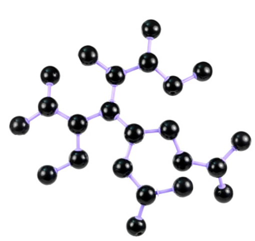
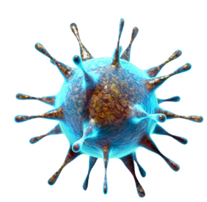
UNDER ATTACK

UNDERSTANDING SOME IMPORTANT BIOLOGICAL AND CHEMICAL FUNDAMENTALS OF TOXICOLOGY AND THEIR RELATION TO SAFETY AND HEALTH PRACTICE

A FOUNDATION FOR UNDERGRADUATE AND ADULT STUDENTS OF SAFETY AND HEALTH





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FRANCIS M. E. LA FERLA

*This book is dedicated to my wife, children and grandchildren,
and to all students who have Committed themselves to years of
intensive study in Occupational Safety and Health,
constrained by daily economic employment and family life
and having limited or no knowledge in one or
more of the Sciences of Biology, Physics, or Chemistry,
my colleagues at the University of Malta and
Prof. Alberto Zucconi, President of IACP
and Secretary General of the World
University Consortium, in appreciation
Of Our continued collaboration and efforts to
advance the promotion of safety and of
health at work.*

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I must acknowledge the enthusiastic students who inspired me to put together the contents of this book. I hope they will now feel more confident in their workplace and that it will help them realise their diploma/degree is not the last rung of the professional ladder. I would also like to acknowledge not only the support of Prof. Godfrey Baldacchino PH.D., who supported the Centre's endeavours throughout the establishment of the Diploma of Occupational Health and Safety, when he was director of the Centre, and indeed continues to encourage its development, and all members of the Centre's staff in the course of its progress, but also Dr. Anna Borg P.hD., the present director of the Centre for her support to the publication of the book. In addition I wish to achnowledge the continued collaboration, efforts and support of IOSH, MOSHPA, IACP and AIAS, to advance the promotion of safety and of health at work.

In particular, I wish to thank my daughter Beverly La Ferla, M.A. (Cantab), M.Res., who as a senior scientific and medical editor has proofed and edited the book. Dr. Manuel DeBono Ph.D. previously a director of the Center, who provided valuable help and advice and reviewed the references and bibliography. Prof. David C. Magri B.Sc. (Hons), Ph.D. (Western) Department of Chemistry, Faculty of Science at the University of Malta for his assistance in reviewing and editing the chemicals referred to in Appendix V, thank Professor Maged Younes, Geneva, for his constructive discussions and my son Nigel La Ferla, BA(Hons)Arch., Dip. Arch. (Lond.) for his advice with the illustrations.

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LIST OF APPENDICES, REFERENCES AND SELECTED BIBLIOGRAPHY

Detailed Chapter Contents

Note on reference citations, Bibliography, Glossary, chemicals referred to in this book and nomenclature and diagrams

All of the above form an important part in understanding the contents of the book and have therefore been presented here to avoid omission by the student reader. Effort spent reviewing any of the above whilst reading will provide greater benefit to the interested reader.

Citations are indicated by a superscript number such as (15) or (45) etc. and can be found in the list of **References**. Those shown with bold numbers indicate the **first citation of each chapter.** Some words (e.g. process) may also have a reference number in superscript. This has been placed there for those readers who wish to read further into the subject and can access the information provided online. In addition, a small selection of books or articles are presented in a separate **Selected Bibliography** and are indicated by a number as superscript with the letter 'B' in bold, e.g. **(B1)** or **(B15)** etc. This material provides a much broader view of what is presented in this book and makes valuable and interesting reading.

Appendix I provides an index to the pages in which major subject matter are referred to.

Appendix II reflects on some reflections on very basic biology and chemistry, as well as useful information and data sources.

The Glossary (**Appendix III**) contains brief explanations of words that may not be understood by some readers. It is not meant to be comprehensive but sufficient to understand the word in context and ensure satisfactory progress through the book. Words in italics and/or underlined words or letters will direct the reader to other parts of the Glossary.

A brief description of the majority of chemicals referred to in this book are presented in **Appendix IV**. Where possible, appropriate formulae have been provided. Again what is provided is sufficient to ensure that the student has some knowledge of the chemical referred to. Chemicals that are also <u>underlined</u> indicates that they are also listed and can be found elsewhere in **Appendix IV.**

To assist those who are unfamiliar with the location/whereabouts of human body organs, some anatomical diagrams (not to scale) have been included to provide a visual image and support reading (**Appendix V**).

FOREWORD

If we understood how and why life and we are changing, we would see that we urgently need to do something about it to prevent or profit from it.[1]

Imagine yourself walking down any busy crowded street in our world of 7.3 billion [2] people speaking 7,102 known languages of which only 23 are common [3]; a vast sea of heads bobbing up and down as a result of the evolution of bipedal locomotion in our species some 4 million years ago. You would invariably be aware of others pacing forward with or towards you, some young, some old. Most of these people would be intent on some particular purpose as they moved along and there is nothing unusual about that and most would hardly reflect very much more about the other beings around them.

The reality, however, is that we are all vast, multicellular organisms [4] – a tremendous integrated network of cells bound together by billions of connections [5]: physically, biologically, chemically and surrounded by a small invisible electromagnetic field within a vaster universal electromagnetic field; men, women and children, all carrying genetic mutations, having received an average of sixty at birth from their parents [6], each exposed to different levels of some toxin or another, whether it be from atmospheric, oceanic, agricultural, natural or synthetic chemicals. You are probably unlikely to think of people in this way every time you came into contact with someone, but you would certainly need to reflect on cellular exposures in relation to their environment, their work and their lifestyles, if you were to establish preventative measures and ensure the safety and health of those for whom you may be responsible as a safety practitioner.

Twentieth-century science is already taking us beyond our knowledge of the human cell and delving deep down into atomic and subatomic levels of the human structure; quantum levels, in fact. Some scientists are carrying out research even beyond these levels, working into the realms of cell network control by energy forces [7]. In other words, they are questioning what is it that is controlling cell communication and response and providing such a unified approach to a task. This goes beyond how the cell itself functions; it assumes that there is some other 'something' that is in overall control of all cells to enable them to function as a network. Intriguing, on-going research shows how much there is yet to learn in this area and that it may have the potential to change the future of medical diagnosis and perhaps treatment in many respects.

Clearly, some basic knowledge of the composition and function of the human cell is of importance in understanding to what extent toxins can damage the structure or function of cells and through them, the many organs and other tissues of the body, which are built of these cells. In reference to these issues, a brief description of the biology of a human cell is presented in Appendix II (Part I: Reflection on some basic biology).

Cells are subject to changes from exposure to toxins but, although they have considerable ability for repair, they cannot always cope and die. Once toxins, whether these are bacteria, viruses, synthetic chemicals, drugs, solar radiation, or some alteration of genetic structure, are absorbed into the body, defence mechanisms come into play. The immune system, perspiration, the gastro intestinal tract (G.I. tract), liver, blood barriers and kidneys are some of the body's major systems in defence from toxic hazards. However, if defence mechanisms fail, the toxin(s) may get into the cells and any part of the cell, including the DNA, may be damaged, sometimes irreparably. Many cells continue to replicate and if damage results in uncontrollable replication, a tumour (excess growth of cell division) may develop. Should cells separate from the tumour then metastasis results (the movement of cells from the tumour to other parts of the body), where these cells will generate new tumours (secondary tumours).

As planet Earth raised mountains, spurted hot gases and lava, formed valuable land and sea resources, developed rivers, lakes and trees four and a half billion years ago, a increase in the size of brain capacity of our species, which started only 70 million years ago, has acceptably been the major power behind the dispersion of humanoid beings from the cradle of Africa and from there on to other faraway lands [(8)].

Exposed to extremes, our flexible and adaptable species bore this onslaught of change, built defence mechanisms and adjusted to the changing inhospitable environments on different continents and in different climates. These dynamic conditions continue today and will continue to change through time as man progresses, developing new technology, new chemicals and changing his attitudes and behaviour towards his living environment.

There are differences in the global estimates of the number of people that have lived on this planet as well as projected figures for many years yet to come. Plagued by pandemics and unexpected catastrophic disasters, populations are reduced and take time to recover. Nevertheless, short term projections show that there continues to be a steady global increase in population size with estimates of 8.185 billion by 2025 [(9)], many of whom will inevitably be exposed to the hazards that current rapid development brings into the living and working environment, and in spite of increasing efforts that will take/are taking place to reduce them. The new wave of international migration will only add to this plight. It could be argued that genetic changes combating some of the exposures are taking place and will continue to do so. Overall, however, we change slowly over time and the many changes identified in insects and other species [(10)] indicates that chemical substances, toxic or more toxic *metabolites*, play a serious part in these changes over time, some perhaps faster than others.

Financial profit, through whatever means, reigns high in both the developed and developing worlds and causes actions by our species too numerous to mention. The development of new products can be so rapid that it becomes difficult to evaluate their possible potential for harm. Only concerted, collaborative investment efforts by all nations, analysing and monitoring chemical and other potentially hazardous new substances and products, together with support to existing institutions, could perhaps reduce this backlog. Time has shown that such efforts have always been limited and slow in their implementation or acceptance for different reasons, some unjustified. Political, industrial and managerial support to education, research and monitoring are essential values still lacking in achieving the standards required that have so easily been established over time. Behaviour of those for whom these standards are developed is also far behind what would be expected in this day and age. Changes are required to make life for everyone safe, healthy and secure. Only through this multiple concerted approach can we recall Sir Winston Churchill's words: *"United we stand, divided we fall* [(11).] Fall may be going a little too far, but it is worth bearing in mind. Perhaps what is really needed is to ensure all the key stakeholders are optimistic and see opportunity in every difficulty.

PREFACE

It had never been my intention to teach students some toxicology, nor did I imagine that I would ever do so. It was a subject that intrigued me in my early days of studying medicine, and one into which I kept delving into as the years went by. This by no means made me a toxicologist. However, following a few years of lecturing students on the course in Safety and Health at the Centre for Labour Studies of the University of Malta, different approaches to the subject and their exemplary attendance it became clear that the majority of adult students attending this subject found it difficult to grasp; they lacked background in biology, chemistry and/or physics. Their past education was not sufficient for them to deal with a subject that essentially required some basic knowledge of all three. I also got the impression that they thought toxicology was extremely dull. Perhaps it is, but even something dull can be brightened up! It was this realisation and my determination to support students in a subject that they obviously felt uneasy about that compelled me to try and address this lack of knowledge in both undergraduates and mature students aspiring to become Safety and Health Practitioners.

The basic approach has been to put together, in what I hope is an engaging way; enough information to provide sufficient resources that can also be used as a reference book containing what they need to know for the management of safety and health at undergraduate level. No more. But also broaden their knowledge in a more general way. Although there are different ways of doing this, I became convinced it was necessary to arouse their curiosity of the organ systems of the human body; their anatomy, function and dependency on other organs to maintain existence in the face of a constant onslaught from their internal and external environments. This, I concluded, would also introduce them to Occupational Health as part of the course in Safety and Health through the implications of the impact of chemical substances on the body's organ systems from accidents to disease prevention. The catalyst to developing this approach was the launch of a global campaign *'No Time to Lose'* focussing on chemical safety by the Institution of Occupational Health and Safety (IOSH) – UK, which would provide a contribution through its emphasis on the potential hazards of chemicals at work, and aspire Safety Professionals and others interested in chemical safety.

The book's content will hopefully support lectures for undergraduate and mature students whose ages range between 25 and 50 and who have committed themselves to several years of intensive study in Occupational Health and Safety, constrained by their day jobs and their family life, and in many cases, insufficient prior knowledge as a consequence of an early start to a working life, in spite of their ability to succeed in what they undertake. A major focus, therefore, has been to ensure students become sufficiently aware of the importance of toxicology in Safety and Health and its application to problems that will undoubtedly confront them in practice. The book's somewhat ambitious sub-title might suggest detailed biological and chemical material. This is far from its objective and only a limited content of both these fields is provided. Other than some basic general aspects of chemical and toxic substances and basic medical and pathological explanations following toxic response of target organs, the reader has been spared complex involvement and provided with broad, relevant, general educational issues. The contents are not directed at safety levels required by very advanced technologies, which is beyond the current needs of the general safety and health student at this educational stage in most countries at this time.

It is difficult to get away with no knowledge of basic chemistry in reading anything dealing with toxicology and assistance with some of the chemicals referred to in the book has been included. The reader is encouraged to refer to Appendix III and IV when in difficulty for more detailed explanations. What I hope it does is educate students not only in the fundamental principles they need in the subject, but also develop their general scientific knowledge in areas related to the conditions they come across in their everyday tasks, in addition to broadening their general interest.

I have often joined students over an evening dinner. These were interesting and instructive evenings at which I gathered vital feedback from them; reactions to educational methods, difficulties encountered, frustrations of the time limitations due to their daily work schedules and trying to meet the pressure of course requirements. Perhaps, the most important experience was learning how much talent and knowledge existed amongst them all; both social and professional skills. The list was, without question, impressive. I found this a most useful source of information that I could use to draw them into discussions during lectures in subjects that they were well versed in, effortlessly passing on knowledge to their colleagues, and often to me!

These 'get togethers' and other time spent informally with students led to an understanding of the value they found in having copies of slide presentations together with lecture notes. Things often become clear graphically and helps those whose recall is much improved with visual input. It also provides a useful resource for revision. I have presented the chapters in this book so that each can be read separately yet stand in their entirety, allowing students to return to unread chapters at a later date.

The more advanced student may find they are already familiar with some topics. This is unavoidable to some extent when writing with the objective to provide subject matter to adult students. I trust, however, that what appears familiar to them will serve to refresh their memories and support new knowledge. A number of words in each chapter have been underlined and printed in *italics* to indicate that their meaning can been found under definitions and explanations in the Glossary (Appendix III).

Adult students ask a lot of questions and learn somewhat differently than those of a younger age. Few of them, however, spend any real time wondering what is in the food they eat, what hazards are posed by substances in bottles or cans at work or at home, and fewer still look at the sky at night and take time to reflect on how chemical reactions probably began and how they are gradually altering the life evolving on this planet.

I find the greatest difficulty in writing is how to begin to capture the reader's continued interest. Furthermore, I cannot hope to cover adequately all that I may wish to include without overburdening the adult student as study time is very restricted. I hope, therefore, that the following chapters will fulfil my intention to *catalyse* the interest of adult undergraduates who enrol for a Diploma or a Degree in Safety and Health at the Centre for Labour Studies, University of Malta, and at other institutions, and encourage them to follow further studies on toxicology aspects important to Safety and Health.

I hope the reader will make use of the general information provided throughout the book and adapt it to whatever specific situations they encounter in their workplace. Safety Professionals, however, are cautioned that although a number of industries and toxic substances have been provided throughout this book to ensure a holistic integrated approach to the subject, they are advised to review the toxic substances in more detail when confronted with any hazardous materials. Occupational Physicians or Occupational Nurses are advised to review medical books with more detailed information on anatomical and medical explanations as the information provided is often too general for their profession and only the tip of the iceberg.

Finally, I trust that by the time students have read this book they will not only have gained a much better appreciation of the many hazards that surround us in everyday life but will also have learnt a lot more of the 'health' side of safety and health. This is an area that needs to be appreciated and seriously addressed, as future demands will focus much more on the prevention of work-induced disease rather than injury, so that safety and health practitioners can better support, through knowledge and observation, the promotion and well-being of all employees and truly live up to their role in the prevention of safety and of health by complimenting, rather than impinging, unnecessarily upon other disciplines and their professional responsibilities.

Professor Edward de Bono, a schoolmate and friend of many years, stated in his book 'Thinking to Create Value' [(12)], Malta 2015, *"As you read this book"* – he was of course referring to his book, not mine, but his words are very applicable here – *"you should be* ***'bonting'****. That means seeking to extract the maximum value out of your reading experience. There may be points with which you might disagree, but that should not inhibit the overall 'bonting' attitude"*.

INTRODUCTION

The human body contains approximately 50 to 70 trillion cells [13] which are constantly exposed to an array of toxic chemicals. Whatever the number and in spite of the cells' cooperative efforts to fight back and alter or eliminate these, the effects of many chemicals often succeed in causing untold damage and even death. The life of a human body can vary with many factors, such as geographical location, food supply, etc., but even at low levels chemical exposure can affect our health and research has shown that the quality of the air we breathe, the food we eat, and the water we drink are vitally important. The potential damage from long-term, low-level exposure is often forgotten; perhaps we should be forgiven for this in view of short-term priorities.

Toxicology is *the study of the harmful, injurious or lethal effects from toxic agents on man, animal, plant and the environment they live in.* It is closely related to people's lives and provides information of fundamental value to human activities, especially tasks undertaken by people at work. There is no task at work, or indeed at home or at leisure, that is devoid of some potential hazard (the likelihood to cause harm), many of which would remain unobserved, silent or unidentified until it is too late for some measure of control.

The science of toxicology benefits from the changing frontiers and new developments of many other disciplines such as molecular biology, genetics, bio-engineering and other newly emerging sciences. The list is a large one. In today's world, thousands of chemicals are constantly being used and many others being produced, the effects of which may be still largely unknown.

The magnitude of the problem to the workforce

The International Labour Organization (ILO) gives the global labour workforce as 3.3 billion as the world entered the year 2012, with a change in age structure and an increasing rate in women employment: In all *"197.1 million were unemployed and a further 327 million in extreme poverty and 967 million of the working population in moderate poverty [14]"*. The World Employment and Social Outlook trends 2016/ ILO – Geneva 2016 also indicates that unemployment reached 197.1 million [14] with 1.5 billion (46% of total employment) in vulnerable employment [16], although it should be noted that there are variations across countries which reflect changing economic conditions. ILO also estimates that there are "*168 million in child labour aged 5-17 of which 85 million are in hazardous work* (*higher for boys)* [14]" but overall this indicates a "*15.5% decrease*" from previous years. Projections for the unemployed show a decreasing rate.

Pairi Hamalainen, Yukka Takala, and Tan boon Kiat in their report on Global Estimates of Occupational accidents and Work-related illness 2017, an update on previously published figures, *"estimated that there were 2.78 million deaths* *occurring annually across countries being attributed to work"* and that *"2.40 million (86.3%) of the total estimated deaths"* were due to work-related illness. (see Data Sources in Appendix II),

The authors indicated that *"including COPD the top three illnesses were circulatory diseases (31%), malignant neoplasms (26%) and respiratory diseases (17%) which had increased").* Europe's share of global work-related mortality was estimated at 11.7%. In all *"more than 7,500 people die every day; 1000 from occupational injuries and 6,500 from work-related illness".* Non-fatal occupational injuries were estimated at 374 million.

Their survey report of 2017 also states that *"nearly 1 million workers died at work attributed to hazardous substances including dusts, vapours and fumes".*

It is undeniably clear one must accept that the total global workforce has a right to a healthy work environment, and that employers and employees alike have specific responsibilities in achieving it. Serious and concerted efforts by many stakeholders are needed to ensure that exposure to people at work is either eliminated or maintained at the lowest reasonable levels.

Europe, Asia and North America account for 92.7% of the world's chemical trade. Europe's contribution is about 21% but together they provide an enormous contribution to world economy (15). Nevertheless, there are a large number of chemicals which are known to be hazardous and others we still know little about. With over 140,000 chemicals in use and an ever-increasing number reaching the market each year, it has proved difficult to adequately analyse the full impact of these chemicals on the environment and human health, and many have not even received basic toxicological testing. The body is often exposed to a combination of chemicals and the combined effect of many chemicals is still not known. Long- term exposure may also have cumulative effects, and many individuals are more susceptible than others.

There are many who have suffered serious health consequences as a result of the type of work in which they have been engaged, and many more who continue to be exposed to hazardous substances. There are over 35,000 synthetic chemicals that are known to have adverse effects on the human body, some of these have serious reproductive outcomes and others the potential of being passed on to future generations.

If the global budgetary expenditure on Safety and Health was totalled, the average per capita investment would be incredibly small. There are a few countries that have, and continue to provide, substantial sums towards the protection of people at work – but these are exceptions. Others still do not appreciate, or if they do, continue to ignore the benefits of preventive investments in the safety and health of their nations' workforce. The economic and social losses due to this attitude are enormous. Nevertheless, it must be remembered that a number of developing countries, in particular, have higher health priorities at their stage of development.

Chemical policies have taken a big step forward since the approval of the *REACH* legislation in Europe (16). This legislation was established on 13 December 2006 to protect public health and the environment from the risks of toxic substances in everyday life. Its influence reached far beyond the shores of European countries, stirring manufactures, importers, the Environment Protection Agency (EPA) and others to overhaul their chemical protection policies

Friend or foe?

It is difficult to ignore the advantages that are gained from many substances, natural or synthetic, in spite of the potential toxic effects they may cause. Some are prevented reaching commercial markets following health and safety trials, whilst others continue to be sold worldwide as no suitable alternatives are currently available. Others, although toxic, may save lives, even at a temporary cost to other bodily functions. At the current rate of investment in research to test the large number of substances that reach commercial markets each year, and the continued yearly increase in the number of chemicals upon which we have insufficient and definite safety knowledge, it has become a monumental task to achieve acceptable clearance for the many products produced, however hard the effort made. Considerable investment and cooperation amongst all stakeholders is needed if such standards are to be met. Systems are currently being developed to accelerate testing.

The budgetary allowance for safety and health made by most countries, on a per capital basis, with very few exceptions, is exceedingly small. There is clear evidence for a lack of knowledge of the enormous national economic and social loss, more important basic health priorities, and the simple inability to implement action. In general, serious political interest in the health and safety of people at work continues to progress very slowly in many countries. The establishment of the European Agency for Safety and Health, United Nation's bodies and other related organisations in other countries, such as IOSH, ROSPHA, NIOSH, RSPH, BSC, OSH *(see Information and Data Sources)* Government authorities, and many other non-governmental organisations (NGOs), assist to their utmost, but overall global progress remains generally slow in many areas.

Before moving on

Before you move on to read the first chapter of the book, just reflect on three common everyday foods; an apple, a bitter almond and a green potato. There are others you could select from; apricots, cherries, peaches or some other product or substance of your choice. Whatever you choose, ask yourself:

What are these? Where do they come from? Is there anything at all that may be toxic about them however small the amount? If there is then at what levels? What would their route of entry into the body be? What happens once they have entered? What damage do they do and to what? How does the body deal with them? Can it alter them into other chemical substances? How does the body get rid of them? Where do they go and how are they eliminated or discharged from the body? Is there any need for concern and does advice need to be given to those that use them? What prevention methods are necessary, if any? These are questions that you should reflect upon. They should serve as very simple examples for you to observe, question, interpret and possibly consider what approach for action may be appropriate for potential hazardous products, whether they are food, natural or synthetic materials or some other substance.

It should now not be difficult to appreciate that today's safety and health manager must be prepared to handle such potential hazards when they are encountered in an effort to eliminate or reduce injury, illness and possibly loss of life. Observation is critical to identification and in some cases analysis, before making decisions on what damage or harm could potentially result from an observed hazard. These decisions then lead to the probability of it happening – the risk level, achieved by the multiplication of the independent rating factors of likelihood by severity; a method used in general routine risk assessments (RA) of existing conditions at the time of assessment, and from which priorities can be identified. Irrespective of who carries out the RA and establishes the final risk level, the end of this process requires a plan for control, vigilance and audit. Control essentially requires the inclusion of existing standards, legislation and regulation pertaining to the identified risks and their levels, aspects often ignored, as well as company organisational elements and worker response.

For students and others in safety and health practice to relate to the stage of making informed decisions to reduce the risks and its effects, which opens a multiplicity of options limited by many factors, and eventually leads to a feasible, often a comprise, but final conclusion, on the way forward for the implementation of control, I had coined the acronym – '***DIPOST'*,** which stands for 'Directional Possibility Thinking' (DPT). Whatever methodology is used, and direction/route taken, to filter through the many possibilities/options open to the decision-making process for control, what you would then be doing is '***diposting'***. This process is vital in achieving acceptable decisions for approval and implementation for the control of the potential for damage, that includes harm and its management.

The justification for the term 'Directional Possibility Thinking' or DPT, and the use of the word 'diposting', arises from the fact that having completed the observational stage and identified a potential hazard/s, those carrying out day-to-day risk assessments generally do these diligently and move on to achieve risk ratings and priorities fairly adequately. However, many, if not most, then tend to take a quantum leap into a decision for control measures without focusing on critical path analyses, reviewing options, legislation, and other important issues in developing a report that would be readily acceptable to both management, supervisors and workers alike.

BACKGROUND

Scientists are in agreement that the universe is approximately 13 to 14 billion years old [17, (18)]. Future research, however, may suggest extended figures. Let us simply go back to a point in time when a speck of dust in an expanding space collided with other dusts, gradually aggregating to form a larger mass and later colliding with asteroids to become, some 200 million years on, Planet Earth, accompanied by a small chunk that we call the Moon [19 & 29]. Billions of years have left many different layers of rock on Earth, each with a story to tell through its layers and embedded fossils which have provided powerful evidence of climatic changes, and most importantly, the living organisms and their many evolutionary changes.

Under assault

There has been no time over the period of our evolution, some 3.8 billion years [20, 21], or so, that living things have not been under attack from toxic substances, both natural and man-made and we have evolved automatic defensive reactions in return. Such substances include atmospheric pollutants like *carbon monoxide (CO,) oxides of nitrogen (NO_x), ozone (O_3), sulphur dioxide (SO_2)* and others, some of which we know little, if anything, about yet. Also, solar radiation, some chemical constituents of water, chemicals in oceans and other food chains, and more recently, food preservatives, agricultural activities, industrial and domestic chemicals, cosmetics, dusts, a multiplicity of natural chemicals manufactured by invading bacteria and viruses, not to mention the natural defence mechanisms of other species that are toxic to humans, such as poisons or irritants.

Defence mechanisms [B1]

There are defence response systems to target hazardous substances, chemicals or pathogens. For example, the body can quickly eliminate some substances in their original configuration via sweating or excretion, or convert harmful substances to less harmful ones in the liver, or alter them at a molecular level to something which can then be rapidly excreted from the body. It can store them temporarily or permanently by placing them into a selected organ in the body, such as fat or bones, but note that this may cause accumulation in those organs to toxic levels which may cause sickness and/or death. For example, dieldrin (used for termite control) is fat soluble and may be stored in body fat if ingested. Dieldrin has been banned in most (but not yet all countries) because it has been linked to health problems such as Parkinson's, breast cancer and immune system, reproductive and nervous system damage. It is also a hormone disruptor and can adversely affect pregnant women.

A major factor in defence is preventing the hazardous substances entering the body. Visual, gustatory (taste) and olfactory (smell) senses are an important first line of defence. Once in, however, then other systems come into play in an effort to stop or reduce interference with the normal function of live cells. The immune system is critical with its many different type of cells to the protection of the body. These are discussed in detail later.

Epigenetics

Epigenetics, which can be described as "a set of modifications to our genetic material that changes the ways genes are switched on and off but which do not alter the genes themselves" [22 p55], also plays a strong role in determining whether humans at some time in their life develop one or other illnesses. To put it simply, this is because chemicals can manipulate our genes to do something without altering their structure in any way. This manipulation may result in varied anatomical and other physical and biological changes that may affect future generations in the descendants of those affected. This is referred to as transgenerational inheritance [23 p101 & 24]. Some substances can mimic hormones essential to body functions, upsetting hormonal balance with undesired effects. These are known as *endocrine disrupters*.

Persistent Organic Pollutants

We must also remain aware of persistent organic pollutants (POP) **[B1,2,3]**. These are synthesised chemicals that are extremely toxic, and which the United Nations Treaty at the Stockholm Convention on 22nd May 2001 [24], mindful of a number of other decisions, declarations and environmental conventions on POP, acknowledged the importance of concerns by all parties, and having taken into account the particular requirements of developing countries, approved *"the need to take measures to prevent adverse effects caused by POP at all stages of their life cycle"* in order "*to protect human health and the environment from the harmful effects of persistent organic pollutants* [24] .

These persistent substances that enter the food chain and accumulate in body and animal fat are still a global threat to us all because they take decades to break down. Some of the persistent *organochlorines* (different formulas) are *"released from thermal sources involving organic matter, and chlorine (Cl_2) is released as a result of incomplete combustion or chemical reactions"*. A number of industrial sources, such as the metallurgical industry and waste incinerators, have the potential to release these chemicals into the environment. Residential combustion sources are another source of persistent organic pollutants.

Atmospheric oxygen [B4]

Joseph Priestly, an English clergyman, described as "one the 18th century's most outstanding scientists" and Carl W. Scheele, born in Sweden of a German family who discovered a number of chemical elements and compounds of these elements, both deserve to be mentioned in connection with the discovery of oxygen, which they did independently in 1774 &1772/3, respectively [25], although Priestly published before Scheele.

The following years 1789–1794 were a difficult time in France [26]. Suspicion alone was sufficient to see you being transported in a cart to the guillotine, which was in fact invented by a surgeon, Antoine Louis, but actually named after Dr. Joseph-Ignace Guillotin [(28)], a French physician, politician and freemason.

Antoine Lavosier [(28)], a French nobleman and chemist, today widely considered "the father of modern chemistry", was beheaded in 1794 along with 16,594 [(28)] others during those difficult years of social upheaval in France referred to as the 'period of terror', although he was publically exonerated by the French government a year and a half later.

Lavoisier was a graduate of law and although he was admitted to the bar, he never practiced law, preferring the sciences. Born in 1743, and wealthy through inheritance at a very young age, he theorised continuously on the subject of chemistry and in addition to a number of chemical experiments he carried out, he is credited with having named the chemical element oxygen [(29)].

Before *archaea* and *bacteria* began to *photosynthesise* carbon dioxide and release oxygen into Earth's atmosphere, there was no oxygen, [(29)] or perhaps just a little or even less than a little **[(B4)].** About 2.5 billion years ago, some of this oxygen first combined with iron (chemical symbol: Fe) which was in a dissolved state in the ocean waters, and later rose out of the waters as a gas into the atmosphere [(29)]. Oxygen in the air would also have been absorbed by land surfaces. Over the millennia oxygen levels continued to rise, reaching up to 35% around 500 million years later [(29)]. Following some fluctuations it later settled at today's level of a little less than 21%. Protosystem II (**water-plastoquinone oxidoreductase)** is a complex protein containing enzymes which capture "photons of light to energize electrons" and then through coenzyme processes Prosystem II is reduced to **plastoquinone.** Water is then split forming "Hydrogen ions and molecular Oxygen" [(30)]. Becky Allen reported in her article Game changer that Professor Bill Rutherford Professor of Biochemistry of Solar Energy at Imperial College London stated "this enzyme change the whole planet" putting oxygen into the atmosphere.[(31).] It is now the third most abundant element in the Universe.

Anyone will tell you that oxygen is essential to life, but how many realise that it can also be toxic at different percentage levels and atmospheric pressures [(30).] We know *anaerobic bacteria* do not survive in oxygen environments. So whilst it is so important to life, how then is oxygen toxic? Oxygen toxicity results from the formation of *free radicals* [(32)] which damage *biological molecules*. Free radicals are involved in many processes but in human biological terms these highly chemical reactive radicals derived from oxygen itself by *reduction* lead to the destruction of cell structure and cell death. The body's defence against free radicals is through the use of *enzymes* which help to repair some of the damage they cause. In addition, these defence mechanisms utilise *vitamins A, C* and *E* (See Appendix III & IV) and the *polyphenol antioxidants*. (See Appendix III & IV). Remember, however, that although free radicals are involved in a number of health conditions, such as arthritis, drug-induced deafness and many others, they are also valuable to the body in that they are also involved in *gene signalling* processes [32 & 29)] and in the destruction of bacteria.

Water

You may wonder why yet another chemical compound essential to life is mentioned here. Water is a molecule made up of two atoms of hydrogen and one of oxygen that can exist in a liquid, solid or gas state. In his excellent book, '*The Bird in the Waterfall*' [33], Jerry Dennis gives the amount of fresh water on Earth as 3%, and states that most of it exists as ice sheets or within glaciers at each pole. Although water is almost everywhere on this planet; the atmosphere, the oceans, lakes, within rocks, soil, trees, plants, and in all organisms including ourselves where it makes up 65−70% of our body and is essential for maintaining a sufficient level of hydration for survival. Water is essential for many of our body's functions, most importantly to help maintain our body temperature balance, cell function, digestion and excretion. It is of no less importance and essential to many industrial processes.

There are many things we require for survival and common salt (chemical formula: *NaCl*) is one. However, we must be very careful with the amount taken as it quickly upsets the normal function of the body's cells which, in their effort to reduce the levels of excessive salt intake, use their water content to allow transportation of soluble salt to be discharged from the body. This, unfortunately, can result in dehydration. Dennis, referred to above, gives impressive and captive descriptions in his chapter on the world's Salt Lakes [33].

Drinking water supplies are to some extent regulated, but many countries do not keep supplies at safe levels. There are a large number of potential contaminants in drinking water supplies that may result in health problems, which may be caused by contact with recreational or other polluted waters. Industrial or domestic roof water tanks may harbour *algae* and *bacteria*. In addition, chemicals used to disinfect leisure water (e.g. in swimming pools), such as *chlorine*, react with *organic material* which then generate other chemical compounds and some of these may be toxic to a certain extent. Such toxic products are known as disinfectant by-products. *Radioactive* substances have also been detected in water supplies from the decay of naturally-occurring radioactive substances, spills or nuclear fallouts [34].

There are a large number of substances used to disinfect drinking water supplies, all of which are strictly regulated, as are the materials used for transporting drinking water to homes or businesses. Nevertheless, the quality of water in some countries still does not reach the water quality standards established by the World Health Organization (WHO) drinking water guidelines [35] and some communities continue to be exposed to toxic substances. Some countries have *fluoride* levels in underground and drinking water supplies higher than the recommended WHO standards of 0.8–1.5ppm, which affects adults and children with dental and bone *fluorosis*. Contaminated drinking water and inadequate hygiene results in large numbers of people developing diarrhoea and many water borne diseases in developing countries.

Air

The film 'AIR', released in 2015 and directed by Christian Cantamessa [36], shows what would happen if a chemical weapon was released that made all air unbreathable on Earth. In the film, the disaster kills almost everyone, leaving two underground workers and some scientists who live in cryogenic sleep chambers and ends with them being released decades later when the air becomes breathable again. Whatever entertainment this film provides, it shows how important it is to avoid releasing man-made hazardous substances into the air and to maintain the balance of our atmosphere, not only for our health today, but that of future generations.

Atmospheric science and climatology are interesting and complex subjects but the points made below may come in useful to safety professionals in planning safe work schedules and reducing exposures in outdoor occupational activities, such as construction projects, roadworks, marine, mining, agriculture etc.

Chemicals, particulates and biological materials are released into the atmosphere continuously from human, animal, plant, natural, man-made and volcanic sources**.** Active volcanoes release, both on land and beneath the sea, ash, sulphur dioxide gas, carbon monoxide (CO), and carbon dioxide (CO_2). The Hawaiian Observatory studies give a figure of 200 million tons annually [37], and although they point out this is less than 1% of the total global fossil fuel release, other researchers have given much higher figures. Other releases include *hydrogen sulphide* (H_2S) and *hydrogen halides*, (hydrogen combined with fluorine, chlorine and bromine: HF, HCL, HBr), all soluble strong acids, as well as pulverised rock, volcanic glass, minerals and water vapour.

Chemical interaction/reactions can occur between molecules in the atmosphere when initiated by solar energy (photochemical reactions) or climatic conditions. These result in products which are sometimes more toxic than the initial substances. For example, nitrogen oxide (*NO*) and sulphur dioxide from emissions react with water molecules in the atmosphere to create sulphuric acid (H_2SO_4) and oxygen (O_2) molecules combine through the action of ultraviolet (UV) light to become *ozone* (O_3). Another common photochemical reaction is the formation of *smog*, which is derived from fine particles released from car exhausts, industrial emissions and fossil fuel burning. This type of air pollution can be visible in the absence of wind and is highly toxic to humans; it can cause severe sickness, shortened life or even death.

Information is collected on air quality [B5] by numerous stations everywhere and there are a number of air pollution data sources where one can obtain information and review air quality conditions, such as the European Environmental Agency in Copenhagen, Denmark and the European Pollutant Release and Transfer Register [38] which provides information on emissions from industrial facilities across Europe [39]

Weather conditions can be very hazardous to those working in high rise buildings and other construction, marine, and many other activities both indoors and outdoors. A basic knowledge of how to review and understand published online daily data from differences in *barometric pressures*, *cloud height and thickness*, *wave height*, *relative humidity*, *cold and warm fronts* are all important and useful in forestry activities and smog. Reviewing the latest satellite and radar images would provide you with a good estimate of a more immediate weather forecast. The prediction of the potential impacts of wind, rain, solar radiation and temperature on task schedules cannot be overstated and the safety professional is encouraged to get a grasp on doing this even more regularly in locations and latitudes where such conditions often prevail. The reader is encouraged to get used to checking for himself/herself the weather conditions online, then compare with meteorological forecast data and also check for specific weather alerts. The wider you extend your regional satellite images for review the more accurate your longer term forecast is likely to be, if that long term prediction is what you require.

Soil

Although the evolution of soil began billions of years ago, soil as we know it today started to appear on this planet some 485 million years ago as a result of the breakdown of rock at the surface of the planet. This process was assisted by erosion, plant roots, dead plants and microbial activity that provided organic material and *clay* as floods and sediment or soil was transported from other locations [40]. These processes take time and result in many different types of soil, and consequently all soils do not contain the same type of elements (*aluminium (Al), calcium (Ca), iron (Fe)* (See Appendix III), *magnesium (Mg), manganese (Mn), nitrogen (N)* and *potassium (K)*) that can be taken up by plants or have the same pH (a number which expresses the acidity or alkalinity of a solution).

The pH value of soil is important and depends on the basic rock, vegetation and climatic conditions. A value of 7 is neutral, with lower values being acidic and higher ones alkaline. Vegetation that produce acidic chemical substances and rainwater which is slightly acidic can alter soil pH. Sulphur will increase acidity and calcium increase alkalinity. Most plants prefer moderately acidic to neutral soils (pH 5.5−7.0), and variations may result in deficient uptake of nutritional elements to the plant or damage to plant roots, among other more complex chemical impacts.

Safety and health professionals should look closely at those whose work activities are linked with this material. Data from many sources such as the World Bank, ILO, FAO indicate that over a billion people work in agriculture, many of whom are women and, in some countries, children. In occupational health, one must be aware of exposure to workers of around 28 different health conditions that can be transmitted from animals (*zoonoses*) [41], although today a few of these are now rare. Grain and poultry dusts contain soil, bacteria, faeces, spores and chemicals. From a safety perspective, the soil-related hazards may not be readily obvious. In addition to the importance of hygiene, the promotion of health, chemical interaction with other products (i.e. *ammonium nitrate* – NH_4NO_3), use and storage of chemical products including spraying of pesticides, *translocation* of chemicals into plants and the food chain, subsidence, soil landslides and mechanical or other injuries which are high in agricultural activities, a knowledge of soil and chemicals in farming activities is helpful when working with other related professional disciplines.

Fire and combustion of materials [B6]

The benefits of fire are indisputable but the destructive force and resultant hazardous materials, a number of which are toxic, either through the chemical's specific characteristics or through the interaction of one or more chemical substances that undergo change, also justify it being briefly referred to here.

Fire and combustion are dependent on a number of factors and it is not simply exposure to the flames or heat that most concern us about the outcome. It is the products of *pyrolysis* and combustion of the materials involved that lead to the formation of smoke. Smoke contains fine particles of carbon and forms soot, and also contains complex *hydrocarbons*, toxic gases like *carbon monoxide (CO)*, *hydrogen sulphide (H_2S)*, *hydrogen cyanide (HCN)*, *oxides of nitrogen (NO_x)*, *ammonia (NH_3)*, *sulphur dioxide (SO_2)*, *carbon dioxide (CO_2)* and many others that finally lead to respiratory difficulties and affect other body systems and can even cause death [42].

It is often difficult to know what to expect from fires. Oxygen is obviously absorbed by the products of combustion and if reduction by volume reaches less than 6%, the lack of oxygen will result in death to those who remain in such atmospheres [43]. Fire personnel, safety officers, families and unfortunate individuals caught in such fires are more often than not exposed to such toxic materials and appropriate regard and some knowledge is needed of such substances.

A number of hazardous materials have to be transported to industrial destinations by truck, train, plane or ship, and one must remember that fires may occur spontaneously, during transportation, in industrial and public areas, as well as at home [B6,B7].

Radioactive substances [B8, B9 and B10]

The chemical elements *uranium*, *plutonium*, and their *isotopes* (*elements that have the same number of protons but a different number of electrons*), thallium or material contaminated with other substances that can emit ionizing radiation [44] (radiation that produces charged particles or ions) are all referred to as *radioactive* substances (*substances that emit radiation*). They may be sealed (enclosed entirely so that the sealing material prevents their release), open (e.g. laboratory chemicals) or portable (e.g. in some testing equipment). They may have a short or long *half-life.* This is the time required for a quantity to reduce to half its initial value; in this case with radioactive material, it is a measure of the rate of decay – the time taken for half of the substance to decay, decay being the loss of an electron or in some cases a proton or even through splitting of the nucleus as in fission [45]. Waste areas of radioactive substances are regulated, and are designated as such when above a specific threshold level or have other specified radioactive properties. Many people often live in areas dangerously close to such waste sites.

A *rem* is a unit of radiation dose (*see Appendix III for more detail*). In general, radioactive substances at low levels will affect blood vessels (*at 100 rems*), the blood cells called lymphocytes (*at 100 rems*), hair will also be lost at *(100 rems)*, the gastro-intestinal tract (*at 200 rems*) and the reproductive system (*at 200 rems*). At high levels: the heart (*at 1000 rems*) and the brain (*at 5000 rems*). The thyroid is susceptible to radioactive iodine. Note that human body cells, which are not yet fully mature, are relatively more sensitive to radiation than other cells [46].

A note on carcinogens

A carcinogen is any substance or radiation which promotes the formation of cancer; this can be a chemical or a substance (natural or synthetic), such as inhaled asbestos or tobacco smoke, a virus, bacteria or, in the case of radiation, gamma rays or alpha particles. Cancer is any disease whereby normal cells are damaged such that they divide uncontrollably and create a tumour. There is usually a period of time (latency) between exposure and detection of cancer, with some being more aggressive than others. Should exposure result from more than one carcinogen, then synergy (individual effect greater than combined/joint effects) may result, although antagonism is also possible. (more detail on synergy can be found on page 39).

Although the body cells do have some capacity to repair themselves in the very early stages of DNA alteration, changes to the DNA may be genetically inherited. Note that not all chemicals are mutagenic and carcinogenic substances may not necessarily be immediately toxic as their effects may be insidious (proceeding in a gradual, subtle way, but with very harmful effects). In some cases, certain cancers require higher or prolonged levels of exposure. Confounding factors, such as lifestyle (tobacco smoking, nutrition, exercise, etc.), may significantly increase the risk of some cancers.

Cancer remains a major concern to everyone. Mortality rates indicate different geographical, gender, occupational and environmental differences and changes have been noted in those who migrate from one country to another. The International Agency for Research on Cancer (IARC) (part of WHO/UN) has and continues to carry out considerable research on the evaluation of carcinogens, as do many other institutions worldwide through epidemiological, animal studies and tissue cultures.

Cancer has been designated into Groups which have been universally adopted. Group 1 (carcinogenic to humans), Group 2 (A and B – probably carcinogenic to humans/limited evidence – the difference between A and B, being the A has sufficient evidence in animals (probably carcinogenic) and B insufficient evidence in animals (possibly carcinogenic)), Group 3 (inadequate evidence in humans and animals), and Group 4 (lack of evidence at this time both in humans and animals) [(47)]. Some countries have developed slightly different designations to those of IARC.

Aggressive recent research on cancer, is showing promise in dealing with affected different body organs, its progression, recurrence and mortality although there is much to learn and be done in this field.

Chapter 1 A popular weapon

If you start off by separating 'TOXIC' from the suffix 'OLOGY' which invariably refers to '*the study of*' some subject or another, then you can focus your attention on that part which you will come across time and again throughout this book.

TOXIC refers to anything which is harmful, injurious or lethal. This could be any agent (synthetic chemical, drink, plant etc. or natural toxins of microorganisms of plant and animal origin) that is known to be 'toxic' (usually referred to as the 'toxicant') that *may* produce a "harmful, injurious or lethal" effect (the toxic effect) to the many cells of which we are made. Toxicants are absorbed either as *molecules*, *ions* or *colloids* and they may travel in the *blood plasma* in their free state, bound to a protein or some fraction in plasma (i.e. albumin, globulin, lipoprotein), as well as bound to red blood cells in the plasma. *Gases* and *vapours* are also dissolved in the plasma. Once absorbed, they alter cell function by chemical reactions with its constituents and if hazardous, either damage or destroy it. It will, however, do this only:

1. When it has entered or been introduced into a living organism, such as the human body, animal or algae; all flora and *fauna*.
2. Upon the circumstances and length of its use.
3. When the amount or concentration is sufficient to cause harm, which then depends on:

   (a) the route of its entry,
   (b) the rate and amount that has been absorbed,
   (c) the rate of metabolism and
   (d) the rate of excretion by the organism affected
   (e) individual susceptibility.

Note that all chemicals can be toxic and they can also be used safely. Toxic chemicals can be administered to select/attack specific targets such as bacteria or cancerous growths by limiting their dose to what is at the time of administration believed to be 'acceptably safe' to render a beneficial effect. The acceptably safe level is found by carrying out studies to measure the harmful effects against different doses of the toxic substance. The information obtained is then kept in data bases for reference and retrieval when required. Note also that the organism absorbing these toxic substances may have an effect on the chemical structure of the absorbed substances, altering or detoxifying it (*biotransformation)*.

What, therefore, is TOXICOLOGY? [B11]

Professor John Timbrell described the derivation of the word **toxicology** originating "*from* ***toxicon,*** *which was a poisonous substance that arrow-heads were dipped into"* in days gone past, and that *"**toxicos** was the word used for a bow"* [48].

Toxicology may be defined as the study of the harmful, injurious or lethal effects (i.e. pathology) from toxic agents on man, animal, plant and the environment they live in. It draws upon the major sciences (biological, medical, chemical, epidemiological and other emerging sciences.) for the identification, quantification, research design, methods and other information in arriving at the toxic outcomes associated with exposure to toxic agents that result in injury, illness and disease. It also includes treatment. This science attempts to define the limits of the safety of toxic agents and predict the level of harm at a given level of exposure.

Toxicology is an important element in environment and occupational health and safety, because it provides information by which policy and decision makers can evaluate and regulate hazards in occupational and non-occupational environments. There is a great lack of information and knowledge on 'human exposure' to toxic substances and the information toxicology provides on potential hazards is critical to the development of occupational health and safety prevention strategies. Since 1980, many countries have given considerable thought to the development of methods by which to use toxicological information in regulatory decision-making. In toxicology, these 'methods' are referred to as 'risk assessments'. It should be noted that risk assessment methods used by countries have not yet all been harmonised internationally but work goes on in this field to try and achieve this. IPCS, OECD *(see Information and Data Sources)* are two of the organisations who support this through their activities and also maintain current information on the national approaches to risk assessment. It goes beyond toxicology encompassing exposure assessment. It is part of 'hazard characterization', which consists of hazard identification (potential to cause harm) and 'dose-response relation'. R.A. thus combines hazard identification and exposure, and uses both toxicological, and epidemiological data as well as mathematical models. IARC carries out the classification of cancer hazard.

Exposure: This word refers to **external exposure** which means the amount or concentration of a substance to which a person or a population may be exposed, whether this is in the volume of air in a workplace, water or even soil. It should not be mixed with **internal exposure** or the word **'dose'** which refers to the amount or concentration that has reached the inside of a person or population and upon which information is often not available. There is a relationship between exposure and dose and the information of this relationship helps in establishing acceptable exposure levels (allowable limits or concentrations) in the workplace. Standards and guidelines are often set on this relationship, although sometimes they are based on dose alone because of the high toxic effects on specific organs within the organism. Decisions are generally not made, however, without reviewing the external exposure levels.

The number of new chemicals continues to rise every day, which also increases the risk of chemical exposure, although today the manufacturing and service industries as well as users of these chemicals are much more strictly monitored and regulated.

The increase in the use of chemicals worldwide is making the study of toxicology very much more important than it used to be. Toxicology is a multidisciplinary subject which continues to develop. It is not easy to bring together all the information that continues to influence and make an impact on: (i) the understanding of the interactions of chemicals, and (ii) the impact on living systems. The *influence of genes on the growth and development of the organs"* [49] are no exception.

Toxicology could be divided into different disciplines such as Industrial Toxicology, Clinical Toxicology, Forensic Toxicology, Environmental Toxicology, Regulatory Toxicology, and so on. It could also be referred to by the target organ or system affected, such as the reproductive system, genetic system, immunological system, etc. At further depth, it could be seen as research toxicology or risk assessment toxicology. Whichever way one wishes to look at it, the aim remains as reasonable prediction of the hazards and their impact on the living organism, such that the science of toxicology strives to define the limits of the safety of toxic agents. The principles and practice of toxicology are relevant to all types of activities and contributions of toxicologists, whether they are academically, commercially or industrially employed in order to ensure the broadest perspectives of the exposure, dose, response, research investigation, regulation and control.

A glance at some aspects of the history of toxicology (B11, B12)

Readers interested in a more detailed history of poisons should refer to the book by Louis Casarett and John Doull (50) and that of John Timbrell(48) – see selected bibliography. This short historical summary is based on their work.

Primitive man was aware of natural poisons from animals and plants and indeed used these on his weapons (50). Myth or true, there are also kings, queens and others through history who may have been murdered with poisons. Their poisoner probably knew it would be difficult – certainly at that time, but not so much today – to identify who was responsible for the foul deed. It was a popular weapon!

"A poison is any substance, natural or synthetic, that has a harmful effect on any living system. The purpose for which it is used decides whether it is regarded as a poison or not".

Through its definition, there is effectively little difference between the words 'toxicant' and '*poison*'. However, many disciplines (nuclear industry, medicine and environment) define 'poison' differently and large quantities of synthetic or natural substances are used in industry to produce other chemicals or added to other substances every day. An example is methyl alcohol [*methanol* (CH_3OH)], which the body can only deal with in extremely small amounts and is poisonous at high levels. It is converted into *formaldehyde* (CH_2O) and *formates* ($HCOO^-$) – there are different ways of representing this formula), both of which damage cells. *Methylated spirit* (C_2H_5OH) is the result of adding methanol to ethanol (C_2H_5OH).

The earliest records of poisons date back to about 1500 BC(50). *Arsenic* and *opium* were known to Hindu medicine around 900 BC and ancient Greeks were aware of poisons around 400 BC (50). The Greeks were also aware of some of the antidotes to poisons and there are many examples where certain substances were used to induce vomiting after the ingestion of a poison.

It was in Rome that "*the first known law against poisoning was passed*"(50). This was in 82 BC "*to protect the public against careless dispensing.*" (50). The use of poisons to commit suicide, assassinate individuals and commit murder underlined to a great extent the origins of toxicology. '*Poisons and their antidotes*' was written by Maimonides (1125–1204) outlining some of the treatments considered to be effective

[50]. The famous words of *Paracelsus*, a sixteenth century scientist, on these issues were: "*All substances are poisons, there is none that is not a poison. The right dose differentiates a poison from a remedy*". He also believed that poisons could damage particular organs within the body. *"Water intoxication, also known as water poisoning or hyperhydration is a potentially fatal disturbance in brain functions that results when the normal balance of electrolytes in the body is pushed outside safe limits by overhydration (excessive water intake)".*[51]

Matthieu Joseph Bonaventura Orfila (1787–1853) was a Spanish physician who made a tremendous contribution to toxicology by finding ways to detect poisonous substances that would provide proof that poisoning had indeed occurred. This is of great importance in *forensic toxicology*. It was, however, *Claude Bernard* (1813–1878) who initiated the identification of the site of action of a poison, which he did by showing that *curare* *($C_{37}H_{42}N_2O_6$)* acted on the *neuromuscular junction* [50].

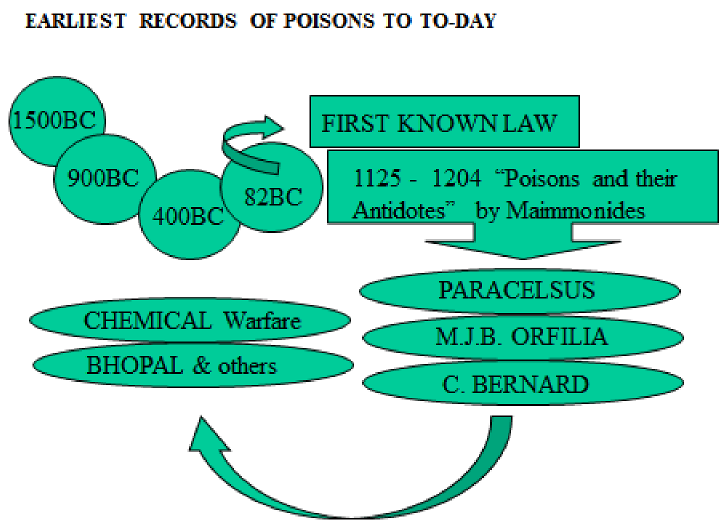


Figure 1. Illustration showing poisons date back to 1500BC and eminent personalities involved in important developments of Toxicology, and the threat of chemical biological warfare that has been reached today.

In relatively more recent times, the Bhopal disaster in India (2 December 1984) led to 600,000 people being exposed and about 16,000 deaths over the years [52]. It provides an example of a compound – *methyl isocyanate* *(C_2H_3NO)* – whose toxicity was not well understood at the time, making treatment of the victims uncertain and emphasising how important knowledge of the toxicity of substances is. There have been other similar incidents since then.

Chemical biological warfare has become a serious threat in more recent times. The use of arsenical war gases in the Second World War and the use of *anthrax* following the September twin tower disaster in New York are clear examples of exposure, once again highlighting the importance of toxicology and the control of hazardous substance abuse.

Entry of toxic substances

Populations are constantly exposed to natural and synthetic compounds and hazardous materials that vary in their level of potential hazard. These compounds (substances) reach populations through three major routes of entry:

1. Ingestion - the gastrointestinal tract
2. Inhalation - the lungs
3. Absorption - the skin or eyes

in that order of importance in toxicology. The *gastrointestinal route* is placed at the top of the list mainly because most compounds such as drugs, contaminated food and water, food additives, plant, animal and bacterial toxins can be ingested directly, and its increased importance is due to fact that very toxic compounds can be ingested in significant quantities.

These are, however, not the only routes. Other routes of entry include the following:

4. Transfer across the placenta to the unborn baby
5. Intravenous (injection into a vein)
6. Intra-muscular (injection into a muscle)
7 Subcutaneous (injection under the skin)
8. Intra-peritoneal (injection inside the membrane that lines the interior wall of the *abdomen*. This method is experimental.

One should remember that for workers in health care, radiological and biomedical activities at work and needle punctures into the skin are significant exposure risks.

The different types of toxicity

There are a number of different types of toxins and these can be simply grouped into the following:

- **Natural** - insect bites, stings, certain plants, seed, fruit, animal, marine
- **Environmental** - natural atmospheric, man-made emissions, waste products etc.
- **Drugs** - medicinal, veterinary, drugs of abuse, also alcohol and tobacco.
- **Food and some food additives** – food contaminants, bacteria, colourings, preservatives etc.
- **Domestic** - bleaches, garden products like paraquat (a herbicide), cosmetics, dyes, oxidisers etc.
- **Industrial** - Solvents, acids, alkalis, and many others
- **Agrochemicals** - pesticides, fertilisers
- **Synthetic chemicals -** There are at this time some 20 million synthetic chemicals [53], a few highly toxic.

The nature of a toxic substance will, in most cases, lead you to the way in which exposure may have taken place, for example, a toxic gas by inhalation. Others may have more than one route of entry, e.g. by both inhalation and via the skin when those working with such chemicals consume food with contaminated hands. Multiple routes of entry may result in a serious contribution to the body's *systemic* load.

So far you have become acquainted with the word toxicant. **Toxicity**, on the other hand**, is the ability of a compound to produce injury** once it has reached the exterior or interior of the body *(see ILO definition* [53]. Toxicity can be referred to as: **unknown, no toxicity**, **slight toxicity**, **moderate toxicity** or **severe toxicity**. Slight, moderate or severe toxicity, can be either sub-acute or sub-chronic or **acute** or **chronic** and each of these may be either **local** or **systemic** depending on the site of action of the toxin. Some compounds accumulate and may pose a longer-term risk such as Dioxins, Mercury and PCB,s.

When referring to toxicity levels such as 'slight toxicity', it is important to define what is meant. It is also useful to differentiate between acute and chronic *exposure* and acute and chronic *effects*.

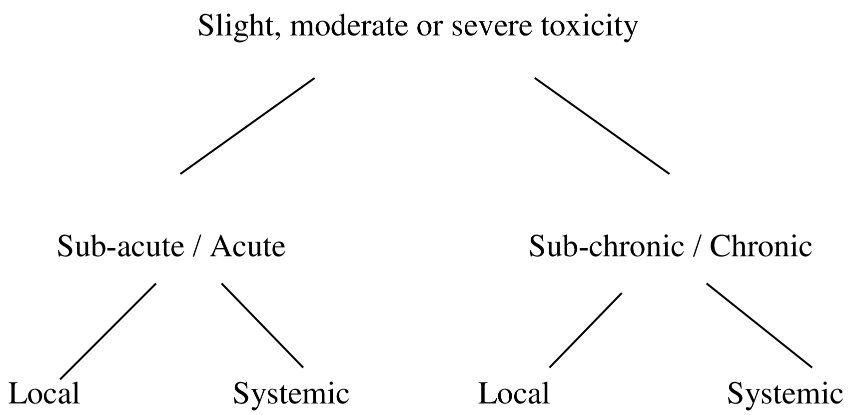


Figure 2. The different types of toxicity.

Acute exposure

This is an exposure of short duration to a *hazardous* (potential to cause harm) **substance.** When referring to ingestion, acute exposure refers to a single dose within 24 hours or less. When referring to inhalation or absorption, it refers to a single exposure the duration of which may be in seconds, minutes or hours.

Acute toxicity results when a sudden single exposure or dose of a toxic or *poisonous* substance results in acute (mild, moderate or severe) effects to some part of the body. The resulting effects may be temporary. One example is poisoning by a bee or a snake.

Chronic exposure: this is **exposure of long duration to a hazardous substance.** The term of duration of exposure may be in days, weeks, months or years.

__**Chronic toxicity**__: refers to **repeated doses of, or repeated exposure to,** a toxic or poisonous substance that results in adverse chronic (long term) health effects. __*Mercury*__ (Hg) and __*n - Hexane*__ (C_6H_{14}) are two examples.

__Note__: 'Chronic' does not refer to the severity of the condition but to the duration of exposure. To have an 'adverse effect', a substance must be able to enter the system.

'Exposure' depends on the amount (dose) of substance and the period (duration) during which it affects the target, for example, humans, animals or bacteria, as well as the route of exposure (entry site). Host factors such as age, sex, resistance and sensitivity, diet and the co-existence of infectious disease, are also important when considering exposure to populations, as they can affect both the exposure and the dose, by modifying absorption, distribution and metabolism.

__Local toxicity__

This is the site of contact or area of the body where the action of the toxin has its effect. Absorption may or may not occur at the site of contact. They include the skin, mucous membranes of the eyes, nose, mouth, throat, and anywhere along the upper respiratory or gastrointestinal system.

__Systemic toxicity__

This refers to the entry of a toxic substance into the blood stream by which it is then transported into the body system. Entry of the toxin may occur directly by injection into the blood stream, or be transferred, e.g. through the placenta, or through absorption, ingestion or inhalation, and then be absorbed into the bloodstream. Since absorption into the bloodstream can occur after **local toxicity,** the systemic effect can be produced some time after the local injury has occurred. This means that some toxic substances can produce harmful effects at a site in the body, through both local and systemic toxicity.

Entry of a substance into the body depends on:

1. The measure of toxicity of a compound when it is introduced into the body. This is called *the __absolute toxicity__*.

2. The properties of the compound which influence the *ease of entry* of that compound. This is called the *__effective toxicity__*.

These properties are due to the compounds' characteristics such as:

(a) Volatility
(b) Dustiness
(c) Solubility
(d) Ability to be absorbed by the skin.

3. The circumstances of its use.

__*VOLATILITY*__ is the tendency of a liquid to evaporate, that is, form a gas or a vapour. Solvents are all relatively volatile.

DUSTINESS refers to particles of solid material that may be microscopic in size, freely floating in air, settling or settled somewhere.

SOLUBILITY in chemistry is defined as the maximum quantity of a substance that can be dissolved in another substance.

SKIN ABSORPTION *See p.41-45 for detail under the heading: 'The Skin'.*

In occupational health, the type of toxicity and the clinical conditions or disease associated with exposure to specific toxic compounds is important because they aid in identifying the organ that is first (or mainly affected) by the toxic compound. The **target organ** is therefore that organ which is affected by the lowest or most severe dose by the toxic compound. The event (sign or condition outside the normal range for that organ, for example, excretion of proteins by kidneys that signals the damage or intoxication to that organ) is known as the **'critical effect'** (see also p. 83-84).

The cell is the smallest unit of biological organisation within organs. Toxic effects manifest their action first at the cellular level, affecting the cell's function, and this response is the first indication of the system's encounter with toxic compounds. The toxic compound may cause cell death, although cells in some organs can be replaced. Cells that are repeatedly injured but do not die may still compromise the function of an affected organ.

Dose and dosage

There is an important difference between **dose** and **dosage**. Dose (internal exposure) refers to the amount or concentration of a substance that has reached the inside of an organism. It becomes useful to know how much of a dose (the level of concentration) will cause toxicity, and sometimes how much of the dose will cause death (lethal). Since many of the studies carried out to understand the level of toxicity of a substance have been done on animals, it can be very difficult to try and relate the information obtained from such studies (*extrapolate*) to the effect they would have on humans. Remember also, that *host factors* can affect the dose received *(see also Chpt.5, p 147 - 149).*

The human body actually requires many substances that in very small quantities (low concentrations) are not toxic, but are known to be poisonous in larger amounts. Copper (Cu), Magnesium (Mg) and Manganese (Mn) are examples of these. There are many others.

'Dosage', in contrast to 'dose', is used when the amount or concentration of a substance (dose) is linked with the body weight or surface area of the organism. So that, if dosage required were 0.5 mg for each kilo of the person's body weight, then for a person weighing 60 kilos, the dose (concentration of the substance) to be given would be 30 mg (0.5 x 60). No reference here has been made as to how often such a dose may have to be given, but this is also important with regard to the effect (response) required. It now becomes clear that it is possible to see what relationship there is between a dose of a specific substance and its response – the 'health effect'. This relationship shows how the different levels of exposure change the severity of the health effect. In studies of dose and response, a number of organisms (usually mice or rats) are used to obtain a response average to a certain dose, and this average becomes the reference percentage. A range of doses will be tested and these percentages can then be plotted as a graph showing the percentage of responses obtained by administering the dose against the dosage (dose per kilo or other parameter selected to represent a characteristic of the organism). The resulting graph is referred to as the 'dose response curve'.

The dose response curve is usually '*sigmoid*' as shown below but is not necessarily so. The slope provides information on the magnitude of the range between a 'no effect level' and a lethal dose, and it is from this graph that one obtains the dose which is expected to be lethal to 50% of the organisms tested (all of the same species). The percentage of organisms which have died from the specific dose administered is known as the LD 50 (lethal dose only in acute exposures). Autopsy will discover which organs were affected. Those who use such data or graphs may wish to know the lowest levels of exposure referred to as LOAEL which can be classified as less (not expected to cause any significant dysfunction) or serious (this refers to some failure which leads to morbidity or mortality). Interpretation also depends on the purpose for which the data is intended (public health, animals etc.) and by whom it is used.

LD50 *is defined as the statistical estimate of the dosage required to kill 50% of a population of the test organism and refers only to acute exposures. It is a convenient standard to describe the toxic level of a substance when comparing the toxicity of different compounds. It is of most value in dealing with toxicity by ingestion.*

The range between the 'no effect level' and zero is known as '***the margin of safety'***, although it is now considered to show the quotient between observed exposure and a NOAEL or a benchmark dose.

A **'no effect level'** *is one at which no response to the dose is observed / measurable. (This is where one is measuring the effect of the dose of a substance on a specific characteristic of the organism, such as its enzyme inhibition) or occurs in any individual in the population tested.* This 'no effect' level is often referred to as the '**no observed adverse effect level' (NOAEL).**

This 'no effect level' may be absent in some toxic substances as there may be a response at all exposure levels. This, of course, means that no safe exposure level can be established for that substance. The NOAEL is based on animal toxicity studies.

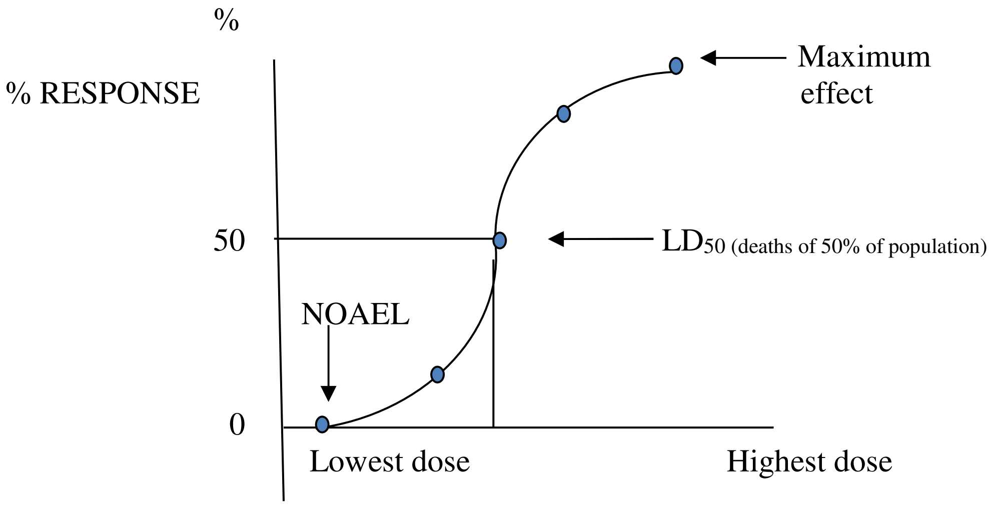


Figure 3. Dose response curve. Note that the curve may take different shapes and may vary in its slope (more or less steeper than sigmoid) and position along its X axis.

Note that because those who are exposed to similar concentrations of a toxic substance do not respond in a similar manner, the variations in response will result in what is known as a normal distribution (Gaussian distribution). This means that a very low or small exposure (dose) will affect those individuals who are susceptible, whilst those who are resistant may respond to a maximal dose concentration. The majority will be affected by a mean concentration. However, remember that it is the cumulative dose response curve (sigmoid) which is used in toxicological work.

In occupational health and safety, exposure to known and potentially hazardous substances is to ensure safe working procedures and therefore safeguard workers' health. The principle by which acceptable safe exposures are established is the use of the no effect level concept, because if there is a no effect level there must then be a level (threshold) at which exposure beyond it becomes hazardous to health. This is referred to as the **Threshold Limit Value (TLV).**

TLVs are published yearly by the Threshold Limit Values Committee of the American Conference of Governmental Industrial Hygienists (ACGIH), and these are periodically revised as the levels change with knowledge and experience of hazardous substances. They were given the status of law in America in 1968 and were also referred to as **Permissible Exposure Limits (PEL).** Note that in some countries such as the UK, the **Maximum Exposure Limit (MEL),** *i.e.* '*maximum level of exposure allowed'* is often used. Both these limits are calculated as exposure over a working day of 8 hours over a five day week, which is *known as a 'time weighted average'* TWA) and a safety margin is built into the final limit of the exposure allowed by regulation. It means that you could repeatedly expose workers to 8 hours per day for five days without expecting any adverse effect.

Time weighted averages allow limited fluctuations (excursions) above the established TLVs during the day, provided that they are compensated for by the same limited excursions below the established TLVs.

Synergy

Exposure may occur to more than one substance at the same time. If the effect of each substance is similar, the overall response may result in a total effect which is the same as the addition of the individual effects (*additive*). If the effect is different (one may be toxic, the other non-toxic), the overall response may result in that one substance increasing (*potentiating*) the effect of the other substance. This is known as *potentiation.* Where the effect of two or more substances are greater than the sum of their individual effects, we have what is termed as SYNERGY that, is *a synergistic effect.*

Antagonism occurs when an interaction between substances may block or reduce the effectiveness of one or more of the drugs, decreasing the response. Where repeated exposure to one or more substances occurs, tolerance may develop and a lower grade of response may occur. On the other hand, however, repeated exposure may result in increased sensitivity and therefore an exaggeration of the response.

These issues are of importance in terms of exposure from potentially hazardous substances. Although no serious injury is expected to occur as the result of exposure to substances to which TLVs exist and are observed, the best possible practice is to maintain exposure levels as low as is practicably possible.

TLVs are expressed as follows for:

1. *Gases* and *vapours* in parts per million **(ppm)**;
2. Fumes and mists in milligrams per cubic meter **(mg/m³)**;
   (note that this is also true for some dusts such as asbestos)
3. Some *dusts* such as *silica*, the expression is in millions of particles per cubic foot **(mppcf);**
4. *Fibres* are stated in number of fibres per cubic meter **(fpcm)**.

It is vitally important to understand that TLVs are guidelines and not boundaries, between what is safe, and what is a dangerous concentration of a substance. Some TLVs bear notations like: 'C' or 'skin'. 'C' refers to *'ceiling limit'*, which means that at no time must this level limit of exposure be exceeded. 'Skin' draws your attention to the fact that the substance can be absorbed via the skin, and this includes the mucous membranes.

TLVs include the values for:

- Chemicals substances;
- Physical agents (heat, ionizing radiation, *lasers*, noise, vibration, radio frequency and microwave radiation, ultraviolet and infrared radiation and visible light);
- Biologic Exposure Indices (BEIs): this term is reserved for biologic monitoring of workers exposed to toxic agents. An example is the measurement of a chemical or its *metabolite* (*small molecule that is the result of metabolism*), such as exposure to *organophosphorus* *insecticides* where the organophosphorus metabolite *alkyl phosphate* (P_2O_{5+}ROH) is found in the urine of a worker using this chemical.

These values are not established for carcinogens *(cancer-producing substances)* because so far it has been assumed that a threshold does not exist, although a range of the estimates of risk (a numerical probability of the risk) are carried out making a number of other assumptions. Where only suggestive evidence of an association to cancer exists [(54)] values are established.

There are a number of chemicals, which are not included in the TLV list established by the TLV Committee. These are included in other sources of recommended exposure limits such as the Workplace Environmental Exposure Limits of the American Industrial Hygiene Association (AIHA). This is the most widely used list. The NIOSH criteria documents also provide a set of references for recommended upper limits for exposures, many of which are lower than the recommended TLVs. ILO had published as long ago as 1980 [(see 53)] occupational exposure limits for airborne toxic substances from all countries, and today one can see that several countries have established lower limits than published TLVs at that time. These clearly underline the 'inadequacy' of TLVs, and the importance of using the information only as a guideline.

Chapter 2 ACCESS INTO THE BODY

Routes of entry

Light, heat, microbes, chemical substances and compounds of chemicals, many disguised as creams, aerosols, liquids, gases and others in various forms such as smoke or dust, all attempt to enter the body. Entry, however, is prevented or limited by bodily responses. Under attack, the body exerts specific methods to defend itself, but much depends on the circumstances at the time of contact, and indeed, on other biological and metabolic factors.

Behaviour and personal attitude, ignorance or unavoidable conditions, such as being caught in a fire without *egress*, are some factors to be aware of that result in contact with toxic substances.

The three major routes of entry into the human body are the skin, the gastro-intestinal tract and the respiratory system by absorption, ingestion or inhalation (but remember that these are not the only routes of entry). In such cases one must remember that a compound is said to have been absorbed when it has entered the blood stream; a route by which it can reach almost every part of the human body.

ABSORPTION	INGESTION	INHALATION
SKIN (dermal)	*GASTROINTESTINAL (oral)*	*LUNGS (respiratory)*
This is very important in industry especially for compounds of high lipid solubility, i.e. fat soluble.	It is seldom that this is important in industry except for very toxic chemicals. It is important to remember, however, that most substances are taken orally (e.g. medicines).	An important route for all compounds that are airborne.

Absorption is very important for entry of toxic substances into the body and a somewhat detailed explanation of the anatomical structure of the route of entry is necessary to understand the process. See also Selected Bibliography. **B37**

The Skin

The skin covers about 1.8 square meters of the human body's surface (55) and, together with its appendages (hair, nails, hooves, feathers etc.), is also referred to as the 'integumentary system'. Its surface has a *pH* of 4.5 to 6.5 (56) and is made up of (from outside inwards): the epidermis, dermis and a subcutaneous layer. Beneath this last layer lies muscle (see Figure 4).

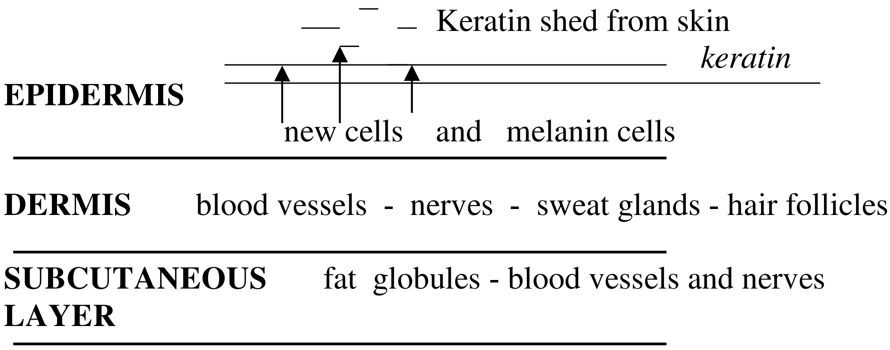


Figure 4. A basic sketch showing the main contents of the skin layers.

See below for a more detailed diagram of the skin layers. These sketches have been drawn to simplify what is in reality quite complex, but it is unnecessary for you to know any more at this stage. Do not, however, consider the skin as being just a barrier to contact with chemicals or air, water or soil pollutants. The skin is a dynamic tissue which has metabolic, *immunological* and other responses and there is probably much more we do not yet understand about its function.

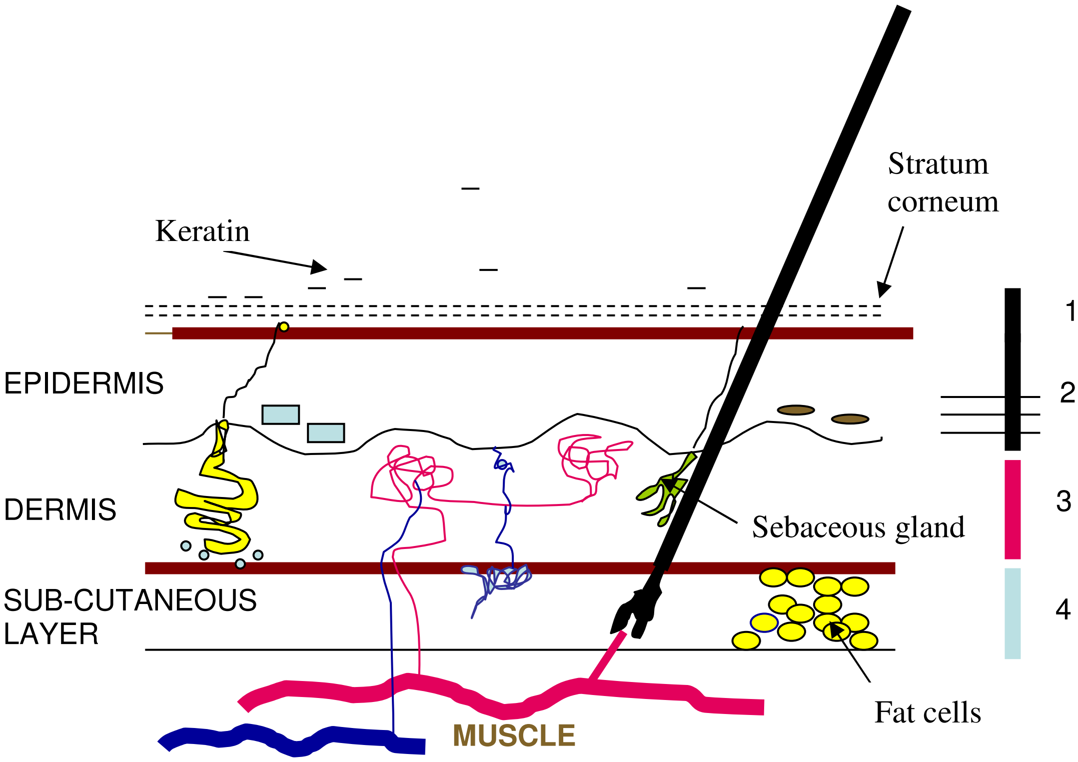


Figure 5. A schematic representation of major constituents of the human skin showing the different layers of which it is composed.

The top layer of the epidermis (the vertical black line marked 1 in the sketch) is made up of flat cells which contain keratin. This is a *fibro-protein* substance containing 40% protein. These flat cells are dead cells and flake off from time to time.

The skin surface (stratum corneum – shown as interrupted lines in the sketch) is a very good barrier (10–40 *μm* thick) [57] and diminishes the absorption of toxic substances through it. This layer, which is the major *diffusion* rate-limiting barrier, can metabolise substances trying to gain entry. The thickness of the skin surface varies in different areas of the body and this alters the rate of penetration. The scrotal skin, for instance, is very highly permeable and absorption can be considerable. Some skin irritants, such as *hydrochloric acid (HCl)* and *sodium lauryl sulfate* ($C_{12}H_{25}NaO_4S$) can cause damage to the barrier and facilitate absorption of other chemical substances. *Nanoparticles* >40 nanometres (nm) do not go past the stratum corneum [58].

The skin surface contains water (15–54% [59]) and a certain amount of water is necessary for the skin to act as a barrier. However, if the amount of water in the skin is increased, then absorption will increase considerably. An issue which is often forgotten is that liquid substances that reach beneath protective clothing or protective gloves remain in contact with the skin and therefore cannot evaporate and this will increase absorption. Temperature and humidity too can have an effect on absorption; skin temperature is normally between 33–36°C [60] but varies with location and environmental conditions. A rise in temperature will increase the blood flow through the vessels in the skin. Lipids (fats of different types) make up 15–20% of the stratum corneum[61], but there is variability between locations of the body [62].

The very lowest layer (basal layer) of the epidermis is composed of five layers in all (marked 2 in Figure 5 – see horizontal lines). Blue cuboidal cells can be seen above the wavy line that separates the epidermis from the dermis. These cells divide forming new cells, so that over a period of about 27 days these cells reach the upper layers of the epidermis, lose their nuclei and eventually die and form the keratin layer. The epidermis is thus continuously renewed. In the layer above the basal layer of the epidermis where the new cells are formed, some cells contain the pigment *'melanin'* (shown as brown oval areas above the wavy line – 2 in Figure 5). These prevent the more dangerous of the sun's rays from damaging the tissues. Some blood vessels and nerves do penetrate into the lower layer of the epidermis to provide the nourishment it needs (not shown).

The dermis lies below the epidermis (vertical pink line 3) and varies in thickness in different parts of the body. The junction between the epidermis and the dermis is not a straight line but a wavy one, so that the upper wavy layers of the dermis (papillae) lock into the lower layers of the epidermis. The dermis provides nourishment to the epidermis through the many blood vessels that lie within it. Many nerve endings of different types are found in the papillae providing our sense of touch. The dermis also contains the sweat glands (yellow spirals), the hair follicles and sebaceous glands, *lymphatics* and layers of thick and thin fibres that make up its framework (not shown). The dermis is alive with activity as many materials that enter or leave the epidermis pass through its layers. Its thickness is greater than that of the epidermis [62]. The epidermal thickness varies with body site and the studies by Sandby Moller *et al.* (2003) indicate that this thickness is "*not correlated with age or skin type*"[62].

The subcutaneous layer lies under the dermis (vertical light blue line 4). Below it is muscle and beneath muscle, in most places, is bone. It is a layer made up of fat globules (small individual pieces of fat), as well the blood vessels that supply the skin and nerves that also pass through it to supply the dermis. It acts as a spongy area between the muscles and the dermis and gives the skin its appearance. With age, the fat is reduced and the skin appears wrinkled.

When the skin is not healthy or damaged (as in *eczema*, *exfoliative dermatitis*, *psoriasis* or a skin burn), this barrier will not be so efficient and a toxicant may penetrate or become absorbed many times faster than it would be when the skin is healthy. It should be remembered that some chemical substances penetrate the skin faster than others depending on their *molecular weight*. The epidermis layer (50–100µ thick) limits the rate of absorption, but absorption varies and is not constant.

The thickness of the skin and the *solubility* of the substances are other important factors that affect penetration. Solubility plays a major role. Some chemical substances have a high solubility, such as *aniline* ($C_6H_5NH_2$), *dimethyl sulfoxide,* $(CH_3)_2SO$ and *nitrobenzene* ($C_6H_5NO_2$). Their solubility increases the penetration rate. The chemical structure of a compound affects its potential to penetrate the skin. The vehicle (solution) in which the chemical substance is concentrated, such as water, alcohol or oil, also affects the rate at which a substance is absorbed.

Once the toxicant reaches the blood vessels of the peripheral circulation, it is then transported via the heart to the systemic circulation and throughout the body.

Workers who have been previously exposed to a solvent may have an increased rate of penetration when exposed to a second toxic substance. Many workers are *atopic*, that is, their skin has sometime in the past been in contact with a substance which has caused the skin to react (recognised previous contact) or, in other cases, without any evidence that anything has happened (an unrecognised previous contact). The skin 'recalls' the contact with that substance to which it is 'allergic' and produces an allergic reaction with visible evidence.

It is difficult for people at work not to have their skin come into some contact with chemicals at some time or another, but even slight contact may result in a person developing toxic and sometimes severe effects, as with *nitroglycol* ($C_2H_4N_2O_6$). It is important, therefore, that careful assessment is made of materials with regard to their potential skin absorption and guidelines provided to those who work with them. The water soluble salts of *thallium* (Tl) are one example that dissolve in contact with skin and absorption is generally much higher than exposure by inhalation. Thallium is also absorbed by the intestine. Small concentrations are found in cigarette smoke. High concentrations are generally needed for symptoms to develop usually within 48 hours or so. Airborne concentrations of chemical substances may be absorbed through the skin too and such conditions are often difficult to detect.

Platinum (Pt) from catalytic convertors can be deposited into road dust just as *cadmium* (Cd) is from vehicle tyres that contain this metal. Substances found in road dusts can be transported by wind to soils and there become *translocated* into plant tissues. *Lead* (Pb) and *iron (Fe)* are two examples of toxic substances that are *translocated* by certain plants. Nevertheless, an airborne potentially toxic substance may reach the body through the skin and result in systemic toxicity. Such toxicity may not show for some time, making it even more difficult to identify the cause. An example of this is *acrylamide* (CH_3H_5NO) exposure.

Sun *et al.* (2002) indicated that powdered solids may penetrate the skin in an unresolved state (63), and Tinkle *et al.* (2003) have suggested that ultra-fine metal particles may pass through the epidermis and into the dermis where they may generate an *immune response* (64).

Remember that considerable absorption may occur through the *conjunctiva* of the eyes which lines the inside of the eyelids and covers the sclera (the white of the eye) and also has a good blood supply. Medicine drops instilled into the eyes for ocular conditions may cause systemic toxicity. In addition, the insertion of suppositories is yet another route of entry for toxic substances, but although it is well to be aware of them, they are unlikely to be of any importance to the safety practitioner.

Nanoparticles have been reported to be in many personal care products such as moisturisers, soap, sunscreen and other products, and studies on mice have indicated that plastic nanoparticles can cross the placenta (65). *Titanium dioxide* (TiO_2) and *zinc oxide* (ZnO) are examples of nanoparticles but not all of their compounds contain are necessarily in nano form. They may contain varying fractions in the nano scale. One study has indicated that plastic nanoparticles can *"transverse the human placenta"* (67)(67) These are clearly some cause for concern, especially as many countries have so far not established requirements for testing or labelling.

Skin Absorption Risks – *What You Should Do*

With the basic background knowledge that you have gathered so far on the absorption of potentially toxic substances through the skin, it is now necessary to consider some general guidelines for skin risk situations at work. How do you alert your attention to what is potentially hazards for workers in terms of skin contact?

A request to view the register / list of materials stocked and or in use by workers is a good start to the identification of potentially hazardous substances. This should be available on demand.

A walk through the stock rooms may identify materials that have recently been received and are not yet listed. Often, courteous questioning will reach the same objective. If you have had the time to research which materials an industry or other place of work is expected to be using in its production processes, warehousing or other activities, then it is useful to make a note of those materials that you feel you should be looking for during your observation of the working areas themselves. Make note of any possible substitutes at the same time.

Many countries have listed Occupational Exposure Limits for a number of chemical substances that have been identified to be potentially hazardous when in contact with human skin (SB2). Airborne concentrations within the exposure limit stipulated for the chemical substance may increase the effect of the potentially toxic hazard. These substances have been given what is essentially *'a skin effect identification'*. This denotation is also given to 'carcinogens' (cancer-producing substances) if it is known that the carcinogens can be absorbed via the skin. However, few workers find themselves in contact with such substances as they are prohibited.

There are over 170 known chemicals that can be absorbed through the skin. Substances which are potentially hazards through skin contact and are listed as having an occupational exposure limit are numerous but include the following groups (see below). For an explanation of these you, should refer to each one in Appendix IV and obtain some understanding of what they mean).

1. *Aliphatic hydrocarbon derivatives (in liquid form)*
2. *Aliphatic amines*
3. *Aromatic amines*
4. *Alcohols*
5. *Halogenated hydrocarbons*
6. *Isocyanates*
7. *Nitriles*
8. *Organophosphorus esters*

It must, however, be remembered that there are a large number of chemicals we do not know enough about in relation to skin contact and that prevention policies are the best policy. Big differences also exist between countries in the lists of substances that they consider are potentially hazardous.

It is important to regularly review the occupational exposure limits as these change along with their annotations, but remember that a substance that does not have a skin denotation does not necessarily mean that there is no skin hazard. Use the skin denotation as a guide only. With more chemicals being banned as research reveals their toxic potential and more detailed labelling being required (e.g. by the European Community), the number of those exposed is gradually decreasing. It is good practice to read labels and note any warnings or instructions.

Ask whether any material safety data sheets are kept by the workplace you are visiting and make a point of reviewing the health and safety data sheets.

Look for substances that are known to make the skin permeable, or are liquid at room temperature. Compounds with a molecular weight of more than 500 penetrate the skin very slowly, but those below this penetrate rapidly [68,69]. Compounds that are both *hydrophilic* (water soluble) and *lipophilic* (fat soluble) penetrate the skin rapidly.

Remember that solid compounds may release concentrations of potentially toxic substances into the air and also affect, or be absorbed by, the skin. Note the type of vehicle that is used for the substance or compound and check its concentration.

Whatever you identify, double check the substance, its properties and effects before taking any steps unless you are absolutely sure of its toxic hazard and level of priority. Remember that dilute solutions of a substance and limited skin contact may not be a hazard. Always consider whether you need to call in further expert support.

The following are a few examples of chemicals that have the potential to be absorbed by the skin and which may affect a specific organ or the whole body system. Refer to Appendix IV for information on the chemicals below.

Acrylamide	*Benzene*	*Dichlorvos*
Acrylonitrile	*Carbon tetrachloride*	*Dimethyl sulphate (DMSO)*
Aniline	*Cresols*	*Malathion*

An example of a substance that has a local effect is a group of compounds called liniments, which contain *methyl salicylate* ($C_8H_8O_3$). This is an oil from plants which is *hydrolysed* in the skin to *salicylic acid* ($C_7H_6O_3$) and then relieves the pain [70].

On any workplace observation round keep an eye on workers' hands, necks and exposed parts of the body. Where you spot skin conditions, report this to the company doctor. Workers may have had previous exposure or are specifically sensitive. Where you see workers with any skin condition, review the work area well and check materials being used by the worker, as well as those in transit through that area.

In industries, such as computer or electronic workplaces, double flooring is often used and contains a multiplicity of wiring and ducting. Bear this air space in mind as potential areas of airborne substance exposure; they are often not continuous between departmental sections. One section may have different potential hazards that can easily travel to other areas of the workplace. If you feel it is necessary, request permission to question the workers on their movements within the workplace, ensuring the workers' safety and health representatives are also informed of what you are proposing. Remember that workers may carry out similar jobs in other locations, even outside the workplace being reviewed. Other more personal questions should be left for the company physician or company nurse to deal with.

The Gastrointestinal (GI) system

The prefix 'gastro' refers to the stomach so the term 'gastrointestinal' directs us to both the stomach and the intestinal system. This extends from the mouth through the *oesophagus* (perhaps more commonly referred to as the gullet) to the stomach, different parts of the small intestine, the large intestine and finally an exit, the anus. See Figure 6.

Three important pairs of glands secrete juices into the mouth almost immediately that anything enters and mastication (chewing) starts. Each has a specific task. *Mucin* is released to lubricate both food and the oesophagus. An *enzyme*, called lingual *lipase* starts to *hydrolyse* fat to smaller molecules; *amylase*, also known as *ptyalin*, breaks down the starches into molecules of glucose and maltose; *lysozyme* kills most of the bacteria in the mouth and *bromelain* liquefies protein. Chewing, of course, breaks down large particles to much smaller ones making it easier for all of the mouth secretions to mix with the food and do their specific tasks before the contents are passed on (by swallowing) down the oesophagus to the stomach where digestion will continue (see Fig. 6).

Whether the toxic substance is in the form of a liquid, an aerosol, a plant leaf, drug or other chemical form, or even in edible food, it does not spend much time in the mouth. Excluding intentional poisoning, taste, irritation and burning will cause immediate expulsion, although certain foods, such as the mistaken identity of a poisonous mushroom, may eventually reach the stomach. Children are often victims through accidental ingestion.

Odours are often valuable warning signs, but these depend on individual sensitivity and the concentration of the substance. *Formaldehyde* is one example.

The blood supply to the mouth is very good and although the mucosa varies in thickness in different parts of the mouth, being thinnest in the *sublingual* area (under the tongue), absorption through the mucosa can be very rapid with permeability many times greater than that of the skin. Permeability from another area of the mouth referred to as the *buccal mucosa* (inside lining of the cheeks and floor of the mouth) is important because substances that come into contact with this area have a slower gradual absorption rate.

Certain substances such as *glycerine trinitrate* ($C_3H_5(NO_2)_3$, which is absorbed in the sublingual area, is used in the treatment of *angina* (constriction of the blood vessels of the heart). *Nicotine* ($C_{10}H_{14}N_2$), which has a large number of side effects, can penetrate the *mucosa* very quickly. Some pesticides are also absorbed through the mouth.

Workplace exposure does not generally create GI system problems from potentially hazardous substances. It is good to remember, however, that workers often eat and drink whilst working; some chew gum and others breathe heavily through their mouths and all of these unfortunate habits help to add to the risks of hazardous substances, and gaseous particulate, absorption.

Saliva is rapidly swallowed taking with it food, toxins, vitamins and all of the enzymes it naturally contains, which reach the stomach and then the small intestine where most toxic absorption commences. It should be noted, however, that certain substances, such as organic chemicals and heavy metals, are excreted in saliva which is then swallowed returning the toxins that originally reached the body’s systemic circulation through other areas of entry. In essence, saliva does little to help with the elimination of toxins.

Your awareness and vigilance of these issues will help to improve the health and indeed the safety of the workforce, through education and training by you or company health care personnel thus reducing sickness absence, maintaining productivity and economic costs.

FOOD ENTRY INTO MOUTH → Immediate secretion of MUCIN

LYSOZYME ↓ → Always present to kill most of the **BACTERIA**

This is then followed by :

LIPASE → To hydrolyse FATS

AMYLASE → To convert STARCHES into GLUCOSE & MALTOSE

BROMELINE → Liquefy PROTEINS

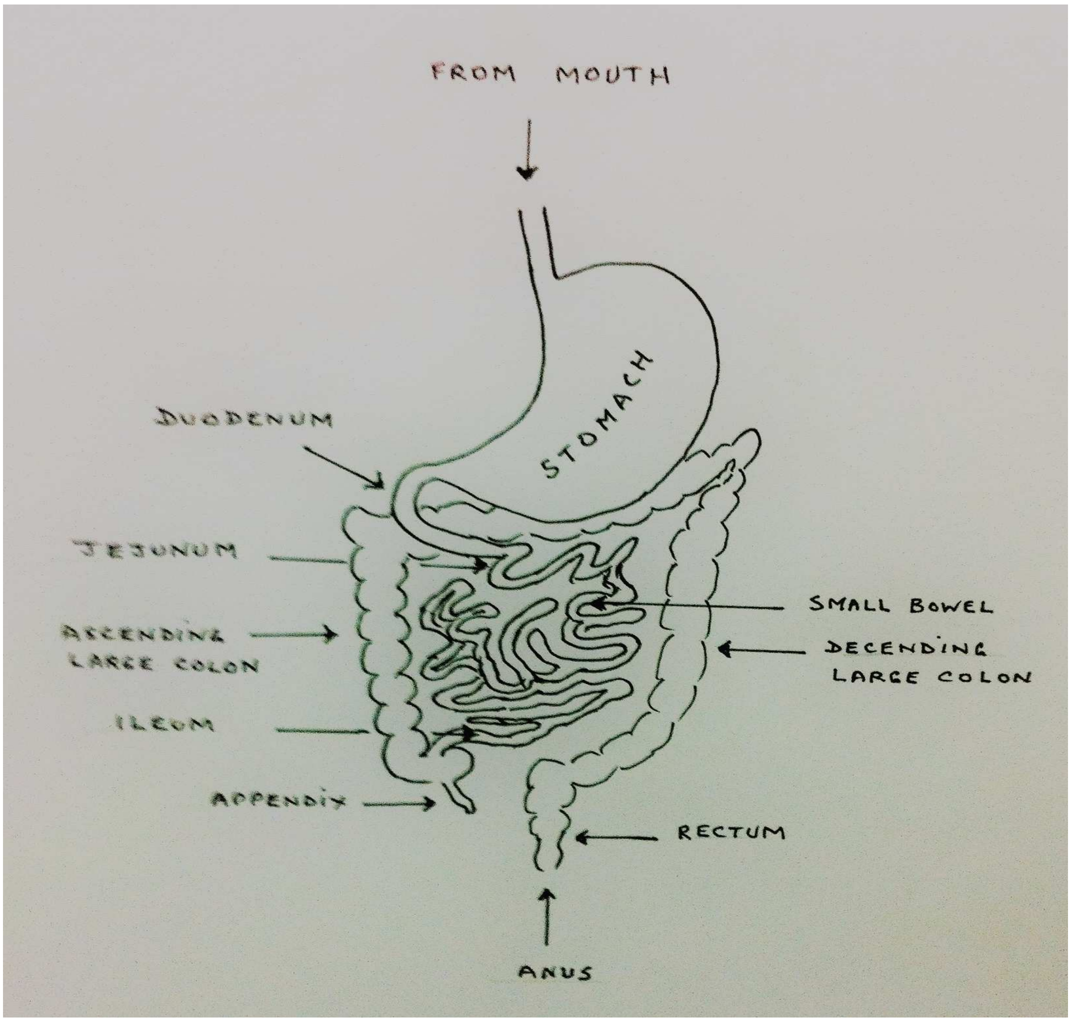


Figure 6. An artist's impression / representation of the GI system from mouth to anus.

For much of the journey from the mouth to the anus, anything entering the mouth is crushed, dissolved by the various gastric digestive juices and pushed along by muscles. Throughout this process, chemical changes take place and absorption occurs, being enhanced at sites that have increased blood flow. The absorptive surface of the gastrointestinal tract (GI tract) is about as large as a football field – roughly 550 square meters – which is a considerable surface area, but researchers consider these estimates too high as they were done at post mortem and suggest 180–300m^2 or even as low as 30–40m^2 in a healthy adult subject [71].

Once food has reached the stomach, which is the most dilated part of the digestive tract and is richly supplied with blood vessels, it passes to the small intestine which is about 6.5 meters long and is made up of three continuous parts known as the *duodenum*, the *jejunum* and the *ileum*.

The diameter of the intestine decreases from the duodenum (4.0–4.5 cm) as it reaches the end of the ileum (3.5 cm). While all these areas are well supplied with blood vessels, the duodenum and jejunum are much more vascular than the ileum, which lies further along the digestive tract.

Note that various studies of the size and diameters of the GI tract give different estimates and more recent studies indicate that many estimates are high.

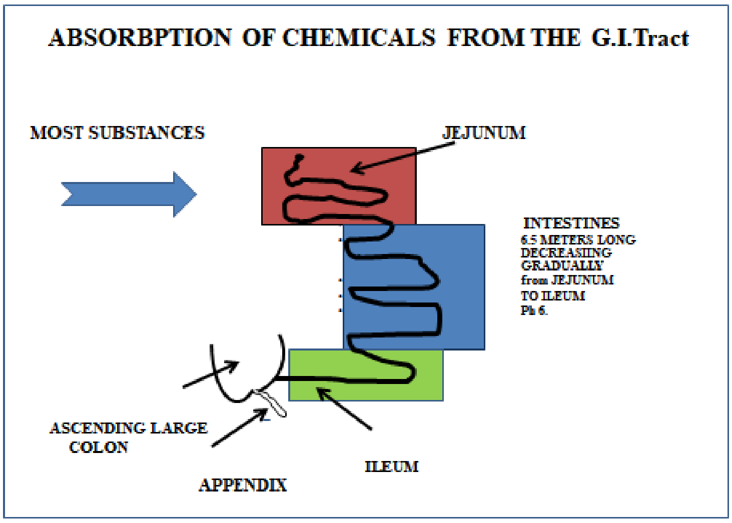


Figure 7. A schematic representation of the intestines showing where most chemical substances are absorbed. Some are absorbed by the bowel beyond the Jejunum and at the distal end of the ileum.

Although, as mentioned earlier, absorption with some compounds can take place in the mouth where it can be very rapid, most toxic substances are absorbed in the small intestine.(see Figures 6 &7). For example, aspirin is given as acetylsalicylic acid tablets which is a derivative of salicylic acid. This is done because the salicylic acid in aspirin irritates the stomach lining. Aspirin passes to the small intestine where it is converted by hydrolysis from acetylsalicylic acid to salicylic acid and then absorbed and finally provides relief. To avoid aspirin irritating the stomach lining, aspirin and other tablets are 'enteric coated'. This means that they have an outer coating which will not dissolve at the pH of the stomach but will at the pH of the small intestine where it is absorbed into the bloodstream. This also allows time for *prostaglandin* in stomach cells to stimulate the release of mucous and neutralise some of the acidity before it reaches the small intestine and before aspirin blocks prostaglandin. There are many other functions that prostaglandins carry out but they need not concern us here [72].

The stomach produces a number of gastric juices which include *hydrochloric acid* (HCL) to create an acidic environment, *pepsin* to digest protein, *intrinsic factor* to help the small intestine absorb *vitamin B12* (important for the metabolism of cells – see Appendix IV), some other enzymes, and *gastrin* which controls the total acidity and the rate at which the stomach empties into the duodenum. Although the stomach does absorb some substances such as alcohol, non-coated aspirin, *barbiturates*, and some fat soluble compounds, very few substances in general are absorbed from the stomach.

There are a number of substances that delay the emptying of the stomach and therefore decrease absorption [73]. Examples include serious bodily injury, high levels of blood glucose that effect nerve conduction, or injury to the nerve supply (*vagus nerve*) to the stomach muscles, drugs that slow down the small intestine's movements, and some medical conditions such as infection with *Helicobacter pylori* bacterium that causes atrophy to the smooth muscles of the stomach or mistaken action on the cells lining the stomach by the immune system. Lack of vitamin B12 (pernicious anaemia) may also be involved [74]. On the other hand, there are substances, such as *cholinergic drugs* (muscle stimulants), that increase the emptying of the stomach and this helps to increase the absorption rate. Remember also that unlike solids such as rice or chicken which take 20 minutes to 4 hours, liquids reaching the stomach leave the stomach in about 15 minutes.

Toxicity is minimised in the gastro-intestinal tract by a number of different processes. Both liquids and food within the G.I. tract can dilute toxic substances or form less soluble compounds. Both gastric and *pancreatic juices* can help to detoxify some toxic substances (hydrolysis and reduction), although gastric juice may affect a toxicant and an even more toxic substance produced. Absorption through the blood vessels transports toxicants to the liver and there metabolic changes immediately commence, changing a toxicant's chemical structure to a less toxic, sometimes more toxic, or inactive one (*biotransformation*).Note that both dermal and intestinal cells contain xenobiotic-metabolizing enzymes and can be responsible for some biotransformation of certain compounds.

The pH of the GI tract is an important factor in absorption because of the difference between pH values of the mouth (pH 7.3–7.4) to that of the stomach (pH ~2 but varies in different individuals) as well as that of the small intestine, which has a pH of about 6 [75]. These will cause different substances, depending on the physical state of the substance, to be absorbed in different areas of the G.I. tract. A low pH for example, facilitates absorption of metals such as iron (Fe) [76,77] and the stomach acidity (pH 2) may inactivate a toxic substance by *hydrolysis*.

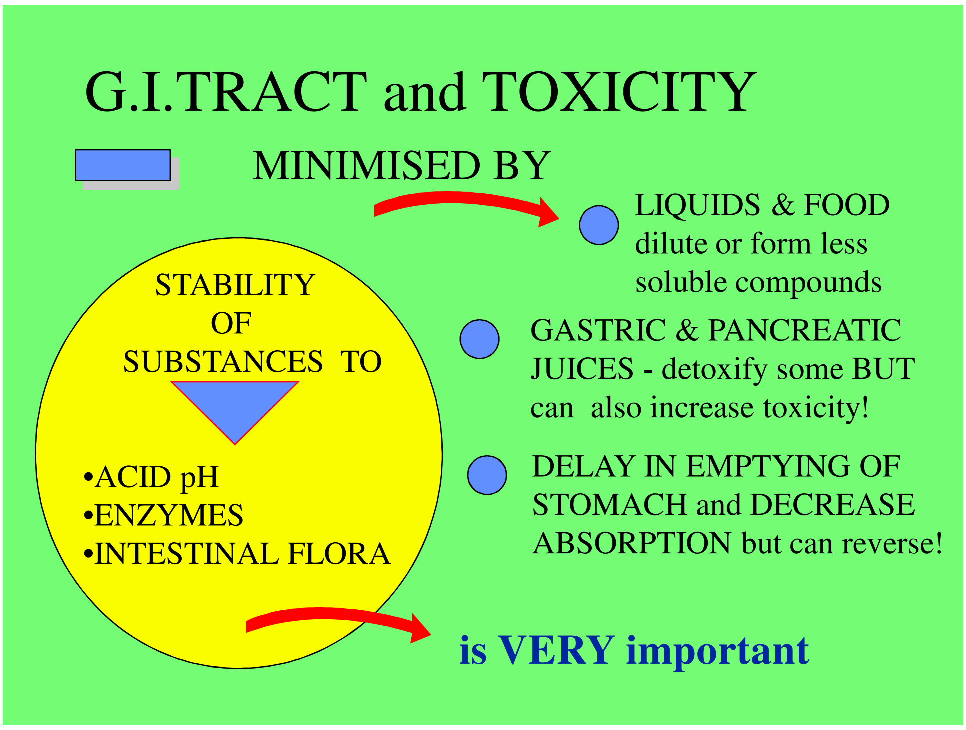


Figure 8. The processes that minimise toxicity in the gastrointestinal tract.

Non-ionised substances will be absorbed along the whole length of the gastro-intestinal tract if they are fat soluble. Other substances, which are *ionisable* if they are also fat soluble, will only be absorbed if they become ionised in the specific section of the GI tract where the pH is suitable to bring this about.

The solution in which a substance is suspended/dissolved can affect the rate of absorption of the substance and, in addition, both enzymes and bacteria present in the GI tract may metabolise these substances.

What is important, therefore, is how stable the substances are when exposed to:

1. Acid pH
2. Enzymes
3. The intestinal flora

This is because the toxicant may be transformed into a new compound even more toxic than the original substance. A common example of this is presented when fish, vegetables and fruit juices which contain *secondary amines* combine with meats or smoked fish which contain *nitrite* to form *carcinogenic nitrosamines* in the stomach [78] (see nitrosamines in Appendix IV).

Most toxicants reaching the GI tract are absorbed by *simple diffusion* (see diffusion in Appendix III) and these are chiefly lipid-soluble substances. Others are absorbed actively (a membrane carrier plus oxygen is required) and some toxicants are absorbed by the *GI tract transport systems* [79,77], for example, *thallium* (TI) uses the *Fe system* (see iron) and *lead* uses the *Ca system* (see calcium).

It should be noted that even particles can be absorbed by the GI tract. Emulsions of polystyrene latex can be absorbed via the intestinal epithelium [79] and are transported to the *lymphatics*. *Azo dye* is absorbed in the duodenal area.
As has been mentioned earlier toxins and other substances are transported to the liver where several other processes take place. These will be elaborated under the chapter that deals with the liver and its metabolism.

GI Tract Absorption Risks – *What You Should Do*

Some general guidelines are presented below on what can be done to prevent risk situations that may occur at places of work. These can be adapted to a specific industry or other establishment.

Education and Information –

- Plan the route for preventive action you have decided to take once you know your options.
- Inform your organisation's management and request that you also inform the Union representative.
- Divide the number of workers into groups if greater than 20 and inform them what you are planning to do with their management's support.
- Request management to attend your first activity to show full support and point out that they should be brief and to the point if they want to say anything (no more than 2 minutes).
- Ensure the activity is during the lunch hour, but inform the group that there will be some food specifically selected and supplied and that they may bring other food with them to complement that provided.
- Choose the canteen or a similar location where workers are comfortable with food being eaten hygienically.
- Prepare a 10-minute – NO LONGER – presentation using the food provided as visual aids.
- Start your presentation by explaining the number of bacteria found in the mouth and the intestinal tract, then the mouth juices and how they deal with the foods you eat (use your visual aids), followed by providing them with the food, which will contain carbohydrates, fats, protein, fruit and liquids.
- Do not exceed your determined time for the activity.

Note: *This session will also form the basis of when to start educational information in the promotion of health at work (Health Promotion). I have found that during lectures this specific information is better carried out when students are studying toxicology where it is much better accepted, remembered and applied, than done within Health Promotion lectures.*

Hygiene – The importance of hygiene cannot be overstressed. A practical demonstration of the transmission of microbes to food makes the best visual experience for workers to encourage the practice of hand washing before meals. Show them how easily contamination results in many other situations at work as well such as from hand tools or when cleaning AC filters. A lasting impression can be made by using a large transparent container such as those used for bread bins and placing his over sliced white bread and some dung or faeces to which a phosphorescent has been added. Collect one or two domestic flies and place under the container. Flies will transmit bacteria from the dung or faeces to the bread which can be seen to glow indicating transmission. This is, of course, easier to perform where flies are in abundance in the southern regions.

Posters – Select a small group of four or five workers to create posters which can be placed in strategic areas to remind their colleague about the use of facilities to maintain hygiene. Extend the subject to skin contact, inhalation and ingestion risks and the importance of emissions from chemicals at work. With management approval allow them some time at work to do this. This is a good investment and creates conversation and comments between workers which strengthens the spread of educational information.

Substitution and transportation – There are a number of chemicals which can be substituted for other less hazardous to those at work. Discuss this matter with the purchasing manager; ask him to review supply chains and take note of the conventions and bilateral agreements in the exporting of chemicals or their waste. Where substitution with some chemicals proves impossible, as in printing, laboratories or research, other methods of prevention can be developed and existing policies improved for implementation.

Arrival of chemicals at the workplace and storage –

The following issues require attention:

Leakage – liquid or solid – separation – flammable or combustive – drainage – ventilation – funnels for transferring liquid chemicals – spill control – corrosive conditions and non-metal containers – open containers – safety chemical container compatibility – electrical bonding – legal responsibilities and liabilities – storage cabinets and locks – personnel responsibility.

Improper storage and handling of flammable liquids is the leading cause of *industrial fires*.

Disposal -

Follow the country-specific regulations on the disposal of chemicals. If uncertain, call for advice from the appropriate authority.

- Decide on the level of hazard of the materials (hazardous or extremely hazardous. Maintain separate lists in records, use CAS registry numbers, concentration and quantities. *(A CAS number is a unique numerical identifier assigned by Chemical Abstracts Service (CAS) to every chemical substance described in the open scientific literature).*
- Identify appropriate sites for hazardous waste and extremely hazardous waste.
- In earthquake regions, take precautions to avoid breakage or possible spills; screw-on caps and secondary compatible containers are invaluable.
- Separate dry solid chemicals or waste from liquid chemical waste.

- Decide on the appropriate type of containers to use. Follow published guidelines for compatibility with chemical waste. These will refer to acids, liquid bases, solvents, volatile and non-volatile liquid substances, flammable substances, compressed gases and substances that react, some violently, with water or air.
- Always label the contents of containers, keep a register and appoint someone accountable for the overall management of chemical waste.
- Do not rinse any empty containers of liquid toxic waste.
- Do not store liquid wastes above solid chemical waste.
- High regional temperatures may require appropriate ventilation but care must be taken in smaller areas to ensure patency of containers from volatile substances.
- Should you come across unidentified chemical waste, inform the appropriate authority.
- Country regulations may differ in the time allowed for storage of hazardous waste – check with the appropriate authority.
- Country regulations on the disposal of chemical/toxic wastes into drains that empty into public sewers are strict as these reach both sewage treatment plants and, in some countries, the sea and other waterways or reservoirs. Check with the appropriate authority on what can and cannot be directed into such drains. These generally include flammable and corrosive substances, some dyes that may contain acids (acetic) or some alcohols (butanol, methanol) or mutagenic chemicals.
- Where private transport facilities are used, ensure that these meet the legislative/regulatory requirements, such as colour codes, trained personnel, etc.

First aid and disasters –

In spite of legislation, emergency operation procedures/plans, training and other preventive measures, fires and disasters due to natural, human, or technical failure continue to occur, causing considerable damage to life, property, economic loss and social problems.

All safety practitioners should be qualified in First Aid and have good knowledge on oxygen administration. With reference to chemicals used in the workplace, it is important to ensure instant availability of the lists of all the chemicals in use at the place of work, their material safety data sheets, the manufacturers' names and phone numbers as well as that of the country's poison center, should these be required. A number of practical guides on First Aid are available for reference and should be readily available at an appropriate site in the workplace to deal with chemical issues.

The contact numbers of the local fire and disaster response teams should be readily available should these be urgently required in the event of transportation spills. Other important contacts should be retained by a responsible person and a back-up representative at each workplace. These include hospital emergency, public health authorities, district council and company doctor, if one is available.

The Respiratory System

Our lungs are essential to life and we are effectively at the mercy of the atmosphere and everything which each breath we inhale brings with it. Man's activities today, as in years past, continue to pollute the air we must rely upon for survival, unbalancing what nature has tried over billions of years to keep in equilibrium. *Environmental chemistry* [B4, B7] is a complex subject. In the atmosphere, chemical interactions occur constantly, resulting in chemical substances to which we may become exposed, many of which we are probably still unaware of in both existence and function.

But this is only one side of the issue of the quality of air and the respiratory system. In spite of the continued efforts of many organisations pressuring industry and decision makers, education, and the provision of other support systems to assist people to stop smoking, the habit has not yet been eliminated. Cigarette smoke contains around 4000 chemicals [80] – *carbon monoxide* (CO), *nitrogen oxides* (NO_x), *ammonia* (NH_3) and *hydrogen cyanide* (HCN) are some examples. Some others are known chemical *carcinogens* and a glance at lung cancer registers shows that a large majority of lung cancers are due to smoking. In addition, the use of aerosol sprays, air fresheners, fragrances and repeated indoor insecticide spraying only add to deterioration of the quality of the air we inhale.

We are told that some species of fish were the first to evolve lungs around 370 million year ago, and if we accept the transition from water to land at about 375 million years ago [81,82] then we have to appreciate that amphibians would have required considerably more oxygen for their activities on land. This was a significant change from acquiring oxygen that was dissolved in water via gills to direct inhalation of gaseous oxygen from the atmosphere via lungs.

The lungs have a number of different types of cells, each with its own function. The human respiratory system includes: (see Figures 9, 10, 11, 12, 13a,13b,15 & 16).

1. The passages inside the nose (*nasal cavities*)

2. The space at the end of the nasal cavities. This space is behind the tongue where it forms different sections together known as the *pharynx*

3. An area which extends beyond the pharynx from the back (root) of the tongue to the wind pipe (*trachea*) and this is referred to as *the larynx, which is the organ of the voice box*

4. The trachea itself, which divides into a right branch (a *bronchus*) and left branch; these then divide again into other branches providing smaller branches *(bronchioles)* to the various lobes of the right and left lungs where they end as *alveolar* ducts. There are between 2−11 alveolar ducts for each bronchiole that open into hallways *(atria)* that lead to the air *saccules*. The walls of the ducts, atria and saccules are lined with very thin walled sacs called *alveoli*. These provide a large surface area for absorption which can be very rapid

5. The lung tissue itself through which the air passages *(bronchial system)* pass and end. Each of the right and left lung is covered in a delicate membrane called the *pleura*. This membrane also covers the inner surface of the chest wall and is continuous, covering both lungs. When healthy, the membrane lining the lung is in contact with the membrane lining the chest wall even during respiration. The potential space between them is called the *pleural cavity*.

The left lung is divided into two lobes with the right into three; the right is larger than the left. All parts of the lungs do not move equally during respiration. Blood deprived of its oxygen (deoxygenated blood) is returned to the lungs, ending in a very dense capillary network in the walls of the alveoli where gas exchange takes place. Oxygenated blood is then returned to the body and may contain other potentially toxic substances which have been absorbed during gas exchange. The blood reaches the heart and is supplied through the vascular system to the other organs of the human body, taking with it any toxins.

As blood flows through the capillaries (the smallest of the body's blood vessels) in the tissues of the body, a clear fluid *(lymph)* passes from the walls of the capillaries and into the tissues around them. When the pressure in the tissues increases sufficiently, this lymph then enters a network of vessels *(lymphatic vessels)* also within the tissues, which then discharge their contents into larger vessels that form part of the lymphatic system, which eventually drains back into the circulatory system (See Lymphatic System Figures 33 & 34). It does not do this, however, until the lymph has passed (been filtered) by *lymph glands* along its vessels on its way back to the heart and into the circulatory system. The glands may become infected, inflamed and enlarged by toxic substances, bacteria, particulate matter and dead *phagocytes* (cells that protect the body by ingesting harmful foreign particles, bacteria, and dead or dying cells).

It is important to note that the lungs and their pleura are also supplied with vessels from the lymphatic system but in the lungs they do not quite reach the alveoli and only go as far as the atria of the lungs.

There are more lymph vessels in tissue than there are veins, although the lymph vessels are much smaller. Moreover, the lymph vessels unlike the blood vessels can take up not only soluble substances but also substances which are insoluble in water.

Absorption through the lungs

The surface area of the lungs can be between 50 to 100 square meters [83]. The volume of air taken in with each inhalation is about 500ml. This, of course, will increase with exertion such as physical exercise.

Air passes through the nasal cavity and the series of tubes that become smaller and smaller and reaches the alveoli (air sacs) that have a total surface area of about 70m^2 [84]. Oxygen is then exchanged for carbon dioxide which is then exhaled. The blood flow to and from the lungs is very high and the alveolar membrane barrier for this exchange to take place is about 0.5–0.75 microns (a micron is = 0.01mm) [85]. Thickness can vary in those born and living at high altitudes [86].

The passage of a potentially toxic substance from the nasal cavities to the alveolar region is presented schematically below (Figure 9) together with some relevant parameters (see also Figures 10–12).

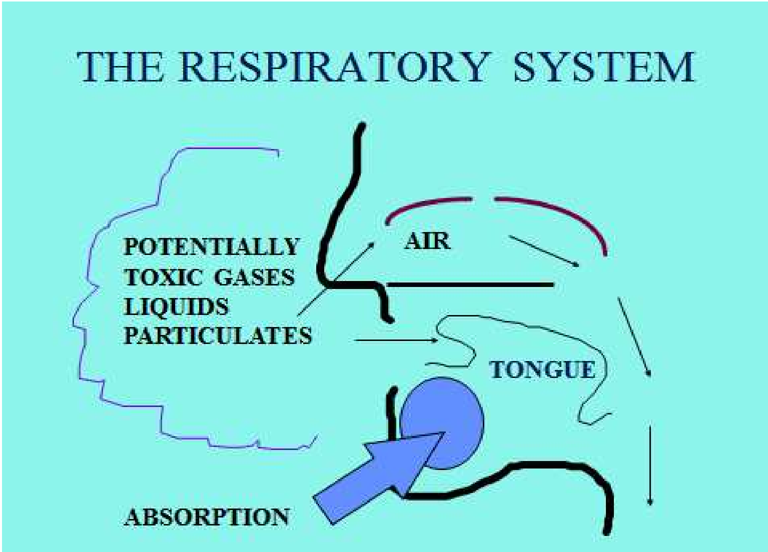


Figure 9. Schematic representation of the entrance of potentially toxic substances to the mouth, indicating that absorption also takes place with some chemical substances below the tongue.

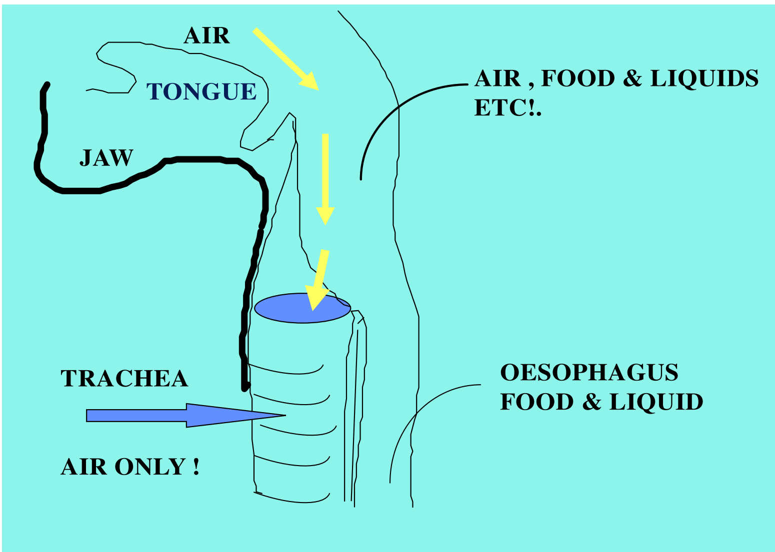


Figure 10. Schematic representations of the entrance of potentially toxic substances to the lungs. Note that the oesophagus (gullet) lies behind the trachea.

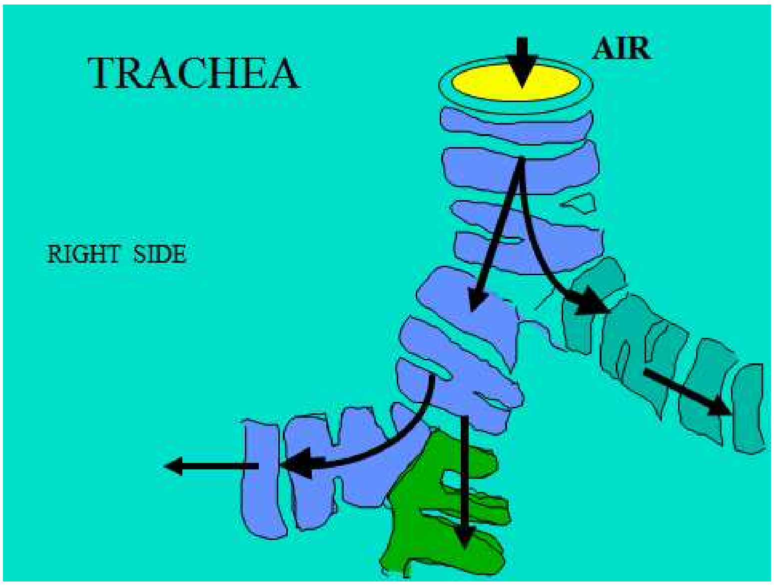


Figure 11. Schematic representation of the upper part of the trachea showing that it divides into two main branches on the right side and one on the left before further divisions on its way to the alveoli.

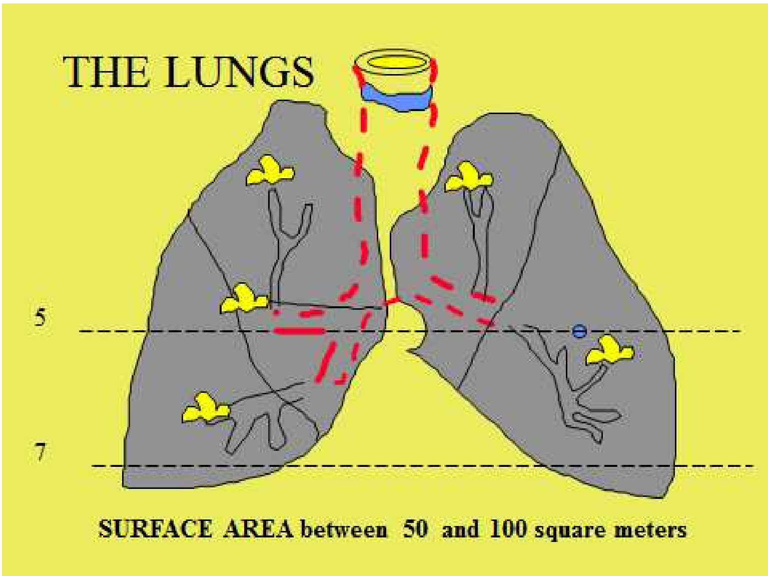


Figure 12. Schematic representation of the lungs indicating the three lobes on the right lung and two on the left lung. Five alveoli are represented in yellow as examples of the many alveoli (300–700 million) in the lungs. See also Figures 13,15 & 16 for detail. The numbers 5 and 7 in the diagram refer to the level of the spinal vertebrae.
Absorption can occur in the form of:

1. GASES
   (carbon monoxide, sulphur dioxide)

VOLATILE **RAPID absorption**

2. LIQUIDS
   (vapours, fumes, mists)

AEROSOL **DIFFUSION** but even more rapid if they are *lipid soluble*

3. PARTICULATE MATTER
   (*dusts, fibres*)

Their absorption in the lungs depends on:

1. The amount inhaled
2. The *partial pressures*
3. Their solubility in the blood
4. The rate of blood flow
5. The rate at which an individual is breathing
6. Particle size

Once toxic substances enter the blood circulation system and the lymphatic system they are then transported to other organs of the body where they may have a biological effect on the heart, kidneys, liver, brain, bones, the reproductive or other systems, or be stored.

Concentration may be higher in one organ than another and there are barriers to the passage of toxic substances, two of which are the blood *brain barrier* (see also p.123) and Figure 47) and the other *the placental barrier*. These will be covered when the toxicology of that system is presented in later chapters, but it is important to mention that substances which can diffuse through the cell membranes will still get through the brain barrier, so do not consider this barrier as a closed door that does not let any chemical or toxic substances through.

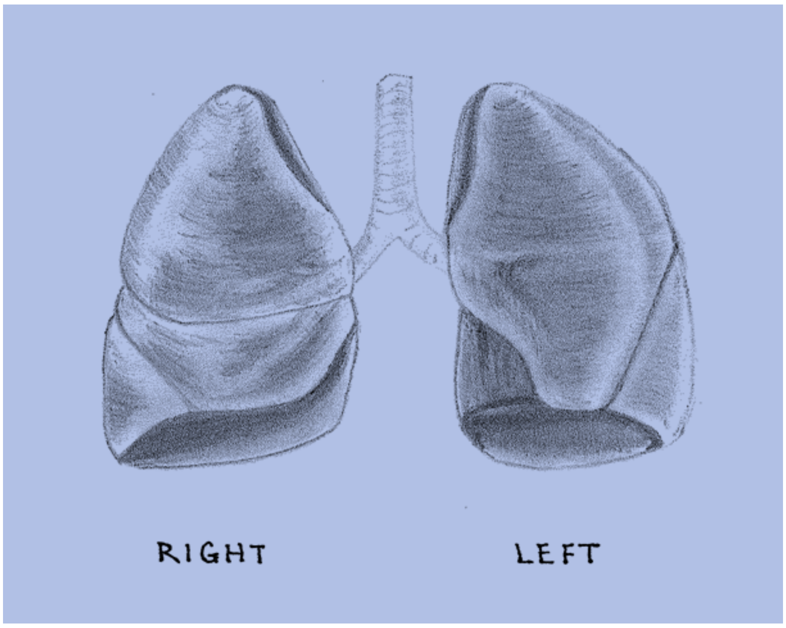


Figure 13a. A sketch of the human lungs and bronchi showing 3 lobes of right lung and two lobes of the left lung.

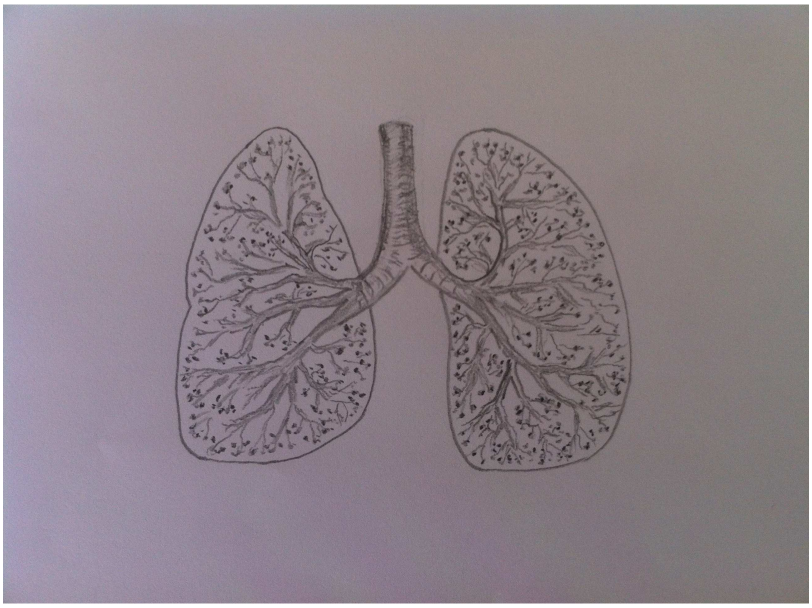


Figure 13 b. A sketch of the human lungs showing the decreasing diameter of the bronchi to bronchioles and the alveoli.

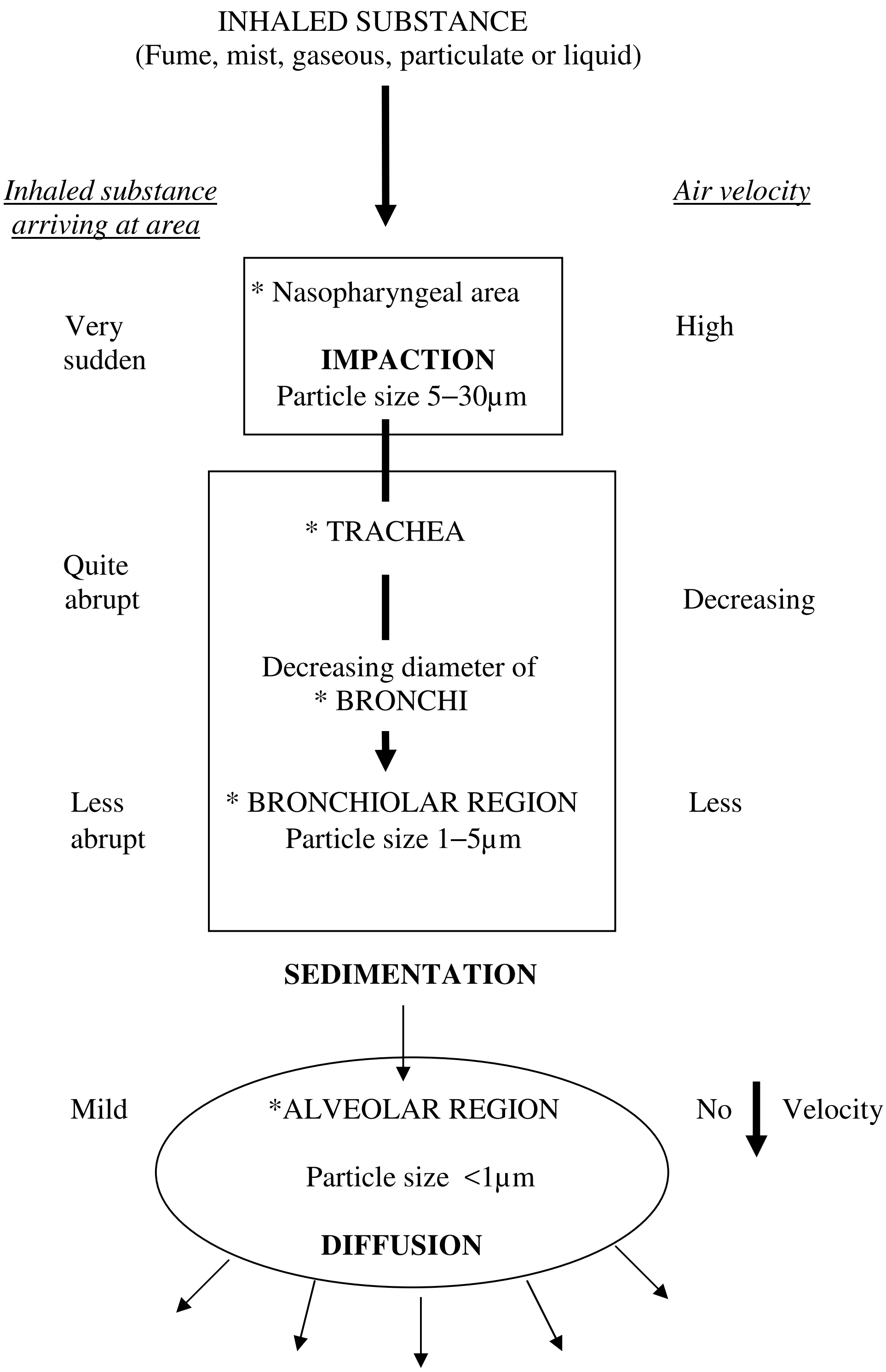


Figure 14. *A schematic presentation of the route of absorption from the nasal cavities to the alveolar regions of the lungs, showing route and velocity changes of inhaled substances as well as the particle size that may reach the various areas.*

Note: asterisk (*) indicates the area through which gaseous, particulate or liquid is travelling.

The vapours of benzene (C_6H_6)B13, toluene (C_7H_8)B14 and xylenes (C_8H_{10})B37 are poisonous; in Appendix IV you will find a list of chemicals and processes where exposure by inhalation may result in adverse effects in the respiratory system and may produce occupational lung diseases [B13, and B14]. Note that the WHO, ILO, IPCS Environmental Health Criteria Series has an extensive list of books on individual chemicals.

Workers travel to and from work and are often on the roads for a considerable time. They are also exposed to many other substances, such as naturally occurring toxins (plant, fungal, microbial), some household products (chlorine, solvents, the burning of certain plastics) and environmental pollutants (nitrogen oxides, volatile hydrocarbons, particulates PM 2.5's and PM 10's), so remain alert to the fact that reported illness may not be attributable to occupational exposure and expert advice should be obtained when in doubt.

During moderate exertion [87] (i.e. when during exercise you do not feel out of breath), a worker will breathe about 10 cubic meters of air over an eight-hour day [88]. Should this air be mixed with a potentially toxic compound, the hazard can be considerable, even more so during heavy exertion. On the other hand, absorption from the respiratory tract is hindered by several factors, which include:

1. Impaction on the mucous membrane of the nasal cavities, pharynx, larynx, and sometimes the upper areas of the bronchi.

2. An immediate return of inhaled substances to the atmosphere by exhalation, especially of fine particulates, which would still be suspended in the upper respiratory tract.

3. Trapping by the mucous that lines the membrane of the air passages and subsequent removal with the sputum and expectoration, or swallowing, which may then either become absorbed or render the substance inactive by the GI tract.

4. Not all matter is absorbed into the blood. Scavenger cells remove inhaled material and either store it or transport it to other tissues or organs where it may also be stored or from where it may be excreted over a period of time. It may also be excreted unchanged by the kidney into the urine.

5. Taken up by the lymph vessels and transported to the lymph glands where it may remain.

Exposure to certain hazardous substances such as asbestos can result in lung conditions where some function of the lung is adversely affected, such as *pulmonary interstitial fibrosis* (see also interstitial fibrosis) or mesothelioma. In consequence, the lung's ability to remove the toxic substance is reduced. Dust particles, mould, *allergens* and chemical ingredients of tobacco smoke could trigger an episode of bronchial constriction such as asthma, and this can result in a build-up of carbon dioxide and reduced intake of oxygen across the alveolar membrane to the blood. Over time, *emphysema* destroys the air sacs in the lungs so that chronic exposure to occupational and environmental pollutants become an important risk factor. *Radon,* which may result in lung cancer, is yet another substance to be aware of when considering chronic exposure to inhaled hazardous substances.

Air quality indices are used in some countries. The values run from 0 to 500 and the higher the value the greater the pollution status [89].

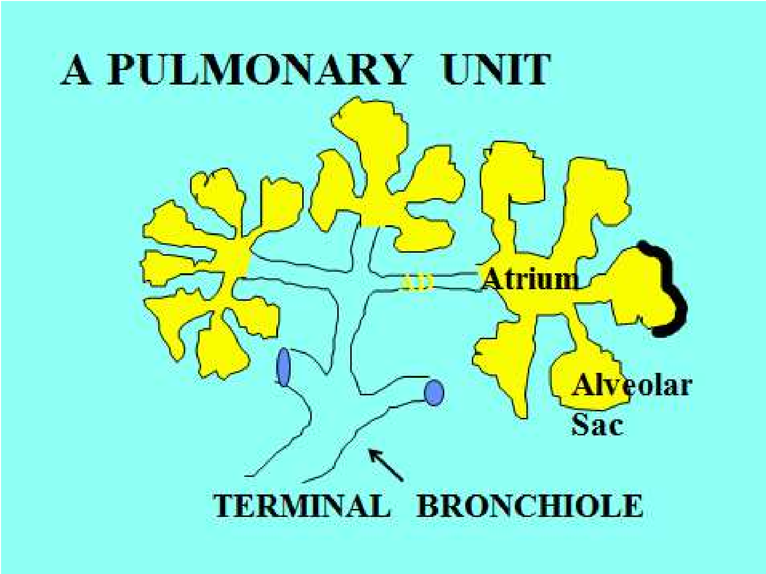


Figure 15. Representation of a pulmonary unit showing the terminal bronchiole dividing into three branches, the presence of an atrium, and the alveolar sacs from the atrium.

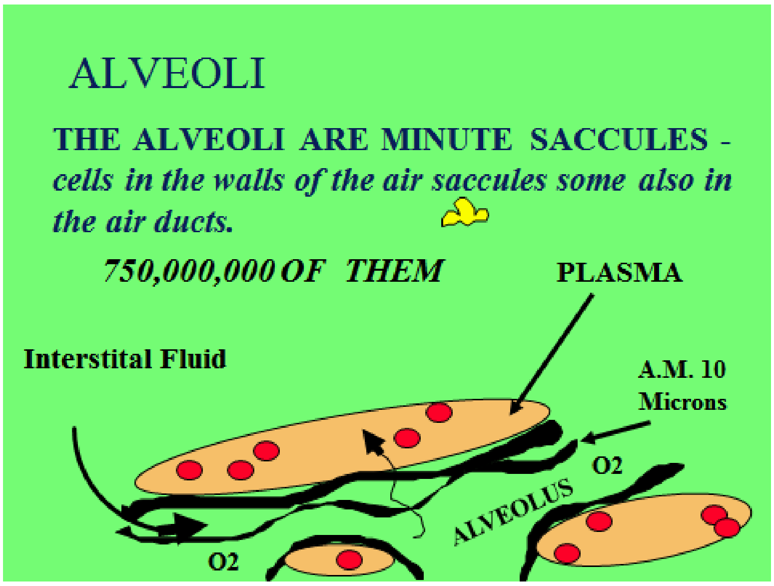


Figure 16.

An impression of the walls of an alveolar saccule showing oxygen transfer to the red blood cells. A.M. = alveolar membrane

Chapter 3 Body Distribution of Toxic Substances

A contribution to chemistry

Jacobus H. van't Hoff [90] received the first Nobel Prize for Chemistry in 1901. Born in Rotterdam, The Netherlands, on August 30 1852 he spent many years (1896–1905) in Berlin as 'Honorary Professor' connected with a membership of the Royal Prussian Academy of Sciences. His contributions to research in Chemistry gained him innumerable honours world-wide. He died on March 1, 1911 at Steglitz near Berlin [91].

There are thousands worldwide who today devote their lives to research in chemistry and develop and contribute many new substances each year to an already extensive existing number of chemical substances. An example is below.

Joachim Schummer [91 & 92] trained in philosophy and chemistry; his major interest is mainly in the philosophical perspectives of chemistry, and like others in this field today takes *"a leading role in the societal and ethical implications of* *nanotechnology"*. This is a relatively new and emerging field of science; it is being mentioned here for you to be aware that as research in the field continues to evolve there may result in toxicological impacts to the general environment, air, soil, water, waste products, effects on plants, biodegradability and indeed during manufacturing processes. As Schumer himself explains, this field may have toxicological implications for nanotechnology researchers. This science will indeed alter manufacturing processes, demand and substitution of some materials, affect waste disposal and safety regulations in the future. In his paper [92], '*Coping with the Growth of Chemical Knowledge – challenges for Chemistry Documentation, Education and Working Chemists',* Joachim Schumer provides a stimulating view of the situation. Once entry to the body has been accomplished, one must then consider the distribution of toxicants.

Nanotechnology

At this point you might ask – what is nanotechnology? Do not even try to define it as so many others keep doing and complicating the issue. The subject incorporates many other technologies and is in consequence very vast. As Schummer states, it may no longer be the correct term to use for this field. One thing is certain; it refers to technology dealing with things that are very, very small – anything smaller than 100 *nanometres* (0.0001mm). You cannot, without very powerful magnification, see anything the size of one nanometre, so to get some perspective of a nanometre just consider how very small a billionth – 1000 million – of a meter would be. You need a microscope to see bacteria and these are a thousand times larger than a nanometre. Odours are made up of gas molecules and many of these are smaller than one nanometre in size. Inhaling smoke would mean you are inhaling particles of around 0.01 microns in size.

Engineers are making so many electronics smaller and smaller, so for simplicity you could for the time being be satisfied with understanding that nanotechnology is the science/technology of researching and developing the structure of materials (used in its widest sense) to a size so small that atomic precision is essential for processing or manufacturing whatever the final product, be they semi-conductors, molecular products or other medical applications.

Into the circulation

Once a toxic substance has been absorbed and entered the blood vessels, it will be transported into the blood system of that organ, for example:

1. SKIN vessels drain into: the peripheral (superficial) blood system;
2. GI tract vessels drain into: the portal (liver) blood system;
3. LUNG vessels drain into: the pulmonary (lung) circulatory system.

All of these systems eventually drain into the right side of the heart. The blood then flows from the right to the left side of the heart and on to the systemic circulatory system which supplies oxygenated blood to the various organs and tissues all over the body. D=duodenum, J=jejunum, I= ileum.

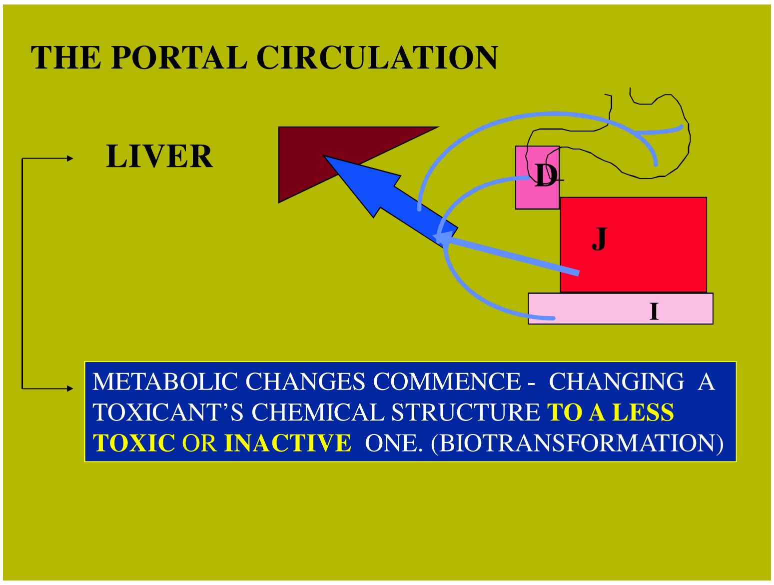


Figure 17. The portal (liver) blood circulation system showing blood reaching it from the stomach, duodenum, jejunum and ileum of the small bowel.

The lymphatic vessels also drain the skin, GI tract and lung, as well as most other body tissues and then drain into a large vein on the right side of the neck. The blood then flows into the right side of the heart, and eventually through the left side, joining the systemic oxygenated blood circulatory system. Throughout this process, a toxicant therefore becomes somewhat diluted within the whole system.
Remember that toxins may affect the site of original contact. Strong acids or bases may cause burns of the skin, and cadmium fumes, ozone (O_3) or nitrogen oxides (NO_x) will all cause acute irritation of the mucous membranes along the bronchial routes and may later result in *pulmonary oedema* (see pulmonary and oedema

separately). Ingestion of *chlorodane* ($C_{10}H_6C_8$), which is an insecticide, may cause burns of the mouth, nausea, vomiting, abdominal pain and severe *gastritis* (inflammation of the stomach) depending on the amount and concentration taken.

Through the membrane

The distribution of a substance into the tissues and organs depends very much on its passage through cell membranes. Very simply described, the structure of membranes are mainly two layers of four different types of *phospholipids* with proteins spaced irregularly between them (see Figure 18 below). Michael D. Fayer in his excellent book "*Absolutely Small*" on quantum theory reminds us that cholesterol is a major component of cell membranes. It forms 20% of the mass of the membrane but *"molecule for molecule the percentage would be more like 30–50%"* of the membrane [93]. Without cholesterol the cells would not function. Its importance lies in the fact that it helps the proteins to maintain their function with active transport of substances through the membrane layers, and makes it difficult for water molecules to get through the outer phospholipid layer, which would otherwise make the membrane much less firm than it needs to be [94]. Note that all membranes are not identical.

Biological membranes are selectively permeable, so whether the toxicant will pass through the membrane depends on its physico-chemical characteristics (size, shape, fat solubility). Proteins in the membrane also have specific functions, such as acting as carriers that assist the transport of molecules through the membrane. Substances which are lipid soluble are altered by the phospholipids assisting their transport through the membrane.

Four of the ways which a substance may use to pass through a *membrane* are listed below. All except simple filtration require that there is a *concentration gradient* across biological membrane, but remember that all this is putting it in its simplest form. It is a lot more complex, both biologically and chemically. The four ways are:

1. Small molecule **filtration** through pores in the membrane.

2. **Diffusion -** the substances must be lipid soluble and *non-ionised.*

3. **Active transport -** by carrier molecules (proteins can be carriers).

3. **Phagocytosis or pinocytosis -** particles are engulfed by phagocytes then transported.

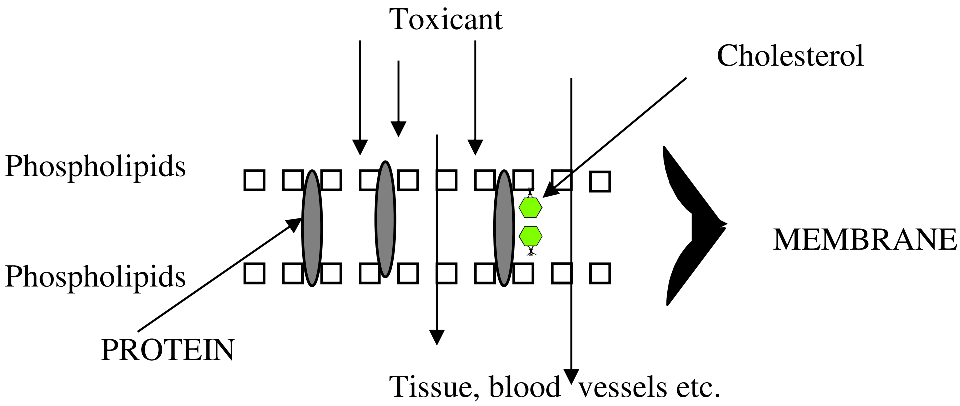


Figure 18. *A simplified sketch to help visualise the layers of a membrane through which a toxicant must pass to get through to the vascular system.*

Interaction versus metabolism

There are some other aspects which affect the distribution of a toxicant (as a foreign substance) to the biological system – these include *interaction* and *metabolism*.

1. **Interaction** may take place between the substance and the proteins in the blood vessels. This happens by the substance binding to the proteins in plasma (the fluid part of the blood). This change (binding of the substance to larger molecules) may make it difficult now for the altered substance to pass through a membrane and therefore its distribution will not be as great.

2. **Metabolism** (a chemical change catalysed by an enzyme that results in a change of the structure of a compound, the formation of a new compound, or destruction of it). This may happen during the absorption process and result in less of the substance getting into the blood vessels and be available for distribution.

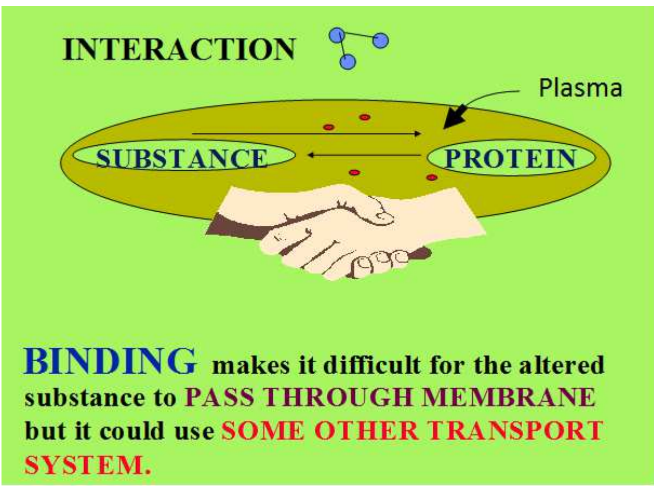


Figure 19. A simplistic sketch of one method of transport systems through membranes, and interaction between the substances and proteins in blood vessels to support paragraph 1 above.

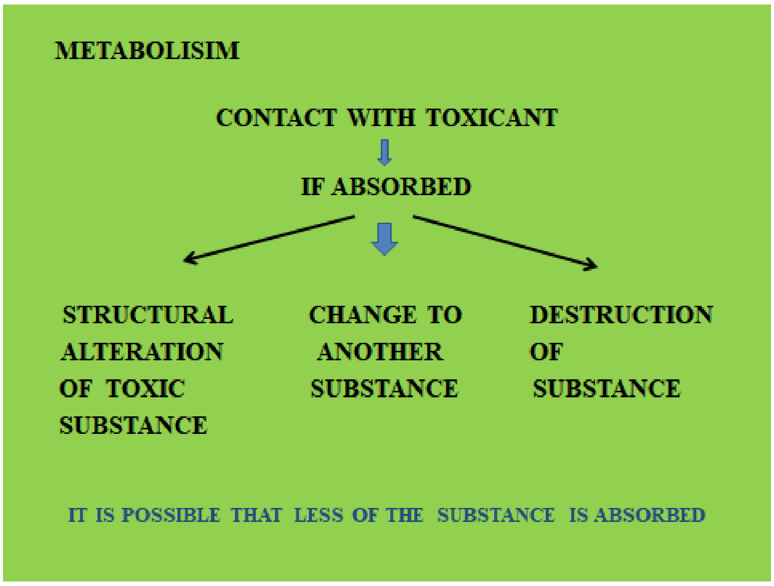


Figure 20. Diagram showing possible changes in the structure of a chemical that has been absorbed.

It should now be clear that the concentration of the substance in blood plasma can provide a useful indication of how much of the substance has already been distributed, because if the substance is lipid soluble then its plasma concentration will be low, as most of it will have passed through the blood vessels and reached their distribution site. Distribution obviously will be large or highly concentrated at the distribution site in this case.

Toxic effects lead to specific organ concentration and half-life.

Through time, people have experienced the effects and often tragic events that have resulted from the toxic properties of many different chemical substances; the poisonous bite of a cobra, inhalation of too much carbon dioxide (CO_2), or in more recent times, the unsuspected ingestion of *Ethanol* ($C_2H_5O_8$) (anti-freeze liquid). Over the years, experts have through post-mortem and/or through the collection of animal experimental data, recorded the damage caused by many toxic chemical substances to the body's different organs. This has led to their classification in terms of those organs where these substances concentrate and do most damage. Both Chemicals and a combination of chemicals have been classified.

Knowledge of the type of substance, with which the body has come into contact, whether dermal, oral or by inhalation, will also provide a good idea where it has been distributed to within the body. It is also possible to calculate the *half life* (the time taken for the plasma concentration to be reduced by 50%) of a substance by knowing the plasma concentration of the substance. The longer the half-life the longer the substance will be in contact with the body tissues and vice versa. This is important in that with a long half-life the substance may accumulate in the system if there is continued or repeated exposure to it.

Remember that the plasma concentration levels also depend on how much of the substance is metabolised and excreted from the body.

Chapter 4 SOME BASIC INFORMATION – ASPECTS OF PHYSIOLOGICAL CHEMISTRY

Chemical processes towards energy and health

There are a number of theories on the origin of life but it is likely that diverse chemical reactions took place in the primeval soup at the beginning of time. Metabolism is a complex area of biological toxicology and unless you are particularly interested you need not go into further depth for the level you need of this subject, other than to grasp the following points:

The human body requires food such as *proteins*, *carbohydrates* and *fats* as well as nutrients which the body itself cannot *synthesise,* such as nine of the 20 essential amino acids, and some vitamins and minerals which it requires for survival. Once these have entered the body, chemical reactions take place that break down molecules or build substances that the cells use for energy or to repair, synthesise compounds like *DNA* (discussed later in this chapter) and ensure the body is maintained in optimum health. The intake of oxygen, food, water, vitamins, minerals, together with the use of *enzymes* to help speed up the chemical reactions, thus provide the body with the essential substances it needs to survive.

A note on Metabolism

Metabolism is thus sometimes referred to as "*biotransformation*" (the alteration of a substance within the body) and "*conjugation*" (the combination of two substances). The structure of a chemical determines how that structure is metabolised. Putting it very simply metabolism can take place :

1. By the alteration of the original compound. This metabolic process is *catalysed* by enzymes (a substance produced by a living organism which acts as a catalyst to bring about a specific biochemical reaction), many of which are found in liver cells, although they occur in most tissues. The enzymes involved may also need other enzymes to help them with their work. This process results in the production of *metabolites* (waste products of metabolism) which can then be excreted from the body.
2. Some metabolites that are produced require the addition (attachment) of some other molecule to the metabolites to alter them so that the change will then allow them either to be excreted or to proceed into some other stage of change before they can be excreted. There are five ways (metabolic reactions) by which this stage of metabolism can be carried out. *Oxidation* and *reduction* are two of these reactions.

3. When the addition of another molecule to the metabolite is insufficient for it to be excreted or inactivated, then further metabolism is necessary and the process moves into another stage of reactions, and again there are other major

metabolic reactions by which this can take place. Sulfation is one of these reactions. Sulfation is the enzyme-catalysed conjugation of a *sulfo group* to another molecule.

The importance of these metabolic processes is that the compound can be made more water soluble (this is done by increasing the *polarity* of the *metabolites*) to increase its excretion, which of course means that its half-life is reduced and therefore its toxic potential is reduced. It then becomes difficult for the compound to accumulate in the tissues or organs. Metabolism may also alter the biological activity of the compound itself or change the duration of its biological activity.

It should be remembered that metabolism may have a reverse effect. For instance, it may reduce solubility which can reduce excretion. Clearly metabolism is an important factor in determining the toxicity of a compound, in addition to its other functions.

Metabolic reactions vary between individuals and are affected by age, disease, a person's environmental conditions, diet and nutrition, as well as genetic traits and the interaction of different drugs. In addition, metabolism does not only take place in the liver but to a certain extent may also take place in the gastrointestinal tract, the skin, the lungs and the kidneys.

In summary, considering the potential hazard of a toxicant having entered, been absorbed into the body, and distributed to organs via the vascular system, metabolic processes at these different stages are important mechanisms because:-

1. A compound can be made more soluble
2. Increase its excretion
3. Reduce its half life
4. Reduce its toxic potential
5. Make it difficult for compounds to accumulate in tissues or organs
6. Alter or change the duration of the compound's biological activity.

Two examples of the metabolism of toxic substances:

1. Acrolein ($C_3H_4O_3$) [95, 97, 105] [B39]

You may have noticed that some food labels have the number E422 as part of their constituents. This particular number indicates that the substance is a food additive called *glycerol* ($C_3H_8O_3$) [96, 97] which is used as a sugar substitute and a sweetener. Note that the European Food Safety Authority (EFSA) has a program for the re-evaluation of food additives and specific dates assigned for this process through Commission Regulation (EU) No 257/2010.

Glycerol, if ingested, is not in itself toxic and it is in fact a valuable product used in medicine, such as cough syrups and in shaving creams amongst others. In food products, it is found in biscuits and beverages, such as liqueurs, where it helps to thicken the liquid or in other drinks where it is used as a sweetener.

However, when heated it is converted to the toxic substance *acrolein* *(C_3H_4O)*. Vegetable oils contain glycerol and fatty acids. Should you inadvertently have forgotten that you placed oil in a frying pan and allowed it to heat to the point where it began to smoke, glycol at that temperature would result in the production of acrolein. At that level of exposure the amount would be so small that there should be little concern other than it could cause irritation of the mucous membranes of the nose, eyes and possibly the lungs. However, at higher levels of exposure, such as those which might result from an accident at a plant manufacturing *acrylic acid* ($C_3H_4O_2$) [98] from *acrolein* *(C_3H_4O)*, this toxic substance would require some consideration to limit accidental exposure. Transportation accidents and spills of acrolein could also result in high level air exposure levels. In industry, acrolein exposure occurs by inhalation and skin contact wherever it is used or manufactured.

Acrolein is emitted to air via vehicle exhaust (consider public garage parking areas), 'side-stream'(*smoke from the lit end of a cigarette*) cigarette smoke, and combustion of fuels (burning of wood and plastics) to which the general population is exposed. Regular smokers inhale acrolein directly in the mainstream of cigarette smoke in which it occurs at up to 90 ppm [99 - 104] not forgetting that there are a few thousand other chemicals in tobacco smoke [101,102]. Costa and Amdur have reported physiological effects at 0.4 ppm of acrolein in animal studies investigating inhalation [103]. IARC has classified it as Group 3 carcinogen. Fires can result in very high levels and it is extremely toxic to aquatic life. Occupational exposures occur in metal plants where welding is used to cut metals coated with anti-corrosives, *thermoplastic* production, and plants where seeds are pressed to produce oil. Acrolein has been found in some wines, fried potatoes and onions, as well as roasted coffee, waste sites and ripened fruit.

What, therefore, happens once it has entered the body? What are acrolein's metabolic pathways? Inhaled, about a third of it is returned from the lungs as carbon dioxide. The remainder combines with protein in the blood and gets involved with protein in *atherosclerosis* while the amount which reaches the liver is *conjugated* with a chemical called *glutathione* and later excreted by the kidney.

2. Chlorine (Cl_2) [105,106, 107, 108]

Almost everyone appreciates how useful and important the chemical *chlorine* (Cl_2) is, both domestically and industrially, but it is not very often that I come across someone who realises how dangerous it can be as well. The lack of understanding of this chemical can be seen by widespread allergies, respiratory and auto immune deficiency problems. How many are aware that PVC contains chlorine and this can leach out when heated? Chlorine can also react violently with many materials, such as fuels.

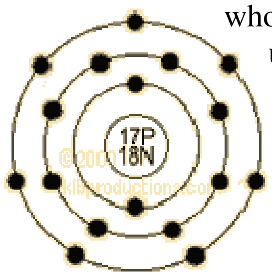


Figure. 21. The diagram shows an atom of chlorine (atomic mass = 35, composed of 17 electrons (black dots) and protons (P). The neutrons (N) share the nucleus of the atom with the protons but do not contribute to the atomic mass. See Appendix II.

Carl Wilhelm Scheele was born to German parents in Sweden on December 9, 1742, [105,107]. He became a chemist and, at the age of 32 in 1774, discovered chlorine. It was, however, another chemist – Sir Humphry Davy – mainly remembered for the invention of the miner's safety lamp, who in 1810 named this important and powerful bleaching, disinfectant and oxidising substance. He showed that it was in fact a new element (Scheele thought it contained oxygen as well). During his 44 years of life, possibly shortened by the toxic conditions in which he worked, Scheele made a number of other discoveries including potassium and sodium in 1807 and calcium, strontium, barium, magnesium and boron the following year, as well as discovering the elemental nature of iodine (as well as chlorine).

Chlorine may be a solid, liquid or a gas which is heavier than air, so that it can accumulate in low lying areas or float like a magic carpet for some distance. It has a strong pungent odour (odour threshold 0.08ppm – this level is below that of toxicity) and a mild irritation may occur between 1–3 ppm, but it becomes very irritating as inflammation increases anywhere between 5–15ppm to the respiratory system. The skin (burns and dermatitis) and eyes (corneal ulceration) are also affected. Beyond these levels a half hour exposure 25–50 ppm are dangerous and could be fatal [(106)].

The American Conference of Governmental Industrial Hygienists (ACGIH) [(108)] has established a short term level exposure level (STEL) of 1ppm (2.9mg per cubic meter) for periods not exceeding 15 minutes: *"Exposures at the STEL concentration should not be repeated more than four times a day and should be separated by intervals of at least 60 minutes"* and assigned a "*threshold limit value (TLV) of 0.5 ppm (1.5mg per cubic meter) as a* <u>*time-weighted average*</u> *TWA) for a normal 8-hour workday and a 40-hour work week"* [(109)].

When a vapour or a soluble gas comes into contact with water in the mucous membranes of the lungs, it dissolves readily producing the corrosive acids – <u>*hypochlorous acid*</u> (HClO) and <u>*hydrochloric acid*</u> (HCl) – and it is this reaction which produces the inflammation. The reaction is shown below where chlorine and water results in hypochlorous acid and hydrochloric acid, both of which are corrosive:

$$Cl_2 + H_20 \quad = \quad HClO + HCl$$

Absorption of some of the gas will therefore take place at the sites of irritation in the upper respiratory tract but depending on the level of concentration in the air, some of the gas may reach deeper into the lungs as far as the alveoli and result in <u>*oedema*</u> (fluid retention). Oedema will occur at around 40–60 ppm [(107)]. The acidity of the gas alters the existing pH of the lungs and of the blood, which reaches other organs in the body. This results in corrosion (<u>*necrosis*</u>) and bleeding of the issues in the organs.

Gases have different ranges of solubility. Different solubility affects the rate of absorption. Chlorine is of intermediate solubility and nitrogen dioxide is almost insoluble making these more likely to reach the alveoli simply because they will not react with water and be absorbed in the upper respiratory tract or partly exhaled. Carbon monoxide has a limited solubility and as the concentration builds up in the lungs, it is rapidly absorbed into the blood preventing it from carrying a sufficient amount of oxygen to sustain life.

The two examples above are not meant to provide a comprehensive picture of either acrolein or chlorine, for which there is ample literature for you to review should you wish to do so. They should, however, have provided an incentive for you to begin to reflect on their metabolic processes and on the impact of potentially toxic chemicals in the workplace and follow up where necessary with your own research for the prevention and control in safety and health management of such substances.

Susceptibility & Sensitivity

Each one of us is unique. Exposure to toxic substances will not affect each of us in the same manner, so that some of us may have a severe reaction and others react mildly. Those who react badly are referred to as 'susceptible individuals'.

Susceptibility depends on a number of factors which include the age of the person, gender, the state of health at the time of exposure, and whether or not there is a genetic disposition in the individual In addition, we all have different lifestyles and this too has a considerable effect on the outcome.

There is, however, another aspect to consider and that is 'sensitivity'. Although, the terms are often used interchangeably, there is a subtle difference between them. An individual who is susceptible is one whose body has the biological capacity to change or modify the effect of a toxic exposure at some specific level of exposure, which then results in a severe reaction. On the other hand, a sensitive individual who has the capacity for risk *(this risk is taken to be higher than that which may be experienced by a normal individual)* may or may not develop a reaction depending on the level of toxic exposure, but if the individual does, then that reaction will be of a milder nature. Such individuals need to be protected by standards of air quality.

Masoli *et al.* gave the global mortality for asthma in 2004 as 250,000 and estimated that around 300 million people suffer from all types and sub-types of this respiratory condition [(109)]. Deaths from asthma are not common [(110)] and the Global Burden of Disease Study report indicated that the levels of mortality fell to 190 million in 2010. It accounts for about 1% of all deaths globally. Those with asthma should not be inclined to live in heavily air polluted areas and with hindsight avoid whatever may trigger an asthmatic attack. Note also that asthmatics may develop sensitivity to certain substances, such as aspirin, and may not realise this is occurring [(111,112)].

One other example to which some individuals are susceptible is *parathion*, an organophosphate insecticide. The very young are generally much more sensitive to chemicals primarily because excretion is not as good during their development as it is in adults. Children in contact with toxic chemicals can also absorb more of these than others.

In terms of susceptibility and sensitivity consider also the synergistic effect of chemicals which was referred to in Chapter 2. Examples include alcohol consumption, or smoking and its effect on the lungs in an air polluted environment.

Enzymes

As mentioned earlier, enzymes help to speed up chemical reactions. These are large protein molecules that accelerate (i.e. catalyse) chemical reactions. The correct environment is important for enzymes to work in – the temperature and pH must be just right for them to function optimally. The result of such reactions are not just the breakdown of molecules into smaller ones but also the build-up of larger ones. In this process enzymes often use what are known as *co-enzymes* to help them with their work. They are divided into six major classes according to the work they perform, so that some will connect molecules to each other, others transfer an electron or add some chemical group and so on.

The human body, like many organisms, has a large number of enzymes essential to metabolism and some of these are used as indicators of disease. Not all of them, however, are specific to the condition for which confirmation may be sought; some enzyme levels are high in more than one condition and confirmation needs therefore to be obtained by also doing other types of blood tests.

Some people metabolise toxins faster than others; as Medical Director of one of the largest oil companies in the world I remember one man in particular who drank more alcohol than was good for him every night. In spite of it, however, the next morning he showed few effects. His body must have detoxified the alcohol fast using an enzyme known as *acetaldehyde dehydrogenase* (ALDH2) found in the liver. This enzyme converted the alcohol to *acetaldehyde* (CH_3CHO) [113] which was then again converted to another chemical – *acetate* ($CH_3CO_2^-$) – by yet another enzyme. A third enzyme extracted the calories (which are then stored in his body as fat), carbon dioxide (CO_2) and water. There is more to it than has been explained as other organs and glands are also involved in this metabolism [114].

Most of the time you have yourself to blame for your hangover, but if you don't want to do that you can always blame acetaldehyde (CH_3CHO) as this is the chemical that really gives you your hangover! However, there are different (genetic) variants of this enzyme, some of which are defective due to genetic mutations. If it does not function as it should, it does not convert acetaldehyde to acetate, which allows acetaldehyde to accumulate in the body. So if you happen to have this particular variant of the enzyme, as some East Asian populations have, you would not want to be drinking alcohol, because apart from a hangover, acetaldehyde build up can lead to other conditions such as liver damage, kidney problems and even in some cases cancer. It is currently classed as a probable carcinogen [113], although WHO/IARC class it as Group 1 carcinogen. Social pressures towards the ingestion of alcohol and continuous exposure to alcohol in some types of employment, both administrative and industrially, remain difficult problems to deal with.

Amino acids ($NH_2CHRCOOH$) [114]

Amino acids are organic compounds containing functional groups - amine (-NH2) and carboxyl (-COOH), along with a side chain (R group) which is specific to each amino acid. The main elements of an amino acid are carbon, hydrogen, oxygen, and nitrogen, although other elements are found in the side chains of certain amino acids. There are about 500 amino acids, although only 20 are in DNA and are found in the body in the form of proteins, but are also used in neurotransmitter transport and biosynthesis.

The first amino acid was discovered in 1806 by two French chemists who called it *asparagine* [115] having isolated it from asparagus, although it can be obtained from other sources, such as potatoes, nuts, eggs and seafood. There are many other sources. In 1969, traces of some amino acids were found in a meteorite that struck Australia, and a 500-million-year-old *trilobite fossil* (see also Appendix III) was also found to contain an amino acid called 'alanine' [116]. This is intriguing to all those who keep searching for the origin of life. By 1935, all types of amino acids within protein were discovered; it was later found that alanine was required by the central nervous system. One amino acid can combine with another amino acid by a ***peptide bond*** (see also Peptide in Appendix IV) and a chain of amino acids that are bonded in this manner form a protein. The protein made up of the chain of amino acids can be very long indeed, which is why they are often referred to as '*polypeptides*'.

There are large numbers of amino acids in nature but the human body has only nine referred to as 'essential amino acids', and these can only be obtained through food or food supplements usually in powder form. The body cannot build them. In addition, it requires 11 others referred to as non-essential meaning it can build them making a total of 20. They are the building blocks of enzymes, proteins, hormones, and other body tissues and are essential for proper nutrition. Two examples are *methionine* ($C_5H_{11}NO_2S$) and *lysine* ($C_6H_{14}N_2O_2$). In industry, amino acids are used in various production processes such as the manufacture of biodegradable plastics, the food industry and very commonly in their addition to animal feed, which often lacks some of the important amino acids for animal nutrition.

The amino group of an amino acid is written NH_2, which is *nitrogen* and two *hydrogen* atoms, and the acid side is the *carboxyl group* written –COOH (see structure below). These lie to either side of a carbon atom to which is attached an oxygen atom on one side and a side chain usually designated by an 'R' on the other. There can be more than one side chain on this peptide bond. The bond linking the amino group and the carboxyl group is known as the peptide bond. Peptides are strong bonds, difficult to break and stable. This structure maintains the shape of the protein and they are only found in proteins.

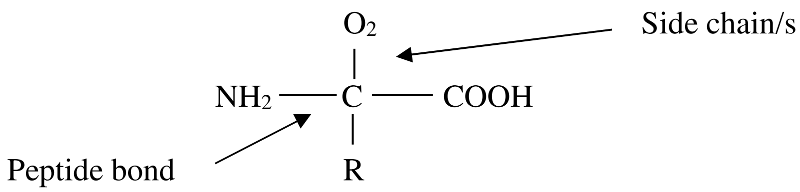


Figure 22. A visual illustration to show the bonds linking the amino and carboxyl groups referred to as the Peptide bond.

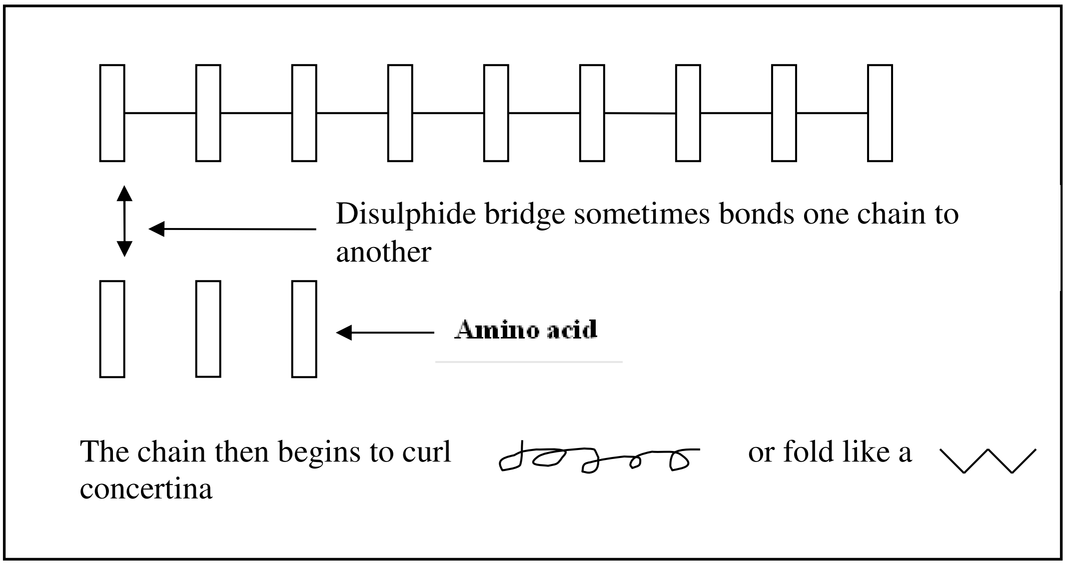


Figure 23. Shows a stylised sketch of amino acids linked by peptide bonds and another chain linked to the first chain by a disulphide bridge.

Peptides

When the amino group (NH) and the carboxyl group (–COOH) have been linked by a *peptide bond* as explained above, the compound is now referred to as a peptide. A peptide has two or more amino acids but when these peptides get longer and they have more than 50 amino acids, they are then referred to as proteins. Proteins, of course, can be very large indeed and may have thousands of amino acids.

Because it can get somewhat confusing, note that in chemistry any chain that is connected by a bond like the peptide bond is also referred to as a *polymer*. This means that a peptide is classified as a *polymer*.

The muscle cells of the blood vessels and both the atria and ventricles of the heart (see Figure 37) secrete peptides. These result because of an increase in pressure or blood volume and help in the excretion of sodium (natriuretic). The B-type *natriuretic* peptide (BNP) helps, reasonably accurately (83%), to differentiate between heart failure and other conditions *(oedema of ankles or difficulties in breathing)* when the levels are higher than normal, i.e. between 100–300 pg/ml (pg means *picograms*), but remember that measurement results differ between laboratories. By helping to reduce salt in the body, blood volume is reduced, the heart pumps better and increased blood pressure is also reduced. The kidney is also an important player in the excretion of sodium.

Proteins and DNA

The long and complex molecules called proteins have a large range of functions in the body. Amongst their many functions they form the main elements of cells which provide structure and support for the cell, transport other molecules around the body, transmit signals to cells and organs, and as enzymes, catalyse most chemical reactions in the body. Insulin and haemoglobin are examples of proteins. There are about 100,000 proteins in the human body (Myers 2007) [B40].

A cell may have thousands of different proteins and you have already gathered that one amino acid can combine with another amino acid by a peptide bond, and a chain of amino acids bonded in this manner then form a protein. But how is this done and what decides to make a protein at a particular time? To answer this we need to glance at the internal structure of a cell and DNA (*deoxyribonucleic acid*) without getting too deeply involved (as this would be the subject of a chapter in its own right).

A nucleus lies inside each and every cell in our body. The nucleus contains DNA, which contains all our genetic information (perhaps 'instructions' might be a simpler word to use) necessary to build every type of cell needed to form and maintain a human body. This is not the only DNA the cell contains. Another structure the cell contains is a *mitochondria* which provides the energy for the cell to function through chemical reactions. Mitochondria have their own DNA (and that again is another story).

DNA is also present in the *chromosomes* found in the eggs of females and sperm of males. Each body cell has 23 pairs of chromosomes (i.e. 46 total), including one pair of 'sex chromosomes' which are XX in females and XY in males, and these divide during reproduction to form eggs and sperm, which contain half the number of chromosomes compared to body cells, i.e. 23. The 'sex chromosomes', i.e. XX or XY, determine gender.

The chromosomes contain the DNA with all the instructions needed for developing and maintaining a human body. Each chromosome contains thousands of 'genes' – the molecular unit of heredity. A gene is a region of DNA that has a specific function (e.g. making a particular protein or an enzyme) and is made up of a sequence containing one or more of four 'bases': adenine, cytosine, guanine, and thymine.

Together the genes make up the 'genome', a word coined by Professor Hans Winkler in 1920. Genes, of which it is believed there are around 25,000, contains the instructions passed on from cell to cell as they divide and also from parents to children, and are necessary to produce the specific proteins required to develop and maintain the human body.

You may be wondering what all this has to do with toxicology. Dr. Sharoon Moalen and Jonathan Prince in their book 'Survival of the Sickest' point out that *'the average human eats somewhere between 5,000 and 10,000 natural toxins every year'*[(117)]. Add synthetic toxins to this figure and you are looking at very large numbers of toxins that the body has to combat. Its importance is that toxic substances can cause serious damage to DNA, and understanding where and what it damages requires getting down to viewing DNA at molecular level. (Note that there are other factors that also damage DNA).

The Nobel Laureates James Watson and Francis Crick described the structure of DNA in 1953 [(B41)]. Rosalind Elsie Franklin also made contributions to the structure of DNA in that she determined by X-Ray diffraction that it had a spiral shape. She unfortunately died of cancer at the age of 38 and never received the credit she deserved to such an important discovery [(118).]

Look at the drawing of the DNA double helix and note the two ribbons joined by horizontal bars called bases. Imagine that you were holding a miniature ladder at each of its ends with your right hand thumb and index fingers touching the vertical rails on one end and your left ones at the other end. If you could now twist one end clockwise and the other anticlockwise you would have replicated what is shown in the drawing below. The rails (verticals) represent the ribbons and the ladder rungs (steps) the bases (coloured rods) of the helix. This twisting continues and stops when a specific number of bases have been reached. The diagram below looks like two blue ribbons that have been twisted together, hence the term 'double helix'.

There are four different bases: adenine, cytosine, guanine, and thymine. The different chemical structure of the ends of these bases where they attach to the inner sides of the 'ribbons' causes a pulling or twisting force on the ribbons, with one ribbon pulling downwards and the other upwards. This is what resulted in the spiral condition of the double helix.

Note also that each ribbon is linked by what in the diagram look like coloured rods. These are the bases explained above. There are four different bases: adenine, cytosine, guanine, and thymine. The different chemical structure of the ends of these bases where they attach to the inner sides of the 'ribbons' causes a pulling or twisting force on the ribbons, with one ribbon pulling downwards and the other upwards. This is what resulted in the spiral condition of the double helix.

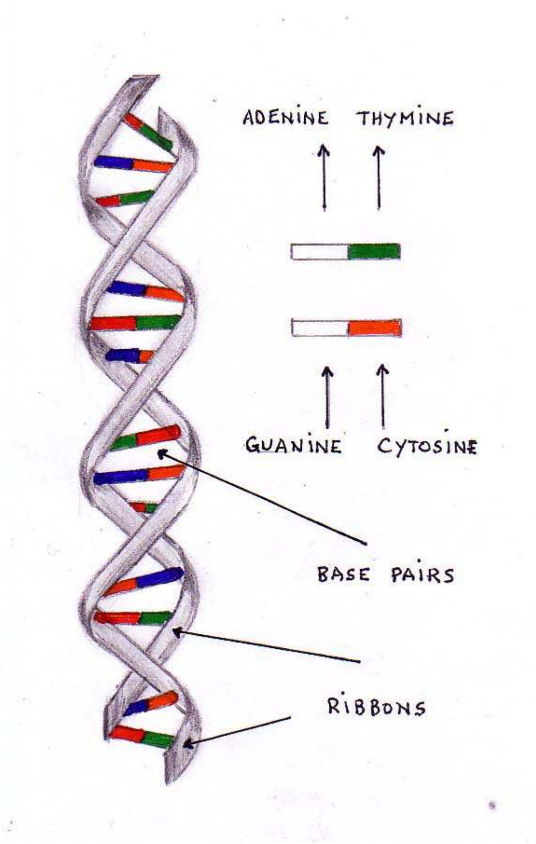


Figure 24. The double helix of DNA.

The bases are shown as oblongs with links between them and to the 'ribbons'.

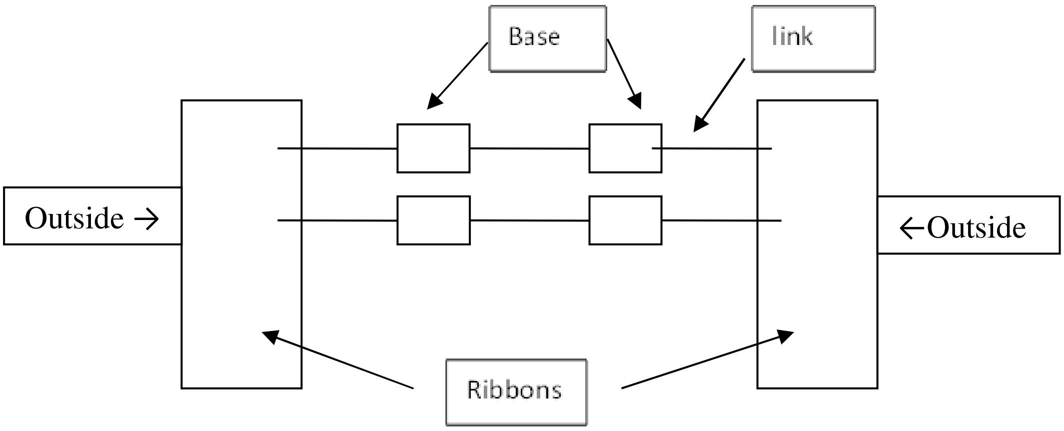


Figure 25. A over simplified flat sketch of an unwound structure of the DNA double helix showing the four bases linked to the chemical structure that are represented as the ‘ribbons’.

You now need to look at what makes up the ‘ribbon’ bands. Figure 25 shows the left ribbon band from outside inwards, that is towards the link with the bases (left to right) there is a molecule of <u>*phosphate*</u> $(PO_4)^{-3}$ indicated by a ‘P’ (see fig.26). This is linked by a hydrogen bond to a molecule of sugar indicated by ‘DR’. This sugar is called <u>*deoxyribose*</u> ($C_5H_{10}O_4$) whose structure you will see further on, as this shows you where and how this molecule combines with a base. The string of molecules from the molecule of phosphate all the way to the molecule of sugar [<u>*deoxyribose*</u> ($C_5H_{10}O_4$)] is repeated all down through what we have called the ‘ribbon’ (helix), each of which is linked to a base.

LEFT RIGHT

Molecule of phosphate	Hydrogen bond	Molecule of sugar	
P	H	DR	BASE
P	H	DR	
P	H	DR	
P	H	DR	
P	H	DR	

Figure 26. Simplified explanation of the molecular structure of a band of the double helix composition. The other band’s molecular structure is the same but starts with the molecule of <u>*phosphate*</u> from outside inwards, i.e. right to left.

This molecular structure is repeated on the other side but note that you read this from right to left starting off with the molecule of <u>*phosphate*</u> $(PO_4)^{-3}$ ending with the sugar molecule which then again joins another base. Each organic base is linked by a hydrogen atom making up the double helix – the DNA. A human DNA molecule has no less than 150 million base pairs; estimates in the literature range from 150 to 200. Note that the base *adenine* always links with the base *thymine* and the base *guanine* with *cytosine* (see Figure 24).

You will have noted earlier that one amino acid can combine with another amino acid by a *peptide bond* and that a chain of *amino acids* bonded in this manner then form a *protein* and that genes contain the instructions needed to build a protein. Whenever proteins are required for repairing tissue, building enzymes or hormones, specific instructions are essential for this task. DNA always remains in the nucleus, so with the help of an enzyme it produces molecules of RNA (ribonucleic acid particles) containing bases with instructions, and RNA sends a **m**essenger called **m**RNA to do the job in the cytoplasm of the cell where the messenger binds and interacts with a *ribosome* *(see also Fig. 68 p.219)* – this is made up of two parts, a large and a small; one reads the instructions and the other assembles one amino acid after another in the order just as the instructions require for the building of a protein. The process of passing the gene instructions in DNA to RNA is referred to as *'transcription'*. Block by block, a protein is built. The cell relies on feedback both from outside and inside the cell to determine when this should be done and when it should stop assembly. The protein is then either dispatched to where it is needed to carry out its work outside the cell or inside. This is a very simple description of what goes on in one of the most important processes in the body.

Mutations

A mutation is a permanent change in the structure (gene sequence) of the *DNA*. Inherited mutations can occur both in the sperm and egg and will be passed on to offspring and inherited abnormal chromosomes from father or mother may give rise to different diseases. Acquired mutations may occur as a result of a number of conditions, such as genetic alterations when DNA is being copied from one cell to another, or modification of proteins or incorrect expression of genes or as a result of factors such as solar radiation or ultraviolet light. These, fortunately, do not happen often. Natural and synthetic chemicals can weaken the hydrogen bonds between the bases of DNA structure and cause a change in the sequence in which the genes are arranged. *Retroviruses* can also find their way into the human genome; these can activate or inactivate human genes. *HIV-1* or *HTLV* are examples of retroviruses. Other destructive activities, such as cancer and other conditions, may cause mutations. A mutation may also result in reproductive damage by affecting the embryo during its development.

Mutations are not just detrimental to the organism as would appear from the conditions listed above. A mutation may actually result in a beneficial effect; for example, altering a chemical process or mechanism within cells that result in an advantage in metabolism or *detoxification* or confer resistance to some disease which the organism did not have before. A classic example is being unable to digest and absorb a sugar called lactose in milk, which is caused by the absence of an enzyme called *lactase* ($C_{12}H_{22}O_{11}$). Lactose is normally broken down by lactase into glucose and *galactose* ($C_6H_{12}O_6$) which the body can absorb easily. In this case, a mutation occurred in an inherited gene which resulted in intolerance to lactose. An infant may be lactose-intolerant showing undesirable gastro-intestinal symptoms, even when parents do not show any signs of intolerance.

CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) is a tool by which DNA can be altered and referred to as gene editing. Several Scientists foremost amongst them is Dr. Carl June and her team at the University of Pennsylvania. Although still controversial the process has been successful in correcting gene defects in mice and rats and may yet prove of great benefit to humanity in the correction of genetic defects [(119)].

The reader should note that some other aspects of physiological chemistry not included here will be found in chapters relevant to the organs targeted by various toxicants.

Chapter 5 Responses to Toxicants by Target Organs

The Great Siege

In Malta at the tip of Valletta facing Sicily (Valletta is sometimes spelt with one 'l' but double 'l' is most commonly used), Fort St. Elmo commands the entrance to both the Grand Harbour and the Sliema (Marsamuscetto) Harbour. Today, few stop to consider its strategic position. In May 1565, the great co-commander of the Turkish fleet Mustapha Pasha was preparing to invade Malta to 'crush and destroy' the Knights of St. John of Jerusalem once and for all on the order of Suleiman the Magnificent, Sultan of Turkey [(120)]. (See Fig.70 & 71 on p.342 & 343 Appendix V).

The Maltese, meanwhile, under orders from the Grand Master Jean Parisot De La Valette, were poisoning the water wells they knew the enemy troops would have to use. Sewage was a major constituent of a number of pollutants they dumped into these wells – a life-threatening weapon of considerable force spreading dysentery and in those days, certain death.

Mustapha Pasha's target was Fort St. Elmo. His soldiers raised their shiny shields to protect themselves and with muskets in hand began the attack to destroy the fort. The dysentery bacterium, *shigella* (there are many variants) covers itself with a fat and a sugar better referred to as a <u>*polysaccaride*</u> (lipopolysaccaride) to protect itself from attack by the body's immune system and fires protein into the host cells at its target sites (the small and large intestine) causing bleeding as it destroys the cells. How, then, does a toxicant select a target site?

Pathological findings, animal experimentation and medical experience has over many years indicated that the distribution of toxicants and their metabolites' selection of target organs depend on their point of entry, molecular size, vapour pressure, pH, affinity for red blood cells, method of distribution (blood or lymph), chemical characteristics, such as its water or lipid solubility, a favourable site for reproduction, and the biochemical conditions at the target site. Biochemical reactions may later result in toxic substances being released from body storage sites (fat tissue, bone, liver or kidney). <u>*Ethanol*</u>, for example, is both fat and water soluble, and therefore passes rapidly through cell membranes. Solvents with a very low vapour pressure have "*a high affinity to water and skin*". *"A low pH in the GI tract facilitates the penetration of metals, and <u>carbon monoxide</u> (CO), <u>hexavalent chromium</u> (CrVI), <u>arsenic</u> (As) and <u>organic mercury</u> (C-Hg) have a high affinity for red blood cells."*[(121)]. *[note: underlining is author's own).* Other toxic substances such as <u>*inorganic mercury*</u> *(Hg)* have a preference for proteins in plasma, rather than red blood cells, and this is important in that less of the toxicant reaches the target organ as most of it will be in the blood plasma [(122)].

Reproduction and spread to other hosts to ensure survival are strong motivators for any species. Killing their host clearly does not work to their advantage, although age, existing disease, virulence of the toxicant, low resistance, and other physical conditions may cause complications and result in death of the host.

Target organs affected by toxic substances include the skin, digestive system *(the GI tract, liver*), the lymphatic system (*spleen, bone, thymus, tonsils, adenoids, appendix and a number of lymph nodes),* the immune system, the cardiovascular System (*blood and blood vessels, and heart*), the nervous system (*brain, spinal cord and nerves*), the reproductive system (*male and female organs*), the endocrine system (*hypothalamus, pituitary, pineal body, thyroid and para-thyroids, adrenals, ovaries and testes, and the pancreas)*, the skeletal system (*the bones and cartilage)*. These will be referred to in this section, although the focus will remain on those of importance for safety and health professionals.

There are a large number of substances that are capable of upsetting target organ function, although the ways in which they can do is quite limited. It is important to understand that a change from normal function occurs in these organs as a result of toxic absorption, distribution and storage. Therefore, knowing how these substances can be identified and what is causing such conditions is essential to plan measures for prevention.

The Skin & Nails

The skin and nails are both sites which are often, especially in the summer months, visible to observant eyes. It is therefore important to understand and be aware of the conditions that affect these areas as they often lead to underlying problems at the workplace that can be prevented.

The multi-layered covering of the human body, which we call the skin (but includes the mucous membranes) is a frequent target as is shown by the number of skin disorders which are commonly reported as occupational diseases. They account for between 20 and 30 percent of all occupational injuries. The increasing numbers of allergies, some of which show dermal symptoms, increase this percentage. It is useful to be aware of allergic conditions that mislead us to carry out unnecessary investigations and which are not work-induced.

An occupational skin injury may be defined as '*an immediate adverse effect on the skin that results from immediate injury or exposure to a toxic agent or agents that involves one single accident in the work environment'*. General estimates of the magnitude of skin injuries and their causes depend on geographical location due to different cultures, education, quality of life, prevention policies, legislation and classification methods of registration. Chemical and thermal burns account for about 15%. Abrasions and radiation injuries would all be below 3%. Radiation would be very low indeed, perhaps 0.02 or 0.03%. Others include: friction, heat, extreme cold and electricity [122].

Cuts and puncture wounds are high, probably above 70%. Whatever will weaken the skin's protective keratin layer, such as dryness and cracking by solvents is worthy of note, because damage to the skin makes it more vulnerable to toxic absorption. Not all chemicals are absorbed at the same rate. Some, like acids and alkalis, result in immediate damage to skin layers; others may require contact to occur multiple times.

The skin's response to toxic stressors (chemical, physical, environmental or microbiological) is the body's first line of defence. The skin has a water-repellent, fibrous protein called the keratin layer and protection is supported by lipids over the skin's surface produced by its sebaceous glands. The skin's selective permeability will also determine its potential passage through the skin layers. The toxicant's size, shape and fat solubility, therefore, play an important part of the response. Enzymatic alteration of the toxic compound, which may result in less of the substance entering into the blood stream, is yet another deterrent.

Response to some substances may be local and immediate, systemic or both local and systemic, and below are listed some examples of agents that may result in skin disorders and should be borne in mind as a guide to broadening your research for workplace assessment and prevention.

Chemical Agents

Acids	-	Chromates
Alkalis	-	Nickel compounds
Oils	-	Rubber chemicals
Solvents	-	Acrylates
Detergents	-	Pesticides
Plastic glass dust	-	*Resins*

Physical agents	***Mechanical factors affecting protective layers***
Wind	Friction
Temperature (high or low)	
Humidity	

Biological agents Bacteria, fungi, parasites, viruses and *Richettsiae* bacteria

Other agents Plants, such as the daffodil (narcissus), contain the poisons lycorine and galanthamine in its leaves and bulb [(123)]. This is are alkaloids, toxic to the nervous system if ingested and inhibit protein synthesis. Alkaloids are found in many plants. Other agents wood, particle board, and treated wood which may contain any of the following toxic substances used to preserve wood such as arsenic (As), creosote (this is a combination of chemicals see citation[(124)], *chromium* (Cr), *copper* (Cu) and *pentachlorophenol* (C_6HCl_5O).

Major skin conditions that may result in a response as a consequence of toxic substances in contact with skin include:

Occupational dermatosis [(125)]

This is a general term that describes skin disorders caused by agents (chemical, physical, plant, short wave *(UVB)* and long wave (*UVA)* ultraviolet radiation, ionising radiation, temperature differences, biological agents etc.) in the working environment. They are all preventable conditions.

Dermatitis [126] on the other hand refers to an inflammatory condition / disease of the skin. The word 'eczema' is often used interchangeably to mean the same thing: redness, swelling, blisters, oozing of fluid (exudation) and later crusting and scaling and possibly even later thickening and a change in pigmentation of the skin. Excluding cuts and puncture wounds, chemical agents come next on the list of causes (solvents, detergents etc.) that produce a large amount of dermatosis which they do by:

1. Mild or moderate irritation of the skin (soaps). These require repeated contact with the skin before they result in inflammation.

2. Strong irritation (acids and alkalis). These will injure the skin immediately on contact.

3. Sensitivity reactions (an irritant may act as a sensitizer). Occupational sensitizers include epoxy *resin*, *chromates* *(CrO_4^{2-})*, solvents, rubber chemicals and many others.

Allergic contact dermatitis [127]

When an *allergen* (also referred to as an *antigen* - this could be pollen, jewellery such as nickel, *rosin* in adhesive plaster, bacteria or a number of other known allergens) comes into contact and is absorbed by the skin or mucous membranes, this activity is recognised by the body's immune system triggering the production of *antibodies* (*glycoprotein* molecules that bind the antigen) to try and neutralise the intruder. The molecular structure of the antibodies are designed specifically to bind to the molecular structure of the antigen. Furthermore, once an antigen binds to the antibody, it signals other cells of the immune system to strengthen and support it in this defensive strategy.

Antibodies are produced in five types referred to as *immunoglobulins*: IgA, IgG, IgD, IgE, and IgM. **IgA** acts as a guard on skin surfaces, nose, saliva, eyes, GI tract. and breast milk. **IgG** prevents spread of infection. **IgD** activates the *B-Lymphocytes*. **IgE** is high in people with allergies responding when pollen, fungus or spores are around, and **IgM** stimulates the immune system when infection is detected. A memory data bank of the invaders is maintained by B- and T-type lymphocytes (see Lymphatic System p.105) so that quick action can be taken should a similar attack occur at some other time.

The immune system may sometimes overreact to the body's absorption of the substance and this may result in *anaphylactic shock* – a very serious condition (an allergic reaction) that may end in death very quickly, although the magnitude of the reaction to the foreign substance varies between individuals.

The clinical outcome of allergic contact dermatitis is varied. There are a number of different conditions that may result. This is not an inherited condition. Although reactions may be immediate, they may show only after 12 to 48 hours at which time the area becomes red, sore, and itchy with blisters developing. These allergic rashes may not be confined to the site of contact and occur anywhere on the skin. It is also possible for someone to develop a rash to an irritant such as nickel or a solvent, whilst already suffering from another type of allergic dermatitis.

Post-inflammatory hyperpigmentation (PIH) [128]

This condition may occur following injury, inflammation or infection of the skin but is also seen following an allergic or skin inflammatory disease such as *atopic* dermatitis (see also p.95). Melanin cells in the epidermis are stimulated by inflammatory mediators (*soluble molecules that are released by white blood cells at the site of inflammation*) increasing their activity with a resulting hypermelanosis. This increase produces the brown and/or grey (tan) colour of the skin.

Photosensitisation dermatitis [129]

This is not a common condition and is not unlike allergic contact dermatitis, except that there is no immediate reaction to first contact with the substance but results only following a second or other exposure. It must be appreciated, however, that there is are a considerable number of chemicals in industry, agriculture and medicine that may sensitise individuals, all of which require solar radiation or other light sources such as *arc lamps*, to initiate activation of the process (referred to as a photoallergic reaction).

Although the condition had been studied in the early years of the 20th century, it was about fifty years later that its biological and medical value was realised. Human tissue absorbs the longer wavelengths of light radiation (700–850 nm) to greater depth than short wavelengths (UV), which can, therefore, destroy cell structures and other supporting tissues. Different photosensitizers have preferential target sites within tissues, and although this knowledge has been used in some countries in the treatment of cancer tumours with impressive but variable success, this technique is still undergoing further research.

Cutaneous melanoma [130]

A large number of cuboidal cells with finger-like projections (*melanocytes*) found in the lower layer of the epidermis of the skin, produce, with the help of an enzyme, the pigment melanin. The cell's projections help to spread the pigment within the epidermis. Their productive activity is also under hormonal control which affects the intensity of the colour of the skin. Although the ultraviolet (UV) spectrum of radiation (100–400 nm) which includes *UVA* and *UVB* is a common stimulant in the process of pigment production by these cells, there are a number of others such as low levels of vitamin D3 that may initiate the process [131]. Some studies have, in contradiction, shown that UVB which initiates the promotion of vitamin D3 synthesis is also protective to the skin. Daily requirement is about 200 international units (IU) but a few minutes of sunshine will provide a much higher amount. Less than 70 nmol/L is considered below reference values [132].

Some of the solar radiation is reflected back from the skin but UVA which has a longer wavelength (280–400 nm) does penetrate the dermis and damage the blood vessels, whilst UVB (290–320 nm) being of shorter wavelength can damage cells in the epidermis and cause cancer of melanocytes, basal and squamous (flat) cells. *Infrared radiation* (IR) like UVA only just enters the dermis and its photon energy releases heat. UVC (100–280 nm) is also part of the solar radiation spectrum but fortunately this short wave dangerous radiation is stopped by the earth's ozone layer). Chronic exposure may also cause dryness and cracking of the skin and affect the elastic fibres (collagen) so that its elasticity is also reduced.

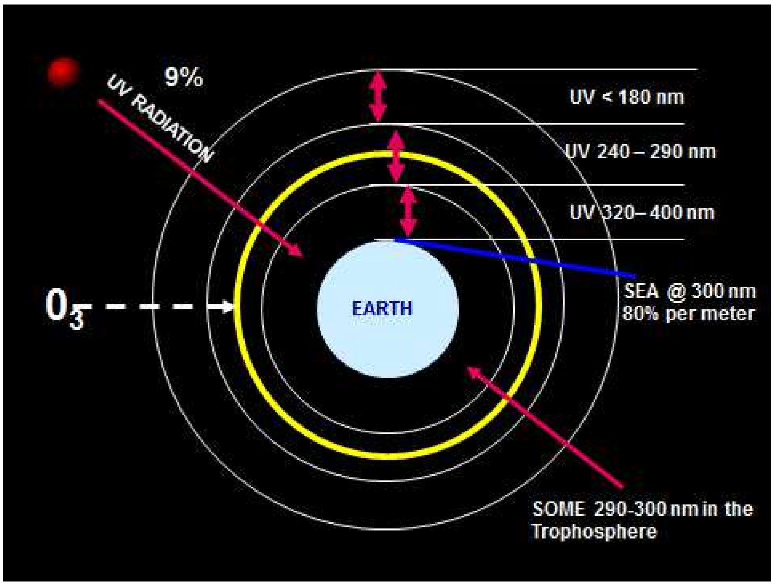


Figure 27. Illustration of the amount of UV radiation reaching Earth, of which 20% is reflected back.

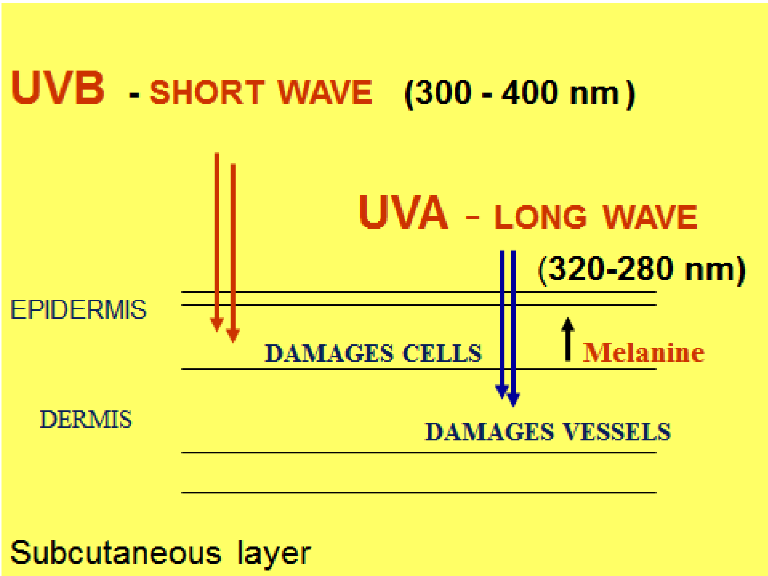


Figure 28. Drawing showing the depth to which UVB and UVA penetrate the epidermis and dermis of the skin.

It is worth remembering that the equatorial region of the world receives higher amounts of UV radiation so that concentrations are lower in the northern countries. Studies have shown that there is a correlation between the colour of the skin of populations in equatorial regions as well as in northern areas and UV radiation levels in those areas (133).

Melanocytes that have become cancerous are identified by their irregular outline, thickness and varied colours of the skin tumour – brown, grey and black. Individuals who are diagnosed with this condition are at risk of developing other melanomas usually within the first two years after treatment. UVB radiation has been shown to be positively related to cutaneous melanoma.

The GLOBOCAN database developed by The International Agency for Research on Cancer (IARC) provides incidence rates on cancer which are estimated age adjusted for 175 of the 196 countries in the world. This is a valuable tool in prevention strategies [134].

Basal cell carcinoma of the skin [135]

Basal-cell carcinoma is quite a common cancer of the skin and usually occurs where the skin is exposed to the sun's radiation, although it can occur on unexposed sites, which indicates that some individuals may be genetically susceptible to this type of cell cancer of the skin and UV radiation is not the only initiator.

Although this cancer grows slowly, it appears as a raised shiny red area that can bleed easily and may vary between a few millimetres to a few centimetres. If untreated, it will destroy the skin surface and also invade through into the dermis and further into the deeper layers of the skin and beyond. Fortunately, it rarely metastasises. Early identification is essential to avoid the destruction of the tissues.

Seamen, fishermen, farmers, construction workers, general labour workers, chemical workers, radiologists and X-Ray technicians are some who may on continuous exposure develop occupational skin neoplasms (any abnormal tumour which can be non-cancerous, pre-cancerous or become cancerous). Today, of course, considerable precautions are taken by many of these professions. Preventive strategies are therefore important in these occupations.

It should be clear that it is much easier to identify skin conditions than other organ disorders and, of course, depending on the part of the body affected it can lead to a loss of productive work time. The incidence of occupational disorders are different amongst workers in different places of work; agriculture, manufacturing and the construction industry have the highest incidence rate.

Nails

There is much you will find in the literature about nails, mainly discussing those who spend their working life in the thousands of nail salons that are found all over the world. Some estimates give numbers of greater than 300,000 nail salons in the United States alone [136]. Workers in these salons are exposed to more than 24 different chemical substances in the products they use, although three of these (which are referred to as 'the toxic trio') are considered to be the most hazardous, namely *toluene (C_7H_8), formaldehyde (CH_2O) and dibutyl phthalate ($CH_{16}H_{22}O_4$). Metacrylate compounds* ($C_5H_8O_2$) [136, 137] are also hazardous. Note that ethyl methyl acrylate (EMA) ($C_6H_{10}O_2$) is present in artificial fingernails and may cause allergies including asthma and dermatitis [138]. Workers are also at risk of blood infections as well as from latex or vinyl gloves. Nitrile gloves should be advised for use.

Workers that use high speed drills to remove thickened areas in nails are also exposed to nail dust which may contain fungi and microbes. Nail dust in air reaches the eyes, nose and, since the particles of dust are below 5 microns, will reach the lungs causing an allergic reaction and/or irritation and lacrimation to the eyes and nose. It is possible that in time (possibly weeks or months later) the worker will become hypersensitive to nail dust triggering the allergic reaction.

The structure, colour, shape and thickness of human nails provide the observer with a insight into a number of health conditions, such as B12 deficiency identified by brittle nails or iron-deficiency anaemia identified by spoon nails. The speed of growth of nails also appears to depend on trace elements, vitamins A, B12 and C and other factors.

Industrial chemicals that affect nails are corrosive substances such as hydrochloric acid, some substances used in nail beauty treatment and nail polishes, such as *triphenylphosphate* (TPP) and *ethylmetaacrylate* (EMA) used in artificial finger nails which may cause allergies, including asthma and dermatitis. High levels of toxic *fluorides* (F^-) may cause white spots on nails. Workers are also at risk from blood infections and from latex or vinyl gloves which may cause skin conditions. Nitrile gloves should be used instead because these are more resistant to tearing, avoid the potential of blood infection and absorption of chemicals, as well as being non allergenic.

The Respiratory System

The Lungs

Work-related diseases of the lungs are still very much underestimated and many are incorrectly recorded. Insufficient investigation is done to identify whether the cause is work related.

The lungs are affected by irritants which can be of low, moderate or high solubility. An irritant is referred to by the ILO as "*a substance, generally in the form of a gas, aerosol or dust, or agent able to cause inflammatory reaction of the respiratory tract, conjunctivae* (mucous membrane around the eyes) *or the skin*". Highly soluble gases and vapours, such as ammonia, act mainly on the upper respiratory tract. On the other hand, less soluble gases and vapours such as nitrogen dioxide penetrate more deeply into the respiratory tract and are more dangerous because of the associated risk of pulmonary oedema (see p. 91 , 92).

Irritants can be:

1. **Low soluble irritants -** will affect the throat, and possibly give some headache, but increased exposure (half a day's work exposure) may result in chest tightness and difficulty in breathing. Welding fumes, *Ozone* (O_3) and *Nitrogen dioxide* (NO_2) can do this. Both are slow soluble irritants.

2. **Moderate soluble irritants –** cause irritation of the mucous membrane and a persistent coughing. Some of these soluble irritants can also cause other problems such as skin burns (Fluorine) and tightening of the

bronchioles (Sulphur dioxide – (SO_2). Chlorine (Cl_2) is a commonly used moderate soluble irritant.

3. **Highly soluble irritants –** The odour of these substances are warning signals, but the worker may be unable to avoid inhalation. They cause shortness of breath and increase the respiration rate. The bronchi can become constricted and oedema may develop with high concentrations. Electroplaters may present with acid burns and again show up with lung problems. Ventilation systems are important in electroplating areas.

As previously explained, dusts containing substances such as toxins may be trapped by the mucous that line the membranes of the airways of the lungs. Once the dust particles pass through the mouth they encounter air resistance in these airways, which is of course related to the particles' shape, density and surface characteristics. However, once it has been trapped by the mucous of an airway wall or the alveolus, it cannot become airborne again.

Many authors have reported that records of the occurrence of silicosis were evident in ancient Egypt [(139)]. Silicosis [(140)] is a condition of the lungs where respirable crystalline silica (SiO_2) dust of less than 5 microns (not visible) reaches the terminal bronchioles and alveoli, and causes localised and nodular peribronchial (around the bronchi) fibrosis (an increase in fibrous tissue). Silicosis is still prevalent today and the chronic form usually takes more than ten years to establish, but once it does it is progressive. One complication of silicosis is tuberculosis. It is important to identify work-related respiratory disease early because once established they are difficult, if not impossible, to reverse. Prevention strategies are therefore vital.

Remember that about half way down the bronchial tree (actually the 19th bronchiole; total number 23) the tubes are covered with cilia (tiny little hairs that exert a wave like motion upward toward the mouth – they help to move the mucous with dust upwards and out of the lung). The remaining hairs, right down to the alveolar sac, are non-ciliated. The deposition of particles <1 micron are expelled in exhaled air and deposition depends on:

(a) Tidal volume of the lungs – the volume of air breathed in one single respiration (the depth of breathing) which is about 500ml and

(b) The respiratory frequency (the rate of your breathing which is increased with effort). In a healthy individual, this is 12 to 18 per minute.

It is useful to measure the amount of air breathed per minute and this would determine the total volume of particles inhaled per minute. The percentage deposition of particles could then be presented in graphical form.

A work-related list of lung disease that could help to maintain a mental picture in relation to the cause is presented below. Note that FIBROSIS means '*a condition marked by an increase in interstitial fibrous tissue*' and that PNEUMOCONIOSES [(141)] (see also the text below) means '*the presence of inhaled mineral dusts in the lungs and their non-neoplastic (neoplastic means abnormal growth – tumour) tissue* *reaction*'. The term was coined by Zenker in 1867 [142]. Mesothelioma is a neoplastic condition that develops on the lining of the lungs and chest wall (and other organ tissues such as the peritoneum and testis). It may result from exposure to asbestos.

Note that PMF refers to Progressive Massive Fibrosis [143,144] which is a complicated pneumoconiosis seen in boiler workers, and that Caplan's syndrome [145,146] is a condition in which the dust renders the lungs vulnerable to the development of circular nodules only in people who suffer from rheumatoid arthritis and are exposed to specific dusts. This condition is found among sandblasters and brass and iron foundry boiler scalers.

Note also that accumulation of dusts in the lung is not a disease until irreversible damage occurs.

Pulmonary disease related to work may therefore be:

1. OBSTRUCTIVE - Asthma (a short inhalation of breath with tightness of the chest). Isocyanates are one example that causes it. There are many causes.

2. RESTRICTIVE - Dyspnoea on exertion (shortness of breath as when going up a flight of stairs) as from silicosis or asbestosis.

3. PULMONARY OEDEMA - A condition where watery frothy mucous accumulates in the lung tissue due to, for example, high concentrations of cadmium fumes as can occur with the smelting of cadmium contained in scrap metals. *Oxides of nitrogen* *(NO_x)*, and *phosgene* *($COCl_2$)* over-exposure will also result in oedema.

4. GRANULOMATA – This is simply explained by the fact that cells which are induced by some irritant or toxic agent respond by becoming surrounded by bundles of collagen (a gelatine-like protein). Exposure to Beryllium (Be) dust in the manufacture of beryllium metal alloys may be in danger of granulomas developing, which then results in a restrictive disease.

Possible causes of lung disease

A work-related list of what may cause lung disease would include:

1. INERT DUSTS - low and high density types which may end in MIXED DUST FIBROSIS.

2. ORGANIC DUSTS - these are non-mineral dusts (fungal spores) ending in either EXTRINSIC ALLERGIC ALVEOLITIS or occupational asthma.

3. MINERAL DUSTS - such as free SILICA (sand, granite) or ASBESTOS.

4. FUMES - such as asphalt, welding fumes (cadmium), lead (Pb), iron oxide (FeO), manganese (Mn), and Zinc (Zn), etc.

5. GASES - these include irritants like ammonia (NH_3) or chlorine (Cl_2) and nitrogen dioxide (NO_2) or hydrogen sulphide (H_2S), etc.

6. MISTS - such as aerosols.

7. INFECTIONS - examples include hepatitis, fungi or Legionnaires disease.

8. CARCINOMA - radiation (alpha particles, radon, plutonium), polyaromatic hydrocarbons (PAH), arsenite (AsO_3), arsenate (AsO_4), tobacco smoke, etc.

Note that today one must also consider Nano Materials of which there are many types and the safety (fire, dust explosion) and health (lung fibrosis, cancer) hazards of these in industrial processes.

While it is not necessary for the Safety Professional to know anything more than the name of some pulmonary diseases caused by the different agents, it is useful to know some of the occupational causes of asthma and what repeated inhalation of an *antigen* may do if it is small enough to reach the bronchiolar and alveolar regions.

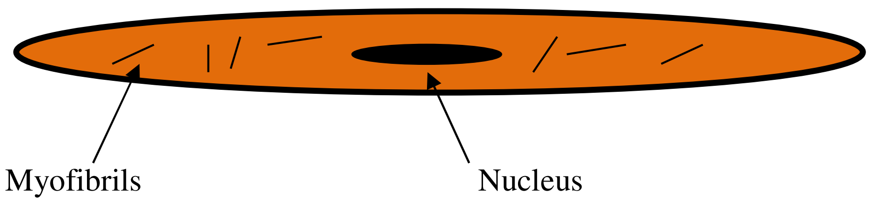
Occupational asthma may be defined as a pulmonary disorder where the airways are narrowed (partially obstructed) in consequence of exposure to inhaled gases, dusts, fumes or vapours. The severity in obstruction varies and it could be reversible. Some of the common industrial exposures that may cause occupational asthma are found in:

1. The food industry
2. The wood industry
3. The agricultural industry
4. The manufacture of enzyme detergents
5. Adhesives and paint manufacture and their use
6. The pharmaceutical industry
7. The electronics industry
8. The manufacture of *polyurethane* foams
9. The construction industry.

In some cases, the mechanism underlying asthmatic reactions are not entirely clear, but much of the evidence lies in the immunological reactions that occur. However, these reactions are not the only cause of occupational asthma.

The respiratory airways contain smooth muscle (long cells with a single nucleus that are bundled together by elastic fibres to help them expand and contract evenly). They are in the wall of the trachea and all the way down to the ducts of the alveoli. Smooth muscle is not under voluntary control and all the muscle cells in a bundle contract together when the proteins actin and myosin in the myofibrils within each smooth muscle cell react to stimulation using ATP as energy.

(a) Longitudinal section of a smooth muscle cell.



(b) Transverse section (below) showing muscle cells and nuclei bundled together surrounded by sarcoplasma recticulum, which acts as support, storage for energy supply and a barrier to some substances.

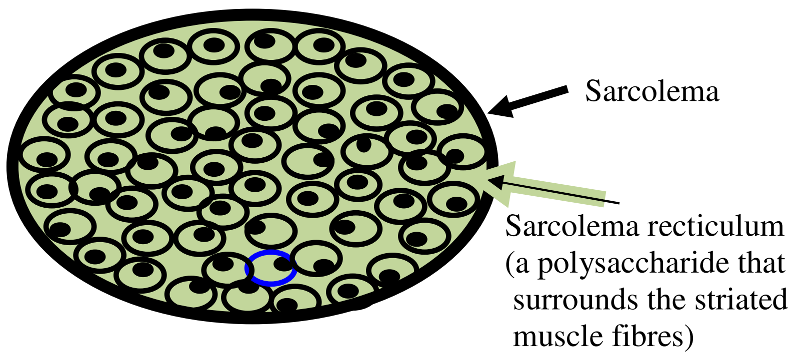


Figure 29. Simplified drawing of a longitudinal (a) and transverse (b) section of a smooth muscle cell.

In healthy subjects, the muscle tone is under the control of different muscle stimulators and a balance of tone is thus maintained. This balance may be increased or decreased, and it is hardly noticeable by an individual with the inhalation of an irritant. Someone who is asthmatic, however, will show some response.

In general, once a chemical or biological agent has entered the body, it may elicit a response on its own or by attaching to another molecule. A 'hapten' is a small molecule that when absorbed by the body attaches to a large carrier such as a protein and on first exposure may only elicit sensitization but on a second exposure induce an immune response stimulating antibodies. The newly formed, combined hapten referred to as a "*hapten-carrier adduct*" [147] may attach itself to an antibody, in which case it may block the immune response. "*Some haptens can cause* <u>*autoimmune disease*</u>" [147]. The genetic structure of the protein in the newly formed, combined hapten is important as it results in asthmatic symptoms [148] (see p. 77, 78 & 86 for more detail on the structure of proteins and asthma).

ANTIGENS - An antigen (also called an allergen) is a large molecular substance (molecular weight about 10,000 or more) and is mainly made up of proteins. They

stimulate the production of antibodies but they differ in their antigenicity (see also page 86).
ANTIBODY - A substance that is stimulated by an antigen and antagonistic to foreign substances such as toxins. Its structure is complementary to the antigen which helps their attraction to each other and keeps antigen-antibody together (see also page 86).

HAPTENS - Substances (chemical groups) which are not themselves antigens but can determine the specificity of the antibody which they stimulate.

HISTAMINE - is a chemical compound which is responsible for the dilatation and increased permeability of blood vessels. It plays a major role in allergic reactions such as asthma.

The most common cause of occupational asthma is 'allergic constriction of the bronchi' which results in the development of antibodies following exposure to workplace antigens. Workers who are *atopic* (previous exposure to some specific antigen and possibly having a hereditary predisposition to developing allergic reactions such as hay fever or asthma) become sensitised more easily than workers who are not atopic, if the antigen is of high molecular weight, such as enzyme detergents. With low molecular weight antigens, such as cedar wood dusts, the atopic issue is generally not a predisposing factor to the response. Over 250 agents are known to cause occupational asthma.

Remember that bronchoconstriction may occur after several hours or even later. Many workers improve soon after leaving their place of work, but some may take a few days to do so. The asthma may come back following the worker's return to the work place, making it clearly obvious where the exposure is occurring. Repeated exposures will result in deterioration of the function of the lungs. The classic symptoms are chest tightness, dyspnoea and wheezing, with those affected complaining of cough, irritation or inflammation of the nose, and sputum production (also referred to as phlegm, which is a viscid mucous from the air passages which is brought up and expectorated or swallowed). Asthma often co-exists with both non-allergic rhinitis due to environmental irritants such as chlorine or perfume, and allergic rhinitis caused by pollen, mould or dust mite. Rhinitis is an inflammation of the cells of the nasal mucous membrane.

The lungs response to toxins depends on whether the substance is a fume, mist, gas, particulate or infectious organisms. Response includes restriction of airflow with smooth muscle contracting which also affects blood flow. Coughing and sneezing occurs. Substances that cause sensitisation involve an immune system response such as Pesticides and other airborne antigens from glove powders [(149)]. Those particles that do not get trapped in the upper airways pass down to the alveoli where macrophages use enzymes to dissolve them and pass to the interstitial fluid or the blood. Those that do not dissolve are carried by the macrophages to the lymphatic system, others may be expectorated or remain in the lungs. Damage occurs when repair cannot overcome the levels of toxicity and injury [(150)].

Pneumoconiosis is a term used to indicate the respiratory tract response to the exposure of an inorganic dust (silica and carbon dusts are examples) which must be less than 5 microns so that it can reach the terminal bronchioles and the alveoli, and which depending on the intensity and duration of the exposure may cause either a local and nodular fibrosis around the bronchi (silica does this) or a diffuse interstitial fibrosis (asbestos does this).

Naturally occurring toxins (plant, fungal, microbial), some household products (chlorine, solvents, the burning of certain plastics) and environmental pollutants (nitrogen oxides - NO_x, volatile *hydrocarbons,* particulates – PM 2.5's, PM10s), in addition to the many potentially toxic industrial chemicals, some of which you will come across in later chapters, are examples of the lung's vulnerability to substances.

The Digestive System & the Gastro-Intestinal Tract (GI tract)

This subject has been explained in chapter 2 and the reader should review this in relation to toxic chemicals affecting the digestive system.

In addition to information provided on pages 47–55 in Chapter 2, "*possible associations between exposure to plutonium and mortality from diseases of the gastrointestinal tract have been examined in studies of workers at plutonium production and/or processing facilities in the United Kingdom (Sellafield)*" [B43]. Collectively, these studies have not found statistically significant associations between mortality rates from diseases of the digestive tract and exposure to plutonium among workers at these facilities.

The Liver

The *Edwin Smith Papyrus* reputed to be the world's oldest known treatise on trauma surgery, written in ancient Egyptian [(153)], is today preserved at the New York Academy of Medicine, USA. This scroll, which was fifteen feet long (it has since been divided into shorter lengths) clearly shows that the liver amongst other body organs was medically recognised as far back as 1600 BC. Earlier references to the liver may have been recorded on clay tablets elsewhere and others not yet found, although several hundred tablets providing medical information are preserved at the British Museum in London [(154)].

Over the millennia, several physicians and philosophers such as Gallen and Harvey studied animal dissections of the liver and theorised about its function [(155)]. However, it was not until repeated dissections of cadavers took place that scientific studies began to show the true nature of this organ. Then in the year AD 1654, Thomas Glisson, an English physician [(156)], (*whom Professor R. Milnes Walker of Bristol University so eloquently described on the 28th October 1965 at the Thomas Vicary Lecture at the Royal College of Surgeons of England)*, published the first book of 458 pages that was exclusively devoted to the liver [(157)]. The liver's physiological factors were, nevertheless, still not well understood at that time, and although much has been elucidated during the nineteenth and twentieth centuries, there are issues in this field that still need to be resolved.

The liver reaches its full potential at about the age of 15 and there are some 500 different functions (biomedical reactions) that it processes [(158)]. There are one hundred or more chemicals that are known to be toxic to the human liver and many of these are found in the work place. These include: paint, insecticides, plastics, synthetic chemicals, rubber, cosmetics, adhesives and many others, such as alcohol and drugs that may enhance their effects. This is a heavy load for the liver to deal with, in spite of it being the largest organ in the body weighing between 1200–1500 grams (about 3 lbs or so) [159]. This reddish brown organ, which appears to be divided into two large lobes (additional smaller appendages are evident in some individuals), also has the remarkable ability to compensate/regenerate even when 75% of its volume has been subjected to damage [160]. When all treatments in a patient have failed and subject to criteria (indications and contra-indications), a transplant is considered. The first liver transplant was performed in 1963 by Dr. Thomas E. Strazi in Denver, Colorado, USA [161]. Until the early 1980s when immunosuppressant medication became available, transplant results were disappointing because of organ rejection by the body.

The liver lies above the ***diaphragm*** (see Fig. 30 below), mainly on the right side sheltered and protected by the ribs and muscles between the ribs and others above them. It spreads from the right side of the chest occupied by the larger right liver lobe, to about the nipple vertical line on the left side of the chest. (See Figures 30, and 31).

The liver is a remarkable organ and no one can live without it. At molecular and sub-atomic level it has the ability, and indeed capacity, to metabolise and detoxify chemicals, synthesise proteins, produce hormones, bile, cholesterol and immune factors, converts ***glucose*** into ***glycogen*** which it can later convert back into glucose when the body requires energy, stores glycogen and iron, regulates blood clotting, and destroys red blood cells but holds on to its iron. In addition, it processes the products of protein metabolism, dumping the end product ***urea*** to be excreted by the kidney. Without any doubt this is a process, manufacturing and warehousing complex that no man-made industry can easily compete with.

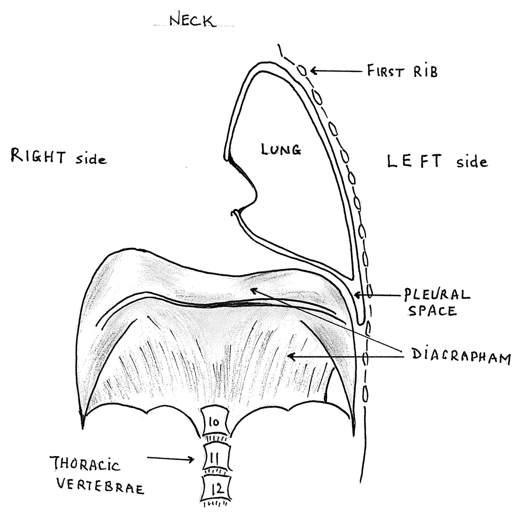


Figure 30. The diaphragm

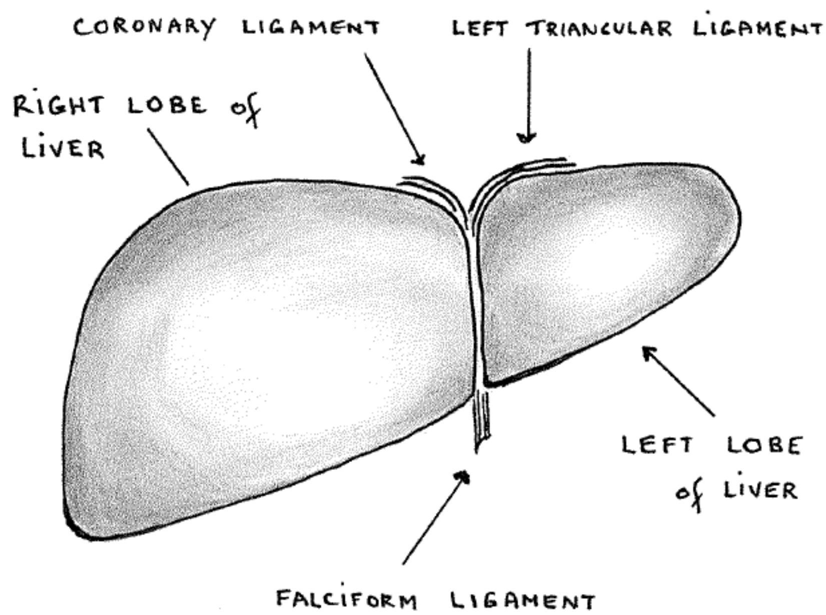


Figure 31. Drawing of the liver indicating the right and left lobes.

Let us take a glance at the structure of the liver but keep our view at macroscopic level. Professor Sheila Sherlock, a world authority on the liver whom I had the pleasure of meeting in London in 1975, recommended that the liver should be viewed as layered sheets of liver cells (*hepatocytes* and *kupffer cells*) in-between which tunnels pass both horizontally and vertically carrying arterial and venous blood and bile (159). The cells are arranged in lobules in the centre of which are two vessels, (artery and vein) and a bile duct, through which the tunnels drain the products of that lobule eventually to reach the heart and the systemic circulation.

In general, most of the toxins that reach the liver cause liver disease only after the many hepatic enzymes that it produces begin to act on them, either to make them more soluble to increase excretion, alter them so that they can proceed to some other phase of metabolism before excretion, or alter the biological activity of the compound.

Metabolism is an important factor in reducing (sometimes unfortunately increasing) toxicity. Some of the metabolic reactions result in unstable intermediates increasing toxicity of the compound and damaging the liver. *Vinyl chloride* (C_2H_3Cl) (161) is an example of a gas that results in an unstable intermediate (an *epoxide*) 162, which is believed to be the cause of its cancer-producing power, and which in consequence may result in either impaired liver function or cancer of the liver following at least five years or more of exposure. These cancers can also get established in other locations such as the lungs and the central nervous system.

It should be noted that many toxins that affect the liver have been replaced by substitutes which are less toxic but accidental inhalation of chemical fumes also toxic to the liver may still occur, such as from *carbon tetrachloride* (CCl_4) fumes used as a degreasing and cleaning agent. This chemical has a synergistic effect with alcohol abuse.

Exposure over many years (10–20 or more) to substances toxic to the liver usually ends in *cirrhosis* or cancer. These are difficult to associate with occupational hazards because of the length of time it takes for a worker to be diagnosed with an enlarged liver.

Major liver conditions that are known or may result in a response to toxic substances include:

Angiosarcoma [161]

This is a rare malignant tumour of the liver that may result from work in the manufacture of polyvinyl chloride (PVC) from vinyl chloride monomer. This is considered as dangerous work and those who work in such plants or buildings should be carefully monitored. It is a reportable occupational disease.

Hepatitis [163,164]

Various entries in the literature indicate that diseases of the liver were probably known as far back as 400–800 BC, including hepatitis [165,166]. The word simply means inflammation of the liver cells. Although one invariably thinks of viruses as the cause of hepatitis primarily because it is the most common, it can be caused by non-viral conditions such as drugs, solvents and other toxic substances.

There are five types of hepatitis; A,B,C,D, and E of which B is the most common. Referred to as HBV, it remains an important infectious occupational disease [163].

Hepatitis A [167] depends on hygiene both at work and elsewhere. This occurs from a virus spread from a person's faeces – person to person. Water from wells can become contaminated with sewage effluent. Employees at risk include marketing personnel on continuous duty travel to endemic countries, homosexuals, and migrants from countries where hygiene culture is poor and who work in food establishments. An effective vaccine is available. It is usually self-limiting and does not proceed to other conditions.

Hepatitis B is spread by infected body fluids and health care workers, dentists, surgeons, emergency personnel and laboratory workers are all at risk. If they come into contact with infected blood, saliva, semen or vaginal secretion, the virus can damage liver cells, cause extreme tiredness and reduced food intake due to loss of appetite, and headaches and can have a considerable effect on work productivity. This condition may become chronic and result in *cirrhosis* or cancer (see p.100). Some countries now vaccinate at birth. People who are allergic to yeast should not have the vaccine [168]. Prevention (personal protective equipment - PPE), work practice and engineering controls continue to be the most important tools in avoiding infection with hepatitis B.

Hepatitis C [169] can remain undetected for a very long time. Many people never realise they have become infected as in its acute stage it is very mild. Spread person to person, many become carriers if the virus is not cleared within six months and it eventually ends in cirrhosis. Today blood transfusion and transplants are not a risk. The effect on work is the extreme tiredness once it becomes chronic, debilitating the worker. No vaccine is available basically because the virus mutates in the liver cell as it replicates itself, and diagnosis requires specific testing.

Hepatitis D [170] cannot replicate itself in liver cells unless the person has already been infected with the Hepatitis B virus which it needs to help it replicate. It is clear, therefore, that prevention from getting infected with Hepatitis B is very important. There is no vaccine for Hepatitis D. It causes the same symptoms as with other hepatitis diseases.

Hepatitis E [171] is similar to hepatitis A and generally self-limiting so that it does not proceed to other conditions.

Cirrhosis

"*Globally, 57% of cirrhosis is attributable to either hepatitis B (30%) or hepatitis C (27%)*" [172]. *Alcohol consumption is another important cause, accounting for about 20% of the cases*" [173,174]. Cirrhosis can take a long time to develop and can result from a large number of medical conditions. Toxins that affect the liver include the solvent *carbon tetrachloride* used in dry cleaning whose use is now rapidly declining, *vinyl chloride* used in making plastics, paraquat a herbicide, and polychlorinated biphenyl, as well as toxic by-products from other substances, which may be even more toxic than the parent substance and created during metabolism in the liver.

It is believed that "*Hippocrates described the first known condition of cirrhosis in the 5th century BC*" [174]. What happens in this condition is that the normal liver structure due to inflammation of its cells from any one of the many causes is gradually destroyed and the liver begins to enlarge. This is then followed by the appearance of nodules in between which collagen fibres (scar tissue) are laid down and the liver now slowly decreases in size. Blood flow through the liver is reduced, which also causes back pressure and other complications. The liver can no longer do its many important functions. Prevention is the ultimate approach. Its importance in safety and health lies in that there are many employees at management, supervisory, technical and entertainment levels where some of the causes of hepatitis ending in cirrhosis have become an increased 'occupational hazard'. The financial investment in human resources to employers of such employees and the financial expenditure in training replacements is a matter of importance. Every effort must be made in creating suitable prevention policies.

Haemochromatosis

Armand Trousseau [175] was a prominent French physician who lived through the first 66 years of the 17th century. He was the first man to carry out a *tracheotomy,* he was an excellent teacher and was well known for the '*Trousseau sign*' [176], the name of two distinct phenomena observed in clinical medicine.

Two years before his death in 1867, he described a syndrome in which the patient had "*bronze skin pigmentation*". Twenty-two years later another physician by the name of Von Recklinghausen [177] named the syndrome 'haemochromatosis', a condition in which iron is continuously stored in the body, damaging tissue and body organs, and which many years later in 1935 a British physician, J.H. Sheldon [178] showed that the disease was inherited due to an error in iron metabolism. In 1996, the control of iron absorption in the body was shown by John M. Feder to be caused by a gene mutation [179].

A person has normally about 3–4 grams of iron in their body [180,181]. Iron is designated as 'Fe' and is essential to human health. Levels of iron that are above 350–500 µg/dL are considered to be toxic [182]. A person weighing 70 kg would require about 3000 µg (3 g) of iron overload to be considered toxic. Some of those with a specific genetic defect are more sensitive to iron uptake and storage, and one must remember that the body has very little means of excreting iron; a little is released from skin cells, faeces and urine [181]. Unlike many other heavy metals which are discussed later in the book, iron is not known to be particularly toxic to workers in industry not even in the mining of iron industry, although several studies indicate more research needs to be done on exposure to respiratory ultra-fine particles such as those found in welding fumes, underground railways, shipyards and engineering manufacturers of machines and tools.

Blocked liver bile ducts [B19 and B20]

Other than to remember that this can occur following hepatitis, cancer, and backflow of pancreatic juices into the bile ducts, the details of the many other causes of blocked bile ducts need not unduly concern Safety and Health practitioners other than to remember that the bile is a source of excretion of toxins from the liver into the gallbladder and from there to the small bowel where hydrolysis by the action of enzymes may result in products that can then be reabsorbed from the bowel back into the liver via the portal vein (see Fig. 17, 32).

Gallbladder (see Fig.32)

It is important to understand what the gallbladder is for and what it does, even though in some cases people lead healthy lives without it. It lies below the right side of the liver and it is a storage tank for bile which it releases into the extreme upper part of the intestine (the duodenum) each time you eat a fatty meal. The fat stimulates a substance which then cause the gallbladder to release the bile and this breaks down and digests the fat.

Cancer of the gallbladder is relatively rare, but those who work in the rubber and metal industry have a relatively higher risk than others in developing this form of cancer. Nitrosamines [183] used in the manufacture and processing within the rubber industry may also damage DNA [184], and genetic changes may occur resulting in a predisposition to the development of cancer of the gallbladder. Asbestos compensation claims for G.I. tract cancer can include the potential risk of gallbladder cancer, however, there does not appear to be any evidence in the literature of such an association except for a mortality study quoted below. No reference to gall bladder cancer from asbestos exposure in the glass, metal or asbestos removal industries could be found.

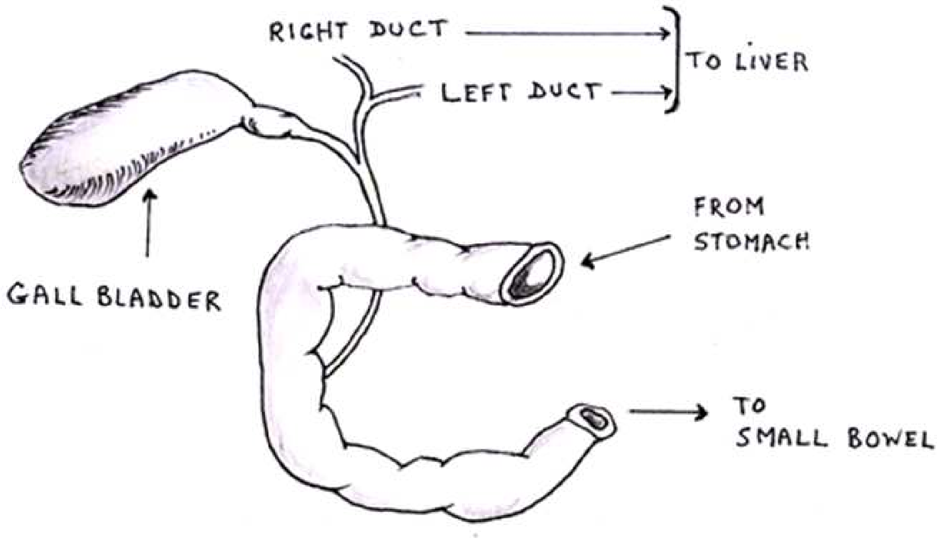


Figure 32. Drawing of the gallbladder and its bile ducts; they empty into the duodenum.

Workers in the textile industry "*are exposed to dyes, optical brighteners, organic solvents and fixatives. Those in finishing operations are frequently exposed to crease-resistance agents (many of which release formaldehyde), flame retardants (including organophosphorus and organobromine compounds) and antimicrobial agents. In the dyeing, printing and finishing processes, workers typically have multiple exposures, which can vary with time and process. One mortality study reported an elevated but non-significant association between cancer of the liver and working with textiles. A similar association was reported for cancer of the gall-bladder in another mortality study. (IARC . Vol.: 48 (1990)*".

It should be noted that there are a number of genes which, if mutated, may play a role in causing gallbladder cancer.

The Lymphatic System [187, 177]

The son of a Swedish bishop, Olaus Rudbeck, (1630–1702) [185] a professor of medicine at Uppsala University Sweden, was a descendent of Alfred Nobel the founder of the Nobel Prizes. He was one of two pioneers (the other was Thomas Bartolin [186], also a professor medicine at the University of Copenhagen, Denmark) who published the discovery of the lymphatic system around 1652/53, although mention of the system was made as far back as the third century BC by several others. It was Thomas Bartolin [186] who referred to the words 'lymphatic vessels'.

The lymphatic system [187] (see Figure 33) is composed of vessels having one way valves, similar to those in the circulatory system reaching tissues and organs all over the body. As oxygenated blood is filtered through the capillaries into the veins about 3 litres of plasma remains in the interstitial tissue. Once it enters the lymph vessels this white liquid is referred to as lymph. This is then picked up by the lymph vessels that move the lymph along its vessels on its way to join the blood circulatory system via the *subclavian vein* (see Figure 34). On its way to join the circulatory system this lymph passes through *lymph nodes* (also referred to as lymph glands) of which there are some 500 or so along the way with some gathered in groups such as the neck, under the armpits, around the elbows, the groin, and back of the knees, the intestines, the pelvis, and inside the chest, indicating that there are both deep and superficial systems of lymph vessels (see p. 108). The lymph nodes contain large numbers of lymphocytes, which are produced in the bone marrow and have millions of *receptors.*

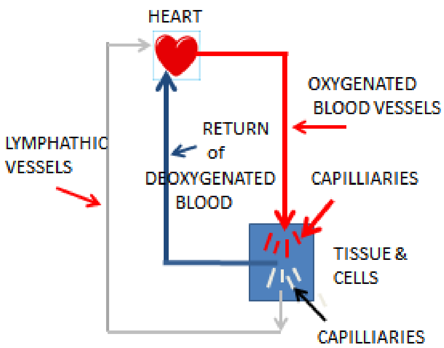


Figure 33. Schematic representation of the lymphatic circulatory system.

There are two types of lymphocytes, B and T, with more T cells than B cells [187] and about 50% of the lymphocytes that are in the body's cardiovascular system circulate in the lymphatic system. The lymph nodes act as filtering stations and thanks to the lymphocytes they stop spread of infection, fine dust particles, white blood cell debris and tumour cells, before the lymph is returned to the blood vascular system. They also have the task of stimulating an immune-related response. It should be noted that if the lymph nodes do not destroy tumour cells, the node itself becomes a tumour. Toxins which are absorbed as molecules and ions can reach into the lymphatic vessels and are then transported to the blood stream.

It should be noted that after the removal of lymph nodes following cancer surgery as, for instance, in the case of removal of the nodes under the armpits, the areas that they normally drain may be unable to deal appropriately with the return of lymph to the circulatory system which then results in accumulation of the lymph, causing swelling of the part affected. In the case of breast cancer, this would be the left or right upper limb depending on whether the right or left breast was surgically removed, which then swells up.

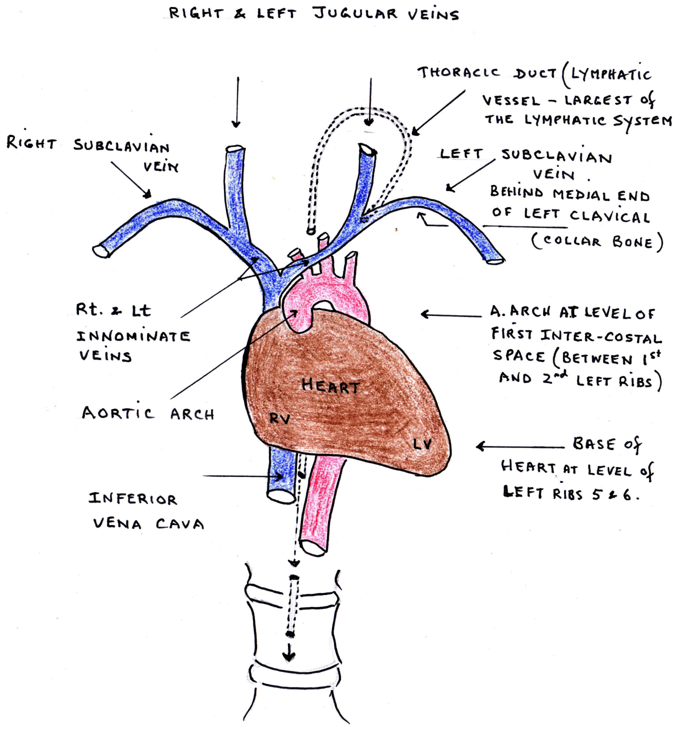


Figure 34. Drawing of the heart showing the lymph vessel joining the subclavian vein, which flows into the innominate vein and on to the right auricle of the heart.

Safety professionals working in tropical or subtropical countries where parasitic diseases, such as filariasis (an infection with roundworm), is still prevalent will have seen swelling of the limbs referred to as *lymphoedema*. Different names are given to the condition depending on the type of worm they are infected with.

The lymphatic system thus has the role of maintaining the body's fluid balance, transporting white blood cells to the bones as part of the processes of the immune system as well as transporting fats, from the small intestine to the blood, except t*riglycerides (fatty acids of glycerol)*, which go directly from the intestine to the liver for processing. Note that the lymph drainage from the liver is returned to the cardiovascular system via a different duct called the *thoracic duct (see Fig.34)* instead of the subclavian duct.

Toxic substances are not filtered by lymph nodes (see page 103) of the lymphatic system. Chemicals that are known to affect the lymphatic system include 1,3-*butadiene* (C_4H_6), *ethylene oxide* (C_2H_4O), *vinyl chloride* (C_2H_3Cl), and *trichloroethylene* (C_2HCl_3) used in degreasing, and asbestos. Where the immune system is involved, a number of industrial chemicals can also have adverse effects. These include *benzene* and halogenated aromatic hydrocarbons such as PCBs found in some electrical products, electronics, adhesives and paints, as well as petroleum products and ionising radiation. There are a number of other chemicals that are suspect but require further research and investigation. Safety professionals should therefore pay careful attention to the dangers that these industrial chemicals may cause to people at work.

The Spleen

Safety professionals should be aware that the spleen is relevant as a body organ which is vulnerable to injury and to a number of chemical hazards. It may rupture as a result of an accident such as a fall from height or a transportation accident. What is important to remember is that the signs and symptoms may not appear at the time, but days or even weeks later. Should you be on site at the time and subject to any other conditions that the injured might have, you can ask if the injured has any pain in his/her upper left arm or left side of the chest or over the spleen location itself, although this may simply be that a rib or ribs may have been broken without injury to the spleen. This information can then be passed to the medical support team on arrival.

The spleen (see Fig.52 page 134) forms part of the lymphatic system lying to the upper left side of the stomach in the abdomen sheltered by the ribs. If you put your right arm horizontally to your left side you would be more or less directly over it. It rests on the stomach, the kidney and the large intestine on the left hand side. Its function is to act as a storage tank for blood – about 6 ounces – should the body need it in an emergency with blood loss. In addition, it acts as a filter for blood to remove toxins and recycle worn out red blood cells, saving the iron inside them for the building of other red blood cells. It also stores platelets – these are cells which help us to stop bleeding by forming a clot, and produces *properdin* a gamma globulin protein taking part in the immune response and helps to neutralise some viruses, as well as assist with the process of engulfing bacteria and *tuftsin* ($C_{11}H_{12}N_2O_2$), a tetrapeptide that binds to specific receptors on the surface of macrophages and polymorphonucler white cells, to stimulate their bactericidal, phagocytic and tumour-generating activity. It also influences antibody formation. Lack of tuftsin has resulted in increased susceptibility to infection [188].

Perhaps even more importantly, it stores three types of white cells, one called **lymphocytes** which produce antibodies to defend the body against some types of bacteria, viruses, fungi and parasites.

The main ones it defends against are *Haemopholus influenzae* and *Streptococcus pneumoniae*, which is why if following injury or other reason the spleen of an individual is removed, the individual would have to be vaccinated against these potential invaders. The second type of white cells that the spleen stores are called **monocytes**. They have a specific importance described in studies that point out that monocytes play a key role in the healing response of a heart attack [189,190].

The researchers discovered that the monocytes are released into the blood stream, adding to the numbers already within the blood, change from monocytes into macrophages once they enter tissue and thus have *'a major role in repair'*[189,190] of the injured site.

The third of the white cells is called a **neutrophil**. The IMIM (Hospital Del Mar Medical Research Institute), in collaboration with researchers from Mount Sinai in New York, determined that these neutrophils are *"the first cells to migrate to a immuno-regulating role"* [191]. This study revealed that *"neutrophils are found in the spleen without there being an infection"*[191]. The researchers revealed and proved that: *"The neutrophils in the spleen are located around B lymphocytes to help their activation and offer a first rapid response when there are pathogens"* [191]. Irene Puga, an IMIM researcher, and an author of the article stated: *"the neutrophils in the spleen acquire the ability to interact with B cells or B lymphocytes, inducing the production of antibodies, a role that lymphocytes circulating in blood are not able to do"* [191].

The spleen, like the gallbladder, is yet another body organ that we can live without.

Chemicals known to affect the spleen include: *benzene* *(C_6H_6)*, *lead* *(Pb)*, *mercury* *(Hg)*, *carbon monoxide* (CO), volatile *nitrites,* pesticides and herbicides, aniline and fine dusts to which one must remember that polyaromatic hydrocarbons (PAHs) adhere. There are about 100 PAHs that may be stored in the spleen among other organs and possibly others still yet to be discovered.

The Thymus [192, 193]

The thymus (See Figure 35) is situated just under the breast bone (sternum) and is made up of two lobes which start gradually to shrink from the onset of puberty. T-lymphocytes produced in the bones travel to the thymus where some mature before they are released into the blood stream. Here they confront and "*destroy pathogens, activate B lymphocyte cells to produce antibodies that stick to the antigens on the surface of pathogens, and store the memory of past infections*" [193]. The remaining T-lymphocytes are destroyed by macrophages because for some reason they will have bound themselves to the body's own antigens and therefore attack and kill the body's own cells rather than foreign invaders (*autoimmune cells*) [193–195].

Lymphocytes are "*very susceptible to the action of toxic chemicals*"[195]. Their nuclei fragment and their internal cytoplasm extrudes from their covering membrane, resulting in a reduction of their size which is then engulfed by the macrophages. It is interesting to note that mention in the literature refers to hard cheeses as another cause of possible damage to T-lymphocytes [195].

The thymus requires two other glands of the body – the pituitary and the adrenal, to function properly. Should the pituitary be overactive it will affect the thymus by reducing its size and therefore its function permanently [196]. This can result because a hormone called *adrenocorticotrophic hormone* (*ACTH)* is released by the pituitary having received another messenger – *C-reactive protein (CRP)* [197] from another part of the brain (the hypothalamus), following which the pituitary then acts to stimulate the adrenal gland to release a substance called *cortisol* *($C_{21}H_{30}O_5$)* [198] (See Figure 51).

Note, however, that whilst the hypothalamus is activated in conditions of stress, cortisol also inhibits the hypothalamus from stimulating the pituitary to release too much ACTH in its effort to balance the levels and control the situation. CRP can also cause depression and sleep disturbances.

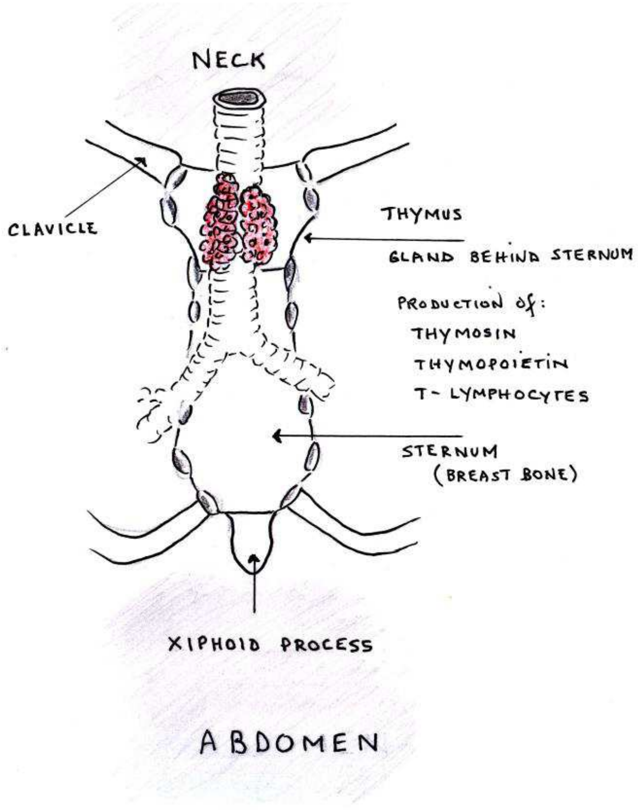


Figure 35.

Drawing of the thymus seen lying beneath the sternum and on the anterior surface of the trachea. It is slightly pinkish in colour.

The thymus gland can be damaged through prolonged exposure to *sodium periodate* (meta) [(199)], which is used in chemical laboratories and is a strong oxidiser. *2,3,7,8-tetrachlorodibenzo-p-dioxin*, better known as Agent Orange [(200)], is used as a herbicide in the Vietnam War and also affects the thymus gland.

A number of other herbicides affect the thymus but most research studies have been carried out on animals and do not refer to their impact on the human thymus gland. Pesticides can disrupt hormones and may affect the thymus, but effects noted in research on animals does not necessarily mean that the same effect can occur in humans.

A substance known as *bee propolis* [(201)] which is found in bee hives and contains resins, wax, pollen and oils amongst other constituents is used for its wax in polishing cars and the manufacture of cosmetics among others. The pollen within bee propolis [(182)] may cause allergies due to pollen being one of its constituents, which you can now relate to the effects on the activation of lymphocytes in the thymus tissue.

Tonsils, Adenoids and Appendix

These organs are well known to everyone.

Masses of lymphoid tissue are situated in areas where entrance to infectious materials or other substances is likely, such as the mouth, and where T-lymphocytes are available, cleverly acting as a first line of defence as many report in the literature.

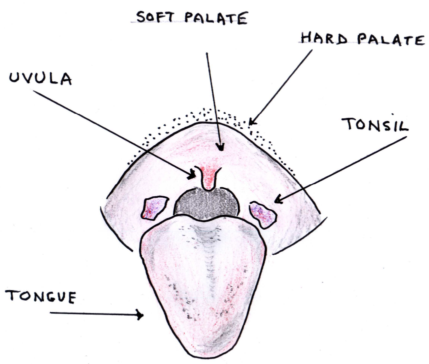


Figure 36. A drawing of the open mouth showing the tongue, the soft palate with the uvula and the hard palate above it, as well as a tonsil on either side of the opening to the pharynx which leads to the oesophagus.

The adenoids are higher than the tonsils, which are found the back of the throat, and lie at the back of the nose and the root of the mouth but are otherwise similar in structure. The appendix (see Figure 6) generally lies in the abdomen low down on the right side; it looks like a narrow short tube. Many theories abound as to the function of the appendix. Recent research (202) has indicated that it may be a storage site for surplus bacteria to supply to the intestine when required. What is known for sure is that it contains some lymphoid tissue, although this should be of no surprise as so does most of the small intestine, and it is quite close to where the small intestine joins the ascending large one. One can assume that this lymphoid tissue would be easily affected by bacteria or other toxic substances travelling through the bowels, settling in the appendix, and with time becoming swollen and inflamed. Extremely rarely a tumour may form.

Inhalation of environmental pollutants, both outdoor, such as vehicle emissions including nitrogen dioxide (NO_2), ozone (O_3), and sulphur dioxide (SO_2), or pesticides, and indoor, such as cigarette smoke, workplace dusts such as *borax* ($Na_2B_4O_710H_2O$) or wood and cement dusts, moulds, fumes and gases, Volatile Organic Compounds (VOCs), chlorine (Cl_2), solvents, and many others have all been reported to cause non-infectious sore throats, all of which may create an inflammatory response in lymphoid tissue. Prolonged exposure may proceed to uncontrolled cell division and tumour formation with some of these. It is well to remember that industries such as waste water treatment, recycling, processing of compost, and some farming activities do result in odours/mixture of odours, affecting the lymphoid tissue in these areas and may result in sore throats.

Lymph Nodes (203,204)

Lymph nodes are small, oval shaped and about 1cm in size and can number into the hundreds (500–700). They contain B and T-lymphocytes and macrophages and filter the lymph that moves within the vessels of the lymphatic system. Lymph nodes are gathered in groups in areas such as the neck, under the armpits, around the elbows, the groin, and back of the knees, inside the chest, the intestines, and the pelvis, indicating that there are both deep and superficial systems of lymph vessels. In the small intestine, chiefly in the ileum, they are referred to as Peyer's patches and B-type lymphocytes are mainly located in the mucosa and the submucosa. The lymph nodes contain large numbers of lymphocytes which are produced in the bone marrow, and have millions of *receptors.* There are two types of lymphocytes, B and T, with more T cells than B cells and about 50% of the lymphocytes that are in the body's cardiovascular system circulate in the lymphatic system. The lymph nodes act as filtering stations and stop the spread of infection due to lymphocytes, and also remove fine dust particles, white blood cell debris and tumour cells before the lymph is returned to the blood vascular system. Lymph nodes also have the task of stimulating an immune-related response. It should be noted that if the lymph nodes do not destroy tumour cells, the node itself becomes a tumour.

Recall that lymphocytes are very susceptible to toxic chemicals. Note, however, that lymph nodes do not filter toxic substances, which is the responsibility of the liver and kidney, although some can also be eliminated via the lungs and skin and the gastro-intestinal tract where toxins reach it via the bile. Nevertheless, lymph nodes themselves are subject to attack by toxic substances travelling in the lymph.

When infected, inflamed or enlarged due to excessive cell division/tumour growth, those nodes that are superficial and not deep within the body can easily be felt by palpation.

The Immune System [(205)]

Through inhalation, skin and injury the body is vulnerable to infection from microorganisms and the many different effects of toxic chemicals, particulates and other foreign substances, such as pollen or mould. The spleen, bone marrow, thymus and lymphoid tissue provide a defence system to maintain health which is monitored by some of the cells these organs contain. In addition, these organs also carry out other functions towards the defence processes. The B-lymphocytes and the T-lymphocytes circulating in the blood and lymphatic circulatory systems aided by phagocytes (all white blood cells) have different functions in defence of the body. Together, these organs and cells form the specific immune system. The non-specific immune system includes mechanical barriers (skin, mucous membranes) and chemical barriers (sweat, gastric juice and other body secretions).

Many workers have asthma or hay fever which is a burden to their daily lives. This is a hyper reaction response to allergens. Some individuals have immune systems that are weaker than others. These may have been genetic or acquired through some condition like HIV/AIDS. Either way, it results in low resistance to infections. Sometimes the immune system fails to respond as it is meant to do and its cells fail to recognise its own body and therefore attack normal cells, a condition referred to as 'autoimmune'. There are a number of *autoimmune* diseases. Silica and some solvents can trigger autoimmune disease [(205)]. *Systemic sclerosis* is one example. Mercury (Hg) may also trigger autoimmune conditions. Workers exposed to infections from viruses, bacteria or parasites may also result in autoimmune disease as a result of the inflammation they cause. Occupational and other environmental exposures including some drugs are being explored to identify what other substances are involved.

The Cardiovascular System

Blood & Blood Vessels [(207)]

Writing in an article '*40 Interesting Facts About the Human Body*' [(206)], *Stephen King* says that it has been estimated there are 60,000 miles of blood vessels in the human body. Someone must have done some complicated mathematical calculations and assuming it is correct, this is a considerable number of vessels transporting potential toxins around the body, in spite of the *'blood brain barrier'* (see Figure 47) which restricts the entry of some substances to the brain..

The circulatory system of the human body contains approximately 4 to 5 litres of blood, of which about 20 litres of oxygenated blood in the blood vessels pass into and through its *capillary system* in 24 hours [207]. Here the blood releases nutrients (and toxins if they are present) and oxygen to the cells. The oxygen is then metabolised to carbon dioxide before it returns to the heart for it to pump back into the lungs to get rid of the carbon dioxide and other gaseous substances, as well as refuel with oxygen again on its never-ending journey around the body. As the heart muscle pumps blood into the circulatory system, it creates a pressure averaging 120 mmHg, although this varies in different people for various reasons. When the heart muscles relax to allow it to refill before it contacts once again, the pressure in the system goes down to an average of 80 mmHg. Blood pressure is therefore recorded as 120/80 mmHg; this is considered the level which, within limitations (race, ethnic, sex and age related differences, social pressures and altitude), should not be exceeded for an average normal human being.

The blood is made up of plasma which forms about 55 to 60% of the whole volume of blood and in which proteins, glucose, fats, salts, antibodies, enzymes and hormones, as well as red blood cells, white blood cells, platelets and a number of other substances float and move within the blood circulatory system of vessels to reach body tissues and organs. These are reached via extremely small capillaries supplying them with oxygen and other nutrients, but during times of exposure, they also carry toxic substances, whether these are prescribed as a form of medical treatment or received through unknown or unexpected exposure. Waste products from metabolic processes are also carried by the plasma. One example is *carbon dioxide* (CO_2) carried to the lungs, which is removed with each exhalation and replaced by oxygen during inhalation. Note that the cornea of each eye does not receive any blood.

There are a number of blood types and each individual has his/her own blood type. The outside surface of all red blood cells support what are known as *antigens,* while their interiors contain *antibodies*. It is the antigens that determine our blood type. It is therefore not difficult to understand that if an unrecognised antigen reaches the outer surface of the red blood cell that the cells' antibodies will attack that antigen and how important it becomes that the correct blood type is given to someone when blood is needed. There are four blood types, namely A, B, AB and O, so that if you have an 'A' antigen on your red blood cells, your blood type would be A. If you do not have either 'A' or 'B' antigen, then you are blood type 'O'. Red blood cells only last about 120 days and are then removed and their iron recycled by the spleen, as described in the lymphatic system under the spleen chapter.

There are a number of different types of white cells (neutrophils, eosinophils, basophils, lymphocytes and monocytes) circulating in the blood and they are found also in the lymphatic tissue, the liver and spleen. They do not last as long as red blood cells, usually about a day or perhaps two. Their importance is the part they play in infection by neutralising bacteria (a job for neutrophils), viruses (a job for eosinophils and *T-type lymphocytes – see lymphatic system Appendix III*), and the immune response (a job for both *B type lymphocytes*, monocytes and basophils). Basophils also release *histamine*, *heparin* and protect against parasites by engulfing them. Eosinophils attack parasites but do not engulf them.

The effects of many solvents can be seen in the blood circulatory system. The bone marrow (where blood cells are created) is affected by the toxic metabolite/s of *benzene* (C_6H_6)), which results in *aplastic anaemia* also called pancytopenia (a rapidly progressive or chronic process condition in which the bone marrow shows a considerable reduction in red and white blood cells). This condition is also caused by certain medical drugs and exposure to radioactive substances and agents such as carbon monoxide, *hydrazines* (N_2H_4) [208] found in the production of plastics used for vinyl flooring and foam cushions, manufacture of agricultural chemicals, and in nickel plating, and cigarette smoke. Long-term exposure to benzene will cause a reduction in red blood cells and platelets.

Nitrous gases from welding and silos, *naphthalene* ($C_{10}H_8$) and *aniline* dyes ($C_6H_5NH_2$) interfere with the normal delivery of oxygen from the red blood cells to the body tissues. *Arsenic* (As) [209] used in the production of alloys, glass manufacture, wood preservation and pesticides found in contaminated water, as well as tobacco amongst others, is a very toxic substance. "*Arsenic targets many enzyme reactions and therefore affects nearly all organs"* [209] although skin is its favourite target (for further reading the reader is referred to the IARC monographs on arsenic). Arsenic intoxication depresses bone marrow function and results in anaemia and leukopenia (a decrease in the number of white blood cells which then increases the risk of infections to the body). Other agents, such as *arsine* (AsH_3) (a compound of arsenic and a very toxic gas), dissolve and burst the red blood cells in the circulatory system. Lead (pottery workers, painters, etc.) interferes with haemoglobin synthesis, particularly in its last enzyme reaction during the formation of heme to make haemoglobin, which affects the creation of red blood cells.

Acute *aniline* ($C_6H_5NH_2$) toxicity [210] causes oxidation of iron in the red blood cells to form *methaemoglobin* which impairs oxygen transport above a level of 5%.

A study in 2007 by Rosenman [211], reported that workers in German vineyards and smelting plants in which they were exposed to arsenic had developed *Raynaud's disease* (spasms/vasoconstriction of the blood vessels in the fingers or toes). Note, however, that pesticides containing arsenical products are now no longer in use and that this disease is also caused by a large number of other conditions, amongst which are *vinyl chloride* (C_2H_3Cl), mercury (Hg) and *vibration tools*. Non-radioactive *thallium* (Ti) also causes vasoconstriction of the blood vessels.

The International Association for Research on Cancer (IARC) – a World Health Organization body – stated in their Monograph (IARC, 1982) *'that there was sufficient evidence of an excess occurrence of leukaemia in workers in the rubber-manufacturing industry* [212].

Heart

The heart is primarily a pump composed of heart muscle, nerves, blood and lymphatic vessels enclosed in a bag of tissue called the pericardium, which is separated from the heart muscle by fluid between its two layers to reduce friction when the muscle contracts and relaxes.

It lies behind and is therefore protected by the breast bone (sternum) about one inch (2 cm) to the right of the sternum and about 3 inches (7 cm) to the left of the sternum, mostly covered by the left and right lungs and rests attached to a small part of the diaphragm (see Fig.30 & 34).

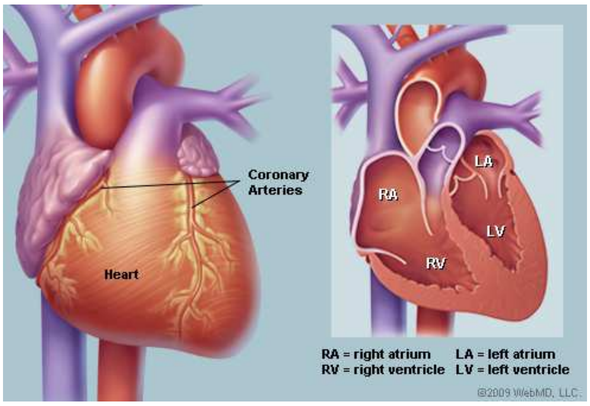
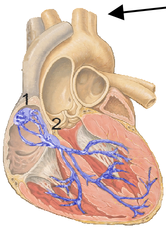


Figure 37. The heart and a section showing the right (RA) and left atria (LA), right (RV) and left (LV) ventricles and their valves. Source: WebMD, LLC: © 2016. Available at www.webmd.com.



Note the external common carotids that give off the internal vessels that supply the brain.

Figure 38. Conduction system of the heart showing SA and AV nodes indicated by the number 1 and 2 in the figure. Source: WikiDoc © 2017. Available at www.wikidoc.org.

The heart is divided into a right and left side, with the left side having a right cavity (atrium – RA in Fig. 37) receiving blood from both the lower and upper half of the body via two large veins that also support the heart in its place. The blood that this atrium receives passes to another larger cavity (the right ventricle), which then pumps the deoxygenated blood to the lungs. The left side also has an atrium and a ventricle, which receives the oxygenated blood from the lungs and pumps it to both the upper and lower parts of the body via a large diameter artery (the aorta and its branches) and also supplies the heart via two arteries – a right and a left – at the point where the aorta leaves the heart. These are the coronary arteries. One-way valves stop back flow in each of the cavities on both sides. These cavities are lined with a very thin smooth layer of cells (the endothelium) so that blood passing through does not adhere to the muscle below this lining.

Toxins reaching the heart may affect the vessels, nerves, muscle or linings and its pacemaker and electrical conduction system. A brief but simplistic explanation may therefore be of some benefit before reference is made to cardiac toxins.

In the left atrium lies a node (*the sinus node: 'SA' – see Fig. 38*) which initiates and controls the heart's contractions and relaxations. It is referred to as the heart's 'pacemaker'. An electrical impulse moves from the SA node to another node (*the atrioventricular node* – 'AV' node) on the muscle wall (*interatrial septum*) that separates the right and left atria. At the AV node, the impulse is delayed momentarily to ensure the atrium is full of blood. It then separates into a right and left branch and passes down the muscular wall (intraventricular septum) that separates the right and left ventricles and on to the muscle of the ventricle walls to initiate the force required to expel the deoxygenated blood out from the right ventricle to the lungs and the oxygenated blood coming back from the lungs from the left ventricle to the rest of the body. The heart then relaxes to allow refilling and the process is repeated. These electrical impulses can be recorded on an ECG (electrocardiogram).

Note that at rest, the heart beats around 103680 times every 24 hours based on an average of 72 beats per minute. There is no specific rate for anyone person as the heart can beat anywhere from 40 to 90 or even more per second. During sleep the rate can be anywhere between 40 and 50 beats per minute. The rate depends on several other factors such as ambient temperature, your physical condition, hormone levels, whether you are overweight (higher heart rate), standing or lying down or in an elderly age group (this may be slower and irregular). New born, infants and children up to the age of 10 or so have a higher rate (60–100 beats per minute) [(213)]. Athletes have a lower rate (40–60 beats per minute). Some types of medication affect the heart rate, as does exercise. The normal resting cardiac output is one litre per minute. This is a useful tool by which to calculate the approximate amount of a toxin absorbed into the blood volume during a particular exposure knowing the *coefficient of solubility* of the toxic substance (see also solubility in Appendix III).

Apart from toxins that affect the nerves and blood vessels (causing vasospasm and thickening of the walls) that have already been outlined earlier, others that affect the heart muscle include arsenic (As), which alters the electrical conduction "*causing arrhythmias and hypertension in some populations*" [(211)].

Long-term inhalation exposure to *Carbon disulfide* (CS_2) [(214)] used in the manufacture of dyes, viscose rayon, cellophane, pesticides, pharmaceuticals, rubber, solvents and many others, as well as the synthesis of chemicals, such as *carbon tetrachloride (CCl_{14})*, is known to cause electrocardiographic changes and arrhythmias. It also reduces blood pressure and increases arteriosclerosis, and as mentioned earlier has neurotoxic affects. *Carbon disulfide* (CS_2) is metabolised to the water-soluble metabolite dithiocarbamate and excreted in the urine.

High levels to sudden chlorine (Cl) exposure have been shown to cause both tachycardia and hypertension [(215,216)]. Studies on long-term cardiovascular effects do not show any effects. Exposure to diesel fuel vapour due to inhalation has also been shown to cause mild hypertension and renal toxicity [(217)]. Research is, however, limited in this area.

Plutonium (Pu) results from the bombardment of uranium with deuterons (^2H) and it has 20 isotopes, although 238 and 239 Pu are the ones that are generally encountered and mainly found in nuclear power stations and in very small quantities in laboratories. Once it reaches soil or water from atmospheric fall out, it can translocate in plants and animals affecting the food chain, but these are very small amounts unless following a nuclear disaster when atmospheric fall out can last many years. Depending on the dose, risk of exposure will of course be higher for those who work in the industry in such cases, but exists for the general population especially children who live downstream from prevailing winds or in areas close to plutonium waste sites due to the inhalation of particles, water intake or the food chain over prolonged periods of time. Chernobyl Children International stated in 2015 that "*today in Ukraine 6,000 children are born every year with genetic heart defects*"[(218)].

Thallium *(Tl)* ions are so similar to *potassium* (K) and *sodium* *(Na)* that the body mistakes it for potassium and it is taken up by the heart cells disrupting their functions (see more under nervous system).

Antimony *(Sb)* and many of its compounds are toxic. It finds a number of uses in glass to remove bubbles, to render glass opaque or as a glaze for ceramics. It is also used in electronics, paints and flame retardants for clothing, engine covers, brake linings, toys, and combined with other metals, it is used in batteries (combined with lead), some solders (lead and tin), as well as cables manufacture. Occupational exposure is either through the inhalation of antimony dust but the ingestion of the substance used in medicine for the treatment of *schistosomiasis* and *leishmaniosis* could result in cardiotoxicity [(219)].

The Nervous System

The nervous system continues to receive so much attention in ongoing research and so much is known today on its function and response that only the barest references can be made here. Consisting of the brain, spinal cord and the nerves, it receives and distributes messages from and to every part of the body, controlling every organ, action, movement and thought.

New and advanced technology continues to show us that this system is very complex to say the least, and to understand its organisation and function it is best to consider it as having central (brain and spinal cord) and peripheral parts(long nerves that are either sensory sending messages to the brain, or motor which can be either voluntary (somatic) or involuntary (autonomic). These reach most parts of the body either from the brain directly or via the spinal cord. The involuntary or automatic nerves are then again divided into what is known as: (a) the sympathetic nerves (these alert the body in response to some emergency that the body should deal with by triggering organs to release the stress hormones, *cortisol* *($C_{21}H_3O_5$)* and *epinephrine* (see also noradrenaline) which are required to prepare the body for such a situation, and (b) the parasympathetic that does the exact opposite by relaxing the body through various signals to the relevant organs. Both these two nerves that form part of the involuntary and voluntary system work together creating whatever balance is required by the circumstances.

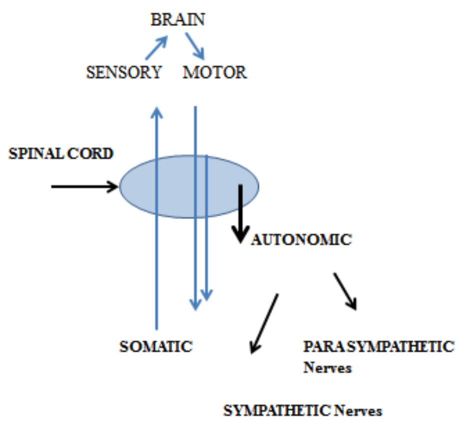


Figure 39. A schematic representation of nerve control to and from the brain.

The nervous system is a target to many toxic and other substances which are essential to its functions. At different doses these can become toxic (e.g. *glutamate*) *(220,221)*. Toxins affecting this system are known as neurotoxins. They effect electrochemical transmission (see below) and inhibit "*neuron control over ion concentrations across the cell membrane or communication between neurons across a synapse*" and can also include *"cell damage or death"* *(220,222)*. The large amount of blood that flows through the brain from the heart allows prolonged exposure although a *'blood-brain barrier'* (see brain p.123 and fig. 47) surrounds the blood vessels that restrict the entry of some substances (223).

Most of the neurotoxins affecting the brain and spinal cord are not selective, that is, they are widespread in their effects, interfering with neuron processing, signal transmission pathways, metabolic injury or cell death. It must be remembered that quite often workers are exposed to a mixture of toxic compounds and not just one toxic substance. In general, neurotoxins have resulted in broad categories of effects. Some are general effects (headache, drowsiness and loss of appetite). Others **sensory** effects (dizziness, pain, impaired colour vision or night blindness, numbness), or **motor** effects (muscle weakness, twitching, lack of coordination and tremors), Psychological and cognitive effects may also occur.

Chakraborti *et al.* (224) have pointed out that "*high (>2mg arsenic (As)/kilogram(kg)/day) or low but repeated exposure (0.03–0.1 mg As/kg/day) to arsenic targets and destroys the axons of neurons which results in peripheral neuropathy*".

Carbon disulfide exposure via the respiratory system results in behavioural (e.g. depression, decreased performance and memory), *histopathological* (e.g. *polyneuropathy*) *and neurophysiological* (e.g. decreased nerve conduction velocity) conditions (225).

Thallium (Tl) (226) is a heavy metal whose isotopes may be radioactive or non-radioactive. It is found in *copper (Cu)*, *zinc (Zn)* and *lead (Pb)* ores so that the mining industry releases small amounts of thallium as flue dust to the atmosphere which ends up in soil and water. It is also found in semiconductor and cement manufacturing as well as refineries, and used in glass and pharmaceutical industries. It is colourless and odourless and the soluble isotopes make it an ideal poison, although it is slow acting and clinically not so easy to identify it as the cause of the patient's symptoms. Exposure may be through inhalation, ingestion, eyes or skin. It affects the nervous system starting by causing headaches, gastrointestinal and muscle problems and affects the peripheral nervous system with *polyneuropathy* (see neuropathy). The water soluble salts of *thallium* (Ti) are absorbed through the skin. Thallium-201 is a radioactive isotope used in medicine in trace amounts that are harmless and is used to investigate how much oxygen the heart is receiving, which it does by emitting gamma rays that can be seen using a gamma camera which it does by counting gamma photons absorbed by a crystal which contains some thallium. Thallium is also used in some type of fireworks.

Brain

Inside the skull, a collection of 22 bones, well fused together in the adult, protect the brain from external injuries. Immediately beneath these bones the brain lies covered by three membranes. Throughout the space beneath the lower two membranes runs what is called the *cerebrospinal fluid*, acting as a cushion and nourishing its fatty tissues, and possibly having other functions yet unknown to us. This fluid also runs down a canal in the centre of the spinal cord. Small blood vessels run along the third membrane supplying every part of the brain's outer surface.

The brain consists of two halves that appear as mirror images of each other (see Figure 40). These are separate halves that are connected together by a bundle of nerve fibres. They include the **diencephalon**, consisting of the thalamus (which relays sensory information) the hypothalamus (which regulates body temperature, and the autonomic nervous system) and the **epithalamus** (which regulates the body's rhythms). Although each half controls the opposite side of the body and can carry out similar functions, each also has its own distinct activities. These two halves of the brain are made up of lobes (frontal, parietal, temporal, and occipital (see Figure 42). The reader is referred to the definitions for more detail. The brain stem (where the brain nerves pass to the spinal cord) is where the **medulla** (that controls respiration and heart beat (see Figure 43), and **pons** (controlling reflexes and acting as its name implies as a bridge to the diencephalon (see Figure 41, 43) are situated. The brain is supplied by two major blood vessels (see Figure 34) the internal left and right carotids and the vertebral arteries both arising from the right and left common carotids from the heart, and many smaller vessels supplying the 25% oxygen [227] that it uses, and sugar (glucose) for the large amount of energy it requires to transport electrochemical signals, lipid soluble substances, as well as *"amino-acids, some gases and water"* [227].

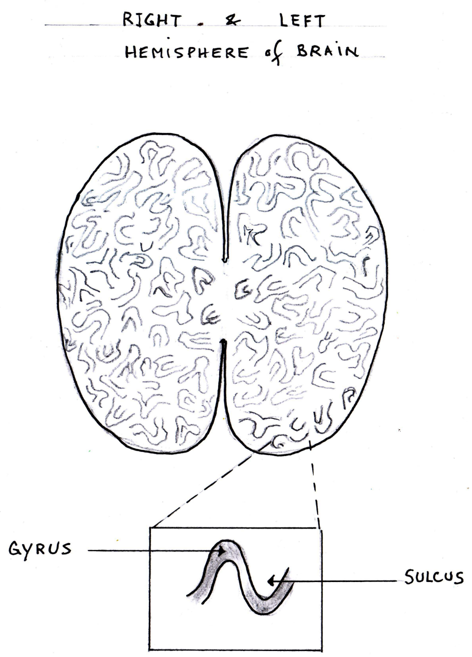


Figure 40. A simplified drawing to indicate the two halves of the brain showing the convolutions of the cortex which serve to expand the size of grey matter and therefore its capacity to process information.

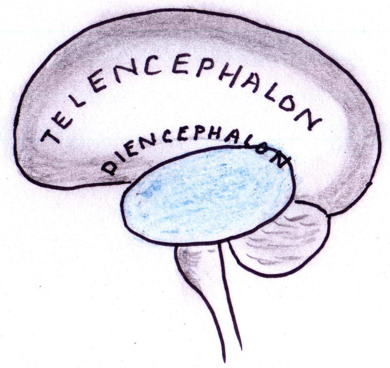


Figure 41. Drawing to show the approximate regions referred to as the telencephalon and diencephalon

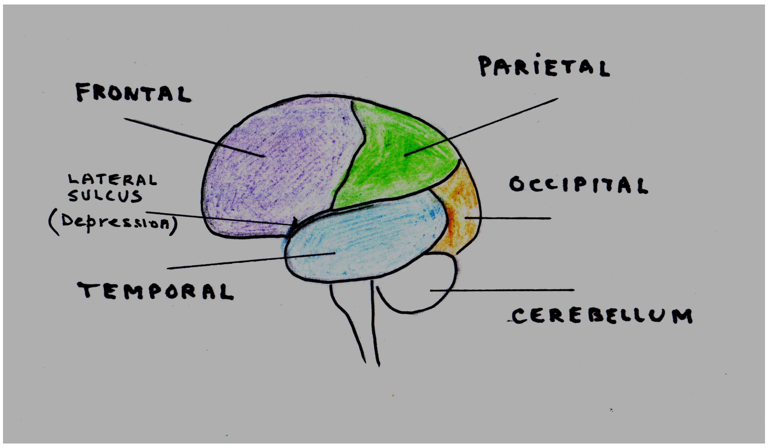


Figure 42. Drawing of the brain showing the brain lobes and lateral sulcus or depression separating the frontal and parietal lobes from the temporal lobes.

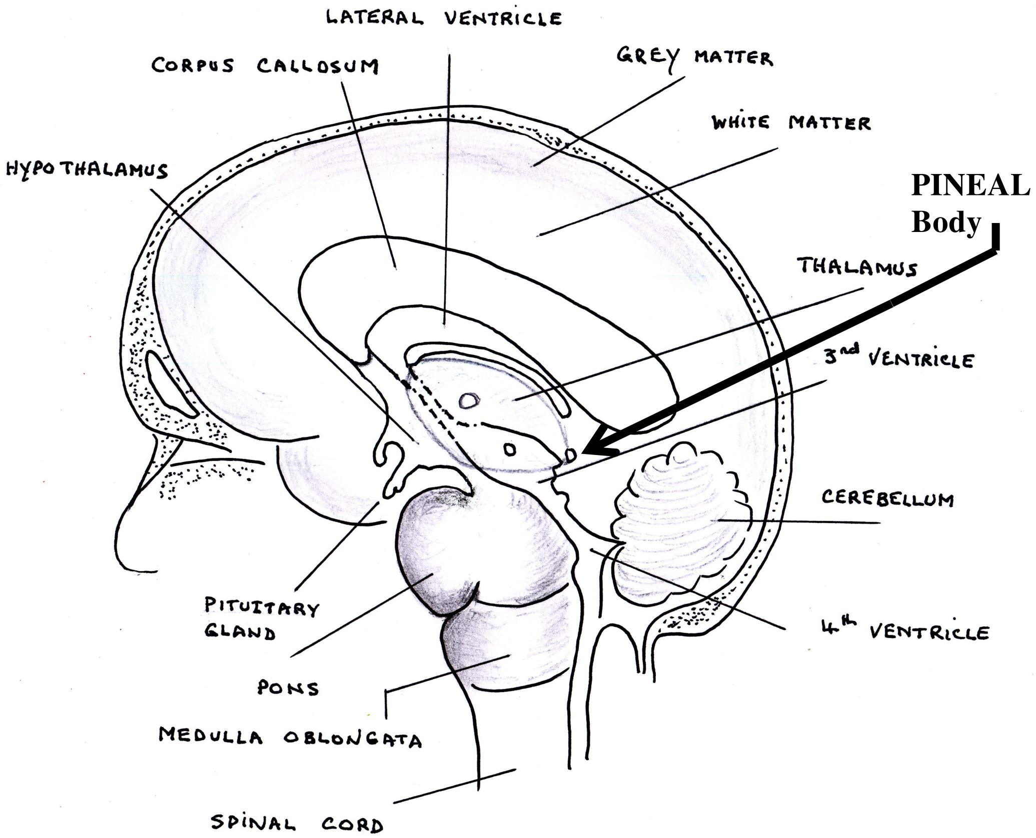


Figure 43. A sagittal sectional drawing of the skull showing the dotted skull bones and the brain, as well as the spinal cord on its way down the vertebrae. Note that the canal from the 3rd ventricle indicated in non-continuous lines runs between the two thalamae (only the left is shown in this section) to the 3rd ventricle. The lateral ventricles are referred to as the first and second ventricles.

Note that the brain's blood vessels contain a membrane which acts as a barrier to many chemicals and toxic substances. This is known as the blood-brain barrier/membrane [228] (see Figure 45), which *endothelial cells* in the innermost layer of the blood vessels and cells called 'astrocytes' that surround them, both control:

(a) the passage of substances due to lower permeability of endothelial cells, and,

(b) the restriction of substances having a large molecular non-lipid (lipophilic) soluble structures into or out of the blood vessels and the intercellular space.

In their role, they are complemented by other cells in tissue called the 'choroid plexus' within the ventricles of the brain that, in addition to providing protection against some substances, also produce the *cerebrospinal fluid.* Those toxic substances that manage to enter through the blood capillaries to the brain, do so either because they inhibit *astrocyte* function or as a result of brain injury and inflammation of the vessels.

It should also be noted that there are some other areas in the brain in the anterior parts of the ventricles (referred to as the *circumventricular organs)* that are not hampered by a blood brain barrier which allows hormones to circulate freely between the blood circulatory system and brain areas. One area of these organs where the spinal cord meets with the brain contains the vomiting centre. This is alerted by toxic/poisonous substances in the blood stream which, defending the body, responds through initiating nausea and vomiting. Furthermore, "*low level ultrasound waves combined with ultrasound contrast media"*(229) has been shown to disrupt the blood brain barrier and thresholds have been established by some researchers. This may become of value in the administration of drugs required to reach the brain tissues bypassing the blood brain barrier (229).

Michael R.Dobbs in the introduction of the book *Clincial Neurotoxicology* (2009) stated that between 750 and 1000 environmental neurotoxins have been classified as *"known potential neurotoxic compounds" (230)*.

James Randerson in *Notes and Theories of Neuroscience* (February 2012) pointed out that Dr. Suzana Herculano-Housel, in a specific method of research on the number of neurons (cells that transmit information via electrochemical signals) in the brain, found that on average brains contain 86 billion neurons (231). Most levels in the literature refer to 100 billion but then no one seems to know where this figure originated from. The other type of cells that make up the matter of the brain provide a framework of physical support for neurons, in addition to removing waste products of dead neurons and an insulation of fatty tissue to their axons. Each neuron has one axon (see Figure 46). This carries information away from the cell via synapses to other neurons and directly to different parts of the body. These cells providing the framework for neurons are called glial cells. Once again, their ratio or estimated numbers are conflicting with some higher and others lower than those of neurons.

A number of industrial and environmental chemicals/toxic substances *(about 150 substances according to Professor Phillipegrandjean (232) "are known to be toxic to the human brain"*. Professors Grandjean and Landrigan stated, "*Children worldwide are being exposed to unrecognised toxic chemicals that are silently eroding intelligence, disrupting behaviours, truncating future achievements and damaging societies (232)*. What they write about points to an important potential long term issue that may show its face in the generation of workers in years to come as most of those chemicals affect the developing brain of children. In the same article, Laura Plunket stated that "*there was no pandemic*" as much depended on the dose to which children are exposed (232).

Some examples include *mercury (Hg), lead (Pb)* – in ceramics, glass, batteries, some paint; *arsenic (As), manganese (Mn)* – in stainless steel; *fluoride (F), toluene* (C_7H_8) – manufacture of plastic bottles, paints, adhesives, chemical laboratories; E*thanol* ($C_2H_5O_8$), *polychlorinated biphenyls* (*PCBs* – fire retardants, coolants and insulation material; *tetrachloroethylene* ($Cl_2C{=}CCl_2$) and other solvents, *polycyclic aromatic hydrocarbons* (*PAHs)* – by-products of burning fuels); *polybrominated diphenylethers* (C12H(9-0)Br(1-10)O-flame retardants), *chlorpyrifos* ($C_9H_{11}Cl_3NO_3PS$) and other pesticides. Many chemical toxins from additives, preservatives and colourings (synthetic dyes made from petroleum products) may be found in the foods we eat, although levels at which they should be included are regulated in some countries. These studies, however, do not always cover very low levels or continued long term exposure, nor does labelled food always provide every constituent that is included in the product.

Response to chemicals and toxic substances reaching the brain varies with the specific areas targeted within it by these substances, and affect the normal function / activities of that site. They may also result in effects at other sites close to or far away from the affected area in other parts of the body. Alcohol and industrial solvents target the cerebellum which affects fine movements.

The brain operates at 7–9 nano amps. (Nano is 0.000,000,001 of a meter and an amp is a unit of electrical current which is equivalent to 1000,000,000 nanoamps) [233,234], so for comparison note that a 60 watt bulb will provide 0.6 amps. Electrochemical transmission of impulses may also be disturbed or damaged. The neurotransmitters can all be affected by chemicals and toxins – serotonin (which reduces anxiety producing a calming effect), and *beta-endorphin*, *norepinephrine* and *dopamine* (affecting alertness among other things).

Workers in the fishing industry may be exposed to a very dangerous toxin produced by some fish. *Tetrodotoxin* ($C_{11}H_{17}N_3O_8$) [235] is one example produced by puffer fish which prevents nerves from transmitting signals by blocking the passage of ions (electrically charged molecules) like sodium (Na), potassium (K) or calcium (Ca) essential for transmission. *Domoic acid* ($C_{15}H_{21}NO_6$) from contaminated mussels, anchovies and sardines is another example. Neurotransmission in agricultural workers can also be blocked by *Clostridium botulinum*, a bacteria of which there are two types and which causes botulism, a rare and potentially fatal illness which causes weakness throughout the body. The bacterial spores which release the toxin can reach the body via an open wound from soil (agricultural workers), street drug injections, and canned or jarred food such as honey (particularly if homemade). Honey with spores fed to children less than 6 months old causes weakness in muscles and possible muscle paralysis so it is recommended not to give honey to children less than 1 year old as protective mechanisms have formed by then. The toxin enters both the neurons and axons and inhibits *acetylcholine* thus blocking signal transmission. It is also used in cosmetics (commonly known as ‘botox’) from where, if present in the injected material, it is possible for the bacteria to travel to other body sites. Note, however, this product is strongly regulated both in cosmetics and the food canning industry, each taking precautions to ensure safety.

Agricultural workers are at times exposed to *chlorotoxin* [236] (secreted by scorpions) and to toxins from snakes (causing headache, disorientation and nausea) bees, wasps, and some plants. Painters, sprayers, mechanics and others that use organic solvents affect both the central nervous system (CNS) as well as the peripheral nervous system (PNS). These symptoms include: CNS – memory, irritability, depression, as well as fatigue and PNS – numbness in hands and feet, muscle weakness and pain. Acute conditions depend on the dose but have other more immediate effects, such as nausea and/or vomiting, headache, dizziness, confusion, which may go on to unconsciousness. Radiological examination (MRI – Magnetic Resonance Imaging) has shown solvents affect selected areas in the brain and usually more than one.

It is unfortunate that although some industrial chemicals have been banned or regulated, they are still in use in many countries, either for economic reasons, lack of knowledge or indifference.

Spinal Cord (see Fig. 44,45,55)

Linking our body to our brain, the spinal cord leaves the brain through an opening at the base of the skull and travels down each vertebra, of which there are 24 in the adult. An additional nine vertebrae, which makes up the total number (33) with which we are born with, are fused into what is known as the sacrum. This lies below the last lumbar vertebra (see Figure 55 p.137). The bony vertebrae help to protect the cord. Through two small openings (a space formed as one vertebra lies above another forming a channel called a *foramen* on the back lateral sides of each vertebra), the cord receives a sensory nerve from the skin, muscles and organs lying within the body, and sends a motor nerve to the same parts. Foramina protect the spinal cord nerves, as well as the blood vessels and some ligaments that pass through it (see fig.44).

Each area that the nerves supply can be quite accurately mapped on the skin, making clinical identification of damage to any of the nerves that supply it easy, although some overlapping does exist. Thirty one nerves emerge from each side of each vertebra which then branch out to cover their destination areas. Some of these are ascending nerves (**sensory** – touch, vibration, temperature, pain and pressure) on their way to the brain via the spinal cord, the others descending (**motor**) nerves to muscles and body organs. The spinal cord only reaches to the 22nd vertebra (which is *lumbar 2)*. The remaining nerves dangle down to reach the spinal bony canal, some to exit from the canals of the lumbar vertebrae 1,3,4, and 5, and the rest go vertically down to reach the fused bones *(the sacrum)* (See Fig.55).

A ganglion (*spinal or 'dorsal' root ganglion containing sensory neurons*) just outside the foramen receives the ascending sensory nerves – one a collection of nerves from the front (anterior) the other from the back (posterior areas of the body). These then go into both the back (posterior horn) and middle (lateral horn) areas of the spinal cord through the foremen at each vertebra on their way to the brain. The descending motor nerves from the brain, which exit the spinal cord at its front (anterior horn) join the descending nerves after it exists from the spinal ganglion (see Figure 43a).

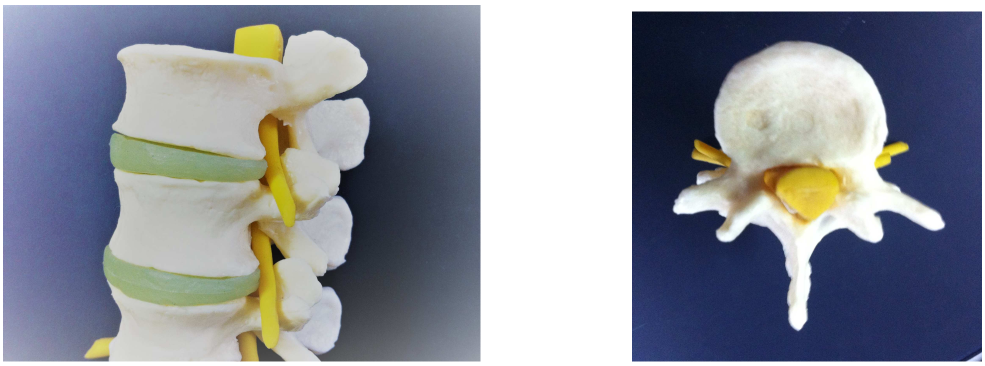


Figure 45. Illustration of vertebrae in the lumbar region clearly showing the nerve roots emerging from the spinal cord through the vertebral canals between each of the vertebrae.

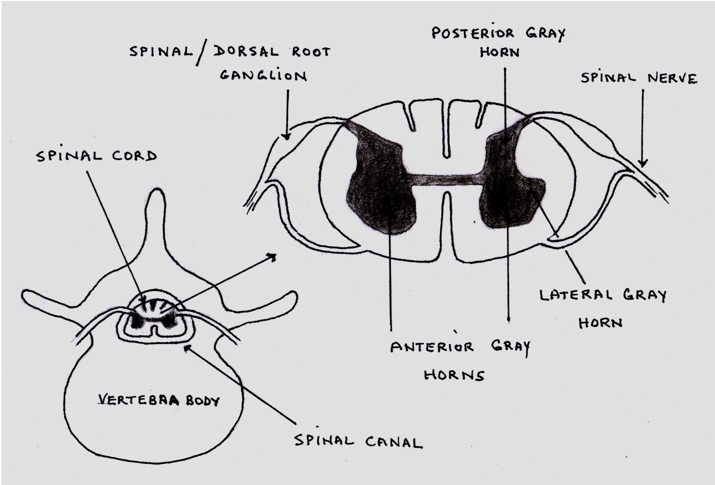


Figure 45. Rough sketch to show a vertebra and its spinal canal through which the spinal cord descends and an inset of a horizontal section of the spinal cord indicating the horns and nerve roots. The white areas surrounding the horns also contain nerves not shown.

An alphabetical list of nerves of the human body from Wikipedia lists 219 nerves, but also points out that this may not *"meet certain standards of completeness"* (237). It may also be interesting to note that in the article '*40 Interesting Facts About the Human Body'* (206) points out that in the adult body there are 46 miles of nerves. How the measurement of a 'nerve' has been defined may be an important aspect of such calculations, either way if correct, an impressive feat!

Nerves are a collection of axons (nerve fibres that originate from neurons) that travel either directly to areas in the head. These are the **cranial nerves** – 12 leave the brain and go to the head (eight to scalp, ears, eyes, nose, muscles, tongue, teeth, throat) with two – one to the heart and the other to the muscles of the shoulders. Other axons travel much longer distances as far as the toes of the feet (these are **peripheral nerves**), some of which go deep into the body to reach organs like the stomach, kidney or uterus, etc.

The nerve cell (neurone) of which there are many types, depending where it is located in the central nervous system, or elsewhere, is made up of the cell body, which has a nucleus, a number of small branches called dendrites that interlace with those of other neurons and one long branch called the axon which is the nerve fibre (see Figure 46). This is very much like copper strands of wire wrapped in plastic for insulation, except that each axon is surrounded by a fatty insulation and lining of connective tissue (called the myelin sheath).

All axons are then bundled together and covered once more by extensions of this connective tissue, before all these bundles receive one more final covering of the same connective tissue. Within each bundle lie the blood vessels through which toxins may reach the axons although they are to some extent protected by fluid in the connective tissue surround. This acts in much the same way as the blood brain barrier.

Acrylamide (CH_3H_5NO) (238) and organophosphorus compounds are two substances which cause axon degeneration. The degeneration is a metabolic process possibly affecting enzyme systems to which chemical substances may become bound and then interfere with normal function. When toxins involve the peripheral nervous system the individual affected will develop numbness and tingling in the hands and feet and later there may be weakness in trying to get hold of objects if they are heavy.

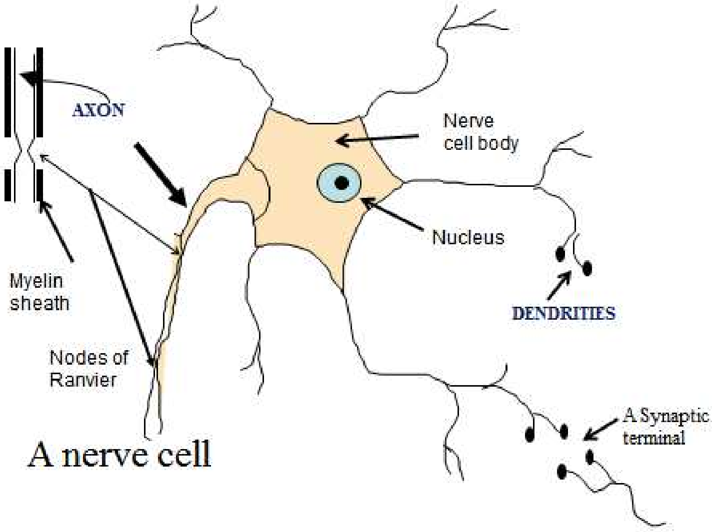


Figure 46. A drawing of a neurone (nerve cell) of the brain showing the link to other neurones through one of many synaptic terminals, and the major structure of its axon, and the Nodes of Ranvier, which are not covered with myelin sheath and serve to increase the speed of action potential of the nerve.

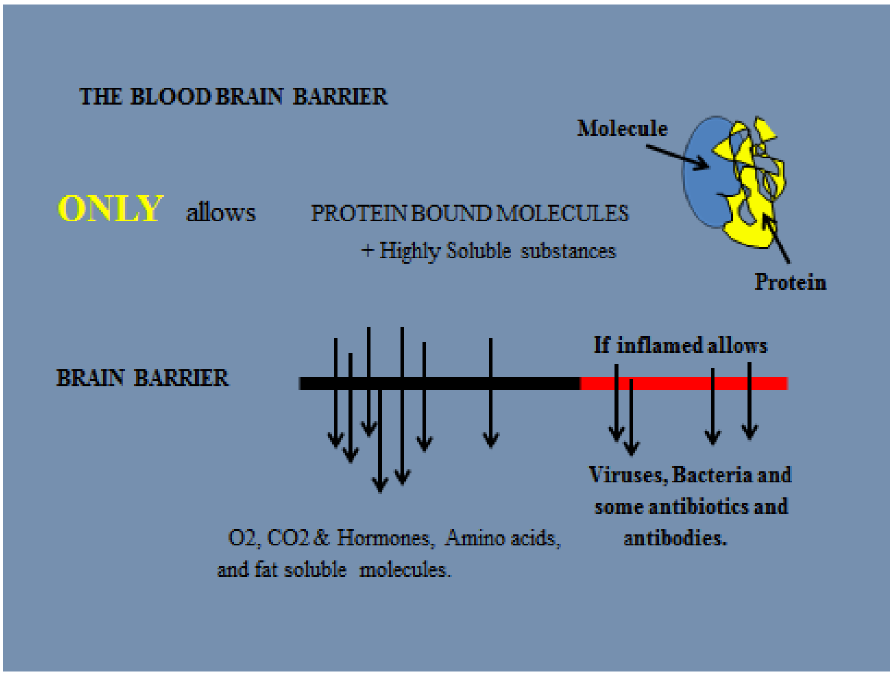


Figure 47. A schematic representation of absorption through the blood brain barrier.

They may also develop ataxia (lack of coordination of voluntary muscular movements). Chronic exposure to *n-Hexane* (C_6H_{14}), which is a solvent, results in a metabolite which is toxic to the nervous system and may cause ataxia. Apart from general symptoms with neurotoxins that affect the peripheral nervous system, there are other symptoms that occur, which are usually specific to the chemical toxin. In some cases, the neuropathy (abnormal condition of the nerve) may develop.

Other common conditions seen by safety and health practitioners are repetitive strain injuries and *carpal tunnel syndrome* (239) where swelling puts pressure on the nerve as a result of some injury, although this can also occur due to other conditions. Note particularly that once signals through the nerve are disrupted they may divert to other areas and the pain may be felt at sites distal to the area involved; this is known as 'referred pain'.

Note, therefore, that neurotoxins that affect the brain tissue can also affect nerves. Peripheral nerves are able to regenerate although vulnerable to many neurotoxins. *Methanol* (CH_3OH) is one example that affects the optic nerve and may cause visual disturbances or even blindness. Others include: *acetone* (C_3H_6O), *acetylene* (C_2H_2), *atrazine* (a weed killer – $C_8H_{14}ClN_5$), *aluminium* (Al), *benzene* (C_6H_6), monosodium glutamate (sometimes referred to as *hydrogenated protein occurs naturally in some foods and used to flavour others – labelled as E621 and not considered toxic*), soya foods and other food additives such as flavourings and spices to some individuals. These are just a few of an unending list of potential neurotoxins.

The Reproductive System

Reproduction is essential to the continued existence of our species and is probably the highest unconsidered priority of any species which can go beyond balanced requirements to maintain existence. Human reproduction is (at the present time) sexual (as opposed to asexual where an organism produces an exact copy of itself), but whether this is an advantage or disadvantage to toxic exposure in utero or after birth still leaves a lot that has as yet to be researched.

Female reproduction (240)

The female labour force continues to enlarge, increasing the number of women that may be at risk from potentially toxic substances. The reproductive process involves different organs of the body and the prevalence *(the frequency of disease at a designated point in time*) of infertility, neonatal and infant deaths, still births, birth deaths and low birth weights available from records in different countries and the need for increased awareness being given to occupational hazards, justifies further studies of possible relationships between these reproductive outcomes and workplace exposures. Legislation specifically requires that the working environment is safe for the health of women within the reproductive period at work.

There are about two million egg cells (*oocytes*) at birth, down from 6 million oocytes in the foetus. Division of egg cells begins in foetal life at about 5 to 6 months, stops at birth, and then restarts at puberty with hormonal stimulation (240). By the time the menopause is reached, the number reduces to about 400,000. Chemicals referred to as *mutagens,* which can cause structural damage to the DNA (genetic material) or cell toxicity, probably causes damage to these cells when the genetic material divides in foetal life. Apart from this genetic damage, cumulative environmental factors may also be involved during cell division. There are many mutagenic chemicals in industry, examples of which are *nickel (Ni),* organic solvents, pesticides and metals such as *lead (Pb).* Various hormones must be in balance, just like an orchestra, to meet all of the requirements in preparing the lining of the uterus for the cell to become embedded, since the process of implantation (which takes about one week) can be affected by toxic substances. Indeed they can affect cell fertilisation, which usually takes place in the ovarian tube (*a tube that links the ovary to the uterus*).

The placenta, like the brain, has a blood barrier that hinders the passage of toxins to the embryo/foetus. Three layers of tissue separate the mother's blood from that of the embryo/foetus. Most of the toxins cross the placenta by diffusion and have an active transport system for many substances. The placenta has to transport nourishment and other substances needed for the development and growth of the foetus so that it is difficult for this tissue to control the passage of many substances. *Lead (Pb)* and *organic mercury* (C-Hg), for instance, can pass through the barrier and reach the brain of the foetus quite easily as its blood brain barrier is not yet properly formed.

The first trimester is the most susceptible to toxicity or structural changes in development of the embryo/foetus by chemical substances that cause birth defects. These chemicals are referred to as teratogens. *Teratogens* interfere with the proliferation rate of the cells as well as cause chromosomal defects, but are not unduly toxic to the mother, which indicates that these particular chemicals are selective to the embryo/foetus. The dose-response curve is usually a steep one.

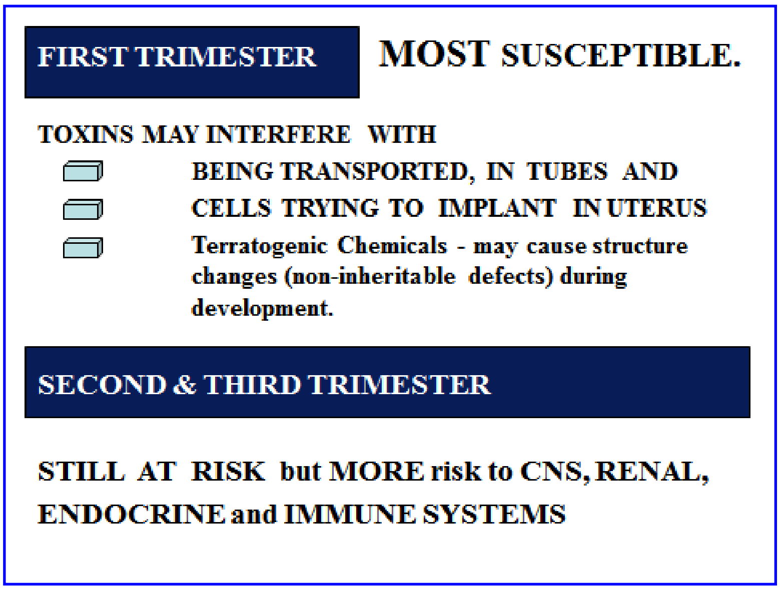


Figure 48. Representation of the most susceptible periods during pregnancy emphasizing the importance to toxic exposure.

Low molecular weight lipoid soluble substances can get through the placenta to cause such damage. Substances such as tobacco smoke, *carbon dioxide (CO_2), sulphur dioxide (SO_2), nitrogen dioxide (NO_2), phenols (C_6H_5OH), phthalates ($C_8H_4O_4$), alcohol (ethanol), PAHs,* substances used in fire retardants such as per fluorinated compounds (polybrominated diphenyl ethers - PBDEs - that are toxic to humans and oceanic organisms, some of which are banned in the E.U.), perchlorates, *bisphenol A (BPA)* have all been shown in studies to affect the female reproductive system. In addition, lead, ionising radiation and some specific drugs are also known to be teratogenic. Benzene has been shown to cause benign tumours of the ovaries. [B11]

Several studies of cord blood have shown that the insecticide repellent *diethyltoluamide* ($C_{12}H_{17}NO$), and the fungicide *vineclozine* ($C_{12}H_9ClNO_3$) pass through the placenta into the developing foetus. Perfluorooctanoic acid (PFOA) ($C_8HF_{15}O_2$) is another fluorinated compound that is found in water, translocated into plants from sewage sludge if applied to agricultural land, and has also been found in cord blood. It has a half-life of 2–4 years in humans and is used in stain repellents, insulating materials and fire extinguishing foams. *Perfluoroalkyl acids* (PFAAs; $C_{12}H_8F_{17}NO_4S$) are another fluorinated organic chemical that has been reported to cause increased pregnancy duration. Endocrine disruptors are yet another of the many substances that attention must be given to in the prevention of exposure during the reproductive period.

As mentioned earlier, exposure to toxic compounds may affect transportation of the egg cell down the ovarian tubes where fertilisation takes place on its way to the uterus or at the implantation site. Still further, there may be malformations, retardation of growth, some functional disorder, abortion or even death. Note that the embryonic period is around 58 days, whilst the foetal period is between 58 and 280 days or so.

Throughout the course of the second or third trimester, the risk (probability) from exposure to the effect of toxic substances is also present. During this period, however, there is more risk to the central nervous system, the hormonal system, the immune system and the urogenital system during the foetus' development. *Lead (Pb)* and *organic mercury (C-Hg)* are two examples in this respect. *Vinyl chloride* exposure may cause foetal loss. A condition referred to as *toxoplasmosis* [(219)] (see more under male reproduction) is another toxin to which female veterinarian workers are specifically exposed to. The toxin passes the blood brain barrier from the mother and through the placental blood barrier into the foetus; even the cysts of the parasite that causes the condition may reach the foetus.

Male reproduction [(241)]

Once the male has reached puberty, sperm are continuously produced. There are a number of phases in the production of sperm which takes about two and a half to three months until maturity. The effect of specific chemical toxins may result in low sperm counts (*benzene* (C_6H_6), *xylene* (C_8H_{10}) *and cadmium Cd)*, affecting fertility and genetic damage (gene mutation or chromosomal changes) to the developing sperm. Excessive heat (hyperthermia) is also believed to be toxic to sperm. Cancer in childhood has also been shown to occur where the male parent has been exposed to specific toxic substances, such as solvents, but although it has been reported in the literature further evidence is needed to confirm these effects. The organic solvents can cause delay in conception, reduce sperm quality and cause birth defects.

Toxins affecting the male reproductive system may have their effects on male hormones, which then exert an effect on sperm development and performance, or directly affect the sperm itself, such as its structure and motility. They could also exert an effect on the seminal fluid through which the sperm can then become affected, so they may not become fully mature. Sperm toxic substances interfere with the *pituitary* and *hypothalamic* areas in the brain which then affects body hormones and may cause impotence. Endocrine disruptors may have an effect on the reproductive tissues and therefore the quality of semen and sperm.

Depression in the sperm count in consequence of toxic exposure occurs gradually after a number of years. In 1977 an incident in a pesticide formulation plant in California,[242] a *nematocide* called dibromo-3-chlopropane (DBCP) which is a broad spectrum plant pesticide that is used to kill nematodes (*very small 3–8 mm worms found in large numbers in the soil)* and is a fumigant which is now banned, was accidentally released. It was shown that the workers' sperm counts varied from around 20,000 million/ml of fluid in some to no sperm that could be identified in other workers. A human sperm count that ranges from around 20 million to 40 million per ml of fluid is considered within normal limits, but sperm counts may be very much larger than this [243].

Ethylene glycol ethers ($C_4H_{10}0_2$), *carbon disulphide (CS_2), lead (Pb) and mercury (Hg)*, some pesticides such as *zineb, ethylene dibromide (banned)*, *carbaryl* and *atrazine* (*a herbicide*) which reaches the water table, and both *2-methoxyethanol* (*$C_3H_8O_2$* – a solvent) and *ethoxyethanol ($C_4H_{10}O_2$)* – a solvent), each of which is used in the electronic industry and dockyards, are other toxic substances that effect the male reproductive system. Note that pesticides include insecticides, herbicides as well as fumigants and fungicides. N-hexane (causes atrophy) and *methyl butyl ketone ($C_6H_{12}O$)* are both solvents and cause damage to the testis.

Welding is a very common task carried out by many everywhere. Unless preventive measures have been taken to avoid welding fumes, substances such as *cadmium (Cd), nickel (Ni), hexavalent chromium (CrVI)* and other constituents of the fumes generated by the specific materials being used must be considered, although there appears to be some controversy in the literature on their effects on the reproductive system.

In the evaluation of the effects of toxic substances on the male reproductive system, other factors such as age, radiation and medical disease must be taken into account as they can confuse the issue. Those who have not been vaccinated would be at risk from infectious conditions such as viral infections, of which hepatitis is one example. Those that are involved in veterinary work are also at risk from a condition called *toxoplasmosis* [244] (a disease caused by a parasite whose *cysts* are found in cats' faeces and insufficiently cooked foods that may contain the parasite's cysts). Note that many people worldwide are infected but have no symptoms. Toxoplasmosis has been linked with schizophrenia (a condition affecting the brain in which the person has delusions, hears voices, develops depression and anxiety, is socially withdrawn and has little motivation). Much of the data is from animal studies, and human data is still limited linking cause and effect.

The Endocrine System

This system includes the following organs; pituitary, thyroid and parathyroids, adrenals, pancreas and the ovaries and testes. The hypothalamus and pineal body have been described here along with these because of their important links with these organs and the production of the many hormones produced and secreted by them.

Each type of hormone reaches specific cells in the target organ via the blood stream and in most cases, through complex chemical reactions, results in the production and release of the hormone/s from that organ to implement its function. A hormone may have an effect on more than one organ.

Solvents play an important part in the toxicity of the endocrine system and the reader is referred to an excellent review paper: *'Endocrinal toxicity of industrial solvents – a mini review'* in the *Indian Journal of Experimental Biology, Vol.47, July 2009, pp 537- 549, by Yeshvandra Verma and Suresh Vir Singh Rana* [B44].

Hypothalamus & Pituitary [245,246,247] (See Fig. 49 p.129 & 43 p.118)

Dictionary.com defines 'hypo' as a prefix to a word meaning 'under' or 'below'. The hypothalamus in the brain lies immediately below and very slightly forward of the thalamus (*a relay system for nerve pathways*) which looks like the shape of an egg with one flat end and lies in the middle of the lower deep part of the brain. The hypothalamus is described in anatomy to be the size of an almond which is about 3–4mm in width. It lies beneath the 3rd ventricle and both of its sides encircle from below the sides of the narrow cavity of the 3rd ventricle) and weighs 4 grams; an average brain weighs 1400 grams [247], equivalent to 3.138 lbs. Its small size, however, does not preclude it from carrying out a considerable number of the most important functions essential to life. Its lower end has nerve pathways which extend to the posterior part of the pituitary – a gland hanging beneath and forward of it in a bony cavity at the base of the skull to protect it, and which is separated by a thin section into anterior and posterior areas. The anterior part receives information from the hypothalamus via the blood.

The hypothalamus is critical to life and has a number of nerve cells packed together into what are referred to as nuclei, two of which are larger than the rest. These sections of packed nerve cells each have a different role to play, synthesising chemicals called hormones, receiving and detecting other hormones or signals reaching them, as well as communicating through signals to other organs in response to prevailing body conditions, such as increased metabolism or temperature amongst others. The signals received by the nucleic areas in the hypothalamus may stimulate or inhibit function of cells in other organs in their response to information from these parts.

The pituitary (see Figures 43 & 49) produces a number of hormones from its anterior lobe. One referred to as <u>melanocyte stimulating hormone</u> is produced by its intermediate lobe, which separates it from its posterior lobe. This lobe only stores hormones from the anterior pituitary, the intermediate lobe and the hypothalamus. The pituitary's anterior lobe hormones include those that affect growth and puberty (see Figure 49 and Figure 58a, and 58b) for detail on the pituitary and these hormones which are referred to as <u>*luteinising hormone*</u> (*LH)* and follicle stimulating hormone *(FSH)*, thyroid stimulating hormone *(TSH)*, <u>*adrenocorticotropic hormone*</u> (*ACTH)* and <u>*prolactin*</u> *(PRL)*[246,247].

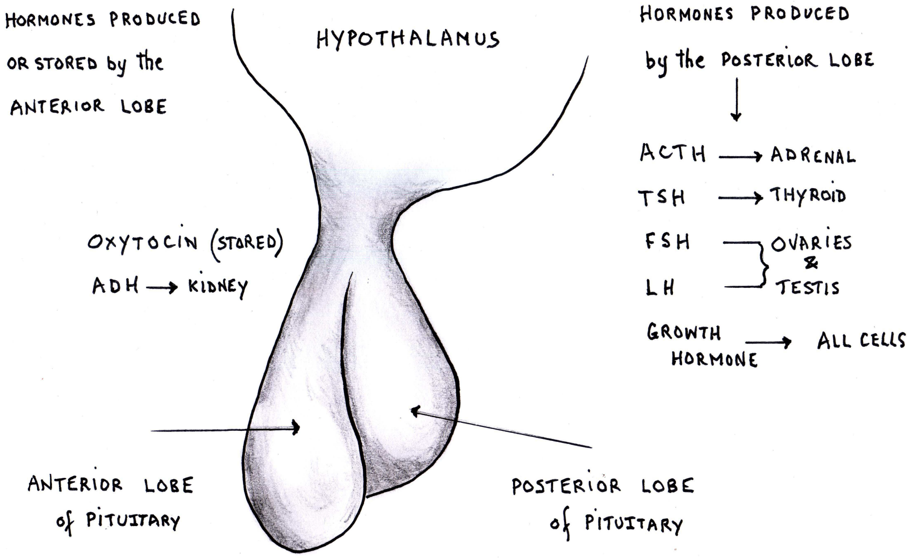


Figure 49. Drawing of the pituitary gland showing its two lobes below directly connected to the hypothalamus above it, together with the hormones produced by each lobe of the pituitary (See also Fig. 43).

Information on the selection of target areas in the brain by toxic substances appears to be limited. However, research evidence exists that fat soluble substances, such as organic solvents, dissolve in brain fatty tissues and cause functional impairment through effects on energy metabolism. *Volatile Organic Compounds (VOCs), hydrogen sulphide (H_2S) and chlorine (Cl_2)* are other toxic substances that can inhibit neuron function. Petrochemicals can lower the ability of the neurons to protect themselves against *free radicals* by impairing their ability to receive nutrients (vitamins and trace elements) necessary for this protection process, as well as reduce blood flow depriving the cells of much needed oxygen to function properly or affect the brain cell membrane. Malathion and endocrine disrupters are other groups of chemical exposure which may cause brain cell impairment.

Molhave,[248] Morrow [249] and Bell [250] have referred to brain sensitisation with repeated exposures to mixtures of organic solvents and VOCs. It is worth noting that toxins may bypass the blood brain barrier and directly affect the nerves at the base of the skull through inhalation via the nose olfactory nerves. Note also that toxic substances reaching the hypothalamus will pass to the anterior and posterior parts of the pituitary gland due to their linked rich blood supply to the anterior part and nerve and blood supply to the posterior part.

The Hypothalamus plays an important part in the communication, regulation and control of blood pressure, temperature changes (heat, sweating, shivering,) thirst and water balance (reabsorption of water from the kidneys), the body's *circadian rhythm* [251] sleep, reproductive processes, emotion (anger, aggression), hunger, fatigue, memory formation and sexual behaviour. Therefore, short or long term exposure to toxic substances that target the Hypothalamus and Pituitary will cause disruption to neuro-communication between them, and the hormones they produce which in consequence will result in a cascade of processes that will affect the function of other body organs and alter the role of these hormones in the body. *Tetrachlorobenzo-p-dioxin* (TCDD), S*tyrene* *(C6H5CH*,CH2) T*etrachloroethylene* ($Cl_2C=CCl_2$) and T*oluene* (C_7H_8) all have effects on the hypothalamus which invariably effects the function of the pituitary.

The Pineal Gland (or Pineal Body) (See Fig. 43 on p.118)

The importance of this gland to Safety Professionals is that it is involved with the circadian rhythm (sleep/wake cycle), and the relationship of the rhythm to the production of melatonin which the gland produces [(251)]. It does produce another substance – *pinoline* *($C_{12}H_{14}N_2O$)* which is an antioxidant and possibly others still undergoing research. Relative to other parts of the brain, it has a considerable supply of blood, and these vessels are not protected by the blood brain barrier, making it an easier target organ for toxins. It also plays a part in the development of the testes and ovaries since melatonin can block the two hormones, LTH and FSH, produced by the pituitary.

Located near the back of the 3rd ventricle, at the back of the thalamus, the pineal gland joins its lobe on the left side of the brain to the lobe on the right side of the brain. In this location, the gland also lies below and forward of the *cerebellum.* The gland is about 0.8cm in size and weighs one tenth of a gram – quite small.

Substances that affect the pineal gland include bromides (Br), chlorine (Cl_2), fluorides (Fl) (found in water and toothpaste), fluoride pesticides, mercury (Hg) in fish (such as tuna, shrimp or prawns), phenylalanine ($C_9H_{11}NO_2$) a neurotoxin found in aspartame, a synthetic sweetener and many foods (eggs, meat, milk and others in small doses), and calcium (water, calcium supplements, etc.).

Experimental evidence that *"fluoride accumulates to strikingly high levels in the pineal gland"* was found by Jennifer Luke in her PhD thesis in 1997 [(252)]. Exposure to fluoride reduces melatonin production which Luke's supervisor and Professor of Chemistry at St. Lawrence University USA, Paul Connett indicated is his note on J. Lukes' thesis, hypothesising that accumulation may result from fluoride inhibiting one of the four enzymes necessary in the conversion of the *amino acid tryptophan* ($C_{11}H_{12}N_2O_2$) from the diet to melatonin.

The increasing importance of sleep and the promotion of health at work in general, the economic costs of sickness absence, and the increase in the number of jobs requiring 'undesirable' working hours justify attention to chemicals targeting this gland.

Thyroid and Parathyroid Glands

Lydatt and Butcher [(253)] referred to Leonardo Da Vinci as the first person to have drawn the thyroid '*as an anatomical organ',* although it was in 1656 that an eminent English physician – Thomas Wharton – working at St. Thomas' Hospital, now part of Guy's Hospital in London, gave it the name 'thyroid' and also described what he knew of its function at that time. The parathyroid glands that lie at the back of the thyroid were discovered in humans in 1880 by a Swedish medical student called Ivar

Viktor Sandstrom [254], who was not aware that these glands had been found in the Indian Rhinoceros by Richard Owen in 1852.

If you gently place the fingers of your right hand over your windpipe (trachea) half way on the front of your neck you will, more or less, have identified the location of the thyroid gland as its two lobes lie to either side of the trachea, each linked by an isthmus across the front of the trachea. To the back of these lobes – two on each lobe a total of 4, but sometimes 3 or more in all – are the parathyroid glands. The two glands behind each lobe are arranged so that one pair lies on each lobe. Each lobe therefore has one pair at the upper part of one lobe and the other pair at the lobes lower end. These four glands are small – about 6 mm long by 0.75 mm in width and 1or 2 mm in thickness.

The thyroid's role is to produce the hormones *thyroxine* (T_4), *triiodothyronine* (T_3), *calcitonin* and *thyroglobulin,* which are stimulated by a hormone from the hypothalamus (TSH) to release the appropriate thyroid hormone to maintain or alter metabolism, body temperature, growth and development. The parathyroids produce, the *parathyroid hormone* whose job it is to regulate the levels of calcium and phosphate. In the case of calcium this is done by stimulating cells (osteoclasts) in the bone to release calcium to the blood or absorb calcium into the bone by inciting the involvement of vitamin D; *phosphate* $(PO_4)^{-3}$ is regulated by inhibiting or increasing absorption of the amount of phosphate in the kidney. From the above explanation you will by now have realised that one may become hyper- (excess or increase) or hypo- (decrease or less) as a result of changes in either the thyroid: hyperthyroid or hypothyroid; and the parathyroid: hyper-parathyroid or hypo-parathyroid.
Toxic substances reach these glands via the blood stream.

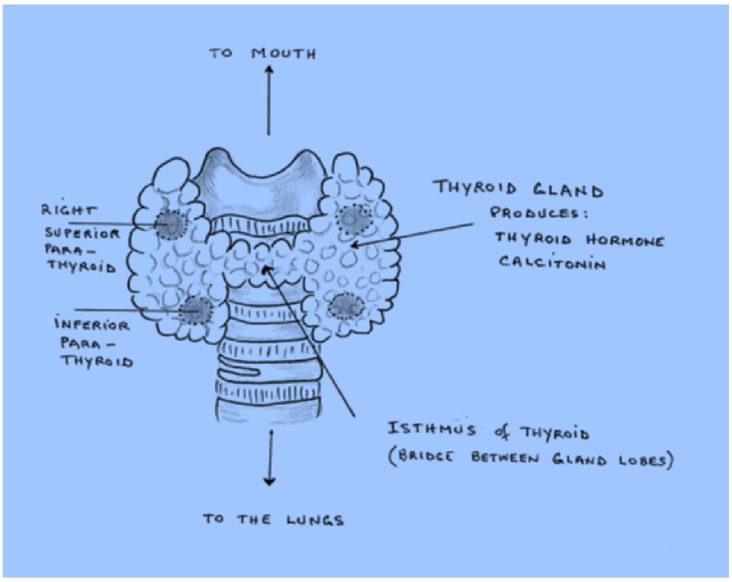


Figure 50. Illustration of the thyroid gland showing the right and left lobes joined by the isthmus surrounding the anterior part of the trachea and the hormones it produces.

The thyroid is affected by heavy metals which can trigger an autoimmune condition. Arsenic (As), aluminium (Al), plastics, flame retardants (CFC use as a flame retardant is now limited), halogens such as fluorine, chlorine, bromine (used as a fumigant), pesticides, *ethyl benzene* *(C_8H_{10})*, and endocrine disrupters, all of which impair or damage the production of the hormonal cells in the gland or interfere with receptors. Aluminium and *di-propylene glycol* ($C_6H_{14}O_3$) affect the parathyroids. Some solvents may affect the parathyroids, but as yet there does not appear to be sufficient research carried out to identify the specific effects.

Adrenals [255]

There are two adrenal glands**.** These triangular, yellowish looking glands, about 5 by 3 cm are located directly on the top of each kidney and separated from it by some connective tissue but still lying within the overall covering (renal fascia) of the kidney. Their role is to secrete hormones, most of which are essential to the function of other organs or systems within the body.

The glands consist of an outer layer which itself is made up of three layers each producing different hormones, the outer one (the cortex) and an inner core (the medulla). The cortex receives signals from the hypothalamus via the anterior pituitary that produces ACTH, which stimulates the production of: (see Fig.51, 58a, & 58b).

(A) three corticosteroid hormones [255] – 1. *mineralocorticoids* secreted by the first layer of the cortex; 2. *glucocorticoids* secreted by the second and; 3. *androgens* secreted by the third layer. The mineralocorticoid is *aldosterone,* the glucocorticoid is *cortisol* (also known as hydrocortisone), and the androgens are *DHEA*, *DHEA-S* and *androstenedione.*

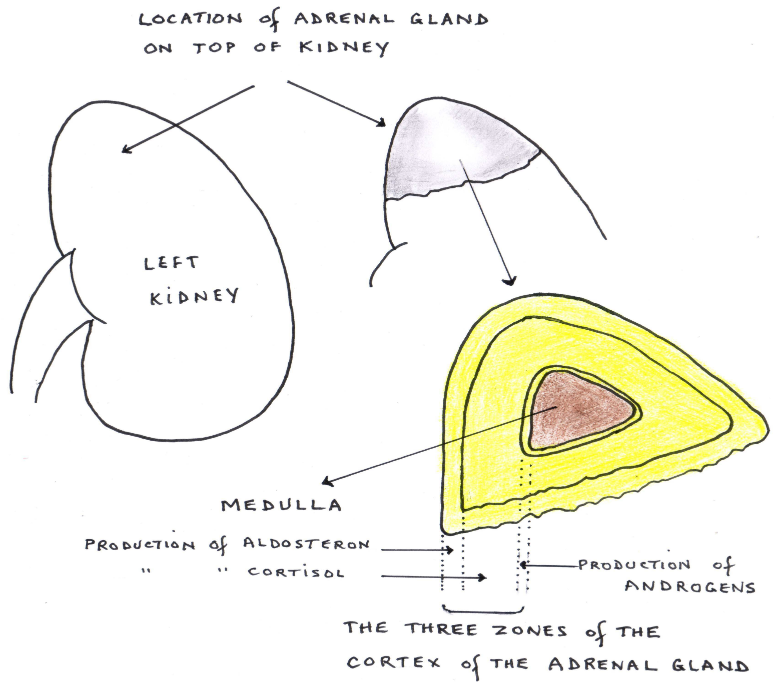


Figure 51. Drawing of the adrenal gland located above a kidney and a cross section to show the cortex and medulla and the hormones they produce.

The glands consist of an outer layer which itself is made up of three layers each producing different hormones, the outer one (the cortex) and an inner core (the medulla). The cortex receives signals from the hypothalamus via the anterior pituitary that produces ACTH, which stimulates the production of: (see Fig. 58b).

(B) three corticosteroid hormones [255] – 1. *mineralocorticoids* secreted by the first layer of the cortex; 2. *glucocorticoids* secreted by the second and; 3. *androgens* secreted by the third layer. The mineralocorticoid is *aldosterone,* the glucocorticoid is *cortisol* (also known as hydrocortisone), and the androgens are *DHEA*, *DHEA-S* and *androstenedione.*

Aldosterone, which for its release is dependent on the concentration of potassium (K) in the blood, regulates salt and blood volume (blood volume changes affect blood pressure levels). Cortisol depends on ACTH released by the hypothalamus, increases the level of blood sugar and the metabolic rate of both fats and proteins as well as decreasing the absorption of calcium in the gastro intestinal tract and suppressing the immune system. Note that both aldosterone and cortisol require the availability of cholesterol catalysed by cytochrome P_{450} for their production.

(B) The medulla produces two *catecholamine hormones* [255] which release two stress hormones: 1. adrenaline (also called epinephrine) and 2. noradrenaline (also called norepinephrine) that increase the heart and respiratory rate and by constricting the blood vessels, increases the blood pressure.

Toxic substances that affect the adrenal glands include the organic solvents such as *trichloroethylene* ($CL_2C=CCl_2$) and carbon tetrachloride (CCl_4). These alter the metabolism of carbohydrates and levels of serum electrolytes, pesticides, herbicides and fungicides, chemicals used in preservatives, and the endocrine disrupters. Others include benzene (C_6H_6), Toluene (C_7H_8), *PCBs*, and *TCDD* *(See Appendix IV).*

Pancreas

The pancreas is an organ about six inches (15 cm) long but may be longer in some cases (25 cm) [256] and lies from right to left just behind the stomach. Its function is to produce enzymes to help with the digestion of food and produce the hormones *insulin* and *glucagon* [256] which regulate the blood sugar levels of the body. This organ is relevant to Safety Professionals because a fall from height could bruise or damage the pancreas.

This organ is part of the endocrine system (see pages 127-128). In his Foreword of the Global Diabetes Plan 2011–2021 [257], Professor Jean Claude Mbanya, President of the International Diabetes Federation stated that: *"Already, 366 million people have diabetes and another 280 million are at identifiably high risk of developing diabetes."* Some people suffer from an insufficient production of insulin or, in some cases, a lack of insulin altogether causing their inability to regulate blood sugar which results in hypoglycaemia. This is known as Type 1 diabetes, which is believed to involve a combination of genetic and environmental factors and can be "*triggered by certain viral infections or some environmental toxin"*. Type 2 diabetes is the result of insufficient insulin and insulin resistance and it "*can be triggered by a variety of interrelated factors some of which are non-modifiable such as increasing age, ethnicity and a family history of diabetes… It accounts for 95% of all diabetes."* [233]

The amount of food eaten each day, as well as stressful conditions and exercise, can affect the levels of blood sugar. Low blood sugar, especially in some jobs such as working at heights, can become a serious work hazard as it results in fatigue, restlessness, aggressive behaviour, impaired vision, dizziness, nausea, and could even result in a seizure.

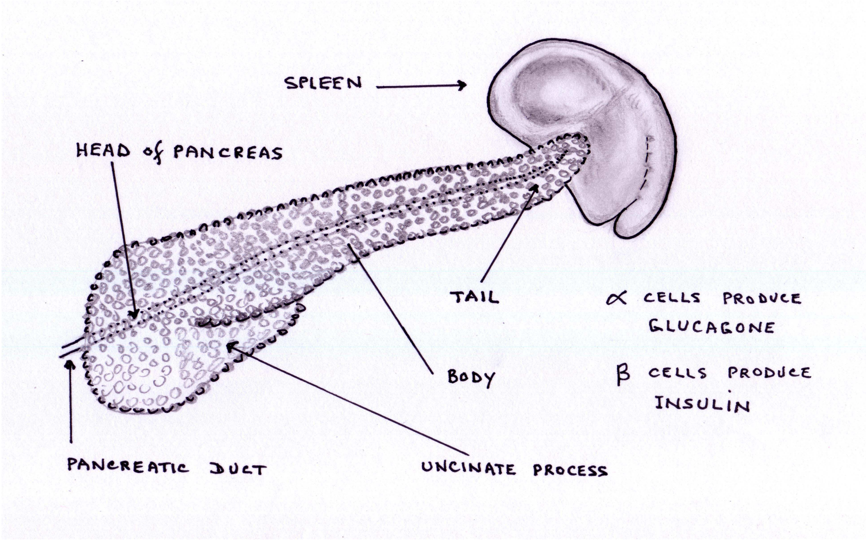


Figure 52. Drawing of the Pancreas that stretches from the duodenum to the spleen showing the pancreatic duct which releases pancreatic hormones into the duodenum just below the bile duct.

Potential ***endocrine disrupters*** (258) are found both as natural and synthetic chemicals and used in industry as solvents, lubricants and their by-products. These substances either mimic or block the function of hormones by "*disrupting the hormones' signalling pathways"* by binding to their receptors, such as they do with oestrogen or androgen receptors, in addition to others within the body and in consequence may affect development, reproduction and behaviour.

Polychlorinated biphenyls (259) (found in plastics, paints, adhesives, inks and dyes), ***polychlorinated dioxins*** (259) (resulting from combustion processes, chemical manufacture sources, metal smelting, cigarette smoking and contained in meat and fish products as well as dairy products) [259,260], pesticides such as ***permethrin*** (261), and ***phthalates*** (262), substances found in plants such as ***isoflavones*** (found in chick peas, soya products and which resemble the female hormone oestrogen), ***lignanes*** (found in barley, oats, flax, rye, wheat and sesame seed), and ***coumestans*** *(*found in split peas and both pinto and lima beans), as well as some cosmetics and personal cleansers such as ***fragrances***, ***glycol ethers*** and ***parabens*** found in 85% of cosmetics and used as an antiseptics, may cause a low sperm count, prostate hypertrophy and cancer of the testis in adult male workers. Cancer of the breast, disruptions in ovulation and uterine fibroids may occur in female workers.

Some chemicals such as *arsenic (As)*, *aluminium (Al)*, *copper (Cu), lead (Pb), mercury (Hg)*, *manganese* (Mn), *tributyltin* (banned 2008 – a very toxic substance used to prevent marine organisms growing on ships hulls) and *zinc (Zn)* may also act as disrupters. The heavy metals target the immune and nervous systems, including the memory areas of the brain. These heavy metals are found in paints, hair dyes, and lipstick. [B45]

A large number of chemicals found in many plants (natural endocrine disrupters) referred to as "*phytoestrogens exist in high levels in broccoli, cauliflower, soya beans, carrots, oats, rice, onions, legumes, apples, potatoes, beer, and coffee, although most are of low potency"* affect blood sugar levels [263].

Nevertheless, one must remember that endocrine disrupters have also been found to be of value in some treatments.

Antimony (Sb) used in medical products to treat schistosomiasis and leishmaniosis may cause pancreatitis in some people in spite of the strict controls and monitoring of patients. It should be noted that traces of *antimony (Sb)* may leak from plastic bottles containing acidic liquids. Studies have shown that in the petrochemical industries and oil refineries *benzene* (C_6H_6), *toluene* (C_7H_8), *ethyl benzene* (C_8H_{10}) and *1,3,-butadiene* (C_4H_6), which are constituents of gasoline, have caused cancer of the pancreas **[B44]** (although study results are "*not conclusive*")[B44], as have the *polyaromatic hydrocarbons (PAHs)*, *xylene* (C_8H_{10}), *trimethyl pentane* (C_8H_{18}) and *methyltertiarytributylether* (MTBE – $\{(CH_3)_3COOH_3\}$.

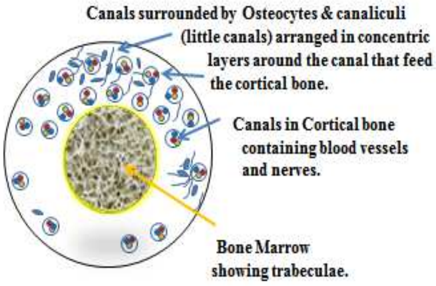
The Skeletal System (See Figures 53, 54, 55)

Bone and Cartilage

Without the 207 bones that form our skeleton we would not be able to stand or move about or support our muscles. Bones act as attachment points for tendons and other organs in our body, store minerals and produce many types of cells which would make things very difficult for us to live without. Some bones are round and others flat. In addition, there are a number of much smaller bones found in the wrists and ankle and one floating just beneath the skin on the front of each knee (knee cap).

Predominantly flat bones, such as those of the skull, sternum (breast bone) and the pelvic girdle, contain red bone marrow but it is also found in the long bones of the femur. As one grows older, the red bone marrow is converted into fatty tissue and contains a much larger proportion of yellow marrow. The yellow fat is different to the fat found elsewhere in the body. Following serious injury with severe loss of blood the yellow marrow can alter to red and provide assistance with the production of cells.

Figure 53. Haversham canals in corticial bone surrounded by osteocytes and canaliculi.



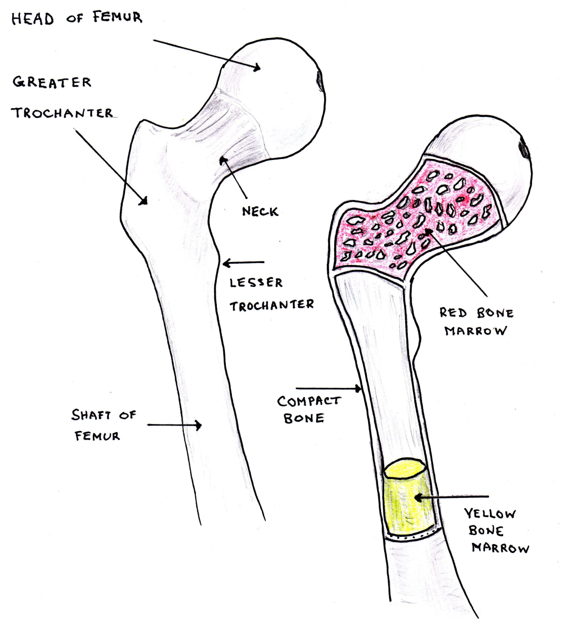


Figure 54. A drawing of the right femur showing the areas of the red marrow where cells are produced and the yellow marrow which contains fat cells.

Bones are dynamic. They contain *stem* cells from which other cells arise. Some are called *osteoblasts* and produce a protein which then hardens to form bone, others become red and white blood cells and platelets. Bone is not only active in manufacturing cells but also produces a cell called *osteocyte* [264] whose task it is to reabsorb the bone assisted by a number of hormones supplied by the thyroid, pancreas and other growth factors. This is a continuous process in bone, although the bone retains its *tensile strength* [265] (this refers to what bone can withstand before breaking apart), *shear* (a cutting that is made parallel to the bones cross-section) and *compressibility* strength. Wikipedia gives the resistible tensile strength of bone as 104–121 MPa,* the shear strength as 51.6 MPa (poor) and the resistible compression strength as 170MPa [266]. F. Gaynor and H. Lissner researched the tensile and compressive strength of the adult human parietal bone of the skull (embalmed cadavers) and found the tensile strength to be 10,230 lbs per square inch [267] (70.53 MPa).

*Note: MPa - '**megapascal'** *is the SI-derived unit of pressure, stress. It is a measure of force per unit area, defined as one newton per square meter*).

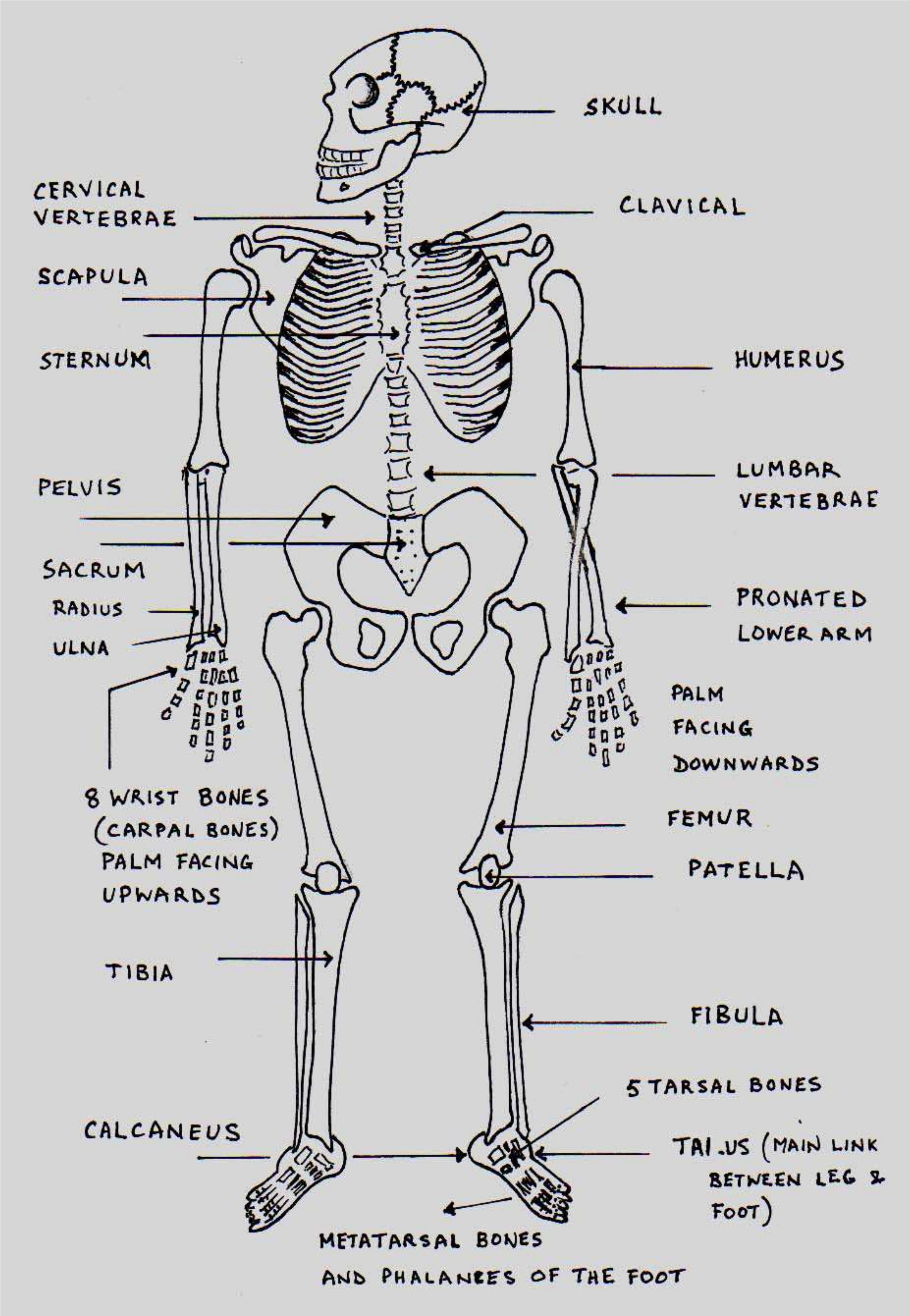


Figure 55. Drawing of the human skeleton indicating major bones sites.

Bone also contains collagen, which provides and adds tensile strength to the overall bone. *Calcium* (Ca) and *phosphate* *(PO_4)$^{-3}$* provide a compressional strength of 205 MPa which is high. Excess *Fluoride* *(F-),* some trace minerals such as *sodium* *(Na),* *magnesium* *(Mg)*, *potassium* *(K)* and *carbonate* *(CO_3^{2-})* also provide strength to bone as does *strontium* *(Sr).* Strengths obviously vary between each bone, much depending on what the location of that bone requires from it, and it must be remembered that with age, both tensile and compressibility are reduced in strength and can become more susceptible to fracture due to the gradual slowing down of the production of cells and reabsorption. Wall et al. in their article *'Age related changes in density and age-related tensile strength of human cortical femoral bone'*[(268)] stated that tensile strength increases up to the fourth decade following which it starts to decrease with age, but that *"rate of decrease of strength is greater than that of density"*[(268)]. Published material varies in the fracture strengths of load bearing bones but one must remember that so much depends on methodologies and many other biological variables, and some figures provided by researchers are higher while others are lower.

Bone is also a storage site for some toxins such as: *aluminium* *(Al),* *lead* *(Pb),* *cadmium* *(Cd),* *plutonium* *(Pu),* *strontium* *(Sr) and radium 226 (Ra).* Cartilage is not affected by *plutonium* *(Pu).*

Other important substances that affect bone, and possibly cartilage, include *benzene* *(C_6H_6)* and some of its derivatives like *phenol* *(C_6H_5O).* Phenol is used in the manufacture of plywood and the preparation of other substances such as disinfectants, aspirin or vanilla. Interestingly, it is present in a number of the proteins of the body. Phenol is a known carcinogen and found in cigarette smoke, plastics, oil refineries, detergents, pesticides, and in motor car exhaust. Long term inhalation exposure to *benzene* (C_6H_6) vapours at petrol stations is something to consider in certain countries.

Aniline ($C_6H_5NH_2$)is another substance affecting bone, which is used in the manufacture of dyes, plastics and polyurethane foam.

Fluorides (*F-)* found naturally in water is generally present in low levels (around 0.05 ppm) and much depends on geological formations, as they may be found in higher levels in some countries. Fluorides are also present in some brands of bottled waters with much controversy as to where the fluoride originated from, e.g. due to leaching from the constituents of plastic bottles made from *polyethylene terephthalate* or PET.

Fluorides *(F-)*[(269)] are also found in some types of tea which translocates into the plant leaf from the soil and water, and some wines. It is also present in some vegetables and fruits. Excess of sodium fluoride causes thickening of the bone (osteofluorosis) [(270)] and white spots in the tooth enamel or in hand/toe nails. Note that in continental European countries (97%) fluoride is not added to drinking water [(271)]. The mineral cryolite (*Na_3AlF_6) - sodium hexafluoroaluminate*), which is used in the production of *aluminium* *(Al),* also causes hardening of the bones resulting in vulnerability to fractures (brittle bones) [(271)].

The burning of coal [(272)], production of cement plants, aluminium smelters and phosphate fertiliser in addition to the output from volcanoes are other sources of fluorine compounds. The ceramic industry is yet one other source of exposure.

The conflicting remarks found in the literature with regard to the levels of the safety of fluoride toxicity is confusing and leaves a lot of uncertainty in what is and what is not a safe level, particularly in long term exposures. What is certain is that it is a very toxic chemical.

Vinyl chloride (C_2H_3Cl) is a gas that is unstable at high temperatures and is made from the breakdown of other substances such as *trichloroethylene* (C_2HCl_3). It is used in the making of a number of plastic products such as *PVC* (polyvinylchloride) for packaging or pipes and it is released into the atmosphere from manufacturing plants, waste sites and contaminates water. Exposure is mainly from inhalation and skin contact. It can cause reabsorption of the bone of the distal (furthest away) bones of the fingers of the hand. It is considered a carcinogen.

Cadmium *(Cd)* is one of the metals found combined with other elements: zinc ores, *copper* *(Cu),* coal, *chlorine* (Cl_2) and sulphur *(S)* amongst others. When I carried out research work measuring the large number of elements present in street dust all over the island of Malta many years back during my time at Imperial College, London, I found that cadmium *(Cd)* was no exception. Although its use globally has decreased, mainly because of its toxicity, which not only affects bones but almost all of the human body systems, it still has many commercial uses. Those who mine or work in smelting ores that contain *cadmium* *(Cd)* or work in Cadmium-Nickel (Cd-Ni) battery plants (some have now substituted these with nickel metal hydride) are exposed to the metal. The glass, printing, tyres, paints and the manufacture of solar panel film cells, and the preparation of absorption rods for nuclear reactors (cadmium absorbs neutrons) to control fission are some of the commercial uses for *cadmium* *(Cd).*

The kidney is cadmium's target organ although it can have direct or indirect effects on the lungs, olfactory nerves, blood and bone. Except in acute high dose exposure, various studies show that indicators of kidney damage do not generally appear for about a decade. Glomerular filtration rate is affected and albumin appears in the urine. *Creatinine* levels also increase, with impairment threshold levels at 2 to 4 nmol/mmol creatinine in the normal population. Industrial atmospheric exposure greater than 300 mg/m^3 and 10 ug/g of creatinine in the urine indicates that the risks to workers exposed to *cadmium* *(Cd)* are high. In the later stages of renal damage, workers are at higher risk than the normal population of having kidney stones.

Cadmium (*Cd)* is stored in the bones but it is believed that once cadmium reaches the bone, even at low levels, the balance between bone formation and its breakdown (*cadmium activates specific bone cells to dissolve the bone*) is altered so that bone loss is accelerated. Maryka Bhattacharyya and a team of researchers working on bone response to *cadmium* *(Cd)* on a project funded by the DOE Office of Science's Biological and Environmental Research Program and the National Institute of Environment Health Sciences showed that cadmium has an effect on bones hours after exposure and at blood concentrations below OSHA's action level of 5ppb [(273)]. Even more importantly, they *'identified specific genes involved in the dose response',* so that *cadmium* *(Cd)* exposure must be having some effect on gene expression causing release of particular proteins in the process of bone loss.

One must not forget that the inhalation of cigarette smoke is also an important source of *cadmium* *(Cd)* and that although cadmium is considered as a probable carcinogen there does not seem to be sufficient evidence of lung cancer in cigarette smokers.

<u>Eyes</u> (See Figures 56a, 56b,)

A symbol of the Maltese islands, the 'luzzu', a Maltese boat believed to date back to Phoenician times, is a fishing vessel painted in bright blue, yellow and red with an 'eye' painted on the bow on both sides. A number of Mediterranean countries and some others still paint what is thought to be the 'lost eye of Horus' which he lost in a battle to avenge his father's death – his father was Osiris, the god of protection against evil. It is possible that the 'eye' also represented 'seeing their way across the seas'. However, if protection against evil is the correct interpretation, should an 'eye' be painted at appropriate workplaces to remind us of this important need and encourage eye surveillance and preventive control? Alternatively, one could consider 'seeing our way safely' through the days of work, as the eye sculptured on the watch towers of bastions or, in more recent times, digital street cameras.

On an observational walk through a workplace, safety or health professionals would be unlikely to look closely at the eyes of those who work there, unless of course some request had been made of eye complaints, or they were aware of what they should be looking for in certain industries where the potential for eye conditions may exist.

Knowledge of such industries and common eye complaints can, however, be of much value not only in the identification of potential problems and prevention of accidents, and the safety of co-workers, but also to those in whom some condition is observed, identified and if possible treated, such as visual acuity assessment. Such evaluation examinations should consider the work tasks undertaken by the worker and the conditions of the workplace.

If you look into an average normal eye all you will see is the skin and margin of the eyelids, eyelashes, the white of the eye (the conjunctiva) over which flow tears, the black circle in the middle of the eye (the pupil), which varies in size between people, the area surrounding the pupil which varies in colour (a pigment) called the iris, and a shiny transparent convex disc over both the iris and pupil (the cornea), which if you look carefully enough you may, in some, notice that the cornea is covered over by a contact lens. Visualisation of the cornea may be difficult if they are wearing corrective lenses (spectacles). Remember that a safety professional is part of a Health and Safety Team and, indeed, the primary observer at most workplaces that lead to prevention and control. Peripheral vision is important to many workers (see Figure 56b).

A number of chemicals irritate the eyes causing excessive watering (tears), redness, swelling or discharge, even damaging the outer layer of the cornea and therefore reduced clarity of vision. Much depends on the strength of the irritating chemical as this may then penetrate through the cornea's second, and then into its third layer of cells, which contains a considerable number of nerves, and causes an increase in pain.

From here, there could be further entry into a fluid (the aqueous humour) that lies behind the corneas third layer and therefore between it and the lens of the eye, which focuses light passing through the pupil in this chamber of fluid into the interior – an area filled with what is called the vitreous humour, to reach the retina (a lining containing nerves and blood vessels that is light sensitive). This light is then transmitted via the optic nerve to the brain for interpretation and clear structural development of whatever object(s) visible light wavelengths (300–700 nm) are being received by the eye.

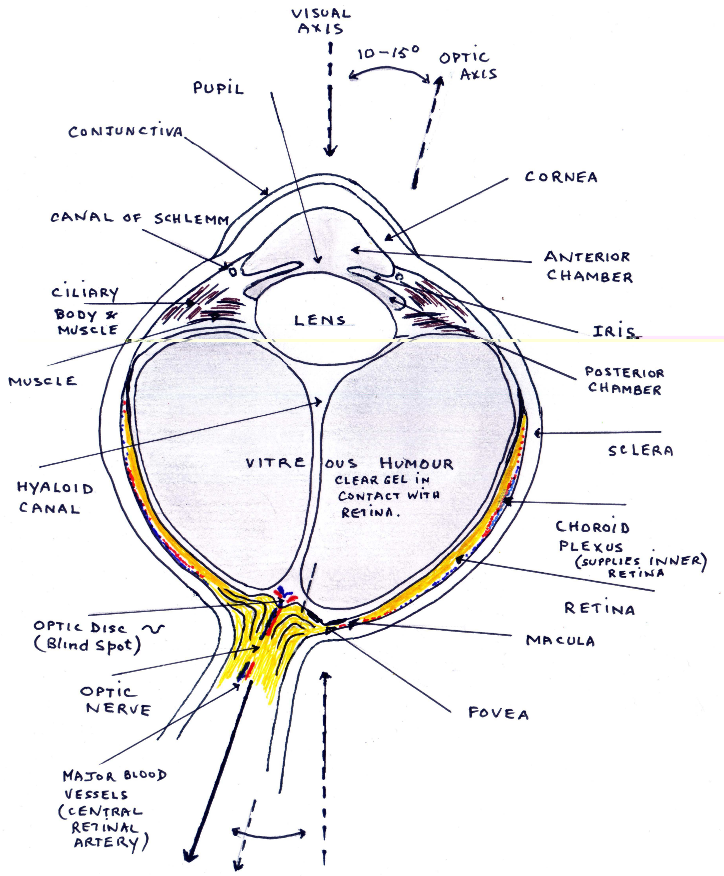


Figure 56a. A sketch of the internal structure of the eye and the peripheral visual field (awareness of objects above, below, to the left and right) of both eyes (note also each individual eye is restricted by the nose – with one eye closed the nasal side of peripheral vision with be restricted to 60°).

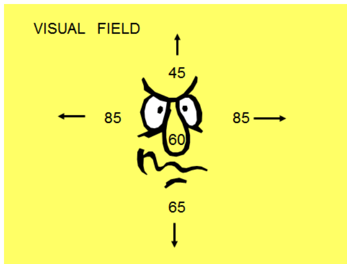


Fig. 56b. Sketch of the peripheral visual field.

Those that work indoors or outdoors whose eyes may become exposed to many chemicals, toxic substances, dusts, gases and fumes are found in chemical laboratories, printing, open and closed mining industries, construction, aircraft paint shops, leather tanning, electroplating, paint manufacture, welding, general offices and many others. Simultaneously, they may also be exposed to wind, heat and poor lighting or radiation.

These substances reach the eyes either via the respiratory system, ingestion from sea fish or dental *amalgam* (mercury alloy, the material of ‘silver’ tooth fillings), the skin, or directly through the conjunctiva, causing red eyes, such as from *sulphur dioxide* (SO_2) exposure or a foreign body. Dry eyes and clouding of the cornea are caused by mercury vapour. Fleshy looking growths referred to as pterygium and pinguecula, due to chronic exposure to dust wood, or silica in sandblasting, arc eye in welders, cataract formation as a result of exposure to solar radiation (UVa, and a little UVb light), or accidental exposure to *ethylene oxide* (C_2H_4O) are some other conditions [274].

The vapours or splashes from organic solvents (fat soluble alkalis and phenols) penetrate the cornea on contact. Acids also damage the cornea causing it to become opaque or destroy its tissue on contact. In addition, surfactants (detergents, and soaps) above certain concentrations are both fat and water soluble making penetration easier.

Ammonium hydroxide, sodium hydroxide and lime (*calcium hydroxide*) all to a lesser extent, as well as cement, produce chemical burns of the eyes. Volatile oils, like those found in onions, are irritants and substances such as pollens or feathers may cause allergic reactions following repeated use.

Other chemicals affecting the eyes include organic mercury such as *methyl mercury* – (CH_3HgCH_3), *cyanide* (CN-), *nitrates* (NO_3^-), *ammonium* (NH_4^+) and acids in mining operations, as well as *barium* (Ba) and *strontium chromate* ($SrCrO_2$), if one is exposed to paint primers in *aluminium* (*Al*) metal painting in the aircraft and other industries. *Ammonia* (NH_3) or ammonium (NH_4^+) exposure causes swelling of the eyelids, irritation and increased watering of the eyes. *Ammonia* (NH_3) is a corrosive substance and a highly irritating gas. Soluble in water, it is used in many industries (agriculture, as a fertilizer, textiles, household cleaners and pesticides, plastics manufacture and other industries [275].

Both *benzene* (C_6H_6) and acrolein may cause eye irritation due to the inhalation of the substance or through skin absorption. Probably the most common complaints of eye irritation and depending on the levels of exposure, redness, itching or a burning sensation of the eyes, are due to exposure to chlorine products.

Eye irritation to *styrene* (C_6H_5CH,CH_2) has also been reported in the literature by several researchers including Carpenter *et al.* (1944) [276], Stewart *et al.* (1968) and (Kohn 1978)[277].

Nail polish and polish removers cause eye irritation. These include *acetone* (C_3H_6O), *butyl acetate* ($C_6H_{12}O_2$) a polish, *ethyl acetate* ($C_4H_8O_2$) also used as a nail glue, *isopropyl acetate* ($C_5H_{10}O_2$) polish remover, and *formaldehyde* (CH_2O).

Naphthalene ($C_{10}H_8$) vapour at exposures of 15 ppm have been reported to cause eye irritation but following long term exposure at higher concentrations may cause cataracts. Eye contact could injure the cornea. Long term exposure to naphthalene has been reported as having caused cataract in workers in naphthalene storage companies.

Carbon disulphide (CS_2) has been reported in the NIOSH Occupational Health and Safety Guidelines to cause decreased ability to seeing in the dark as well as blind spots, whilst Hernberg *et al.* (1970) [278], Sugimoto et al (1983) [279], and others have reported dot haemorrhages and micro aneurysms of the retina.

In spite of the many hazards from chemical and toxic substances, it should be remembered that even water will cause temporary ‘red eyes’ and that the eyes have a response system for their own protection. Tears help to dilute and carry away substances reaching the eye and contain antimicrobials as well as *immunoglobulins* (IgA and IgG) that can bind to bacteria and attack viruses. The cornea also provides a defence to substances trying to gain entrance to the inner aspects of the eyeball, as well as secreting substances called *cytokines* or ‘immunomodulating’ agents, which help to stimulate the movement of protective mechanisms to the site of the invading substances.

<u>Ears</u> [254] (see Figure 57)

Mark Anthony, in William Shakespeare's play 'Julius Caesar', said at his funeral: "*Friends, Romans, Countrymen, Lend me your ears"*[279]. As obvious as the ear is in communication, it took up to the 19th century before it became evident that it had other functions as well including maintaining our balance or equilibrium and in reflex responses to sound.

Our range of hearing is 20–20,000 Hertz. When testing for workers' hearing loss the range of frequencies tested are generally from 125 to 8000Hz [280]. Sound waves that are within our hearing frequency (Hz), which have a loudness (an ***<u>intensity</u>*** measured in decibels (dB) as watts/m^2, or measured as pressure *(newtons/m^2)* in relation to atmospheric pressure) are referred to as *<u>audible sound</u>*. The lower threshold frequency limit is taken as 1000 Hz, which is referenced as zero intensity, although it is actually at 4 dB. The threshold of hearing varies with the frequency [281].

Audible sound, in dry air and a comfortable room temperature of 20°C (68°F), travels to the outer ear (the pinna) at about 344 meters/sec (11.296 ft/sec). The pinna helps to amplify the sound on its way into the canal of the outer ear to reach a disc (ear drum) somewhat vertically oblique and attached to three small bones, the last of which is in contact with another disc (the oval window), all forming part of what is called the middle ear. This has an opening to a small tube that connects to the back of the throat. Remember swallowing as you are landing at some airport? It helps to equalise the pressure on your ear drum as you descend from higher altitudes, but it is also an easy route to infections to the middle ear from the mouth and throat.

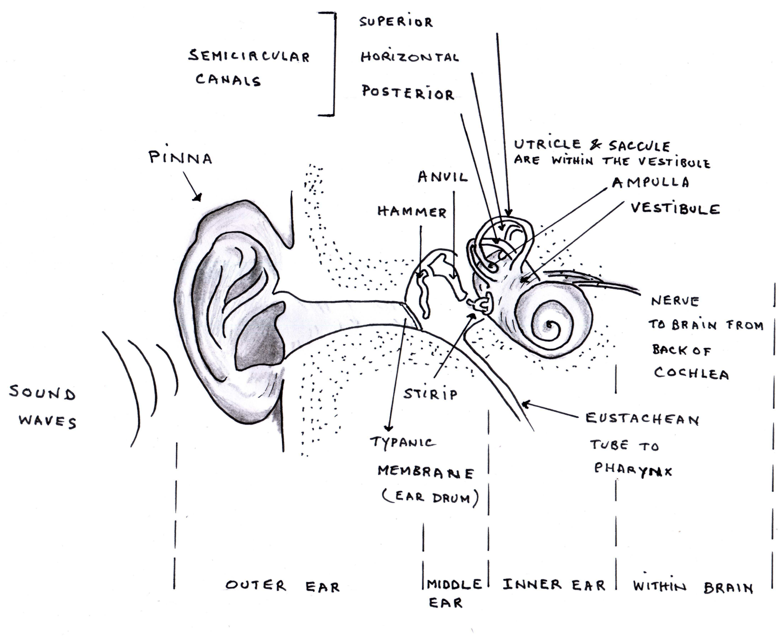


Figure 57. A drawing of the four sections of the right ear. Bone is indicated by spotted areas which extend further as part of the skull than is indicated in the drawing

From the time that sound waves reach the pinna to when they arrive at the oval window, sound is amplified up to about 20 dB. The oval window then vibrates a liquid inside a small canal containing between 16–2,000 tiny 'hairs' [281], each receptive to different frequencies (some 1,500 of them) that move the signals to a nerve (*cochlear nerve*) and on to the brain for interpretation and response. This tiny canal about 3.2 cm (2¾ inches) long is not a straight tube, so mentally roll it up and it looks like it really is, a rolled up tube looking like the shell of a snail, and referred to as the *cochlea.* The hairs at the front end receive the high frequencies and are the first to deteriorate with age, while the ones at the end are receptive to low frequencies. They may be damaged either by mechanical stress or the absorption of toxins.

Above and to the front of the cochlea, lying partly above the middle ear are three loops called the semi-circular canals that contain tiny hairs in a liquid *(endolymph).* Every movement of our body disturbs the liquid which then causes the hairs to sway and signals are sent to the brain (via the *vestibular nerve*) to maintain or correct our balance. This nerve joins the cochlear nerve on its way to the brain. These three canals lie in different positions. The horizontal one senses rotation like looking to the left or right, the vertical canal (facing the pinna of the ear) senses vertical balance (forward or backward), and the inferior (also vertical but at an angle to one or other side depending on the ear's location (left or right) and at right angles to the vertical canal facing the back of the eyes) senses bending movements of the body to the left or to the right.

Hearing loss, equilibrium and brain (hearing or auditory) reflex responses can all be affected by chemicals and toxic substances. Some of these substances may also create a synergy with other substances increasing or decreasing the effects. In some cases when exposure ceases, the effects no longer remain and an example of this is tinnitus *(buzzing in the ears)* but in others it may be permanent.

A number of substances toxic to the eyes also affect the ears such as: *mercury (Hg),* (hearing loss in all frequencies but greater in higher frequencies), styrene (abnormal hearing reflex and hearing loss, *carbon disulphide* *(CS_2)* abnormal hearing reflex and balance, but also affects low and high frequencies, *xylene* *(C_8H_{10})* - affects sensory cells in cochlea, *trichloroethylene* *($Cl_2C=CCl_2$)* - affects balance and high frequency hearing loss.

There are others such as arsenic (As) which target the cochlea resulting in hearing loss in low frequencies (125–500Hz) and also affects balance, lead (Pb) causes demyelination of the cochlear nerve and hearing loss in high frequencies, carbon dioxide can induce mild or large threshold shifts, depending on exposure levels, and also causes synergy with noise in all frequencies, *toluene* *(C_6H_{12})* which causes cochlear damage, hearing reflex and balance and *hexane* *(C_6H_{12})* which affects the semi-circular canals causing dizziness, *manganese* *(Mn)* - hearing loss in high and low frequencies, and *butyl nitrite* *($C_4H_9NO_2$)*, have all been described in earlier chapters.

Some chemicals used in medical treatment such as salicylates (aspirin is an example that may cause both tinnitus and hearing loss with long term usage), or additives to other substances, such as to some antibiotics, can be absorbed by and damage the hairs cells in the cochlea.

It may be worth recalling that when the semi-circular canals are affected by toxic substances the brain may rely on visual inputs to help correct any imbalance of the body. This effect is seen because the eyes move from side to side (nystagmus), and this results in the person feeling dizzy (vertigo) from the eye movements.

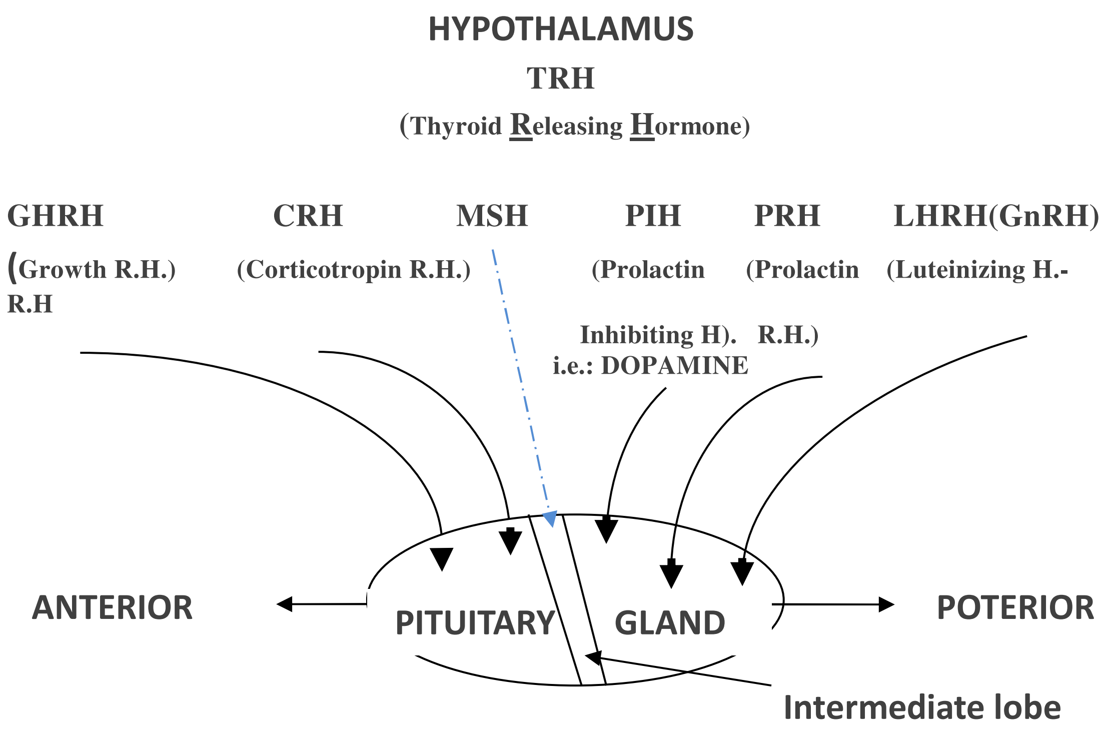


Figure 58a. An expanded representation to show which part of the Pituitary gland hormones are stored and released.

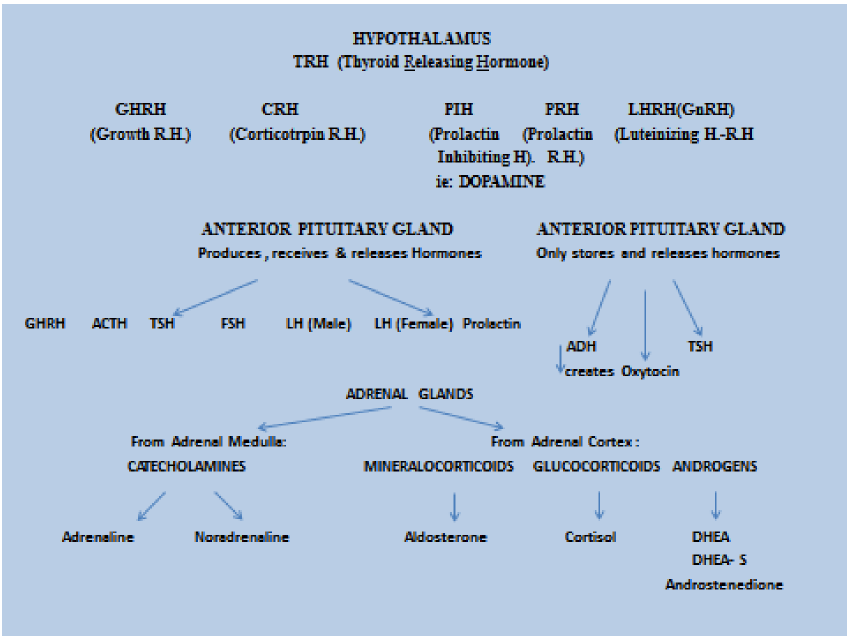


Figure 58b. A visual demonstration of the hormones produced and stored by organs described in chapter 5 p.131-135.

Note: MSH *(melanocyte stimulating hormone)* is stored in the intermediate lobe between the anterior and posterior lobes of the pituitary.

The Kidneys (See Figures 59-62).

The kidneys appear like two large butter beans in a pad of fat, with the adrenals sitting on top of them. They are both enclosed in a sheet of connective tissue (this is the renal (*kidney)* capsule), and lie high up inside and at the back of the abdomen outside the *peritoneum*, one on each side of the body, and protected by the lower ribs and the muscles of the back inside the abdomen on which they lie.

Externally, the muscles of the back also provide additional protection. The concave side of each kidney (which faces the spine towards the middle of the body) as it lies on the back muscles internally, extends into a triangular (funnel-like) shaped bag (the pelvis) which receives the filtered fluid (urine) before it passes into a tube (the ureter) that travels vertically down along the back inside muscles to a bigger bag (the bladder) before it passes via another tube (the urethra) directly from the bladder as waste to the outside.

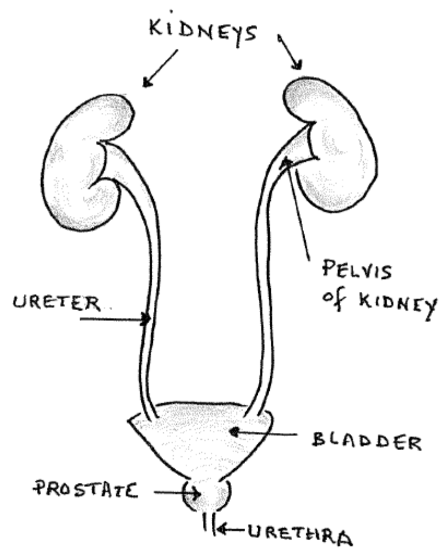


Figure 59. Sketch of the right and left kidneys.

The kidneys receive about 25% of the blood pumped out of the heart, which means that they are exposed to large amounts of any potentially toxic substances present in the blood supply to them. At a macro level, the kidneys are made up of a cortex just beneath the renal capsule and a medulla more internally below the cortex (see Figure 61).

Unfortunately, of the many toxins that the kidneys deal with (it is a substantial target organ for toxins), there are only a few that produce easily recognizable acute (immediate) syndromes. Toxins in the kidneys produce more chronic (long-term) conditions and exposures often go unnoticed at first. The kidneys, however, have a good reserve capacity and can work well even with the gradual loss of some of their filtering units (the *nephrons*) of which there are about one million or so in each kidney. Due to improvements that have taken place in industry as a consequence of better occupational hygiene practice, few cases of acute kidney malfunction are seen today. Nevertheless, acute exposure to heavy metals such as *chromium (Cr), mercury (Hg), cadmium (Cd), lead (Pb)*, can produce necrosis of the kidney *tubules* which are part of the nephron (see Fig. 61 & 62). *Cadmium (Cd)* is one to watch out for because acute exposure may be above warning signals (i.e. symptoms of cadmium poisoning) [(282)]. Lead is rarer today.

Other causes of acute kidney dysfunction include the halogenated hydrocarbons-like solvents – *carbon tetrachloride*, *chloroform, trichloroethylene* and *tetrachlorethane*, the non-halogenated hydrocarbons such as toluene, *phenol and pentachlorophenol (a preservative for timber), and some pesticides* such as the *organophosphates* and *dioxin*. *Arsine* is another to watch out for; it is a haemolytic agent which dissolves red blood cells, is a colourless gas, has no warning signal and is almost odourless if pure.

Naphthalene ($C_{10}H_8$) inhalation may also cause red blood cells to dissolve (haemolysis) with resulting anaemia. This substance is used in treating wool and when packing cloths, carpets, etc. for long term storage. It is also used in public toilet urinals where environmental levels in certain areas may be higher than they should be.

Chronic exposure to *lead (Pb)*, *cadmium (Cd)*, *mercury (Hg)* fumes, *beryllium (Be)*, *silicates* (SiO_4^{4-}), organic solvents, *carbon disulphide* (CS_2), and others can all lead to kidney dysfunction of different severity. When referring to any chemical compounds one should take care to ensure that the correct compound is identified in relation to its action on target organs. An example is *mercury (Hg)* which exists in three different compounds all of which are toxic but have different or multiple target organs. *Elemental mercury* is in liquid form at room temperature and can be inhaled as a vapour; it affects the lungs, C.N.S and kidneys. Inorganic *mercury* (Hg) is a combination of mercury with other elements, such as oxygen, and mainly causes kidney but also respiratory, C.N.S. and GI tract damage, while *organic methyl mercury* (CH_3HgCH_3) causes central nervous system damage.

Biological Factors That Effect Toxic Substances

Important biological factors that affect toxicity include:

1. Species differences - susceptibility, different metabolism
2. Genetic disposition - genetic defects, lower metabolic activity
3. Age - response of an ageing workforce
4. Sex - different male and female response to toxic substances
5. Diet - may cause a change in metabolism
6. The presence of disease - affects metabolism and enzyme function.

Species

Species vary in their response to chemical substances, and there are metabolic differences between them. The metabolic rate of one species may be different to that of another. In consequence, response to toxic substances will not be the same. Some species can be a lot more sensitive than others, or one species may be sensitive and the other insensitive to substances foreign to the organism, thus eliciting a different toxic response. Species difference can be of value, and the extent and particulars of how a particular species responds is made use of when investigating some chemicals, e.g. pesticides such as the organophosphorus compounds which are much more toxic to insects than they are to humans.

Genetic Disposition

There are genetic metabolic differences in individuals and medical drugs sometimes elicit adverse reactions in some of these individuals as a result of these differences. Some individuals are born with genetic defects like an absence of the enzyme system cytochrome P450. This enzyme system, of which there are about 27 different types, is normally found in most tissues but its highest concentration is in the liver and it catalyses the first stage of metabolism of many foreign substances that enter the body.

There are other enzymes which vary genetically. Alcohol dehydrogenase is one, and some individuals find that they are more sensitive to the ingestion of alcohol because they metabolise it at a much lower rate. Other individuals may actually develop a reaction to alcohol. It is the body' defence to alcohol ingestion. Present in liver (it alters the alcohol to *acetaldehyde* *(CH_3CHO)*, which is a more toxic substance and converts this to acetate, which is used by the body cells. Note however, that this enzyme converts *methanol* *(CH_3OH)* to *formaldehyde* *(CH_2O)*, which is carcinogenic and damages proteins in the retina which can lead to blindness. In the liver *naphthalene* ($C_{10}H_8$) is broken down to other compounds, one of which is alpha-naphthol ($C_{10}H_7O_8$) a toxic organic compound that lowers testosterone levels. This is also linked to the breakdown of red blood cells as a consequence of a genetic deficiency of an enzyme called G6PD (glucose 6 phosphate dehydrogenase). G6PD is a deficiency on the X-chromosome; its function is to protect red blood cells as well as convert carbohydrates to energy. It is a fairly common deficiency in Mediterranean countries and predisposes a person to non-immune haemolytic anaemia (for more detail see MSDS of alpha-naphthol).

Human response to foreign chemicals can be very different. Hyper susceptibility is an unusually high response to some does of a substance (a deviation from the normal). Hypersensitivity is a form of hyper susceptibility and it is an acquired sensitisation to a substance. Some individuals are 'hypo' susceptible and show a low response to a substance.

At places of work, hypersensitivity reactions are mostly seen as:

1. Asthmatic responses. The chemical TDI (toluene-2,4-diisocyanide) used in the manufacture of foams and plastics will (if the length and concentration of exposure to it is sufficient) result in an asthmatic attack.

2. A skin reaction: itching skin, following which the skin erupts. This could happen with epoxy resins and metallic nickel (Ni).

Age The elderly metabolise many chemicals much less efficiently than younger individuals. With an increasing elderly workforce this must be taken into account in the evaluation of risk.

Sex Hormonal differences between genders can result in different responses to many chemicals. Hormones can affect metabolism and different enzyme systems, which in turn can also affect metabolism. Males may metabolise substances faster than females in some species. There are also gender differences in excretion of chemical substances. A particular tumour of the liver occurs more in males than females because the methods of excretion of the chemical is different (in the male excretion it is via the biliary system, whilst in the female it is excreted via the urinary system).

Diet The nutritional state of the individual may have some effect upon the susceptibility of toxic compounds, probably due to the effect upon the metabolism of the individual or the inability of the body systems to develop or maintain essential enzymes or other cellular structures and poor nutrition can effect an individual's immunological status. However, most of the studies that have been carried out have been on animals and it is difficult to extrapolate these to humans.

The presence of disease

Metabolism is affected by the presence of disease. Influenza is known to do this. Unfortunately, we do not yet have sufficient knowledge on health status and biological response to toxicants in this or some other conditions. Disease of the liver may affect the function of the biliary system and toxins that are excreted via this system may accumulate and toxicity therefore increases.

It should be noted that biological response to toxic exposure may be either acute or chronic. The effect may also either be reversible or irreversible. Chronic lead (Pb) poisoning effects, except those to the kidney in the late stages, are reversible, but those of acute mercury (Hg) poisoning are irreversible.

Environmental Aspects

Environmental factors such as levels of barometric pressure, temperature, or relative humidity, quality of air and water, biological, and chemical factors may all affect the metabolism, and toxic response of an individual, who may also be exposed to chemical substances including medical drugs. In consequence, enzymes in the body may be altered (increased or decreased in their number), and some of these enzymes may be the specific enzymes that normally deal with the toxic substance to which the individual is exposed. This will result in either an increase or decrease in the toxicity of the substance in the body. Workers are often exposed to a mixture of toxic substances so that some chemicals in the environment can have an effect on the toxicity of other chemicals by inhibiting enzyme activity. Workers exposed to a solvent, toxic to the liver, may inhibit metabolism of other substances such as *ethanol*(C_2H_5OH). Individual absorption, metabolic processes and elimination of toxic substances may therefore be affected. It is important to consider environmental aspects in this respect.

Chapter 6 Excretion of Toxic Substances

The cells of the body undergo many processes, producing or converting other products, altering proteins, detoxifying both chemicals and toxic substances, and the waste products must be eliminated from the body to avoid their accumulation. The length of time that a toxin remains in the body defines how much damage it may cause.

The Kidneys

Although the kidneys are the major route of excretion for most substances, they are not the only route of excretion. Excretion also occurs via the lungs in the expired air, and via the GI tract in the faeces, as well as via sweat, human milk and other body fluids such as tears. This also happens with volatile and gaseous substances, including fumes, which may be a mixture of a gas and small particles, mists (a dispersion of liquids in a gas), dusts and radioactive substances, which may be attached to dusts or smoke, such as radon.

Blood reaches a kidney via a main artery which then branches out towards a kidney's many filters (glomeruli – see Fig. 60) before moving on to supply other areas of the nephron (a unit of filtration - see Fig. 61) and other tissues of the kidney outside the nephron and where reabsorption also takes place, prior to exiting as the renal vein, to join the venous system taking blood back to the heart. There are about one million glomeruli in each kidney, which are the starting point for filtration in the nephrons, (see Fig. 62) composed of the glomerulus, a capsule and proximal tubule, where absorption/secretion takes place, a descending tube/limb, a loop that feeds an ascending tube/limb and a distal tubule where more reabsorption into the blood stream goes on, so that only about 1% of what is filtered results as waste and passes into the ureter to reach the bladder from where it is excreted from the body [283].

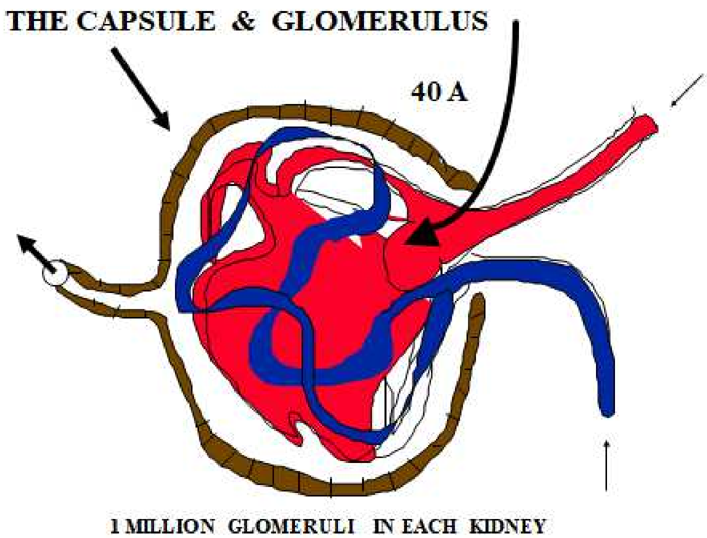


Figure 60. A diagrammatic representation of a glomerulus. There are about 1 million glomeruli in each kidney, which are the starting point for filtration in the nephrons.

The glomerulus has large pores [40A (A = angstrom = 0.1 nanometre = 1 millionth of a millimetre)], and compounds will be filtered unless their molecular weight (which is the sum of the weight of all its atoms) is greater than 70,000. Most toxicants do not have a molecular weight more than 70,000. The glomerulus is negatively charged.

The energy required for filtration to take place depends on the pressure of the blood circulating in the body, generally 120 mmHg, which reaches the kidney together with a supply of oxygen. The pressure in the glomerulus vessels is about 75% of the pressure in blood vessels, meaning the glomerulus requires a minimum of about 90 mmHg to function correctly. The pressure difference between that of the blood vessels in the glomerulus and the tissues in the glomerulus, including the thickness of the membrane, is necessary for filtration to take place. Note that a pressure gradient exists along the whole renal excretory system from the glomerulus to the bladder.

A male excretes about 125ml of filtered fluid every minute, but only about one ml reaches the ureter and bladder from this amount. Females about 115 ml. The remaining quantity is reabsorbed during its passage down the tubules within the nephron. The degree of filtration is affected by *protein binding* (see Fig.19 p.68). If the compound is bound, it is then too large to be filtered through the pores of the glomerulus. Protein binding does not affect *active transport* which utilises carrier systems. The problem with carrier systems is that the system (carriers) may become saturated, and as the concentration of the toxin in the blood fluid increases, accumulation occurs. This is because the rate of elimination with *active transport* is constant, unlike absorption and filtration where it depends on the concentration pressure gradient. However, once filtered, the toxicant can then either be excreted or reabsorbed via the tubules.

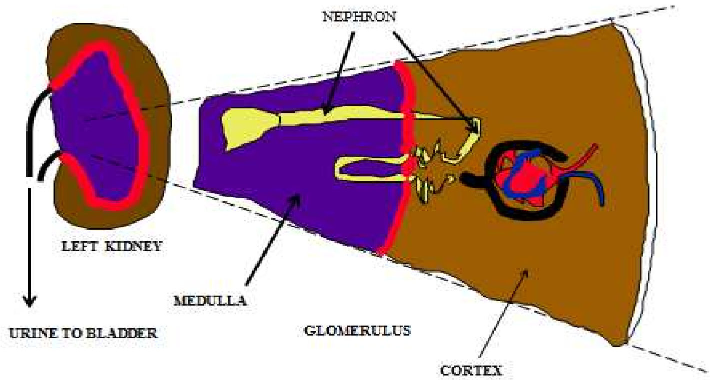


Figure 61. A rough sketch to demonstrate the cortex and medulla of the left kidney, showing in cross-section the location of a unit of excretion, the nephron, as it passes from the cortex to the medulla to excrete urine to the kidney pelvis (see Fig. 59 p. 146). The tube from the pelvis, called the ureter, to the bladder is not shown.

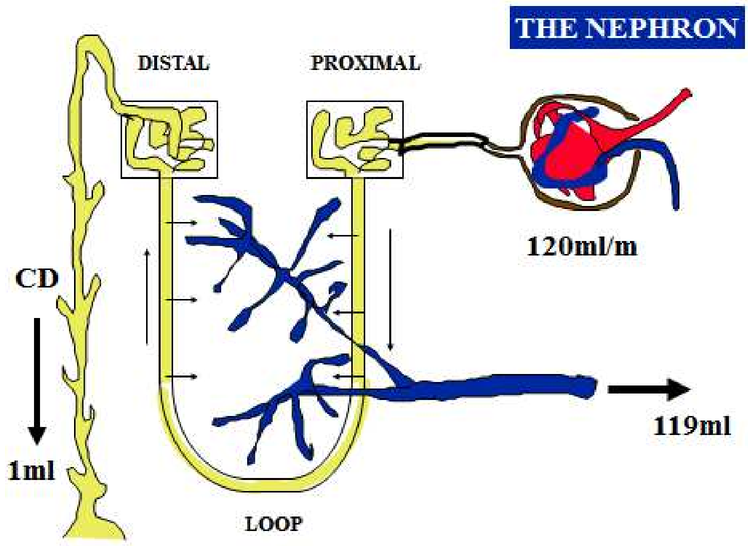


Figure 62. A rough schematic representation of one nephron consisting of the glomerulus, a proximal tubule where absorption takes place, a descending tubule, a distal tubule for more reabsorption and a collecting tubule, which then excretes the urine into the ureter and on to the bladder. CD = collecting duct.

No blood cells or albumin (an anion of 3.5nm molecular diameter) can pass through a healthy filter, and no glucose is excreted unless the distal reabsorption tubule is impaired. Water and fat soluble substances pass through the filter easily, and fat soluble molecules will diffuse out of the blood and into the tubules provided a concentration gradient exists at the time between the pressure in the blood and that within the tubules. The more lipid soluble molecules there are in the blood, the more will diffuse into the tubules. Fat soluble molecules that are toxic and reabsorbed means that toxicity levels are, to some extent, maintained in the circulating blood. Age or previous damage by infections of the kidney, as well as the pH of the urine (alkaline or acid), affects substance *ionization*. Increase in alkalinity increases ionization and this results in better elimination of filtered substances such as weak acids (an acid that is only partially dissociated in a water solution).

As already explained, the kidneys receive 25% of the circulating blood, which they filter to the best of their ability, removing waste products such as *uric acid* ($C_5H_4N_4O_3$), *urea* *[*($CO(NH_2)_2$,*]* *ammonia* (NH_3) and *creatinine* ($C_4H_7N_3O$), and many others. However, to maintain body balance of metabolic processes, some wastes may be needed to deal with more toxic products still in the body systems and the kidney then reabsorbs some of these into the blood. Urea is one example.

It also reabsorbs other substances like calcium (Ca) with the aid of the *parathyroid hormone*, *potassium (K)*, and *magnesium (Mg)*. It reabsorbs water with the help of the hormone ADH (anti-diuretic hormone), as well as salt (Na and Cl ions) with the assistance of the adrenal hormone *aldosterone ($C_{21}H_{28}O_5$)*. *Glucose ($C_6H_{12}O_6$)* or *amino acids* (see p.75) that pass through the filter, are also reabsorbed as these are important to maintain the required levels for the proper function of many organs in the body. Should there be too much water in the system (e.g. swollen ankles), with the help of another hormone atrial natriuretic peptide *(ANP – a vasodilator*) produced by the heart, an increase in the excretion of the Na and Cl ions results in more water being excreted as waste. This increased excretion or reabsorption of water is also linked with the production of a substance called *renin* produced by the kidneys which assists in regulating the body's water volume and in turn the body's blood pressure levels, which the kidney requires to maintain its filtration pressure (90 mmHg) and below which the filter tends to fail.

Toxic substances that have been metabolised by the liver facilitates excretion and are eliminated either via the bile (which excretes large ionised molecules greater than 300 microns) into the GI tract and faeces or the kidneys. The levels of these metabolites can serve as indicators of existing toxicity of a particular foreign or toxic substance. You will recall that transformation by the liver may result in intermediate metabolites which are more toxic than the original toxin and these must be further transformed for excretion.

There are other factors that affect kidney excretion. Posture (lying down or standing up) affects urine flow – increasing excretion on lying down and decreasing it on standing, although this depends on many factors. Sodium and chloride balance effect excretion and are also altered by posture. Temperature of the blood also affects filtration, which increases at lower body temperatures. *Dirunal* (night) rhythm shows a typical fall in filtration during the night hours, which increases in the morning. Exercise gradually reduces the blood flow to the kidney, which is diverted to the muscles and then stabilises even though the exercise continues. This does not reduce kidney filtration. However, if the exercise is more severe, then the decrease in blood flow will cause a reduction in the filtration rate. In hot environments (bakeries, kitchens, foundries, glass manufacture, deep closed mining, etc.), the filtration rates are already reduced to some extent and any severe exercise aggravates the condition. The pH of the urine is another factor which affects excretion. A metabolite may be ionised at an acid urine pH or at an alkaline urine pH affecting re-absorption in the tubules and, in consequence, excretion is affected. The body's entire blood volume is filtered in about 40 minutes or so in a health individual.

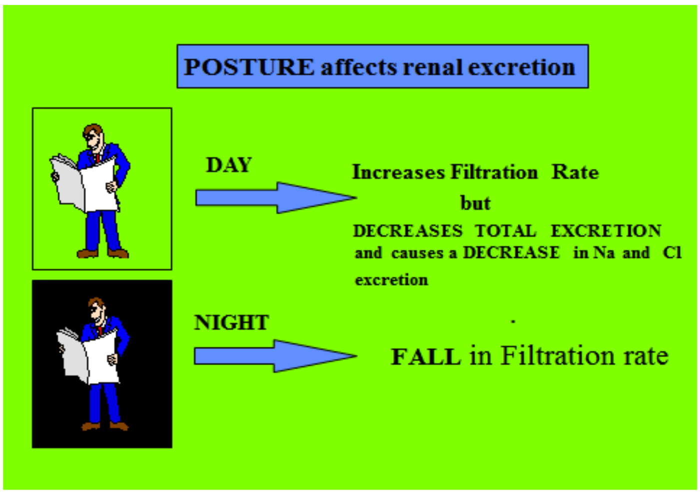
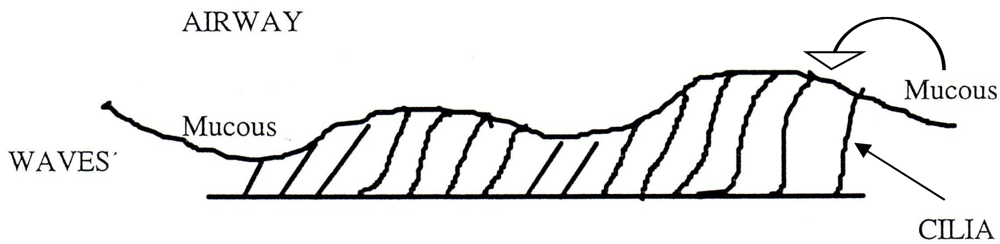


Figure 63. A schematic representation of the effect of day and night time on posture (**B48**).

The Lungs

Excretion from the lungs is assisted considerably by a rate of ventilation greater than 18 to 20 per minute. The tidal volume (the normal average amount is 500ml of inspired or expired air per breath at rest), returns inhaled particulates from the lungs mucociliary and lymphatic systems. An appreciation of the structure of the alveoli and its negatively charged membrane (see Fig. 15 & 16), and a number of animal research experiments have indicated the importance of alveoli permeability in the rapid excretion of gases from the blood capillaries lying within the alveolar membrane (B48).

The rough sketch below shows a ciliated cell, as well as a goblet cell (a cell that secrets mainly mucin but also other types of secretions) within the mucosa of conducting airways, (i.e. the bronchial region, which has ciliated cells upon the basement membrane of the airways). A human cilium is about 6 microns in length and up to 1 micron in width. Together they beat at between 700 and 1000 times a minute. They continue to beat for several hours even after death and are more complex anatomically than shown in the diagram. There is much yet to be learnt about their defects / diseases and related genetic causation.



METACHRONAL WAVES

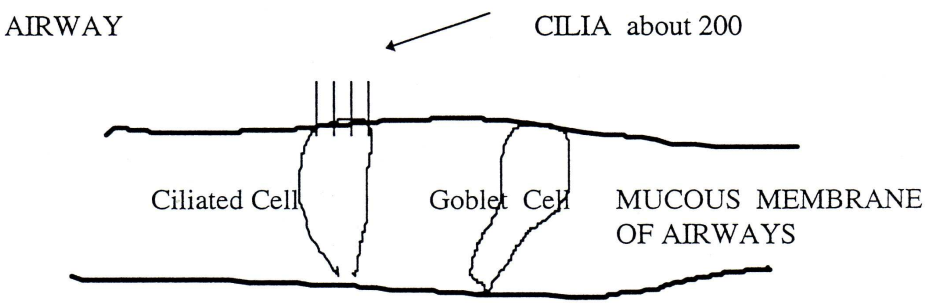


Figure 64. A schematic impression of the bronchial airways showing the cells and their cilia moving mucous and inhaled particulates upwards to the mouth with wave motion. There are approx. 200 cilia per cell. Below these cells lie Basal cells which divide frequently to form new cells making them sensitive to cancer causing agents.

The mucous in the trachea flows at 1–2 cm per minute and in the bronchioles it flows at 1/10th to 1/20th of that in the trachea. The total volume of secretion in a healthy individual is about 1 to -100 ml per day, whilst in Bronchitis (an inflammation of the mucous membranes of the bronchi) they are more likely to be between 200 – 300 ml per day.

Inhaled particle/s between 1 – 30 microns will generally be impacted in the mucosa of the nasal area, pharynx or larynx and excreted through the nose or swallowed. Dust particles, plants particles, mould, *allergens*, microbials and chemical ingredients of tobacco smoke, between 1–5 microns will get trapped by the mucociliary system of the bronchioles and gradually excreted or impacted in the bronchioles with others sedimenting down and reaching the alveoli, particularly those less than 1 micron in size. Scavengers (macrophages) will engulf some, and these will be either stored within them or transported to other organs for excretion. Other particles are taken up by the lymph and eventually also excreted. Asbestos fibres will, depending on their length to width ratio, sediment to the alveoli to become embedded or penetrate the pleura and result in serious pathology of the sector of the lung involved.

Excretion by the lungs is by passive diffusion from the blood into the alveolus, where it is also assisted across the alveolar membrane by the difference in the pressure gradient. The lung has an abundant flow of blood, and volatile compounds and gaseous metabolites are rapidly removed from the expired air. Lipid soluble compounds (vapours, fumes and mists) can easily cross the thin alveolar membrane from the blood capillaries. Concentration gradients between the alveoli and the capillary blood in the lungs will result in *passive diffusion* of blood gases and the rate will depend on the solubility of the gases. If they are very soluble, they are more likely to remain in the blood (see **B**[48] for detail).

Irritants (these are substances which cause inflammation or tissues necrosis to the lungs), such as *chlorine* (Cl_2) or ammonia (NH_3), that are more soluble than nitrogen dioxide, carbon monoxide (CO) and ozone (O_3), will affect the mucous membranes of the upper respiratory tract, whilst the not-so-soluble gases will pass further into the depths of the lungs before they dissolve and cause inflammation or damage. It is the less soluble gases that one should watch as their effects are not noticed for several hours after inhalation and could cause permanent damage, while the more soluble types result in immediate irritation, urging those affected to exhale, withdraw from exposure and request urgent medical attention. Carbon dioxide passes from the blood vessels in the alveolus into the lungs and is exhaled.

Breast milk

Throughout the nine months of pregnancy, diet and nutrition are important to the development of the foetus, and there will be considerable variation between women in this respect. Differences in the levels of potentially toxic substances that they may have inhaled, ingested or absorbed during this period of time, such as in the composition of water, substances contained in soya milk, excessive intake of trace elements or vitamins that at accepted daily doses are beneficial, intake of *methymercury* (CH_3CHgCH_3) from bottom-feeding fish, and preservatives present in food, to mention but a few may, during pregnancy, be at undesirable levels in the mother's circulating blood and pass to the foetus.

Once a baby is born and breastfeeding, excretion via breast milk is an important route for lipid soluble compounds. Studies in 28 countries worldwide have shown that breast milk can contain one or more heavy metals (Pb, Cd, Hg) [284,285], and other studies have indicated higher levels of trace elements in selected infant formulas than in human breast milk.

It is also important to consider the levels of environmental contaminants in terms of their excretion into the milk, such as indoor air, cigarette smoke, volatile organic compounds (VOCs), chemicals that accumulate in the food chain, and other substances that the mother may use such as *perfluorinated* chemicals (floor cleaners, etc.) and personal products, as well as medical drugs that are required to be taken during the time of breast feeding. Radioactive substances in relation to nuclear plant explosions and time-related fall out contaminating milk and food should be no exception. In spite of such concerns, it should be noted that the retention in breast milk of indoor air contaminants are considerably lower than those found in the environment.

The Bile

Excretion of toxicants and their metabolites into the bile is affected by three different systems in the liver. One system is used for the transport of neutral compounds (these are compounds in which the ions have an equal charge), another for anions (negatively charge ions) and the third for cations (positively charge ions). These transport systems may, just like they do in the kidney, become saturated and result in the accumulation of the toxin in the liver. A decrease in the excretion of bile may result in liver disease, although some drugs can increase the excretion of bile from the liver.

Substances excreted by the bile via the different transport systems used are generally water soluble large molecules greater than 300 microns. These pass in the GI tract and are excreted in the faeces. Some may be reabsorbed back to the liver after having reacted with water in the gut and broken down into two separate compounds (*hydrolysed*) by certain gut enzymes. It should be noted that the GI tract has the ability to absorb toxins directly from the circulating blood and excrete these in the faeces. This may happen when circulating levels are high or other excretory organs are slow for some reason in dealing with them.

The Hair

Human hair can be a valuable part of physical medical examinations, due not only to workplace, environmental and cultural exposure but also as a consequence of its hormonal and immunological involvement. The reader is referred to a review of 'The Human Hair: from Anatomy to Physiology' by Barbara Buffoli et al. in the *International Journal of Dermatology* [286].

The hair stores a large number of toxic metals which are fixed in the protein structure of the hair tissue. These are absorbed from the contamination of drinking water such as aluminium (Al), antiperspirants, from bleaching and dyes, cleansing products such as shampoos, conditioning products, and hair sprays or other styling agents used in hair treatment, kitchen utensils, foods and many metals such as: arsenic, antimony, bismuth, cadmium, calcium, copper, cobalt, mercury, nickel, potassium, selenium, tin, vanadium, etc. Bleaching commonly involves the use of *hydrogen peroxide* (H_2O_2) in a solution of ammonia (NH_3). Permanent dyes may contain a number of different dyes and other chemicals may be used to remove them.

Human hair varies in different people and within each individual as a consequence of their nutrition, endocrine condition, occupation, the general environment, ageing and hair dressing fashions. The normal periodic loss of hair and hair cutting practice assists excretion processes reducing the body burden of toxins.

The Sweat Glands

Hardly anyone in medicine has not heard of 'Gray's Anatomy' [B18], an excellent book of human anatomy written by Henry Gray, a famous English surgeon and anatomist (1827–1861) and first published in 1858. Its 41st edition was available in 2015. It was in this book that he described in great detail the anatomy and function of the sweat glands.

There are two main types of sweat glands, the 'eccrine', which are found all over the body, mainly palms and feet. These assist in the regulation of body temperature by secreting water, together with some other substances, such as sodium and urea, followed by evaporation of the fluid to release excess heat, and the 'apocrine', mainly found in the armpits and the groin (*perianal region*).These glands are also found in the skin secreting an oily liquid and contain water and protein in the shaft of each hair, which then passes from the hair to the surface of the skin. This secretion is decomposed by bacteria and soon creates an unpleasant smell. Various researchers have pointed out that in all there are between one and two million sweat glands all over the body and that they appear to be involved in hormone regulation. Apocrine glands also excrete steroids that many studies have shown affect mood and sexual attraction (*pheromones*). Note that apocrine glands do not become active until puberty. Sweat glands are a first line protection to the entry of substances via the skin.

Prof. Dr. Charli Kruse and his team at the Fraunhofer Research Institution for Marine Biotechnology EMB in Lubeck, Germany, described that they *'obtained stem cells from less than 3mm of underarm skin'*, and that they have an important role in healing. Research is still ongoing together with Bioenergy CellTec GmbH now also in Lubeck *'working to develop new products for wound repair'* [287]. Clearly this has great advantages as it would avoid rejection by the host, and also avoid needing to obtain stem cells from other areas of the body currently in use such as the pelvic bone, live human embryos etc.

Substances, such as arsenic (As), bisphenol A ($C_{15}H_{16}O_2$), cadmium (Cd), mercury (Hg), lead (Pb), urea [$CO(NH_2)_2$], water (H_2O), sodium (Na), potassium (K) some proteins and fats, and some steroids, are effectively excreted from the sweat glands.

Chapter 7 Toxic Chemicals & Occupational Cancer

Cancer

A large amount of research has been carried out on cancer and its causes, including toxicants and the decision on what and how much is essential to the Safety Professional is a difficult one. This is an area where so much more still needs to be researched and understood. What will be attempted here is to highlight some relevant aspects for the reader to appreciate the importance of toxic chemicals in safety and health that have the potential to result in occupational cancer.

Although the word originally used to describe a cancer goes back to Hippocrates, the word 'cancer' dates back to 460–370 BC [(288)]. Busheck Lecia [(289)] in her article 'A Brief History of Cancer' (June 25, 2015) points out that the first tumour to be recorded was in Ancient Egypt. It was not, however, until the middle of the 18th century that an Italian physician led the way to the study of cancer followed by the encouragement to carry out surgery by others.

The International Association for Cancer Registries (IACR), a non-governmental organisation, was founded in 1966 and IARC, the International Agency for Research on Cancer (WHO), acts as its secretariat based in Lyon, France. The GLOBOCAN PROJECT of IARC [(290)] "*provides contemporary estimates of the incidence, mortality and prevalence for major cancer types at national level for the 184 countries of the world*". In their 2012 Fact Sheet: "*the number of new cases for that year were recorded as 14.1 million with 8.2 million cases of deaths and 32.6 million people living with cancer within 5 years of diagnosis*". The "*overall age standardised cancer incidence rate is almost 25% higher in males than in females with rates of 205 and 165 per 100,000 respectively*". Mortality is given as 25% higher in more developed countries for men.

The European Network for Cancer Registries (ENCR) [(291)] which was established in 1989 with '*the objective of improving the quality, comparability and availability of cancer incidence data*' provides an '*overview of cancer disease and mortality data of the European Region based on data provided from the registries all over Europe*'. ENCR also '*promotes collaboration between cancer registries, defines data collection standards, provides training for cancer registry personnel and regularly disseminates information on incidence and mortality from cancer in the European Union and Europe*'. The ENCR 2014 Fact Sheet indicates, amongst other data, that 410,000 Europeans were diagnosed with lung cancer in 2012 and mortality in that same year was 353,000 [(292)]. The global economic costs of disability and death from all cancers is considerable. The reader is directed to review ENCR and IACR Fact Sheets for further information.

An International Classification of Diseases for Oncology is used worldwide by cancer registries and departments of pathology and oncologists ensuring improved morphology (describes the cell type of the tumour and biological activity) and topography (describes the site of origin) as well as accurate death certification. A Cancer Atlas [(293)] was created by the IARC, The American Cancer Society and the Union for International Cancer Control.

Occupational cancer

It is difficult to say exactly how many of the global working industrial population may end up in developing occupational cancer, but different authors have placed estimates as high as 30% and even 50%. Any estimate of work-induced cancer based on known or probable carcinogens are clearly difficult and subject to considerable uncertainty, and many countries do not yet identify a cancer as having been caused as a result of specific work exposures. In addition, the latent period – years may pass between the initial exposure and identification or the development of cancer – added to which the migration of workers from one job to another, and delay in obtaining medical/surgical attention, increase the difficulty in determining the cause. Many countries do not have surveillance programs specifically for occupational cancers. IOSH has referred to estimates of "*666,000 worldwide – one death in every 47 seconds*" [(294)].

The body's many trillions of cells, as has already been mentioned in earlier chapters, are exposed to an ever-increasing number of chemicals, some of which are very toxic and may cause changes to the genes that control cell function and induce errors in normal division of cells. Other causes include a person's lifestyle, including diet, physical activity, tobacco use, occupational exposure and other environmental exposures such as some types of radiation, chemical exposures, exhaust fumes, silica, some type of infections, shift work, and asbestos, although today many countries have strict controls on its management and use.

The American Cancer Society (ACS) [(295)] indicates that some type of infections with bacteria, viruses or parasites are risk factors to certain types of cancer and linked to about 25% of cancers worldwide [(295).] Viruses can insert their own genes into cells affecting growth, but although the risk is higher this does not mean that cancer will develop.

Infections that result in long term inflammation and infections (hepatitis B, HIV) that suppress the immune system both increase the risk of cancer developing [(296)].

Bacteria such as *Helicobacter pylori* [(297)] (may cause stomach ulcers and has the potential to promote cancer) and *Chlamydia trachomat* [(298)] (infects the reproductive system in both males and females) both increase the risk of cancer.

Examples of two well-known parasites are: the flat worm (liver fluke) – *Opisthorchis viverrini* [(299)] which may cause cancer of the bile ducts, common in South East Asia, and *Schistosoma haematobium* [(300)] which may cause cancer of the bladder, are risk factors to cancer developing, mainly occurring in the Middle East and Africa.

The importance of the effects of radiation are from:

(a) **Natural** sources: terrestrial, i.e. radioactive materials in rocks (decay of uranium-238 and radon), some building materials (bricks, granite, alum shale) and radioactive substances received from air, food (K40, polonium-210 in fish, shellfish and reindeer), and water (radon)

(b) **Cosmic**: medical – ionizing radiation (X-rays, alpha, beta and gamma), newer technologies (computed tomography, magnetic resonance imaging), and

(c) **Nuclear** sources: nuclear plants – explosions and nuclear fallout, which came to the foreground and created serious concern in the early 1950s following the Hiroshima and Nagasaki bombings. The burning of coal as fuel and air travel also contribute to the doses of radiation received that may initiate cancer. Although experts point out that air travel does not expose pilots or crew to dangerous levels of radiation, indeed the levels measured in milli Sieverts are low and well within the recommended current occupational levels (20mSv/yr). Nevertheless in northern latitudes where radiation exposure is greater, and on continuous long haul journeys throughout their working life, those that have a family history of cancer or vulnerable individuals (pregnancy) may be at higher risk or pass genetic mutations to their future generations [(B46)].

What is a carcinogen?

A carcinogen is a substance than can initiate cancer. A carcinogen is an initiator and many chemicals, including viruses, bacteria, infections, radiation and exposure to other initiators can be carcinogens. Dr Lesley Rushton OBE of Imperial College, London, peer reviewed the IOSH article on occupational cancer which stated that 'IARC lists over 50 substances which are known or probable causes of workplace cancer, and over 100 other possible carcinogens' [(301)]. There are several lists of carcinogens with some including mixtures of carcinogens, and almost all are based on the work of IARC (WHO) and other institutions and ongoing programs in different countries.

Interested readers are referred to the IARC Group 1 list *(definitely carcinogenic to humans*) [(302)]. It should, however, be remembered that from time to time these lists are updated and reference should be made to current lists and the country where these specific lists are regulated and apply. IARC in its book *'Environmental Burden of Disease Series, No. 6 Occupational carcinogens, Assessing the environmental burden of disease at national and local levels'* [(303)] *states that "The probability that a worker will develop cancer is influenced by the total dose of carcinogen received, the potency of the carcinogen, the presence of other exposures (notably tobacco smoking), and individual susceptibility",* and there must have been identified a causal relationship between the exposure to that particular carcinogen and the cancer before a substance is classified as a carcinogen (e.g. asbestos and asbestosis). The strength of the evidence of the relationship established is also important. The European Union 'CAREX carcinogen exposure data base' [(304)], ILO, The World Bank and IARC documentation, are resources that provide information for estimating exposure to carcinogens in industrial sectors.

Cells normally divide at a specific constant rate. If this rate changes, either because the cell division is not being controlled by the genes (DNA) within the nucleus of the cell or because of some cell defect, then increased cell division results. During the initiating stage, of which there are three stages to be considered in the process of cancer production, there is interaction between the carcinogen and the cell genetic material. This may become damaged irreversibly or mutate if the cell cannot repair itself before the damage takes hold. This process depends also on the effectiveness of the individual's immune system and any other agents that can inhibit tumour development, such as a tumour suppressor gene that is present in every normal cell.

However, once the DNA (genetic material) has altered or mutated (this happens because the initiator is metabolised to some more active form and binds to the genetic material) a second step is needed to commence tumour development. A 'promoter' which can be another carcinogen (cigarette smoke is an example of being both an initiator and a promoter) acts by disrupting the cell's control mechanisms and facilitating the replication of cells or a promoter gene. When cells divide, each cell receives a copy of each chromosome. Initiation is not reversible and occurs some time before a tumour appears. Avoidance or removal from exposure to promoters obviously decreases the risk. Cancer cells need nutrients and oxygen to grow and blood must reach them to provide these. New blood vessels are triggered to grow and provide an adequate supply of blood to support the tumour's growth.

A cancer therefore arises from one abnormal cell which, following what has been just explained above, then begins to divide repeatedly to form a clump of tumour cells, literally multiplying, and in some cases spreading, out of control. An estimate of the risk of developing cancer in an exposed and a control group is referred to as the '*cumulative incidence*'. This figure is simply obtained by dividing the number of those with cancer by the total number of both groups. To compare the risk of both the groups, one must calculate what is called the '*relative risk*' also known as the *'risk ratio' (RR)* [305], which is obtained by dividing the cumulative incidence of those with cancer by the cumulative incidence of those without cancer. The result of this RR will provide how large or how small the risk would be. RR differs by region, gender, age and the cancer involved.

The term 'statistically significant' is used to explain that the connection between the health outcome and the exposure was strong enough that it was unlikely to be due to chance.

The odds ratio [305] is a measure which indicates what the odds are that an exposure will result in an outcome as opposed to a situation where the outcome would not occur if there was no exposure. If the odds ratio is greater than 1, then the odds are high that an outcome results. If the odds ratio is 1 then there is no effect.

To estimate the precision of the odds ratio, a 95% confidence interval is used. A high level of precision is indicated if the confidence interval is low and vice versa. This is not measuring statistical significance. For method of calculation, see definitions in Appendix III.

The reader will come across the term '*the cancer burden*', this refers to the number of people living with cancer. Some examples of carcinogenic exposures resulting in occupational cancers are given below:-

***Skin cancers** – (See also Fig. 27 & 28 p.88)*

The major causes of occupational skin cancer are caused by ultraviolet radiation, ionising radiation, and polycyclic hydrocarbons. Workers in construction, the fishing industry and agriculture, and all those who work outdoors (transportation, sport) are at risk from UV electromagnetic radiation (wave length 400–100 nm). UVA and UVB radiation is the most damaging and may damage DNA. Should mutation take place, cells may proliferate and cancer results. Ionizing radiation has been under strict control for some time and little skin cancer is seen from this source. Melanoma is one type of skin cancer. Sun beds (UV is emitted by passing electric current through a vaporised gas) also emit UV radiation that may result in skin cancer and skin ageing. *Arsenic* (As) and arsenic inorganic compounds such as *arsenic pentoxide* (As_2O5) and *arsenic trioxide* *(As_2O_3)* exposure are also known to cause skin cancer. Unrefined or slightly refined mineral oils, soot, coal tar and coal tar pitches, and exposure to cyclohexane-soluble compounds (cyclohexane (C_6H_{12}) in the rubber industry is yet another risks factor for skin cancer. Mehlman who reviewed the scientific literature on malignant melanoma has concluded that it *"is causally related to employment-related chemical exposures in the petroleum-refining industry"*. [306]

Lung, trachea and bronchial cancers [307]

Occupational lung cancers account for a large number of deaths. Smoking the burning leaves of the tobacco plant is a risk factor and enhances the effects of some carcinogens. There are four major types of cancers that result in the lung and these are classified according to the cell type from which they arise. Causes of occupational cancer include those that may result from the inhalation of fumes in aluminium factories, arsenic, asbestos (*malignant mesothelioma* affecting the pleura), beryllium and some of its compounds, cadmium, cobalt, coal and coal tar and pitch from the mining of tin, chemical, electronic, ceramic industries, nickel, phthalates, radon, respirable silica, chloromethyl ether (CMME), in the ion exchange resin industry, as well as the petrochemical, the rubber (PAHs, phthalates) and steel industries, and vehicle exhaust.

In the rubber-manufacturing industry, which today covers a considerable number of products, workers are exposed to dusts and fumes from a very large variety of chemicals used in production processes of producing and re-treading of tyres and manufacture of other rubber goods. Inhalation exposure to N-nitrosamines (during vulcanising), and *cyclohexane-soluble compounds* (C_6H_{12}) are other risk factors for lung cancer.

Cancer of the kidney, bladder and urinary tract [308,309,310]

Most cancers of the kidney appear after the age of 50, and the commonest type of cancer is a renal cell carcinoma located in the lining of the proximal convoluted tubule of the kidney. This type of tumour which may contain watery cysts can spread to other parts of the body. There are a number of subtypes of this tumour but these rarely occur. The incidence in men is higher than that of women. Assigning a renal cancer occupational status is still very controversial, but there is little doubt that the kidney receives 25% of the circulating blood volume and both toxic substances and metabolites to filter and excrete, raising reasonable doubt of the impact of long-term exposure from such substances once genetic or other conditions have definitely been excluded. The lining of the renal pelvis (see Fig.59), which like the bladder is composed of *transitional cells*, is reportedly the site where occupational cancer occurs in the kidney.

Cancer of the kidney has been reported to occur in petrochemical workers, as well as in those working in the steel industry and the manufacture of graphite and electrodes with exposure to coke oven emissions, (*distillation or carbonisation of coke results in the presence of particulate matter containing benzene*), and solvents (e.g. *trichloroethylene* – C_2HCl_3). *arsenic* (As_2), *cadmium* (Cd) and *lead* (Pb) workers have also been reported to have developed kidney tumours [308,309].

Bladder cancer was known to occur in workers manufacturing *aniline* ($C_6H_5NH_2$) dyes as far back as 1895, although in Egypt reference had been made to bladder cancer generally as far back as 1600 BC [311]. Bladder cancer appears to be on the increase. Exposure to carcinogenic *amines* such as *benzidine* $(C_{12}H_{12}N_2)$ and dyes metabolised to benzidine, *(also referred to as 2-napthylamine –* $C_{10}H_9N$*)*, now mainly used in research laboratories but found in cigarette smoke, are all responsible for bladder cancer, (IARC[333]) as is sulphur inhalation during the manufacturing process of auramine in dye manufacture. Recent studies indicate risk of bladder cancer from prolonged exposure to *trihalomethanes* (-) [312]. Some studies suggest links to high levels of exposure to cadmium (Cd) [308,309]. Other studies point to smoking, *aromatic amines* and solvents as well as to electromagnetic fields, but more research evidence is needed to confirm such findings.

Textile and leather dyeing processes exposes workers to *aromatic amines*, which are metabolised so that they release benzidine. Aromatic amines are also used in plastics cable and rubber manufacture [313]. Tar-based wood preservatives also have a risk of causing bladder cancer. Metal-working fluids, diesel engine exhausts and benzo-a-pyrene have a similar risk as do workers in aluminium-reducing plants, due to the coal and tar pitch volatiles. Worker exposure in the production of the dye magenta has been associated with an increased risk of bladder cancer. 4-Aminobiphenyl, used in dye manufacturing, is a known carcinogen that has been linked to bladder cancer and is no longer readily available [313].

There is a delay in time between exposure and the development of bladder cancer, which can vary between 5 and 35 or more years. It is interesting that occupational bladder cancers appear many years earlier than similar type cancers in the general population.

It should be remembered that many chemical substances, such as 2-naphtylamine and *benzidine* ($C_6H_4N_2$), are prohibited substances whilst there are others that are under control but not prohibited like some benzidine derivatives.

Cancer of the blood *(see also p.108,109,111 and Fig. 54)*

The plasma and cells within the blood vascular system are the major carriers to all parts of the body for toxic substances. A group of carcinogens referred to as *'leukaemogens'* affect different cells in the bone marrow causing *leukaemia*, with each type of leukaemia named after the cell it affects. Nomenclature depends on the type of classification used. The term 'leukaemia' is reserved for cells that may affect the production of stem cells and other cells in the process of being formed from stem cells in the bone marrow. This is what differentiates acute from chronic leukaemia. There are two types of stem cells that derive from the basic immature stem cells in bone marrow – the *myeloid* and the *lymphoid* stem cells. From the lymphoid stem cells develops the blast cells that become lymphocytes (3 types) and from the myeloid stem cells develop the remainder of blast cells that then change into the blood cells. These are the **red blood cells**, and **white blood cells** (basophils, eosinophils, neutrophils. Neutrophils may be referred to as granulocytes and monocytes and **platelets** that pass into the circulating blood.

Leukaemia arises either from lymphoid or myeloid cells. Risk factors include genetic, environmental (electromagnetic fields and ionizing radiation), cytotoxic drugs, life style, and a specific virus referred to as *human T-cell leukaemia virus, type II (HTLV-II)*, which appears to be spreading amongst drug users [314]. The abnormal cells that cause leukaemia quickly move into the blood circulating system affecting other organs.

IARC points out that over 10 million workers are employed in the manufacture of textile fabrics, carpet and clothing industries worldwide. Those workers who specifically work in the finishing sectors of the manufactured products are exposed to solvents, formaldehyde, flame retardants and antimicrobial agents, but in the literature, other than formaldehyde [315], there appears to be insufficient evidence for an association between leukaemia and textile manufacture (excluding asbestos manufacture) or processing with the use of these agents, although they do cause other very important health impacts.

Leukaemia has been reported in the production of Benzene and its use as a solvent in the refining industries, and automobile repair. An excess of leukaemia has been shown from exposure to styrene-butadiene, and there is *'limited evidence in humans for a causal association for ethylene oxide* with haematopoietic cancers [316] (cancers that arise from 'blood forming' cells in bone marrow usually myeloid cells. These type of tumours are malignant and affect the immune system).

Ionizing radiation – a number of studies have shown a positive relationship between increasing doses of exposure to ionizing radiation and leukaemia [317].

There are large numbers of workers in the rubber production industries (re-treading of tyres, shoe soles, extrusion of electrical cable insulation, gloves, etc.), who are at risk from numerous chemical substances and their by-products via inhalation and skin exposure. Insufficient research has so far been carried out on all of the chemicals in use to significantly implicate many of these, although in 1982 an IARC monograph referring to the rubber industry had at that time concluded *"sufficient evidence existed to associate leukaemia with occupational solvent exposure"* [315].

Pesticides [318] – a large number of studies have reported higher than average levels of cancers due to some pesticides, although the strength of the associations in general are weak. *Ethylene oxide* *(C_2H_4O)*, arsenic (As which is not used today), *lindane* *($C_6H_6Cl_6$)*, as well as TCDD (2,3,7,8 – tetrachlorodibenzeno-p-dioxin) that may occur as a contaminant, are listed as group 1 carcinogens by IARC. *Pentachlorophenol* (C_6HCl_5O) as a contaminant of *dioxin* ($C_4H_4O_2$) has been shown to cause *multiple* myeloma in pesticide applicators [319]. Note: multiple myeloma is a cancer of plasma cells in the bone marrow. These plasma cells are B-Lymphocytes that turn into plasma cells when they mature.

Cancer of the stomach, pharynx, larynx and colon

Gastric cancer has been studied widely by many researchers that have looked at social status, education, lifestyle, including diet and the relationship of chemical substances. The global differences from cancer deaths are also well known and confounding factors and bias in some studies do have some effect on the results, although these have been shown by Siemiatycki *et al.* [320] not to be greater than 15%. Studies that have also been carried out reviewing occupational risk factors covering a large number of occupations have shown positive findings for the occurrence of gastric cancer and occupations. For a detailed review of the subject the reader is referred to the paper by Pierluigi *et al.* on *'Occupational Risk Factors for Gastric Cancer: An Overview'* (1996) wherein they have also advocated the need for further research, in particular to dust exposure risk and stomach cancer [320].

Whether the substances involved are dusts contaminated with other substances, known carcinogens, ionizing gamma (γ) radiation, or other toxic chemicals to which workers are exposed in the multiplicity of work places, gastritis may be initiated and cause damage to the DNA of cells in the stomach lining. Whether this results directly or indirectly through one or other chemical process, it remains that stomach cancers need to be studied further in order to ensure future prevention in today's changing working conditions. Improved models for monitoring legislative and regulatory standards need to be developed and implemented for preventive policies to become seriously effective.

The manufacture of electrical capacitors and silica carbide, potteries, ceramics, glass, foundries, construction, cement plants, mining of tin (Sn), zinc (Zn), iron (Fe) and silver (Ag), asbestos and silica (Si), the aerospace industries, cement production, oil refineries, paper pulping sector of paper manufacture, pesticide manufacture, rubber works and metal working are some of the workplaces in which people may be at risk from substances that could result in stomach cancers.

Dusts can be ingested through swallowing following inhalation and removal from the air by the bronchial cilia and may act as irritants to the stomach lining.

Construction workers are also exposed to silica (Si), asbestos and chlorinated solvents. Metal workers are exposed to fine dusts and those working in the rubber industry to sulphuric acid and other inorganic acids. Firefighters to a mixture of combustion materials, dusts, sulphur dioxide (SO_2), hydrogen chloride (HCl), PAHs, asbestos, and fine particulates, to mention a few. Grain millers to fumigants and other fermenting gases and other airborne contaminants, all of which are potential risks to cancer of the larynx [321,322].

Occupational cancer of the throat (pharynx) is rare. Asbestos has been associated to cancer of the pharynx but the evidence from several cohort studies was *"suggestive but insufficient"* [323]

Oesophageal cancer has been linked to tetrachloroethylene ($Cl_3C=CLC_2$), but the evidence appears to have been for high levels during the mid-20th century, although it is widely known to have caused other cancers. IARC classifies it as a probable carcinogen [(324)].

The colon or large intestine is about 1.5 meters long (see Fig. 6 p.49) and located in the abdomen it starts on the lower right hand side, below the point where the small intestine/bowel joins it, and from where the appendix lies, continues vertically upwards just reaching under the liver, crossing and rising to the left side under the left rib cage where it makes a 360 degree bend to descend vertically downwards on the left side, then curving backwards and downwards to end its last 12 centimetres or so as the rectum, which then ends in the anal canal and its sphincter. Its purpose is to remove water and salt which helps to solidify the moving faeces, remove the gases produced by bacteria that reside within it and withhold its contents until stimulated to remove it. These bacteria are important as they produce vitamin K and one of the vitamin B complex group called *biotin*, as well as break down some still undigested fibres.

Most (about 60%) of colon cancers develop on the descending section (left side). There are several types that occur, depending on the cells from which they develop and a host of risk factors that do not include environmental/occupational risks.

In their contribution to the book '*Cancer epidemiology and Prevention',* Ward pointed out that there was an "*association between rectal cancer and machinist exposed to mineral-based metalworking fluids" and* Boice indicated that ionizing radiation was not shown to be associated with colon cancer in "*radiologists, underground miners, nuclear workers, or uranium processors*" [(325)]. Various studies show an unclear conclusion on the risk of exposure to asbestos and colon cancer in spite of data that supports a link. Raymond *et al.* in their paper on '*The Identification of Occupational Cancer Risks in British Columbia, Canada: a Population Based Case-Control Study of 1155 Cases of Colon Cancer*', observed "*significant associations between colon cancer and a number of occupations and industries"*[(326)] and suggest that exposure to wood dust and ammonia may carry an increased risk.

Cancer of the nose and neighbouring sinuses *(See Fig. 65)*

The nasal and oral cavities are the gateways to the inhalation of air and its almost inevitable pollution from the exposure to natural and industrial conditions in spite of its defences through the presence of mucous membrane, cilia (nose hairs), nasal secretions, immunological response through columnar epithelium cells that line the nasal turbinates – three bony downward curved shelves, protruding and running from the front of each side of the nasal cavity sloping downwards towards the back of the nasal cavity, and dividing the nasal cavity space into four levels. The mucous lining of each turbinate with a rich blood supply to help warm inhaled air contains enzymes which swells and contracts every 1–7 hours, possibly to relieve congestion. Environmental irritants can also cause swelling of the mucous lining of these turbinates. The upper turbinates propel inhaled air to the nerve odour receptors that pass through minute holes in the skull into the upper surface of the nasal cavity [(327, & B18)].

Estimating a breathing frequency of 7 ml/kg of body weight, or using the more usually quoted figure of 500 ml for tidal volume, and taking the average number of breaths inhaled per minute by a normal individual (which is approximately 12), one can calculate that in an 8-hour day at rest one is taking between 2.88 million ml of air which is equal to 2,880 litres, or 2.8 cubic meters of air. This figure expresses the amount of particles and toxins that pass through the nasal areas. The rate of respiration varies under different exercise circumstances, health status, emotional conditions, driving, altitude, etc. [(328)].

As of 2005, the European Legislation limit for ambient particulates was 50µg/m^3 for particles less than ten microns (PM10), over a period of 24 hours and these should average 40µg/m^3 over 12 months. This means that the level for 35 days of the year should not be more than 50µg/m^3. Standard for fine particulates (PM2.5) put into force in 2015 were 25µg/m^3 averaging over 12 months. One must remember that particulates are subject to variation due to climatic and other urban conditions causing turbulence, irrespective of the sources (Channel streets, high rise buildings etc.) Although models do provide fair representation of air quality measurements, measurements taken at fixed stations must also be considered with care as they too have their problems: one example of this is that measurements taken some meters away from a fixed station can be entirely different within the same area. Air quality standards are available for a number of other pollutants.

Inhalation of particulates can be very high in cities everywhere and one study in London (several studies have been carried out elsewhere) showed levels of pollution is highest in the centre of a street than on the sides, and those within a car would inhale about 4 times more polluted air due to the levels accumulating in the inside of the car entering through the engine compartment and filters [(329)]. Depending on the height of the buildings in the street, the width of the street and vehicle speed and volume, pedestrians would inhale less particulates than those within a car.

Dust levels in underground tube stations have been shown to be higher for *PM10* particulates than they are in streets. Other research has shown averages of 35–40µg/m^3 with large daily variability exceeding the standard of 50µg/m.

The nasal cavity defences (including pharynx but not larynx) catch particulates of size greater than 5–30 microns but some finer particulates < 2.5 microns will also be caught in mucous membranes, all eventually to be exhaled, sneezed away or in some individuals to be swallowed. Accepting the inhalation of 3 cubic meters of air over an 8-hour day, and based on an average particulate exposure to half the established standard for PM10, this would mean that a fair percentage of the total of level of elements in air as PM10 particulates are inhaled on any one day in spite of the fact that most of these will once again be exhaled or removed through the nasal, oral and pharyngeal defences (impaction, coughing, sneezing, forced deep exhalation through the nose, talking and laughing).

According to International Institute for Applied Systems Analysis (IIASA) researcher Gregor Kiesewetter who led a study that analysed particulate matter at individual monitoring stations in Europe said: *'An estimated 80% of Europe's urban population is still exposed to PM levels above WHO air quality guidelines, and a significant proportion of the region still exceeds the air quality limit values set by EU law, according to the European Environmental Agency'* [(330)].

Other types of air pollution in streets differ in many countries and different locations within those countries. Paris, Rome and Berlin were reported in general News on 7th July 2014 by Rachel Holdsworth as having NO_2 levels of 82.61 mcg/m^3, 72.62 mcg/m^3, and 60.49 mcg/m^3, respectively, with the London shopping strip as 135 mcg/m^3 [331]. Some Far East cities have much higher levels of pollution levels [331].

Cancers of the nasal cavity, which includes the sinuses (maxillary, frontal, ethmoid and sphenoid) are not common. These cancers may or may not be malignant but they can arise from the olfactory nerves, bone, and the different type of cells in the nasal cavity including melanin cells causing melanoma. Risk factors and long term occupational exposure to several chemical substances have been shown to have an association with nasal cavity cancers. Most occur about or after the age of 50 except with those resulting from papillomas which occur in younger ages groups, but these form only 0.5% of nasal tumours from the 20–30% that occur in the nasal cavity, 60–70% occur in the maxillary sinuses and 10–15% occur in the ethmoid sinuses [332].

Chromium, wood dusts such as textile, leather and wood, particularly hard woods and chipboard, chromium VI, nickel, and solvent vapours from formaldehyde, as well as adhesives have been shown to have a relationship to nasal and sinus cancer. Inheritance and gene mutation that occurs should also be considered.

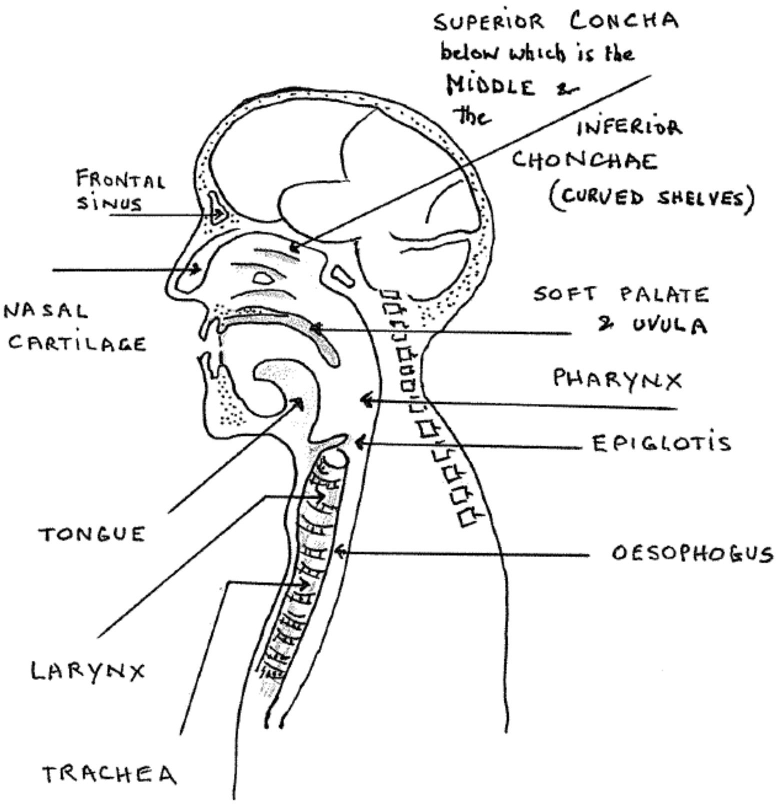


Figure 65. Drawing of the nasal cavity showing the nasal cartilage and the three conchae leading to the pharynx and trachea.

Cancer of the eye [334]

"*The role of occupational cancer of the eye to UV exposure*" on the risk of developing melanoma of the eye has been studied in France by Guenel *et al.* [333] and several others.

There are several sites at which melanoma of the eye may occur. In general, there appears to be agreement on UV radiation and the potential development of ocular melanoma and a dose-response with job duration has been shown in welders [334]. Many, however, are increasingly using protective equipment, but one must remember that welders are subjected to a large number of exposures. Guenel *et al.* have also pointed out that their study showed "*increased risk of ocular melanoma among male cooks, female metal workers and material handling operators*" [334].

A study carried out by Holley *et al.* has indicated that the colour of the iris (green, grey or hazel) has an increased risk to the development of ocular melanoma at a specific location (the uvea) in the eye following exposure to UV light [335]. Although Tucker *et al.* also pointed out "*that sunlight exposure is an important risk factor"* see [430], another study by Lutz did not find such an association with sunlight and considers the matter still controversial [336].

Melanoma of the eye is a primary cancer and is not very common.

Cancer of the liver and gallbladder

The liver receives around 1.4 litres of blood per minute [337]. 75% of this comes from the GI tract (stomach, pancreas, large and small bowels), the spleen, and 25% directly from the systemic blood circulation [337] It is a very large organ and can hold around one tenth of the body's blood volume on which it carries out around 500 functions [338], in the process of which many chemicals in the blood are metabolised for excretion mainly by the kidneys, bile or lungs.

Most cancers of the liver are due to cancer cells received from malignant tumours that have established themselves in other parts of the body and then settled in the liver (metastasis). Primary cancer of the liver can occur due to infection with the viruses of *Hepatitis B and C*, *aflatoxins* produced by fungus on corn and peanuts, and has also been found in the meat of animals fed on contaminated animal food. Agricultural workers are also exposed to dusts from contaminated crops. Long term exposure to *vinyl chloride* (C_2H_3Cl), a Group A carcinogen used in the manufacture of PVC and to which exposure may also occur from release of the gas from new plastics in cars, furniture and leaching from PVC water pipes as well as PCBs, can also cause a rare primary live cancer. Probably other substances not yet studied within the occupational environment may also be involved.

Thorium dioxide (ThO_2) [339] is a carcinogen and broken down to radioactive substances in the body. Used in some electrodes for welding and incandescent lamp manufacture, and the nuclear reactor industry, continue to be its main use as substitutes are today being used for thorium (ThO_2) in other occupational sectors. Arsenic and arsenical compounds and plutonium have caused liver cancer but exposure is now much lower than it used to be.

An association has been shown with PCBs and gallbladder cancer in the manufacture of electrical capacitors [340].

Brain cancer *[341,342,346]*

There are three primary cancers that affect the brain – two of these are the most common and survival rates are low. Each of these then divide into other types [341,342]. In small cohort studies of exposed workers to *epichlorohydrin* (C_3H_5CLO) - a reactive compound used in the production of resins, glycerol and epoxy glues[343] - some deaths have been observed *with standardised mortality rates* (*SMRs)* < 1.0. Studies of the risk estimates for brain cancer due to pesticides are conflicting and there is insufficient evidence connected to vinyl chloride, work in the rubber industry, laboratories, and radio frequency fields emitted from mobile and cordless phones and their cumulative use [343,344,346].

Cervical and testicular cancer

The cervix is a tubular canal, wider at its middle than at both ends which joins the uterus to the vagina. It varies in length but is around 2–3 cm long.

Occupational exposures [347] of the chlorinated solvents *tetrachloroethylene* (C_2Cl_4) also referred to as perchloroethylene or PERC, and *trichloroethylene* (C_2HCl_{3-}) which was replaced by *tetrachloroethylene* (assumed to be less toxic) and its use in the food industry, pharmaceuticals and anaesthesia is banned, but it may be still used by some as a spot remover) found in dry cleaning and metal degreasing workplaces where levels can be quite high.

Increased cervical cancer has be observed by Ruder *et al.* in 2001 [347], and Blair *et al.* in 2003 [348]. It should be noted that laundry and dry cleaning workers may also be exposed to petroleum solvents and a positive association with chlorinated solvents has been shown. In public laundries where dry cleaning machines have been placed, exposure levels may also be high, especially when machines are loaded or unloaded increasing air concentration. Newer machines have reduced exposure by the introduction of vapour recovery before opening and the introduction of air conditioning and improved maintenance in the work environment. Dry cleaned clothes stored in wardrobes at home would also show elevated levels of *tetrachloroethylene* for some days. Exposure level guidelines for a TWA for 8 hours of 20 ppm and a STEL of 40 ppm for 15 minutes has been recommended by the Scientific Committee for Occupational Exposure Limit values (SCOEL) [349]. Tetrachloroethylene [349] is only slowly metabolised and is stored in fat. Exposure causes headache, dizziness, nausea and fatigue in addition to red eyes and skin irritation, and depending on exposure levels and duration, unconsciousness.

Whether or not chemical substances that interfere with hormone receptors (hormone disrupters) have an association to cervical cancer still requires further evaluation and broad research approaches are being taken in the study of hormone disrupters.

The testes are located in the scrotal pouch between the upper parts of both thighs, outside the abdomen, and are suspended in the pouch by a cord. This helps to keep them at temperatures below body temperature. Their structure includes three type of cells, one of which, the germ cell, matures into spermatozoa (sperm) containing chromosomes taking about 42–76 days to mature. Sperm has only one set of chromosomes, from the 23 pairs (46 in all) received from the parents (one pair from the father and the other from the mother) which are in each cell in the body. Of the 23 pairs, one pair is an X and Y chromosome. When sperm and female egg unite and the division of the egg cell takes place, the newly formed cells may receive an X and a Y chromosome or an X and another X. If an X and a Y are received, then the developing foetus will be a male. Females have two X chromosomes. This happens by random selection of the chromosomes.

Cancer of the testis is rare but considerable research has been done in this area. Many papers also focus on the decrease in semen quality (number, motility and morphology, i.e. form and structure). Mester *et al.* based at the Western Institute of Medical Research have indicated that an association with solvents, particularly *dimethylformamide* (C_3H_7NO)*,* has been suggested and that "*electromagnetic radiation may have sub thermal effects or may disrupt hormone release*" [(350)] . Tina Kold Jensen *et al.* have reviewed a number of studies for the period 1990–2005 on "The influence of occupational exposure on male reproductive function" that covered metals and welding, inorganic lead, ionizing radiation, the solvents – glycol ethers, acetone (C_3H_6O), carbon disulphide (CS_2), *tetrachloroethylene* ($Cl_2C{=}CCl_2$), *trichlorethylene* (*C2HCl3*), 2-*bromopropane* (C_3H_7Br), pesticides, physical and psychological exposures, and concluded that "*the evidence is strongly supported in well-designed epidemiological studies*" for some specific agents, "*such as heat, ionizing radiation, inorganic lead, DBCP, EDB, some ethylene glycol ethers, carbon disulphide and welding operations*" but that for others "*the association is only suspected and needs further evaluation*" [(351)]. The reader is encouraged to read these papers for more information on this subject (see note below).

The testes also produce testosterone stimulated by the release of two hormones under the control of the hypothalamus, which signals the pituitary to supply and regulate its levels, and animal studies have shown that *PCBs* and *phthalates* acting as endocrine disruptors disturb the function of the testes.

Breast cancer

The breasts lie over four chest muscles and their shape results from their content, which includes a number of lobules containing smaller lobules that produce breast milk, ducts that lead milk to the nipple and a quantity of fat. The ratio of fat to other tissues alters after menopause. They are vulnerable to malignant and non-malignant tumours, apart from other conditions, from the lobules and ducts within the breasts, although duct cancer is more common.

Potential environmental and occupational risks form about 3% of these cancers and include: ionizing radiation (alpha particles, radon, plutonium), tobacco smoke, PAHs, a*rsenite* (AsO_3) *and arsenate* (AsO_4)*, ethylene oxide* (C_2H_4O)*, organochlorines*, and shift work [(352)].

Note: *DBCP, referred to in the cited quotation refers to a pesticide and EDB to ethylene dibromide* ($C_2H_4Br_2$)*.*

Shift work – nurses, flight personnel and many others [(353, 354)]

The International Labour Office defines shift work as "*a method of organisation of working time in which workers succeed one another at the workplace so that the establishment can operate longer than the hours of work of individual workers*." Most countries have adopted their own definitions but in general they all have the same objective.

The official global number of people in shift work provided by ILO in 2006 was more than 2.5 billion but they point out that reliable data are difficult to obtain from countries. The hours of work established vary between organisations but are usually of 8 hours' duration with a range of 6−12, and some are simply an extension of time worked and do not involve night hours. Erin *et al.* have indicated that "*approximately 15–20% of the working population in Europe and North America are involved in shift work that involves working at night"* [(354)] and that the IARC Working group on shift work concluded "*shift work that involves circadian disruption is probably carcinogenic to humans"* [(353,354).] A survey carried out in 2005 by The European Foundation for the Improvement of Living and Working Conditions indicated that the prevalence of "s*hift work, including night work, involved more than 17% of the total European Union (EU) working population"* [(355)] The prevalence level in Malta was 22.3% at that time [(355)] but has since grown probably due to increase in tourism, inter-country transport of goods, security operations and the service industries. The highest level in Europe was in Croatia at 33.5% [(355)] and the lowest in Turkey at 6.4% [(355)].

In my experience, most workers on shift work would keep away from it if they had immediate other choices, but some do prefer night work perhaps due to their own personal reasons, social attitude and behaviour or possibly yet unknown genetic conditions. The occupations in which the large number of people employed on shift work is large, and one must remember that in addition to the burden of potential health impairment from shift work, there may also be exposure to other health and safety risks.

Professor Franz Halberg who died in 2013 coined the word *'circadian'*. This is a rhythm or better still, a periodic fluctuation, over a 24-hour period that remains constant and is often referred to as the body's biological clock. Surrounding environmental stimuli such as light or darkness establishes our behaviour affecting physiological functions by raising or lowering specific chemical levels through signalling selected organs in the body to do so. A group of cells that make up our biological clock located in the brain's hypothalamus is what regulates our sleep-wake cycle. Among other responses, these cells signal the pituitary which releases melatonin *(6-hydroxymelatonin sulphate [aMT6s])* which is high at night and low at wake time and during the daylight hours. Airline and ships' crews travelling through different time zones disrupt their circadian rhythms due to loss of time across the time zones, and depending on the distance travelled can take some time to readjust, particularly in airline crew.

Research indicates that it may be linked to metabolic disorders, and Straff *et al.* in 2007 ((Lancet Oncol, 8:1065-66, 2007) [(355)] indicated that the working group on shift work (IARC – International Agency for Research on Cancer) had concluded that shift work that causes circadian rhythm dysfunction may be carcinogenic to humans [(355)]. Other researchers had linked the rhythm with hypertension and other health disorders such as depression. Schernhammer *et al* [(356)] have linked shift work with human breast cancer and have shown that night shift workers have a risk of developing colorectal cancer [(356)].

For the protection of workers, an ILO 'Code of practice on working time' (1995) and Convention no. 171 (C171) on 'Night work' (1990), and the European Directive No. 93/104/EC "concerning certain aspects of the organisation of working time" (1993), was implemented in European countries through national legislation.

Cancer of the bone and articular cartilage (see also p.136-140)

Cancer of bone and cartilage are not common and when they have occurred, latency has been recorded as 10 years or more. Exposure to ionizing radiation of nuclear workers, personnel involved in disaster clean ups, underground mining operations, and aircraft crew who work close to cosmic radiation have been shown to be at risk.

Cartilage is a form of connective tissue which is not rigid like bone but a little flexible which helps to assist in the movement of nutrients into its cells (chondrocytes) as there is no blood or nerve supply to cartilage and it does not contain calcium. It is from these cells that, although rarely, cartilage cancer arises. The ribs in the chest are joined to the breast bone (sternum) by cartilage, and it is also found in the knee, hip at the end of long bones where it articulates with other bones, and occurs at other sites. Cartilage can wear away causing pain and immobility but if damaged it is only replaced in the body with a fibrous tissue, like scar tissue. Cartilage tumours may be benign. There is currently insufficient information on what causes cancer of the cartilage but repeated injury and ionizing radiation are risk factors.

The body skeleton has 213 bones, some are short or long, and others flat (ribs) or irregular (face). Bone is a tough and rigid material and considerable pressure is needed to cause a fracture until, mostly in later life, it becomes osteoporotic. The bone centre running along the bone's length (see Fig.54), is a tube like structure filled with fat – the bone yellow marrow which is where stem cells develop and stimulation/initiation of other cells takes place. The ends of these long bones are filled with spongy bone that is full of cavities to allow blood vessels and nerves and nutrients through. It is the outside layer of this that is covered with cartilage. Surrounding the marrow are many tubes running parallel to it, which have a centre canal for blood vessels and nerves surrounded by layers of very hard bone cells making a very compact bone structure that can withstand great force. This is then surrounded by the outer layer of bone to which muscles are attached. The red and white cells, as well as the platelets of the blood, develop in the red bone marrow and are mainly found in flat bones and the ends of long bones.

There are three main types of malignant primary bone cancers and these are not common, as well as five types of benign ones. Most bone tumours metastasise from other sites. Occupational exposure risks to bone are similar to that of cartilage.

A closing note on all occupational cancers

What has been provided in this chapter on occupational cancers is by no means exhaustive but nevertheless sufficient to guide and alert the interested reader to the occupational exposure risks involved. Biomarkers exist by which it is possible to roughly determine exposure to the toxic materials and whether or not the individual is susceptible.

Note that 'The Directive 2004/37/EC - Carcinogens or Mutagens at Work of 29 April 2004' (357) on the protection of workers from the risks related to exposure to carcinogens or mutagens at work (Sixth Individual Directive within the meaning of Article 16(1) Directive 89/391/EEC), which is proposing to limit or develop new limits of maximal concentration and therefore exposure from 13 cancers at the workplace, does not apply to radiation. It is likely that other chemicals still under review and analysis will be included later. Note that animal experiments have recently indicated that the National Toxicology Program of the U.S. Department of Health and Human Services (NTP) has recently listed trichloroethylene ($Cl_2C{=}CCl_2$), as 'a known human carcinogen' (Reported in *The Engineer* by Envirotech on 22 November 2016) (358).

In conclusion, it is as well to recollect that powerful economic interests, under reporting, methodology of estimates of occupational cancer that are providing very conservative figures, and political reluctance to funding preventive approaches to the reduction of cancer rather than the current trends of focussing on treatment, are considerable hurdles yet to be overcome in the management and reduction of occupational cancer. The available literature has shown substantial evidence of the potential risks from exposure to occupational chemicals, in spite of the difficulties and limitations in many studies, so that the present knowledge and experience and ongoing research provided by expert groups worldwide, can be used to direct and develop additional ways to contribute to strong, creative occupational cancer preventive policies and programmes that would also result in considerable reduction of health care costs. Hopefully current important and promising research on treatment of cancer will not encourage anyone to diminish prevention policies in the light of genetically editing cancer cells through the *'clustered regularly interspaced short palindromic repeats'* (CRISPR) technology, that viruses developed long before us! (See Alice Park 19 Dec. 2017, in The CRISPR Pioneers, Time Magazine) (359).

Occupationally-induced cancers – what can be done by the team

On Monday the 4th November 2015, IOSH (UK) led and launched a campaign to cut cancer deaths at work, referred to as the **"No Time to Lose campaign"**, backed by *"business leaders, academics and charity Macmillan Cancer Support, that called for collaboration of government and employers 'to beat occupational cancer'*. The objectives are to see developed "*a national database of work-related carcinogen exposures, more research into the potential cancer risks of new technologies, a greater focus on work cancer in medical courses and awareness training for apprentices, and publish guidance for employers to help identify and deal with cancer risks"*. It also "*wants businesses to sign a pledge demonstrating their commitment to controlling carcinogenic exposures in their workplaces"*. Since then, the IOSH lead campaign has received considerable interest and continues to gain ground towards their objectives. Readers are referred to the IOSH "News and Events" for more detail on these issues or contact the campaign team. See www.notimetolose.org.uk.

The scope of primary prevention of cancer at work lies in:

- Careful attention to type of chemicals and products purchased. The purchasing department or personnel should be made aware of the important aspects and impact of hazardous chemicals and products that in manufacturing or work activities could result in a serious impact to health.
- Substitution with alternative safe or less hazardous substances or products.
- Review and assessment of the work processes and implementation of adjustments where appropriate.
- Request for the evaluation of *relative and attributable* risk by appropriate personnel.
- Engineering controls including enclosure, ventilation, wet processes, ambient temperatures for storage, filtration or cleaning, and any other measures that would eliminate, reduce or meet established standards of exposure to ensure safe working environments internally and externally.
- Prohibiting the use of asbestos or substitution of the product.
- Identification of any presence of radon at the workplace location and institution of measures for lowering internal levels.
- Adherence to and monitoring of established chemical standards of concentration by appropriate measurements.
- Requests for pre-employment evaluation of potential employees to avoid hazardous placement of vulnerable/susceptible persons.
- Requests for periodic examinations where appropriate.
- Identification of susceptible individuals, biological monitoring and cancer screening and awareness of any cluster conditions.
- Counselling employees of the dangers of personal choices in smoking, diets, cooking techniques, physical activities and atmospheric pollution.
- Consider the prohibition of smoking in work environments.
- Counselling and informing employees of potential hazards should policies on chemical and product use not be observed.
- Maintaining records of all primary prevention measures/activities carried out.

If the stage of secondary prevention (screening and detection of disease) is reached, wherever possible, every guidance or support should then be provided in the hope that further advance may be halted and a third stage avoided.

It should be quite clear that prevention approaches cannot entirely be carried out by the safety professional but requires a team approach involving management, purchasing, medical personnel, engineers and carers and at times the assistance of epidemiologists. In addition, one must move into yet another phase that considers 'Return to Work after Cancer' (see IOSH [Institute of Occupational Safety and Health] document research carried out by the Institute of Occupational Medicine (IOM) Loughborough University and Affinity Health at Work: www.iom-world.org/news-events/news/2017/return-to-work-after-cancer/).

Chapter 8 A glance at some Industrial Materials and exposure to other products

Chemicals

The often-quoted figure of 100,000 existing chemicals has long been exceeded and the number is currently greater than 140,000 and will continue to rise making it difficult to study and review the potential hazards, or indeed the benefits so many of these chemical products. The cost-benefit dilemma, as is the case with pesticide use, most particularly in developing countries, adds to the complexity of chemical production, their use for safety, health and the environment. Broad regulation and careful chemical management programs (guidance, prevention (regulation, substitution, reduction, engineering controls, risk assessment, information and training, personal protective equipment (PPE), storage, handling and transportation, policies and permits, monitoring, health surveillance, disaster controls, waste disposal and the external macro-environment) are essential to reduce these problems.

Newer methods of dealing with the issue of chemical risk evaluation is fortunately underway. Sales of basic chemicals (petrochemicals and inorganic chemicals), the starting point for downstream production, is continuing to increase as new industries and changes in technology arise to produce new products and emerging economies demand them. The global population will have reached 9 billion by 2040 and developing countries must have energy and basic industrial chemical to meet downstream production requirements. According to Exxon Mobil, energy requirements are expected to increase by 25% by then, and *"oil, natural gas and coal will continue to meet about 80% of global demand"*[(360)], and "*global carbon dioxide emissions by almost 30%*" [(360)] during this period. The production and sale of chemical products is a competitive business, but it must be remembered that a number of products have been abandoned or discontinued due to environmental pollution, carcinogenicity, disposal of waste, new products or high costs. There are also a number of hazardous chemicals that are prohibited from importation or supply at work in some countries.

Clearly, it becomes essential to select a few from the global production of current industrial and domestic chemicals, highlighting some of those used in larger quantities with known potential and/or greater impact on safety and health to present here. One must also ensure that careful attention is maintained when labelling a condition as 'occupational' at any specific workplace because this may have been initiated in a domestic environment or elsewhere. On 8 April 2015 Japan's Ministry of Health designated 24 domestic amines as harmful substances in domestic products.

Although the focus of selection of the chemicals in this chapter are common among those found on the islands of Malta and Gozo, overall the selected material is, nevertheless, of similar importance to those in other countries. The importance of consideration to origin and supply chains, signatories to the Basel Convention on transboundary movements of hazardous wastes, bilateral agreements on export/import of chemicals, and insurance of small and medium size industries, cannot be overemphasised in chemical management to avoid the very high costs involved as a consequence of inadequate responsibility to risk.

Adhesives and Sealants [(B23)]

Although adhesives have considerable industrial production and economic benefits, careful attention must be given to exposure in manufacturing and the application of some of the types by end-users, as these include a large number of workers in other industries and the general public. Whilst adhesives are made to hold materials together, the purpose of sealants is to fill gaps and act as a barrier to air, dusts, liquids or reduce noise transmission through gaps, although depending on how they are derived/formulated they may also act as adhesives that cure at room temperatures. Silicone is the classical example. During production, compounds/chemicals such as silica or clay, colours, plasticisers to increase workability *benzoate* ($C_7H_5O_2$) or additives (fungicides, fire retardants, catalysts (amines or anhydrides to accelerate reactions) may be added to adhesives. Similarly, sealants receive stabilisers to increase their shelf life or alter their level of flexibility (viscosity). Some types are resistant to UV radiation, *ozone* (O_3) and extreme temperatures.

It is not difficult for anyone to realise that the construction, wood and automotive industries use considerable amounts of adhesives and sealants. Electronics, aircraft and publishing are some of the many other end users. Adhesives are either water, solvent or hot-melt based, and *polymers* are used in manufacturing every type. Polymers are made up of chains of *monomers* which are organic molecules that *polymerise* (a chemical reaction that results in the linking of one monomer to another) to form polymers. To achieve their objective, adhesives must cure (solidify) which require either, heat, moisture, radiation or the addition of a chemical hardener. When a hardener is supplied to cure the adhesive component, the adhesive is referred to as a combination of two components.

Solvents [(B24)]

These are extremely common petroleum-based chemical substances, many of which are mixtures of chemicals, used as cleaners, degreasers and paint thinners, at places of work.

Most are volatile and rapidly absorbed by the skin and the respiratory system. Volatile gases and vapours that are very fat soluble store and persist in adipose tissues but those that are less fat soluble are fairly quickly exhaled. *Benzene, toluene, xylene, acetone* (all used in the production of many organic chemicals), *methyl ethyl ketone (MEK), methyl n-propyl ketone (MPK), methyl n-butyl ketone (MBK), and methyl isobutyl ketone (MIBK), trichloroethylene (TCE), carbon tetrachloride, carbon disulphide* (manufacture of viscose rayon and many other uses), the ethylene glycols (used in paints, varnishes, inks, dyes and adhesives) are some examples.

Solvents are toxic to the central and peripheral nervous system, the heart, kidneys, liver, reproduction (many women work in the electronic industry where cleaning and degreasing activities are routine procedures), and affect blood and bone marrow through metabolic processing of solvents. It should also be noted that ultraviolet radiation can decompose chlorinated hydrocarbon solvents into toxic gases [(361)]. Those who work in offices are not excluded from exposure to solvents.

Aromatic amines [(362, 363,)]

An amine is derived from ammonia (NH_3) [(362 & 364)]. If one of the hydrogens is replaced by an alkyl or aryl (aromatic) group then this would form a primary amine. When two hydrogens are replaced this would form a secondary amine, whilst the replacement of three hydrogens would make it a tertiary amine, thus providing three main groups. It is also possible for the nitrogen of the amine to be connected to an alkyl or aryl group and this would result in a fourth group referred to as a quaternary ammonium compound used as antimicrobials and disinfectants, etc. Amines may be liquid or gaseous. The three types of aromatic amines are referred to as monocyclic, polycyclic and heterocyclic. The neurotransmitters are amines [(363)]. The simplest amine where the hydrogen is replaced by an aryl group, is aniline (ethylbenzene).

Many aromatic amines have been banned in the EU, although not all are carcinogenic, and some are used as antihistamines, tranquillizers and analgesics. Aromatic amines are also found in tobacco smoke, diesel exhaust, dyes, pesticides, surfactants, polymers, burning wood, and rubber. Japan's Ministry of Health designated 24 aromatic amines as harmful substances in domestic products (Amended Act 112 of 1973 see Data Sources Appendix II). Some of the aromatic amines, in particular the primary amines, cause contact dermatitis - the delayed hypersensitivity type - although some skin reaction may occur on contact. Cross-reaction between different aromatic amines can occur. An excess risk of bladder cancer in textile dyeing, rubber and cable industries has been observed by many, and lung and stomach cancers have also been observed. Concern has also been raised for the occupational risk to barbers, and hairdressers [(364)] from amines in products they use. It should be noted, however, that these chemicals which were extensively used in the early- and mid-1900s also contained many impurities/additives.

It is interesting to note that at temperatures above 300 degrees Fahrenheit, fire flames will contain polyaromatic hydrocarbons (PAHs) which in the preparation of food such as cooking over open fires (smoking of meats or fish), will adhere to the surface of the meat or fish. Once eaten and absorbed these are metabolised by body enzymes and then have the potential of damaging DNA. Charred foods also contain PAHs. The levels of PAHs would be insignificant when cooking meat or fish at temperatures that are below 300° F [(365)].

Ammonia (NH_3) [(366)]

In 1774, Joseph Priestly, an English physician-scientist [(366)], was the first to prepare pure ammonia, although a French chemist, Claude Louis Berthollet, determined its exact composition in 1785. This chemical, corrosive, hydroscopic, and a very pungent gas, which can also be in solution if put under pressure, is used in the production of many important compounds, and the manufacture of plastics, dyes, pesticides, fertilisers, as well as in the purification of water supplies. One derivative of *ammonia (NH_3)* is *hydrazine (N_2H_4)*[(367)]. This is used as a reducing agent, insecticides, fungicides and algaecides, as well as rocket fuel and a blowing agent. More commonly, ammonia is found in household cleaners which contain between 5–10%. Domestic cleaners in industry more often than not do not understand that ammonia should not be mixed with bleach which contains *chlorine* *(Cl_2)*, as this will form toxic chloramine gas and could result in collapse and unconsciousness, as well as produce toxic hydrazine, which has the potential to explode if the concentration of ammonia is high.

Ammonia can dissolve in water (liquid ammonia) forming *ammonium hydroxide* *(NH_4OH),* and it reacts with oxygen to produce *nitric oxide* *(NO)*. *Ammonia* also results from the decomposition of organic matter and animal waste.

Ammonia is not highly flammable but could explode if exposed to heat, with mixtures of 16–25% of air, and reactions with acetaldehyde, or hypochlorites in solution. It reacts violently with halogens.

The irritating vapour of ammonia is a good warning signal but continuous exposure to the substance can dampen sensitivity to exposure and therefore explosion danger. Ammonia is corrosive and exposure is by contact with skin, mucous membranes, and inhalation, which results in necrosis of tissues and pulmonary oedema. Contact with eyes may end up in blindness. Accidental ingestion is possible and would result in corrosion of tissues along its path.

As a gas (anhydrous ammonia, meaning without water), ammonia will boil at below room temperature. This is important in that it must be contained under pressure in suitable pressure containers. Transportation of ammonia is strictly regulated.

Formaldehyde (CH_2O) [366, B25]

As *formaldehyde* dissolves in water, it is more commonly seen in liquid form as formalin, which is a 37% solution of formaldehyde. It is otherwise a colourless and flammable gas, which has considerable industrial uses. It is used in the production of resins, adhesives, urea, paper and textiles. It is used in embalming solutions, disinfectants, fungicides and chemical laboratories. Note that adhesives are used in the manufacture of plywood and particle board from which *formaldehyde* evaporates, polluting indoor air, although the levels decrease with time. Products used in hair salons may contain *formaldehyde* which pollutes the air in blow drying. Note that products may refer to formaldehyde by its other names such as *methylene glycol* or *methylene oxide.*

Some individuals are more sensitive to *formaldehyde* than others. Exposure is mainly by inhalation, but skin contact may result in allergic contact dermatitis. It is an irritant to the eyes but contact with liquid formaldehyde may cause serious injury to the cornea such as an opacity. Inhalation of formaldehyde will cause severe irritation to the respiratory system and result in bronchial constriction, pulmonary oedema or even death depending on the level of exposure, usually above 50 ppm. Accidental or intentional ingestion, even in small amounts will cause severe injury to the stomach and may be fatal. *Formaldehyde* is classified as a carcinogen.

Silica (SiO_2) [369]

Silica is a common name used for silicon dioxide, which is one component of sand. As an element in its natural crystalline state, silica is found in quartz which is found in granite and sandstone rocks. The concentration or saturation of quartz in rocks varies. You will commonly come across the words: silicon, silicone and silicates as well as silica. *SILICON* is a natural element but with oxygen it forms *SILICATES*. Quartz is a silicate and it can be pure and referred to a SILICA or 'free silica' but when quartz contains other elements, it is then referred to as 'combined'. Silicone (note the 'e'), is made synthetically from silicon.

When silica is heated to high temperatures and then quickly cooled down it does not crystallise, which is rather useful in the manufacture of glass. Workers are exposed to respirable free Silica in sand used in foundries, maintenance to sand filters, building construction, quarrying, tunnelling, in its use as an abrasive in sandblasting and grinding, in the chemical industry, and as a filler in paints, rubber and adhesives.

Very large numbers of workers worldwide are exposed to free silica in many industrial and other operations, in addition to those shown above. Dust of less than 5 microns of free silica are respirable and reach the alveoli. Inhalation of the crystalline 'free silica' fine dust particles results in a condition referred to as 'silicosis', which is characterised by nodular areas whose centre consists of the quartz particles, around which collagen forms that later results in hyaline fibrosis (loss of elastic and formation of scar tissue) by the free silica mainly in the upper lobes of the lungs causing difficulty in breathing. These nodules may grow around the bronchi narrowing the airways. Silica dust also reaches the lymph nodes where fibrosis also occurs and later calcify.

Silicosis remains an important occupational disease and a hazard to many occupations.

Wood Dusts

Generally speaking woods are either hard or soft woods. However, one must note that many new wood products are mixtures of soft and hardwoods such as chipboard or MDF (Medium Density Fibreboard). In addition, there are so many types of wood available one would really need to know a lot more about the species of the wood to assess what toxic effects that particular wood may have. Dusts are irregular shaped particles in air which may aggregate to form larger particles and settle under the influence of gravity. Dusts are hydroscopic.

Both hard and soft woods may cause health effects, although it is the hard woods such as African mahogany, red cedar, oak, rosewood or teak that cause most problems. Workers in forestry, saw wood mills, and the furniture industry may be affected following long term exposure. These hardwoods cause irritation of the mucosa of the nose, throat and lungs, and may also cause asthma as well as carcinoma of the nose and nasal sinuses. Wood mould which lives between the bark of the tree and the wood may also trigger sensitivity reactions [370]. Contact with skin in sensitive individuals may result in irritant or allergic dermatitis [371].

Sodium hydroxide (NaOH) (B26)

Sodium hydroxide is also known as caustic soda and is a very corrosive alkaline and toxic white crystalline solid which has exceptional solubility in water. The solid absorbs water vapour. It has considerable industrial uses but mainly applied in neutralising acids in chemical processes, and in the paper and rayon industries to separate cellulose by dissolving the lignin that adheres them together. It is also used in the soap, textile, petroleum and food industries, and as degreasers for stainless steel and glass. Cleaners are exposed to sodium hydroxide in drain cleaners. It is found as a solid, liquid, and packaged as flakes or gel.

Some metals react with *sodium hydroxide*. In concentrated solutions of *sodium hydroxide,* aluminium (Al), lead (Pb) and zinc (Zn) will corrode. Materials, such as wool and silk as well as fats, dissolve in sodium hydroxide solution and contact with human and animal living tissue will result in severe burns. Exposure is by inhalation of the vapour, ingestion or skin contact.

The heat from the reaction of sodium hydroxide solution with materials is sufficient to cause ignition although the solution is not in itself flammable. Accidental ingestion may result in strictures of the oesophagus and may be fatal. Ensure that caustic soda is ALWAYS added to water and not the water to caustic soda, as the heat generated could splash back violently onto the user's face or body.

Metals – inorganic chemicals (B27, B28)

Over 70% of the earth's elements are made up of metals. They are not usually pure but fused with oxygen so are found as metal oxides and they react very easily with other elements which makes it difficult to extract metals from rock. As natural elements, metals are either:

(1) BASE METALS (a common metal that is not considered precious, i.e. copper, tin or zinc) and usually refers to a metal that can be oxidised or corroded easily;

(2) PRECIOUS METALS (gold, silver or platinum) – these do not corrode easily;

(3) RADIOACTIVE METALS (some heavy metals (atomic number > 21) such as Caesium or Plutonium are radioactive).

If you study the Periodic Table below, you will see that metals are arranged in groups and that in addition to their broad characteristics, groups also provide specific information about each group and other useful information which is not repeated here.

A substance can be a pure element, a mixture of two or more substances, or a compound, and the compound can be inorganic or organic (organic are carbon based). Inorganic metals are minerals, found in many geological areas of the Earth usually in combination with other matter as a compound. These inorganic compounds are not carbon based, that is, they do not contain carbon bonded to hydrogen like organic chemical compounds. These metal chemical compounds have two or more elements, and conduct heat and electricity. Some are reflective, some are difficult to ignite (iron), some ignite in very fine powdered form (aluminium, Be, Cd, Mg, S), some are readily combustible, i.e. flammable in contact with an ignition source or heat generated by friction (potassium), and others highly combustible (magnesium).

Exposure results from inhalation of extremely fine particulates and fumes; Metal Fume Fever from heating cadmium is an example. It also results from skin contact (nickel, chromium) and ingestion. Metals in soil are translocated and bio accumulated in roots and plant leaves. Animals eat these plants and the metals get into the food chain and ingested by humans. Bottom-feeding fish and shellfish are other sources. The heavier metals (As, Cd, Cr, Pb, Hg and Se) all have an impact on health. It is useful to remember that exposure to metals at work is often a mixture of metals.

The applications and uses of inorganic metals are considerable and in respect to this fact, attention should be paid to identifying the risks and establishing preventive measures in mining, processing, manufacturing, storage, packaging, transportation and disposal of metals.

Hydraulic Fluids

These are mixtures of chemicals. These chemicals vary in type and concentration in different hydraulic fluids of which there are three main types; mineral oil, organophosphate esters (no oil in these and they do not burn) and polyalphaolefin (these are mainly synthetic hydrocarbons). Hydraulic fluids are materials that transmit pressure in a closed system and the chemicals in them help to reduce wear and tear, and maintain a level of flow in low temperature environments. These systems are essential in vehicles (trucks etc.) aircraft, heavy equipment, such as tractors, and in military equipment, and wherever heavy mechanical lifting is necessary [(372)].

The mineral oils are the ones you will come across more commonly. These are produced from crude oil from which wax is removed and to which Silicone oils, organophosphorus esters (these provide anti-wear and fire resistance properties) and corrosion inhibitors are added. Their major chemical components are therefore aliphatic and aromatic hydrocarbons.

Workers exposed to mineral hydraulic fluids include mechanics, many who work in engineering workshops, car assembly, and those who work with military equipment, though these are more exposed to the *polyalphaolefin hydraulic fluids* since they are more fire resistant fluids. Note that motor vehicle hydraulic fluids contain *polyalkylene* glycols to which such mechanics are exposed [(373)]. Exposure is commonest through skin contact and soaked work cloths but mists and vapours may be inhaled from engineering workshops, open container/reservoir and other sources. Accidental ingestion is occasionally seen in children.

There appears to be limited information on the human toxic effects of mineral oil hydraulic fluids in the general literature. Most studies have been carried out on animals. However, long term and heavy exposure has resulted in skin, respiratory, GI tract and neurotoxic conditions [(374).] The highly refined mineral oils are not considered to be carcinogenic, but *"untreated and mildly treated mineral oils are considered* *carcinogenic to humans*" (IARC) [(375)]. It is probable that workers susceptible to mineral oils for any number of reasons such as age, general health and nutritional status or genetic conditions, may develop and exhibit toxic symptoms while others do not.

Disposal of the older type hydraulic fluids are regulated but the newer types may be recycled or incinerated.

In general, it is well to be vigilant on any changes in production processes, maintenance of guidelines on mists in the immediate environment and the purchasing of new or different mineral oil products for use at work.

Asphalt (bitumen) [(B29)]

Asphalt is produced from crude oil after refining/removing other fuels from it. This is not coal tar, which is the residue from the burning organic materials like wood, coal or peat and is sometimes used as a sealant on asphalt.

Asphalt is continuously used in large quantities for paving roads, airport runways, car parks and domestic driveways all over the world. Other uses include the manufacture of sound deadening pads for automobiles, domestic metal sink basins to reduce the noise of water falling on stainless steel, roofing (this is oxidised asphalt), and batteries. Different grades of asphalt are used for the different purposes and these grades cure differently, some rapidly because evaporation of the solvent used is fast and the asphalt hardens quickly, others more gradually. This is important as the asphalt flash point is lower in the rapidly curing asphalts and that means the explosion hazard is high.

In the application of asphalt a solvent is added to increase its liquid state. These solvents contain *benzene, toluene, dioxin and naphtha* which have different flash points. *Benzene* has a flash point of −11.63°C (11.07°F) [(376)] and toluene 6°C (43°F.) [(377).] Note, however, that when asphalt and solvent are mixed together the flash point rises and is higher.

The hazards of asphalt are double: firstly, the effects of the health impact on workers and, secondly, fire and explosion because when heated, asphalt releases vapours of *hydrogen sulphide (H_2S)*. The fumes irritate the respiratory system causing headache, dizziness, nausea and sometimes vomiting. Long term exposure can result in changes to the pigment of the skin which sunlight makes worse. It may cause acne and if hot asphalt splashes on to the skin, it can cause burns. In long term health effects, carcinoma cannot be ruled out especially in those that smoke, mainly due to the exposure to the constituents of the solvent vapours. The TLV guideline is 5 $mg/m^{3,}$ at the present time. Where exposure is above 6.5 mg/m^3, workers should use a full face respirator that has an organic vapour and particulate filter attached [(378)].

Polyaromatic Hydrocarbons [(B30)]

These are organic compounds that only contain carbon and hydrogen. They are produced by incomplete combustion (burning of organic matter, garbage, engines exhausts, forest fires, as well as occurring naturally in deposits of oil, coal and tar.

They are derivatives of <u>*benzene*</u>, stable and therefore not very reactive, insoluble in water and colourless. They are usually complex mixtures. Atmospheric degradation can lead to toxic compounds being produced [(379)].

Worker are exposed to <u>*PAHs*</u> during the manufacture and processing of asphalt, rubber, distillation processes, dyes, plastics, and through direct or passive tobacco smoke. PAHs are also found in air as vapour or attached to dust, and in sediments in soil. They could end up in underground water, reservoirs or the sea through rain water or hazardous waste disposal sites, because as they are not soluble they sediment down.

Short term health effects on the skin and immune system are well known and chronic inhalation and skin exposure have resulted in malignant carcinomas. Cancer of the bladder has also been noted. IARC has classified the less refined mineral oil mists as carcinogenic and others as 'possible' carcinogenic substances (e.g. pyrene which is used to make dyes and is toxic to the liver and kidneys) or 'probable' (e.g. benzo(a)anthracene). Although the body can store <u>*PAHs*</u> for a short time in fat and other organs, these organic compounds are soon excreted in the urine and faeces.

Volatile Organic Compounds [(380)]

These are a group of chemical organic compounds which at room temperature are volatile. They vaporise from liquids which contain the organic solvents, such as paints, fuels, and varnishes but also from some solids. They are also found in building materials, cleaning products, and are emitted from office copying and printing machines, permanent markers, carpets and upholstery.

The acute health effects are irritation to the throat, nose and lungs (dyspnoea), headache, dizziness and fatigue. Nausea may also occur. Exposure in some individuals has resulted in skin allergic reactions and the elderly are more vulnerable. There are a large number of VOCs and each has different potential levels of toxicity.

Paints that dry fast have low levels of VOCs. Current trends are to use water as the primary solvent, but oil which takes longer to dry is still used. Oil-based paints are made from synthetic (i.e. alkyd) which are mixed with other solvents, but are also made with linseed oil. Latex paints have a low level of VOCs and therefore dry quickly. Whilst they may not be good for certain jobs, one advantage is that the paint brushes do not require solvents that you would have to use to clean them as they clean up well with soap and water. Examples of VOCs include benzene, perchloroethylene and acetone.

Note that plants emit VOCs from their leaves mainly at night time. The eucalyptus tree is an example of one tree that emits VOCs. The main compound is ISOPRENE [(381)] (this is a hydrocarbon which is also present in human breath). This chemical in combination with high levels of nitrogen oxides produces photochemical smog and brings about further health effects.

Plastics (polymers) [B31, B32]

Plastics are synthesised from primary chemicals that are derived from oil or natural gas. These are materials that either by heat or by pressure or by both together become soft enough to form solid shapes. The primary chemicals are in powder or pellets and as they are brought into a liquid state and to which other ingredients (additives such as flame retardants, colourants or catalysts) may be added, are sometimes referred to as 'resins'. Most plastic are 'thermoplastics', which means that they can be melted repeatedly and recast again into other shapes. Thermoset plastics indicates that they cannot be re-melted. Thermoplastics can be altered to thermoset products. The reference to 'polymers' arises because plastics are long chain polymers (these are groups of atoms called monomers that form the units that repeatedly combine, this repeating forming the polymer chain. Structuring a chemical change in these chains results in the production of different plastic products such as polycarbonates, polyethylene, etc. (Dissertation, H&S Council (UK) Styrene, F. La Ferla, 1976).

The burning of plastics is a common and serious matter. The pollutants released which include *PCBs, dioxins and furans, styrene, mercury* and others depending on the plastic product (polystyrene or PVC etc.), enter the atmosphere and can travel far, settling in gardens and agricultural land and water where some persist and bio-accumulate. This results in their getting into the food chain through fish, meat or milk and also effect wild life. These substances accumulate in body fat.

The plastic industry employs large numbers of workers. The health effects depend on the type of additives used and considerable existing literature searches may have to be made by those who wish to review the potential toxic effects of such additives. Some produce irritation to tissues, others allergic responses (e.g. amine compounds, *isocyanates*). Some are suspected carcinogens (polyethylene and polystyrene), others *endocrine disruptors* (e.g.: Phthalates (DEHP [382]).

Chapter 9 The External Environment and Chemical Exposure

Environmental pollution

Faculties of Occupational Medicine and their members as well as safety organisations and their professionals are becoming, and indeed should be, more concerned with external environmental pollution and health impact. Investment and industrial development in Africa, the Near and Far East and other transitional small island states are being exposed to the same problems that developed countries have had, and in some cases continue to experience, with emissions, increased chemical usage, altered agricultures practices, climate change, the management of waste, new technologies including medical applications and ionizing radiation, noise, water contamination, fires and other industrial and transportation spills and disasters.

The reduction of environmental pollution and prevention of ill health extends beyond industrial sources and people at work, to communities, and across borders. Economic development should be balanced with environmental control. Products essential to industrial manufacture and of danger to the environment and to health are many, and the by-products that can result from manufacturing processes only increase the list of exposures to toxic substances.

Man-made sources of air pollution emissions, include: manufacturing industry, quarrying, mining, agriculture, transportation, construction, electrical generation, incineration and other forms of combustion, domestic and industrial heating and waste. Beyond these major chemical considerations one would, of course, include noise and the effects of chemical odours. These sources produce a large number of chemicals and include *nitrogen (N) and sulphur oxides (SO_x), hydrocarbons (HC), particulates, carbon dioxide (CO_2), carbon monoxide (CO),* acids and aldehydes.

Some of these industrial potentially toxic substances have already been referred to earlier in other chapters or information provided in the appendices. They include Volatile Organic Compounds (VOCs), which as vapours or gas are easily dispersed, such as the *solvents methyl ethyl ketone (MEK), acetone (C_3H_6O), isopropyl alcohol (C_3H_80), xylene* (C_8H_{10}) and *toluene (C_7H_8).* Exposure to *VOCs* are generally higher in work environments such as chemical manufacturing plants, fuelling stations, storage and distribution, and chemical laboratories. Nevertheless, communities living near manufacturing, oil refinery plants, or waste disposal sites are at risk from VOCs. Today many companies produce wireless VOC detectors to control environmental levels within and beyond the workplace.

Air pollution from natural sources include: volcanic eruptions, wild fires, the transfer of materials between oceans, land and air reservoirs, and both lighting and heat which drive the chemical reactions and interactions that take place in the atmosphere.

Differences in atmospheric temperature create air pressure differences and these create winds which are influenced by rural or urban ground topography. Wind velocity increases with height, but at night velocity decreases due to ground friction, but this applies only to surface wind and not that above 3000 feet or so. Particles that become airborne, particularly small particles, can be moved by winds for great distances, although dispersion does dilute the concentration. Air turbulence (unpredictable air movement) usually caused by the circulatory movement of air cells, will concentrate particle pollution to particular areas. These usually occur downstream from a point source, such as a *stack's* continuous emissions. The height, shape and direction of stack plumes varies considerably and depends on the wind velocity, temperature and direction.

The shape of a plume is also affected by *temperature inversions* which usually result in smog. Inversion happens because during a period of high pressure with low wind velocity, the air at higher altitude is at a higher temperature than that below it at ground level. This traps pollutants below the layer of higher temperature which may take some time to disperse and pollutants to settle. Particle pollutants are also removed from the air by water droplets or rain and washed away to drains, the sea, or settle into soil or onto buildings, which, depending on the building surface may cause discolouration. Note that particulates may aggregate in air increasing their mass and lowering the time taken to sediment.

The interactions that occur between solar radiation, the Earth's crust (siliceous rocks – oxygen (O_2) combined with silicon (Si-O-Si), - and mainly *iron* (Fe), *aluminium* (Al), *magnesium* (Mg), *potassium* (K) and *sodium* (Na)), its hydrosphere (oceans and all waters) and the atmosphere (*oxygen, nitrogen (N)*, *carbon dioxide (CO_2)*, water vapour and argon (Ar) that surrounds the Earth, form the framework of the chemical conditions of the Earth's external environment. The dynamic balance of this framework is maintained by solar radiation and its impact on plant photosynthesis, microorganisms and oxidation processes. The many chemical interactions that take place in the atmosphere are the result of these major chemical reactions in continuously changing weather patterns. It should be noted, however, that up to an altitude of about 100 kilometres or so, i.e. the thermosphere or upper atmosphere (the area were the air is not as dense as in the lower atmosphere and temperatures may reach 1500–2000 degrees)[383] the proportion of the main gases referred to are generally constant.

The effects of atmospheric air pollutants whether they act singly or in combination, can result in the formation of acid rain (*sulphur dioxide (SO_2)* emissions combined with water droplets forming *sulphuric acid (H_2SO_4)* and *ozone (O_3)* and their serious impact (bronchitis, pneumonia, allergy) on the respiratory system. The alteration of the *nitrogen (N)* content of the soil from air pollutants causes damage to vegetation, and water reservoirs. Fresh water chemistry, fish and other water organisms as well as animal life are also affected. Increasing levels of *carbon dioxide (CO_2) and methane (CH_4)* add to global warming and its impact are another issue for consideration. Reduction in visibility is an important aspect in construction and transportation at work. Asbestos, *carbon monoxide (CO_2)*, halogens and their compounds, *silica* and *phosphorus (PO_4)*, heavy metals, *radon* and other radionuclides are other important pollutants that reach and effect the external environmental and the health of those exposed.

The knowledge of the atmospheric air pollutant effects on health at work outdoors require constant attention to prevailing conditions and intervention, as far as is possible, by adopting reasonable safety margins, if one is to reduce the impact of risk.

Disaster products

Everyone in safety practice will remember the Bhopal pesticide plant disaster in India due to a leak that released a cloud of *methyl isocyanide* *(C_2H_3NO)* that killed thousands of people [384]. However, smaller spills are more common than large ones and these can be explosive, corrosive or toxic and can be just as damaging to people and the environment. Trucks and train cars in many countries continuously carry such hazardous materials.

In order to rapidly assist in identification and provision of other information that could result from exposure to hazardous materials/substances involved in emergencies such as spills, fires, storage or shipping, a number of directives, regulations and other information was developed in different countries. These were directed at different but very specific purposes and are currently in use, such as the **NFPA 704 Diamond** (Standard System for the Identification of the Hazards of Materials for Emergency Response) [385], **DOT** (Department of transport U.S.A. which regulates the transport of goods by ground, air, rail, inland waterways and sea) [386] and OSHA **HazCom 2012** in the United States [387]and **Hazchem** in the UK, Australia, New Zealand and Malaysia [388].

The United Nations adopted a globally harmonised system which is periodically updated and provides uniformity (*A Guide to The Globally Harmonized System of Classification and Labelling of Chemicals (GHS))*[389]. This was implemented in the European Union in 2008 by regulation (EC) No.1272/2008 and referred to as *The Classification, Labelling and Packaging of Substances and Mixtures Regulation* (CLP Regulation) [390] which came into force one year later. In the EU, the Registration, Evaluation, Authorisation, and Restriction of Chemicals otherwise referred to as the **REACH** regulation, which entered into force in June 2007, affects all chemical manufacturers (except those outside the EU), importers and downstream users (p.204)

There are also European treaties, such as the *European Agreement Concerning the International Carriage of Dangerous Goods by Road* (ADR regulation) [391] (N.B. ADR is French for Accord Dangereux Routier) affecting cross border and internal transport of goods, which has been updated as of 1 January 2017 and *The Regulation of International Transport of Dangerous Goods by Rail* (RID regulation) [392]. These regulations include transportation by river or inland waterways and are based on the UN system guidelines. The International Air Transport Association Dangerous Goods Regulations (IATA) established the international standard for the transport of dangerous goods by air.

Those who advise on the transportation of goods whether by land, inland water ways or rail, must conform to the EC Directive 96/35/EC of 3 June 1996, [393] which requires them to be trained and qualified as a Dangerous Goods Safety Advisor. The directive came into effect on 1 January 2000. Vehicle transport personnel need not be qualified to transport dangerous goods, but basic emergency knowledge and training is advisable.

The Atex Directive 2014/EU [394] (that states what equipment and work environments are allowed in places with potential explosive atmospheres) became mandatory on 26 April 2016 and is available on line.

It should be noted that for labelling, certain materials have their own specific requirements, and in the EU countries, labelling must conform to and clearly indicate such information as trade name, manufacturer information, danger symbols, etc. For more detailed information on the subject the interested reader is referred to ILO documents such as 'The Identification, Classification and Labelling of Chemicals' and 'Lists of Substances with Risk Phrases' [395].

The NFPA 704 Diamond system used in the USA (NFPA stands for National Fire Protection Association) [396] requires the display of a label/diamond shaped card having a number that identifies the material being carried, as well as a rating number over colour symbols (BLUE at left = health, with rating number providing the type of injury; RED at top = flammability, with rating number providing flash points; YELLOW right at bottom = stability/reactivity, with rating number providing sensitivity to light, heat or shock and capability to detonation, and WHITE = special hazard information such as radiation, water reactive or oxidiser, etc.) thus indicating whether the material is poisonous, corrosive, reactive, flammable, *cryogenic*, infective or radioactive. When materials above certain weights or volumes are stored in a building it may be required to have the appropriate card displayed and these cards must conform to specific sizes. There are nine hazard classes which also includes compatibility, all of which allow for immediate identification of the materials for the appropriate action to be taken.

HAZCOM 2012 (Hazard Communication) [397] system in the USA is aligned with the United Nations Globally Harmonized System of Classification and Labeling of Chemicals (GHS). This was carried out by OHSA in Washington D.C., but it did not adopt all of the GHS. The final date for all of the HazCom's 2012 system requirements came into force in June 2016 are were followed by a transition period to completion.

In their Hazard Communication and GHS Frequently Asked Questions, J.J. Keller & Associates state that, *"This standard applies to general industry, shipyard, marine terminals, long shoring, and construction employment and covers chemical manufacturers, importers, employers, and employees exposed to chemical hazards"* [398] The standard has some limited provisions for laboratory employees, those handling sealed chemical containers and office workers, but there are exemptions for some substances.

DOT (Department of Transport in the USA) is a hazard communication standard aligned with the GHS. It regulates the transport of goods by ground, air, rail, inland waterways and sea. (see Ref.386)

HAZCHEM [B48] (hazardous chemicals) is a warning system of signs used to indicate the presence of hazardous chemicals/materials for use in workplaces and of considerable value in emergency situations, such as spills, fires and contamination. It is used in the United Kingdom, Australia, New Zealand and Malaysia.

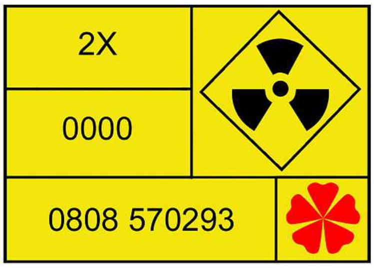


Figure 66. An example of a warning sign for hazardous chemicals.
Credit: Wikipaedia (13Jan. 2018).
https://en.wikipedia.org/wiki/Hazchem

As is indicated by the Wikipedia Encyclopaedia (2016) (see **B45** in Selected Bibliography), this particular sign shows:

1) 2X = the emergency action to be taken
2) 0000 = the U.N. Substance Identification Number
3) The telephone number to use
4)  = the warning symbol
5) The company logo (this flower is just an example of a company logo).

For much more detailed guidance, the reader is advised to visit the National Chemical Emergency Centre (NCEC in the UK) that provides a free online Hazchem Guide and also review material such as the United Nations Recommendations on the Transport of Dangerous Goods, and the Australian Government Department of Infrastructure and Transport (2008) Australian Dangerous Goods Code, and the Hazardous Materials Regulations of the Department of Transport, U.S.A.

CHEMDATA [399] is an interactive data base of thousands of chemicals used by fire and emergency services worldwide, which can provide advice on emergency spills, fires and contamination.

Chlorine, ammonia (acutely toxic), ammonium nitrate, petrol (benzene, toluene and VOCs), acids, caustic substances, 2,4,5-Trichlorophenol which releases dioxin (a carcinogen and used in pesticide manufacture and an example of chronic toxicity), the chemicals used in fireworks manufacture, fertilisers, and some fine dusts (explosive) and many other organic chemicals that are made from petroleum, are some examples of chemicals that can precipitate or result in chemical disasters. A complete list of *'substances and quantities potential to cause major accidents'* can be found in Annex 7 in the ILO guide for the 'Identification, Classification and Labelling of Chemicals, Nov. 30 2004' [400] and a guide on chemical accident awareness, preparedness and response for health professionals and emergency responders can be found in a IPCS/OECD/UNEP/WHO document - ENVIRONMENT MONOGRAPH NO. 81 [401].

Chapter 10 Ageing, women at work, disability and exposure to toxic substances [B33,B34,B35]

Ageing

Many have defined and others quantified ageing in various ways and there is little doubt that almost everyone is familiar with the concept of ageing as no day passes by without its appearance in whatever form or reason: birth, mortality, physiologically, biochemically, socially, economically or administratively.

In light of all this I would attempt to define it, at this point in time and the evolution of our species, as '*ageing is a very complex genetic, developmental and deteriorative biological process that lacks the regeneration of cells throughout the passage of time influenced by intervention, pathology, lifestyle, and the multiple conditions of its living environment to clinical death'*. The social, geographical location, economic and policy implication aspects important to ageing populations vary and would serve to supplement a baseline definition on ageing.

Quantifiably from a statistical point of view, the World Health Organization refers to 'aged' as 60 and over, and if calculated as the number per 100 persons under 15, gives what is known as the Ageing Index [(402,403)]. Comparing men to women, today women generally have a longer life expectancy, that is, the average number of years they would live provided mortality at that age does not change, although the difference is much smaller in less developed countries. Life expectancy is not 'life span', which is the maximum number of years that a human can live.

The Department of Economic and Social Affairs Population Division (DESA) report on World Population Ageing – 2013, United Nations [(404)] indicates that mortality rises exponentially after the age of 30 and the ageing populations are currently higher in the developed countries and increasing in the developing countries. In relation to the '*proportion of older persons to the rest of the population'*, DESA also reported that globally in 2000, one in every 10 persons were over 60, and projects that 1 in every 5 will be over 60 by the year 2050 and that about 37% of these will be within the European region [(404)]. The number of adults aged over 60 that suffer from some mental disorder is estimated at about 15% (WHO) [(405)]. Over time, migration from less developed and developing regions and their cultural lifestyles may have some effect, however small, on these figures.

The economically active aged population is diminishing although flexibility to continue working could and should be seriously encouraged, not only to avoid the loss of the many years' experience gained by such persons which can be passed down to the ageing and the younger generation at work, but to ensure as far as is reasonably possible their continued activity, lifestyle and health maintenance. The main concern here, however, is therefore the impact of chemicals on aging as well as any aged population at work.

Over the centuries, populations have become unavoidably dependent on chemicals at home and at work. Human chemical exposure from specific individual chemicals or a mixture of chemicals is influenced by the macro and micro environments and their complex pathways (atmospheric conditions, emissions, agricultural, manufacturing processes, metabolism, transformation, food, water, drugs, wastes), as well as a person's lifestyle (smoking, eating and nutritional status). The cumulative effects of low level exposures may affect life expectancy although it has been pointed out that there can also be beneficial, as well as damaging, effects to health.

Accepting that physical and sexual maturity ends no later than the age of 16–18 years of age, adulthood is likely reached by 18 and no later than 25. The frontal cortex is fully developed in most people at 25 years of age and it is this area of the brain that is the centre of the working memory and its network of reciprocal connections, giving one the ability to interpret, analyse, respond and be behaviourally and commercially/academically responsible, excluding any accidental damage to the organ. However, information processing speed has already peaked by 18 and short-term memory is strongest at 25. By 30, the brain has begun to structurally deteriorate which continues through to the time of death.

There are a number of theories of ageing (the *telomere,* gene regulation, mitochondrial, *free radical*, *immunological, triage,* etc.) all of which provide some important aspects in understanding the many complex processes that take place in ageing. The interested reader is referred to the many reviews on the subject. It should be noted, however, that Professor Jun-Ichi Hayashi [(406)] and his team compared mitochondrial *DNA* function in children aged 12 and those aged over 80 and discovered that the DNA in the aged was not any more damaged than that of the children, leading them to understand that epigenetic regulation (causing genes to be turned on or off) was involved in cellular function, and therefore it could be possible to reverse and reprogram cells to their stem cell state and possibly alter/reverse the ageing process [(407)].

These changes, which are slow in some and faster in others, as they depend on so many different and variable factors (genetic, environmental etc.), affect body structural, molecular, cellular, physiological, biochemical, genetic and psychological processes and increase susceptibility to the effects of chemicals.

Although the many thousands of available chemicals have undoubtedly improved the standard of living for most of the global population, it has not been without cost to their well-being and in many cases, their lives. Nevertheless, chemicals are here to stay and some of the changes to the genetic code of our ancestors that were caused by chemical exposure are, with our present scientific knowledge, irreversible and are likely to be passed on to future generations. They may also put at risk future family descendants by epigenetic regulation as a result of *DNA* methylation which is triggered by chemical exposures.

In addition to what is already known about chemicals affecting ageing workers and the aged, it would be useful to identify macro- and micro-environmental chemical substances and the concentrations of those substances. These have the potential to affect the ageing process or cause increased sensitivity or toxicity in the aged. This would establish databases which would be invaluable. It would also identify that those chemicals (and no other agents) are in fact causing the damage.

Genetic effects

Khan [407] and others have shown that there are a number of genes that can influence aging. The GenAge Database of Ageing-related Genes provides the figure of >1500 genes that can alter aging. Some specific mutations accelerate the onset at which ageing occurs, such as that which occurs with Downs syndrome [408].

Chemicals certainly interfere with biochemical processes causing damage. Long term exposure may exacerbate the condition and this could accelerate the ageing process. Potentially harmful chemicals that are absorbed can alter DNA (e.g. by epigenetic regulation or protein addition to DNA, etc.) affecting cellular and organ function, resulting in disease that then affects the ageing processes. Whether or not improvement of function could result (see research by Prof. Jun-Ichi Hayashi *et al.* [see 406]) requires further research.

Automobile emissions due to hydroxyl radicals and superoxide free radicals, heavy metals, pesticides, alkylating agents and cigarette smoke can all cause DNA damage. Some compounds such as 2-aminopurine (a substitute for the nucleotide bases guanine and adenine used in laboratory research) can bond to DNA and cause mutations. In addition, high temperatures and ionizing radiation such as ultraviolet rays (UV-B: 280–315 nm) can affect the DNA helix structure [409].

Major body system effects (see also pages 147, 109 -114)

The Brain

In spite of genetic influences (*heritability, i.e. genetic contribution to differences among individuals)* of abilities or disabilities, the brain with its intricate architecture, electrical energy and its axon system pathways to every part of the body, is a kingpin of human structure. Absorption, distribution, metabolism and excretion, of potentially damaging neurotoxic substances, however, can affect and alter brain function.

As age increases, deterioration progresses and results in:

(a) a diminishing number of neurones and dendrites;
(b) increasing plaques (*fat surrounded by dead nuclei*);
(c) atrophy of both the grey and white matter (*non-myelinated neurones process information received and transmit to white myelinated to execute*);
(d) changes in the concentration of important chemicals and hormones (dopamine, serotonin, acetylcholine, epinephrine, glutamate, GABA *(neurotransmitter*) and glycine) that affect communication, as well as an accumulation of *lipofuscin (a pigment)*;
(e) alteration in the brains vascular flow, and
(f) changes to peripheral sensory and motor input.

In most aged people, performance ability declines. In general, behaviour, reaction time, coordination and mobility are slower. Vision and hearing deteriorate and although the olfactory cilia in the nose are reduced, in some the sense of smell may increase. Taste, touch, pressure and vibration sense as well as cold, heat and pain are reduced in the aged. Sleep patterns are also altered.

The literature is abundant with information on the immune system and aging. This defence mechanism is complex and receives signals from the nervous system and relates to other systems. It seems clear, however, that there is deterioration with age. Srinivasan *et al.* provided evidence that the rate of antibody production is affected by activated *B-cells* (410). The system is slower in responding and it may begin to damage/destroy its own healthy tissue by mistake, because it fails to distinguish between one's own healthy tissues and antigens. This is referred to as an autoimmune disorder. *Myasthenia gravis* is an example of a condition that results when this happens and, in this case, neurotransmission of signals are not received by the muscles causing muscular weakness due to the production of antibodies.

A number of neurotoxic chemicals that affect the brain are provided on page 119.

The Heart and Blood Vessels (See also p. 110–114)

The symbol of the heart was used in pictograms by hunters before the last Ice Age about 1.8 million years ago. It has changed from being the symbol of life and the centre of the soul with great importance in Christian theology, to its use much later (1250 A.D.) when it became a reflection of love and heraldry, and is today widely used in Valentine cards. These descriptions certainly do not show any links to the potential of toxicity of the heart.

The value and level of toxicity from cardiac glycosides (*these chemicals are sugars and affect the heart muscle by reducing the heart rate*) found in the plant 'common foxglove' (*Digitalis purpurea*) was recognised in 1785 by Dr. William Withering FRS, an English physician (411). Glycosides are used in congestive heart failure and arrhythmias (*irregular heartbeats*). Note that not all glycosides are poisonous and they are widely distributed in plants. Toxicity results in effects on:

(a) the heart (alteration of the electrical conduction shown in electrocardiogram (ECG) changes – *AV conduction block* and sinus *bradycardia)*;

(b) GIT (nausea, vomiting, diarrhoea);

(c) nervous system (headache, drowsiness, disorientation, fainting, lethargy and depression);

(d) eyes resulting in blurred vision and different coloured halos, and;

(e) the kidneys, by lowering glomerular filtration rate (this also checks how well the kidneys are working (normal 90 ml/min) and inhibition of renal tubular absorption (return of substances to the blood needed by the body before total urine excretion).

Cardiac toxins may affect the conduction system, the vessels or the muscle and the tissue (pericardium) in which the heart is enclosed and protected. However, one must remember that ageing alone results in changes in conduction and muscle tissue, to which must be added a contribution made by choice of lifestyle, disease and environmental conditions.

Common conditions that impact on muscle by toxins are hypertrophy, deposition of fat and *lipofuscin* (a pigment).

Other possible toxins that can affect the heart include: solvents, organic nitrates, *carbon monoxide (CO),* heavy metals and alloys, pesticides and radioactive plutonium (Pu). More information on a number of cardiotoxic chemicals that affect the heart are provided on pages 113–114. Viruses and other infectious diseases to which most workers are vulnerable also affect the heart and, this factor brings into play the importance of vaccination to those at work, in particular the elderly. Indeed WHO has also considered the prevention of infectious diseases in the elderly as an important health priority [(412)].

There is an unavoidable link between blood vessels and the heart so that the ageing or damage to vessels contribute to the development affecting function of the heart, although the level and rate of change is unlikely to be the same in everyone, including those who may be genetically vulnerable. Studies have shown that in those whose arterial walls have thickened and have therefore become less elastic, the heart walls are also thicker. Over many years, lifestyle factors such as smoking and diet, fats including cholesterol, calcium (Ca) and blood cells can build up and adhere to the inside of arterial walls (plaque). This narrows the lumen and initiates the development of what is referred to as 'atherosclerosis of the blood vessels'; a risk of arterial blockage affecting more commonly the heart and/or brain.

In addition to physiological effects on blood vessels, those working in extreme thermal environments or those sensitive to changes in temperature (chilblains, frostbite, gangrene) and those who use manual vibratory tools (vibration white finger – also referred to as hand-arm vibration), antihistamines, smoke tobacco or hyperventilation, which causes a reduction in their blood levels of CO_2, are at risk of blood vessel constriction. *Vinyl chloride* used in the plastics industry causes constriction of vessels in hands and feet (*Raynaud's disease*). *Histamines*, nitric oxide (NO) and a number of medical drugs will dilate the vessels altering blood flow.

Solvents (amyl nitrite and butyl nitrite) used in medicine and by sniffers will dilate blood vessels, and other solvents have been shown to reduce regional brain blood supply. Alcohol also has dilatory effects as can petrol or perfumes. Dilatation of the blood vessels invariably causes headaches, lowers blood pressure, and the supply of blood to all body organ systems affecting function. At work a decrease in concentration, possible mobility unbalance and fainting may occur, so that delegation of some tasks may place the worker at risk.

Susceptibility changes (see also p.74)

It is important not to confuse susceptibility with sensitivity. The difference must be taken within the context of the subject matter in which it is discussed. For our purpose sensitivity is the degree to which one responds to some stimulus whilst susceptibility is the vulnerability to such stimuli. Susceptibility is related to genetic makeup, previous exposure experience and overall health status. Note also that people may become susceptible due to the hazardous work in which they are involved, their habitat and culture.

The fact that degenerative conditions occur and body functions alter over time in the ageing, as many of us are experiencing, is indisputable. However, the evidence for the precise causes of these alterations still leaves much to be done, in spite of concentrated ongoing research. Our increasing immobility, cardiac and respiratory function, skin changes, altered cycle of urinary excretion, vision, hearing and short memory retention, are some or all of the changes that are undeniable in most of us, and often lead to dependence on others because of our frailty. Some, of course, remain healthier than others.

Many ageing and aged individuals take increasing numbers of medications, the side effects of which they could be susceptible. Metabolism changes with age and susceptibility to bacterial infection is increased. This has also been shown following injury [413]. Climate change and exposure to environmental pollutants (work, domestic or atmospheric), is unrelenting and an added burden to body function in the elderly, particularly if the immune system is compromised and kidney function is reduced since the rate of excretion of metabolites and other substances is more limited than in the younger age group.

With advancing age, changes in absorption of chemical substances from the skin, gastro-intestinal system and the lungs have been well documented. Dermal, GI tract, and alveolar absorption is generally decreased. The gas exchange in the alveoli of the lungs due to membrane permeability is altered in the aged and may exacerbate toxic effects. Skin absorption is reduced, and the reduction of absorption from the gastro-intestinal tract results in extended periods of time in which the toxic substances remain in the gut and facilitate further absorption. The aged are also at risk from heat- and cold-related exposure and illness at work. In addition, heat waves may affect the aged by exacerbating existing health conditions.

The visual system is affected by a number of environmental toxic substances. Accommodation of the lens of the eye (visual acuity) is affected by discoloration of the lens (metals such as *copper* (Cu) or *organic mercury (C-Hg)*. Also common in old age is cataract formation of the eye lenses which may result from long term exposure to solar radiation and many toxic chemicals used in manufacturing processes such as dyeing, perfumes, and paints. Ocular vascular changes also occur.

In conclusion, following these few points provided on ageing, it is important to understand and take into consideration the extent of the elderly's vulnerability, identifying the vulnerable groups, so as to plan and implement policies for prevention. (If interested see **B34** for more information).

Psychological changes [B34]

There are many different but related topics of psychology: genetics, childhood roots and development, body organ functions, environment, deprivation, etc. Of considerable practical importance at work is to *'get along'* with everyone else and relate to their safety and your own, which often requires some adjustment to what one knows about one's personality traits such as physical limitations, personal ambition/drives, emotion, aggressiveness, envy and jealousy, sociability etc. Workplaces are more than just about work. They represent new relationships, friends, credibility, reliability, achievement, behaviour, happiness or depression, experience, safety, security and social networks.

The periods of transition from adolescence to ageing and the aged in which hormonal, physical changes, learning experience, independence, social relationships and pressures, as well as the inevitable occupational/economic objectives, make up a complex system that shapes our overall psychological responses. An understanding of behaviour is therefore paramount at work, as indeed it is for everyone else throughout life.

There are many who are affected by psychological illness. These could be of an organic nature, such as alcohol addiction, head injuries and such conditions as anxiety, fear, phobias, and obsessions, all of which may affect behaviour and affect work activities.

Excluding any organic factors, medicinal therapy and specific toxic exposure, changes may be expected once hormonal functions begin to alter in the early or mid-forties, although the hypothalamus and pituitary in the brain do not reduce their hormonal supply to any great extent, but the organs that receive their messages alter in their response. These responses affect metabolism, blood volume, sexual drive, bone structure and electrolyte balance.

Over the years these changes/alterations provide warning signs of fatigue, altered sleep patterns, sensory impairments, changes in personal appearance, anxiety, and sometimes loss of interest, withdrawal and confusion. The use of therapeutic drugs and inability to adjust to technological change at work and family loss add to any existing depression and other mental health status. A change in immunity may also be noticeable. Toxicity from exposure to previous substances such as lead (Pb) which can be released in later life from body storage, and levels of *copper (Cu), zinc (Zn), iron (Fe), aluminium (Al) and mercury (Hg),* may lead to neurodegenerative changes and behaviour.

Women at work

The World Bank reported that the Total Global Labour Force in 2014 reached 3.384 million [(414)]. The Intelligence Unit of the Economist in an article that presented a profile of the present (2016) and future of the global workforce [(415)] indicated that more than 50% of the world's population are women and these outnumbered males in tertiary education globally. These numbers are expected to increase over time, especially in the younger age groups, and it is difficult to accept that this will not happen with increasing education, expanding service industries, lower birth rates, and an ageing population. A large number of those at work in 2015 were employed in agriculture, although this trend was switching to an increase in the service industries [(416)]. Note that whenever reviewing population sector statistics, there are differences in the way countries record/ include part-time, unpaid, the armed forces and others, some of whom may be under recorded due to survey difficulties.

There are many sectors of employment from which women are banned by legislation [417], such as mining or industries in which they would be at increased risk. Much depends on the particular country legislation and the manner in which terminology is defined, such as the meaning of 'heavy work' [see 415]. However, with strict preventive safety and health policies, and monitoring of conditions at work in some places, there would not be many occupations in which women cannot be employed in.

Most women continue working to the late stages of pregnancy, but the necessity of taking maternity leave clearly precludes them from employment for varying periods of time. This is also a matter of importance to ensure adequate breast feeding time in view of the knowledge that breast milk is protective to both the infant and mother. Flexibility of working hours or part time employment is another important factor in their adjustment when returning to work. This would reduce the stress that develops and still provide maximal efficiency during the allocated employment periods. Both flexibility and part time work are also important for the aged at work.

An important factor to consider is that there are physical and biological differences between men and women, and between women themselves, and these must be taken into consideration in assessment of risks at work. Women who continue in employment and are over the age of 65 and over suffer from dizziness much more than men. Many women select work in social sectors such as supermarkets, health care facilities, pharmacies, social work and school education. This selection brings them in contact with large members of the general population and is often the cause of difficult situations and conflict, resulting in considerable psychological stress.

Many surveys have shown that women are exposed to violence, sexual harassment and bullying at work. In addition they are exposed to chemicals, ergonomic hazards repetitive strain syndrome, the hazards of piece work and fast high demand sorting by hand, monotony, shift work, radiation on long haul aircraft duties, lifting and needle injuries in health and social care, hazards of night duty in some sectors, as well as other more general physiological (such as response to heat) and biological hazards. The burden of domestic and other duties at their homes only adds to this list.

With many countries moving into delayed retirement, one cannot ignore the potential physical and health implications of retirement-age women who return or remain at work past retiring age.

The risk of injury is known to increase with age. Slipping and falling are commonplace. Women's vulnerability to osteoporosis, arthritis, fatigue and indeed many chemicals because of differences in chemical metabolism, must also be considered. Harassment is yet another issue affecting work performance that must be considered.

Legislation is gradually changing in many countries in relation to women at work as equality gathers momentum but much depends on culture and attitude in both developed and developing countries. Responsibility to ensure equality is essential but it must be accompanied by stricter safety and health policies, if the male-to-female gap in work-induced disease and injury is to be maintained rather than reduced. The reader is referred to J. Hassard's paper on 'Women at Work: An Introduction' (2016) [418].

Disability

At the 54th World Health Assembly on the 22 May 2001 the World Health Organization (WHO) Member states unanimously endorsed a resolution to describe and measure health and disability as an International Standard at both individual and population levels. This is referred to as the International Classification of Functioning, Disability and Health (ICF). Many countries now use the resources of the ICF that include data bases, surveys, indicators etc. Note that the ICF allows for the impact of the environment on both an individual and a population.

There is a difference between disability and incapacity as these terms can cause confusion in decision making since an individual may be unable to work as a result of some medical condition and yet not be disabled. Disability is a functional limitation.

Incapacity, whether temporary or permanent, has many origins; for example, it can arise in the very early stages of life, toxic chemical exposure at work and agents used in wars, radiation and air pollutants (fires, *sulphur dioxide* (SO_2) etc.), as well as physical (extensive skin burns, vertebral injuries, corneal damage, etc.), physiological (respiratory or reproductive damage) and mental damage. In some cases toxicity may lead from work incapacity to cancer and death.

Although compensation schemes exist in many countries, and litigation may have to be pursued, this is little consolation to the family and social life of the individual. Responsibility to the management (including the education of workers and others) of potentially toxic substances of whatever nature (e.g. asbestos) is vital to the reduction of disability. Some occupational conditions do not appear for many years, making compensation application difficult to prove. Albeit there are many other issues to consider in dealing with incapacity, such as return to work and personal adjustment in possible new working environments.

Chapter 11 Culture, social conditions, geographical habitat and exposure to toxic substances

The cradle of human civilization today consisting of 7.4 billion people contains a huge number, diversity and uniqueness of cultures. Many have mixed with other cultures and current increasing immigration is facilitating a gradual decline in diversity in spite of the important efforts of UNESCO and other international organisations who endeavour to protect and promote this uniqueness in language, art, music, lifestyle, beliefs, attitudes, behaviour and values, and cultural identity. Note, however, that as Helen Spencer-Oatey put it: "*Culture is a notoriously difficult term to define*" as it has *"multiple meanings, usages and understanding, some attached to different political and ideological agendas"* [B36].

Food cultures and toxicity

The immense volume of published books on food and its preparation, each one dedicated to its particular country, is clear evidence of the diversity of local cuisine adopted by people of different cultures who become exposed to long term and often low level effects of a variety of indigenous food ingredients, some of which have undesirable toxic properties even at low levels and others which have immense health benefits. The methods of cooking, and utensils used, can play a significant part in the toxicity of the ingested food. Storage too may have an impact on the retention of some of the ingredients in food.

In some countries it is customary to farm and eat large quantities of kelp. This is a sea weed called 'bladder wrack' (*Fucus vesiculosus*), which contains 30+ valuable minerals and absorbs toxins such as heavy metals (arsenic, etc.). It also contains alginate which prevents the GI tract from absorbing fat [419, 420]. However, it also contains iodine (I_2) which is useful but if taken in large amounts can affect the thyroid causing hyperthyroidism. The seaweed's high salt content may also affect those with elevated blood pressure. The effect of *alginate* on fats was shown by Prof. Jeff Pearson *et al.* of Newcastle University in a study published in Food Chemistry (2014) [419].

Cassava is an important carbohydrate eaten by millions of people everywhere and is a staple food in some countries. It contains valuable nutrients but again also contains a toxic substance called *linamarin* [421], (note it may also contain other toxins not yet identified) which if not cooked correctly is converted to cyanide in the GI tract and unfortunately deaths continue to occur. In Japan, cassava consumption is prohibited. The almond is an example of a seed that naturally contains cyanide and is commonly used in foods. Heating/roasting destroys the content of cyanide, but this bitter almond continues to be grated into foods for its flavour. The seeds of cherries belong to the same family as almonds and sucking or chewing them when eating cherries releases prussic acid (hydrogen cyanide – HCN).

The training of chefs who are learning to prepare foods often includes the knowledge required to process edible poisonous plants, fish and other substances and render them safe to eat. This is particularly so in the preparation of the Puffer fish whose flesh is very mildly toxic but has a very poisonous liver. Mushrooms (the toadstool is one example) and the castor bean (toxic ingredient is ricin) are both poisonous. Workers who collect castor beans are at risk unless they follow the strict prevention policies for collection.

Potatoes form part of everyday diets in many countries. Both contain high levels of *glycoalkaloids* in their leaves and stems which should not be eaten even if cooked. Some people eat green potatoes, and or drink potato leaf tea, both of which contain high levels of the toxin.

What has been presented above are just a few examples of the relationship between cultural conditions of food intake and toxicity. Should the reader choose to research the composition of foods, it will be increasingly clear that in addition to composition, once absorbed, metabolic transformation may alter chemical substances, and some may result in toxic metabolites irrespective of their level of toxicity, many of which are at very low levels indeed. Furthermore one must remember that the dose or amount ingested is a critical factor in poisoning. Excellent examples are the apple seed, cherry pits and almonds, which contain cyanogenic glycosides, yet one would need to ingest a fair amount. However, they are best avoided as the cyanide reaching the GI tract cuts off the oxygen uptake by red blood cells. Inhaling *cyanide* is of course extremely dangerous and may be fatal.

The function of target organs and general health balance are altered by inherited or physical limitation. In addition different cultural practices and traditions or beliefs can affect body organs. Plant translocation/uptake and plant concentration of soil constituents such as metals or starch may also alter organ function as a result of seasonal consumption of plant foods.

Where supply of marine food is continually abundant as in fishing communities, many rely on food from the sea as their stable diet. This exposes them to *volatile organic pollutants and methyl mercury (CH_3HgCH_3)*. In some areas *methyl mercury* levels in some fish are high. Molluscs (mussels, snails, squid, octopus, and the bivalves – clams, oysters and scallops) also play an important part in the food chain. Due to their unique way of feeding, bivalves absorb many contaminants toxic to humans by ingesting and retaining them in their bodies, which humans then eat. Some may have fed on other marine creatures such as phytoplankton that are very toxic. Ingestion of contaminated oysters may cause neurotoxic problems in humans. In addition, contamination with bacteria and viruses may also affect those eating molluscs.

A large number of synthetic chemical ingredients can be found in most processed foods which serves multiple but useful purposes for commercial desirability, preservation, stabilisation, colour, texture, rapid availability/convenience, etc. Processed foods are usually relatively high in salt and sugars which are mostly synthetic. Some have added vitamins. For example: sulphites aggravate asthma and destroy vitamin B1; *butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA)* are both currently being considered for possible genetic damage; *aspartame*

[422] breaks down in the GI tract into methanol and other products and there is much controversy on its dangers; and various colourings may cause hyperactivity. Therapeutic drugs may cause gastric, bone, heart and other organ disruption even though these may be temporary.

Culture and geographic location

The geographical location of where different populations make their homes cannot be separated from the risk of toxic exposure at work or otherwise. Most rocks contain uranium and its radioactive decay forms radon and radium. Some locations have higher levels of radon than others and because radon is a very mobile gas it moves easily between rock cracks and soil and enters the air in workplaces and homes where, without adequate ventilation it can concentrate. Its atoms can attach to dust which is then inhaled and emits alpha radiation that damages lung cells and may later result in lung cancer. It is also found in areas where ground water is used. If used for drinking in some locations where arsenic deposits heavily contaminate ground water, this very toxic substance can become a very serious problem affecting many organs, pigmenting skin, badly damaging blood vessels and causes cancer in spite of it being rapidly eliminated from the body. Those living in volcanic or near mining and smelting locations, are also at risk from inhalation of soluble arsenic compounds that also attach to dust particles. Smoking increases the risk. Other areas, (*where many expatriates find more lucrative work, but not excluding local inhabitants*), such as deserts, dense woodlands and wetlands, also present other risks from silica, fungus, microbes and venom.

Poverty

Low income levels, general sanitation and personal hygiene are other factors to be considered. Over the years in my extended work and travels in developing countries I have seen open channel sewers in streets, dug out open latrines, sheep and other animals living in homes in close contact with children and the elderly, and unprecedented poor personal hygiene at home and at work. These factors in combination with the repeated use of aerosol insecticides (to avoid insect vector transmission) weigh heavily on toxic exposure.

Poverty, however, is not solely correlated to the level of household income and much depends on the value that individuals or families allocate to the conditions in which they live. To some it has become a standard of living and no effort is made to alter it. Such conditions are indicative of insufficient attention and support from those who have the power to improve inequality, avoid social conflict, reduce morbidity and mortality, support education and create positive social change.

It is not a matter of simply increasing minimum wages, where these exist, useful as these may be. A holistic approach to a gradual change in a population that deserves an equal chance to progress, with opportunities for work and the development of choices and values through educational support in many essential areas would go a long way to changing the unfortunate conditions of so many worldwide.

The few points made here will, I hope, alert the reader to aspects of the exposure of workers to toxins from ecological concepts, natural resources, cultural, habitats, diets and contaminated sites, beyond the general industrial scenes to which safety professionals are usually confined and to which they should, together with occupational health personnel, give consideration when and where appropriate.

Migration

Historically human migration began about 1.75 million years ago ( ). Movements from a migrant's place of origin to other areas was probably initiated by factors such as lack of food supply, a change in climatic conditions, raiding by others groups and slave exploitation, exploration or some yet unknown factors of those times. Over the millennia there have been peaks in the numbers of those migrating far from their homeland; in the 19th century 50 million people left Europe for America" ( ). A similar peak in migration is taking place today as a result of civil wars, violence, genocide, persecutions, or geographical divisions within a country that results in people's displacement. Some simply seek better economic conditions, education and a safer family life. Migration from rural to urban areas continues to this day. Although migration may be legal or illegal today many countries are posing restrictions on such movements and impose other conditions such as the learning of the country's language. All this being said one must note that some of these migrants are highly qualified workers and turn out to integrate well and become an asset to their country of choice where choice is possible.

The U.N. International Migration Report 2017 states that *"migrants had continued to grow and reached 208 Million worldwide"* of which "*78 million live in Europe*." Women make up *"48% of all migrants."* In Europe female migrants outnumbered males migrants in 2017( ). The report also indicates that "the median age of international migrants worldwide was 39 years." The U.N. General assembly adopted the New York Declaration for refuges and migrants *"reaffirming the commitment of Member States to protect the human rights of all migrants, regardless of status."*( ).

Globalization of business has initiated labour immigration throughout many countries that are resulting in flexible immigration policies. These bring about temporary allocation of specialists or highly experienced employees of large organizations to their subsidiaries which contribute to the countries' economy and further education and skills of those who are employed by these multinational subsidiaries. To this effect on 15 May 2014 Europe adopted the European Union Directive 2014/66, - the conditions of entry and residence of third-country nationals in the framework of an intra-corporate transfer." ( ).

Many migrants obtain work in the construction industry and although proficient in their activities have little or no knowledge of safety or health policy requirements. This group is at high risk from injury and illness at work. Difficulties with interpreting language on what is demanded of them and more often than not, having long hours of work, increase their risks considerably. Unawareness of the hazards of dusts, fumes and potentially toxic substances, possibly undernourished and inappropriately immunized migrants are vulnerable to many existing unsafe work environments. Other service employment activities are not necessarily free of similar potential hazards.

Chapter 12 Toxic substances and European Law

The chemical industry

The chemical industry is an essential global pillar that supports many other industries both directly and indirectly, supplying raw materials, employing millions of workers, and forming part of a chemical chain from supply to disposal, generating billions of dollars and contributing to GDP. In Europe alone in 2012 it provided '*1.2 million directly highly skilled jobs'* (see 416). Clearly, safety, health and environmental protection requires serious attention by all stakeholders.

Worldwide information on the toxicity of chemicals from research institutions, production processes, industrial chemical incidents, transportation, transboundary air pollution, import and export of chemicals amongst others, have contributed to international and national legislation. In spite of the current lack of toxicity testing, due to the considerable existing and daily increase in the number of available chemicals and existing current methods employed in testing, this accumulated data has resulted in a vast improvement in the prevention policies of public health, safety at work and the environment. There is, nevertheless, a lot more to be done.

European Union (EU) Legislation has been transcribed into or affected the laws of many countries , which not only made toxicity testing compulsory for chemicals that are produced or imported into Europe but also places a responsibility on the safety of chemicals of very high concern (e.g. carcinogen, mutagenic, teratogenic, persistent). A time limitation for registration was established for these, and those that remain on the markets must prove that they can be appropriately controlled or undergo a chemical substitution.

The **Registration, Evaluation, and Authorization of Chemicals** (REACH) (423) recommends the substitution of hazardous chemicals where reasonably possible and a Safety Data Sheet must be provided to users. This ensures an information communication process through the whole of the supply system in line with the 'right to know'. Such advances inevitably bring with them industrial and commercial impacts as well as the need for easy access to chemical information, conflict, disputes and political effects.

REACH initiated not only a European, but a global movement, establishing standards in the implementation of chemical legislation, focusing on research, substitution and disclosure. Through such legislation, potential risks can be prevented before widespread damage ensues, whether this is as a result of its use, some intermediate action or disposal.

REACH makes no difference between 'existing' and 'new' chemicals. It requires that all substances produced or imported into the EU must be registered with the

European Chemical Agency (ECA). A minimum quantity was established on the production and importation levels of the substances, as well as minimum toxicity data required, which includes both risk (carcinogen, persistent etc.) and hazard (analysis of human exposure) data. This has served as an incentive for producers or exporters to provide the information.

Whilst it may be argued that the cost of the implementation of the REACH legislation may have been and continues to be high, in relation to the overall revenue from chemicals 'this is probably very low. In addition, the gains resulting from the reduction in health effects, loss of life, social impact and litigation, as well as the reduction of the costs involved in each of these, are well worth the preventive policies and their resultant impact on people at work, the public and the broad general environment.

European legislation lays down a number of obligations on its Member States in different aspects of chemical management and control through Directives. In addition to the Chemical Agents Directive and the Safety Health and Welfare Chemical Agent and Carcinogens Regulations, many other aspects and specific groups of chemicals are covered by their own legislation together with amendments. These include: 'Good Laboratory Practice', 'Classification, Labelling and Packaging', biocides, pesticides, fertilisers, drugs, oils, pyrotechnics, cosmetics, detergents, explosives, storage, transportation, skin and eye irritation, endocrine disruptors, import and export of dangerous chemicals, etc.

Most countries had legislation in place long before EU legislation was proposed, although there were significant differences in the comprehensiveness of their approaches. In countries where the directives had to be adopted by EU Member States, they have and continue to show improvement in safety and health conditions. The influence of EU legislation has undoubtedly had some effect on the efforts made by countries beyond the European Union Member States too. The details and interpretation of any specific country's legislation is beyond the scope of a general overview here.

Individual country legislation often goes beyond the minimum standards of the EU directives in some aspect or another. The monitoring and inspection of Safety and Health conditions at places of work depends very much on the availability of staff and financial resources. Many small and medium size industries (SMEs) within the chemical chain are limited in how much they are willing or can comply with the burdens of chemical legislation in spite of prosecution and the penalties involved in some countries. Assessment of risk is therefore not always what it should be, when or if carried out at all. Such conditions erode the inestimable value of existing chemical legislation and invite potential danger to workers, their families and the environment.

Chapter 13 General Principles of Prevention

Reducing Risk

There is no intention here to explain the management of risk and the reader is directed to volume 2 of the books on this subject edited by John Ridley & John Channing published by Butterworth Heinemann, and Health and Safety: Risk Management by Dr. Tony Boyle printed by Lavenham Press Ltd, UK. but simply to note that in addition to many other responsibilities, safety practitioners have a responsibility to reduce the risk of exposures to potentially hazardous substances. This requires the development of an occupational prevention strategy and a plan of action establishing specific targets by which to achieve the activities planned. Such a plan essentially needs an input from others within the workplace for which it is intended. This is usually obtained from members of a safety committee which should include plant and production managers, the company physician/nurse, the safety practitioner, and others brought in as required, such as maintenance workers, necessary to achieve the planned objectives. A company policy that provides commitment to the health and safety of all employees, including management itself, is essential to success.

Each worker becomes an 'expert' in their specific job, and their participation is of the greatest value in determining or refining what and how much should be done. This issue is most important when new materials or tools, machinery or other equipment, are brought in for them to use, making education another important aspect of the principles for the prevention of potentially toxic exposures. Job safety analysis has proved a very useful tool for the purpose of identification and prevention of exposure hazards in which the worker himself has an essential role to play.

Prevention programmes

Occupational Physicians and Occupational Hygienists also have a strong role in prevention programmes which they carry out by careful observation, measurement and screening of possible health changes in the workforce, in particular when the change occurs in more than one individual worker, and consequently take immediate action to prevent further exposure.

Each country's legislative and regulatory rules on the control of substances hazardous to health, labelling, personal protective equipment at work, fire and disaster precautions, and, where appropriate, the mining and quarrying regulations, as well as the minimum workplace health and safety requirements, provide standards to follow. These can also be supplemented by the many codes of practice, ILO's conventions and guides to occupations to ensure a successful outcome to prevention programs. There are also lists of chemicals that use risk and safety phrases. In addition to the above, there are other specific standards for e.g. carcinogens and a useful list of known carcinogens, which includes other names used for the substances, as well as carcinogens and chemicals which have been banned.

Employer duty

The general duty of every employer, and indeed every employee, to ensure that as far as is reasonably practical, no employee suffers any impairment of health or functional capacity from toxic exposure is quite specific. Threshold Limit Levels (TLV's) are only recommended guidelines because they are not totally adequate but can help to protect against exposure to toxic substances.

The 'right to know' and to refuse hazardous work is a preventive/protective mechanism for employees. The requirement to educate and provide safety regulations give further support to preventive programs.

Prevention

General principles of prevention should apply to all resources such as:

(a) labour (personal protective equipment, appropriate instruction, training and information);

(b) operations and equipment (engineering controls, adaptation to new technology, research and other progress);

(c) materials (purchasing, elimination, substitution, potential explosive materials, administrative policies);

(d) transportation (where appropriate, education and training of drivers, health examinations, emergency response, legal requirements), and;

(e) the internal and external environments (using a system approach), access and egress, air quality, ventilation, electrical considerations;

(f) occupational hygiene measurement where required, fire, etc. These should apply both at the design, implementation, alterations/extensions and following monitoring stages.

Other general principles for the prevention of exposure to potentially toxic hazards directed to the workplace therefore include:

1. Changing work practices;
2. Installation of engineering devices, if appropriate;
3. Elimination of hazardous, or substitution by non-hazardous, substances
4. Planned surveillance / monitoring;
5. Risk assessment including surrounding neighbourhood;
6. Training in emergency response.

The above principles assist in the removal of the hazard at source which is good practice. Those directed specifically at the worker cover:

The provision of advice, education, training, periodic re-training and where appropriate specific training for job tasks / activities, such as transport spills etc.;

1. Pre-placement examinations to avoid exposure to susceptible individuals;
2. Safe working procedures;
3. Hazard communication (labelling/safety databases/specific health risk
4. information to employees);
5. Reduction of the exposure;
6. Remove or rotation of workers to reduce exposure time;
7. The use of personal protective equipment;
8. Exposure bans for pregnant employees and breastfeeding mothers
9. Codes of practice on shop floors;
10. Codes of practice on the changing of jobs within workplaces;
11. Codes of practice for the disaster drill involving toxic materials;
12. Training in first level first aid and resuscitation.

Primary and secondary prevention methods

Most of the above are primary prevention methods. Secondary prevention would include the provision of first aid and emergency treatment for acute poisoning and screening of employees.

Practical prevention measures (choosing safe/safer solutions) should start when planning any new workplace, workplace extensions, or new materials / processes are being considered. Such changes in work organisation happen more often than one realises, although one is more often involved in planning interventions for already existing places of work.

Small enterprises often have very little funding available for investment in practical prevention. They continually face the problems that legislation and human rights to the health and safety of all at work brings about. However, simple low cost solutions exist or can be identified to carry out prevention measures and these should be given priority so long as they achieve what is needed to meet requirements. Many at top management of larger companies often see little of the efforts that underlie the production of their organisation's products and services, and digital photography and other technologies today provides a cheap system to bring information to their desk, portraying the dangers and legal liabilities to the company of exposing their staff and for which solutions must be found.

A NOTE on handling a toxic incident [401]

This is something that everyone must approach with great care, because it can result in needless loss of life. Except for some general action, much depends on the specific toxic substance involved. You may be called to the scene of an incident at the place of work (or outside the place of work) involving your company's employees, e.g. a spillage that occurred during the transport of a hazardous substance. Clearly, there are many scenarios. In the event that toxic material(s) are present at the place of work you should:

1. Already have some knowledge of the probable toxic substance/s that the specific worksite or type of organisation is likely to be using. Failing this, request someone to bring the company's specific chemical database to you, and the chemical emergency response policy report

(based on previous risk assessments). This should be available at all times.

2. Evaluate the situation and decide what general action you should take to protect those involved and any others around the site, including company property and/or neighbourhood (such as fire responses, incompatibility of chemicals, evacuation, shut down of electrical supplies or machinery, sector isolation, request for chemical absorbers or respiratory protection equipment, call internal emergency response team, first aid assistance or hospital services). Always make sure you have an escape route planned.

3. Be sure to follow all policies for the specific situation.

4. In the event of surrounding external chemical fire incidents within the grounds of the organisation, take note of wind direction and based on extent of fire and smoke, ensure isolation of the workplace to avoid spread if possible and need for safe evacuation of personnel. Evaluate possible need for informing fire brigade, especially where cooling sprays may be required on external storage, cylinders, silos, vehicles or other items, including any vulnerable building structures and potential explosion.

5. In the event of large chemical transport spills, identify the toxic product/material involved by checking the transport labels and any documentation that is being carried by the driver. Call Fire Brigade to assist with containment. If it is not possible to obtain information on the product / chemical involved, contact the company transporting the material, or investigate via the vehicle number plates.

6. If a spill is within company grounds and small, then make sure you are dealing with the right substance and check with data sources and inform the Fire Brigade. Assess whether you can contain any small spill or leak and ensure that it is diverted from any sewers, drains and prevent mixing with any other chemicals.

7. Identify any trained personnel that you may need to help or apparatus to be used and place these upwind from the spill of the toxic substance. Decide your escape route. Always make sure you have an escape route planned. Ensure that personnel are protected and that you have rescue personnel available to help if needed.

8. Make sure you use the correct protective equipment for the job in hand.

9. If the toxic spill is small but flammable, or may be already burning, you will need to take other precautions.

10. Decontamination may be necessary once the incident is under control. This includes equipment, clothing, skin and any water or other liquid run off.

11. Once the situation is under control and completed, ensure that a report is prepared, submitted to management and should any alterations, correction to policies, procedures, employee training, or increased practice sessions be required, develop a request for future implementation.

Note that the above only provides some general guidelines. These should direct you to carry out further research in more detail of the subject/s related specifically to your responsibilities at your place of work.

Postscript

In retrospect, although my target audience has been safety undergraduates, I am confident that some sections of this book may refresh the memories of Safety Professionals, Occupational Nurses and Occupational Physicians through many of its chapters as well as help others forming part of the team necessary towards the pursuit of the holistic and effective management of Safety and Health. Hopefully, it will benefit them as a means of reference and resource and provide an understanding of its wider context. Safety is a dynamic subject with considerable overlap in health, occupational hygiene and environmental issues to say the least. It might also serve as a fundamental introduction to other interested parties and to those aspiring to learn a little more within these disciplines, and serve to create an appreciation or better understanding of the chemicals used by workers in different jobs and types of industry, as well as the many issues that exist at different workplaces throughout our world.

LIST OF APPENDICES, REFERENCES AND SELECTED BIBLIOGRAPHY

Appendix I

INDEX

This index provides an alphabetical list of subject matter and where it appears in the book for reference. Descriptions of words and chemicals can be found in Appendices III and IV.

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Appendix II

Part 1: Reflection on some basic biology

What is a cell?

The cell is the smallest unit of every living organism. It may form part of a community of cells (multicellular – such as plants or animals) or function as a single unit (unicellular – single cell, such as bacteria or *amoeba [single cell with ability to alter its shape]*). Multicellular organisms form tissues (the skin, muscle or bone), and tissues form organs (the brain, heart or kidney etc.). Each organ has its own special function and together they make up the organs that form a multicellular organism such as the human body.

The first type of cells that evolved on Earth were PROKARYOTIC cells [424]. These had one *chromosome* but no nucleus. From these cells arose two types of bacteria (Archaea and Eubacteria) and a related species called Eukarya (Eukaryote cells that developed a nucleus). See Figure 67. These Eukaryote cells that arose from the prokaryotic cells gave rise to animals and then the rise of man as we understand things today. Human cells are multicellular and mainly Eukaryote, unlike those of bacteria which are unicellular. There are about 200 different types of specialised cells [424].

PROKARYOTIC CELLS
Unicellular; no nucleus but have one chromosome

ARCHAEA **EUBACTERIA**

Related Species called
EUKARYA
Multicellular with Nucleus

ANIMALS

HUMANS
Eukaryotic cells forming organ systems

Figure 67. Cell development on earth from the first type of cells believed to have evolved around "3*.5 - 3.8 billion years ago*" [424] although "*one study (2015) found remains of biotic life from 4.1 Billion years ago*" [425].

A cell has a MEMBRANE consisting of a thin, semi-permeable barrier made of *phospholipids* and protein molecules arranged into a bilayer. Protein receptors/sensors at the surface of the membrane (also called 7TM receptor - TM means transmembrane) control the movement of substances through PORES between the inside and outer surroundings of the cell [426]. The inside of the cell is composed of CYTOPLASM (a thick fluid in which all the cell content lies and consists mainly of water and salt. Within the cell are a number of structural elements made of proteins and also bodies called organelles, each of which has its own special function [427].

Each cell has a NUCLEUS which contains the DNA or 'blueprint' of the information required to replicate itself (split into two identical cells – you will learn more about DNA, its types and roles later in the book). This information is the same in every type of cell whether it is a nerve cell, a skin cell or a heart cell. The DNA is folded into spirals within the nucleus, which helps to make space for other elements such as the NUCLEOLOUS (a smaller nucleus that produces RNA [ribonucleic acid] and carries instructions from the DNA in the production and control of proteins), and *ribosomes* (cells that assemble proteins from amino acids) [426]. See also Appendix III p.232 for more detail.

Within the cytoplasm of the cell are other important structures/bodies (see Fig. 68), the most important of which are as follows:

(1) The MITROCHONDRIA [426] produce the energy required for all the cell's activities by oxidative phosphorylation. This is a metabolic pathway where cells use enzymes to oxidise nutrients and release energy, a complex process which produces ATP (adenosine triphosphate) the energy-supplying molecule. The cell stores it for use and maintains it at a level of around 60%. The process can be anaerobic or aerobic, depending on whether oxygen is used or not in the breakdown of *glucose* from food intake. About one third of the energy of the cell is used up in maintaining a balanced concentration of *sodium* (Na) and *potassium* (K), which is required to raise or lower the osmotic pressure in the cell (pressure needed to maintain the equilibrium between the d6fferent concentrations of substances in liquids on either side of a membrane) [427].

(2) The RIBOSOMES [426] which are minute particles that help assemble proteins from amino acids according to instructions provided by the mDNA (m = messenger) which comes from DNA in the nucleus. There are two parts (units) in ribosomes, one reads instructions, the other assembles. Ribosomes can be seen to float in the cytoplasm of the cell or surround the endoplastic reticulum.

(3) The GOLGI APPARATUS [426] which receives the proteins produced from the ribosomes and distributes them to where they are needed.

(4) The LYSOSOMES [426] that contain *enzymes* to break down all cell debris.

(5) The NUCLEAR PORES [426] (channels) that control the exchange between the nucleus and the cytoplasm.

(6) ENDOPLASMIC RETICULUM [426] containing vesicles and two type types of tubules: a rough type that synthesises proteins and a smooth type to synthesise fats.

(7) MICROFILAMENTS [426] which are proteins that make up the cytoskeleton, which help the cell keep its shape.

Cell division, where a cell divides into an exact copy of itself (mitosis), is divided into different phases and each phase is controlled by the correct level of a substance called CYCLIN [427]. Division commences once the correct level of cyclin has been reached but before it physically divides, it produces copies of its own DNA, one copy for each daughter cell. Any error in copying results in a mutation – where the structure of a gene is altered and will be passed on to subsequent generations – although generally replication is pretty accurate. Once complete, separation takes place and two daughter cells are formed and each cell starts the process of mitosis all over again. Later, each cell may begin to specialise into its specific function, thus forming the various organs with their respective specialised activities in a multicellular organism.

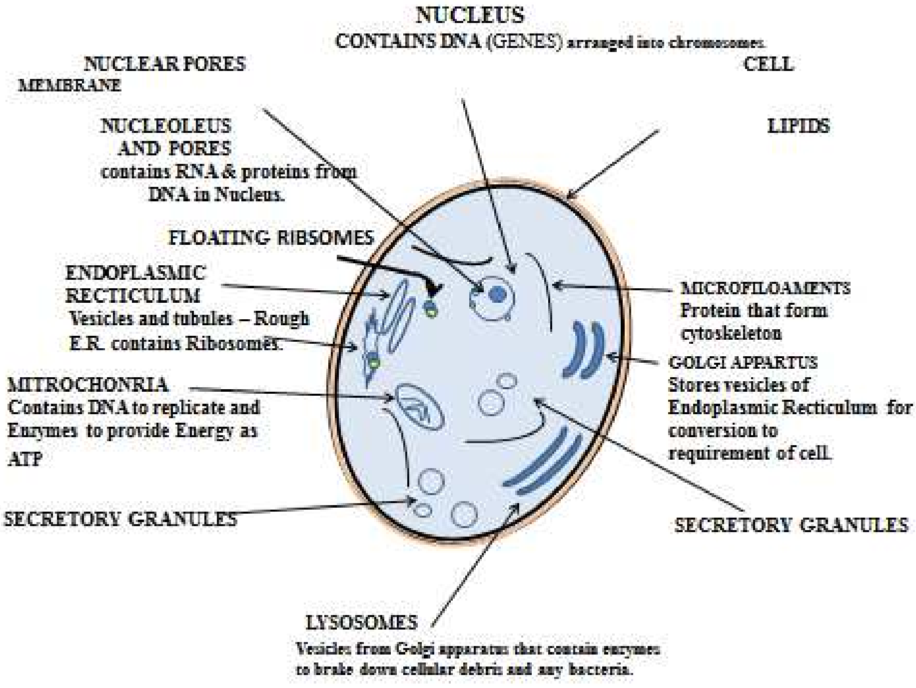


Figure 68. Structure of a human cell containing its organelles. The cell was discovered by Robert Hooke in 1665 and emerged on Earth at least 3.8 billion years ago. Note that "*one study (2015) found remains of biotic life from 4.1 Billion years ago in Australia*" [(425)(426)].

<u>Part 2</u>: <u>Reflection on some very basic chemistry information and data sources for safety and health students</u>

For those who have not studied any chemistry, some of which is important in understanding the hazards and assessing the risks practitioners are confronted in many areas of safety and health, grappling with it in toxicology and adult life can hardly be considered an easy task. For those who covered the subject many years back, what is provided here will perhaps serve to refresh memories and encourage a closer look and a better understanding of some of the hazards at work.

MATTER

Matter is everything of which our planet and all things around us are made. Matter is made up of elements of which 118 have so far being discovered; 94 of these are natural and 24 are synthetic, produced by nuclear reactions. These elements cannot be broken down into anything smaller. Matter has mass and mass has weight and since it occupies space it has volume. The weight of mass, however, depends on the force of gravitational attraction, so that weight of the same mass varies depending on where the mass may be located. If it was on the moon it would be much lighter but its mass would remain the same!

These elements consist of small particles (atoms) that are constantly in motion and change their structure to be in gaseous, liquid, solid form and plasma [(428)]. Their constant motion and change in structure is an alteration in the relationship of their atoms. Particles can therefore be referred to as atoms, a molecule (groups of atoms bonded together) or ions (electrically charged particles). The scientific study of these particles is the science of chemistry.

The atom itself is made up of smaller particles. Each atom has a nucleus, which contains one or more neutrons (neutral electrical charge) and one or more protons (positively charged), surrounded by one or more electrons bound to the nucleus. Note that the proton number differs in every element, and the number of electrons (negatively charged) is equal to the number of protons. These electrons can be envisaged as forming ‘shells’ (one shell being a layer around the nucleus). There may be more than one shell, with each ‘shell’ surrounding the previous one, and they all revolve in orbits of different shapes (spherical or oval etc.) around the nucleus within sub-shells of each ‘shell’ which can be visualised like the layers of onions. The maximum number of electrons that the first shell can take is 2 electrons, the next 8, the third 18, the fourth 32, fifth 50, and sixth 72. Note that this explanation is sound but elementary to say the least. The actual number of electrons in the outermost orbit of the atom is referred to as the atom’s valency which is a measure of the atoms combining power with other atoms. The difference between the maximum number the atom can take on its outermost shell and the actual number in its outermost shell, indicates the number of bonds that an atom can make with other atoms. Atoms may gain or lose electrons.

BONDS

The bonds, that is the connectivity, is the electrostatic force of attraction; strong between atoms but weaker between molecules. Those atoms which have only one chemical bond (i.e. combine with only one other atom), are said to have only one valency (the combining power of an element – in other words valency is the number of bonds that an atom can make. There are different types of chemical bonds. The main four types are **ionic** (a bond between two ions of opposite charges), **covalent** (when a pair of electrons are shared between atoms – they can be single, double or triple bonds and are strong bonds), **polar** (negative electrons are not evenly distributed between the two atoms) and **hydrogen** (a weak bond in which negative electrons are attracted to bond hydrogen atoms) .

Atoms have been assigned an atomic number. This is the number of protons in the nucleus of the atom. Adding the number of protons to the number of neutrons gives the mass of the atom. Electrons have negligible mass so are not included in the mass of the atom. When the number of electrons is different to the number of protons the atom is referred to as an 'ion'. If the number of neutrons are different to the number of electrons, then the atom is referred to as an ISOTOPE, but note that the number of protons does not change. Chlorine, for instance, has different forms of itself and these are its isotopes. Carbon has three isotopes.

THE PERIODIC TABLE

Dmitri Mendeleev devised the Periodic Table (see Fig.69) in which he placed the elements known at that time (about 62) in some order according to their atomic mass and other variables leaving spaces for other elements that he predicted would be discovered to fit in between. His work was published in 1869. Other scientists have continued to add to this table ever since with the number of elements today being 118.

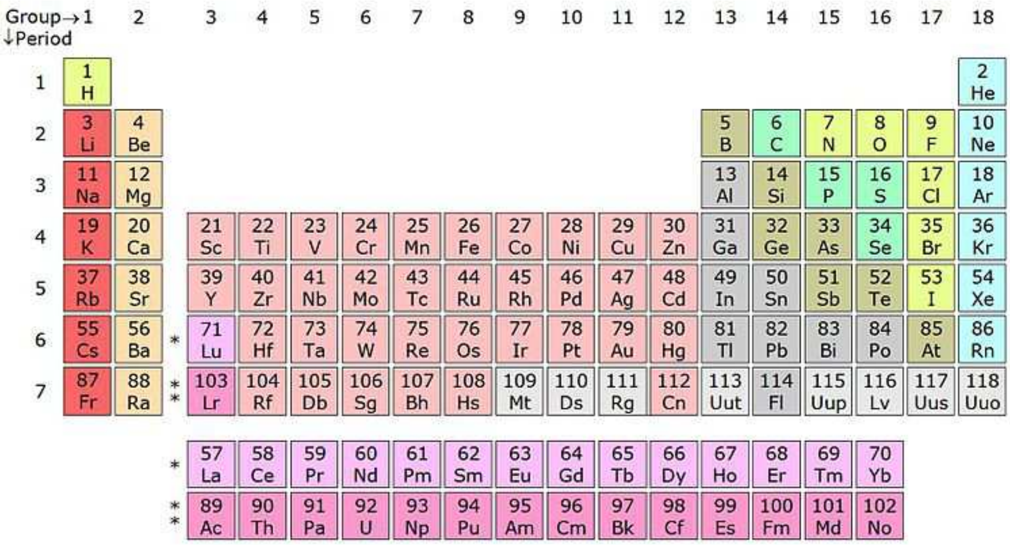


Figure 69. The Periodic Table. Source: Wikipedia © 2017. Available at https://en.wikipedia.org/wiki/Periodic_table

For greater detail see ILO Encylopaedia Appendicies under 'Basic Data'. (see Selected Bibliography **B15**). The table is read from left to right. Elements have been assigned symbols. Note that symbols have capital and lowercase letters which you must be careful with, as minor changes alter the name of the substance in the field of chemistry. The classical example is ‘Co’ for cobalt but the compound carbon monoxide is ‘CO’.

The main elements in living organisms are carbon (C), hydrogen (H), oxygen (O), nitrogen (N) and phosphorus (P).

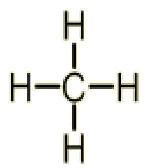
Elements may be **metallic** such as gold (Ag) or iron (Fe) or non-metallic such as carbon (C) or chlorine (Cl). There are also elements which are in-between metallic and non-metallic and referred to as ‘**metalloids**’. Metallic elements that give away electrons to form positive ions are referred to as *cations,* and **non-metallic** elements take up electrons to form negative ions called *anions.* The colour scheme assists by grouping the different elements within each of these types. The Periodic Table helps to categorise the different characteristics of each element, such as the chemical reaction that could result or if it is electrically conductive, among other things.

The elements in each row have the same number of electron orbitals. The first has one, the second two and so on up to seven. The elements in each of the vertical rows referred to as ‘groups’ have the same number of electrons in their outer electron orbital (remember that the outer orbital electrons are called the elements valency).

Today’s industrial resources from which many other products are also manufactured are provided by all the 118 (94 occur in nature and 24 are synthetically produced) different elements in the earth’s crust. Elements are made from one type of atom. These are pure elements (they cannot be split into any other element), although there are elements which by nuclear fusion can be broken down into smaller elements. What defines one type of element from another is the number of atoms that they contain, and when different atoms combine with other atoms, a compound is formed.

INTERPRETATION OF SOME PHYSICAL AND CHEMICAL PROPERTIES

In order to interpret physical and chemical properties, and other characteristics of substances, mixtures or chemical compounds and understand the chemical profiles you will inevitably come across, you must remain aware of some fundamental aspects of chemistry. You will come across figures like this:



These represent STRUCTURAL FORMULAS which if represented like this: CH_4 , represents its CHEMICAL FORMULA. This means that this molecule contains one atom of carbon and four atoms of hydrogen. An element which is represented as follows: $^{16}\mathbf{O}_8$ – *(the subscript 8 should be written below and on the same side of the superscript 16 on the left side of the **O**)* indicates that the element oxygen whose symbol is ‘O’ has an atomic number of 8 and a weight of 16. A formula that is represented as follows: $Ca(HCO_3)_2$ which is calcium bicarbonate contains more than one group of atoms. Because the bicarbonate is a compound made up of two bicarbonate (HCO_3) groups indicated by the '2' and a calcium atom, the HCO_3 is put in brackets. An aqueous solution may be indicated by '(aq)' in brackets next to the chemical symbol (see examples below). Note that how you write an aqueous solution may depend on whether the substances are molecules or ions at which time you may see that their charge is also indicated. This is a little more complex but if interested you may wish to research this further.

Note the 2 here

$$Ca(HCO_3)_2$$

$$KNO_3\,(aq)$$

As a safety officer, your toxic assessment of chemicals will require that you ask yourself a large number of questions each of which may follow on with other questions that need answering, such as appearance (is it solid, liquid or a gas ? etc.), odour, colour, density, pH, pressure and others. The more relevant information on these physical and chemical characteristics is presented at the end of this chapter.

ACIDS and BASES

Both acids and bases are corrosive substances. They destroy tissues by contact in a process that dehydrates the skin, a reaction which generates heat and then causes a burn, destroying the tissue. The concentration of acids and bases differ and the more concentrated they are, the more corrosive they are. Weak acids are safe to handle. It is the strong ones that are dangerous. Some corrosive materials can ignite organic matter. Acids have many general and industrial applications. Acids are used as food preservatives and in the beverage industry, the manufacture of fertilisers, detergents and explosives, in electroplating, batteries, and in products for use as domestic cleaners.

Acids are of two types, inorganic (mineral) or organic (biological). Both have a similar molecular structure containing a carboxyl group, [(COOH) often found in amino acids and fats].They are flammable, although the ignition temperature of the organic acids which contain carbon is higher than that of the inorganic type that do not carbon and not flammable). Some of the acids have an oxygen like nitric acid (HNO_3) combined with an element, and others do not have an oxygen. Hydrogen chloride (HCl) is one example of an acid that does not have an oxygen.

Acids may dissolve in water yielding hydrogen ions. An example is hydrogen sulphide (H_2S) where two hydrogens are combined with a single atom of sulphur. The bonding could also be with a group of negative ions such as NO_3, which is a salt of nitric acid. Examples of acids are hydrogen chloride (HCl), hydrogen Bromide (HBr), hydrogen Iodide (HI), Perchloric Acid ($HCLO_4$), sulphuric acid (H_2SO_4), and nitric acid (HNO_3).

A base is a metal oxide (a compound that has at a metal element and at least one oxygen atom). When dissolved in water any of these chemical compounds release hydroxide ions (OH) and are referred to as alkalis. The more OHs there are, the more alkali the resulting solution is. The terms 'alkali' and 'base' are often used interchangeably, although this is not quite correct. Alkalis react with acids, salts and metals. Examples are sodium hydroxide (NaOH) and potassium hydroxide (KOH). Alkalis are used in the manufacture of soaps, detergents, fertilisers and the treatment of sewage, as well as in products for domestic cleaning.

SALTS

Salts are formed when acids and alkali (base) are mixed. Hydrogen ions are replaced by the metal ions. For example: hydrogen ions (H^+) in chlorine are replaced by the metal sodium (Na) to form NaCl. There are a large number of salts that can be formed, which can be done in different ways; they derive their names by placing the name of the metal first and adding the negative ion. Since salts do not release either H^+ ions or OH^- ions they have a neutral pH. Whilst acids taste sour and alkalis taste bitter, the taste of salts vary and as some are toxic, tasting should never be attempted although some expert chemists knowing this would taste the differences between the different salts.

Some salts like Na, K, and most chlorides or sulphates and others like Mg and Ca are partially soluble, whilst most carbonates are insoluble.

Salts are used in cosmetics, fertilisers, water treatment, food industries and many other industries including the production of other salts. Health hazards are specific to the type of salt, dose, and other properties of the salt in question. Refer to MSDS for detail on those of interest.

OXIDIZERS

An oxidizer is an element or compound that receives or gains oxygen electrons from another element or compound that is then referred to as the reducing agent. Since oxygen allows a substance to burn it may become a potential explosion hazard. Examples include O_2, O_3, hydrogen peroxide (H_2O_2), and the synthetically produced fertiliser ammonium nitrate (NH_4NO_3). Heat invariably accompanies most oxidation reactions.

CHEMICAL REACTIONS

Much of what has been said in previous chapters clearly indicates that chemicals can combine in many different ways. Their combination results in new chemicals being formed. The reactions that take place in these combinations produce heat and combustion may result, and if the compound contains oxygen its decomposition will accelerate combustion. The changes that take place in reactions when one chemical state alters into another chemical state may involve a change from solid to gas, gas to liquid or vice versa. The rate of chemical reactions vary. Some react instantaneously whilst others require sunlight, heat, catalysts or ignition. These and other aspects make it important to understand the relevant practical meaning of chemical profiles when needed. A chemical profile which requires basic toxicological knowledge and points to items from which you can select those that are relevant to planning prevention or emergency response in specific situations, is given below and a brief explanation of the physical and chemical properties is provided. It is presented to remind and direct you to search further, and refer to other reference and information sources for each of the properties.

An example of such a chemical profile to follow includes:

Physical and chemical properties (see below)
Occurrence
Uses
Potential substitution
Acceptable standards and guidelines
Transport
Occupational exposure
Acute and chronic human exposure effects
General population effects
Environmental levels and exposure
Absorption
Metabolism
Acute aquatic toxicity
Storage
Disposal
Factors that modify toxicity
Carcinogenicity
Mutagenicity
Reproductive toxicity – embryotoxicity and teratogenicity
Immunotoxicity
Explosion and fire hazard
Spillage
Emergency response, including advice to others and evacuation
First aid

<u>The chemical's LABELLING & PACKAGING information</u>

Trade name
Name, address, and telephone of manufacturer/importer/distributor
Chemical name of substance/other names
Molecular and empirical formula
CAS number or IUPAC 'Compendium of Chemical Terminology'
Risk phrases (R-phrases)
Safety phrases (s-phrases)
Quantity of contents/volume and container.

A BRIEF EXPLANATION OF IMPORTANT PHYSICAL AND CHEMICAL PROPERTIES

What one should be aware of in terms of the physical and chemical properties of a substance (one component chemical) or preparation (a mixture of two or more substances).

1. Appearance: Solid, liquid or gas

Solids *may be friction-sensitive, corrosive, stable, create toxic fumes or gases and vapours, leach, contaminate other products, water or land. Solids may contain dust in the respirable range. Some metals and non-metals in fine respirable particles are flammable.*

Liquids *are flammable if their flash points are at or below 37.8* °C (105 °F). *There is a range which limits flammability/burning as below or above these limits the substance will not burn because the concentration of vapour will be too rich or too lean to burn. Flammable liquids are more dangerous (i.e. fires) than combustible ones. They are combustible if their flash points are greater than 37.8 °C and below 93.3 °C because they do not produce a vapour below this temperature.*

Gases* (see Note p.227) *develop pressure on their surrounding depending on the temperature and pressure. When heat or temperature increases, vapour pressure increases within the container and if the container's relief valve does not hold the excessive pressures, explosions may result. Compressed gases may be natural or synthesised, some inflammatory or non-inflammatory.*

2. **Odour:** Refers to concentration in air. Some chemical odours can be detected at very low levels in air (e.g. H_2S, NH_3).

3. **Colour:** One aspect of the importance of colour interpretation is the colour on labels. The colours and numbers on these provide useful information on reactivity (yellow), health (blue), fire (red) and other special hazards (white). The numbers 1 to 4 indicate the level of the hazard (minimal to severe).

4. **pH:** a figure expressing the acidity or alkalinity of a solution on a logarithmic scale on which 7 is neutral, lower values are more acid and higher values more alkaline. It is the '**p**otential or power of **H**ydrogen' Scale: acidic 1–6.5, neutral 7 and alkali >7.5–14. (Note: 11.5–14 is corrosive).

5. **Boiling point:** The boiling point at which a liquid boils and turns to vapour. The boiling point determines the speed at which a substance evaporates. The lower the boiling point, the higher the vapour pressure and therefore the easier the liquid evaporates – a change from liquid to gas. It is dependent on pressure. Containers may build up pressure and explode. Storage outdoors in hot climates may cause fires as well as storing materials indoors near furnaces or other forms of heat.

6. **Melting point:** The temperature at which a substance changes from solid to a liquid state at normal atmospheric pressure (760 mm Hg = 14.7 psi). Note that the temperature below zero (freezing point) on the Celsius scale goes as far as (minus) –273K where 'K' refers to Kelvin (the name given to the scale below freezing point). The degrees are equal on both scales. A substance cannot solidify any further as there is no more heat left in the reaction causing the change. No temperatures exist beyond –273°C. This temperature is referred to as ABSOLUTE ZERO. Care must be paid to melting points of materials as attention to temperature is important with hazardous substances that could expand and overflow and react possibly violently with other hazardous substances.

7. **Flash point:** the lowest temperature at which a liquid or a solid produces enough vapour to form a flammable air-vapour mixture near its surface so that it can be ignited by a spark or flame at atmospheric pressure. The lower the flash point, the greater the risk of fire and explosion.

8. **Ignition temperature:** This is the temperature at which material will self-ignite. Ignition temperatures of flammable and combustible materials are between 300 and 550°C.

9. **Flammability:** The ability of a substance to ignite and burn easily. Liquids that have a flammability point below 0°C, or a boiling point below 35°C and liquefied gases are extremely flammable.

10. **Explosive:** Chemicals that release gas and heat instantaneously when subjected to certain conditions. Usually shown as the LOWER and UPPER explosion limits. They are given in volume percentage of air. Benzene, for example is 1.2–8.0%. The manner in which explosives are handled and stored is extremely important.

11. **Vapour density:** This compares the vapour density of air with that of the substance. Since air=1, if the vapour density of the substance is less than 1, it is heavier than air. An important aspect to note with gases.

12. **Vapour pressure:** The pressure in millimetres of mercury (Hg) of the vapour of a liquid or a solid when it is in equilibrium with that liquid or solid at a given temperature.

13. **Relative density:** Tells you whether the substance floats or sinks in water. This happens when the RD is greater than 1. Air=1. Note that density for solids and liquids is given in g/cm^3, for gas in g/litre.

14. **Solubility:** May be poor, moderate or high. Important because of hazardous reactions that may occur under certain conditions such as high or low temperatures, contact with other substances or different pressures that affect the substance when exposed to these conditions. Substances that are very soluble are unlikely to found in air.

15. **Molecular formula:** This identifies each atom and the number of every atom in a molecule of a compound. It does not provide information on the bonding.

***Note:** Pressure must not be misinterpreted for force. Pressure will change depending on the size of the area on which force is applied. This is because the distribution of force would be distributed on a larger or smaller area. Pressure is measured in pounds per square inch (psi). Note also that 'psig' refer to pounds per square inch gauge which means that this is the pressure indicated in the container since the gauge is set at zero when empty. It does not take into account atmospheric pressure. You would have to add 14.7 psi – pressure at sea level to the gauge reading to indicate the correct pressure. With reference to pressure and altitude there is approximately a decrease of half a psi for every 1000ft of increase in altitude.

INFORMATION AND DATA SOURCES

This list only provides some of the many available data sources for information.

The Advisory Committee on Safety and Health's Working Party on chemicals
The American Chemistry Council (ACC)
The American Conference of Governmental Industrial Hygienists (ACGIH)
The Association of the European Adhesive & Sealant Industry (FEICA)
The Agency for Toxic Substances and Disease Registry (ATSDR)
The National toxicological Program (NTP) - Division of the US Department of Health and Human services.
The Council of Chemistry Associations (ICCA)
The Chemical Industry Association (UK)
The Chemical Carcinogenesis Research Information System (CCRIS) maintained by the National Cancer Institute (NCI).
The Chemical Risk Information Platform (CHRIP)
The Chemical Weapons Convention
The Control of Chemical Substances Hazardous to Health 1994, Stationery Office, London, UK
The European Agency for Safety and Health at Work (FACT SHEETS)
The European Inventory of Existing Chemicals (EINECS)
ERG 2012 (Emergency Response Guidebook) (mobile app)
The European Inventory of Existing Commercial substances (EU), Luxembourg
The European List of Notified Chemical Substances (EU), Luxembourg.
The European Chemical Industry Association (CEFIC)
The European Chemical Agency (ECHA)
The European Commission Directive 96/55/EC, the second adaptation to technical progress of the Marketing and Use Directive; Individual directives can be found under 89/391/EEC, Art.16 (1) E.g.:
Council Directive 2004/37/EEC – risks of carcinogens.
Council Directive 98/24/EC – risks to chemical agents at work.
The Occupational Safety and Health (OSH) Framework Directive 89/391/EEC and those Directives specifically dealing with chemical risks – notably

the Chemical Agents Directive and the Carcinogens and Mutagens Directive (CMD)
The Occupational Health and Safety Authority Malta.
The European Chemicals Agency and the International Agency for Research on Cancer (IARC)
The European Union’s Registration, Evaluation and Authorization of Chemicals (REACH)
The European Environmental Agency (EEA)
The European Pollutant Release and Transfer Register
FEMA (Federal Emergency Management Agency) (mobile app)
Global Estimates of Occupational Injuries and Work-related Illnesses 2017 Workplace Safety and Health Institute, Singapore & Ministry of social Affairs and Health, Finland.
The Hazardous Substances Database (HSDP)
History of Human Migration. (See WIKIPEDIA, 30 January 2018.
Household Products Database (HPD) http://hazmap.nlm.nih.gov/index.php
HazMap (mobile website)
The ILO Conventions and Recommendations (ILO encyclopaedia)
The International chemical Secretariat (ChemSec) [See the SIN List for chemical substitution]
The International Council on Mining and Metals (ICMM)
The International Labour Office (ILO)
Interteck Vol. 828, May 06.2015. Act on control of household products containing harmful substances, Amended Act of 112, 1973. (Kenny Chan & Dicti Wong)
Government Sources of Data in Countries
National Technical Information Services (NTIS)/ United States Department of Commerce
The NEPSI GREEMENT – (OJ2006/279/02). The European Network for Silica
The Organization of Economic Cooperation and Development (OECD)
The OSHA Occupational Chemical Database
PEPID (mobile app)
Regulation (EC) No 1272.2008-classification, labelling and packaging of substances and mixtures
REMM (Radiation Emergency Medical Management) (mobile app)
The Scientific Committee on Occupational Exposure Limits (SCOEL)
Toxipedia – an encyclopaedia
The Toxic Substances Control Act Inventory (TSCA) - (USEPA)
The United Nations Environmental Programme (UNEP)
The United Nations food and Agricultural Organization (FAO)
The United Nations Industrial Development Organization (UNIDO)
The World Health Organization – IPCS (International Program on Chemical Safety)
CICADs (Concise International Chemical Assessment Documents)
EHC (Environmental Health Criteria Documents)
TSCA (Toxic Substances Control Act) [chemical inventory free of charge online – March 15, 2010].
TOXNET (mobile website) LactMed (mobile app)
TOXMAP
Union for International Cancer Control

Appendix III

GLOSSARY

ACKNOWLEDGEMENT

The importance of information/knowledge provided by encyclopaedias, journals, books, researchers, institutions, u-tube providers, and many others is invaluable to all of us who have to ensure that the knowledge passed on to students at all levels is accurate and updated as far as is reasonably possible. I would, therefore, like to acknowledge the support that all of these have provided by their work through documentation and on line, in my effort to ensure the provision of concise but simple explanations related to biology chemistry and other general knowledge to adult part time undergraduates whose knowledge of such subjects is often limited and may have long disappeared from memory.

It was not practical in writing these definitions that accompany this book to mention every reference/support to every definition individually, but special acknowledgement is made to WIKIPEDIA and all its supporters, The Encylopaedia Brittanica, The Free Dictionary by Farlex, Study.com, News Medicine Live Science and Medicine, those who provide U-tube on a diversity of subject matter, and so many others whose review of their work have helped in designing the structure, presentation, verification on what has been written, and information to keep the definitions and explanations as simple as possible.

'The general knowledge obtained from many other disciplines is knowledge gained that can be beneficially applied to Safety and Health'

Explanatory Note: Underlined words that are also in Italics indicate that the specific word can be found in other parts of the glossary. In some cases the reader is directed to Appendix IV or other sections of the book.

A

Abdomen

The belly. Space between the diagphragm and the pelvis.

Absolute toxicity

The effects of a compound once it has entered the body.

Acrylic acid

($C_3H_4O_2$) A synthetic organic compound that is a corrosive liquid. It is a *monomer* used as a chemical intermediate and to make plastics, paints, etc. Hazardous by inhallation, contact with skin and mucous membranes. Could cause blindness.

Active Transport

This is the movement of substances /molecules through a membrane. There is a concentration gradient between the indside and outside of the membrane.

Additive

Exposure often occurs to more than one substance. If the effect of each substance is similar the over response results from the additon of the effects of each substance.

Adenine

This is one of the four nucleotides bases which always links with the base Thymine that link to the 'ribbons' of the *DNA Helix*. See p.78 & 79.

ACTH

Adrenocorticotropic hormone – produced by the pitutary gland in the brain which then stimulates the adrenal gland's cortex to release cortisol. *Cortisol* levels are generally high in the morning, but can be high at other times as in stressful conditions or low as in some diseases such as *Cushings syndrome.*

Allergic reaction

A reaction of the immune system to an allergen such as pollen, dust mite or some food to which the person is sensitive. These normally harmless allergens triger the production of immunoglobulin IgE.

Allergens

These are proteins that brings about an immune response (*allergy*) or specific hypersensitivity (pollen or eggs are example).

Algae

Uni or multicellular organisims that have no roots or leaves but contain chlorophyll and grow in water.

Alginate

Brown *Algae* contain 30-60% of Alginate which is a colloid (jelly like material) resulting from alginic acid and minerals and contains some fibre.

Amalgam

(See Appenix IV p.284).

Amines

When Hydrogen atoms in *Ammonia* (NH_3) are replaced by hydrocarbon groups they are refered to as amines. There are primary, secondary and teritiary amines which depends on how many hydrogens are replaced. In primary one hydrogen, in secondary two and in teriary all hydrogens are replaced.

ANP

A cardiac *peptide* hormone that regulates blood pressure and volume. It is produced in the heart's atrial chambers and suppresses kidney *renin* secretion and blocks *Aldosterone*.

Alveoli

Very small air sacs that are in clusters at the end of the lungs' ducts from the bronchioles, and where the exchange of CO2 and O2 takes place.

Alveolar ducts

An alveolar duct is the continuation of the respiratory bronchiole which then ends in a cluster of alveoli of the lung.

Amino acid tryptophan

This is an essential *amino acid.* An important building block for proteins. Inability to absorb fructose reduces *tryptophane* from the intestine lowering its blood level. Some bacteria synthesize tryptophane. It is found in oats, dates, bananas, chic peas, milk, sesame seeds, and other foods. Vitamin B3 is synthesized from tryptophane.

Amylase

This is an enzyme which is found in the saliva and pancreatic juice and breaks down starches and glycogen into sugars.

Anaphilactic shock

A severe allergic reaction that occurs to anything to which the person is allergic to, and could result in death. Person goes into shock and may vomit. It requires immediate emergency treatment**.**

Anaerobic Bacteria Bacteria that do not require oxygen to live and grow. Some die in the presence of O2. They are present in the digestive system and can cause infections invarious organs in the body.

Androgens Hormones produced buy the Adrenal glands, responsible for male characteristics. Females also produce some.

Angina A mild or severe pain in the chest that may extend to the neck and arms due to a reduced supply of blood to the heart muscle by a block in the arteries of the heart.

Antagonism When the effect of one substance or a mixture of substances counteract the effects of other substance/s. It can reduce the response of the other substance/s.

Antibodies When the immune system is stimulated by an antigen (virus or bacteria etc.) it produces a protein in the blood or lymph to neutralize the antigen. This protein is an *antibody* (an immunoglobulin) produced by a B lymphocyte which then attaches to the *antigen*.

Antigen A substance (bacteria, virus, toxin) that is foreign to the body. It stimulates the immune system to produce antibodies. Each antigen is different to another so that different antibodies are produced to neutralize different antigens. Once the body has produced an antibody to a particular antigen the next time the body receives that particular antigen again it will be neutralized immediately and not cause a problem.

Antioxidants Substances that inhibit oxidation. Protects cells from the damaging effects of free radicals (molecules containing an unpaired electron). Vitamin C is one example. They are found in many foods such as cranberries and blackberries, black olives, and some herbs, etc.

Antrax An infectious disease caused by the bacterium 'Bacillus anthracis', transmitted to humans or to contaminated meat.

Archea A single cell microorganism called Prokaryotes (no nucleus or organelles). Not a bacteria.

Arc lamps When an a high voltage is passed between two electrodes usually in a gas it produces an arc of light. It was superseeded by the incandescent light bulb. It is used today for high intensity point sources.

Arrythmia

An abnormal rhythm or speed of rhythm of the heartbeat.

Asbestos

A mineral that occurs in six types naturally and generally divided into two major classes. Their value is that they are resistant to heat, fire and many chemicals. Asbestos is strictly controlled and banned in many countries.

Ash

Ash is what is left after anything that is burnt. What it contains depends on what the sunbstance was made of.

Aspartame

A synthetic sweetener used in many foods, drinks and pharmaceutical products. The current evidence as to its helath effects are still unclear. An ADI (daily intake) of 50mg/Kg has been assigned to the use of Aspartame in Europe by EFSA (European food safety authority).

Astrocyte

These are 'glial cells' found in the brain.Their number varies in different parts of the brain and they are present in the *blood-brain barrier*.

Aterosclerosis

Commonly refered to as 'hardening of the arteries'. An accumulation of cholesterol and other fats in the artery walls that can eventually block the artery.

Atopic

A pre-disposition to developing an allergic reaction. It may be herediatary. See also p.92.

ATP

Adenosine triphosphate. It is the energy produced inside cells and is important in nerve transmission and muscle contraction.

Atria

The chambers above each ventrical in the human heart. The left atrium receives deoxygenated blood and the right oxygenated blood.

Autoimmune

The response by antibodies (T-cells) against the body's own cells and tissues that normally should not be attacked resulting in an autoimmune diseases such as arthritis or multiple sclerosis.

AV conduction block

AV = Atrioventricular. A block or delay in the conduction (the pulse that causes the heart to beat) between the atria and the ventricles of the heart. It can be causes by ischemia, fibrosis or infarction.

B

B-Cell

A type of lymphocytes (white blood cell) that develops in the bone marrow and has B-*receptors* so that it can bind to antigens which then release antibodies.

Bacteria

Single cell micro-organisms. They can be spherical, rod or spiral shaped but there are many variations of these. They do not have a nucleus and are therefore *prokaryotes* (See Fig. 67 p.217). They can be aerobic or anerobic. Some destructive (causing tuberculosis or diarhoea) others beneficial (digesting food) to humans.

Barbiturates

Used as sedatives and some mental illness but mostly replaced today by tranquilizers because these are safer. They acted by depression of the CNS and are addictive.

Barometric pressures

The weight of the air in the atmosphere which extends about 3 miles up is measured by an aneroid barometer in millibars (mb). This is a small evacuated tank which contracts and expands that then moves a needle on a scale. At sea level barometric pressure is 760 ml. Hg pressures indicate fair or good weather and low pressure unstable weather.

BEI

Biological Exposure Indices. These are guidelines (like the TLV's), to be used only by Occupational Hygienists and not a legal standard. *'They are health based values'(ACGIH)* and have limitations.

Biochemistry

The study of the chemistry and processes of molecules in living organisms.

Biological molecules

Organic molecules such as carbohydrates or proteins found in living organisms and consist of *Carbon, Hydrogen*, *Oxygen*, *Nitrogen*, *Sulphur* and *Phosporous*.

Biotin

A water soluble vitamin of the B complex group (Vit. B7) found in liver and egg yolk, bananas etc. which synthesizes fatty acids and glucose. Deficiency rare. Believed to promote healthy skin, nails and hair.

Biotransformation

Alteration of chemical substances or toxins in the body by enzyme acticvity. This occurs mainly in the liver.

B-Lymphocytes

One type of the blood cells produced in the bone marrow. They are capable of discriminating between different *antigens* - *a foreign substance* in order to bind themselves to a receptor on a specific antigen following which the antigen is destroyed. They can also differentiate into *Plasma cells* which then secrete *antibodies.*

Bonting

Seeking to extract maximum value out of your reading experience.

Bradicardia

A heartbeat slower than 60 beats per minute.

Brain Barrier

A highly selective barrier that prevents certain substances from entering the brain or placenta and protects it.

Bromaline

A protein that breaks down fibrin (a blood clotting substance) obtained from the stem of a pineapple and used as a meat tenderizer.

Bronchial system

Air reaching the trachea from the mouth via the pharynx and larynx passes down the right and left bronchus on its way through the bronchioles and the alveoli. No exchange of oxygen and *carbon dioxide* occur in the bronchi.

Bronchioles

The trachea divides into two bronchi (one = bronchus) which again divide smaller air passages called bronchioles. About 1mm in diameter they are surrounded by elastic fibres and smooth muscle but have no cartilage.

Buccal Mucosa

This is the lining (mucosa) on the inside of the mouth (cheeks).

C

'C'

Many countries have different skin exposure limits denoted by the skin notation 'C', which is an indicator of the hazard and 'ceiling limit' for skin absorption of the chemical.

Carpal tunnel Syndrome

'Carpal' means referring to bones of the wrist.The carpal tunnel is narrow and contains the tendons from the muscles of the arm to the fingers and the median nerve in both hands. It is surrounded by the small bones of the wrist and a fibrous tough band called the 'flexor retinaculum' which forms its roof and on top of which lie the Ulnar artery and nerve. Repeated motion (eg: typists, twisting of the wrist (cleaners) causes imflamation. Since the tunnel cannot expand it puts pressure on the median nerve compressing it causing severe pain in the wrist. The roof of the tunnel is surgically cut to release pressure.

Ca System

Referes to calcium metabolism/regulation of the body organs. The concentration of the *Calcium* ions in the blood is kept within very precise limits. This critical point is maintained by the Thyroid and Para-thyroid Glands. (See pp. 127 of book).

Calcitonin

A hormone produced by the thyroid to control *Calcium* and *Potassium* levels in the blood which it does by releasing Calcium from bone and reducing re-absorption from the kidneys.

Capilliary system

Body cells and tissues require Oxygen and other nutiritional substances which are exchanged through very tiny vessels. They also need to remove waste products such as Carbon dioxide and water. These vessels make up the capillary system.

Carbohydrates

Food nutrients mainly sugars and starches which are found in bread, rice, pasta, fruit, etc. The DRI (daily reference intake) is 45-65 % of the daily intake number of calories. They provide the energy needed by the body.

Catalyze

The initiation, that can modify or increase the reaction of a chemical process.

Catecholamine

Produced by the brain, nerves and the adrenal glands these chemicals act as neurotransmitters or hormones. They include *dopamine,* *epinephrine* and *norepinephrine*.

Ceiling Limit

Under OSHA's regulation standards for air contaminats, such as Chlorine or Methyl bromide, Table z-1-1910-1000 limits inhalation of substances preceded by "C"-Ceiling Values. It states that "*An employee's exposure to any substance in Table Z-1, the exposure limit of which is preceded by a "C", shall at no time exceed the exposure limit given for that substance. If instantaneous monitoring is not feasible, then the ceiling shall be assessed as a 15-minute time weighted average exposure which shall not be exceeded at any time during the working day". Reader is referred to* (https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=9992) for more detail.

Cerebrospinal fluid

A clear colourless fluid found in the brain and spinal cord. It is produced in the ventricles of the brain and circulates around the brain and spinal cord and is continuously absorbed. It acts as a cushion for the brain and assists in providing nutrients to the cells.

Cholinergic drugs

Note first that a substance called Acetylcholine is released by motor nerve cells to pass signals on to other nerve cells, ie: it is a Neurotransmitter. It functions within the brain as well as in the peripheral nervous system which includes the Parasympathetic (effects all body systems in everyday functions like salivation, digestions etc.) and Sympathetic Nervous System (acts under stressful situations). Cholinergic drugs act by producing the same effects as *acetylcholine* or blocking effects of acetylcholinesterase, that is, effects of the Parasyhmpathetic Nervous System.

Chromosomes

These are structures that contain the *DNA* in the nucleus of each cell. During replication the chromosome divides into two and forms an 'X' structure with the new chromosome. A protein called the 'centromere' is the point of the 'x' intersection. The centromere has specific roles to play in chromosome assembly. (See also p.78 of book).

Circumventricular

Some organs in the brain do not have a blood brain barrier and are refered to as 'circumventricular' which means that although they still protect the brain from toxic substances like the blood brain barrier they have an alternative method by which to allow hormones from the brain to enter the peripheral blood circulation system. Some of these circumventricular organs are secretory and others sensory.

Cirrhosis

Any damage – most commonly, alcohol, hepatitis or a fatty liver – stimulates the liver to repair itself. This happens by replaceing damaged tissue with scar tissue which gradually over time reduces the liver's important functions. This condition is referred to as cirrhosis.

Clay $(Al,Si)_3O_4)$

Wickipedia Encyclopedia describes clay as "*Clay is a fine-grained natural rock or soil material that combines one or more clay minerals with traces of metal oxides and organic matter.*" Different types of clay will have different chemicals in them such as manganese and the glazes applied require particular attention in their use.

Cloud height and Thickness

Cloud height refers to the height from the ground (also referred to as cloud ceiling), and thickness to its depth ie: base to top of cloud. Thickness is relative to the amount of percipitation it contains. Low clouds do not usually go further that 2000 meters up. Cloud formation is important for predicting weather in outdoor safety and health activities, amongst others such as aircraft flight plans etc.

Co-enzymes

A co-enzyme – many are derived from vitamins – are small organic molecules and necessary to catalyze enzymes which are proteins.

Cohort

A group of individuals that have shared some experience, such as an exposure, or some similar health condition.

Cold Front

Usually depicted as pyramids on a line. It is a fast, dense advancing edge of a cool mass of air, that comes in over a less dense hot mass of air (warm area). The air behind it is colder and drier. If sufficient moisture is present thunder storms and rain results. Atmospheric pressure high but decreases as it moves forward.

Colloids

A mixture of two substances in which one substance - the particles which are usually extremely small - do not settle to the bottom of the container and are therefore either translucent or opaque to light.

Concentration gradient

This is the level of change in the concentration of a substance as it continues to reach a uniform concentration throughtout. Concentration gradients are important around cell membranes as molecules or ions move in or out of the cells.

Conjugated/conjugation

This referes to the bonding or linking of atoms or electrons and to be conjugated must have a minimum of 3 'p-orbitals' that link them. These orbitals which are the distances from the nucleus – also referred to as 'shells'- refer to the electron configuration around the atom. Their energy increases as the distances away from the atom increases. The 'p' referes to one particular shell/orbit. Conjugation strengthens the chemical's stabilization.

Conjunctiva

This is a thin layer of mucous membrane that covers the inside of the eyelids and the front of the eyeball. (See Fig. 56a p.141).

Critical Effect

When an organ is affected by some toxic substance, the first adverse effect to occur once the threshold of that substance is reached is called the critical effect.

Cycline/s

Proteins that have a common ancestor (refered to as a 'family of proteins') of which there are two main groups and many sub-types each of which has a different role in the different phases of the cycle of cells. This is done through the activation of specific enzymes. Concentration of Cycline rises as the cell starts to divide. Some Cylines induce DNA replication others error correction and so on.

Cyclohexane

A clear flammable liquid that smells a little like petroleum. Used as a solvent, paint removers and in the production of othr chemicals.

Cytokines

Signalling proteins produced by many different cells including those of the immune system. Their role is communication between cells and regulation of growth the manner in which a cell responds to injury and infection. Each cell has a different function. They are biomarkers of imflamatory disease.

Cysteine

A non essential amino acid and antioxident. Important in the formation of proteins. Found in poultry and a number of vegetables. Mainly used to flavour foods and labelled as E920. An antidote to the toxic chemical *Acetaldehyde*.

Cystosine

This is one of the four nucleotides bases which always links with the base *Guanine* that link to the 'ribbons' of the *DNA Helix*. See page 79 & 80.

D

Decay

Referring to radioactive decay – decay or loss of energy from the nucleus of a radioactive substance results when it losses alpha, beta or gamma radiation

Dehydroepiandrosterone(DHEA)

An androgenic hormone secreted by the adrenal cortex, the brain and testis. As a drug supplement there are many claims of what this substance can do but insufficient evidence. It requires prescription in many countries. It does, however, have some nerurological and psychological functions.

DHEA – S

This is the same as DHEA (see above) but sulphate is added to the chemical compound. It is used as a test to estimate the adrenal glands function or causes of infertility and amenorrhea.

Detoxification

The process of metabolic removal of toxins by altering them from a toxic to a less toxic or non toxic chemicals which accelerates excretion of the toxin from the body.

Diaphragm

This is an umbrella shaped collection of muscle that not only separates the abdomen from the thorax but also assists with the process of respiration.

Diffusion

In order that substances enter or leave through the cell membranes, either a concentration gradient is required or some other means of transport, such as a protein to help the substance across. This is diffusion of which there are several types.

Diethyltolumide

(DEET) An insect repellent that can be applied to the skin.

DNA

Deoxyribonucleic acid (See p. 77 - 78 of book).

Dipost and Diposting

Dipost referes to 'Directional Possibility Thinking'. In safety and health, observation is a pre-requisit to the analyses of the many possibilites that could result from an observed hazard, and the probability of its happening., ie: the risk level. The total process of carrying out these activities is referred to as DIPOSTING.

Diurnal

A rythm that results in a fall in urine filtration during night the night.

Duodenum

This is the first segment (20-25 cm long) of the small intestine which is attached to the stomach and into which the stomach directly empties. Here the enzymes secreted by the pancreas and liver bile digest the food received from the stomach.

Dusts

Dust consists of very small particles – some finer than others – it arises from volcanoes, agricultural activities, construction, streets, materials used such as tyres on cars, inside homes, desert or dry areas, which become airborne and can be inhalled. Some fine dusts may ignite and explode, such as Flour or *Magnesium*. Small dusts have a negative electrical charge and when these dusts are seperated from larger dusts an electrical field is established.

Dustiness

The concentration of dust particles usually of a size between 1 and 100 μm in or over an area. A dustiness index was developed sometime in 1985 to provide for a ranking of materials causing dustiness. There are different methods for testing depending whether the dust is a powder, an aerosol or within a liquid.

E

Effective toxicity

Also refered to as the ED50. It is the amount of the dose or the maximum amount of the dose that obtains the desired effect in 50% of a selected population.

Egress

This refers to exiting from a building or a place of work.

Electrons

These are negatively charged sub-atomic particles. Electrons that orbit/spin around the nucleus in opposite directions neutralize the magnetic field that would otherwise be created. Electron energy increases as the distances from the nucleus increases.

Emphysema

Once the alveolar walls break down as a result of damage from toxins (inhaled occupational dusts or chemicals), or in rare instances a genetic congenital deficiency of α1-antitripsin – (this is a protein produced in the liver that protects the lungs and some other organs from other proteins) the collapsed alveoli or groups of larger alveolar sacs make it difficult to breath efficiently and coughing results. This put simply is emphysema.

Endothelial cells

These cells line the inside of blood vessels, the chambers of the heart and the lymphatic system for smooth flow and act as a barrier to bacteria and other toxic substances (see blood brain barrier). They also produce *Nitric oxide* which dilates the vessels and help build new vessels. Damage to endothelieal lining can have serious consequences especially in the heart.

Endocrine disruptor

Any substance that mimics and therefore disrupts/alters the function of the hormone systems of the body and may cause serious changes both to the individual and offspring.

Environmental Chemistry

The study of the effects and fate of chemicals including human activities in the environment.

Enzymes

An enzyme is a protein which catalyzes or accelerates a chemical reaction. They require specific temperature and pH levels to function optimally.

Epinephrine

Also refered to as *Adrenaline* and produced and released by the medulla of the Adrenal gland in times of stress. Can be made synthetically. It raises blood pressure by constricting the blood vessels, increases the heart rate and relaxes the smooth muscles in the lungs dilating the bronchial tubes. Important in treatment of anaphilatic shock. (See also Nor Adrenaline)

Epoxide

Epoxides are very reactive cyclic ethers (Cyclic = atoms connected in the form of a ring – and an ether is an oxygen atom linked to an *alkyl* or *aryl* group). Many epoxides are very toxic. Epoxy glues are produced by the reaction of epoxides with *amines*. Important industrial epoxides are *ethylene oxide* and propylene oxide. (see also Appendix IV)

Ethanol

(ETHYL ALCOHOL) A colourless liquid made from different types of grain, mainly corn as this is so abundant. It dissolves fats well, and has many workplace applications such as solvents, disinfectants, fuels and the production of chemicals. Ingestion is the main hazard, although skin contact may cause irritation.

Exfoliated Dermatitis

This is an inflamation of the skin in which a large area of the skin becomes red and peels off. Cause so far not really known, but seen to occur following other skin conditions or sensitivity to some medication.

Exzema

A skin imflammation, that could be dry and itchy, and of which there are several types. The cause may be difficult to find as several different factors may be involved. Bacterial infection can complicate the condition.

Extrapolate

To reach an estimate or conclusion from available known data or information such as extrapolating from animal experimental data to humans.

F

Faeces

These are the waste products of the digestive system that are discharged from the large bowel – 1 to 1.5 meters or so in length and their consistency depends on the amount of water(fluids) that are reabsord from the large bowel on their way through it, in additon to other possible health issues. Note that the total length of the G.I.T is around 7 – 9 meters in length of which the large bowel is 1-1.5 m.

Fats

Essential food nutrients made from fatty acids and may be saturated, unsaturated or polysaturated (eg: Omega 3 fatty acids). All types provide equal amount of calories which is 9 calories per gram. Excess intake is stored as body fat. RDI for total fat intake is 95 grams (G) for males and 70 G for females. The RDI for saturated fats is 30 G and 20 G respectively. (British Nutrition Foundation - 2016).

Fauna

This refers to the animals that are found in some region or another or at some particular time in history

Fe System

This refers to iron (Fe) metabolism of the body. Iron is essential for the red blood cells which is needed for the transport of oxygen to other cells in the body. Fe can be toxic and it is therefore usually combined with protein which reduces the danger. The body hardly excretes any iron (about 1 – 2 mg /day) which means it is stored (mainly in bones). Most iron is absorbed by the duodenum and absorption is better in the presence of *Vitamin C*. Tannins prsent in black tea reduce iron absorption. Some genetic diseases cause iron overload.

•

Fibers

Fibres may be natural, regenerated or synthetic (totally made from chemicals) and usually longer than they are wide. The hazards of man made mineral fibres (MMMF) are well documented. Those of natural fibres are related to agricultural practice and manufacturing processes. One must also consider the hazards to the environment from all fibres including those of plastic fibres.

Fibromyalgia

A common chronic condition, often misdiagnosed affecting the muscles and joints. Symptoms include pain and fatigue which may lead to depression.

Fibroprotein

Fibroprotein is described in the literature as "*highly repetitive amino-acid sequences that provide mechanical and achitectural functions in nature*" such as strength, plasticity and support. They are found in fruits like bananas, collagen in human tissues and spider silk.

Fibrosis

In the process of repair following injury or damage as by occupational exposure to hazardous substances, fibrous connective tissue is laid down (scar tissue). Macrophages may also carry hazardous substances such as MMMF to the lymph nodes where they envelope them by fibrous tissue. *Silica* and *Absestos* are examples which can result in *fibrosis*.

Filtration

There are four ways by which substances can pass through a biological membrane of which one is simple filtration through the pours of the membrane, and this depends on the physical and chemical characteristics of the substance and in some internal organs, the hydrostic pressure within the blood circulatory system. Note that the pores of different body organs are not of the same size.

Fission

This happens when an atom is split into smaller parts with the release of energy. The atom is usually bombarded by a neutron which initiates the process. A self-sustaining chain reaction will occur if more neturons are released. Neutrons have no charge. Do not confuse with FUSSION where atoms combine to produce larger and heavier atoms.

Fluoride

A compound of Fluorine (Fluorine and another element such as NaF). Found in varying concentrations in underground water, gelatin and tea. Calcium Fluoride (CaF_2) is used in the glass and enamel industries as well as a flux in smelting. CaF_2 is toxic by ingestion. Corrosive in high concentration as fluoride in solution.

Fluorosis

This results from over exposure to *Fluorides* whether this is due to excessive ingestion or high levels of Fuoride in natural or drinking water or occupational exposure from dust and vapours. It causes a mottled (white) appearence in teeth and changes in bone (osteofluorosis).

Forensic Toxicology

The study of poisons/toxic substances. The subject requires a knowledge of the chemicals, absorption, distribution and elimination by the body, as well as analytical and other proceedures. In addition a knowledge of epidemiolgy, physiology and pathology are essetnial.

fpcm

Exposure to fibres needs to be expressed in some form of measurement. Conversion factors are also necessary even though they are not that accurate. They may be different for different technological processess. 'fpcm' stands for fibres per cubic meter.

Free – Radicals

These are highly reactive atoms or groups of atoms, because they have an unpaired electron. They are produced in the body (atoms that lose whilst others gain an electron) or they may form as a result of exposure to light or heat. Many substances are susceptible to the formation of free radicals such as carbohydrates, fats and proteins, DNA and RNA and Oxygen. They cause damage to proteins, DNA, through oxidation, and when they affect the nerves through them. They have been linked to the ageing process. (International Dermal Institute, La, USA).

FSH

Follical Stimulating Hormone. Secreted by the pitutary followoing stimulation by the Hypothalamus. It is part of the control of sperm production and menstrual cycle as it works with another hormone called Leutotropic hormone (LTH) .

G

Gas

A gas consists of particles that occupy all of the space/volume in which the gas resides. These particles are continuously in motion. Collision does not alter the gas kinetic energy, which is the same at any given temperature *(See Kinetic & Molecular theory of gases)*

Gastro-intestinal Route

This extends from the mouth to the anus. Approximately 7 - 9 meters (20-30 feet) long. The route through which food and other intake passes, is digested and nutrients with the help of enzymes and bacteria, are then absorbed into the blood stream. The upper part serves as a short passage for air into the trachea, and peristalsis moves the contents along and its waste for excretion.

Gastric

Anything relating to the stomach.

Gastrin

This is a hormone released by G-cells – a specific nucleated cell in the stomach. Some of these cells are also found in the duodenum and pancreas. This release is stimulated by distension of the stomach, undigested amino-acids and hypercalcaemia. Gastrin itself stimulates the release of Hydrochoric acid and pepsinogen for digestion. It also has other functions.

Gastritis

An imflamation of the lining of the stomach, commonly caused by Helicobacterpylori, drugs, as well as alcohol and smoking. Painful and may cause nausea.

Gene

A string of DNA in a cell's nucleus. A gene may be 'On'or'Off'. They control DNA replication and 'protein synthesis'. The ways in which all this is carried out is referred to as 'expression'.

Gene Signalling

A complex system of communication to provide specific instructions – referred to as 'codeing'. The interested reader is referred to '*SITABLE by nature education'* for detailed information - http://www.nature.com/scitable/topic/gene-expression-and-regulation-15 and other similar links.

G.I.T. Transport Systems

The absorption of nutients from the intake of food, vitamins and other substances into the blood stream requires different systems to achieve absorption, although some direct absorption occurs. Each phase of digestion and absorption along the whole GIT route is different, some is through active and others through passive transport of the nutrients or toxins.

Glucose

($C_6H_{12}O_6$). A carbohydrate, also referred to as DEXTROSE. It has one half the sweetness of ordinary sugar. Concentrtion depends on when the blood is tested. Fasting it would be between 77 to 90 mg/DL but reference should be made to the investigating laboratory. It is usually higher in diabetes. Through complex metabolic ractions it provides energy needed by the cells which also require the assistance of insulin to use it. It is measured in mg/dL.

Glutathione

This antioxident is found in every living human cell, mostly in the liver. It forms part of the body's immune system which is compromised if glutathione is low. It is also recycled in the body. Important for many enzymes and probably has other effects on metabolism.

Glycerol

($C_3H_8O_3$). Also referred to as GLYCERINE. Used in food, soaps, creams, toothpaste and pharmaceuticals. Non-toxic and sweet.

Glycogen

See Appendix IV.

Glycoprotein molecules

These are proteins with a sugar attached and are located on the outside of the membrane of cells, and connective tissues, as well as in blood plasma. They have several functions being important in clotting, identification of Blood types and skin cell structural support.

Gray (Gy)

This is defined as *"the absorption of one joule of radiation energy per kilogram of matter"*. A 'rad' which is still in use is equivalent to O.O1 Gy**.**

Guanine

This is one of the four nucleotides bases which always links with the base Cytosine that link to the 'ribbons' of the *DNA Helix*. See page 79 of book.

H

Half life

The period of time during which one half of a population or radioactive substance alter or decay. The remaining half then alters or decays over the same time period. This may be in milliseconds or millions of years.

Hepatocytes

These are cuboidal, epithelial cells that line the sinusoids of the liver and carry out most of the liver functions. Bile is secreted by the hepatocytes and these cells can and do regenerate to maintain a constant weight balance of the liver mass.

Histamine

Produced within the White Blood cells (Basophils and Eosinophils) as well as mast cells in various places within the body (nose, mouth, stomach and the brain). Histamine is realsed once an antigen is exposed to an allergen and binds to the IgE antibody. It dilates the capillary vessels so that the white cells can enter the tissues to attack foreign invaders.

Heparin

Produced by the white blood cells (Basophils) and mast cells. An anticoagulant used in medicine. Also made synthetically and believed to have other functions yet unknown.

HIV-1

HIV stands for Human Immuno deficiency Virus. The two major groups are HIV-1 and HIV-2, but there are many sub-groups and again these are divided into types. It is the M-sub-group that is mostly responsible for Aids although HIV-2 also causes Aids. The difference between them is genetic and HIV-2 is found mainly in West Africa and progresses slowly. HIV enters the immune system and attaches to a receptor on the W.B.C's.

HTLV

This means 'Human T-cell Lymphotrophic Virus'. It is a retrovirus (a virus that has a protective covering to protect it from the host's immune system) that effects the T-lymphocytes. There are 4 types but HTL-1 is the more important as it can cause a type of leukaemia which is fatal.

Host factors

In order to prevention the potential transmission of an infection, an individual (the host) utilizes a number of different defence mechanisms to prevent entry, remove the offending infection or damage to the body. These, such as age, gender, race, and many other systems are examples of what are referred to as 'host factors'.

Hydrolise

A chemical process that results in making a chemical compound into simpler chemicals.

Hydrolysis

This refers to the 'breaking down of a bond in a molecule with water. There are 3 main types by which hydrolysis is achieved – acids, alkalis and enzymes.

Hydrocarbons

Compounds that only contain two elements, Hydrogen and Carbon. They are found in crude oil, coal and vechicle emission of gases following combustion and cause enivronmental pollution.

Hydrogenated

A chemical reaction that adds hydrogen to an atom of carbon. Some foods such as oils are hydrogenated which changes their molecular structure making them solid. This is done because the food then last/stay fresher for a longer period of time. This process produces trans fats which may result in many undesired medical conditions such as increasing the LDL (bad cholesterol).

I

Ileum

The third part of the interstinal tract approximatly 3m long. This is where bile acids and vitamin B12 are absorbed via villi similar to those in the Jejunum.

Immunological

Referring to the immune system. Its structure, function and disorders.

Immunoglobulin/s

Lymphocytes and Plasma cells produce a protein referred to as immunoglobulin (Ig). These are *antibodies* and there are five types. IgA, IgG, IgD, IgM and IgE. Each one has a different role to destroy intruding foreign substances.

Immune response

When the body's immune sytem recognizes the presence of a foreign substance invader it defends the body by responding to destroy the *antigen* on the invading substance. Note that the body has its own antigens (called HLA antigens) but it knows this and normally does not destroy them. Immunity can develop over time as the body builds a defence against antigens. Immunization is another way of acquiring immunity but this has a life time and does not last forever.

Infra red radiation

That part of the Electromagnetic radiation spectrum that lies between visible light and radio waves (700 nm to 2 Million nm). Wavelength is long (about 30cm) and energy low. Cannot be seen by human eyes but can be felt as heat. Water vaour in the air absorbs IR. One half the sun's emitted energy is IR. Uses: thermal imaging, remote controls, and astronomy are examples.

Insecticide

A type of pesticide that is specifically formulated to destroy insects. Thee are two main types which destroy insects by contact (short term) or systemic (long term).

Interaction

For the purposes of this book this refers to the effect of one chemcial/ toxin /drug upon some other. This can be additive, snergistic or antagonistic.

Interstitial fibrosis

Chronic exposure to dusts (silica, grain, etc.) and fibres (*asbestos*), as well as certain medical conditions and drugs, can result in a repair process where fibrous tissue is laid down. This is irreversible. The interstitial tissue is a supporting framework of the lungs through which blood and lymph vessels and nerves are contained. It is this area which become scarred ie. fibrotic.

Intrinsic factor

This is a *Glycoprotein* produced in the stomach which passes to the less acidic small inestine where it then binds to *Vitamin B12* to assist in its safe transport to the ileum where it is normally absorbed to the circulatory system and tranported to the liver. Following oral ingestion of the vitamin B12 a protein produced by the salivary glands binds to B12 to transport it through the stomach without the acid harming it, as B12 is very sensitive to acid media. This carrier is digested by pancreatic enzymes before the intrinsic factor takes over.

Ions

An atom or group of atoms (Polyions) that have an electrical charge. The may be NEUTRAL ions, which means the charges are balanced, CATIONS = positively charged and have more positive ions, or ANIONS = negatively charged and have more negative ions. They have an important role in body functions as well as in industrial processes.

Ionizable/Ionization

Capable of being ionized. The alteration or change of atoms into a positive or negatively charged state. Some (7) of the human body's amino-acids can be ionized amongst many other molecules.

Ioniozing Radiation

This is electromagnetic radiation that has sufficient energy that "*overcomes the binding energy of electrons.*" They include gamma rays and X-rays having a short wave length and a high frequency, as well as alpha particles, netrons and protons. Ionizing radiation is dangerous as it damages internal body structures. The unit is the Becquerel. In the International system of Units, 1 Bq = 1/s where 's' = Sievert.

Isotopes

A different version of an element is called as an isotope. It has the same number of protons but a different number of electrons. The parent element always has the same atomic number (protons) , but the number of neutrons will be different.

J

Jejunum

This is the second part of the small intestine extending for 2.5 m from the duodenum to the *Ileum*. It has larger microvilli than the other two parts of the small intestine and tranports food nutirents to the blood via active and passive transport through the large villi.

K

Keratin

This is a *fibroprotein* and a structural component of hair and nails. It is also found in the outer dead layers of the skin which helps to protect the skin.

Kupffer cells

These cells are mainly found in the liver and are in fact macrophages that protect the liver. Since they are located in the sinusoids of the liver they are in contact with all toxins reaching the liver and in response they release various substances as part of the livers action again infection, damage or toxicity.

L

Lactase

Many individuals cannot tolerate milk and some milk products (other foods have added lactose) because it contains a sugar called Lactose. *Lactase* is an enzyme produced by the intestine which converts lactose to glucose and galactose (simpler sugars that the body can digest). Lactose is needed to digest food and if not enough of this sugar is not produced one becomes lactose intolerant – generally a genetic condition but bowel disease or medication may cause it. A lactase supplement is available.

Larynx

Located between the pharynx and the trachea about 5cm long (2inches) long. It contains the vocal chords. A flap (epiglottis) closes the layrnx entry to the respiratory system when food is swallowed. Cartilage and bone (Adam's apple) keep the larynx from collapsing.

Lasers

These are beams of electromagnetic radiation. The beam is formed by the excitation of atoms which then emit photons in a continuing reaction as other atoms are stimulated to emit more photons. The resulting beam is of one colour only.

LD50

"A statistical estimate of the doseage required to kill 50% of a population of the test organisms"It is a convienent standard to describe the toxic level of a substance when comparing the toxicity of different compounds. It is of most value in dealing with toxicity by ingestion .

Legionnaires Disease

This is a Pnuemonia caused by a bacterium called legionella. EXP: inhallation (not person to person) but Inhallation of micro water droplets from water systems such as showers, air conditioners, cooling towers in buildings, swimming pools etc. Symptoms like influenza with very high fever. A weak immune system or smokers are more likely to get infected.

Linamarin

Found in the roots and leaves of the Cassava plant, which is a stable diet in some countries. Once ingested its alteration in the intestines results in the production of low levels of the toxic compound *Cyanide*, unless the flour or food prepared from the plant (there are other plants that contain this cyanogenic glucoside) is carefully cooked so that the cyanide which is volatile is removed before eating the final preparation of the food.

Lipase

An enzyme produced by the pancreas, liver, saliva and other tissues as well as by some bacteria and fungi in the bowel. Not all these function on food in the small intestine to digest the fats. These are also used widely in industry in baking, to convert vegetable oil into fuel, detergents and others.

Lipoid

This is a small molecule of fat which of course is insoluble in water. *Cholesterol* is a lipid (but this also contains protein). *Triglycerides* are key components of lipoids (these are LDH and VKDL). They are important in the structure of cell membranes, production of hormones and the storage of energy. For a more accurate and detailed definition, classification and discription the interested reader is referred to *Fahy, E. et al. A comprehensive classification system for lipids. J. Lipid Res., 46, 839-862 (2005) (DOI: 10.1002/ejlt.200405001) - reprinted in Eur. J. Lipid Sci. Technol., 107, 337-364 (2005).*

Lipofuscin

An important pigment which accumulates in the brain, retina, liver kidney, heart and colon and contains fat, sugars, Hg, Al, Fe, Cu and Zn.

LTH

Leuteo**t**ropic **H**ormone, also refered to as PROLACTIN. This is produced by the anterior pitutary in the brain, breast and prostate and has several functions (production of breast milk, metabolism, immune system and others). It is under regulation by the Hypothalamus. Its level can be measured in blood or urine.

Luetinizing Hormone

Produced by the anterior pitutary this hormone stimulates ovulation in women and the production of testosterone in men.

Lymphatic system

This system is similar to the circulatory system. It contains lymph – a milky fluid which transports lymphocytes (white blood cells - B and T-lymphocytes are produced in bone that produces antibodies to fight infections, toxins remember the invader should they attack again at some time and carry dead cells ie. waste). It maintains fluid balance in the interstitial tissue and has hundreds of nodes – lymph nodes – which filtre the contents in its vessels before the lymph passes on through the system. The spleen, thymus, tonsils and adenoids are all parts of the lymphatic system. It does not extend to the nervous system.

Lymphedema

An obstruction in the lymphatic circulatory system will slow or block the low of lymph return to the blood circulatory system and result in swelling due to fluid retention and occurs usually in the ankles, legs or arms. It may be caused months after surgery for breast cancer due to removal of the lymph nodes, damage to the lymph vessels, and a tropical infection with filaria – a parasite). It can also occur genetically due to insufficient lymph nodes or lymph vessel abnormalities.

Lymph glands

Also referred to as Lymph Nodes. These are filtres along the vessels to remove debris before the lymph passes back to the circulatory system.

Lymphatics

These are the small vessels that form the lymphatic system through which lymph flows.

Lymph

A watery clear and slightly yellowish fluid that runs through the lymphatic vessels.

M

Maltose

($C_{12}H_{22}O_{11}$) A malt sugar which is white, crystalline and soluble in water. A type of carbohydrate which is slightly sweet and important in digestion and as an energy provider for the body. It is made up of two glucose units. Malt refers what is left over by one of a number of cereal grains such as barley, that is processed by wetting drying and heating and later allowing an enzyme like diastase to convert it into sugar.

Melanin

A pigment in the skin and a protective factor from exposure to *Ultra Violet radiation* which can induce skin cancer. UV increases the production of melanin which rises through the layers of the epidermis and gives the skin its dark colour

Melanocytes

These are cells in the bottom layer of the epidermis of the skin which produce the melanin pigment. They are also found in other areas of the body such as the eyes and the hair.

Membrane

A layer or layers of tissue that acts as a barrier to the passage of particles, molecules or ions from one side of the membrane to another. It may be a covering of a cell organ or layers that form the skin. (see Fig.18 p.68).

Metabolism

This describes the breakdown of molecules and the synthesis of chemical compounds to provide nutrition, energy for cells, and also results in less toxic substances for body excretion. This is carried out by the help of *enzymes*. fats, proteins and carbohydrates are all metabolized in the body.

Mesothelioma

A malignant cancer that affect the tissue lining the lungs. It can also affect the peritoneum in the abdomen, the pericarium of the heart and the tissue surrounding the testis. Exposure to asbestos fibres predisposes to mesotheliom but this may also be due to other causes which today are not known.

Metabolite

A small molecule which is an intermediate product in the process of metabolism. Primary metabolites are produced by cells that requires them for their growth. Secondary metabolites refer to those that are not required for growth of the cell. Metabolites are used widely in industry (perfume, drugs, vaccines, cosmetics etc.

MEL

This refers to 'Maximal Exposure Limit'. They are usually established for serious occupational health exposures, such as occupational asthma. They are given as the airborne concentration which is averaged over a period of time – long (8 hr.) or short (15 min) to ensure that there is no significant risk.

Mists

This is the result of small droplets in air. It appears a little bluish. Some countries have regulations of the visibility range for driving on roads. This helps to differentiate between mist and fog. It usually occurs near shores where moist warm air comes into contact with cooler areas.

Methaemoglobin

Haeme is a component of haemoglobin. It contains Ferrous iron (Fe^{2+}) which carries oxygen in the red blood cells. When ferrous iron is altered to ferric iron ($Fe3^{+}$) haemoglobin is converted to methaemoglobin. This substance cannot then be released to the cells in tissues for oxygenation and the condition results in hypoxia (lack of oxygen supply). Methaemoglobinaemia results at levels >1% of methaemoglobin. Skin colour due to blood colour alteration changes at 15% and death occurs at 75%. The condition may be genetic (absense of an *enzyme* called Cytochrome b5 reductase which controls iron in the red blood cells) but is usually acquired.

Mitrochondria

Located in most but not all cells (ie, not in red blood cells) the number of mitrochondria varies in different cells. They provide a number of functions to the cell such as generate energy from fats and fatty acids, synthesize protein, and are understood to cause certain medical conditions. Mitrochondria has its own genome. *(Information from Wikipedia Encyclopaedia).*

mg

Milligram. This is a unit of mass or weight and equivalent to 1000 of a Gram. A 'mcg' is a millionth of a gram. Note tha 'Mg' (large 'M') refers to the chemical *Magnesium*.

Molecule

These are atoms which chemical bonds hold together and make up a chemical compound. They vary in their size and some compounds can have thousands of molecules. As they are always in motion their speed increases with absolute temperature. (zero temp – lowest temp at which an system is at its lowest energy level). To convert Celcius to absolute add 273.15 which now becomes Kelvin temperature – not Celcius.

Molecular Biology

The science that studies the characteristics and biological process at molecular level. Started seriously in 1960 after *DNA* structure was explained by Dr. F. Crick et al. at Cambridge University UK.

Molecular weight

This is the same as the atomic mass (m_a) of a molecule. Atomic mass is indicated by 'u' which is the value of the sum of all the protons and neutrons in the neucleus of the atom. Note that the mass number changes in radioactive decay. Molecular weight is therefore the sum of all the values of all the atoms in the molecule.

Monomers

A atom / molecule that can combine with other atoms/molecules to form polymers such as vinyl chloride to form *Polyvinyl chloride*.

mRNA

This stands for 'messenger RiboNucleic Acid'. Since *RNA* cannot move out of the nucleus because it is such a long molecule, *mRNA* receives the information (*refered to as transcription)* transports the information of the sequence of amino-acids from the gene in the nucleus to the ribosomes in the cytoplasm of the cells where the proteins are then formed according to that sequence.

Mucin

A group of high molecular weight glycoproteins found in mucous secretions such as saliva and eye tears. The two main types have different functions although both are protective. Mucin has a high carbohydrate content and some protein.

Mucosa

Also refered to as 'mucous membrane'. It is continuous with the skin in some areas such as the mouth and nose. It lies over connective tissue and has a protective role such as keeping areas moist or removing pathogens from the nose through the prodcution of mucin. The mucosa can absorb drugs and toxins at a rapid rate.

N

Nanometers

A unit of measurement that is equal to one billionth of a meter (0.000000001, or 10^{-9}). You require a scanning probe microscope to see the size of a nanometer. For comparison one inch = 25.4 million nanometers and a virus varies between 30 to 50 nanometers.

Nanoparticles

Originally refered to as Ultra-fine particles and 100 nanometers in size. Note that the term refers to inorganic materials not molecules. They absorb solar radiation better than film sheets and have optical properties.

Nanotechnology

Several definitions exist. The European Commision (2011/696/EU) has defined nanomaterial and has been reviewing the recomendations based on experience for publication by the end of 2016. (See http://ec.europa.eu/environment/chemicals/nanotech/faq/definition_en.htm (5/8/2016). In general one might look at this as the science and application of extreemly small particles.

Nasal Cavities

The nose is divided into two passages lined with mucous membrane. They heat moisture in the air inhalled protecting the lungs. Hairs in the nose trap dust and other particles. From the walls of each passage protrude three conchae (twirls of cartilage) that help to increase the nasal surface area and slow the speed at which air is inhalled. Sinuses in the skull on the front of the face drain into the nasal cavities – all except one sinus. The roof of the nasal cavity contains the olfactory nerves (sense of smell). A tube from the nose rises upward to the middle ear to equalize pressure.

Natriuretic

This refers to the excretion of large amounts of Sodium (Na) in the urine. It lowers blood Na levels and blood volume. Caused by diuretics and some medical conditions and cardiac atrial peptide hormones (α-ANP), which is present in heart failure. This hormone has other functions such as increasing capillary function and secretion of renin and other substances.

Necrosis

Cell damage and eventually cell death caused by blocked blood supply, injury, infection, and toxins. There are six types of necrosis. Gangrene is one example. It can also be the normal process of what is known as 'Apoptosis' which is the natural process of a cell that has come to an end of its life cycle and dies. In necrosis the cell protein dies and the cell releases the enzymes to digest the dead cell.

Nematode

Commonly refere to as Roundworms. About 60 species are parasites that live in the intestines of humans. Millions of individual espescially children are infected world wide. Many nematodes live in the top layers of soil. They eat bacteria and some insects. They are both beneficial and harmful. Eosinophil IgE blood levels are high with human nematode infections. Some types cause anaemia and others serious imedical conditions and nutitional deficiencies.

Neuropathy

Numbness, tingling, pain and weakness in the affected part or loss of temperature recognition and results from damage to a peripheral nerve is refered to as neuropathy. The causes are varied and may be injury or compression to a nerve. And as such these are called mononeuropathies. *Polyneuropathy* is more common and is caused by exposure to toxins (alcohol), nutrional deficiencies (*Vitamin B12*) or diabetes.

Neuromuscular Junction

This is the junction between the axon of a neuron and the dentrite of another neuron. Signals are transmitted by the release of *Acetylcholine* through this junction. Motor neurons transmit signals to muscles to contract. Genetic, *autoimmune* problems and certain chemicals effect neurotransmission.

NOAEL

A 'no level effect' is "*a level at which no response to the dose is measurable.* It refer to the dose of the substance being measured on a specific characteristic of the organism. The 'no effect level' is often referred to as the "No observed adverse effect" – that is NOAEL.

Non-ionized

A state when insufficient (< 10eV-electron volts) photon energy is available in that part of the electromagnetic radition to ionize atoms or molecules. The figure of 10eV varies in the literature. Visible light and radiowaves are examples of non-ionizing radiation.

Nucleotide

An organic compound which is a precursor of NUCLEIC ACID (this lies in the nucleus of all cells and contains the genetic material and is also important in cell signalling and metabolism). The BASES of *DNA* are composed of two types of nucleotides ie: Purine (these are the BASES *Adenine* & *Guanine*) and Pyramidine (the BASES *Thymine* & *Cystosine*). In RNA one of the Pyramidines (Thymine) is replaced by Uracil (this is a Thymine without a methyl group).

Other nucleotides composed of a nitrogen base sugar and a phosphate are present in the body such as muscle.

O

Odds Ratio

In a study /trial off some intervention it is useful to measure the effect by comparing the control group (receiving a placebo) with the group that is receiving, lets say, some medication. To do this one calculates the Odds Ratio. This is done by dividing the results of the intervention group with that of the control group. If the answer is the same then the odds ratio will be 1. Meaning there is no difference between the two groups. If it is more than 1 then the control group is better but if it is better than the intervention group is better than the control group.

Oedema

This is the result of excessive fluid in the intestitial tissue spaces and a more than average/large circulating blood volume which moves into the tissues and is not returned from the tisues to the venous blood system. Balance is therefore disrupted.

Oesophagus

This is a tube that lies behind the trachea and in fron of the spine (Thoracic vertebrae). It connects the back of the mouth (Pharynx) to the stomach after it passes through the daigrapham. It is about 35cm = 10 inches long.

Opisthorchis Viverrini

A liver fluke that has a similar life cycle to that of the blood fluke which causes Schistosomiasis (see Schistosoma Haematobium), except that it goes through two hosts – the snail and some species of fish – before it infects man through the food chain by eating raw/ fish. It passes fron the small bowel into the bile ducts where it develops and causes cancer of the bile ducts. IARC classification a Group 1 carcinogen. Humans pass the eggs into the feaces which infects water via sewage. It is common in Asian countries particularly in Thailand.

Organic materials

These are carbon based compounds such as wood derived from natural material, leather from animals or synthetic, such as plastics from oils. Plants decay, and over time convert to what is known as humous which contains valuable nutrients for the soil.

Oxidation

This occurs when a substance gains oxygen. The substance looses electrons or hydrogen which are replaced by oxygen. Examples are iron which is oxidized and rusts. It continues to loose electrons as long as oxygen is around!.

P

P-450

An enzyme of which there are many types (around 50 in the body). They help to make cholesterol and steroids but also metabolize potentially toxic substances forming metabolites for excretion. Deficiency in some of these enzymes can result in infections or difficulty in clearing some chemicals such as warfarin products.

Pancreatic jucies

These are alkaline fluids, that contain enzymes and hormones produced by the pancreas. Their alkalinity helps to reduce the acidity of the stomach contents as it passes into the first part of the small intestine, and the enzymes help to digest the carbohydrates, fats and proteins of which food is made up. They are stimulated by hormones produced in the duodenum in response to acidic food reaching it. Insulin, is one of the important substances produced by the pancreas.

Parathyroid Hormone

(**PTH).** The Plasma in blood has about 360mg of dissolved Calcium in the circulation of a health person and the bones about 1000 mg (1Kg)(wikipedia 2016). The parathyroids secrete parathyroid hormone to control the levels of calcium in the bood by increasing the release or reabsorption of calcium from the bones or stimuating calcium uptake by the intestine through a process of assisting the kidney to convert vitamin D to Vitamin D3 (cholecalciferol)., which is the active form of Vitamin D to enhance the uptake of calcium. Another control system is by inhibition of reabsorption of Phosphate (HPO^{2-}) from the proximal tubule of the kidney which then increases plasma calcium. Note that a low level of Magnesium in the blood inhibits PTH secretion. Medical conditions result in consequence of increae or decrease of the PTH.

Parathion

An Organophasphate insecticide. This is a very toxic cholinesterase inhibitor.

Partial pressure

This can be defined as the 'pressure of that portion of gas that together with the pressure of all the other gas molecules gives us the total pressure of a gas. Atmosphere is made up of portions of Nitrogen gas, Oxygen gas etc., and its total pressure is 760mmHg. To calculate the gas partial pressure take the portion (a decimal of its percentage in the gas) and multiply by the total pressure.

Partical size

Particles may be solid, liquid or gaseous and there are various methods of measuring them as they may be spherical or irregular in shape. There are International Standards on how particle sizes should be described. Measurments are often in microns (1 millionth of a meter). The eye cannot see particles below 40 microns. A particle of lead dust is about 2 microns.

Passive Difussion

The movement of molecules to pass/move/diffuse from a concentrated to a less concentrated across a membrane. See also Diffuse Appemdix III p.241.

PEL

Refers to 'Permisable Exposure Level'. They were established by OSHA in the USA as legal limits to the concentration of hazardous substances in the air. They are not guidelines like TLV's. However, the levels are considered by some as being too high and need to be adjusted for the safe exposure of workers from adverse effects.

Perianal region

The area between the scrotum and the annus in the male and the vulva and annus in the female.

Peptide Bond

These are strong chemical bonds that bind one amino acid to the carboxyl group of another amino acid. Proteins consist of long chains of amino acids held together by these peptide bonds. Short chains are refered to as peptides. (See also p.74 of book).

Peripheral Neuropathy

See Neuropathy p.253 Appenix III..

Peripheral system

The Central Nervous system has two parts to it, the central and the peripheral. The peripheral sends and receives information to and from the central system. The peripheral nerves extend to all the organs, muscles and glands of the body and also receives and sends information from external stimuli. Being outside the skull and spine it is more vunerable to injury.

Pepsin

This is an inactive enzyme that is activated from pepsinogen in the acid medium of the stomach. It digests the larger petide bonds of proteins. Note that there are also other proteolytic enzymes to digest (the smaller peptide bonds of proteins in the stomach.

pH

A logarithmic scale that measures the level of acidity or alkalinity in a liquid. A level >7 is alkaline and <7 acid.

Phagocytes

These are cells (mainly White cells called neutophils and monocytes) that engulf bacteria and foreign matter to protect the body.

Phagocytosis

The ingestion of foreign particles (bacteria, toxin, debris etc) by macrophages or other cells in the body.

Pharynx

This is the cavity (31.75 cm = 12.5 inches long) that connects the nose and mouth to the oesophagus, and is the passage for air to the larynx.

Pinolin

Believed to be produced by the pineal gland. Its major role is to promote the generation of neurons from nerve stem cells, and its antioxidant activity. It may have some effect on aluminium toxicity through its antioxidant activity on fats in the brain.

Phospholipids

Phospholipids are part of the cell membranes. They contain phosphorus and fats as their name implies. They form a two layer structure where the outer layers of the membrane contains the phosphate molecule (a polar molecule meaning it has a chemical charge) and the inner layer, the two fatty acids (non-polar meaning no chemical charge). These fatty acids are attached to a *glycerol* molecule at one end and the glycerol is attached to a phosphate at the other end. The glycerol is often also attached to an alcohol. Thus one end – the outer side of the membrane - the molecule is hydrophilic (water attracting) the other end hydrophobic (water repelling). These phospholipds line up parallel to each other and make up the membrane structure. They have several different functions. (see also Fig. 18 p.68).

Photosynthesis

The process by which green plants and algae absorb light to convert carbon dioxide and water into glucose to provide energy. This energy can be stored in its roots, stems and leaves in the form of starch. Oxygen is released by the plant during the process of photosynthesis.

Placental barrier

Three layers of tissue seperate the foetus from the mothers blood. These layers in the placenta act as a selective filter to what is transported across to the foetus from the maternal blood. The placental barrier alters throughout the term of pregnancy. The passage of substances across the placental layer which has and continues to receive much attention is complex. It is possible that some nanoparticles may also cross this barrier – research is still limited.

Plasma

A clear, yellowish, watery fluid in which the cells of the blood are suspended in the blood circulatory system. The Plasma cells are white cells produced in the bone marrow and secrete antibodies for release into the blood and lymph circulation system to bind antigen for destruction.

Platelets

These are produced in the bone marrow along with other blood cells. They are very small cells and respond to signals from damaged blood vessels to help repair by adhering to the damaged area. Low levels resulting in skin bruising or excessive bleeding (eg. nose bleed), whilst a high count may result in blood clots and cause serious conditions (eg. arteries to block). Certain diseases can increase the level of platelets as some drugs can which later get back to normal.

Plural cavity/ Pleura

Each lung is covered by pleura which also lines the chest wall so that a cavity is formed over the lung. This cavity is filled with fluid to avoid friction as the lungs expand and contract during respiration.

PM 2.5 & PM10

'PM' refers to Particuate Matter. Airborne particles whose aerodynamic diameter of 2.5 microns or less are referred to as PM 2.5. PM 10's do not exceed 10 microns are referred to as PM10. Measured in micrograms per cubic meter. An average human hair is about 50 microns in diameter but could be larger.they include dusts and airborne bacteria but not gas pollutants.

Poison Any substance that can cause harm, injury or death to cells and organs in any part of the body. Can also be referred to as 'toxin'.

Polarity Polarity referring to a molecule means 'unequal distribution of the electrical charge of electrons' with an electrical charge being greater at one end of the molecule than the other. A molecule can be polar or non-polar. The difference is that a polar molecule (H_2O or NH_3) is one where the electrons are NOT electrically symetrically distributed, and non-polar that are symetrical ie. there is no abundance of electrons on one side of the molecule – and the charges cancel each other out. (O_2 or N_2). Molecules of the same polarity mix to form a solution, while polar and non-polar molecules do not mix. Oil and water are examples.

Polymerise A chemical reaction that results in one monomer to another to form polymers.

Polyneuropathy See Neuropathy p.260.

Polymer This is a long chain of molecules called monomers that bind to others identical to itself to form a polymer. This long chain binding is called polyerization.

Polypeptides See 'Peptide Bonds' p.257 Appendix III. A chain of amino acids that are linked together by peptide bonds.

Polysaccarides A sugar may be refered to as a saccaride which is a crytalline sweet carbohydrate. Simple sugars are called monossacrides, disaccarides have two monosaccarides and a chain of monosaccarides is a polysaccaride. *Glucose* is one example. They serve as enercy storage.

Portal System This consists of the veins from the large and small intestines and the spleen, which go to the Hepatic Portal Vein and on to the liver, as well as the artery from the spleen, panceas, and an artery from the aorta. Toxins from these organs in the abdomen all pass through the liver.

Potentiates Refers to making more effective, powerful or more potent which may be toxicity or a beneficial condition.

ppm

Refers to 'parts per million'. It is a measurement of the pollutant per unit of a volume of water. It is the same as mg/L. Zane Zatterfield an engineering scientist, explains this simply by noting that 1mg in 1 kg is 1ppm or he states *"Another way to say it is a liter of water weighs 1,000 grams or 1 million milligrams. Therefore, 1 mg in 1 liter is l mg in 1 million milligrams or 1 part per million"*.

PRL

Stands for **PROLACTIN (**See LTH – Luteotropic hormone). Produced by the pitutary in response to stimulation by the hypothalamus, and is important in the production of breast milk, metabolism and the immune system. It counteracts dopamine production. High levels decrease the levels of testosterone and oestrogen.

Protons

A sub-atomic particle found in the nucleus of every atom which has a positive charge. The number of protons present defines the number of electrons of the atom. Adding a proton to an atom results in a totally new element.

Prostaglandin

This is a fatty chemical produced at sites of injury or infection anywhere in the body which responds by causing imflamation and swelling as a part of the healing process. It also causes pain. Aspirin stops the production of prostglandin to relieve pain amongst other things that Apirin does. There is more than one type of prostglandin and they have different important functions.

Proteomics

This refers to the study of the function of the many different proteins, their structure, expression and interaction.

Protein/s

Molecules made up of very large numbers of amino acids in long chains. 20 different types in humans. Each has a different function in the body ie: as an enzyme, antibody or transport etc. Found in many foods.

Psoriasis

A chronic skin disease the triger of which is still not known, although at this time a protein that binds to *DNA* and regulates gene expression reduces psorias imflamation when activated is being studied. *(National Psoriasis Foundation article by Melissa Leavitt on 5th June 2015 referring to work of Paola Di Meglio lead author of the study and published in the June issue of Immunity).*

Ptylin

An enzyme found in saliva. It helps to breakdown starches and *glycogen* (this is obtained from beef, chicken and pork). Once it reaches the stomach the stomach acid destroys it.

Pulmonary

A word used when referring to anything that has to do with the lungs such as the condition of 'Pulmonary fibrosis'.

Pulmonary Interstial Fibrosis

A lung condition in which excessive fibrous connective tissue is laid down in the lung causing thickening of the tissue and difficulty in breathing. Occupational and Environmental pollution from Asbestos, Silica, coal, metals as well as arthritis, tuberculosis and radiation therapy may end up in pulmonary fibrosis.

Pulmonary System

This refers to structure, and functions of the whole of the Pulmonary system, respiration; lungs, inhallation and exhallation, exchange of gases etc.

Pyrolysis

This is the thermal or chemical breakdown of materials such as wood or certain types of fabrics etc. Heat gradually starts to decompose the materials lowering the materials ignition temperature until it catches fire.

Q

R

Radicals

A free radical is an unstable molecule (because it lacks an electron) that has resulted from the spliting apart of a chemical bond of another molecule. To stablize, the radical must gain an electron from some other stable electron which can set up a chain reaction. This happens in the process of metabolic, enzyme reactions and from initiation by pollutants, such a smoking and by some body cells themselves, such as the mitrochonria in the process of phagocytosis. Free radicals damage/destroy carbohydrates, lipid, proteins and DNA trigering disease. *Vit C* and *E*, fruit and vegetables, all contain antioxidants and neutralize free radicals by donating an electron.

Radioactive

A substance that can emit radiation whether this is alpha, beta, or gamma radiation which damage tissues.

Radon

A radioactive very heavy single atom gas and therefore can penentrate materials easily. It emits alpha radiation. It has two isotopes – 220 and 222 with 222 being the more common and occurs in the environment. 222 is the decay of Uranium and 220 of Thorium-232. Found in igneous (magma which cools and hardens) rock and soil and therefore in mines and homes. Exposure by inhallation but also found in underground water and therefore includes exposure by ingestion. Several countries have maped radon levels where housing is erected.

Raynaud's Disease

This is condition affecting the mainly the fingers and toes although it can affect the ears, nose and lips as well, which results from spasm of the very small arteries supplying these areas which results in the affected parts turning both blue (lack of oxygen and white. On warming these areas return to the normal pink colour, but this can take from a few minutes to several minutes or more. There are two types a primary (cause unkonwn) and secondary which occurs in the elerly due to exposure to vibration tools, injury, connective tissue diseases or nicotine from smoking.

REACH

Refers to 'Registration Evaluation Authorization and Restriction of Chemicals'. This is an EU regulation developed to protect the environment and human health from the hazards of chemical substances. The reader is advised to review the regulation (EC) No. 1907/2006 and its modifications.

Receptor

Biology on line (5/6/2009) defines receptor as "A molecular structure within a cell or on the surface characterised by selective binding of a specific substance and a specific physiological effect that accompanies the binding, for example, cell surface receptors for peptide hormones, neurotransmitters, antigens, complement fragments and immunoglobulins and cytoplasmic receptors for steroid hormones"

Reduction

In this context, reduction refers to the gain or loss of oxygen electrons. Some chemicals undergo reduction by gaining oxygen (eg: Copper) others by loosing electrons eg: Magnesium). This process alters the charge of the atom. Note that when an oxidizing substance gives off an oxygen it is reduced but the substance receiving gains, as it is oxidized.

Relative Humidity

Relative humidity refers to the level of saturation of moisture in the air. Do not confuse with Dew Point which refers to the amount/quantity of moisture in the air. Optimum level of RH for comfort is around 60% at a temperature of $19^{\circ}C = 67^{\circ}F$.

Rems

A unit of radiation. In other words a measure of how much radiation dose is absorbed by the body and the effect on tissue and health that this absorbed energy has on the body in relation to the period of time in which it is received. A dose of < 10 rem is small and one does not expect any health effects. A number of health effects begin to occur above > 50 and at 500 may cause death, although this depends on whether it is localized or widespread. Above 500 the risk of death is very high indeed.

Ribosome

This is a spherical particle of protein and *RNA* (ribonucleic acid – see RNA below) each making up a unit of the particle, (ie: the ribosome) floating in the cytoplasm of a cell which according to instructions received from mRNA, (a messenger from the nucleus of the cell, which has instructions of how to link in proper sequence amino acids to make proteins – a copy of the DNA) together then produce specific proteins needed for the cell and others that will leave the cell.

RNA

Refers to Ribonucleic Acid. There is more than one type and shape. They are single strand molecules containing Ribose, involved in the synthesis of proteins, transmission of genetic information from the DNA to the ribosome and can act as enzymes. (See also page 78 of book).

Renin

This is a protein that has enzymatic activity and is produced by smooth muscle cells in the afferent arterioles that supply the kidney with blood. It is released by the cells to regulate blood pressure and increase *Sodium* or *Chloride ion* (Cl^-) concentration.

Retroviruses

A virus that is made up of *RNA* and has the capability of entering a hosts cell's and altering the RNA. The virus consists of *DNA*. This results in the hosts cell replicating itself in the exact compostion of the virus. infecting the host with more viruses. It is refered to as retrovirus because this alteration of RNA to DNA is the reverse of what normally happens and is called 'reverse transcription'. *HIV* is one example of a retrovirus.

Rosin

A yellow or black solid resin obtained from some plants that consists chiefly of Abietic acid (an allergen and on the toxic substances list in USA). Rosin melts at around 300-350° and used in flux for soldering, varnishes, soaps, adhesives and has other applications such as its use on violine strings. Labelled as E915 OR E445 if used in soft drinks (Wikipedia 27 Dec. 2016).

S

Saccules

The vestibule which is part of the inner human ear and lies in the temporal bone of the skull and consists of a saccule, 3 semi-circular cannals and an atrium. They are all important in reference to our balance. The saccule which contains sensory hairs detects head movements and acceration in the vertical plane (head tilting forward and backword) and transmits the impulses via the 8th Nerve to the brain.

Saliva

A fluid containing a number of enzymes and secreted by glands within and around the mouth, for the purpose of commencing the digesting process of foods making food easier to swallow before it reaches the stomach and small intestine. It also has an antibacterial effect on bacteria in the mouth and acts a lubricant.

Schistosoma Haematobium

This is a blood fluke that causes the disease Schistosomiasis. It is endemic in the middle east and Africa. Also called BILHARZIA. When humans are in contact with infected water the larvae make their way the skin, enter the blood vessels and go to the liver where adult flukes develop. They then go to the bladder, mate and lay eggs which infect the urethers, kidney and bladder walls. Excreted into the urine they penentrate snails who later infect the water.

Sievert (Sv)

In the SI system of units this is a unit of the radiation absorption. It takes into consideration the biological effectiveness on tissue of the radiation being absorped which varies with the type of radiation. It is a large unit so millisievert (1000th of a sievert) is more commonly used. An accute exposure of 10Sv is generally fatal. Regulations limit radiation exposure to workers.

Sigmoid

This can refer to an 'S' curve as in the Dose response curve or to the Sigmoid colon which is the portion of the large intestine before reaching the rectum and has a curve in both directions

Skin absorbtion

The structure of the skin is such that it can absorb chemicals, toxins, liquids, vapours and pharmaceutical products to the blood circulatory system. It is permeable to other substances such as radiation. A number of factors affect the rate and extent of absorption such as dose, solubility, molecular size and transport systems in the skin. Therefore there are both benefits and disadvantages to skin absorption. The risks to absorption of hazardous substances is reduced by establishing safety margins for the products.

Smog

Pollutants from industrial activities, vehicle exhausts, incomplete combustion etc., react with UV light creating ozone at low levels and other chemical substances that result in smog causing a severe reduction in visibility.

SMR

A ratio that shows the increase or decrease in mortality of a cohort in reference to the general population. This is the Observed deaths to Expected deaths in some population. Multiple by 100 to change to a percentage.

Solubility

This refers to the ability of how much a substance can dissolve into another substance. Temperature, pressure and pH all effect solubility. If a substance is insoluble then it will percipitate into the other or not at all, although to some extent it is possible to make anything soluble. Solubility is expressed in grams per 100 cc. of water at a given temperature.

Soot

Carbon particles that result from incomplete combustion of hydrocarbons from home or forest fires, furnaces and motor diesel exhaust etc., and may become airborne polluting the atmosphere. Fine soot particles may be less than 2.5 micrometers or larger. Note that dust is usually around 10 micrometers.

Spores Spores are unicellular organisms and have only one chromosome. Plant spores are part of their life cycle and produced by cell division (meiosis). They can develop into a new organism and do not require sexual reproduction. They are also produced by bacteria and fungi.

Stack A chimney draws air into its inside hollow structure (the flue) to maintain combustion. This process is referred to as the 'stack effect'.

Sublingual The area or space under the tongue which is very vascular and useful when direct absorption into the blood is quickly required as it avoids the substance to be absorped from having to be processed by the liver which delays its action.

Sulpho group A functional group is a part of a molecule and gives the molecule its properties. These may be simple atoms or groups of atoms. Sulpho groups are a functional group and they have an affinity for oxygen. For example So_3H^-) is one which is derived from Sulpuric Acid (H_2SO_4).

Sulphur dioxide (SO_2). A gas which reacts with other chemcials to form hazardous substances such as sulphuric acid. Formed in industrial activities such as fuel combustion, the chemical industry, or released from minerals containing sulphur which is then oxidized. As H_2SO_4 can travel large distances. It is hydroscopic and hazardous to health.

Synergy This is the greater potential that can be created by two or more substances (chemicals), or two or more people (team work) that could be obtained by the substance or individual person on their own. Sometimes stated as 'the combination of certain chemicals can be greater then their individual elements'.

Systemic In this context this term refers to the effect of a substance/toxin beyond any local effect it may have. Its systemic effect (on any internal organ or sytem of the body) may occur some time after the local effect.

Systemic Sclerosis

Although it is refered to as 'systemic' this disease can be either local (skin) or systemic (affects internal organs). It is an autoimmune connective tissue condition. May be caused by organic solvents and other chemical toxins. May be hereditary.

Synthesize

Refers to forming a new substance in the process of some chemical reactivity such as combining two chemicals.

T

Thallium

See Appendix IV p. 330.

Target Organ

An organ which is the first to be effected or mostly affected by a toxin. Any cell in the body that has a functional receptor (these vary in their number and their presence is due to the instructions from DNA in the cell) for a particular chemical becomes a target cell otherwise it will not accept the toxin. The number of receptors increases the cells response to the toxin.

Telomere

A nucleotide that protects the end of the chromosome from attaching to another chromosome. They deteriorate with age.

Temperature inversion

Normally temperature decreases with height. When air in the centre of a high pressure area sinks it compresses the air beneath it and this causes the temperature below to increase more than the ground surface air. This hot air does not decrease as it should in rising, it increases with altitude resulting in what is referred to as an inversion of temperature. Air pollutants are trapped in a temperature inversion which causes smog. *Note that there are other causes of temperature inversion.*

Teratogens

Chemicals, drugs radiation or other agent such as a virus that can cause birth defects are refered to as teratogens. Their effect depends on the time during which the foetus is developing as some only have an effect at particular periods of pregnacy. Rubella, HIV endocrine disruptors *(Dioxins)*and environmental toxins such as *Lead*, and *Mercury* are examples.

Thermoplastics

These are materials made of chains of polymers. (Acrylic which is a glass substitute is a polymer, Nylon or polycarbonates are other examples). By raising the temperature of these materials they melt and therefore their shape can be altered. *NOTE that they are not thermoset materials which set when heated.* Thermoplastics are good electrical and thermal insulators. They can be of high strength and light in weight. Some can be subject to degradation by UV Radiation and stress, and may deform them. Their application is wide.

Threshold

Exposure to a toxic substance beyond a ‘no effect level’ of that toxin is the threshold limit value of that substance.

TLV

TLV’s are guidelines by which exposure levels can me maintained as low as is practically possible. They are not legal standards. See page 39 for details.

Toxic

Anything which can produce a harmful, injurous or lethal effect on the cell/s of the organ/s that they target.

Toxicity

This is the ability of a compound to produce injury and may be slight, moderate or severe in addition to also being acute, chronic, local or systematic.

Toxoplasmosis

A disease caused by the parasite Toxoplasma gondi. Found in contaminated food or water, in cats faeces and soil. Infection developed during pregnancy can result in congenital transmission may cause serious eye damage to the infant. A test is available to see if you have had or have toxoplasmosis.

Transcription

This is the process of making a copy of the genetic information in *DNA* into the messenger mRNA which then produces the proteins in correct sequence in the Ribisome of the cell replicating the DNA.

Translocation

Here, this is referring to the transfer of nutrients from the soil through bundles in the roots and stems of plants to the veins in the leaves. The word means a change in location.

Trachea

Windpipe. A tube (10.16 cm (4 inches) long and about 2.5cm (1 inch) wide) surrounded by cartilage that extends from the larynx (where the Adams apple is) to where it branches into two major Bronchi once to each lung carrying air via other bronchi and bronchioles to the alveoli in the lungs.

Tachycardia

A heartbeat faster than 100. The cardiac atria or the cardiac ventricles beat faster, so that pumping is not as efficient as it should be. It indicates that the heart requires more oxygen for a number of possible reasons. It is a disruption of the normal nerve conduction signals. Remember the heart also has its own conduction system which can be disrupted in its rhythm.

Thymine

This is one of the four nucleotides bases which always links with the base Adenine that link to the 'ribbons' of the *DNA Helix*. (See pp.78 & 79 of book).

Thyroglobulin

A protein produced by the thyroid gland and used by it to produce the thyroid hormones T3 and T4. (See TSH for detail).

Triiodothyronine

See TSH p. 276 below.

Tracheotomy

This refers to the operation proceedure and not the opening which is made in the trachea which is referred to as 'tracheostomy' ie: that an opening has been made. Usually carried out in an emergency situation because of air being unable to get through the trachea into the lungs as a result of injury, blockage such as a tumour or other object etc. This is a proceedure which can have serious complications and care and attention are required. Not a matter for the layman to dea with.

Tribolite fossil

A tribolite is an extinct marine anthropod (one that has an external skeleton to protect its body unlike humans that have an internal skeleton). Their fossils date back to >500 million years.

Trousseau's sign

This is an involuntary medical sign where the wrist and fingers of the hand hyper flex. It is seen in patients with a low blood calcium level (50% of normal values) and tetany which causes the involuntary contraction of muscles. It can also be caused by an increased ratio of phosphate to calcium and low levels of magnesium as well as an underactive thyroid.

TSH

Thyroid Stimulating Hormone. Produced by the pituitary gland to stimulate the thyroid gland to produce T3 (Triiodothyronine which effects metabolism, heart rate, muscle control and temperature) and T4 (thyroxine which is activated by the liver to T3). Low Iodine levels lowers both T3 and t4 blood levels and may result in goiter. High levels result in Hyperthyroidism and low ones in Hypothyroidism and their respective symptoms.

TWA

This refers to a chemical/toxic exposure over a specified period of time, usually 8 hours over a 40 hour week, and to which a worker should not have an adverse effect from that exposure. The exposure is expressed in either parts per million or milligrams per cubic meter and is only a guideline.

Thyroxine

See TSH p. 276 above.

U

µm

An SI unit of length refered to as Micrometer or Micron. It is equal to 1000th of a millimeter = 0.001mm.

Ultra violet radiation

(UV). Radiation emitted by the sun with a wavelenth of between 100 – 400 nanometers, shorter than the wavelength of visible light and therefore has more energy. It can cause electrons away from atoms and molecules to split, thus damaging tissue and the DNA. Three types – *UVA*, *UVB* and UVC in that order of their energy with UVA being the least. UVC is absorbed by the ozone layer but can be hazardous resulting from welding.

Urea

See Appendix IV.

Uric Acid

See Appendix IV

Uric Acid

($C5H4N4O3$). Purines found in drinks, dried beans, anchiovies, peas and beer dissolve in the blood and break down to form uric acid which is excreted in the urine. A little is excreted in the faeces. If the concentration of uric acid in the blood is higher than the kidney can deal with then crystals of uric acid form hard deposits in joints which are painful. This condition is refered to as gout. These crystals may aggragate and form stones in the kidney. Purines found in drinks, dried beans, anchiovies, peas and beer dissolve in the blood and break down to form uric acid which is excreted in the urine. A little is excreted in the faeces. If the concentration of uric acid in the blood is higher than the kidney can deal with then crystals of uric acid form hard deposits in joints which are painful. This condition is refered to as gout. These crystals may aggragate and form stones in the kidney.

UVA

See also Ultra Violet radiation. UVA (A long wave) penentrates the deeper layers of the skin – up to the dermis. Wavelength 400-320nm. May cause genetic mutation by damaging DNA. Sun protection factor (SPF) should be > 15. Note that the SPF's may not be that accurate.

UVB

See also Ultra Violet radiation. UVB (A shorter wave than UVA) penentrates up to the epidermis. Wavelength 320-290 nm. UVB causes sunburn and increases the colouration of the skin. Sun protection factor should be > 15. Note that the SPF's may not be that accurate.

V

Vagus nerve

One of the 12 cranial nerves and the longest. It has 2 branches and supplies the pharynx, stomach, heart and other areas of the body. It sends and receives signals. It regulates the heart beat and inervates muscles that help with breathing and can at times affect swallowing in the elderly due to the health status of the nerve.

Vapour

Molecules that have or have gained sufficient energy to escape from a liquid or solid are said to be in a vapour state. It is a gas that is below its critical temperature (ie: the temperature at which the density of the vapour and liquid are equal) In a closed container the vapour may become saturated.

Volatility

This refers to the rate at which a substance has a tendency to vaporize. It depends on pressure, the strength of molecular forces and temperature. It increases with a rising temperature and decreases with lowering of pressure.

Vibration tools

Vibration equipment creates pressure waves. Workers exposed to the oscillations are exposed either to their whole body (eg: vehicle drivers) or a part such as the hand and arm with hand held tools. A guideline would be to keep at $2.5m/s^2$ over an hour period and if this is not possible alter the way work is carried out or consider protective gloves that meet your requirements. Avoid more than $5.0m/sec_2$ over a full days work.

W

Wave Height

The distance from the top to the bottom (trough) of the wave). Important for weather reporting together with other information on waves, such as swell, frequency, speed, length etc., and research work such as information on sedimentation. Most sediments are loaded with toxic and other substances.

Warm Front

This is usualy down as a line with circles on its front. It is warmer and more moist at its rear than the front it is heading into and replacing. It therefore feels humid and warmer with the Dew point rising. Atmospheric pressure falls and visibility is poorer.

X

Y

Z

Zoonoses

Diseases transmitted to humans by animals such as Malaria, Rabies or Lyme disease. Transmission occurs by mosquito bite, viruses, bacteria, as well as saliva, urine or faeces of an infected animal.

Appendix IV

SOME INFORMATION ON CHEMICALS REFERRED TO IN THIS BOOK

ACKNOWLEDGEMENT

The importance of information/knowledge provided by encyclopaedias, journals, books, researchers, institutions, u-tube providers, and many others is invaluable to all of us who have to ensure that the knowledge passed on to students at all levels is accurate and up updated as far as is reasonably possible. I would, therefore. like to acknowledge the support that all of these have provided by their work through documentation and on line in my effort to ensure the provision of concise but simple explanations related to biology, chemistry and other general knowledge to adult part time undergraduates whose knowledge of such subjects is limited any may have long disappeared from memory.

It is inpractical in writing the explanations of chemicals that accompany the contents of this book to mention every support to each definition individually but special acknowledgement is made to WIKIPEDIA and all its supporters, The Encylopaedia Brittanica, The Free Dictionary by Farlex, Study.com, News Medicine Live Science and Medicine, those who provide U-tube on a diversity of subject matter, and many others whose works have helped in designing the structure, presentation, verification and information on what has been written, and to keep the explanations as simple as possible. They are by no means meant to be comprehensive or replace the scientific descriptions of any chemicals which is beyond the scope of the glossary, but just sufficient to motivate and encourage the student to feel they know something about it and delve more deeply into each chemical with interest towards a practical approach in their work. In particular I wish to acknowledge the assistance of Prof. David C. Magri B.Sc.(Hons), Ph.D. (Western) Department of Chemistry, Faculty of Science at the University of Malta for his assistance in reviewing and editing the chemicals referred to in Appendix V.

'The general knowledge obtained from many other disciplines is knowledge gained that can be beneficially applied to Safety and Health'

<u>Explanatory Notes/Abreviations used in writing the definitions</u>:

Chemical or molecular formulas have been provided for most chemicals but it should be noted that a student is not expected to learn these although many of the more common ones will become familiar over time. Nevertheless they help to ensure that the correct chemical is sought should further research to any one is carried out. A major objective was to broaden student knowledge and be aware of where these chemicals are commonly found industrialy and otherwise to improve chemical risk assesment.

Ca = carcinogen,
VOC = volatile organic chemical compound
EXP: = exposure
A dash, ie. '–' signifies the meaning of the symbol or word in front of it.
Emm = emmissions
PD or Mnfc. = produced or manufactured
(-) = not available, because the make up of different chemical formulas, may have diverse structures or requires the reader to have further chemical information and knowledge which makes it of little value to provide the formula at this level.
<u>Underlined words</u> that are also in *<u>Italics</u>* indicate that the specific word can be found in other parts of Appendix III or IV but at times the reader is directed to contents within the book.

A

Acetaldehyde Dehydrogenase (ALDH $_2$)

Enzyme - 15types. ALDH 2 maintains body balance of *<u>acetaldehyde</u>* (*CH3CHO - a <u>VOC</u> group 1 carcinogen but methabolized in liver).* Catalyses oxidation of aldehydes. EXP: Air water, Both indoors and outdoors. Wood and chipboard, paints (water&matt), tobacco smoke Exhaust and building materials.

Acetaldehyde (CH_3CHO)

Group 1 Ca., VOC. Demand now decreasing. EXP- air, water, Cigarettes Wood, plastic, water based paints, and fuel EMM: Metabolized in Liver. Excreted in Urine. Thermal degradatiion of plastic bottles (*<u>Polyethylene terephthaltate</u>* (PETE).

Acetylene **(C_2H_2)**

A hydrocarbon. Colourless Gas which is. unstable in the pure state. At the torch where it is mixed with oxygen it may reach tempertures of > (5700°F). "*Stored under special conditions. May explode in excess temperture, pressure or mechanical shock*"(421). The reader *is advised and* MUST review instructions on its potential hazards.

Acetate **($CH_3CO_2^-$)**

A Salt made from Acetic Acid. Found in industrial solvents.

Acetone **(C_3H_6O)**

A solvent. Colourless, flammable liquid and volatile. Not toxic but desquamates the skin on contact. A building block for many chemicals in production of acrylic plastics (eg: plexiglass), adhesives etc. Used in fragrancies, nail polish remover, hair spray, and cleaning laboratory glassware.

Acetylcholine **($C_7H_{16}NO_2$)**

A neurotransmitter released by neurones to the central nervouse and peropheral ssytems to contract skeletal muscle, and in activate cholinergic system in CNS. Involved also in pain sensation, endocrine activity and rapid eye movements in sleep. Broken down quickly by the enzyme acetylcholinesterase.

Acrolein **(C_3H_4O)**

An aldehyde. *Glycerol* in fat alters to to acrolein. Toxic. A Biocide.

Acrylamide **(CH_3H_5NO)**

PD: in manufacture of Polymers**.**
Group 2A Ca. Used in Water treatment and Sewage industry. Present in Foods heated at high temp. In baked and fried starchy foods and cigarettes.

Acrylic Acid **($C_3H_4O_2$)**

Found in many household products(floor polish, plastics textiles and paints). EXP: skin contact, eyes, inhallatation and ingestion. Corrosive substance with an increasing industrial demand. Considered a teratogen and embryotoxic.

Acrylonitrile **(C_3H_3N)**

Volatile and Toxic at low doses.PR: Plastics, Synthetic rubbers. Group 2B Ca. It is flammable and exposive.

Adrenocorticotrophic Hormone **(ACTH)**

Secreted by the Anterior Pituitary. Response to Stress and responsible for release of *Cortisol*.

Adenine **($C_5H_5N_5$)**

A building block of *DNA* and *RNA.*

Adrenaline **($C_9H_{13}NO_3$)**

Also called *Epinephrine*. By the stimulation of receptors causes vasoconstriction, increase cardiac muscle contraction and bronch-dilatation.

Agent Orange **(2,4,5-T + 2,4-D)**

A herbicide mixture contaminated with *8-Tetrachlorodibenzo-dioxin* (TCDD). Extremly toxic affecting skin and causes Cancer.

Alcohol **(C_2H_5OH)**

Organic compound. Most common are *Ethanol* and *Methanol*.

Alcohol dehydrogenase (-)

An enzyme found mainly in the liver and some in the stomach. Several types are present each with a different function. Can have both a useful and toxic effect. Converts alcohol into acetaldehye (toxic molecule) but this is quickly converted into acetate for use by body cells. Note, however also converts methyl alcohol (*Methanol*) which is metabolised into formaldehyde and other toxic substances. It is the bodies defence mechanism to alcohol intake.

Aldosterone **($C_{21}H_{28}O_5$).**

A *mineralcorticoid* produced by the cortex of the adrenal gland. See Fig. 51 p.132.

Alkaloids **(-)**

Single molecules that occur naturally in plants and contain a Carbon and at least one *Nitrogen*. Basic substances. Isolated from plants and used in medicine.

Alkyl (designated R)

Part of a larger molecule. A *Benzene* ring missing one Hydrogen.

Alkyl phosphate (P_2O_5 + ROH)

P_20_5 = Phosphoric Pentoxide.

R = ALYKL/ARYL group on alcohol mixed in PR: of the type of *Phosphate* made. EX: Vapour, Mists, Liquids, effects Eyes, skin, lung, GIT. Reacts with alkalis, Al, Zn and liberates Hydrogen gas.

Aliphatic amines (-)

See also '*Amine*'. An Aliphatic Amine is an amine molecule in which the aromatic ring (like the benzene ring) is NOT attached to the Nitrogen atom of the molecule. One example is methylamine.

Aliphatic Hydrocarbon derivatives

Arbitraly placed into 3 main groups. Alkanes, Alkenes and Alkynes and each depends on their type of bonds. In the order shown – single, double or triple bonds. **Alkanes** are saturated but the other two are unsaturated HC's. Examples are Ethane, Methane and Propane. Derived from petroleum deposits and burn in air. **Alkenes** are oils and pigments of plants and trees. They form starting points for the production of epoxides. **Alkynes sometimes refered to as Acetylenes.** Ethene C_2H_4) also referred to as Ethylene is an example. Occurs as a plant hormone involved in leaf growth and found in ripened fruit promoting ripening. It has agricultural, industrial and other applications.

Aluminum (Al)

Soft, flexible mineral. Strong affinity for O_2. Usually found as oxides or *Silicates*. Deposited in bone and CNS. Competes with *Calcium*. EXP: Al welding fumes, antacids, flavour to cakes and bread, antiperspirants, powdered Al. is also explosive.

Amalgam (Ag2Hg3)

An alloy of a metal such as tin, copper or silver combined with Mercury. Used in dentistry they are regulated by ISO

1559. Alternatives are available for use in dentistry.

Amine **(-)**

Derivates of <u>*Ammonia*</u> (**NH_3**) where one, two or three of the'H's of NH_3 are replaced by an atom or group of atoms so so that there can result 3 types of amines. **Strong** bases of low Mol.wt., **Soluble** in water, and **Toxic**. and easily absorbed via the skin. They react with mineral acids to form amonium salts. Breakdown of amino acids release amines. Used in the mnfc. of deeply coloured AZO) dyes. *Note that neurotransmitters are amines.*

Amino-Acids ($NH_2CHRCOOH$)

(See p.75 of book). These are organic acids which contain an amino group (-NH_2) and carboxylic acid (-COOH) the form the building blocks of proteins. Not all can be synthesized in the body. 8 are ESSENTIAL (cannot be synthesized in the body) and 12 non essential. They contain C,H,O N.and a side chain which consists of different types of atoms. It is the side chain that makes each one of the amino acids unique. Sources of essential amino acids include, fish, meats (note that meats also contain high levels of saturated fats and <u>*Cholesterol*</u>), poultry, eggs, milk and some vegetables

Ammonia **(NH_3)**

Gas or liquid. Found in fertilizers and many household cleaners in water solution as <u>*Ammonium hydroxide*</u>. Caustic. Toxic. Converted to Urea in humans.

Ammonium **(NH_4^+)**

A positively charged ion. Formed by the neutralization of amonia with an acid (eg: Ammonium Sulphate = <u>*Ammonium*</u> plus <u>*Sulpuric acid*</u>).

Ammonium Hydroxide (NH_4OH)

A solution of water and <u>*Ammonia*</u>. Used in laboratories, agriculture, cleaners, and production of some foods. Hazardous.

Corrosive and toxic. Heated results in ammonia vapour.

Ammonium Nitrate	**(NH_4NO_3)**	Salt of *Ammonium* (NH_4). Nitrogen Fertilizer. Still used in explosives. Requires strict handling and storage procedures. Fire risk.
Aniline	**($C_6H_5NH_2$)**	*Aromatic amine*. Used in the Mnfc.of many industrial chemicals, additive to dyes, rubber and preparation of other chemicals. Toxic. Non- essential Amino acid with benefical functions. Found in Avocados,beans, gelatine & whole grains.
Androgens	**(-)**	A steroid hormone present in males and females. Produced by the adrenal cortex, and responsible for male sex characteristics.
Antimony	**(Sb)**	Soft mineraloid used in alloys, flame retardants, pigments and glass industries. Powder explosive. Absorption via lungs and by skin contact. Excreted in Urine.
Aromatic amines	**(-)**	Aromatic (aryl) ring attached to an amine. They are derivates of *Aniline*. Very stable ie: *Benzene, Toluene*. 3 types of aromatic amines. Mnfc: dyes, pharmaceuticals, pesticides, rubber and Polymers. A Probable carcinogen and *Endocrine disruptor*.
Arsenic	**(As)**	Natural element in many different minerals. Mining,pesticides, preservation of wood, volcanic eruptions, food and water. Inorganic As. is more toxic than organic As. and is easily abosrbed. Excreted in Urine. Carcinogenic.
Arsenic Pentoxide	**(As_2O_5)**	A white powder which is used in solution in the glass and electronic industries and in the production of insecticides and fungicides. Not much used today and barred in many countries. Has an affinity for *Cystein.* EXP: skin and eye contact, inhallation. Chronic

exposure affects the peripheral nervous system and results in nose ulceration or '*a hole in the nose*'. A carcinogen.

Arsine	**(AsH_3)**	Toxic gas. Formed when the metal antimony comes into contact with an acid in metal refining. EXP: Via skin andInhallation. Destroys the Red Blood cells and damages the kidneys. Used in the semiconductors industries.
Aryl	**(Ar)**	An organic group derived from *Benzene* or a Benzene derivative.
Asparagine	**($C_4H_8N_2O_3$)**	An amino acid. Synthesized in the body for protein structure. In the human body the isomer L-aspargine is one used for protein structure. Not an essential amino acid. It reacts with simple sugars ie: Glucose in baked foods to produce *Acrylamides.* Found in meats, eggs, aspargus and potatoes.
Atrazine	**($C_8H_{14}ClN_5$)**	A Herbicide banned in Europe due to contamination of ground water. Degrades slowly in soil. Controversial evidence and still under review.
Azo dye	**(R-N=N-R)**	R=aryl or alkyl group.N = N represents Azo Dye. AZO refers to 'deeply coloured.' Used in textiles, printing, paper and food colouring industries. Some are toxic and could result in tumours (eg: bladder). Not easily degradable and discharged into water resources will effect aquatic organisms.

B

Barbiturates	**(-)**	Derived from Barbituric Acid. CNS depressant. Now replaced by benzodiazopines in medical practice, but

		still in use for certain conditions eg: eplilepsy under the control of physicians.
Barium	**(Ba)**	Occurs naturally in combination with other chemicals. Mined. It reacts with non metals forming toxic substances. Some Ba compounds dissolve in water and these are toxic. Others are insoluble. Used in the oil, glass, paint, ceramic and other industries. Present in Barium nitrate firework displays.
'Base' in chemistry		A molecule that has a high pH. greater than 7**.** It accepts Hydrogen ions rather than repels them and neutralizes acids. Eg: soap or detergent.
Benzene	**(C_6H_6)**	EXP: Crude oil, gasoline, Forest fires, cigarette smoke. Exhaust, burning coal and oil. Used in production of many chemicals for plastics, rubber, lubricants, pesticides. Effects bone marrow and the Immune system. Carcinogen.
Benzidine	**($C_{12}H_{12}N_2$)**	A cyrstaline aromatic amine. Very toxic substance. Group A carcinogen (bladder cancer). Used in dye manufacturing. Can leach from clothing and comes in contact with skin. also used in printing inks, laboratories and paints.
Beryllium	**($C_{10}H_9N$)**	A grey very strong metal mainly used as an alloy. Exposure occurs by skin contact, and inhallation of mists, dusts or fumes, in foundries, engineering, the aircraft, automobile and electronic industries, welders dental laboratories and many others. Beryllium results in sensitization, a chronic condition of the lungs (breathing difficulties, night sweats and cough). May progress to lung cancer.
Beta-Endorphin	**(-)**	Released by the pitutary gland in response to stress, injury or exercise. This substance enters the cells in the central and peripheral nervous system trigering opiate receptors.

Beta-naphthalene **(-)**

An isomer of *Naphthalene*. (See Naphthalene p. 315).

BHT

Butylated Hydroxytoluene. An synthetic antioxidant used in medicine, cosmetics, as an additive to fuel oil and also in small amounts as a food preservative. Currently considered safe to use in cosmetic preparations. Mildly irritant.

BHA

Butlated Hydroxyanisole. An antioxident and prservative this chemical has wide applications in food products, cosmetics (such as lipstick and eye shadow) and pharmaceutical products /preparations. Occupational exposure: rubber tyre handlers, fast food handlers, consumer food and animal food production industries by inhallation, skin contact and ingestion of food products. Considered to be an *Endocrine disruptor*, causes allergic reactions and a probable carcinogen. Regulated concentrations apply. EU prohibits its use as a fragrance.

Bisphenol A **($C_{15}H_{16}O_2$)**

Synthetic compound used in the preparation of plastics, eye lenses and epoxy resins. It is a colourless solid that is soluble in organic solvents and as a coating for food metal containers. An endocrine disruptor. Baned from use in baby bottles and considered a chemical of concern due to studies having linked a number of diseases with it.

Borax **($Na_2B_4O_7{\cdot}10H_2O$)**

(Sodium Borate) This is a mineral. It is a Salt of Boric Acid. Used in the Production of Fire retardants, flux, anti-fungals, glass, pottery and ceramics. Prohibited as E-285 (acid regulator) in some countries and requires labelling in EU. Low toxicity but over exposure may cause irritation to lungs and skin.

Bromine	**(Br)**	A liquid at room temperature but evaporates easily above this temperature forming a brown toxic gas. Many of its compounds are no longer in use. A hazard to transport requiring lead containers. 3ppm *"immediately dangerous to life"* (NIOSH).
Bromopropane	**(C_3H_7Br)**	A solvent used in the furniture, aircraft, electronic and synthetic fibre industries. that have substituted CFC's and tetrachloroethylene. Overexposure affects the nervous system. EXP: skin contact and inhalation. Easily absorbed via skin.
2-Bromopropane	**(C_3H_7Br)**	There is a 1- and a 2- Bromopropane. They have the same formula but different physical properties. EXP: skin, eye and inhalation. May cause effects on fertility (animal studies) Irritant to eyes, lungs and G.I.T. and may cause liver, kidney and CNS system damage. See also Bromopropane above.
1, 3-Butadiene	**(C_4H_6)**	A synthetic colourless gas. Toxic with risk of leukaemia. A human carcinogen. Used in the production of synthetic rubber and the production of other industrial chemicals. Present in vehicle exhaust but broken down in the air.
Butyl Acetate	**($C_6H_{12}O_2$)**	A solvent for lacquers and a food flavouring agent. A colorless flammable liquid. In Butyl Acetate fires CO and CO_2 are released. Very reactive substance. Containers usually have an inhibitor to prevent explosions. Keep below 100° F = 38°C. Flash point 120°F = 49°C. Exposure via skin, eyes and inhalation. Irritant and may cause allergic contact dermatitis.
Butyl Nitrite	**($C_4H_9NO_2$)**	A yellow oily ligand. Absorbed by ingestion and inhalation. Low toxicity. Known as 'Poppers' in dance clubs.

Amyl nitrites are used to treat angina and cyanide poisoning.

C

C-reactive Protein (CRP)

This is a protein produced by the liver in response to any imflamation that may occur in the body. As a test it is not specific and therefore when used it is done in combination with other investigations as a stronger indiction of whatever condition the tests are directed at.

Cadmium (Cd)

A soft metal by-product of the refining of Zinc. It has a number of isotopes incuding some that are radioactive. Used mainly for the Mnfc. of NiCd batteries and colouring paints where worker exposure is due to the cadmium being in powder form. Present in cigarette smoke, liver and kidney foods. Particularly toxic to kidneys and liver. IARC classifies it as " a known human carcinogen but other institutions have labelled it as probable or suspected carcinogen.

Carbon tetrachloride (CCl_4)

A solvent for oils, varnishes and resins. No longer in general use in dry cleaning and refrigeration because of its effect on *Ozone*, but still in use in the manufacture of some industrial organic chemicals. Hazardous by inhallation, effects the CNS, kidney and liver.

Calcium (Ca)

Generally found combined with other chemicals such as Calcium Sulphate (Gypsum) or Calcium Carbonate (Limestone), in bones, teeth, vegetables, nuts and milk. Essential for life. Used in fireworks, medicine, buildings etc. Strictly controlled by the parathyroid glands in the human body to maintain accurate balance in the blood. Calcium is important in communication between cells. *Aluminium* competes with *Calcium*

Calcium Hydroxide	**(CaH_2O_2)**	A white powder that is formed when lime ($CaOH_2$) is mixed with water. Used in laboratories, the food industry, building restoration, and as a flocculant in sewage treatment plants. Caustic to skin, eyes and lungs. Chronic exposure to skin results in dermatitis and ulceration.
Carbaryl	**($C_{12}H_{11}NO_2$)**	An insecticide. And a *cholinesterase* inhibitor. Illegal in some countries. Not stored in fat and milk.
Carbonate	**(CO_3^{2-})**	Salt of carbonic acid, eg: $CaCo_3$. Used in cement, lime and ceramics.
Carbon Monoxide	**(CO)**	A odourless and poisonous gas from incomplete combustion – Engines, Furnaces, wood etc. – materials that contain carbon. If inhalled will replace the oxygen in the blood causing loss of consciousness and death. Confined spaces, boiler rooms and stores where petrol vechicle engines are used are at risk.
Carbon Dioxide	**(CO_2)**	A heavier than air odourless, colourless gas. It is present in the atmosphere, absorbed by plants, released during respiration and results from the burning of carbon materials and natural gas. Used as a fire extinguisher, and a refrigerant. Absorbs reflected heat from the earth causing global warming.
Carbon Disulphide	**(CS_2)**	Volatile and foul smelling. Used as a solvent, fungal insecticides, fruit conservation and in the manufacture of rayon. Affects the nervous system.
Chloride	**(Cl^-)**	A negitively charged ion. An electrolyte that helps in the regulatin of fluid in and out of the tissues.
Chlorine	**(Cl_2)**	A very toxic gas. See p.72 of book for this.

Chlorodane **($C_{10}H_6C_8$)**

An *Organochlorine insecticide*. (See Organo Chlorines (-). Toxic via inhallation, ingestion or skin absorption. Effects on CNS, Bood, Respiration, Liver and Kidneys and G.I.T. Persistant in the environment and banned in many countries.

Chlorotoxin

($C_{158}H_{249}N_{53}O_{47}S_{11}$) This is the very toxic neurotoxic venom of a yellow scorpion found in deserts. Produces *anaphylactic shock* and paralyses very quickly. Its target organs are the glial cells in the brain and pancreas. An antitoxin is available.

Cholinergic drugs **(-)**

See also the definition of the Parasympathetic Nervous system (page 110 of book) as these drugs have the same effect, increasing muscles tone, slowing the heart rate, increasing salivation and stomach secretions. They can block the enzyme acetylcholinesterase and therefore destroy *Acetylcholine*.

Cholesterol **($C_{27}H_{46}O$)**

A Lipoprotein (molecules of fat and protein). Produced in the liver and found in all body cells. Present in most foods. There are two types referred to as LDL (low density) and HDL (high density because they contain more proteins (± 48 different). *Cholesterol* is necessary for integrety of membranes and production of hormones. but high levels of LDL which ae very rich in cholesterol accumulate in and may block blood vessels. Research is complex, moving forward showing unexpected results, such as ‘dysfunctional HDL etc. – *interested readers should review the works of Jay Heinecke et al of the University of Washington and others.*

Chlorpyrifos ($C_9H_{11}Cl_3NO_3PS$)

An *Insecticide*. Used to control termites, cockroach infestation, fleas and ticks (dog collars) and crop pests. Modertely toxic (WHO) and Effects neurotransmitters such as <u>*Acetylcholine*</u>. Its metabolite 'TCYp' excreted in human urine. May be ingested as residue in food and water. Its application is limited by regulation and a safety protocol exists for agricultural workers.

Chromium	**(Cr)**	Hard but brittle metal and resistant to corrosion. When added to steel will produce stainless steel.thee are several compounds of Cr of which Cr VI is toxic and carcinogenic. Different compounds have varied production uses. Cr III is may be an essential trace element nutrient (see Wikipaedia (31 Dec. 2017).
Chromates	**$(CrO_4)^{2-}$**	An ion. Used in <u>*Chromium*</u> plating to avoid corrosion. Oxidizer. Carcinogen if inhaled.
Copper	**(Cu)**	A natural element. Released into the atmosphere from combustion of fossil fuels and industrial activities (Mining, Agriculture). Found in river water sediment. A trace element important to the body. Cu binds to organic matter in soil. Not present in ground water. Chronic exposure may result in Metal Fume Fever and Wilsons Disease (Cu in corneas of the eyes and damage to liver, kidneys and brain).
Cortisol	**$(C_{21}H_{30}O_5)$**	A glucocorticoid (See p.132-133 of book). This is a steroid hormone secreted by the cortex of the Adrenal Gland. It is involved in the metabolism of carbohydrates, fats and proteins and increases blood sugar levels. It is involved in many other body functions including the immune system.
Coumestans	**$(C_{15}H_8O_3)$**	A low molecular weight (therefore Passes easily through cell membranes) natural compound. Found in spinach, brussels sprouts, some type of chick pea and other vegetables. It mimicks

biolocical activity of oestrogen. Has many effects, such as, on bone, reproduction, metabolism etc.

Creatinine **($C_4H_7N_3O$)**

A waste product of muscle metabolism and ingestion of meats. Corelates with body muscle mass, and increases with exercise. Excreted by the kidney's and an indicator of kidney function. *Creatinine* levels rise if the glomerulus fails to excret it.

Cresols **(C_7H_8O)**

Aromatic compounds which are classifed as *Phenols* (a methyl group onto a phenol ring.). Hazardous by skin contact, inhallation or ingestion and may cause burns at these sites. Extracted from coal tar and used in the manufacture of pesticides, plastics and dyes.

Creosote **(-)**

Still in use as a wood preservative. New alternatives now in use due to carcinogenic potential. This is a phenol compound. Commerically used in the extraction of other chemicals such as carbolic acid, *Naphthalene* and anthracene. Health hazard by skin contact, inhallation and ingestion but this depends on durtion of exposure.

CRP – **(-)**

C-reactive Protein. This protein is made in the liver and its level in the blood will rise when there is inflamation. It can be measured by a blood test and elevated levels may indicate possible disease.

Curare **($C_{37}H_{41}N_2O_6$)**

A highly poisonous alkaloid substance which is extracted from the wood bark of certain tropical plants that used to be used on the tips of arrows. It effects the neuromuscular junctions and causes muscle weakness and depending on the dose may paralyse the diaphgram effecting respiration and death. A cholinesterase inhibitior will reverse the muscular weakness.

Cryolite **(Na_3AlF_6)** See Sodium Hexafluoroaluminate.

Cyanide **(CN)** There are a number of cyanide compounds eg: *Hydrogen cyanide* (HCN). Present in some fruit seeds (apple, appricot, peaches). It is released from some foods such as almonds and cassava. Present also in cigarette smoke and in the smoke from combustion of fires. Used in plastics and textile Mfc. EXP: Skin contact with soil, inhallation from cyanide gas and ingestion. Antidote – Hydroxocobalamine. Cyanide inhibits enzymes which are needed for respiration and may be quickly fatal.

Cyclohexane **(C_6H_{12})** A clear flammable liquid. Heavier than air. Used as a solvent and int the Mfc. of other chemicals and calibration of laboratory and othe t echnological equipment equipment.

Cytosine **($C_4H_5N_3O$)** A component of DNA and RNA and forms the base pair with Guanine. (See also Proteins on pp. 77, 78, 79 of book.

D

Deoxyribose **($C_5H_{10}O_4$)** **(2-deoxyribose)** This is a a monosaccharide, a simple sugar (Mono). The saccharides is the sugar. '2-deoxyribose' is theprecursor of the *DNA* nucleotide deoxyribonucleic acid. A nucleotide is a base plus a sugar ie. Ribose. DNA contains a string of nucleotides.

Dibutyl Phthalate **($H_{16}H_{22}O_4$)** This has many industrial applications. Used to soften materials, such as adhesives,inks, varnishes and as a solvent. ie. Cosmetics and fixatives for nail extensions. Also found in childrens toys. EU restricts use in cosmetics, child care items and toys. Evidence of toxicity appears insufficient at the present time except in animal studies.

Dichlorvos **($C_4H_7Cl_2O_4P$)** **An Organophosphate.**
EXP: Inhalation, ingestion, skin absorption and eyes. Inhibits acetylcholinesterase (*an Enzyme that breaks down Acetylcholine which is a Neurotransmitter and the way the brain processes information. Also causes slowing of the heart rate, blood pressure and secretions, bowel movements and cause bronchi to constrict*.) Carcinogenic.

Dieldrin **($C_{12}H_8C_6O$)** **An Organochloride.** A persistent organic pollutant. Biomagnifies (*concentration increases as it moves up the food chain)*. Toxic to CNS, reproduction, and the immune system. Also an *Endocrine disruptor*. This substance is banned.

Diethyltoluamide **($C_{12}H_{17}NO$)** Also known as **DEET.** An insect repellent. Used as a spray or lotion. Toxic if more more than 6 mg/L.in plasma. May cause insomnia and mood changes in workers. In high exposures. Its a pplication to the skin may cause irritation and rarely an allergic reaction in the epidermis. It may, very rarely, also cause a seizure.

Dimethylformamide **(C_3H_7NO)** **DMF.** A solvent for chemical reactions. Used also in production of plastics and fibres, pesticides, adhesives and paints. Females often bared from working with it as it may results in birth defects. It is not easily eliminated from the body.

Dimethyl Sulphate **($(CH_3O)_2SO_2$)** **(DMSO).**
Absorped via the Skin Inhallation, GIT. Mucous membranes including eyes Carcinogenic and mutagenic. Hazardous to the environment. It is used in industry as a methylating agent for many organic chemicals, to make dyes, perfumes and the seperation of mineral oils.

Dimethylsulpoxide **$(CH_3)_2SO$**

A solvent that dissolves *Salts* (ie. *formed by chemical reaction of a base, eg: NH_3 and an acid HCl), giving the salt NH4Cl, or a metal and an acid etc. Can be solid or liquid).* Found in many foods, and rainwater. Also in sea water from the end product of algae metabolism. Quickly absorped via the skin and neoprene or similar gloves should be used. Useful in medicine to increase absoption of some drugs.

Dioxin **$(C_4H_4O_2)$**

TCTD (2,3,7,8-tetrachlordibenzo para dioxin). Persistant environmental pollutants. Very toxic. stored by body fat with a long half life (years). Many types of related compounds but not all toxic. TCTD ie: Dioxan most toxic. These result from incomplete incineration (<850°C = 1562°F as a minimum) of waste, but present also result from forest fires and volanic erruption. Dioxins have been found in food and identified it was due to animal feed. For more detail review WHO and GEMS/FOOD documentation.

Dipropylene glycol **$(C_6H_{14}O_3)$**

Solvent and plasticizer. Used in fog machines, perfumes, incense, cosmetic emulsions, and as an intermediatry for many industrrial chemical reactions. Low toxicity.

Domoic Acid **$(C_{15}H_{21}NO_6)$**

A neurotoxin that Wikipedia explains is *"produced by algae and accumulates in shellfish, sardines and anchiovies"*.This neurotransmitter damages specific brain regions which results in "*short term memory loss*". The reader is refered to the WIKIPEDIA Encyclopedia (4/1/2017). https://en.wikipedia.org/wiki/Domoic_acid

Dopamine **($C_8H_{11}NO2$)**

A neurotransmitter produced in the brain (hypothalamus and substantia nigra). A decrease causes incoordination of movement whilst an increases results in repeated and unecessary movements and improved short term memory. Food and other pleasurable situations stimulate its release. It is involved in other brain functions.

E

Epoxide **(-)**

A chemical compound in which an Oxygen atom is linked to two different other Groups that are bonded to each other making a ring. These other two groups may themselves also link to other groups. One example is *Ethylene oxide* used for the sterlization of medical equipment, etc.. Epoxy resins contain epoxide groups. The hardner used with the epoxy is toxic and possibly carcinogenic.

Epichlorhydrin **(C_3H_5ClO)**

A colourless liquid organochlorine compound that is slighly soluble in water and hydrolizes to a substance found in food and is a carcinogen. Used in synthesizing organic compounds. Found in the Mfc. of solvents, plastics, epoxy glue and resins. EXP: skin contact, eyes and inhallation. A carcinogen. Flammable and explosion hazard. May cause allergic reaction, liver and kidney damage.

Epinephrine

See Appendix III. p. 243

Ethanol **(C_2H_5OH)**

Also referred to as alcohol or ethyl alcohol. An ethyl group (an alkyl that is substituted for a hydrogen on the parent chain of a hydrocarbon) linked to a hydroxyl group. Produced by fermentation for use as drinking alcohol or by extraction from sugar or corn for use as a fuel. When ingested has toxic properties in high doses. Effects, Brain, liver, digestive system and skin.

Ethoxyethanol	**($C_4H_{10}O_2$)**	Solvent that dissolves many chemical compounds.. Flammable and toxic by inhallation. To be stored below 30° centigrade. Has many industrial applications.
Ethyl Acetate	**($C_4H_8O_2$)**	Organic compound used in adhesives, nail polish removers, cosmetics, confectionary, as a solvent and in entomology. Low toxicity. Present in wines (provides the fruity taste and to which some individiuals are sensitive). Very high concentrations in industry cause nose and throat irritation and drowsiness. A flammable substance.
Ethylbenzene	**(C_8H_{10})**	A colourless liquid with a low flash point used in the Mfc. of *Styrene* and as a solvent. Vapour heavier than air and floats on water. Acute exposure causes irritation to eyes, throat and bronchial constriction as well as dizziness.
Ethylene Glycol Ethyl Ethers		**($C_4H_{10}O_2$).** These are all solvents and depending what chemicals they are produced from identifies their application. Some are of low toxicity. Occupational exposure has been known to cause low sperm motility. Insufficient information on longer term exposure in humans.
Ethylene Oxide	**(C_2H_4O)**	**Oxirane.** Colourless flamable gas at room temperature. Found in crude oil and petrol. Very hazardous. Carcinogenic. Sweet smelling and used in Mfc. of detergents, solvents and plastics as well as hospital disinfection (sterilization). EXP: skin, inhallation. Easily absorbed. Low toxicity and occupational exposures very low because of closed processes in manufacturing.

Ethylmetacrylate	**(EMA)**	**($C_6H_{10}O_2$).** A colourless liquid. Exposure is by ingestion or inhalation. Toxicity is low, but irritates skin, eyes and respiratory system. Occupational exposure occurs during the production of polymer based products (inks, paints etc.), as well as the use of products that contain the liquid monomer.

F

Fermones	**(-)**	Molecules that become airborne and transmit messages to members of the same species. A means of communication, distinguishing between other members of society, attraction and/or possibly as defence or attack mechanism in some insects.
Fixatives	**(-)**	Its meaning depends on what it isused for. Many types in solutionor spray are used as reservative in art or to fix cell's histology eg: *Phosphate* buffered Formaline. Some are toxic. Difficult to obtain full chemical composition even for substitutes.
Formaldehyde	**(CH_2O)**	Very widely used. A Volatile Organic compound. Toxic and Carcinogenic. Found in the atmosphere, smog, cigarette smoke and exhaust emissions. Metabolized to Formic acid in body. Used in embalming, medicine, wood panelling, construction materials, and foam insulation. Banned in some applications. Some limitations to exposures from emissions.
Formates	**(HCO_2)**	A salt or ester of Formic Acid (*this is a carboxilic acid which is an organic compound found in amino-acids).*
Fluoride	**(F^-)**	Natural element. Most abundant in mineral fluorite (CaF_2). Present in tea, raisins and wine and some other foods.

Soluble fluoride salts eg: Sodium fluoride are toxic and concentrated topical solutions are corrosive.

Fragrances

Pleasant smelling ingriedients that are found in perfumes eg: the synthetic chemical Tricyclodecenyl allyl ether. (this is also an insect repelant). Perfumes are volatile complex chemical mixtures from essential oils and synthetic chemicals. Also found in air freshners, soaps, detergents and candles. Very little information on the health effects are available due to the secrecy of product contents and there is limited regulation. Can cause allergies to some individuals.

G

Gama rays **(y)**

Short wave, high frequency, and of high energy electromagnetic radiation. This is ionizing radiation. Results from radiactive decay and nucler fussion (sun and stars). Mostly absorbed or scattered in earths atmosphere. Hazardous biologically as it penetrates deeply.
Note: a Photon is a extreemly small particle in all of the electromagnetic radiation waves whose energy depends on the wavelengths.

Galactose **($C_6H_{12}O_6$)**

A water soluble monosacaride (**a** simple carbohydrate). A sugar found in milk, tomatoes and vegetables. Does not require digestion and is absobed directly into the blood stream. Present in Lactose and Pectine.

Glycerol **($C_3H_8O_3$)**

Also referred to as GLYCERINE. Used in food, soaps, creams, toothpaste and pharmaceuticals. Non-toxic and sweet.

Glycogen **($C_{24}H_{42}O_{21}$)**

Derived from foods. *Glucose* is stored as glycogen to provide energy when needed by the body. Metabolized in the liver by stimulation of the liver cells by insulin.

Glycol ethers (-)

Water based solvents of which there are two groups depending whether they are made from **E**thylene or **P**ropylene derived from Naphtha from crude oil. The former E-type are used in cosmetics and paints and the P-type in cleaning products, adhesives and degreasing. Regulated . See **REACH** Regulations Appendix III p.269.

Glyceryl Trinitrate ($C_3H_5(ONO2)_3$

A vasodilator of smooth muscle. Administration under the tongue results in lowering of vascular resistance and systolic blood pressure. May produce severe headache, nausea, vomiting and collapse. Contact with skin may produce skin eruptions *(Windholz M. ed. 1976. See Merck Index).* Glyceryl trinitrate has some contraindications and may have a number of interactions with other substances such as with alcohol etc..Tolerance is generally good.

Glucagon ($C_{29}H_{41}N_9O_{10}$)

This hormone is produced by the pancreas instructing the liver to convert *glycogen* to *glucose* in order to raise the concentration of glucose in the blood. Also produced in the stomach.

Glucocorticoids (-)

Chemical formula depends on the particular chemical. These are *Cholesterol* based steroids. – one example is *Cortisol* produced by the adrenal glands. They increase the production of sugar by the liver and suppress proteins that produce imflamation. They are produced synthetically to treat autoimmune disease (all cause excessive imflamation of tissues) and replace *Cortisol* if necessary. They have a number of possible side effects.

Glucose ($C_6H_{12}O_6$)

A carbohydrate which breaks down to single (monosaccharide) or double (disaccharide) sugars, which are mainly glucose. Through further metabolic processess it results in the production of ATP. *Glucose* is stored in the body as glycogen in muscles, liver and fat. It is also important in the body synthesis of *Vit C*. Medical conditions such as diabetes may result, due to disruption of the control of glucose levels in the body.

Glutamate ($C_5H_9NO_4$)

A neurotransmitter effectiing certain areas of the brain. Should it overstimulate the brain it is referred to as an 'exitotoxin' and may cause neuro degeneration which results in medical conditions such as *fibromyalgia* or alzheimer's. GABA (gamma-amino-n-butyric acid) is another neurotransmitter which has the opposite function to glutamate, counteracting varying levels of glutamate in the brain.

Guanine ($C_5H_5N_5O$)

A building block of *DNA* and *RNA*. It is the base pair with *Cystosine*. (See p.78 and 79 of book).

H

Halogenated Hydrocarbons (-)

These are HC's that contain halogen atoms within their structure such as those of *Bromine*, chlorine and fluorine. They can be generated in forest fires and incineration of waste. Generally produced synthetically. CFC's are one example. Halogenated organic solvents are health and environmental hazards – some carcinogenic. Halogenated Hydrocarbons have many industrial and commerical uses.

Herbicides (-)

This is a pesticide that falls under the class of herbicides which is manufactured either (a) specifically to kill particular species of weeds and not to effect other plants or to be (b) non-specific for site clearings. Others may be manufactured simple to control growth rather than kill unwanted plants. Paraquat is an example of a non-specific type. They may be incorporated into the soil before planting. Residual time may be short or long, and depending on solubility of the herbicides may leach to unerground water. Occupational exposure by skin contact, inhallation and accidental ingestion or poor hygiene. Resistance to herbicides may occur.

Hexane (C_6H_{14})

A colourless highly flammable substance. Explosive in air. Irritant to eyes and causes dizziness if inhaled. Made from crude oil and present in petrol. Absobed by skin and lung tissue. Used in shoe glues, leather products, degreasing and as a solvent in medical laboratories (chromatography). Replaced by n-hexane due to its long term toxicity. (See also *n-hexane* p. 315).

Hexavalent Chromium (CrVI)

A chemical compound that contains the metallic element Chromium and has six electrons. It is the more toxic of all the *Chromium* compounds. It is used as an alloy with steel and other metals (eg: stainless steel) and paints (as *Chromates*) to inhibit corrosion. Occupational exposure is via inhallation of the vapour as in electroplating or welding, brazing, skin contact, as well as sanding and grinding. Carcinogenic. Effects the nasal passages (ulceration of nasal septa) lungs (asthma and cancer), stomach (ulcers and perforation of stomach) and skin (dermatitis). CrVI is strictly regulated.

Hydrochloric Acid (HCl)

This is Hydrogen Chloride. This gas forms Hydrochoric acid in solution with water. The fumes from the gas in contact with moisture in the air therefore produce hydrocloric acid. Used in the semiconductor and textile industries.

Very corrosive in contact with skin, eyes, and all of the respiratory system. May cause death from pulmonary oedema.

Hormones **(-)**

The endocrine glands produce a large number of chemicals that are transported in the blood circulatory system or via ducts act directly to regulate various body physiolocial functions, called 'Hormones'. They act as signalling molecules for communication between cells /organs which then result in the required response from that/those cells or organs. Examples are the effect they have on levels of blood sugar or calcium. Some are water and others fat soluble.

Hydrazine **(N_2H_4)**

Flammable liquid and smells like *Ammonia*. In anhydrous form it is very toxic.Used as fuel for thrusters in space shuttles but attemps to replace it with alternatives are being made. Very corrosive and effects many body organs.

Hydrocarbons **(HC)**

Organic **c**hemicals which consist only of Hydrogen and Carbon. If the carbons are arranged in the form of a ring then they are designated as aromatic H.C. If in the form of a chain or branches then referred to as Aliphatic H.C. When a hydrogen atom in the aromatic group is substituted by a halogen theyu are refered to as halogenated HC. These are the most toxic of the H.C.'s. H.C.'s may be saturated which only have single bonds or unsaturated which have double or triple bonds. Most occur naturally in crude oil. They may be solid *(bitumen)*, liquid (propane) or gas (methane). Most are highly flammable and some like benzene are carcinogenic. During combustion produce CO which is Toxic. Hightly reactive with Fluorine compounds. H.C. mainly affect the lungs causing pnuemonitis but they also affect the acns, liver and kidney and blood.

Hydrogen **(H_2)**

The lightest gas and most abundent element in the Universe. Exists mainly as water. It has 3 isotopes, one of which is Deutrium (^2H) referred to as 'heavy water' which is used to cool nuclear reactors. Hydrogen is used in the production of ammonia for fertilizer, but has other uses. Highly flammable. Reacts with *Chlorine* and Fluorine to produce dangerous and toxic acids.

Hydrogen Halides **(HX)**

H = Hydrogen and **X** = one of the Halides. A 'halide' is a Hydrogen attached to one of the Halogens [Cl.,Br.,Fl.,I., and Astatine (At)], which are negatively charged ions. Hydrogen Halides are colourless gases that dissolve in water. This reaction gives off strong acids, except for the formation of Hydrogen fluoride which is a weak acid and different to the others due to its hydrogen bonding. Used in solder paste, high pressure sodium street lamps. Health effects depend on which of the halides are involved.

Hydrogenated Hydrocarbons (-)

Hydrogenation is a chemical reaction requiring an catalyist like Nickel plus hydrogen ions to the hydrocarbons to remove the double bond between carbon atoms. The amount of Hydrodgen introduced controls the reaction. This converts unsaturated fats that have a double bond to saturated fats that end up with a single bond. This reaction results in liquid fats being altered to solid fats (eg: margarine).

Hydrogen Peroxide **(H_2O_2)**

A weak acid that is an oxidizing agent. Unstable. Can combust with organic matrial. Used in textile and paper bleaching and manufacture of foam rubber. This is a hazardous substance to use and can be fatal by ingestion. Irritant to skin, eyes and lungs even at low dilution.

Hydrogen sulphide **(H_2S)**

An extremely toxic gas. Heavier than air. Occurs in crude petroleum and natural gas, in around sewage treatment plants, tanneries and is broken down by bacteria in food waste in the intestine. Occupational exposure is by inhallation causing irritation to the eyes and respiratory system including pulmonary oedema and asphyxia. Effects may be very rapid. H_2S is also available in liquid form.

Hydrogen Cyanide **(HCN)**

A colourless gas or liquid. Used in the production of synthetic fibres, plastics, dyes and in other production processes. Extreemly hazardous and rapidly lethal. Exposure through food, smoking, via inhallation and skin. Converted to thiocyanate in the body if in low concentration. Affects oxygen uptake in the lungs resulting in asphxia, loss of consciousness and possibly death. Antidotes available. Easily ignited and explosive in air.

Hypochlorous acid **(HOCl)**

Formed when *Chlorine* is dissolved in water. HCl is also formed at the same time. Used as a disinfectant, and a cleanser in cosmetics. When added to salts like Na or Ca it forms Sodium or Calcium Hypochlorite which is used in bleach. It can react with a number of other chemical molecules in the body. It is a strong oxidizer and may form explosive mixtures.

I

Inorganic Mercury **(Hg)**

See Mercury p. 312 Appendix IV.

Insulin **(-)**

A Peptide that is involved in the metabolism /absorption of glucose, and promotes fat storage and amino acid in cells. It is a hormone produced by the pancreas. If the production stops diabetes type 1 results. If person becomes insulin resistant ie. c*annot use the insulin to* *mainatine blood glucose levels,* then type 2 diabetes results.

Iron **(Fe)**

Common and an abundant element the Oxides easily form rust. There are about 4 gm in humans and these needed to bind with haem to form haemoglobin and this transports oxygen to tissues. Mixed with other metals and carbon produces steel. Toxicity is genetic or acquired. Can be chelated from the body if levels are excessive.

Isoflavones **($C_{15}H_{10}O_2$)**

These are easily abosrbed *Polyphenols*. Structurally similar to oestrogens, giving them ability to mimic them. Found in soya foods and the plant red clover. Several possible health benefits such as reduction of prostate enlargement, osteoporosis, cancer risks, reduction of *cholesterol* and menopause symptoms.

Isocyanates **(- NHO)**

Organic compounds that are linked to a cynanide group. Powerful irritants to lungs, gastrointestinal membranes and skin. Exposed workers can become sensitized and then develop asthma. Used in the Manufacture of foams, paint, varnishes and construction, as well as polyurethane sprays that have many applications.The most used compounds are TDI, MDI and HDI.

Isopropyl Acetate **($C_5H_{10}O_2$)**

A clear liquid solvent. vapour heavier than air. Irritant to skin and eyes.

Isopropyl alcohol **(C_3H_8O)**

A colourless flammable liquid. Very unstable and reactive. Can explode if it forms organic peroxides (compounds that have a carbon in combination with an oxygen combined with another oxygen by a single bond - Hydrogen peroxide is n example). Used in industry as a solvent, as well as in pharmaceuticals and health care products such as rubbing alcohol and preservatives. Absorbed by skin, inhallation and G.I.T.

J

K

L

Lactase **($C_{12}H_{22}O_{11}$)**

An Enzyme (two sugars linked by an atom of oxygen). Abundant in milk, whey, canned fruit, baked items and pharmaceutical tablets.

Lead **(Pb)**

Not radioactive. Stable and heavy element. It has 3 of 4 isotopes that decay to Uranium 235 and 238, and Thorium 232. Very toxic. Stored in bones. Damages the nervous system and the kidneys heart and immune system. Exposure is via Inhalation, ingestion, skin and eye contact.

Lindane **($C_6H_6Cl_6$)**

Insecticide and pharmaceutical used in the treatment of lice and scabes. A neurotoxin and *Endocrine disruptor*. Effects liver and kidneys. A regulated substance and banned in agriculture and garden use due to concern of the occurance of breast cancer as Lindane is very volatile. Occupational hazard for those who work with Lindane.

Lysine **($C_6H_{14}N_2O_2$)**

An essential amino acid. Obtained from food (poultry, pork and beef, cod, sardines, eggs and parmesian cheese) as it is not made by the body. Helps in calcium absorption and conversion of fatty acid into energy. Believed to be antiviral and used in cold sores creams.

M

Magnesium (Mg)

Occurs in combination with other metals such as O_2, and Ca. It is Abundant in seawater and the Earth's crust as MgO. Present in many foods such as spinach and foods containing fibre as well as in the body in bones, blood and soft tissues. Absorption from the gut about 30-40% but high levels of Zn and some medications interfere with the absorbtion of Mg. Important for *enzymes*, *DNA*, *RNA* and nerve conduction. It effects the concentration of *Vit. D* and the parathyroid hormone. Industrially used in fertilizers, fireworks, alloys and batteries. Highly flammable and expolsive. The burning of Mg as in welding produces UV radiation. Water should not be used to extinguish fires.

Manganese (Mn)

A hard but brittle metal, found with other minerals. Found in drinking water, bones, as well as in liver, kidney, some in brain and as nodules in deep ocean floors. Used in alloys (stainless steel), Pigments, dry cell batteries, Occupational exposure from dusts and fumes. Toxic to nervous system and liver at high exposure levels. Excreted by the bile.

Malathione ($C_{10}H_{19}O_6PS_2$)

A widely used Insecticide – Once sprayed residue may remain in soil, on plants and other surfaces from a few days, to weeks before being broken down by sunlight, water and bacteria. Forms 'malaoxon' a toxic compound with air. Unlikely to get into underground water as it is easily broken down by water and bacteria. Slower breakdown on other surfaces. Exposure by skin contact, inhallation and ingestion. Mainly effects CNS. Overexposure occurs if workers return to sprayed areas/fields before one week or so. Transported to other areas by winds.

Metabolized in the liver and excreted in the urine.

Mercury **(Hg)**

Derived from the ore Cinnabar (Mercury Sulphide). Its use in thermometers and blood pressure units (sphygmomanometers) but has been substituted by alcohol, other substances, and mechanical devices, although many are still available and in use especially for high temperature thermometers. Other uses include mercury vapour lamps, mirrors in telescopes and some cosmetic creams. *Methyl mercury* is found in some fish and shell fish and is highly toxic. Exposure via skin contact, inhallation and results in acute and chronic toxicity. Must be handled with care.

Methacrylate **($C_5H_8O_2$)**

A volatile synthetic chemical used in Acrylic plastic manufacture. Also used in adhesives, sealants, floor polish. Skin irritant and may induce sensitization and asthma.

Methane **(CH_4)**

Colourles odourless gas. Found in natural gas, fuel and in human intestines and breath. Lighter than air and explosive in high temperatures.

Methanol **(CH_3OH)**

A constituent of many common organic Solvents and incorrectly prepared alcohol by amatures. Causes metabolic acidosis. It is toxic. Damages optic disc and retina, causes sinus tacchycardia and results in other ECG changes as well as muscle spasm. Formic Acid is the toxic metabolite.

Methaemoglobin **(-)**

The inability of the red blood cell to release oxygen to the body tissues results in Methaemoglobin giving rise to the condition of Methaemogobinaemia. The oxygen is carried in the red blood cell haemoglobin by the Ferrous iron (Fe_2). When the Ferrous iron is oxidized to the Ferric iron (Fe_3) haemoglobin is converted to methaemoglobin. This is caused by irregularities with the enzymes due to excessive abosorption of nitrates, a metabolic disorder or a hereditary gene.

Methionine ($C_5H_{11}NO_2S$)

An essential amino acid. Not produced by the body and must be obtained from food (cereals, eggs, fish, meats). Excess by suplimentation may be hazardous. Low levels have been linked to the loss of hair colour due to excess of hydrogen peroxide in the hair follicle.

Methylbutyl Ether ($C_5H_{12}O$)

Methyl Tertiary Butyl Ether – MTBE.

$(CH_3)_3COCH_3$. Mnfc**:** From crude oil in a reaction between Isobylene (an isomer of Butylene, a flammable gas) and *Methanol* (solvent). Has been used to reduced engine knock but now substituted by *Ethanol*, though still in use in some countries, as well as a solvent in industry or to dissolve gallstones in medicine. It is very water soluble and has been known to leach from tanks into underground water. Volatile and flammable. Occupational exposure through handling, contact with skin and inhallation. Irritant to nose and throat. Causes headache, nausea, Symptoms may occur some time after exposure. Not compatablie with oxidizing agent and strong acids or bases. Training employees is essential to handle this substance.

Methoxyethanol ($C_3H_8O_2$)

A liquid solvent for varnishes and resins and in deicing solutions. Present in some cleaning products. Exposure via skin contact and inhallation. Chronic exposure results in toxicity to bone effecting the blood forming cells and the testis causing a low sperm count.

Methyl Butyl Ketone (MBK)

($C_6H_{12}O$). Mnfc: from *Acetone* - A ketone that is found as a solvent in paints, varnishes and resins, and the extraction of precious metals.

Incompatable with oxidizing agents, and strong bases. Occupational exposure from skin contact and inhallation. Irritant to eyes, nose and throat. May damage liver and kidney. A Flammable liquid and fire hazard.

Methyl Ethyl Ketone (MEK)

Also refered to as Ethyl Methyl Ketone and Methyl Acetate. A solvent. Found naturally and in many foods such as chicken and honey. Used in adhesives, polymers and surface coatings. Low toxicity.

Methylated spirits (C_2H_5OH)

Mainly consists of Methyl Alcohol *(Ethanol)* but it also contains *Methanol* and other substances like MEK. Methanol is very toxic and small amounts can cause blindness. Methylated spirits are solvents and should not be confused with what is refered to as 'white spirit' which is made from parrafin.

Methyl Isocyanate (C_2H_3NO)

A colourless flammable liquid used in the production of carbamate pesticides, adhesives and rubber. Toxic by skin contact, inhallation and ingestion at low doses. The Bhopal disaster is an excellent example of it toxicity effects.

Methylmercury (CH_3HgCH_3)

Accumulates in fish and when bacteria in sediments react with elemental mercury in river or lake water and oceans. Once in the food chain it may cause methylmercury poisoning. Used in latex paints, batteries, and PVC. Effects the CNS and causes irreversible damge to the brain.

Methyl Salicylate ($C_8H_8O_3$)

Produce synthetically and naturally by plants probably as a defence mechanism. Toxic when pure or absorbed in repeated large amounts by ointment application to skin or accidental ingestion. Used as a muscle pain reliever, an antiseptic and in the printing industry to restore rubber rollers. Found also in mints in very small amount. In the body it converts to salycilic acid and its derivate salyicilates to which some individuals are intolerant.

Mineralocorticoids **(-)**

This is one of the 3 types (Glucosteroids, Mineralocorticoids and Androgens) of the steroid hormones (ie: Corticoids) produced by the kidney cortex. Production is triggered by *ACTH* from the anterior pitutary in the brain. Mineralocorticoids effects mineral metabloism, Aldosterone is the main mineralcorticoid in the body and acts on the kidney to reabsorb sodium and water to maintain the body's blood volume and pressure. It also effects the sweat glands to reduce Na loss.

N

Naphthalene **($C_{10}H_8$)**

Mothballs. These are **P**olycyclic **A**romatic **H**ydrocarbons [Benzene rings attached to each other (*fused*) because they share two or more atoms]. Found in coal tar and purified from petroleum. Uses as a fumigant and in the production of phthalic anhydride in the preparation of plastizers such as PVC., and Azo dyes. Volitile, and toxic via inhallation and ingestion. May cause haemolytic aneamia and damage to neurological and liver systems. IARC classifies it as a Group B. carcinogen.

n-Hexane **(C_6H_{14})**

A constituent of petrol. Used as a Solvent, in shoe glues, degreasing and extraction of oils. Flammable with oxidizing agents. Exposure irritant to skin, eyes, respiratory and neurological nervous systems.

Nickel **(Ni)**

A mined soft metal element. Good electrical conductor and has some magnetic properties. Reasonably resistant to corrosion. Used mainly as an alloy. Many applications such as batteries, propellers, electrolyses, jewelry, etc. Occupational exposure from refining, dust and fumes, welding and electroplating. Has caused skin allergy, pneumonitis and lung cancer as well as oxidative stress. Present in dried tea leaves and vegetables depending on soil content. IARC classified as Group 2 carcinogen.

Nicotine		**($C_{10}H_{14}N_2$)** This is an <u>*alkaloid*</u> (-) found in tobacco leaves. Present in cigarette smoke. Addictive. Occupational exposure mainly due to skin contact with wet tobacco leaves and inhallation of tobacco smoke. Toxic if ingested. Penentrates the blood brain barrier. Nicotine has many interactions on body functions. Metabolized in the liver and has several metabolites that can be found in the urine such as Cotinine.
Nitriles	**(-)**	Organic compounds, solids or liqids where the organic group is attached to a cyano group i.e: **−C≡N** group. An example is <u>*Acrylonitrile*</u>. They are important in the formation of other chemicals and as solvents. They are toxic products of combustion as they release <u>*Hydrogen cyanide*</u> and <u>*CO*</u>.
Nitrite	**(NO_2^-)**	A salt or ester containing the group NO_2. *(**Salt** referes to an ionic compound which has a cation (positive charged ion which is the metal part) an anion (negative charged ion which is a non-metal, eg: sodium chloride. The total charge of the compound is Zero -.An '**Ester**' results by the reaction of an acid with an alcohol and the release of a molecule of water in the process, eg: ethyl acetate).* Important in the food industry as a preservative and especially to avoid botulism. An example of a preservative is sodium nitrite. It has many industrial uses, such as the perfume and polymer industries, as solvents, etc.

Nitrate **(NO_3^-)**

Inorganic water soluble compound which occurs naturally in soil, found in vegetables, processed, food and drinking water. By ingestion converted into *Nitrites* (NO_2). Also converts to (1) toxic Nitric oxide gas through the loss of an oxygen, but is important in physiological body functions (signalling, mitrochondrial production etc), and (2) also converts to *nitrosamines* in acid pH of stomach which are carcinogenic substances. Industrial uses include fertilizers, glass, preservatives and explosives because they generate *O_3*, once heated. Indusdrial exposure is by inhalation.

Nitrogen **(N_2)**

Inert gas and can be in liquid form. It is present in the atmosphere (78.082% by volume). Found in all organisms mostly as proteins as it is essential in building aminoacids. Replaces O_2 and therfore hazardous particularly in confined spaces. It is absorbed in the blood under conditions of rapid decompression. Liquid nitrogen is used in the removal of skin growths can cause burns due to rapid freezing of the skin. Used in the semiconductor, welding and oil industries.

Nitrobenzene **($C_6H_5NO_2$)**

Produced from *Benzene* to make *Aniline* ($C_6H_5NH_2$) used in the production of polyurethanes and other materials such as rubber and dyes etc. Nitrobenzene is very toxic with exposure is via inhallation, skin and ingestion. Causes liver, spleen and kidney damage, nausea, vomiting. headache, visual disturbances and cyanosis. IARC classfied as a Group 2B carcinogen.

Nitrogen Oxides **(NO_X)**

The 'x' refers to both NO (nitric oxides) and NO_2. being present. Results from combustion of fuels – N combines with oxygen to form NO which is not generally hazardous but the formation of

NO_2 may cause respirtory problems such as bronchitis, and asthma. NO_x's react in the air with water vapour, ammonia and other compounds forming fine respirable particles. In sunlight VOC's and NO_x's react forming *Ozone* (O_3) resulting in smog and to which many individuals are vulnerable. In combination with Sulphur dioxide in the air, acid rain (a reaction in which Nitric acid or Sulphuric acid are formed) results causng transboundary pollution.

Nitroglycerol **($C_2H_4N_2O_6$)** Also refered to as GLYCEROL TRINITRATE. Developed by Alfred Nobel "as a blasting explosive". Very dangerous to transport. Used in Medicine to treat angina. Dr. William Mussel discovered its medical value in 1888. EXP: skin, lungs and eyes. PEL (OSHA) IS) is 0.2 ppm = 2 mg/m 3.

Nitrosamines **(H_2N_2O)** These are NO groups (Nitroso) attached to an amine (molecules in which the hydrogen atoms in *NH_3* have been replaced with an organic group, ie: a hydrocarbon radical (a radical is a molecule that has an unpaired electron). *Note that Hydrocarbons only contain carbon and hydrogen. Methane* (CH_4) is one example of a hydrocarbon. Used in production of cosmetics and pesticides. Frying foods at high temperatures may produce nitrosamines. They are also produced in the stomach and small intestine. Carcinogenic in animals and probable carcinogens in humans.

Nor-Adrenaline **($C_9H_{13}NO_3$)** Also referred to as **NOR-EPINEPHRINE.** Produced by the adrenaline glands and the pons in the brain. In response to stress (danger) the body levels rise. These levels are low at night and higher during the day. It raises the heart rate, blood pressure and blood glucose to deal with the situation and makes the individual more alert and attentive to what is going on. It is an important neurotransmitter.

Nor-Epinephrine **(-)** See Nor-adrenaline above p. 318..

O

Organic Compound

Compounds that contain Carbon and Hydrogen but do sometimes contain other elements like nitrogen.

Opium **(-)**

A mixture of natural *alkaloids*. A white liquid (latex) which coagulates in contact with air and obtained from the opium poppy seed pod. It contains the alkaloid morphine and drugs that have an analgesic effect eg: coedine. The reader is refered to United Nations Single Convention on Narcotic drugs.

Organo Bromine Compounds **(-)**

Compounds that contain Carbon bonded to *Bromine*. Produced industrially but large numbers exist in nature are formed by marine organisims. One example of an organobromine compound is *Polybrominated diphenyl ether* (PBDE) which is used as a flame retardent in plastics, electronics and textiles. Another is *PCB* now widley banned. Production waste is regulated and some compounds are more toxic than others.

Organo Chlorines **(-)**

Compounds that contain Carbon bonded to *Chlorine*. Many of the compounds exist and some like pesticide and solvents have been banned in Europe. Others phased out such as DDT. Not all are toxic. Skin, respiratory system, CNS, kidneys, liver and Blood can be effected.

Organic Mercury **(C-Hg)**

The 'C referes to having a least one carbon atom attached to the Mercury. Toxic. An example is *Methylmercury* which is highly lipophilic and accumulates in the myelin sheats that protect the brain and nerves in the body reaching these through eating fish as it bioaccumulates in fish muscle tissue. It also binds to *Cystein* and mimicks *Methionine* in the body.

Organphosphorus Esters (C-P)

The ‘C referes to having a least one carbon atom attached to the *Phosphorous*. An ester is recognized by the suffix ‘oate’. One example is Methyl Butanate Organophosphorus which is an organic compound that contains an ester of *Phosphorus*. Insecticides, but has effect on enzyme acetylcholinesterase and inhibits its action. They degrade rapidly in sunlight. Acute and chronic toxicity.

Oganophosphorus Insecticide

Effectively used for insect and mosquito control. Compounds containing phosphorus that are cholinesterase inhibitors. This inhibition may last some time. Very toxic by skin, inhallation and ingestion. Affects central and peripheral nervous, muscular, respiratory, cardiac and most organ systems. The reader is refered to the IPCS (WHO) documents due to the importance of Organo Posphorous Pesticides (OPP’s).

Oxides of Nitrogen (NO_x)

A general term for ***Nitric Oxide*** (NO) & Nitrogen Dioxide (NO_2). An Emmision Polluter from automobiles. Industrial and forest fires. These gases react to form Smog in sunlight. Irritant to nose, throat, eyes, the respiratory tract and lungs. May cause premature death.

Ozone (O_3)

Formed by action of short wave ultraviolet light on O_2. in the Stratosphere, and any electrical discharges in the atmosphere. O_3 layer lies 10 to 50 km above the earth. Reacts with HC’s and NO_x when formed by sunlight on automobile emissions. O_3 is a strong oxidizing agent and irritant to respirtatory system and the eyes.

P

PAH/s **(-)**

Polyaromatic Hydrocarbons. This is a large goup of chemicals that are released from volcanic erruption, forest fires, vehicle exhaust, asphalt, burning coal or organic materials and also made synthetically. Persistant organic pollutants. Used in plastics, dyes and pesticides. Occupational exposure wide and varied and include oil refineries, mining, foundries, metal works, wood preservations etc. Some are considered carciinogenic.

Parabens **(more than one)**

An Ester of Hydrobenzoic Acid. Preservative, Bactericial and fungicidal. Uses: Cosmetics, food additives, shampos and pharmaceuticals. May cause skin dermatitis in those who are allergic to Parabens. Insufficent evidence of other toxicity.

Parathion **($C_{10}H_{14}NO_5PS$)**

An *Organophosphorus insecticide* and acaricide. (It is a cholinersterase inhibitor. Extreemly toxic. Industrial exposure during its manufacture. Other exposure includes air drift from agricultural spraying or ingestion from contaminated (residue) on food, contact with eyes, skin and inhallation. Otherwise rather limited information available regarding toxicity.

PCBs **($C_{12}H_{10}$-xClx)**

Polychlorinated Biphenyls. These are organic chemicals insoluble in water but very soluble in fats. They resist heat, acids and bases and persist in the environment although eventually degrade. They were used in electrical equipment dumped as waste and contaminated the soil, water and the atmosphere. Much of this equipment is still around. PCB's are found in sediments, fish, meat and milk. They are stored in fatty tissue and the liver in humans. IARC classification (2013). Group 1. They are *Endocrine disruptors* and neurotoxic.

Pentachlorophenol **(C_6HCl_5O)**

An Organochlorine compound.
Use: Herbicide and a dinsinfectant, Antifoulant and wood preservative. EXP: by inhallation and skin contact. Toxic to blood, liver, kidney, and nervous system. It is quickly absorbed in GIT., with good elimination in urine. It's half life is 20-50 hours.

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Pepsin **(-)**

Digestive enzyme produced in the stomach. Breaks down the food proteins to peptides and amino-acids for absorption in G.I.T.

Peptide **(-)**

Chains of amino acids that make up a protein. Different peptides have different types of activity. All have the ability of cell communication. They are susceptible to breakdown by enzymes.

Perfluorinated **(-)**

This referes to chemicals where hydrogen has be replaced by fluorine. Most perfluorinated compounds are synthetic. Some fluorocarbons are considered hazardous to the environment and tend to bioaccumulate. Fluorosurfacants ae used in waterproofing textiles.

Perfloroalkyl Acid

($C_{12}H_8F_{17}NO_4S$) or PFAA.
Several compounds. Those with longer chains are more persistant, ie. years. Exposure unclear but dusts inhaled and food are the apparent pathways. Detected in blood of those near manufacture of PFAA's. Found also in soil. The compounds PFOS & PFOA cause cancer, endocrine disruption and effect the immune system.

Perfluorooctanic Acid (PFOA) **($C_8H_{15}O_2$).** This is an strong acid that persists in the environment. It has been shown to be toxic and carcinogenic to workers in chemical plants producing it, but it has been identified in industrial wastes, ground water, soil, air, food and house dust. The environmental levels were reported as too low to cause health problems.

Perianal region The area between the scrotum and the annus in the male and the vulva and annus in the female.

Permethrin **($C_{21}H_{20}$)** An insecticide. Can be sprayed on to mosquito nets and used to treat lice and scabies.

Pheromone **(-)** Molecules that become airborne and Transmit messages to members of the Same species. A means of communication, distinguishing between other members of society, attraction and/or posibly as defence or attack mechanisim in some insects.

Phenol **(C_6H_5OH)** **Carbolic acid.** A volatile crytalline solid. Used as a precursor for parmaceutical, plastics and herbicides. It is a component of many products. Absorbed by the skin, mucous membranes and lungs. Corrosive and toxic. Can cause burns, oedema of the lungs and central nervous system effects. Long term exposure affects liver and kidneys.

Phosgene **($COCl_2$)** Very toxic gas that appears yellow. Used in the production of isocyanates and polycarbonates. Also found in laboratories. Inhallation results in suffocation.

Phosphate **($(PO_4)^{-3}$)** Salt of Phophoric Acid. Important in metabolism (added or removed from protein in cells) and for bones and teeth. $^{-3}$ refers to the phosphate ion charge.

Phthalates	**($C_8H_4O_4$)**	Chemicals added to plastics to make them more flexible. Wide range of uses (packaging materials, cooking containers, pharaceuticals, cosmetics, electronics, etc.). EXP: From food, air and skin. Believed to cause allergies, asthma and act as endocrine disruptors. Industies being encouraged to use alternatives although these are more expensive to use. Restricted use in toys in Europe and USA and possibly some other countries.
Pinoline	**($C_{12}H_{14}N_2O$)**	A poweful antioxidant. Believed to be produced in the pineal body in the brain. Promotes brain development.
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Platinum	**(Pt)**	Rare scarce precious heavy metal. Uses: Dentistry, and Electrical contacts as well as catalytic converters.
Plutonium	**(Pu)**	**Pu 224 -** Radioactive chemical element. Has 5 isotopes. Used in the atom bomb. Stored in Bones. Very long half life. Decays into Uranium 224. Used in nucelar plants for energy production. Hazardoous to handle.
Polyalphaolefin/s	**(-)**	Colourless high viscoisty, non toxic hydraulic fluids/lubricants.
Polyalkaline Glycols	**(-)**	Synthetic lubricants used in hydraulic fluids, industrial worm gears to reduce friction and relatively more recently in gas turbine and tunel boring equipment. Irritant to skin. Exposue also by inhalation and G.IT. Midly toxic. *(see article by Dr. Martin R. Greaves on Polyalkaline Glycols, http://www.dow.com/ucon/pdfs/greaves_stle.pdf*

Polyphenols (-)

Also referred to as Phenolics. Present in edible plants such as tea, as well as in red wine, olive oil, capers, some dried herbs such as sage and rosemary, berries such as blackcurrent, strawberries, blueberries. They are one of the 3 main groups of antioxidants (these protect cells from free radicals), which are themselves then grouped into 4 others and Phenolics are one of these groups. The colour in fruit is due to Polyphenols. They are fat soluble and importantly reduce the clumping of platelets as one of the activities of antioxidents.

Polypeptides (-)

(See peptides pp. 77 of Book & 263 Appendix III). Peptides are stong bonds, difficult to break and stable. They are only found in proteins and maintain their shape. Polypeptides are peptides that that bind more than 50 amino acids. A protein has more than 50 amino acids.

Polybrominated Diphenyl Ethers

$C_{12}H(9\text{-}O)Br(1\text{-}1O)O$. These are compounds in which carbon is bonded to bromine atoms. The number and position of the bromines may vary with the compound which are produced synthetically. They are found in air, soil, and water in which they are not soluble. They adhere to particlate matter and sediment in water. Also present in waste recyling plants and waste sites. Occupational exposure is via inhallation and ingestion, on manufcturing plants, and waste areas, but include confined spaces where material containing these products may be present. Sunlight degrades PBDE's seperating the bromine atoms from the chemical compound. Considered *Endocrine disrupters.*

Polyethylene Terephthalate (-)

A strong synthetic fibre used in synthetic plastic bottles for strength and thickness packaging and in materials such as wool, cotton and rayon fabrics. May leach *Phthalates* and *Antimony*. Considered an *Endocrine disruptor*.

Polychlorinated Biphenyls (-)

PCB's. Synthetic organic chemicals which are persistent in the environment. Soluble in fats. Now banned or restricted in most countries. Wide and varied health effects. IARC classificed as Group 1 carciinogen.

Polychlorinated Dioxin/s (-)

See *DIOXIN* p.291. This is a large family of chemical compounds which depend on the number of chlorine atoms in the compound.

Polyurethanes (-)

A varied number of thermoplastic polymers containing isocyanide. Used in seating, packaging and many other uses. Ignites exposed to flames. May be teated with flame retardents also hazardous in themselves. Spraying may result in sensitization of the induvidual at work.

Potassium (K)

A radionuclide that is unstable. It is both beneficial and harmful. Essential for body cells, neurotransmission, heart and muscle. Industrial uses include leather, fertilizers, textiles, fireworks, inks, food preservatives and laboratories.

Properdin

A gamma globulin protein. Assists in the processes of immune system, phagotycotsis and inflamation.

PVC ( )

Polyvinylchloride. A polymer of vinylchloride that may be rigid (melamine resin) or flexible (polyethylene). PVC is hazardous especially if it contains chlorine and burnt which releases *dioxin*. PVC contains plastisizers and is found almost everywhere.

Q

R

Resins **($C_{19}H_{29}COOH$)**

Mostly mixtures of organic compounds, but natural to plants. Amber is fossilized resin. The resin <u>*Bisphenol A*</u> *diglycidyl ether plus a hardener* produces an epoxy glue. Used in plastics, varnishes and the bonding of many materials, Electrical winding and as fillers. Exposure is by inhalation of dusts particles fumes and Skin contact. May cause, irritation, sensitisation or allergy.

Rickettsiae **(-)**

A small (0.3 µm x 0.1 µm) Bacteria transmitted from faeces of lice, & fleas, and the bites of mites, and mammals. Consider the infected host for geographic distribution. Cause spotted fevers and typhus (3types). Vaccines are available for some. Others are susceptible to the Broad Spectrum antibiotics. Prevent exposure to hosts.

S

Salicylic Acid **($C_7H_6O_3$)**

Metabolite of Acetylsalicilic Acid. ie. Aspirin. Salicylic Acid salts are **Salicilates**. Salicylic Acid is an analgesic. Has many uses. Present in ripe Fruits and vegetables, some herebs, mushrooms, olives, almonds, tomatoes, and peanuts.

Salt in chemistry **(-)**

SALT referes to an ionic compound which has a cation (positive charged ion which is the metal part) an anion (negative charged ion which is a non-metal. The total charge of the compound is Zero.). <u>*NaCl*</u> is an example.

Secondary Amines **(-)**

See <u>*Amine*</u> before reading this. There are 3 types of amines which are derivates of NH_3. Primary, secondary and tertiary. The secondary amine is one in which two of the hydrogen groups in the <u>*NH_3*</u> is replaced by a hydrocarbon group.

Silica **(SiO_2)**

An Element, chemically oxide of silicone. Insoluble in H_2O but soluble forms exist ie: *Salicilates*. Deficiency can cause health problems. silica dust leads to Silicosis, and sometimes cancer. *Note* that *Silicone dioxide* ie: Quartz, is mined used as sand for casting in foundries, in glass, ceramics, electronics, etc. Silica is also used as an additive in foods and pharmecuticals.

Silicates **(SiO_4)**

An abundant mineral. Silicon and oxygen that combines with metals such as Mg, Fe or Al etc. form Silicates. These are salts of Silicates. Water flowing over natural mineral deposits will dissolve some silicates thus affecting water systems and the ecosystems. Silicates have innumerable useds (glass, ceramincs etc).

Sodium **(Na)**

Found in many minerals and a very soluble substance. Easily oxidized and of immense industrial, commercial and human metabolic importance (influences blood pressure and osmotic equilibrium). It forms alloys with other metals. Used as a food preservative.

Sodium Chloride **(NaCl)**

Common salt. Widely used to de-ice roadways, as a Preservative, and synthesis of other chemicals, textiles, pulp and paper, rubber and water softening. Salt is Hygroscopic.

Sodium Hexafluoroaluminate

(NA_3AlF_6). A rare mineral called CYROLITE. Produced synthetically and with Aluminium trifluoride is used as a solvent in Aluminium processing of Aluminium oxides to metalic aluminium by electrolysis. Corrosive to skin and eyes. Toxic by ingestion and harmful by inhallation. Not flammable.

Sodium Hydroxide **(NaOH)**

Caustic Soda. Crystalline solid which if dissolved in water releases heat and can result in combustion. Present in drain and oven cleaners and used in electroplating, bleaching, metal cleaning, and manufacture of paper, soap and dyes. A corrosive substance to eyes, skin, lungs and G.I.T.

Sodium Lauryl Sulphate (-)

A foaming agent and emulsifier. Found in detergents, soaps, toothpaste and shampoos. Toxicity due to contamination by 1,4 dioxane during production from coconuts. Irritant if concentration is more than 1%.

Strontium (Sr)

A natural element. Stable except as the synthetic isotope which is radioactive and found in nuclear fallout. Deposits in human bone. Used in glass manufacture and fireworks. Consideration is being given to the use of Strontium Ranelate being use in osteoporosis but its value is still uncertain. Calcium prevents its absorption and sensitivity reactions have occured.

Strontium Chromate ($SrCrO_4$)

A yellow powder or solid that is used in fireworks, as a colourant and in protective coatings because it is a corrosive substance. Toxic when heated due to the *Chromium* fumes.

Styrene (C_6H_5CH,CH_2)

Toxic. Used in the production of polystyrene plastics and other *polymers.* There are short term and long term health effects. IARC has classified styrene as Group 2B carcinogen.

Sulphuric Acid (H_2SO_4)

Very corrosive substance. Used in lead acid batteries, laboratories, cleaning agent, Synthesis of chemicals, wastewater treatment, fertilizers, detergents and many other applications. Exposure via Inhallation and skin contact. Handle with great care. It is present in acid rain.

Sulphur dioxide **(SO_2)**

Atmospheric pollutant from volcanic eruptions and the burning of fuels. Used as a preservative to which some people are sensitive resulting in difficult breathing. SO_2 has important biochemical /physiological effects in the body on fat, smooth muscle, and the cardio-vascular system.

T

Tetrachlorobenzene-p-dioxin

($C_{12}H_4Cl_4O_2$). TCDD. Produced as a result of the burning of organic material. A persistent pollutant. Regulated by the Seveso II Directive following the Seveso disaster in Italy when it was released from a manufacturing plant. IARC group 1 carcinogen.

2,3,7,8-tetrachlordibenzo-p-dioxin **(Agent Orange)**

A by product of incomplete combustion ie: incineration of wastes. A Herbicide. B2 carcinogen. Lung and stomach cancers in exposed workers. Used in research of chemical substances. EXP: meats, fish and dairy products.

Tetrachloroethylene **($Cl_2C=CCl_2$)**

PERC. A colourless liquid solvent. Used in drycleaning and as a paint stripper. IARC Group 2A carcinogen. Depresses the nervous system. At high temperatures (315°C = 599°F) oxidizes to *Phosgene* gas. Banned in some countries.

Thallium **(Tl)**

Mineral element found in *Lead, Copper* and Zinc in trace amounts. Has 25 isotopes. Soluble salts are extreemly toxic. Exposure by inhalation, skin, GIT and eye contact. Hazardous sources are, smelting, cement industry emission water. A possible carcinogen.

Tetrodotoxin ($C_{11}H_{17}N_3O_8$)

A neurotoxin found in some species of fish. Although toxicity varies between species this substance is extreemly toxic. No known antidote but activated charcoal may help. Following ingestion person is paralyzed but remains conscious till death, although some have recovered after 24 hours.

Tin (Sn)

Element occurs as SnO_2 (ie: Tin Dioxide). A metal which is extracted from ore. It has 10 isotopes. Used in tin plating, solder, and as alloy with other metals. Note tin dust may irritate skin eyes and lungs affect neurotransmission.

Titanium Dioxide (TiO_2)

A abundant ore. Metal element that can also be mined from other minerals. Used in paints, varnishes, inks, plastics, cosmetics, rubber and glass, and some food as colouring, (ie. E171). Also in sunscreens workers in TiO_2 prodcution are exposed to inhalation of dust especially ultra fine dust causing lung fibrosis. Group B carcinogen.

Thorium dioxide (ThO_2)

Radioactive material referred to as THORIANITE. Used in nuclear reactors, in TIG (Tungsten Inert gas) welding rods as a fuel in aircraft engines and ceramics. Emits alpha particles. Stored in bones, lungs and other organs. Also effects red blood cell formation in bones.

Thymine ($C_5H_6N_2$)

A Building block of *DNA* and *RNA*.

Toluene (C_7H_8)

METHYLBENZENE
An aromatic hydrocarbon. Used as precursor to *Benzene*, *Xylene* and other Synthetic chemicals. Solvent for paints, rubber, inks and adhesives. Less toxic than Benzene. Also present in Laboratories. EXP. Skin, GIT. and inhalation. CNS main target. Insufficient evidence of carcinogencity.

Tributyltin	**($C_{12}H_{28}Sn$)**	**TBT.** A blanket term used for compounds based on tin linked to a H.C. A Biocide in anti-fouling paint for boat hulls. Leaches and sediments to bottom. Toxic to marine organisms and up the food chain including humans. Has a two year half life.
Trichlorodiethyl (TCD		More accurately reads as **2,3,7,8, tetrachlordibenzo-p-dioxin.** This is a product of incomplete combustion of wood, industrial and domestic and waste. Can also be produced by bleaching processes in paper mills. Use: Chemical research. Found in air, soil, food and may leach from waste dumping areas into the sea. Acute and chronic exposure results in chloracne (acne which appears on the cheeks, behind the ear armpits and the groins) and cancer in various organs in the body.
Trichlorethylene	**(C_2HCl_3)**	Degreasing solvent. No longer available in Europe (21April 2016) without special permission. Can be replaced with EnSolv, or used as an alternative to solvent degreasing eg: water based cleaning systems.
Triglycerides	**(-)**	Esters of fatty acids and Acohol *(Glycerol).* Referred to as unsaturated fats. Present in foods and also synthesized in the liver. It is transported in blood by very low density lipoprotein. (VLDL). They may be removed from VLDL and used by body tissues or stored in adipose tissue. Glucagon or Insulin hormones control the release of triglycerides.
Trihalomethane	**(-)**	Composed of four chemicals – Chloroform, Bromoform, Dibromochloromethane and Bromodichlormethane. Environmental pollutant. Formed when *Chlorine* is used to disinfect water. Vapourises easily. Exposure by skin contact and inhallation.

Hazard in pools and showers. Carciinogenic.

Trimethylpentane (C_8H_{18})

ISOCTANE or 2,2,3-**TRIMETHYLPENTANE**

Organic compound, isomer of octane. Pentane is parent name – 'pent' gives number of carbons in chemical and ane tell you it is an alkane ie; single bonds. The numbers tell you where the groups ie: methyl in this case – is attached. Used in gasoline to reduce engine knocking.

Triphenylphosphate

(TPP) ($OP(OC_6H_5)_3$) An ester of Phosphoric acid. Flame retardant (blocks heat Transfer) and a plasticizer. In Europe considered toxic. Also present in nail polish.

Tryptophan ($C_{11}H_{12}N_2O_2$)

An essential amino acid. Not produced by the body and must be supplied by food. Low levels due to fructose malabsorption causes depression. It has a role in chemical reactions to produce other important chemicals such as serotonin which converts to Melatonin and others. Found in oats, milk, yogurt, chickpeas, some seeds, fish, poultry and many other foods.

Tuftsin ($C_{21}H_{40}N_8O_6$)

Produced in the Spleen. It is a peptide of 4 amino acids and binds to the surface of the Macrophages and the White Blood cells to stimulate their activity. Used in immune-therapy.

U

Urea ($CO(NH_2)_2$

An organic compound – note that it has two NH groups. The liver combines these groups with CO_2 to make urea which is then excreted by the kidney. It is an indicator of kidney function and because of its high nitrogen content is widely used in industry to make resins and fertilizers apart from a number of other uses.

Uric Acid

(C5H4N4O3). Purines found in drinks, dried beans, anchiovies, peas and beer dissolve in the blood and break down to form uric acid which is excreted in the urine. A little is excreted in the faeces. If the concentration of uric acid in the blood is higher than the kidney can deal with then crystals of uric acid form hard deposits in joints which are painful. This condition is refered to as gout. These crystals may aggragate and form stones in the kidney.

Uranium **(U)**

A Very Heavy Metal. Two common important isotopes. U- 238 and U- 235 (nuclear fission). Decay in Millions of years.

V

Vinclozine **($C_{12}H_9ClNO_3$)**

A fungicide that can pass through the placenta into the developing fetus. Used on golf courses. Banned in a number of European countries as it is an *Endocrine disrupter*.

Vitamin A **($C_{20}H_{30}$)**

The Daily requirement is 700µg. For ages 20 onwards. Others vary. eg: pregnancy, deficient for one or other reason. Found in milk, liver, fish, eggs, tomatoes and added to some foods such as cereals or to tablets. Acute or chronic toxicity if taken in excess due to its accumulation in liver. Could damage liver, kidney and result in excess calcium in blood by the removal of it from bone. Should be kept in dark bottles.

Vitamin B12 **(-)**

CYANOCOBALAMINE. There are three chemical types of B12, Cyan- , hydroxy- methy- . Each is added to –

cobalamin which contains cobalt. Daily requirment 2.4 µg for ages 14 onwards. Found in meats, liver, fish, milk, eggs, some yeast products and tablets. Low toxicity. Potential deficiency (170-250pg/ml = 0.00017 µg - 0.00025 µg) in vegetarians, elderly, protein-pump users, G.I.T., surgery and those with pernicious anaemia. No health danger known from excess intake of 1 mg (1000 µg) for 5 years.

Vitamin C **(C_6H_8)**

An Antioxidant. The daily adult Requirments 90mg male and for females 75mg. Unless adult is deficient, excess is extrected in the urine. Not stored in body. Found in vegetables & fruits and fortified foods. Helps iron absorbtion,skin to heal and make a protein for health of blood vessels. Deficiency leads to bleeding Nose and, weak tooth enamel, bruising, slow wound healing. Cooking, steaming microwave, reduces vitamin rich foods.

Vitamin E **($C_{29}H_{44}O$)**

Alphatocopherol. All other forms are excreted. A fat soluble antioxident. Helps with reducing platelets to aggregate by dilating blood vessels. It is involved in gene expression and metabolism, immune system and cell signalling. Found in wheat germ oil, sunflower oil, almonds, hazel nuts, raw tomatoes, green vegetables and fortified foods. Daily adult requirement 15mg = 22.14 IU. Deficiency is rare.

Vinyl Chloride **(C_2H_3Cl)**

Used in the production of PVC (see p.315 Appendix IV). A vinyl chloride monomer derived from petroleum and produced through different chemical reactions. Stored as a liquid in double spherical containers filled with inert gas. It is the monomer that is unstable and most hazardous. Classed as a flammable liquid. Explosive if mixed with air and emits hydrogen chloride and phosgene.

Group 1 carcinogen. Mutagenic. Effects eyes, skin lungs and liver.

X

Xylene **(C_8H_{10})** **(Dimethylbenzene)**

An aromatic HC. derived from petroleum. 3 isomers. Used as a solvent and in the production of plastic bottles and polyester cloth in ink, rubber and laboratories. Irritant to skin. Vapour moderately toxic, causes CNS depression, long term exposure, incoordination and short term memory.

Y

Z

Zineb **($C_4H_6N_2S_4Zn$)**

Fungicide. Many different trade names. Spray or dust exposure toxic to skin and lung mucous membranes. No neurotoxic effects, but metabolized to *Carbon disulphide* can damage nerve tissue. Baned in some countries and requires PPE used in home gardens.

Zinc **(Zn)**

A metal and an important element for the body. May occur with the metal *Cadmium.* Deficiency can result in a number of different medical conditions such as growth, low insulin levels, malabsorption and retinal effects. Excess intake may result in copper deficiency and ataxic gait. Used in galvanizing as an alloy and in the paint and rubber industries. It **Nitroglycerol** has other uses.

Zinc Oxide **(ZnO)**

White powder insoluble in water. A semiconductor. Used in electronics, Plastics, rubber, ceramics, paints, glass, hand cream, sun screens fire retardants electronics. Hazardous if inhalled as fumes in welding zinc plated steel.

Appendix V

Illustrations

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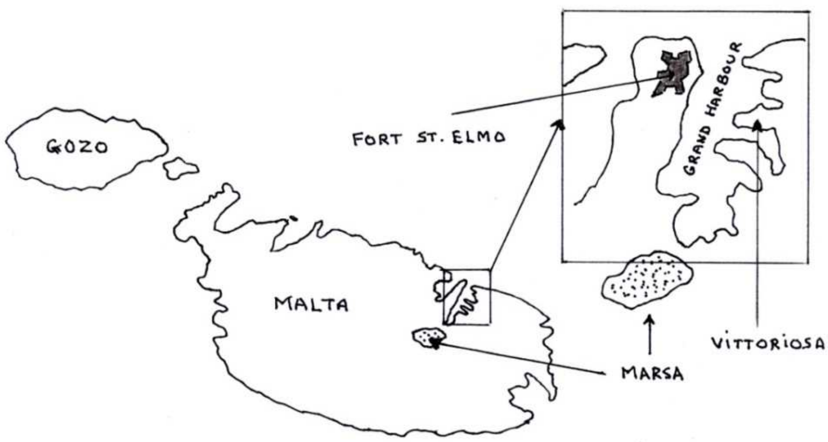
343. **Figure 71.** A rough sketch of the island of Malta and inset showing Fort St. Elmo in what was then a barren area (now the capital of the island Valletta). The fort guarded the entrance to the Grand Harbour. The inset also indicates the area of Vittoriosa (also refered to as Birgu) which then housed the main stronghold of the Knights and people in that city. The area of Marsa (dotted area – not to scale) was where the invaders camped to attack Vittoriosa thereby hindering reinforcements from reaching Fort St. Elmo, and where the water wells essential for drinking water supplies to the invaders where polluted with sewage. *(For more detail the interested reader is refered to the excellent book 'the great siege of Malta' by Ernie Bradford).*



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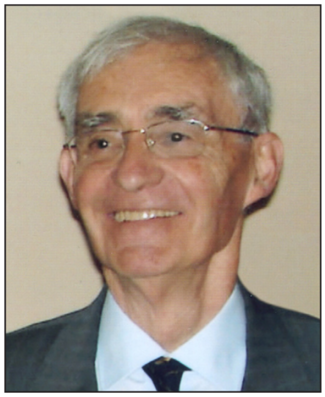

Dr. Francis M.E. La Ferla was born in Malta in 1931 and was educated at St. Edward's College, a private English School in Malta. He is currently an international consultant in Occupational Medicine, Health, Safety and Environmental Sciences, having received degrees in the United Kingdom and Ireland. He is a Fellow of The Royal College of Physicians and Surgeons of Occupational Medicine in Dublin and in London, a Fellow of the Royal Institute of Public Health, a Fellow of the Royal Society of Arts, an Honorary Fellow of the Institution of Occupational Safety and Health (UK), and a Fellow of the Society of Tropical Medicine. Dr La Ferla has been honoured with Membership of the Malta Order of Merit for his international and local work in his field. He has been a full staff member of the World Health Organization Regional Office in Copenhagen, Denmark, and collaborated with work in other United Nations member organisations, worked both in developed and developing countries, and was a Director with Mobil Oil based in Africa for many years. As Malta's first consultant in Occupational Medicine, he started the first University of Malta courses in these subjects for medical students, initiated the setting up of Malta's Occupational Health and Safety body and later, at the Centre for Labour Studies at the University of Malta, was instrumental in the development of the first Safety and Health course to be held at University level accredited by IOSH (UK). He is Scientific Director of IACP in Rome, Italy, and is currently engaged in furthering educational knowledge and skills in Safety and Health.

UNDER ATTACK

Written for undergraduates, adult students and practitioners of Safety and Health, this book provides the reader with basic knowledge of the ever-increasing number of substances that people at work are exposed to on a daily basis and their importance in safety and health. The book covers how workers are exposed, entry into the body and the impact on the body's systems, while its hand drawn anatomical diagrams illustrate the pathways of substances and the organs targeted by them. Prior knowledge of chemistry, physics or biology is not necessary and an extensive glossary is included for those new to these subjects. Relevant historical anecdotes capture the reader's interest and information is presented on what should be done to encourage preventative approaches.

This book will broaden your horizons and help you plan and implement approaches to identify and reduce the health impact of potentially hazardous substances in the workplace environment.

L-Università ta' Malta
Centre for Labour Studies

IN COLLABORATION WITH

THE MALTA OCCUPATIONAL SAFETY & HEALTH PRACTITIONERS ASSOCIATION

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