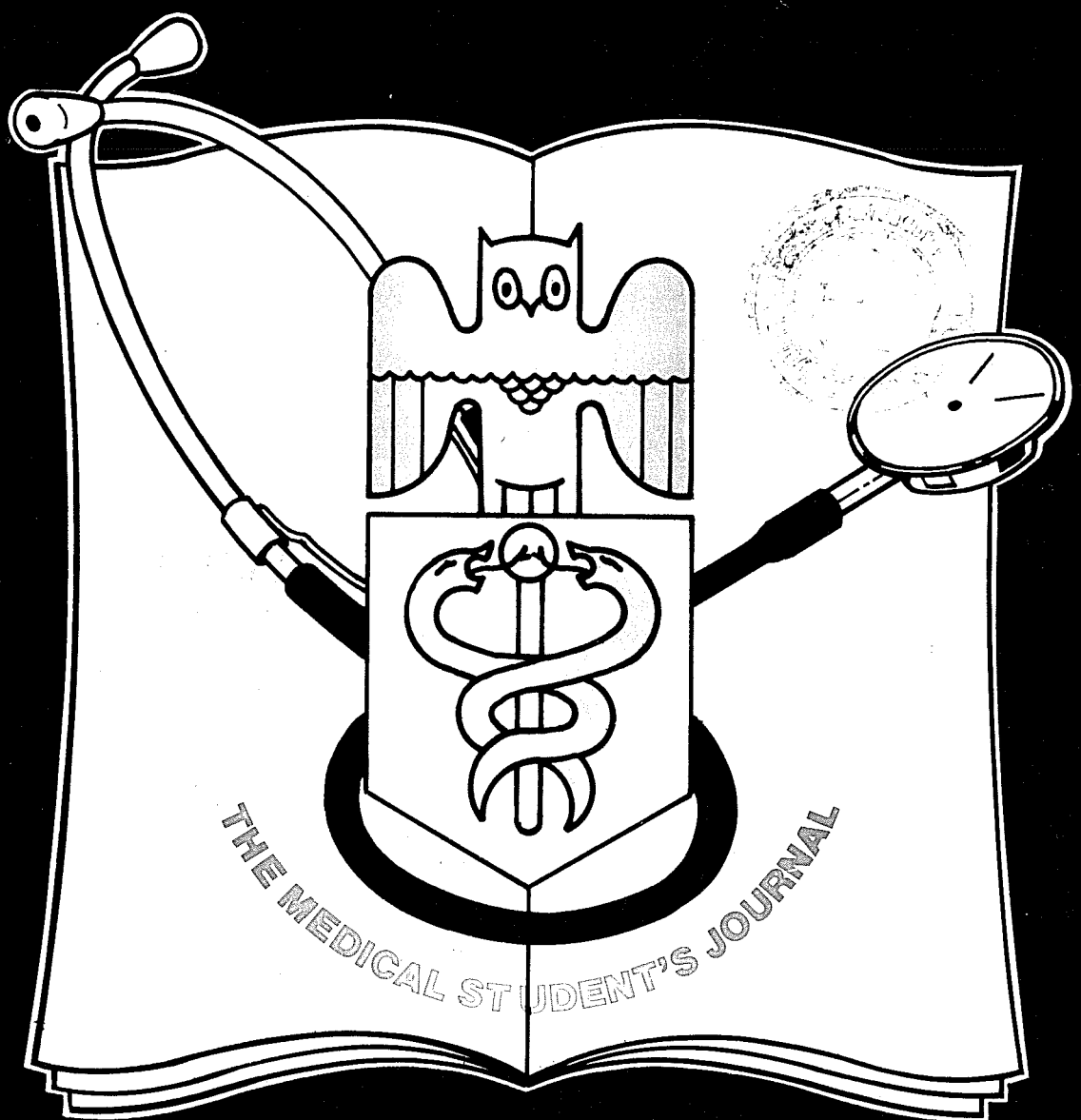
Medi-Scope

ISSUE No. 2 APRIL - JUNE 1983



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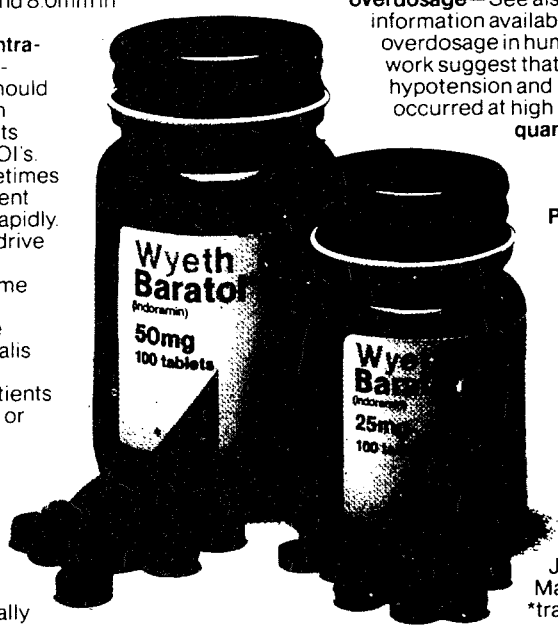
Hospital Price: As per local contract.

Product Licence number: 25mg tablets PL 0011/0071; PA/22/34/1, 50mg tablets PL0011/0058; PA/22/34/1

References:

1. Carballo, R. In *'Arterial Hypertension'* Ed. Velasco, M., 1977, Excerpta Medica, Amsterdam & Oxford, p.129. 2. Marks, P. Awaiting Publication.



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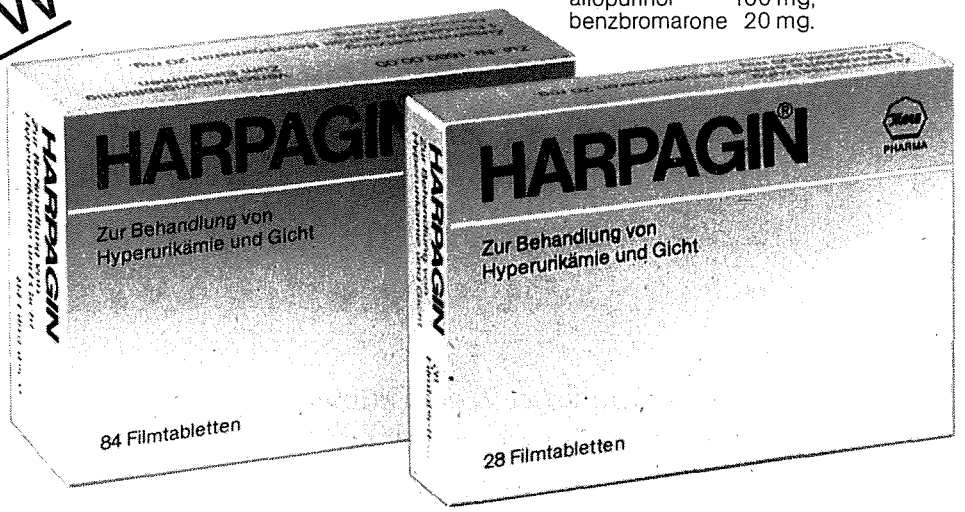

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Editor's Letter

Medi-Scope **Issue No. 2 Apr-Jun '83**

Medical Students Journal
University of Malta Medical School
G'Mangia.

To our great satisfaction, ***Medi-Scope*** has attained the desired popularity amongst students, doctors and others. It was certainly worth all the trouble it took to get started; it was appreciated by one and all. Thanks to Mr. Zammit Ciantar whose knowledge in printing assisted us considerably through the first issue.

In this issue we have not failed to note, however, that we are still lacking the participation from the student at large; after all it is a student's magazine, the medium through which the student is provided with the opportunity to get versed in presenting cases and other material in a scientific manner. Sooner or later we are all bound to face the problems of writing medical papers and before the material can be read by intellectual people, the presentation must be of a high standard. The technique of writing must be achieved now before we ever become doctors at which stage we will be expected to know how to forward our ideas.

I would like to appeal to all the agents to make early bookings for their advertisements as well as to co-operate with us in an efficient manner. As future doctors, I am sure that all the agents would want similar co-operation from us.It is, after all, through such advertising that medical products can be made known to the medical profession and this journal has certainly a good circulation amongst doctors and students alike.

Printing a magazine of this nature involves a lot of work, we must admit. Also, we are not eternal members of the editorial board hence, we will be very pleased to have more students participating in this work, helping us by sharing the burden and eventually to take over the publication. The end-product is always gratifying if carried out properly, whole-heartedly and enthusiastically. Dedication is the secret of success and satisfaction.

One last point that I ought to mention is that though the magazine is intended to contain several medical articles a touch of humour and some brain-twisting quizes will certainly give a sweet flavour to the publication and induce more participation. Moreover, it will make more pleasant reading. As the saying goes *all work and no play makes Jack a dull boy.*

THE EDITOR

Contents

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Acupuncture

NAZZARENU AZZOPARDI MD FFARC
HEAD OF DEPT. OF ANAESTHESIA
RONNIE BORG MEDICAL STUDENT

In the popular mind acupuncture conjures a picture of a patient riddled with pins; rather like a pin cushion but this great scientific discovery expounded by the Chinese philosophers thousands of years ago has gained scientific recognition among European scientists only in the last decade or so. Is it a hoax? Does it work?

Chi

The Chinese explanation for the success of acupuncture is that the insertion and movement of the needles in certain specified points in the body can affect the body's life giving energy, the *Chi*. The Chinese identify 1000 points in the skin divided into 12 systems or meridians, each meridian is linked with a major body organ. *Chi* flows in the meridians and is composed of two elements; the *Yin* and its opposite the *Yang*, symbolised as water (Yin) and fire (Yang). Dynamic balance of the body implies dynamic balance of Yin and Yang, - this is a state of good health. In illness the balance is disturbed and one of the elements predominates. To restore the balance it is necessary to resort to acupuncture. Also the partaking of certain foods rich in these elements can be of benefit. So the Chinese believe in Yin and Yang foods. Acupuncture is said to restore good health by correcting the Yin Yang imbalance.

Melzack Gate Theory of Pain

Western science has adopted a different approach to explain pain. The control of pain can only be achieved if its actions and transmission is known and understood. Melzack proposed the gate theory of pain control and relief after observing in the First World War injured soldiers still fighting, intent in their purpose and oblivious of their severe wounds, only to collapse at the end of the stressful situation. Melzack argued that the mind intent on a stressful situation shuts the gate to other incoming impulses, all the attention being diverted to one purpose. Pain transmission and its perception is subject to modification depending on presynaptic inhibition. Evoked potentials in the cerebral cortex are modified if two kinds of splanchnic stimuli are transmitted or if a somatic stimulus is superimposed on a splanchnic one.

Acupuncture

In acupuncture, modern science has finally discovered the connecting link between traditional folk medicine and real scientific medicine. The subject has now been upgraded from fringe medicine to a reputable medical practice with the appointment in Tennessee, America, of a professorhip in Acupuncture. Using the latest biochemical methods Koesterlitz, working in Edinburgh, produced evidence of natural opiates - the endomorphines were discovered. These brain hormones act as neuromodulators lasting a few hours but modifing pain impulses.

Acupuncture modifies the action of cells of the caudate nucleus which is rich in opiate receptors and hence by increasing the release of endomorphines supplies the pain killing effect directly on the cells that appreciate pain, i.e. thalamic cells. Naloxone, a total inhibitor to opiates, reverses the pain relief obtained by acupuncture - a further proof that acupuncture acts centrally. As time passes so more natural opiates are being discovered. One hormone *Dynorphine* is 200 times as potent as morphine.

Anaesthetists have extended the use of the drug morphine by giving it in very small doses intrathecally and achieving good pain relief at the cost of the undesirable side effects of the opiate, such as vomiting and some respiratory depression.

The acupuncture points

Traditional Chinese acupuncture is guided by charts that show the path of the meridians for internal organs. Even psychosomatic illnesses are curable by acupuncture according to the old philosophers of China. So far modern science has failed to explain how a psychosomatic effect may be elicited by the use of the needles. But the evidence of the meridians has in some cases been proved ... today we call these points reference points. Every student knows that pain over the right scapula indicates biliary disease . the Boas sign. In fact the Chinese acupuncture meridian for the liver is in the interscapular region.

The use of embrocations, deep heat and the old system of cupping (fintusi) was all directed to the same purpose, stimulating the skin and therby reaching an internal organ.If the condition is localised to the skin or to the muscles underneath then the existence of 'trigger points' as reported by Lewit is proved because

acupuncture on these points relieves the condition. Some acupuncturists use a machine to determine the site of these trigger points, as in these areas there is a change in potential due to cellular oedema. Other acupuncturists theorise that if the process involved is the building up centrally of a sufficient level of endorphines then any point that is stimulated can reproduce the same effect, so bypassing the study of trigger points.

Diagnosis in acupuncture

A complete physical examination including radiographic studies is an essential part of the therapy. Nobody should practice acupuncture who is not a physician alert to the syndromes of malignancy and to the diagnosis of bone lesions. Today the theory of the Chinese acupuncturist about the 12 pulses, 6 on the wrist and 6 on the meridians, is now forgotten.

The technique.

The needles used vary from one acupuncturist to another, but all claim good results. Some still use hand stimulation, rubbing the needle hub between thumb and index finger while most use electrostimulation. A current of a varying intensity is passed through the needles, the current being pulsed at 700 μsecs and a frequency of 2 Hertz. The variable intensity is determined by the patient's reaction. While on one hand it is a rule never to cause any pain during acupuncture yet it is essential to tell the patient to forbear any slight pain. The number of treatment sessions is much reduced if the patient's cooperation is obtained. The duration of each treatment session varies from five to twenty minutes, and the frequency of application is determined by the intensity of the pain.

The use of the Laser is a new approach updating this science to modern times. The laser beam is emitted from a pencil like probe attached to a generator with an output of 2mW. The probes, which operate in the infra-red spectrum, are held between six and twelve mm away from the skin, and simulate the twirling of the needle. The advantages of laser acupuncture is that it is completely painless, and can scan a wider area than a needle technique can achieve. The drawback of this technique is that it cannot reach points which are deep down as any increase in intensity is accompanied by burning the skin. A latest approach is the use of ultrasound in acupuncture.

The Dangers

The main danger of acupuncture is that a malignant process is missed until too late. That is why we emphasised that the therapy should be administered by a medically qualified person who has investigated the patient's complaints thoroughly. The introduction of the needles calls for the utmost sterility as viral hepatitis and an occasional skin abscess has occured.

Discussion.

The acceptance of acupuncture as a form of therapy is justified not only by tradition but by proved medical and scientific researches.

It may seem puzzling that noxious stimuli applied to the skin may relieve pain yet Hippocrates had an aphorism 'If the patient is subjected to two pains in different parts of the body simultaneously the stronger blunts the other.' The build up of endorphines in the brain by repeated sub-noxious stimuli is the best explanation given to explain the beneficial effect of acupuncture therapy.

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Notice

This periodical is published quarterly.

Contributions (articles, advertisements, etc.) for the various issues must reach the Editor ***1 month*** *before the issue is due and not later.*

Articles must be typewritten with double spacing. References should be given by the author's name & by the year of publication.

Materials sent to us for printing will not be returned unless otherwise specified.

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EDITOR

The Deaf Person in Hospital

MISS JOSEPHINE CUOMO SRN MRSH
NURSING OFFICER ST. JOHN'S MEDICAL BRIGADE
& HANDICAPPED EDUCATIONAL AND AIDS RESEARCH UNIT
CITY OF LONDON POLYTECHNIC
CO-ORDINATOR DAR TAL-PROVIDENZA, SIĠĠIEWI

Most people with normal hearing, find that entering hospital causes them anxiety. For a deaf person, going to hospital can be an especially traumatic experience. Their inability to hear and to communicate can bring distress, confusion and embarrassment.

Not only is it difficult for them to communicate with the hospital staff and these, with them, but their handicap can isolate them from other patients around them. They can be left out of the general ward which often keeps patients cheerful, despite their illness and which may even aid in their recovery.

For patients who are hard of hearing or who are totally deaf, this can be a nerve-shattering experience. The doctors give all their professional help and the *guardian angels,* the nurses, give wonderful care and attention... but still they find it exasperating when they cannot hear what the doctor is saying to them. Everybody just nods his head and moves on and the poor patient is left in a world of silence and ignorance from which there seems to be no escape!

I personally feel that it is of the utmost importance that nurses and doctors should be aware of the needs of people with this handicapping condition; in fact my intention is to smooth the path of the deaf patient in hospital. Here are some hints and ways in which hospital staff can help:

1. Many patients have defective hearing; so any patient may well turn out to be deaf.
2. If patients are admitted by appointment, ask if their hearing is normal, if not, try to find out whether they have a hearing aid, and what type it is and if they can lip read.
3. Profoundly deaf people may have defective speech. In this case it would help to know the name and telephone number of a social worker with the deaf or a member of their family or someone else who can communicate with them.
4. Please remember - deaf people who are waiting in out-patients clinics will not know that their names are being called when their turn to see the doctor comes.
5. Have patience when communicating with someone whose hearing is impaired - your frustration is likely to be theirs too.
6. To overcome loneliness we all need company and conversation. For a deaf person these may present difficulties. Try to see that some attempt is made to befriend the deaf person in hospital. Nurses may not have time. But visitors could be advised that a deaf person needs frequent visiting.
7. Deaf patients who are to undergo a surgical intervention should be allowed to keep their hearing aid up to the point of anaesthesia. It can be so distressing to them to lose their communication link at a critical moment!
8. There are five main methods of communication used by the deaf:
   (a) Hearing aids
   (b) Lip reading (d) Sign language
   (c) Finger spelling (e) Hand writing

   All patients would want to know about their progress. Deaf persons are no exception. Using one of the above mentioned methods of communication even in writing, will certainly help them psychologically and helps them gain confidence in the staff.
9. Children deaf from birth have even greater problems than acquired deafness in adults. For instance, their vocabulary is generally limited to simple words only. Like any other child, a deaf youngster longs for friendly, uncomplicated conversations. In Medical matters it is of course best to deal with the child through the parents or guardian. When possible it is essential not to separate the deaf child from his mother.
10. Speak clearly but don't shout. Shouting at a deaf person will get you nowhere; shouting at a patient who uses a hearing aid can cause great discomfort and in some cases pain. It also reduces the clarity of speech and distorts the shape of the mouth making lip reading more difficult.
11. Speak slightly more slowly than you do normally and be prepared to use different words if understanding seems difficult. Some words are much more difficult to lip read than others, even though they have the same meaning.
12. Make sure that you are standing in good light, so that your face can be clearly seen. Deaf patients are often seen at ENT clinics which are usually *dark-rooms*... such environment is thus far from ideal!
13. Don't expect someone to be able to lip read you if you are eating, smoking or face down reading at the same time.
14. If possible note the patient's degree of deafness on his or her medical records. When this this information is included on the notes attached to the bed, it will save repeated explanation to doctors, nurses and visitors consequently reducing to a minimum further embarrassment and frustration to our dear friends who suffer from impaired hearing.

Love works in ways, that are wonderous and strange.
There is nothing in life that love cannot change!

An Integrated Approach to the Management of Health Care in Malta

A.J. PSAILA, MD, MRCP, DCH
PROFESSOR OF MEDICINE
THE UNIVERSITY OF MALTA
SENIOR CONSULTANT PHYSICIAN AND HEAD
DEPARTMENT OF MEDICINE,
ST. LUKE'S HOSPITAL.

Paper read at The Institute of Pharmacy Management Annual Conference - Malta 1982

A successful health care programme depends directly on the team work of a group of people who care about and who care for patients in the management of their sickness with the aim of allaying the symptoms in all cases and of a complete cure whenever possible. This team is made up of general practitioners, hospital medical officers, consultants, pharmacists, dentists, physiotherapists, occupational therapists, speech therapists, nurses and social workers.

According to the front cover of the Pharmaceutical Journal of September 18th, 1982, in the 16th Century the physician and pharmacist worked closely together, but today we rarely see them depicted together. This might be so in other countries, but I am pleased to say, it is not the case in Malta. The pharmacist is an important member of the team looking after the sick. His place as a prominent member of this team has been enhanced by a working programme planned between the Department of Medicine and the Department of Pharmacy of our University under the auspices of the Ministry of Health. This working programme will be discussed later in this paper; at this stage I am going to dwell on the situation in Malta vis-a-vis the traditional relationship between the pharmacist and the physician.

Malta is a small country with a population of about one third of a million packed in about 100 square miles of land area. Everyone is known to and by everyone else especially so in the same sphere of work or in the same professional activity. There is only one University in Malta. The end result is that most pharmacists and doctors of the same age have rubbed shoulder to shoulder in their university years not only in the lecture rooms but also and even more so in the extracurricular activities such as sports. This bond of present and past friendships leads naturally to excellent team work spirit between most pharmacists and doctors; they treat each other as colleagues and discuss common health problems together.

It is interesting to point out that up to the late fifties, medical students were allowed to follow the Course of Pharmacy (leading to the B.Pharm. Degree) concurrently with the M.D. course. As a result a large number of doctors in Malta (of average age forty-eight years) have qualified as pharmacists as well as doctors.

Another factor which strengthens the bond between pharmacists and physicians is the fact that in Malta it is common practice for community pharmacists to provide rooms for visiting general practitioners and consultants. The proximity between the two enables further direct and frequent contacts between pharmacist and physician.

In hospital work, keeping in mind that in Malta we have only one general hospital the relationship between doctor and pharmacist has traditionally been excellent, one helping the other. Frequent administrative meetings take place between the Chief Pharmacist and physicians regarding:

a. The ready availability of most commonly used drugs;
b. the date of expiry of stock medicines, e.g. antibiotics; (When expiry date is near, a circular is sent to all doctors to attract their attention and ask their cooperation about this fact.)
c. the newest drugs as described in the world's leading journals of Medicine and Pharmacy are discerned and if applicable stocks are bought for the hospital;
d. preparations of IV infusions; their problems are discerned e.g. 5% Dextrose, Normal Saline solutions.
e. the Hospital Formulary is reviewed from time to time to
   i. add new drugs
   ii. remove from stock old fashioned drugs, no longer in use.

With the rising costs of medicine this job is not only beneficial to the patient's health but also to the country's economy.

For a great number of years this job was the responsibility of a sub-committee of the Hospital Management Committee, chaired by the Professor of Medicine.

Since 1981 there has been an adhoc Committee (Drugs and Therapeutics Committee) appointed by the Government with advice and help from the World Health Organisation to look into this matter.

The Ministry of Health (administrative) is represented by one of the Principal Medical Officers, the Department of Medicine is represented by the Head of the Department and the Department of Pharmacy by the Senior Hospital Pharmacist who is also the Committee's Secretary.

Drugs which are not in the hospital formulary are discussed in the Committee in the appropriate items of the agenda under the following headings:

a. A case may be made for a particular drug which has become popular recently, and which has superceded previous drugs to enter the formulary. A case for this drug has to be made by physicians, surgeons dealing with the particular disease, taking into account cost, clinical findings, availability of drug and amount of stock needed per year.

b. A case may be made for a particular drug not in the formulary to be issued and purchased by Government for a particular patient who is not doing well on the formulary drugs usually taken for his illness. Asthmatics, arthritic and cardiac patients very often fall in this category.

The majority of patients with chronic illnesses of the type mentioned irrespective of their income, can obtain free medicines from the Government Dispensaries. This is over and above free hospitalisation and out-patient treatment.

I shall now discuss the working programme planned jointly by the Department of Pharmacy and the Department of Medicine since the establishment of the Student-Worker Scheme in 1978.

Pharmacy students are taught physiology, applied physiology and pharmacology in the medical wards. A group of students studies a group of patients with a particular illness, e.g. hypertension. Under the supervision of the staff of the Professional Unit they assess the effect of a variety of drugs on a particular disease taking into consideration age, severity, concomitant disease, sex, body weight, patient's personality, patient's cooperation, etc. The same group of students studies one particular drug either in a group of patients with one disease eg. hypertension or in a group of patients with different diseases eg. the use of ß blockers in hypertension, angina pectoris and cardiac arrythmias. With this approach, the students learn more, faster and are gaining fruitful experience not only in their subject but on humanity in general. They work hand in hand with doctors, nurses, medical students, physiotherapists and others. On their qualifying as pharmacists, they are mature enough to be trusted with ward pharmacy and other responsible jobs. The concept of ward pharmacy has been prompted by a joint venture between the Department of Pharmacy and that of Medicine. The medical wards at St. Luke's Hospital were the first to be used to develop the system. Now other hospital wards are being included; list of stock drugs were drawn up by each ward; each ward is treated on an individual basis. The Professor of Medicine and the Hospital Senior Pharmacist discuss and approve the list of drugs required for each ward. Each ward pharmacist is responsible for a number of wards which he or she visits daily. The pharmacist checks the storage and distribution of drugs in the ward and deals with any problem regarding drugs which the nursing staff might bring to his or her attention. Adverse reactions and interactions are documented and discussed between physicians and pharmacists. The main responsibilities of the ward pharmacists are as follows:

a. to ensure a rational use of drugs and avoid abuse;
b. to ensure the proper storage of drugs and avoid excessive storage;
c. to give to the medical and nursing staff all the necessary information regarding proper usage of drugs.

Another outcome of this joint venture is the new Drug Information Unit. It is part of the Drugs and Therapeutics Committee mentioned before in the paper. Information about new drugs, dosages and side-effects are given immediately to any member of the medical or nursing staff who requests it.

The Drug Information Unit is also publishing pamphlets for the general public of great value as information, for example drugs dangerous for drivers and drugs which should not be mixed with alcohol. Press, television and radio programmes to educate and inform the public are also organised.

In conclusion, the aim of all this is that the pharmacist and the pharmacy student are:

a. getting out of the pharmacy and the classroom and coming into contact with whoever matters most - the patient;
b. becoming automatically part of the team looking after the sick;
c. contributing to the research programme of the University and supplying valuable general information to the public.

Drugs can be life saving. However, abuse can cause serious illness and DEATH!

Osmotic Pressure in Biological Fluids

Application to Patients in General Practice

PROF. J. GATT MD. MSc,
FRCP, FRC Path, DTM +H
DEPT. DIRECTOR. DEPARTMENT OF PATHOLOGY

Dr. V. HOLECEK, MD, BSc
CONSULTANT BIOCHEMIST. DEPARTMENT OF PATHOLOGY

Osmotic pressure in biological fluids is one of the most important physical values. Different solutions at the same temperature and the same concentration (activity) of ions have the same osmotic pressure. This means that a big molecule of protein for instance has the same osmotic effect as the small ion of sodium. Osmolality expresses the number of dissolved particles in a given weight of solvent. The solution of one mole of each fully dissociated compound has the osmotic pressure of 22.412 atm. The formula for checking the osmotic pressure is:

$$P = R \times T \times c$$

Where P = osmotic pressure, R = universal gas constant (0.08204), T = temperature in the Kelvin's scale, c = concentration in moles.

If we want to imagine the force which the osmotic pressure can produce, the following experiment could be done: (Fig. 1)

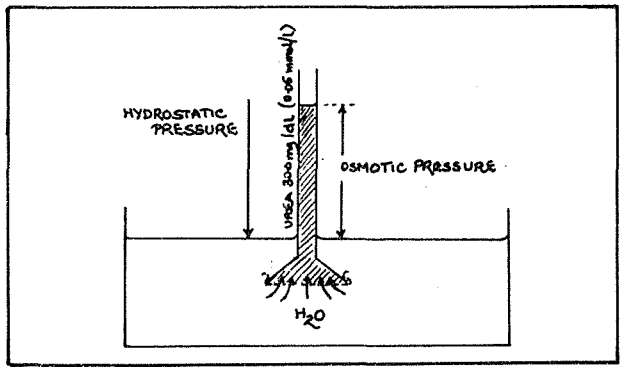

Figure 1

In the vessel there is distilled water, in the funnel there is a 300 mg% solution of urea (0.05 mol/ℓ). Both fluids are separated by a semipermeable membrane, which enables the passage of water into the compartment with the urea solution. According to the law of isoosmolality, when two solutions are separated by a semipermeable membrane and on both sides of the membrane there are different osmotic pressures, the water and the ions will pass through the membrane until the osmotic pressures on both sides are equal; the water from the vessel will dilute the solution in the funnel. The equilibrium occurs when the hydrostatic pressure will be in balance by the osmotic pressure (shown by the column of fluid in the funnel.)

We can calculate the absolute osmotic pressure (at 20° C and the barometric pressure of 760 mm Hg):

$$P = 0.08204 \times 293 \times 0.05 = 1.2 \text{ atm}$$

This pressure corresponds to: 760 x 1.2 = 912 mm Hg (=14.2 m of water). If we realise that the patients with renal insufficiency often have such a urea concentration in the blood and that there are many other ions in high concentrations (Na^+, K^+, HCO_3^-, glucose etc.) we can easily imagine how changes in osmotic pressure of body fluids can be fatal.

We have to distinguish the terms osmolarity (osmotic pressure in 1 litre of the solution) and osmolality (osmotic pressure in 1 kg of the solution). Both these values in the serum are not much different. Usually we use osmolality due to the methods of estimation. Mostly we use the cryoscopic method (by dissolving of a solute (compound) the properties of the solvent change, e.g. 1 mole of a substance dissolved in 1 kg lowers the freezing point of water by 1.86° C.) The boiling point of the solution also increases; the vapour tension decreases; osmotic pressure and conductivity increase. The estimation of other physical parameters as conductometry, densitometry of the solution etc. are complicated and inaccurate and therefore not in use.

In biochemistry in the past we used a unit the osmol (Osm), equal to 10^{-3} x a smaller unit, the milliosmol (mOsm). In the new SI units convention we use mmol as a unit. There is no change in the numerical value. 1 mmol/kg = 2.58 kPa at 37° C.

The osmotic pressure (osmolality) can be calculated according to the formula:

$$\text{mmol/kg} = \frac{\text{mg of the compound in 1 kg x the number of active compounds (ions)}}{\text{relative molecular mass}}$$

For example the osmotic pressure of the saline isotonic solution (0.9%) is:

$$\text{mmol/kg} = \frac{9000\ \text{mg/kg} \times 2\ (\text{number of ions, i.e. } Na^+ + Cl^-)}{58.5\ (\text{relative molecular mass of NaCl})} = \mathbf{308\ mmol/kg}$$

But we know that the normal osmolality of the blood is 285 ± 10 mmol/kg. (Higher values = hyperosmolality, lower values = hypoosmolality).

Blood is not an ideal water solution and therefore NaCl is dissociated by 93% only = 308 x 0.93 = **286 mmol/kg** and this osmolality already corresponds with the osmolality of the blood. This so called "physiological solution" is not really "physiological" due to the lack of Na^+ in correlation to Cl^-, yet this solution is isotonic.

The osmolality of the blood is lower than the calculated amount of the osmotic active compounds. (Fig 2). Collectively there is, in the serum, 150 mmol/kg of cations, the same amount of anions + 10 mmol/kg (urea & glucose) = 310 mmol/kg. The osmolality of 285 mmol/kg is lower due to the incomplete dissociation rate of the solute; i.e. 25 mmol/kg lower. It is well known that the erythrocytes in hypertonic solutions lose water and reduce volume, in hypotonic solution the erythrocytes absorb water, their volume increases and this can lead to haemolysis due to the rupture of the membrane.

There are several formulas available which help us calculate the osmolality of the serum. A very simple formula is the following:

mmol/kg = 1.86 (Na^+ + K^+ mmol/kg) + urea mmol/l + blood glucose mmol/l + 10 (for simplification we use osmolality and osmolarity together).

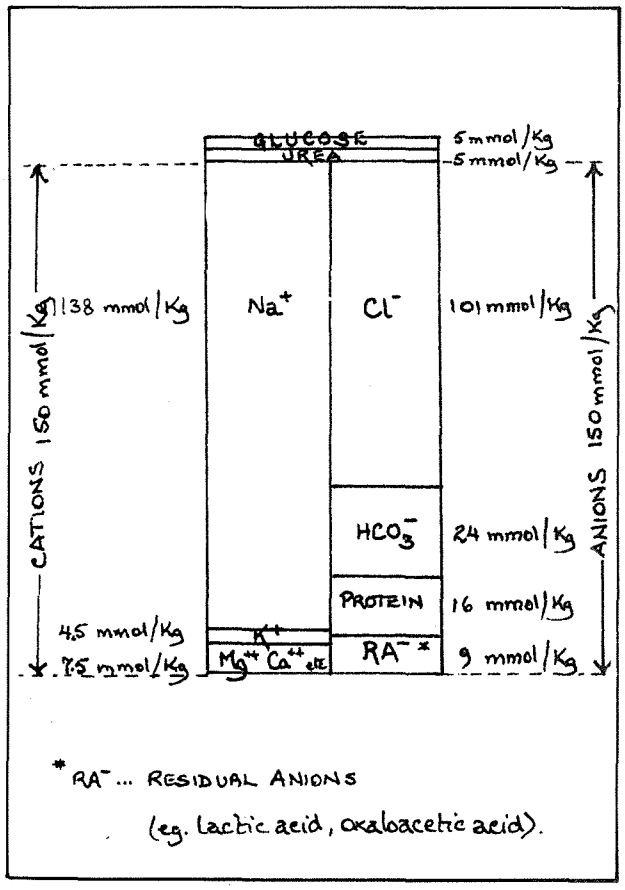

Figure 2.

But no calculation can substitute the actually measured osmolality. It is well known that in healthy people the calculated osmolality is very near to the real (i.e. measured) osmolality. But that in patients where catabolism predominates, the difference between the calculated and measured osmolality is greater. Some authors (e.g. in toxicology) consider the high difference between these values to be the indications for dialysis. Other possibilities of higher measured osmolalities compared with calculated osmolalities are: decrease of serum water or the presence of uncalculated substances if present (e.g. mannitol, sorbitol, acetone, ethanol, glycerol, trichlorethane etc.)

The osmotic pressure in nature is sometimes very high, but it can act only in those cases where there is a difference between two or more systems. Slight differences of osmolality enable the transport of ions and compounds across the semipermeable membranes. It sometimes happens that the osmotic pressure suddenly increases. For example: after dislocation of a joint, at one point of the anatomy at a specific point in time, haemorrhage occurs. The extravasated blood proteins in the tissues are haemolysed and degraded to smaller compounds at a geometrical rate and the osmotic pressure locally increases quickly. From the surrounding tissues with lower osmolality the water flows (according to the law of isoosmolality) and the joint becomes swollen. Similar changes can occur in the brain when e.g. in diabetic coma and injection of insulin, the blood glucose and blood osmolality rapidly decrease. These changes in the central nervous system are delayed, the glucose level in cerebrospinal fluid decreases slowly and the water is attracted into the brain spaces and this leads to oedema of the brain sometimes with lethal consequence. Therefore, the therapeutic decrease of the hyperosmolality must be slow (2-4 mmol/hour). Another example: Alcohol produces hyperosmolality due to dehydration as the urine volume increases. After alcohol intoxication and loss of water osmolality increases and the osmotic receptors of the body provoke the sense of thirst. After drinking of water the osmolality decreases, but again the delayed response (slower decrease of osmolality) in the central nervous system and in cerebrospinal fluid leads to severe headache. Administration of salts will help with water by reducing the differential values. In the therapy of brain oedema we can use the administration of urea to the patient. Urea is distributed very quickly in the body with the exception of cerebrospinal fluid. The penetration of urea into the CSF is delayed and this fact can turn the water-flow from the brain compartment back to the body fluid compartment. Similar changes can occur after a rapid haemodialysis in cases of renal insufficiency.

From these examples we can see the importance of changes in osmolality in clinical medicine.

Increased serum osmolality occurs in water depletion, infantile gastroenteritis (high milk osmolality), in hyperosmolar non-ketonic diabetic acidosis and in diabetic ketoacidosis. Low blood pH values also lead to high dissociation rate of some compounds and leading to the increase of osmolality. Increased breakdown of proteins leads to hyperosmolality, e.g. after burns cases (alas often treated with high protein intake). Cerebral lesions, diabetes insipidus, alcohol intoxication (increased elimination of water) lead to hyperosmolality as well. Inability to drink (e.g. unconsciousness), loss of sense of thirst (old age), lack of water of low electrolyte concentration (shipwrecked person, wrong parenteral nutrition) and hypostenuria are other causes of hyperosmolality.

Decreased serum osmolality occurs in adrenocortical insufficiency, untreated severe panhypopituitarism; salt loss, water intoxication, wrong parenteral nutrition and inappropriate ADH secretion. Catabolic states lead to decrease of protein (albumin), lower oncotic pressure (osmotic pressure of proteins) and therefore to the flow of water from the blood vessels into the tissues (hypoproteinamicoedemas). Similar changes occur in renal diseases with albuminuria. In catabolic conditions the body weight and osmolality are decreasing in a parallel fashion. However when the tissue mass only decreases and not osmolality we expect oedema to appear; (the patient begins to retain water and ions) therefore the loss of body weight is masked by the oedema. If the osmolality is decreasing, but not the body weight there is a danger of water intoxication.

Under physiological conditions the osmotic pressure is controlled by osmoreceptors. Hypo-osmolality leads to stimulation of osmoreceptors and causes decreased secretion of antidiuretic hormone. The water resorption in the kidneys is diminished and the kidneys excrete the excess of water during 2-3 hours. A close correlation is seen between osmolality and viscosity of the body fluids. The increase of osmolality leads to the decrease of blood flow (especially in arteriosclerosis). Hyperosmolality leads to the highly concentrated urine excretion (and/or bile excretion) and increases the danger of lithiasis and infection.

Acute disorders of osmolality. Rapid injury of the cells, due to toxic agents or hypoxia, leads to catabolism in the cells; the amount of degradation products increases and even osmolality increases. The cells absorb water by imbibition, necrotic cells increase the amount of catabolites and the kidneys are unable to eliminate all these osmotically active compounds with sufficient speed; as a result, osmolality increases.

Chronic disorders of osmolality. Severely ill persons are not able to restore all the cell structures and plasma protein levels, especially, fail to return to normal levels. The ability of retaining cations and anions in the body fluids is diminished and the osmolality decreases.

Practical Problems

Example A

1. The patient weighs 60 kg, his blood osmolality is 285 mmol/kg. What happens if he receives an infusion of 3 litres of isotonic NaCl solution?

   Usually the total amount of water is 60% of body weight = 60× 0.6 = 36 l(kg)
   Intracellular fluid is usually 40% = 60 × 0.4 = 24 l(kg)
   Extracellular fluid is usually 20% = 60 × 0.2 = 12 l(kg)

   Na^+ and Cl^- are extracellular ions and therefore the 3 litres are retained in the extracellular fluid = 12l + 3l = 15l. Due to isotonicity, the osmotic pressure will not change but the extracellular volume will increase. (Fig. 3)

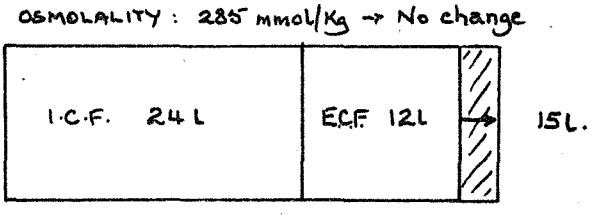

Figure 3

Example B

2. What happens if the same patient receives an infusion of 3l 5% glucose?

   Glucose is metabolised to water and CO_2. 3 litres of water will dilute intracellular and extracellular fluid according to the law of isosmolality, i.e. 2 litres go to intracellular fluid and 1 litre goes to extracellular fluid. The osmolality of the blood of the patient was 285 mmol/kg. Total amount in both body fluids of osmotic active compounds was 36 (kg) x 285 = 10260 mmol. The new volume (weight) of body water is 36 + 3 kg = 39 kg. The new osmolality is 10260 ÷ 39 = 263 mmol/kg, i.e. decrease of 22 mmol/kg. Therefore there has been a drop in the osmolality of intra and extracellular fluid. (Fig. 4).

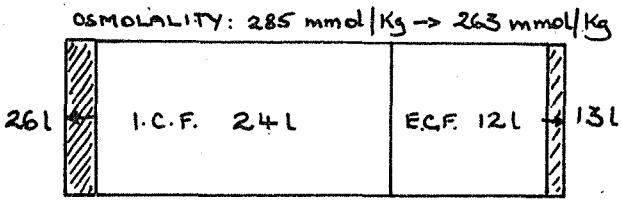

Figure 4

Example C

3. What happens if the same patient receives an infusion of 1 litre of isotonic NaCl solution and 2 litres of 5% solution of glucose?

   1 litre of isotonic saline solution increases the amount of the extra-cellular fluid. 2 litres of 5% glucose after its oxidation to water increase the amount of both fluids in relation 2:1. Intracellular fluid therefore increases from 24 l to 24 + (2:2/3) = 25.33 l. Extra-cellular fluid increases from 12 l to 12 + l + 2:1/3 = 13.66 l. The osmolality will change (for simplification we consider litre = kg) : total amount of osmotic active compounds is 10260 + 285 = 10545 mmol. The amount of water is 39 l. The new osmolality is 10545 : 39 = 270.4 mmol/kg. Therefore there has been a drop of osmolality in the extracellular and intracellular fluid from 285 to 270.4 mmol/Kg. (Fig. 5)

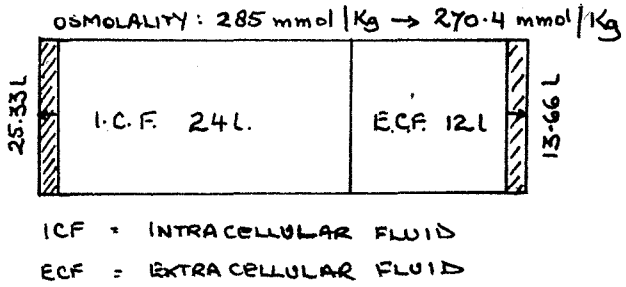

Figure 5

The checking of the osmolality of any solutions is a quick quality control.

Example D

4. We need to give 1 litre of infusion solution 0.3g KCl and 0.33g $CaCl_2$. How many g of NaCl we must add to the solution, if final osmolality should be 295 mmol/kg?

   Molecular weight of KCl: 74.6, $CaCl_2$: 111.1 and NaCl : 58.5

   The amount of g K in 0.3 g KCl:

$$\frac{\text{at. wt. of K} \times 0.3}{\text{mol. wt. of KCl}} = \frac{39.1 \times 0.3}{74.6} = 0.157 \text{ g } (= 157 \text{ mg})$$

   The amount of mmol K in 0.3 g KCl:

$$\frac{157}{39.1} = \mathbf{4 \text{ mmol/l}}$$

   The amount of Cl in 0.3g KCl:

$$\frac{35.5 \times 0.3}{74.6} \times \frac{1000}{35.5} = 4.0 \text{ mmol/l}$$

   The amount of mmol Ca in 0.33 g $CaCl_2$:

$$\frac{40.1 \times 0.33}{111.1} \times \frac{1000}{40.1} = \mathbf{3.0 \text{ mmol/l}}$$

   The amount of mmol Cl in 0.33 g $CaCl_2$ must be 2 times higher than Ca = **6.0 mmol/l**

   Total osmolality of 0.3 g KCl and 0.33 g $CaCl_2$ is 4+4+4+3+6 = 17 mmol/l

   295 (wanted osmolality) - 17 mmol/l = 278 mmol/l = we must add 278:2 = 139 mmol of Na and 139 mmol Cl: 139 x 58.5 = 7131.5 mg NaCl = **7.1315g NaCl**

Example E

5. A patient weighs 60.0 kg and ingests 29.25g of NaCl. What happens to his osmolality (previous was 285 mmol/kg) and to his extra - and intracellular fluids?

   29.25g NaCl corresponds 29.25: 58.5 = 0.5 mol of NaCl — 500 mmol NaCl = 1000 mmol of osmotically active compounds.

   Before the intake of NaCl the body fluid osmotic active compounds divided into:
   total body fluids = 36 x 285 + 10260 mmol

   extracellular fluid 12 x 285 = 3420 mmol
   intracellular fluid 24 x 285 = 6840 mmol

   New amount of mmol = 10260 + 1000 + 11260 mmol (in total body fluid) NaCl increased only the amount of osmotic active compounds in the extracellular fluid: 3420 + 1000 = 4420 mmol

   The new osmolality in the body will be 11260: 36 =312.777 mmol/kg. The volume of the extracellular fluid will be = 4420 ÷ 312.777 = 14.13l.

   After ingestion of 19.25g NaCl increases the osmolality to 312.777 mmol/kg and the extracellular fluid volume increased to 14.13ℓ (2.13ℓ more) the intracellular fluid volume decreased to 21.87ℓ

   These calculations show the importance of deionisation of drinking water. Increase of extracellular volume puts a greater load on the heart, but healthy kidneys can regulate the electrolyte balance and correct for extra load.

Urine Osmolality

Under physiological conditions the water and the ion uptake is very variable. The smallest quantity of water which is needed for the elimination of all the catabolites in urine (resting adult people, maximal concentration rate of the kidneys) is 500-600 ml/24 hours. The urine osmolality increases to 800-1100 mmol/kg. The concentration index of osmolality (I_{OSM}) can reach the value:

$$I_{OSM} = \frac{U_{OSM}}{P_{OSM}} = \frac{1100}{285} = 3.86$$

(U_{OSM}= osmolality of the urine in mmol/kg, P_{OSM} = osmolality of the plasma in mmol/kg).

I_{OSM} expresses the objective concentration ability of the kidneys. The higher values are reached by 15-19 years old individuals. The concentration rate of kidneys is age dependent and at the age of 60-69 years has its highest values of 796 mmol/kg. In young healthy people 1 mmol of osmotic active compounds can be eliminated by 0.8 - 10.0 ml of water. The amount of osmotically active catabolite during 24 hours during fasting and at rest is 200-500 mmol. People under normal conditions and normal nutrition produce 600-1200 mmol/24 hours. Heavy catabolism in patients produces 1200-1400 mmol/24 hours and more. The daily amount of osmotically active compounds which should be eliminated by urine is increased by: physical load, uptake of electrolytes and food, increased (body) temperature, pathological conditions, operation, infection, intoxication, x-rays, necrosis, increased proteolysis, metabolic disturbancies (diabetes, hypoxia, fasting). As a result the urine shows very high level of urea. Again glucose in diabetics needs much more water to be excreted (45g of glucose need 250-1000 ml of water).

When the kidneys of a patient lose their concentrating and diluting ability, I_{OSM} is near to 1.00. In such cases the kidneys will need 1200-1700 ml of water (sometimes more) for elimination of the catabolites under resting conditions. For elimination of 1 mmol/kg of osmotic active compounds such patients need 3.5 ml of water.

Clearance of osmotic active compounds (C_{OSM})

C_{OSM} is the amount of plasma in ml which is cleared of osmotic active compounds during 1 minute. It is calculated as follows:

$$C_{OSM} = \frac{U_{OSM} \times V}{P_{OSM}}$$

(U_{OSM} urine osmolality in mmol/kg, V.. 1-minute volume of urine, P_{OSM}•• average plasma osmolality in mmol/kg). In healthy people the osmotic clearance is 2.0-3.0 ml/min.

In renal insufficiency the kidneys are unable to excrete enough of the osmotically active compounds. This leads to an increase of plasma osmolality, C_{OSM} decreases. Increase of osmotic clearance (osmotic diuresis) is an important datum for the physician since it reflects upon the metabolism of drugs which have been administrated to the patient. These are eliminated in urine at a higher rate i.e. proportional to C_{OSM}• Other values are often caluclated, i.e.: EF_{OSM} (Excretion fraction of osmotically active compounds in % shows us what part of filtrated amount of osmotic active compounds is actually eliminated into the urine (C_{Cr}•• clearance of creatinine)

$$EF_{OSM} = \frac{C_{OSM}}{C_{Cr}} \times 100\ (\%)$$

Normal values: up to 3.5%. Resorption fraction is 100 - EF_{OSM}•

When hypertonic urine is formed (U_{OSM} is higher than P_{OSM}) the so called non-solute water (T_{H_2O}) in the collecting tubules is resorbed. The intensity of the resorption of the non-solute water is calculated:

$$T^c_{H_2O} = C_{OSM} - V\ (ml/min) \qquad (V = \text{minute volume of urine})$$

related to C_{Cr}:

$$\frac{T^c_{H_2O}}{C_{Cr}} \times 100\ (\%)$$

Normal values: maximum by osmotic diuresis: 5%.

When hypotonic urine is formed (U_{OSM} is lower than P_{OSM}) the cells in such urine are quickly destroyed; relatively higher resorption of osmotically active compounds takes place in the distal part of nephron than that of water. The intensity of resorption of osmotically active compounds without water is the renal clearance of non-solute water (C_{H_2O}):

$$C_{H_2O} = V - C_{OSM}\ (ml/min)$$

related to C_{Cr}:

$$\frac{C_{H_2O}}{C_{Cr}} \times 100\ (\%)$$

Normal values: average 10.38%

All these biochemical parameters enable us to evaluate even the slight disturbances of kidney function. There are many other important estimations of osmolality in practice, but in this paper we wanted to give the reader only the rudimentary informations

Conclusions:

A summary of osmotic relationships in the human body fluids has been given. The importance of the osmolality is great, the application of it saves lives. The osmolality of urine cannot be substituted by urine density estimation or other examinations. Monitoring of urine osmolality is another important parameter in the diagnosis of kidney insufficiency. Intravenous infusion of electrolytes, hypervolaemia or hypovolaemic states, parenteral feeding and electrolyte imbalance cannot be managed efficiently without the knowledge of plasma and urine osmotic parameters.

Reference: NEJEDLY B (1980): *Internal Environment*, AVICENUM, PRAGUE.

Renal Transplantation

MARK BUGEJA MEDICAL STUDENT
Revised by DR. BUHAGIAR MRCP MRCS LRCP.

The first Renal Transplantation ever to be carried out in Malta was performed on the 22nd April, 1983, a day that may well be included in the Medical History of our Islands. This event is another step forward following the introduction, not very long ago, at St. Luke's Hospital, of Haemodialysis or as the lay-man would call it, the *'Kidney Machine'*.

What follows is not meant to be a case-presentation proper but is intended to serve as a base over which some pros and cons of renal transplantation, the subsequent management of the recipient and the possible complications that may commonly arise, could be forwarded to the reader in a hopefully simple and palatable manner.

Case:

A 45- year old, unmarried postman came to hospital in March '83 complaining of:

1. Intense Itching
2. Increasing pallor } since summer 1982
3. Increasing fatigue
4. Progressive breathlessness - worst in February 1983
5. Vomiting of eaten food

The patient has a history of albuminuria (at around the age of 20) following an upper respiratory tract infection. Since the age of 18 he has been a heavy smoker (approx. 50 cigarettes daily). About 18 months before his admission to hospital (March '83) the patient had a respiratory tract infection and his symptoms as listed above seem to have started then and continued since. There were no other significant findings in his Past History or in his Family History.

Following a medical examination and a battery of laboratory investigations, the patient was diagnosed as having ACUTE RENAL FAILURE.

The patient's health deteriorated rapidly and peritoneal dialysis was instituted. Improvement followed. Kidney transplantation was contemplated for this middle-aged bachelor and after the decision was finalised he was put on haemodialysis (towards the beginning of April '83). The surgeons concerned stated that the operation was feasible at St. Luke's Hospital itself.

Choice of Donor:

The donor in this case was the living sister of the patient. A close blood relative was chosen as the best possible donor since, as a survey published in April 1973 showed, the closer the relation between donor and recipient the higher the survival rate over an 8-year period was. The success rate for unrelated cadaver donors was considerably less, for the same 8-year period. Apart from this, cadaver donors in Malta present many other problems - availability as well as moral and ethical.

Two main criteria may have to be fulfilled if the tendencies for rejection of the allograft are to be minimised:

1. HL-A compatibility
2. Blood Group (ABO) compatibility

between donor and recipient.

The HL-A system is said to be a strong one and therefore thought to assume a major importance in considering transplantation of tissues. These antigens are widely distributed in tissues but are not present in red blood cells. The RBC's on the other hand, contain antigens of the ABO system (ABH antigens). Since leucocytes carry all the known HL-Antigens, leucocyte agglutination and cytotoxicity tests are carried out to detect the presence or absence of the antigens. A *cross-match* between donor lymphocytes and recipient serum is then performed to confirm the results of the above tests. Well matched transplants (HLA-wise) sometimes do poorly whilst poorly matched transplants can do well. Although most units continue to match, some no longer do and simply rely on the ABO compatibility.

When a live donor is chosen he must essentially be medically healthy: preferably no hypertension; no systemic disease; no renal disease; and donor must possess two well functioning kidneys. The donor must therefore be adequately screened. Preferably the kidney to be transplanted must by supplied by not more than two arteries, hence a flush renal arteriogram and a selective renal angiogram are carried out on donor preoperatively. An ultrasound investigation or an intravenous pyelography are also done.

The patient himself must be thoroughly assessed medically: a Barium meal may be necessary to exclude peptic ulceration which, if present, could be aggravated by steroid therapy post-operatively. A chest X-Ray is necessary to exclude chest infection particularly tuberculosis; intractable urinary tract infection is an indication for bilateral nephrectomy.

Surgical Technique:

The left kidney from the donor is opted for since it has longer blood vessels leading to and from it. This kidney is rotated and placed extraperitoneally in the patient's right hemipelvis. The renal artery is anastomosed usually end-to-end to the internal iliac artery or if a cadaveric kidney is used the renal artery together with a patch of aorta is anastomosed end-to-side to the internal iliac artery. The renal vein is sutured end-to-side to the external or common iliac vein. The ureter is implanted in the bladder through a submucosal tunnel. Alternatively, the recipient's ureter may be anastomosed to the renal pelvis of the donor kidney.

If a right kidney (from a cadaver usually) is to be implanted, it is rotated and put in the recipient's left hemipelvis.

Management:

1. Suppression of Immunological Reaction which causes Graft Rejection:
   - AZATHIOPRINE 2-3 mg/kg body weight It is started before operation and continued post-operatively. The doses are decreased as renal function resumes.
   - ANTILYMPHOCYTIC SERUM (purified to IgG) can be a potent immunosuppressive but is still in the experimental stage.
2. Steroids
   - PREDNISOLONE 2 mg/kg started on the day of operation. Doses are decreased over 3 months gradually to a maintenance dose of 15 mg daily.
3. Fluid Balance
   - Hourly measurements of urinary output. The same volume is replaced with Dextrose Saline up to a urinary output of 200 ml/hr.
   - Insensible loss is replaced by 20 ml Normal Saline/hr.

Complications:

(A) Of Renal Transplantation itself:

1. Acute Tubular Necrosis
2. Rejection (a) Hyperacute (b) Acute (c) Chronic
3. Stricture or Fistula at Ureteric Anastomosis
4. Renal Artery (or vein) Thrombosis or Stenosis.
5. Urinary Tract Infection
6. Tertiary Hyperparathyroidism

- Acute Tubular Necrosis
  - — usually seen in cadaveric kidney due to prolonged total ischaemia time.
  - — donor was hypotensive before death
- Hyperacute Rejection
  - — is seen in some cases during the operation itself.
  - — antibody dependent.
  - — occurs if prior exposure has led to sensitisation.
- Acute Rejection
  - — 5-7 days post-op. Usually happens in cycles, the periods between which progressively becomes longer.
  - — T-cell dependent
  - — Clinical features:

  Symptoms: Lassitude, patient feels unwell, anorexia, oliguria, anuria, haematuria.

  Signs: Fever, ↑Blood Pressure, Kidney is enlarged and tender, ↑weight, unilateral leg oedema (on side of transplant) and scrotal swelling.

  Investigations: Leucocytosis, ↑B.U.N and serum creatinine, ↓Na^+ excretion, Proteinuria (in recurrent renal disease), Ultrasound:- enlarged kidney with echolucent areas in substance of kidney. Arteriogram:- decreased vascularity; vessels irregular (these features are reversed by Prednisolone therapy). Biopsy:- perivascular lymphocytic infiltration; interstitial oedema.
- Chronic Rejection
  - — detectable by biopsy long before clinical deterioration.
- Stricture or fistula at ureteric anastomosis
  - — inadequate blood supply of donor ureter.
  - — poor healing due to uraemia and immunosuppression.
  - — leakage of urine may follow.
- Urinary Tract Infection
  - — susceptibility is increased by immunosuppression.
  - — catheterisation of ureter for splinting the ureterostomy.
  - — catheterisation of urethra to protect cystostomy.
  - — any microbe can be responsible; bacteria, viruses, protozoa, fungi.
  - — septicaemia is a constant threat.
- Tertiary Hyperparathyroidism
  - — hypercalcaemia due to hypertrophy of parathyroid glands during long period of antecedent chronic renal failure.
  - — may be due to adenoma of parathyroids in some cases.
- N.B. Hypertension
  - — post-transplant hypertension may accompany acute or chronic rejection or renal artery thrombosis or stenosis.
  - — occurs in 18-83% of patients.
  - — Hypertension due to other causes must be excluded e.g. essential hypertension, recipient's original renal disease if nephrectomy has not been performed.
  - — It is an important risk factor for myocardial infarction and cerebrovascular accidents as well as for Renal Failure.
  - — a bruit is not always detectable in renal artery stenosis.

— angiography is an essential investigation to detect renal artery stenosis, however this is invasive and requires the use of a nephrotoxic contrast medium.
— Doppler ultrasonography sound-spectrum analysis is being used as a non-invasive screening procedure. (For a more detailed account, the reader is asked to refer to reference No.8 below.)

(B) Of Immunosuppression

1. Steroids (a) Impaired wound healing
   (b) Increased susceptibility to infection & sepsis
   (c) GIT bleeding; Pancreatitis
   (d) Avascular bone necrosis; Osteoporosis
   (e) Cushing's Syndrome
   (f) Cataract
   (g) Diabetes
   (h) Psychosis
2. Azathioprine (antimetabolite)
   (a) Hepatotoxicity
   (b) Bone marrow suppression

N.B. Sepsis

— is still a major cause of death in patients who have received a renal transplant. The severity and frequency of infection have been reduced by less aggressive immunosuppression.
— There is a place for perioperative antibiotic coverage but long-term antibiotics should be avoided.

(C) Long-term Complications include:

1. Atherosclerosis
2. Malignancy e.g. Lymphomas (reticulum cell sarcoma) and sarcomas of brain and skin after Antilymphocytic globulin.
3. Cushing's Syndrome with hypertension and Diabetes mellitus.
4. Peptic Ulceration and its complications.

Treatment of Rejection:

1. Prednisolone and Azathioprine together with intermittent high dose prednisolone.
2. Antilymphocytic globulin
3. Drainage of thoracic duct to deplete patient of lymphocytes.
4. CYCLOSPORIN A a cyclic polypeptide that has been shown to be a powerful immunosuppressant. Some investigators have been able to use it alone in the management of renal transplant patients whilst others have found it to be more effective in combination with low dose steroids.

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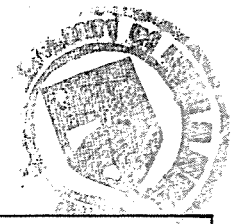
An Overview of Arteriosclerosis and Surgical Considerations of Coronary Arteriosclerosis.



A. YATES, MD., FRCS.
CONSULTANT CARDIOTHORACIC SURGEON
HEAD OF DEPT. OF CARDIOTHORACIC SURGERY
GUY'S HOSPITAL, LONDON.

In the western civilisation arteriosclerosis has become the major cause of death, accounting for approximately 65% of all deaths. In recent years it has increased in almost epidemic proportions.

Studies have shown that the disease process is initiated early in teenage life and progresses insidiously thereafter to produce extensive morbidity and death in later life due to ischaemic damage to the myocardium, brain, lower limbs and viscera.

The aetiology is multifocal and has strong social implications. The financially richer a society becomes the greater is the development of arteriosclerosis.

I. Diet

There can be little doubt that the major cause is dietary due to increasing intake of animal lipoprotein products such as cheese, cream and butter. It is interesting that all these foods are judged to be highly nutritious and desirable by poorer societies and are avidly sought after when income increases.

The offending constituents are probably saturated fats (found in all these foods) and to be more specific perhaps the low density lipoprotein fraction.

Not surprisingly the incidence of arteriosclerosis is markedly reduced in societies eating *poorer* diets of high carbohydrate and low animal protein content, eg. Japanese fisherfolk and Central African tribes. In populations that have suddenly acquired wealth, eg. certain Arab populations, and who have within one generation changed their dietary intake from low to high animal lipoprotein intake the incidence of arteriosclerotic disease has exhibited a dramatic step-like increase.

It is interesting to note that the *normal* range of blood lipids in high animal protein intake populations, eg. British, is higher than the *normal* range in low animal protein intake populations, eg. Japanese fisherfolk.

In England the Milk Marketing Board has for many years extolled us to "drink a pint of milk a day" from childhood to adulthood. I know of no better way of priming a population for arteriosclerosis!

There are other important aetiological factors:-

II. Inadequate Physical Exercise

Lack of regular physical exercise results in lack of episodes of vasodilated high blood velocity circulation. It is perhaps not simplistic to view periods of rapid blood circulation as a flushing mechanism of the vascular tree, not unlike how episodes of fast river flow stop silting. It would appear that significant physical exertion needs to be taken at least three times per week to be of benefit, and the level of physical exercise must make one at least breathe heavily.

III. Smoking

There is no doubt that smoking is an aggravating factor. A person smoking twenty cigarettes per day is eight times more likely to suffer symptomatic arteriosclerotic disease. Nicotine increases vascular endothelial permeability and it can be surmised that this allows greater passage of saturated fats into the sub-endothelial area where it cannot be cleared quickly enough to stop deposition which is the beginning of arteriosclerosis.

IV. Certain Other Diseases

These increase propensity to arteriosclerosis. Among these are:

(a) Familial Hyperlipidaemias:-
Again it is easy to surmise that the high blood fat levels in these families increases the tendency to sub-endothelial deposition. Many of these families give a history of generations of early death in the fourth and fifth decades of life from arteriosclerosis.

(b) Diabetes Mellitus:-
Again associated with increased blood fat levels.

(c) Systemic Hypertension:-
If the hydrodynamic pressure on the arteries is abnormally raised the blood fats will be increasingly pushed into the arterial wall with the same result as in Familial Hyperlipidaemia and Diabetes Mellitus.

When considering the pathology of arteriosclerosis there is initially a deposition of saturated fats in the vascular sub-endothelium of the major arteries. This is often more marked in the posterior wall, perhaps because of the significant proportion of one's life spent in the horizontal position sleeping.

The lesions that cause reducing blood flow and subsequent ischaemic damage are however localised accentuation of the arteriosclerotic process. These stenoses characteristically occur at points of arterial branching or occasionally where arteries are relatively fixed and immobile e.g. Adductor opening in the lower thigh. Experimental studies in the Angiology Department of Guys Medical School and elsewhere have revealed that at these arterial anatomical points a minor reduction in arterial lumen by early fat deposition causes haemodynamic mismatching which produces a retrograde reflection pressure wave from each pulse. In turn this retrograde reflection pressure wave quickly meets the next pulse and opposing forces produce a stationary standing pressure wave. This standing pressure wave is an expression of kinetic energy (in contrast to the potential energy) and exerts a damaging effect on the local arterial wall which in turn locally accelerates the arteriosclerotic process to produce localised progressive stenosis, often with ulceration. Further progress in this vicious cycle ends by producing local total arterial occlusion.

Blood flow down an artery begins to reduce when its cross sectional area is diminished by 75% i.e. quite late in the disease process. It is only then that tissue hypoxia begins to develop, producing symptoms such as angina and claudication. When occlusion occurs, and if there are inadequate collateral vessels and flow stops, then tissue death occurs causing myocardial infarction, strokes or gangrene of lower extremities or bowel.

It is only because of this mechanism of localised accentuation of the disease that it is possible for operative vascular reconstruction to be successful in relieving symptoms and avoiding tissue death. This surgical principle applies to all arteriosclerotic disease in the body where the offending stenosis or occlusion can be technically bypassed or removed.

Considering Coronary Artery Disease.

Modern investigating equipment and medical expertise allows studies of the afflicted heart by such methods as Thallium scan, Gated red cell studies and cardiac catheterisation with coronary arteriography to accurately detail the extent of any myocardial damage, extent of myocardial hypoxia and exact localisation of coronary stenosis or occlusions.

From these studies it is possible to accurately assess the operative possibilities, risks and prognosis of bypassing the coronary lesions. When the risk is low and potential benefits high, operation is advised.

The operation involves cardiopulmonary bypass, high technical expertise and teamwork including high quality post-operative intensive care. The long saphenous vein is removed and appropriate lengths are used to bypass the coronary lesions by micro-vascular surgical techniques.

Today the operative risk is usually only 1-2% and the patient is usually fit to leave hopsital on the seventh post-operative day. The number of bypass grafts varies, as indicated, from one to seven with most patients having three or four.

The operation is advised if the patient is crippled with angina despite full medical therapy. There is an 87% success rate in relieving the angina. More importantly coronary artery grafting is indicated if there are certain specific patterns of coronary artery disease, to increase life expectancy:

(i) Left main stem stenosis
(ii) Three separate lesions affecting major coronary artery branches - known as *triple vessel disease*
(iii) Stenosis at beginning of left anterior descending artery - known as the *widow maker*

A prospective controlled trial, the *European Coronary Control Trial,* involving over 750 patients in which my unit at Guys participated, has established that operating on the above groups of patients not only usually relieves angina but also significantly prolongs life.

It is because of the good surgical results in these types of patients that the operation of coronary grafting has become a major industry in Western Civilisation. In the U.S.A. 350 - 400 people per million population are being grafted *each year.*

Other operations on hearts afflicted by myocardial infarction can be life saving e.g. excision of left ventricular aneurysm, closure of ruptured ventricular septum and replacement of severely regurgitant mitral valves because of papillary muscle infarction.

There can be no doubt that primary prevention of this disease by population education with appropriate dietary and social changes is all important. This is proving to be a difficult problem to overcome but perhaps the forecasted world wide shortage of food will automatically produce the desired effect!

Meanwhile as long as arteriosclerosis exists in such major proportion surgery plays a very important part in alleviating hypoxic problems and avoiding ischaemic damage in the heart. There are also, of course, vascular operations to relieve the same problems with regard of blood flow to the brain, viscera and lower limbs.

Diabetes:

Aetiology and Pathophysiology of Diabetes Mellitus.

ANTOINE G. SCHRANZ MD
SENIOR DIABETOLOGIST SLH
LECTURER IN MEDICINE UNIVERSITY OF MALTA
PRESIDENT OF THE DIABETES ASSOCIATION

In the *Second report of the WHO Expert Committee on Diabetes Mellitus,* diabetes mellitus is defined as a state of chronic hyperglycaemia which may result from many environmental and genetic factors, often acting jointly. The major regulator of glucose concentration in the blood is insulin, a hormone synthesized in and secreted by the ß-cells of the Islets of Langerhans in the pancreas. Hyperglycaemia may be due to a lack of insulin or to an excess of factors that oppose its action. This imbalance leads to abnormalities of carbohydrate, protein and lipid metabolism. The major effects of diabetes include characteristic symptoms, ketoacidosis, the progressive development of disease of the capillaries of the kidney and retina, damage to the peripheral nerves, and excessive arteriosclerosis.

Aetiology

N. Freinkel's recent review on the aetiology of diabetes confirms that significant developments in the last few years have clearly indicated that *primary* or *idiopathic* diabetes represents a syndrome characterized by absolute or relative insulin insufficiency but mediated by a number of different causes. In the least, insulin-dependent diabetes mellitus, IDDM, (i.e., Type I, formerly designated as juvenile-onset or ketosis-prone diabetes) and non-insulin-dependent diabetes mellitus, NIDDM, (i.e., Type II, formerly designated as maturity-onset or ketosis-resistant diabetes) represent wholly different entities rather than simple quantitative gradations of insulinopenia.

The high concordance rates for NIDDM in monozygotic twins, even when they are geographically separated, suggests that intrinsic factors are of greatest aetiological significance in this population. Unfortunately, however, the site and nature of these intrinsic determinants have not yet been identified. The inborn defect(s) in NIDDM probably reside in some aspect of islet function.The variable patterns of insulin secretion in NIDDM are strongly suggestive of aetiological heterogeneity, and the differences between non obese and obese NIDDM are particularly noteworthy in this regard. Total secretion of insulin is most frequently attenuated in the lean, whereas the obese more often display exuberant insulin release. The delineation of a new subgroup of NIDDM with unique genetic properties, i.e., maturity-onset type of diabetes in young people (MODY), has provided some of the best evidence for aetiological heterogeneity. However, for the moment, it can only be concluded that environmental modifications may not appreciably modify the incidence of any type of NIDDM in view of the strong genetic overlay. Such manipulations should however, modify the severity, and perhaps even the time of appearance.

The less constant genetic pattern in IDDM than in NIDDM suggests that environmental factors may exert a greater aetiological impact. It seems probable that the correlations between HLA and IDDM reflect linkage disequilibria between genes determining vulnerabilities to IDDM and those coding for HLA antigens. As regards the environmental factor to which IDDM are genetically vulnerable, mounting evidence implicates virus in some instances, possibly variants related to Coxsackie virus B_4.

Chemicals may also be contributory, however, the impact of these may be mediated in a complex fashion. The underlying genetic vulnerability seems to reside in the manner in which the beta cell handles the environmental factor.

Genetic factors could determine the initiation of autoimmune processes spontaneously or in combination with the traumatizing variables cited above.

Pathogenesis

In J.S. Skyler et al's recent article on insulin update in Type I diabetes, one reads that current formulation of the pathogenesis of Type I or insulin - dependent diabetes mellitus (IDDM) is that a combination of genetic and environmental factors cause this condition. There appears to be a genetic predisposition conferred by a *diabetogenic* gene,

which resides on the short arm of chromosome 6 near the HLA region. The question of whether more than one diabetogenic gene exists or whether such genes might reside on other chromosomes is the subject of ongoing investigation. It appears that environmental triggers, in susceptible individuals, may initiate a pathogenetic sequence that results in pancreatic islet ß-cell damage. The most likely candidates as environmental triggers are viral infections and chemical toxins. The initial ß-cell damage appears to be perpetuated and sustained by an immune response, leading to further ß-cell destruction and consequent absolute insulinopenia. A period of partial remission, in which some ß-cell function recovers, may occur shortly after the onset of IDDM. Such remissions generally are of short duration. After the remission, absolute insulinopenia again emerges, although minimal endogenous residual insulin secretion can be demonstrated in some patients.

The impairment of insulin secretion in IDDM involves both meal-related incremental insulin secretion, responsible for utilization and storage of nutrients, and basal insulin secretion between meals, responsible for modulating hepatic glucose and metabolic homeostasis in the postabsorptive period.

The same author in an editorial on the improved understanding of Type II diabetes states that still not clearly defined is the fundamental defect or defects involved in the pathogenesis of Type II non-insulin dependent diabetes mellitus. Abnormalities in both insulin secretion and insulin action have been demonstrated, and there has been considerable debate as to which is the predominant lesion.

Impaired islet ß-cell function in Type II diabetes is manifested in at least three ways:

(1) absence of first phase insulin response to glucose, resulting in an overall *delayed* insulin secretory response to glucose; in most circumstances, however, second phase insulin response is sufficient to control postprandial glucose excursions, restoring plasma glucose to basal (preprandial) levels before the next meal, albeit prolonged postprandial glucose elevation;

(2) decreased sensitivity of insulin response to glucose, such that insulin response to glucose is attenuated, and that the islet ß-Cell shows a relative *blindness* to hyperglycaemia;

(3) decreased overall insulin secretory capacity, particularly in more severe Type II diabetes. It can be generalized, from various studies recently carried out, that patients with the most severe degree of Type II diabetes evidenced by significant fasting hyperglycaemia (i.e. fasting plasma glucose > 200 mg/dl), have the greatest impairment of islet ß-cell function and are relatively insulin deficient.

Impaired insulin action in Type II diabetes, i.e., insulin resistance, can be demonstrated in terms of both decreased insulin-mediated glucose disposal and subnormal suppression of hepatic glucose output. The insulin resistance in Type II diabetes is due to an impairment of insulin action at target cells. Although there is variability in the degree and nature of insulin resistance among different individuals and among different tissues within an individual, two categories of insulin resistance have been identified:

(1) decreased insulin binding to cellular receptors;

(2) defective insulin action as a consequence of defects in the effector system beyond the level of insulin binding to cellular receptors, collectively referred to as *postreceptor defects*.

In patients with impaired glucose tolerance or mild Type II diabetes, the degree of postreceptor defect is minimal, whereas in patients with more severe degrees of type II diabetes, evidenced by significant fasting hyperglycaemia (i.e., fasting plasma glucose>200mg/dl), the degree of postreceptor defect is marked, resulting in the greatest degree of insulin resistance.

R.S. Sherwin and P.H. Felig's account on the pathophysiology of diabetes further explains that inadequate insulin availability is the primary factor underlying the alterations in fuel homeostasis and counterregulatory hormone secretion which characterise the diabetic syndrome. With regards to fuel homeostasis the metabolic alterations observed in diabetes reflect the degree to which there is an absolute or relative deficiency of insulin. Viewed in the context of insulin as the major storage hormone, a minimal deficiency results in a diminished ability to increase effectively the storage reservoir of body fuels because of inadequate disposal of ingested food stuffs (e.g., glucose intolerance). With a major deficiency of insulin, not only is fuel accumulation hampered in the fed state, but excessive mobilization or production of endogenous metabolic fuels also occurs in the fasted condition (e.g., fasting hyperglycaemia, hyperaminoacidaemia, and elevated free fatty acids). In its most severe form (diabetic ketoacidosis), there is overproduction of glucose and marked acceleration of all catabolic processes (lipolysis proteolysis).

With regards to the role of insulin antagonistic hormones, glucagon contributes to the diabetic state primarily in circumstances of insulin deficiency. In diabetes suppression of glucagon by glucose is lost and protein-stimulated glucagon secretion is augmented. Glucagon hypersecretion may exaggerate the metabolic alterations accompanying insulin deficiency. However, relative or absolute insulin lack is the essential factor necessary for the changes in fuel mobilization and utilization which characterize diabetes. In contrast to glucagon, physiological elevations of cortisol or epinephrine markedly accentuate hyperglycaemia and hyperketonaemia in diabetics even in the face of insulin treatment.

The Assessment of Competence of Students in the Health Field

DR. ABRAHAM GALEA M.D.
FRCP(G), FRCP(ED), FRCPsych, D.P.M.
PHYSICIAN SUPERINTENDENT MT. CARMEL HOSPITAL
SENIOR LECTURER IN PSYCHIATRY
UNIVERSITY OF MALTA

A summary on a Report of a WHO Working Group, (Sept, 1980)

In September 1980, the World Health Organisation set up a *Working Group* entrusted with the task of re-examining assessment systems currently employed by Member States of the WHO in the evaluation of competence of students in the health field, the finding of faults within these systems, the identification of general principles involved in the planning of an adequate assessment programme, and the suggestion of practical ways whereby these principles could be implemented.

The members of the Working Group met over a 4-day period (23-26th Sept. 1980) during which assessment practices throughout Europe were reviewed, and associated difficulties and problems were discussed.

The purpose of the Working Group was to indicate what action might be taken by Member States to improve existing assessment arrangements. During the course of the meeting, the following *principles* were identified:

An *assessment programme* is *essential* in Medical Training:

a) for *the student*, because it provides information as to "where he stands" in comparison to his peers and to a standard norm, i.e. it demonstrates whether he has learned the facts and skills that are expected of him. In this way, *the programme has a great bearing on how and what a student learns.*

b) for *the teacher*, since it indicates how effectively learning and teaching are progressing.

Being so important, it is essential that the assessment programme be appropriate, relevant, effective and efficient and that the information obtained from it be valid and reliable.

A wide variety of programmes exist; there is no fixed 'ideal' one that can be employed by all Member States. Any assessment system must be planned as an integral component part of an institution's total educational programme; it must take into consideration the needs, plans and policies of the individual country.

Assessments tend to concentrate too much on the *recall of factual knowledge,* which is just ONE of the several pre-requisites of the would-be-doctor or health worker. Other vital attributes, like, for instance, the ability to generate and test, hypotheses, to solve problems, to communicate and work with others, to make relevant observation, to examine patients, to write clear concise readable case-notes, to execute diagnostic and therapeutic procedures etc., are *NOT TESTED* and are of equal importance.

Thus many currently used assessment programmes are *inappropriate and unreliable.* Assessment should not emphasise the recall of factual information but should concentrate on the application of such knowledge, the performance of tasks and the solution of problems. More emphasis needs to be placed on what the student *can actually do.*

The student should be assessed on 'the whole' rather than on the 'details of a part'; he must not fail to see the wood for the trees.

Assessment questions should be closely related to real-life situations, and should examine performance of students on medical emergencies and life-threatening situations rather than proficiency in academic detail. Assessment should concentrate upon performance in real-life settings.

The aim of the assesment should be to guide the student through his studies, rather than to "pass or fail" him. Consequently, continuous informal assessment by tutors and self-assessment by the student himself should be encouraged.

The assessment programme should not interfere unduly with student learning and should be based upon the observations of a number of examiners made over a period of time.

Change from traditional examining methods is necessarily difficult because old methods tend to become traditional and time-honoured. Each Member State should however re-examine its own systems and establish new and alternative methods and techniques.

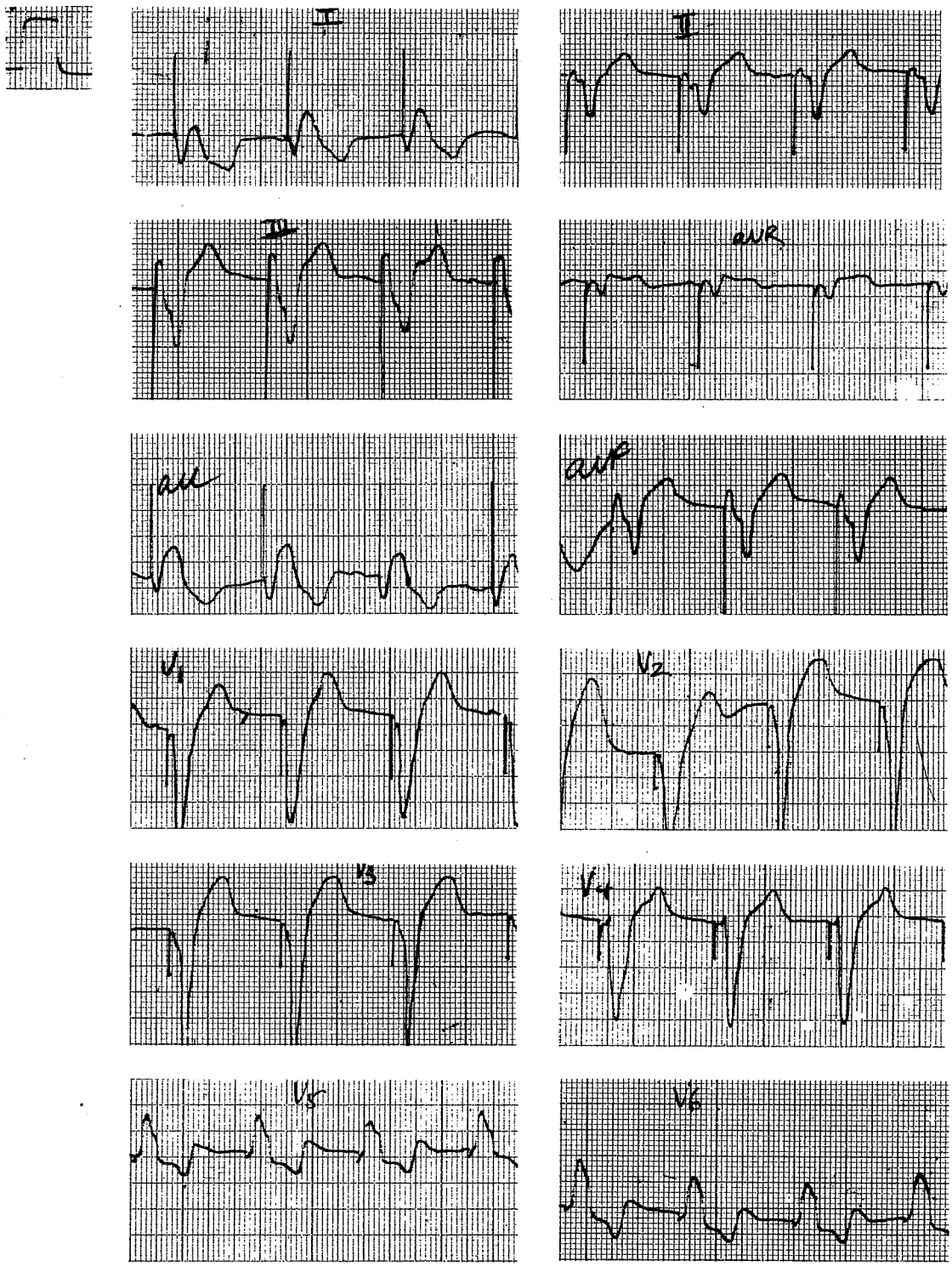
Both teaching and administrative staff should have a sound practical knowledge of available assessment techniques and of the educational principles behind them.

Also, the student should always be informed of the function and detailed nature of the assessment system, and of what is reasonably expected of him.

Clinical Diagnosis

What characteristic feature can you spot in this ECG tracing?

What could the patient be suffering from?



Send your answers to THE EDITOR. The answer will be published in the next issue. One correct answer will be drawn by lot and the winner will receive an appropriate prize.

Collis Williams

300 REPUBLIC STREET, VALLETTA

Tels. 24104 624567

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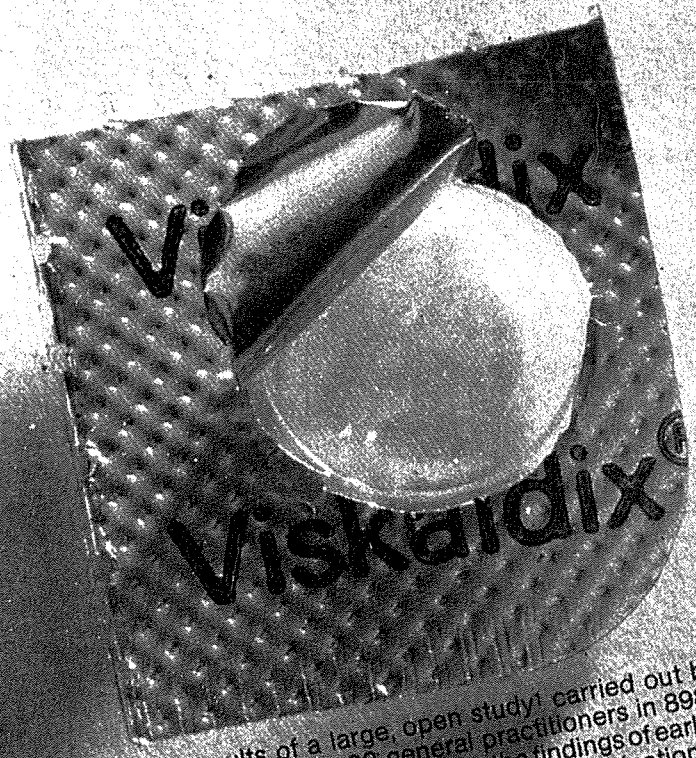

Betablocker + Diuretic in a single tablet

The results of a large, open study[1] carried out by approximately 4000 general practitioners in 8989 hypertensive patients confirm the findings of earlier investigations in showing that the combination of 10 mg of the beta-adrenoreceptor blocking agent pindolol and 5 mg of the diuretic clopamide in a single tablet is a very effective treatment for mild to moderate hypertension in patients of all ages. Only one tablet daily was required by 83% of the patients.

1 "Current Medical Research and Opinion" Vol. 6, No. 8, 1979, pages 342–350 Crowder, D. and Cameron, C. M.

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"The property of cardioselectivity in a beta blocker is not 'all-or-none'; it is a relative quality. Atenolol ['Tenormin'] appeared to be the most cardioselective compound available."

Benson, M.K. *et al* (1977)

Hepatitis B

Hepatitis B accounts for almost a third of the cases of viral hepatitis which occur today. Its incubation period is long, its effects can be severe or even fatal, and its complications far-reaching. Curative therapy is non-existent, and a number of those infected become asymptomatic carriers.

Hepatitis B - The risk of infection

18.5% of a sample of U.S.A. doctors showed serological evidence of previous hepatitis B infection.

Contamination of skin abrasions.

Accidental needle puncture.

Present in urine.

Hepatitis B - The tip of the iceberg

50 to 60% of infections are sub-clinical, asymptomatic, and at the time of infection usually undetected.

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