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JOURNAL OF THE MALTA MEDICAL STUDENTS' ASSOCIATION

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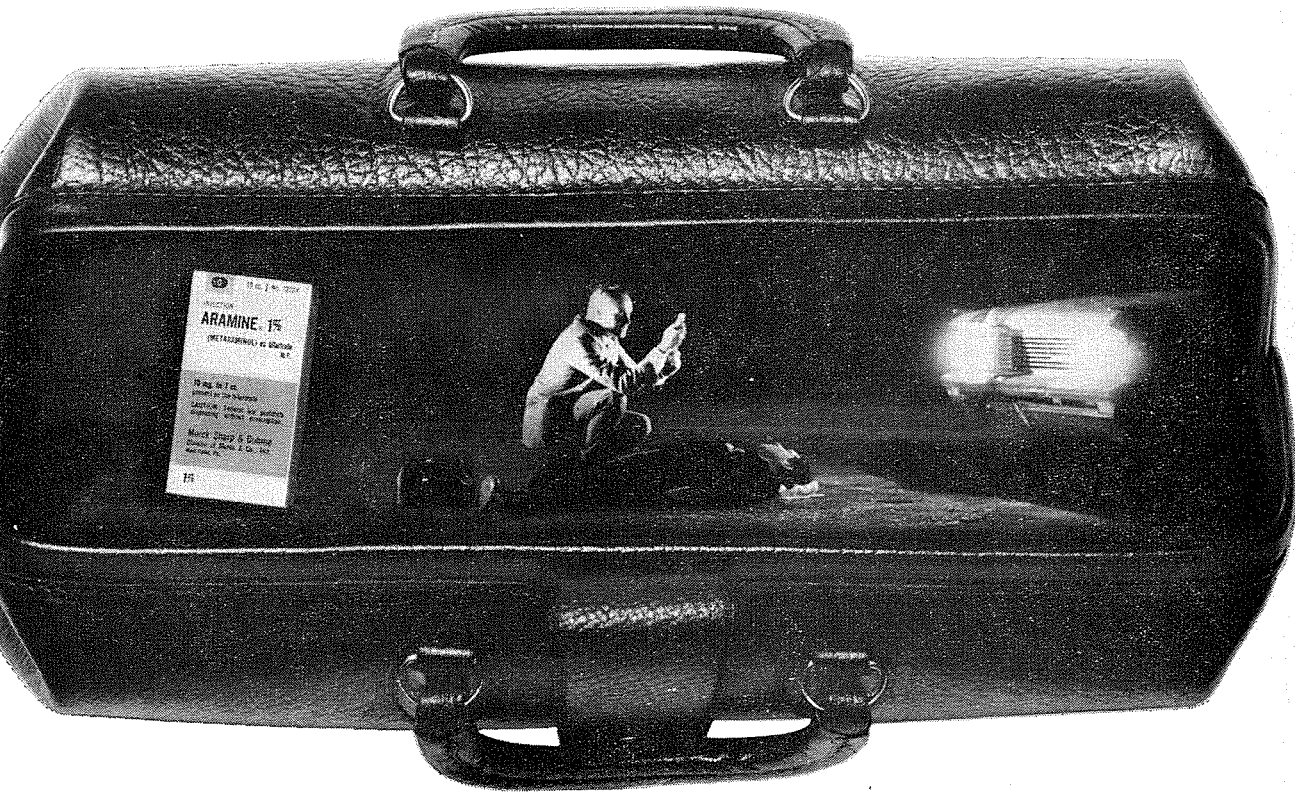

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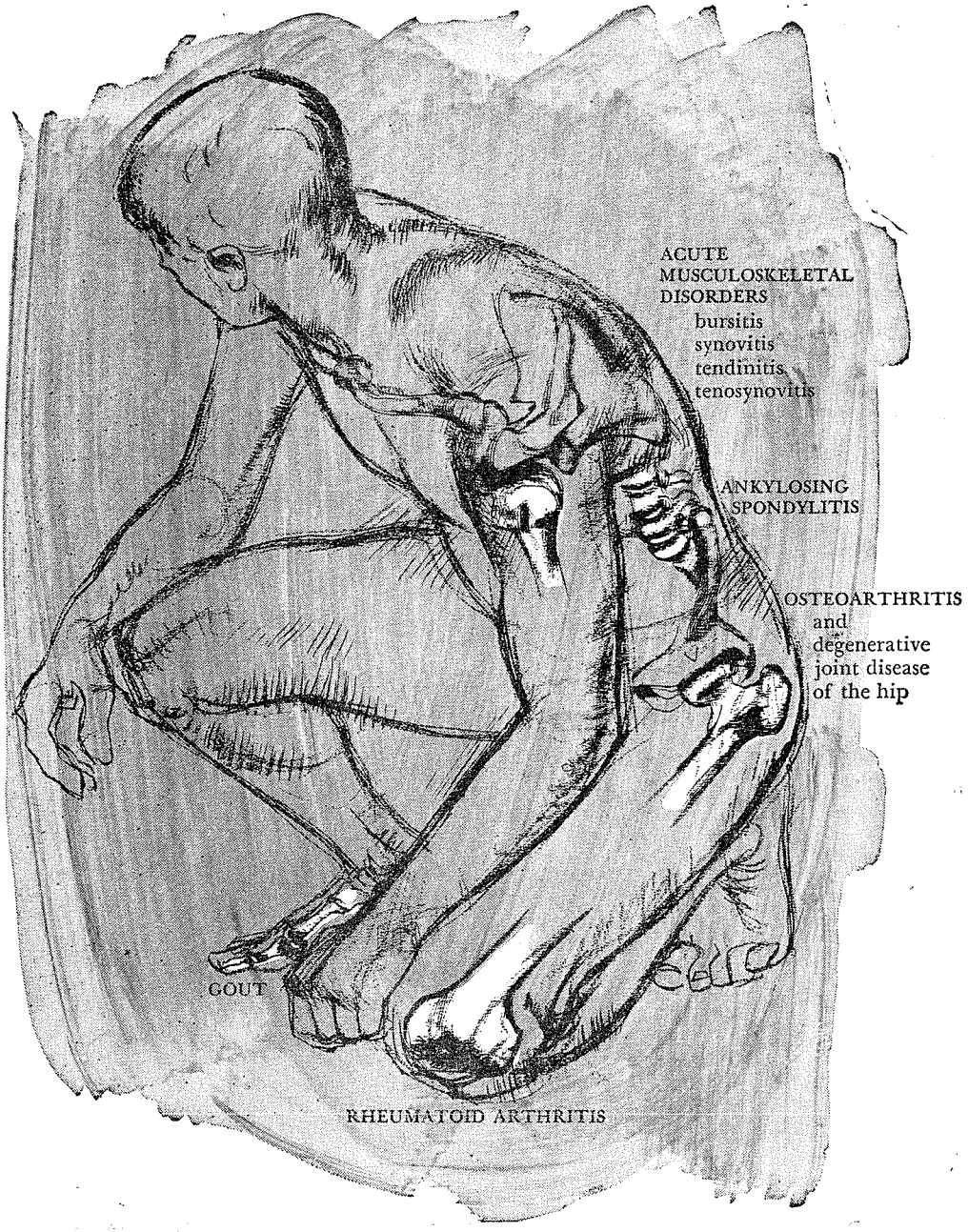
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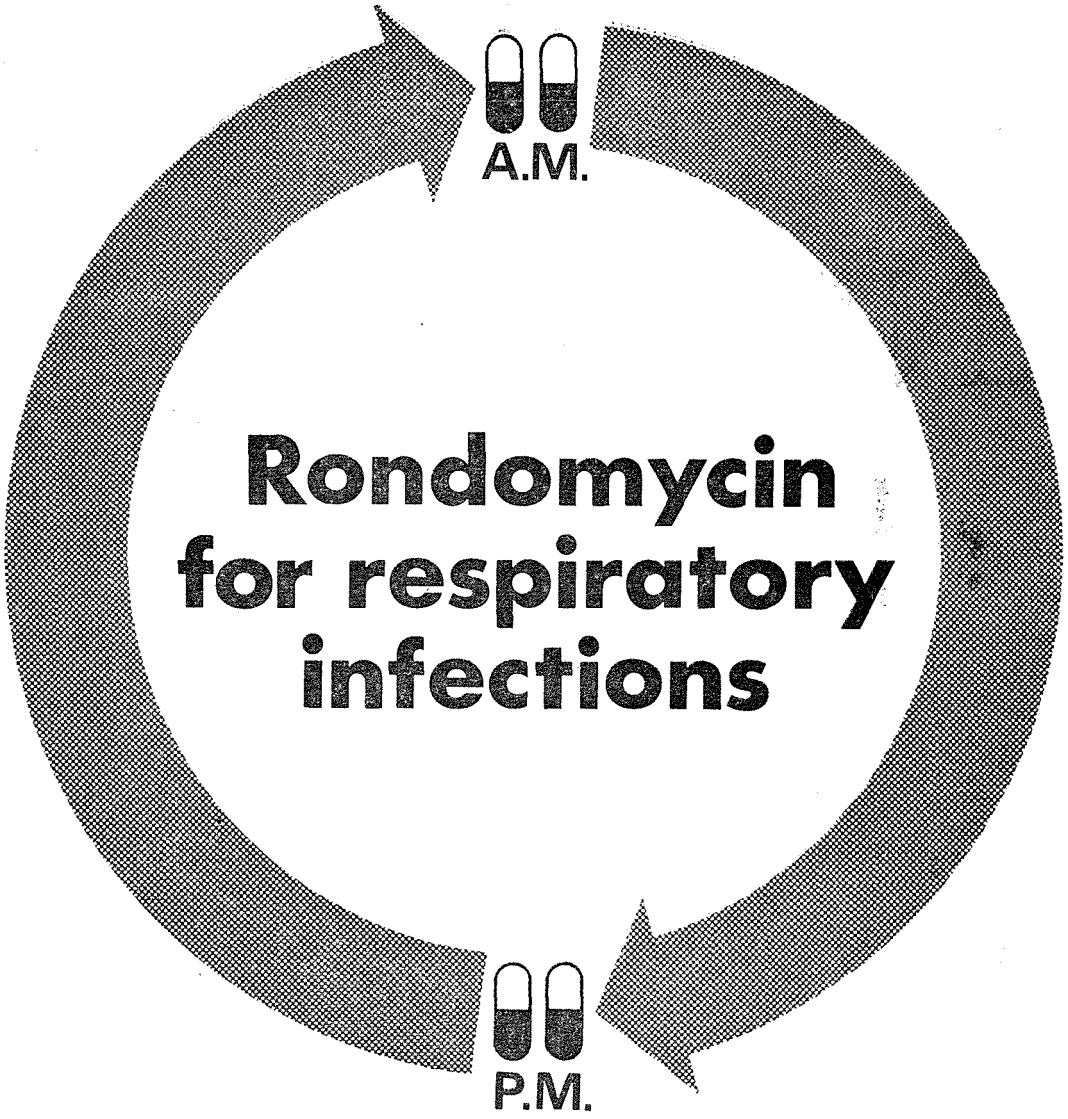

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EDITORIAL

Important changes in medical teaching will be taking place within the next few years in Malta, due to a number of causes among which are: the larger intake of students, their greater preparedness and maturity due to the recent imposition of an age limit on University entrants and to changes in premedical and preclinical teaching. The Medical School has been in operation for three years and its facilities are being gradually expanded. There will be more students from overseas following the invitation by the Minister of Health to Commonwealth countries at Edinburgh last October.

By that time, students in the present course will have already qualified. What they need are changes right now in areas which immediately affect them. The ambition of every medical student is first of all to become a good doctor. To attain this he needs adequate opportunity to learn as much as he needs during his student days, in preparation for the lifelong postgraduate education he will have to embark upon once he is qualified, if he is to remain a good doctor.

Present conditions are not ideal for this. The student is being subjected to an ever increasing volume of instruction which is not leaving him enough time to assimilate well and in full what is being taught him. The culprit here is the lecture. There is an excess of lectures which is robbing students of time for reading and revision. The Final Course is at present having a total of 4 hours of lecturing each day. It is impossible even to keep up with reading of what has been lectured upon, let alone with any reading arising out of clinical work, etc.

What is needed is not so much a drastic cutting down on lectures as a short term measure, but a fresh examination of the needs of modern medical teaching. A reassessment of what is important and what is not in the curriculum, and what should be done in undergraduate days and what should be left to postgraduate specialist teaching, will automatically bring in its wake a cutting down of unimportant detail, and therefore of an amount of lecturing. Such reappraisal is going on in Medical Schools around the world. The I.F.M.S.A. is taking a part in this, largely through the Standing Committee on Medical Education, and reports on such changes in its journal Intermedica.

This has been done in a number of departments, where it has resulted in a notable relief in the work load of the students, who follow their work in those departments more keenly and enthusiastically, and with better results, both immediate and long term. If something similar is done in those departments where it has not been done, it would allow students to get a better grasp of principles and to get on with their work. It is important that as much as possible is done now. After all, the Final Course has only one and a half more years to go.

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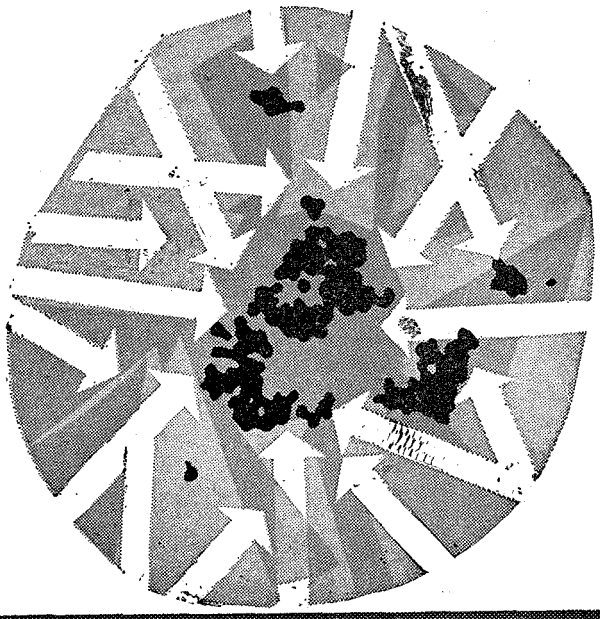

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A SHORT HISTORY OF VIROLOGY

EMANUEL AGIUS, B.Sc., M.D., D.P.H., D.Bact., F.C. Path.

When W.W.C. Topley and G.S. Wilson in their famous textbook, as long ago as 1936, prophesied that "the years ahead of us will be the eighteen eighties over again", referring to the great age of bacteriological discovery, they were, like all prophets, risking their reputation. In fact they have been right perhaps even beyond their expectations for at that time both the electron microscope and tissue culture methods were still in their earliest days. Virology has progressed with gigantic strides and it has now not only shed light on previously obscure medical problems but provided the biologist and the geneticist with tools with which to pursue many fundamental studies.

It would be accurate to say that two of the most useful applications of virology were made before viruses as such were known and studied. Jenner's discovery of vaccination as a preventive measure against smallpox has a long and complicated history, starting in 1789 when he tentatively inoculated his firstborn son first with pus from a case of swinepox and then, for 5 times with virulent smallpox, and progressing to 1807 when his methods were widely accepted and the House of Commons voted him a large award as an expression of Britain's gratitude. Pasteur's discovery of the vaccine against hydrophobia, first put to human use in 1885, was the second case in which a dramatic effect was obtained in spite of the fact that the scientific rationale was still deficient in details.

The first person to see viruses was the Scotsman John Brown Buist, who, in 1887, being a bacteriologist in the university of Edinburgh, examined pus from a cowpox lesion. Guarnieri in 1892 described what are now known as the inclusion bodies of smallpox and cowpox. The Frenchman Amedèe Borrel reported seeing the virus of fowlpox in 1904, and in 1906 Paschen described the elementary bodies of cowpox which were the actual virus. All these findings could occur since the cowpox and smallpox viruses are among the larger, being from 150 to 260 millimicrons in size and therefore just come within the powers of resolution of the ordinary light microscope.

Dmitri Ivanowski in 1892 read a paper to the Academy of Sciences in St. Petersburg (which is now Leningrad) on the mosaic disease of the tobacco plant. He did not apparently attribute the disease to an infective agent, but towards the end of the paper he stated that he had found the juice extracted from affected leaves was still infective after filtration through a Chamberland candle. Martinus William Beijerinck, a plant pathologist and bacteriologist (1851-1931) is best known for his extensive studies of bacteria symbiotic on leguminous plants. He worked on tobacco mosaic disease and discovered a filterable infective agent to which he attributed far greater importance than Ivanowski had done, but unfortunately he thought of the agent as a fluid, as a *contagium vivum fluidum* and thereby the value of his discovery escaped him.

In the veterinary world Friedrich Loeffler and Paul Frosch in 1898 discovered

foot-and-mouth disease to be caused by a filterable agent, whilst the first human disease to be definitely attributed to a virus was yellow fever, discovered to be so by Walter Reed and James Carroll in 1901. Once the technique had been developed many other illnesses became attributable to viruses. William Elford of the National Institute for Medical Research of Great Britain by his development of collodion membranes to act as filters round about 1931 not only gave the death blow to any lingering conception of a fluid infective agent, but definitely established the size of the more important viruses then known.

Two of the most interesting discoveries in medical science were the independent ones by Frederick Twort in 1915 and by Felix D'Herelle, first made public in 1917, of bacteriophages. Twort had observed a glassy clearing on a culture slope, proved its transmissible nature and rightly attributed to what he called "an acute infectious disease of the (bacterial) colonies". He also detected the filterable nature of the agent and its specificity. Twort's report duly appeared in a 1915 issue of the "Lancet", and established his priority. When D'Herelle was in Mexico in 1910 at the time of a locust invasion, he had his attention drawn to a diarrhoeic disease from which the insects were suffering. He discovered that a specific microorganism was causing this and on cultures of these he noticed clear spots. D'Herelle used the bacteria to start an epidemic amongst locusts which in 1915 were invading Tunisia and there he again observed the phenomenon, having this time the opportunity to discuss the matter with Charles Nicolle, who supported his idea that a filterable agent might be the cause. This was confirmed when D'Herelle observed the phenomenon once again in connection with cases of dysentery in France in 1915, this time definitely proving the filterability. D'Herelle's complete researches were published in 1921 in a long monograph entitled "The bacteriophage, its role in immunity". Though bacteriophages have not yet come to play the therapeutic role for which their discoverers had hoped they were cast, yet they have assumed an importance almost as great in the study of the intimate structure of living things.

The development of virology has run concurrently with developments in technique. What had made the work difficult was the smallness of the microorganisms which set them beyond the reach of ordinary microscopes and the impossibility of growing them away from living cells and it was as these obstacles were overcome that progress was made, researchers being driven by the impellent necessity to find ways of preventing some of the most widespread and dangerous diseases, mainly yellow fever, influenza and poliomyelitis.

Yellow fever became an illness of direct interest to a country highly organised scientifically with the involvement of the United States of America in Cuba in the last years of the nineteenth century. It was the American investigators Reed, Carroll, Agramonte and Lazear who, acting on the theory of Carlos J. Finlay of Havana established the fact that yellow fever was transmitted by special mosquitoes and discovered in 1901 that the illness could be produced in human volunteers by bacteria-free filtrates of serum from patients. This was not fully established until Adrian Stokes, Bauer and Hudson succeeded in infecting a *Macacus rhesus* monkey in the Gold Coast as late as 1927. The terrible illness took toll of many of those who investigated it. Stokes died in 1927 in Nigeria, Hideyo Noguchi in Accra in 1928, William Young at 40 a few months later, Paul Lewis aged 50 in 1929 in Brazil and

Theodore Hayne at 32 in 1930 in Nigeria. The construction of the Panama Canal through what was a yellow fever zone started, for the second time in 1906, and fully completed in 1920, put the entomological findings to a severe test. The Rockefeller foundation, founded in 1913, made the study of yellow fever its special objective and since 1916 has spend over fourteen million dollars in research on it. In 1929 Sellards of the Harvard Medical School carried to America a monkey liver infected with yellow fever from a Syrian patient in Dakar. Sellards's partner was Max Theiler, of Swiss origin, who had been born in South Africa, had graduated in medicine in London and studied at the London School of Hygiene. Theiler discovered that mice could be infected if inoculated intracerebrally and that whilst mouse passage heightened the virus' virulence for that species it lessened it for monkeys. Theiler himself contracted an infection and had only a mild attack, prhaps because the virus had been attenuated by passage. Theiler also discovered the neutralisation test as applied to mice for yellow fever, using serum from human laboratory infections. The French faced with the stern necessity of safeguarding the people in their equatorial possessions against yellow fever, promptly adopted the use of the modified Dakar virus by inoculation in the skin and administered the mouse brain cultures to fiftysix million persons between 1939 and 1953.

Theiler was concerned with developing a more secure vaccine. He cultivated the Asibi strain — later known as 17D — on a Maitland type of tissue culture. consisting for the first passages of whole chicken embryos and for the next, to avoid neurotropicity, of chicken embryos without their central nervous system. In November 1936 Theiler, Smith and Lloyd tested the virus which had now been attenuated on thmmselves and on Dr. Thomas Francis Jr., all four having immunity against yellow fever through previous accidental infections. They had some reaction and developed a rise of antibodies. It was next tested on 8 persons with no previous immunity. In March 1937 it was announced that a yellow fever vaccine for an extended trial was available. Theiler later adopted the egg membrance method of culture. Between 1940 and 1947 the Rockefeller Foundation had produced over 28 million doses of vaccine distributing them gratis, and thus a great pestilential disease was effectively halted: the millions which old John D. had made out of that oil which his father had once peddled as a cureall had been put to excellent medical use after all.

The history of influenza so far is as interesting as that of yellow fever though not yet so successful. Attention has remained focussed on the illness since 1918-19 when a pandemic, the greatest in history, attacked some five hundred million people killing, through its pulmonary complications, twentyone million. An influenza epidemic amongst swine also appeared first in 1918 in Western Illinois, U.S.A., the disease running roughly parallel to that in man, although it persisted in swine after the human epidemic had died out. The epidemiology of swine influenza was studied by Shope and some very complex cycles were discovered involving the swine lungworm and the earthworm.

The discovery of the influenza virus was made in 1933 at the National Institute for Medical Research at Hampstead by Wilson Smith, Christopher Andrews and Sir Patrick Laidlaw, largely consequent on the discovery of a suitable experimental animal the ferret, which had come into use in studies on canine distemper. The

etiological connexion of the ferret-passaged virus was clinched when an infected ferret sneezed in Dr. Wilson Smith's face and infected him with influenza, furnishing the first strain of human influenza to be definitely isolated, which was appropriately labelled W.S. Later this strain was successfully passed to anaesthetised mice by intranasal inoculation. Another well-known strain, the PR8 strain was isolated by Francis from Porto Rico cases and served to produced the first vaccines.

Laidlaw formulated the theory that the virus of swine influenza was the human 1918 virus adapted to swine. British and American workers found antibodies against swine influenza to be generally present in the blood of adults even if they had had no contact with swine and absent from the blood of persons born after 1920. In 1941 George Hirst discovered that the influenza virus agglutinates chicken red blood cells and that there was also specific agglutination inhibition by antibodies. It became evident that the antibodies present in a person's serum showed which virus had infected him in his early years.

The World Health Organisation in 1948 instituted the World Influenza Centre located quite fittingly at the National Institute in Hampstead.

A new type of A virus appeared first in a place near Kweichow in China in February 1957. It spread to Hong Kong where 10% of the population was affected. First samples were obtained by the 406 Medical General Laboratory of the American Forces at Zama in Japan, sent to the Walter Reed Medical Centre at Washington and identified as a new type, the Asian type. Antibodies against it could only be found in survivors from the 1889-92 epidemic. It was mild but highly infectious.

The millenial history of poliomyelitis as a clinical entity has now, following its study as a virus disease, reached a dramatic climax and one may reasonably hope it will reach a happy conclusion. Landsteiner and Popper in 1909 succeded in infecting monkeys and Flexner and Lewis showed that the illness could also be produced by filtrates, thus proving its viral etiology. Until about 1396 the view had prevailed that the poliomyelitis virus was exclusively neurotropic and an important landmark was the discovery by Paul and Sabin that the virus was commonly found in the faeces. In 1939 Charles Armstrong of the U.S. Public Health service found the virus to be transmissible to the cottonrat, and Jungeblat and Sanders that the rat-adapted strain could be passed to white mice.

The most interesting developments have been those associated with the attempts to produce a prophylactic since this illness could not be dealt with by non-specific hygienic measures. These attempts were closely linked with unusual circumstances. Franklin Delano Roosevelt had suffered from a paralytic form of poliomyelitis and when he later became president of the United States of America, at the suggestion of the well-known researcher and medical publicist Paul de Kruif, he founded in 1938, the National Foundation for Infantile Paralysis, with at its head for the first three years De Kruif himself and Mr. Basil O'Connor, an ex-president of the American Red Cross Society. De Kruif eventually withdrew leaving the leadership to O'Connor. O'Connor, an Irish-Catholic lawyer with a Harvard training had a dynamic and inspiring personality and was it seems completely resolved that he would give the medical profession no peace till it had given him and the world the means of preventing poliomyelitis. He organised the collection of funds, especial-

ly through the "March of Dimes" campaign about 1945 and was in a position to finance research very strongly.

Backed by a grant from the N.F.I.P. John Enders, Fred Robbins, and Tom Weller in 1947 set to work on virus diseases in the Jimmy Fund Building attached to the Children's Hospital at Harvard Medical School in the celebrated, colonnaded and imposing Lanwood Quadrangle. Their immediate objective was the cultivation of the mumps virus in tissue culture mainly on Maitland lines. They adopted a system of changing the medium rather than subculturing on the new cells and started the use of antibiotics to prevent infection. Weller was using skin and muscle human embryo tissue for culture of the chicken-pox virus. Having some flasks left over he inoculated them with poliomyelitis virus and found it survived and multiplied. Poliomyelitis could therefore be grown in cells other than nerve cells and it could be grown in vitro. It was also grown in intestinal cells. The first announcement was made in "Science" for the 28th. January 1949 and at last the road was opened for the preparation of vaccines, and O'Connor announced that the Foundation had fifteen million dollars available for such purposes.

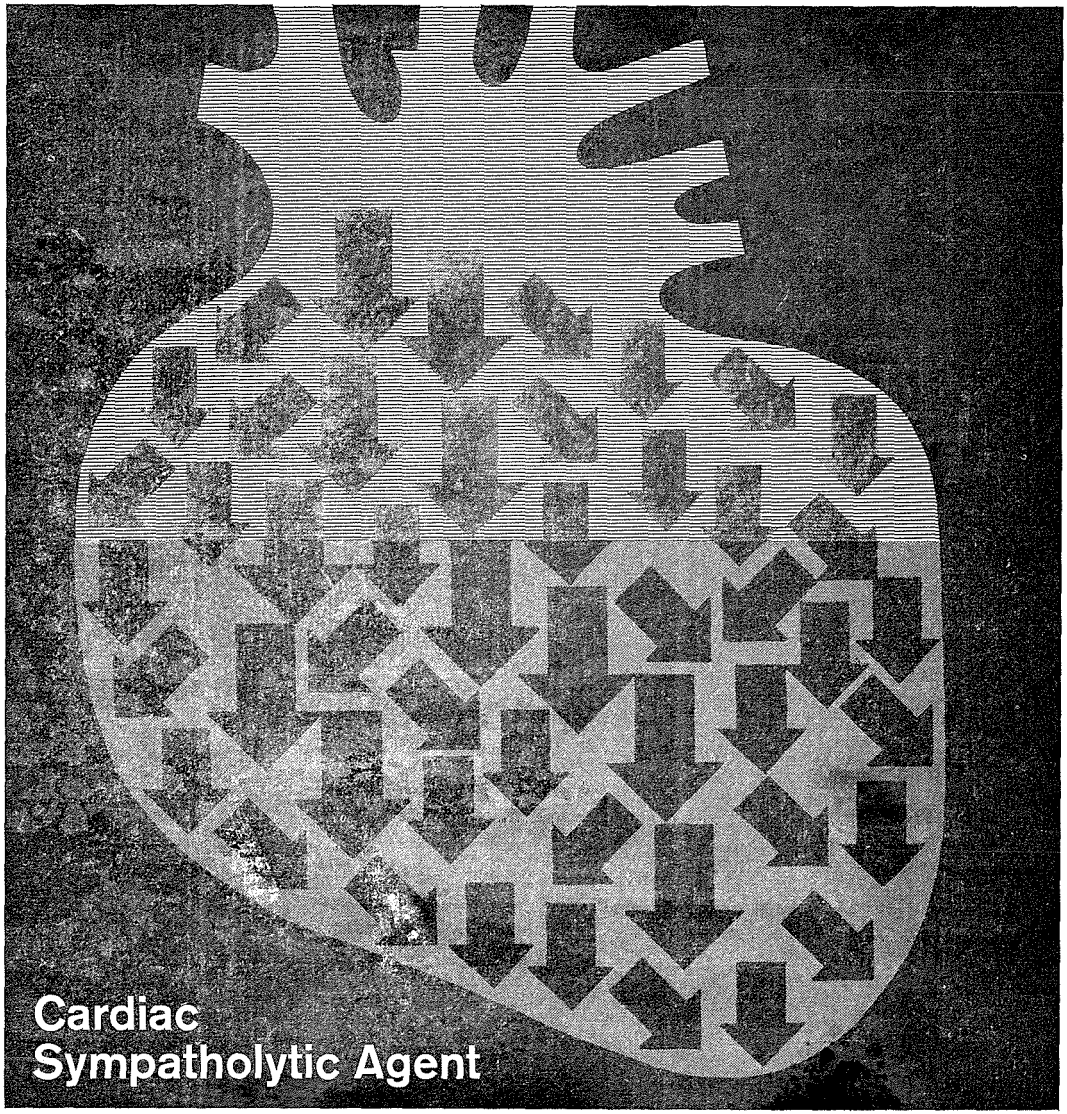
Many workers had tried their hand at vaccines before this, using monkey nervous tissue, notably Maurice Brodie using a formal killed virus and John Kolmer with an attenuated living virus. Both were tried out in 1935 somewhat ineffectively and inconclusively: their safety was, to say the least, suspect, and no more was heard of them. Brodie died in 1939 at the age of thirty under rather tragic circumstances. Fundamental work on poliomyelitis included the discovery in 1949 by Bodian, Howe and Mountain at Johns Hopkins of the three types of virus, and in 1952 by Bodian and Horstman independently of the viraemic phase of the illness. The National Foundation had a "Typing Committee" which included Sabin and Salk, which finished its work in 1951 and became the "Immunization Committee". Many accepted the financial backing of the foundation for research, including Salk and Sabin, and O'Connor felt it his duty to see that not a day should be wasted in developing an effective vaccine and in making it available to the public.

Jonas Salk had graduated from New York University in 1939, gone in 1942 to the University of Michigan at Ann Arbor on a fellowship from the National Foundation, and, in 1947 to the University of Pittsburgh School of Medicine. Being director of the Virus Research Laboratory he was in an excellent situation for developing a poliomyelitis vaccine to which he devoted all his attention. He decided on the use of a formalin-killed virus and the problem mainly was the necessity of making absolutely certain that no single particle of virus survived the treatment. In fact the preparation of every batch of vaccine was a research project by itself. Once sterility was ascertained, once the safety factor had been assured, the remaining problem was that of testing the vaccine's efficiency. This was first done on survivors of the illness in whom it was possible to note a rise in viral antibody titre, then on persons who had no natural antibodies. In May 1953 Salk vaccinated himself, his wife and his three young children. Others, first some hundreds and then some thousands were vaccinated, but in the last resort the effectiveness of this vaccine had to be assessed by a comparison of incidence in protected and in unprotected groups and numbers had to be enormous to give information of any

value. Thomas Francis of the University of Michigan was prevailed upon to devise and supervise such a test and eventually to assess its results. This he did, insisting on his own terms for conducting the vast experiment. The number of children involved was over a million and eight hundred thousand. Never before had any prophylactic measure been studied quite so scientifically, and never before probably had there been so much at stake. The result obviously could not be expressed in some few short phrases nor in a few percentage figures, but the gist of the Francis report was that Salk's vaccine was a safe and effective way of preventing the illness, especially its paralytic form. The Francis report was published on the 12th April 1955, which, purely by coincidence but a lucky one none the less, happened to be the tenth anniversary of the death of Franklin Roosevelt, who had inspired the great undertaking. Both Salk and Francis were careful to conduct the enquiry in a spirit of scientific detachment, but the event was such that it attracted the attention of the public at large and chiefly of the press who made of it front page news with the largest possible types. After a fortnight it became apparent that a tragedy was to mar the completeness of this success, when a batch of vaccine was found to have been incompletely treated and 77 cases of poliomyelitis were produced with 11 deaths. This was the sort of accident which everybody had been so careful to guard against. It soon became certain that this was due to a fault in the preparation of the special batch, but there had been nothing wrong with the method itself. Since then millions of doses of vaccine have been used without any untoward result and surely a large number of cases of poliomyelitis must have been prevented.

Meanwhile Albert Sabin at Cincinnati and Hilary Koprowski at Philadelphia were working on a vaccine with live but attenuated viruses. Sabin since 1955 has succeeded in producing attenuated strains of viruses of each type, and since 1957 his vaccine has been tried first on monkeys and chimpanzees, then on Dr. Sabin, his wife and children (doing something which is no less heroic because it has become almost traditional amongst researchers) then on a few hundred volunteers mainly from penitentiaries and subsequently on several million people in Russia and elsewhere. Sabin maintains that live vaccine by mouth produces a local and cellular intestinal resistance which prevents the passage of poliomyelitis virus, and he hopes that the vaccine virus will ultimately lead to the extinction of the pathogenic strains. The great problem in this and in the case of any live vaccine is the question of any possible reversion of the attenuated viruses to virulence. There does not appear to be any evidence that this has happened or is likely to happen. On the contrary there can be little doubt that the widespread use of Sabin's vaccine has effectively nipped in the bud epidemics in Singapore, in Hull and in Malta. Even there the results are not beyond questioning by statistical rules but workers in the field who saw the vaccine's effectiveness would be persuaded with the greatest difficulty if at all to refrain from using a measure so potent for good.

In 1947, working at the New York State Health department laboratory in Albany, by the use of new born mice, Gilbert Daledorf discovered the Coxsackie group of viruses, so called after a village with under three thousand inhabitants in the Hudson River Valley where the first patients came from. This discovery shed a great deal of light on polio-like cases. ECHO (enteric cytopathogenic human orphan) viruses, of which there are at least twenty types, were first identified in Ender's



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laboratory. These too could produce fever, and muscular pain, and were sometimes responsible for cases which, before they were known, would have been diagnosed as non-paralytic poliomyelitis. At the laboratory of Infectious Diseases in the National Institute of Infectious Diseases of the American Public Health Service in Bethesda, near Washington, the first virus of the adenovirus group was discovered, the whole group numbering over twentyfour types. Wallace P. Rowe and Robert Huebner cultivated it from adenoidal tissue removed at operations. One type, type 3, causing conjunctivitis, pharyngitis and fever was first isolated from Huebner himself and later from a laboratory technician and from a pediatrician, the latter, at least, having contracted the infection through his work.

Measles had in 1911 been proved by Joseph Goldberger, who had also discovered the cause of pellagra, to be a virus disease. In 1938 Harry Plotz, then working at the Paris Pasteur Institute cultivated the virus on chicken embryos. In 1939 G.W. Rake of the Squibb Institute for Medical Research and Morris Shaffer grew it on egg membranes. In 1953 Enders and T.C. Peebles grew the Edmonston strain (so called after a patient David Edmonston) on monkey and on human kidney cells. Samuel L. Katz and Enders himself in 1957 succeeded in attenuating the virus by prolonged passage and by its use in protecting monkeys. Tests on children so far can, at least, be considered promising and it appears likely that measles also will soon be under specific prophylactic control.

By an admirable process of exchange, virology has benefited enormously from pure research in other sciences such as biochemistry and optics and in its turn has contributed to the development of such sciences as genetics. As far back as 1935 William H. Stanley a chemist working in a laboratory of plant pathology of the Rockefeller Institute, succeeded in obtaining the virus of tobacco mosaic disease in crystalline form, and showed that it was an organism if within a cell and a chemical particle when out of it. Stanley first believed the virus particle to be a protein, but Bawden and Pirie of Cambridge found it to contain phosphorus through its content of ribonucleic acid, being a nucleoprotein with 94% of proten and 6% of nucleic acid. Tobacco mosaic virus has a molecular weight ranging from 40 to 50 million, being heavier than any known protein. In 1955 Carlton E. Schweldt and F.L. Schaffer succeeded in crystallising the poliomyelitis virus, obtaining just one crystal out of nine hundred litres of liquid monkey kidney tissue, obtained from the Connaught Laboratory in Toronto, a laboratory which has played a vital part in research, such as in that on poliomyelitis vaccination.

Virology owes its greatest debt to the development of the electron microscope, the first such instrument having been completed in Germany in 1931, by Ruska and Knoll. The first photographs were taken in 1933, the first virus to be photographed being that of tobacco mosaic disease by G.A. Kausche, E. Pfankuch and Helmut Ruska. Robley Williams ,at the time in the University of Michigan, was an astrophysicist who had concerned himself with the task of preparing thin metal layers for use in telescope mirrors; he met Ralph Wyckoff, a biophysicist who, as a lecturer in the same university, interested himself in viruses, and they found the method of metal shadowing viruses by exposing them to a shower of gold particles from a gold laden tungsten filament in vacuum. Since this was placed sideways the gold was deposited laterally producing a shadow effect as if the particles had been hit

by snow driven by a strong wind. Subsequently palladium and uranium shadowing were used. In actual fact the heat produced destroys the virus but the metal produces a cast. Technique has now advanced to a point when investigators have in their hands methods for cutting tissue sections only 100 atoms thick and when electron microscopes can resolve detail only 10 atoms across.

Yet another and most important technical development consisted in progress in *in vitro* culture. Naturally no really fundamental advance of an academic character could be made until viruses could be grown away from an animal host. In 1907 Ross G. Harrison of Yale, working at Johns Hopkins, cultivated nerve cells in a plasma hanging drop preparation, and Edna Steinhards and her assistants first cultivated the smallpox virus in guinea pig or rabbit corneal cells, but although the virus survived there was no multiplication. One eminent worker in the tissue culture field was Alexis Carrel of the Rockefeller Institute who developed many of the methods still in use, but had to contend with the difficult business of preventing contamination at a time when antibiotics had not yet come into use. Frederick Parker Jr. and Robert Nye at Boston City Hospital in 1925 obtained reproduction of smallpox virus in rabbit testicle cells. A method which for a long time proved extremely useful was developed by Hugh and Mary Maitland of Manchester University, who devised a way of growing smallpox in a mixture of chicken kidney cells, serum and mineral salts. This was a real tissue culture system since cells definitely multiplied. The method was later also used for growing the 17 D yellow fever virus and it was the starting point for much of Ender's historical work. A great breakthrough in virus work came when the various parts of the developing chicken embryo could be made use of for growing viruses. Borrel apparently was the first person to use eggs for this purpose. In 1906 Constantin Levaditi first grew Spirilla in fertilised eggs, and Peyton Rous and James B. Murphy in 1910 used the membranes of the developing egg to grow fowl sarcoma virus. Still egg membranes as they are used to-day did not come into the virus laboratory until the classic work of Alice and Eugene Woodruffe, and Ernest Goodpasture of Vanderbilt University. They were all three working on avian pox and Alice Woodruffe, at Goodpasture's suggestion, used fertilised chicken egg membrane to grow the pox virus, her husband Eugene helping her to overcome the difficulties of contamination. The first evidence of success was a swollen leg in a chicken embryo. Then "colonies" were noticed on the membranes. The practicability of using eggs for this purpose was described in 1931 in the "American Journal of Pathology". Within a year egg membranes were being used for smallpox and herpes and since then, as is well known, their use has spread very widely indeed, especially for the purpose of producing vaccines, such as those for influenza, and rabies, the longer incubating duck eggs being used for the latter. Herald Cox used egg membranes very extensively during the last war for the large scale production of typhus vaccines.

It is possible that, in spite of the history of virology so far having been so varied and so fruitful, the most important contributions are yet to be made, for the last great outstanding problem in pathology is the origin of new growths and virology has already made important contributions towards the solution of this and may yet not only provide us with a complete answer to the conundrum but also supply us with a remedy for this sinister abnormality.

Peyton Rous of the Rockefeller Institute published in the "Journal of the American Medical Association" as far back as 1911 an article on "The transmission of malignant neoplasia by a cell-free filtrate". It dealt with a sarcoma in Plymouth Rock fowls. In 1919 U.J. Wile and L.B. Kingery of the University of Michigan proved that the common wart is attributable to a virus. Richard Shope proved the virus origin of fibromas in rabbits in 1930 and of rabbit warts in 1931. In 1936, John Bittner of the Jackson Laboratory in Maine, and later of the University of Minnesota discovered what for a long time was called a "principle" which was present in the milk of mice and transmitted to their offspring cancer of the breast. This was later on, at least partly proven to be a virus acting together with an inherited predisposition. In 1950 Ludwig Gross of the Bronx Veterans Administration Hospital of New York produced convincing evidence that leukaemia of mice was produced by a virus. Most pathologists agree that leukaemia is a neoplasia and when Gross's discovery was confirmed by Sarah Stewart, Bernice Eddy, and Charlotte Friend it was clear that an important contribution had been made in the etiology of a new growth type of illness which frequently occurs in man. Stephen O. Schwartz, primarily an internist but also the director of the Hektoen Institute for Medical Research of the Cook County Hospital in Chicago, has proved, mainly through the use of intracerebral inoculation in mice, that human leukaemia also appears to be of viral origin.

One interesting field of studies in virology which must not be left unmentioned simply for the reason that the historian who does so risks cutting a very poor figure in the future should any of its many possibilities come true is that of interference. G.M. Findlay and F.O. MacCallum as far back as 1937 established that an infection with Rift Valley Fever virus protected monkeys from infection with the immunologically unrelated yellow fever virus. This was the first definite example of viral interference. It was later found that the interfering virus can induce the same effect when it has been inactivated, and later still it was established that when certain cells are treated with different strains of myxovirus (the influenza group) a substance is produced which inhibits the growth of a wide variety of viruses. This has been largely the work of A. Isaacs and his associates of the National Institute for Medical Research at Mill Hill in London. The inhibiting substance has been named interferon. It must have been hoped that it could do in the virus field what penicillin did in the bacterial field, and, although progress has been relatively slow, this may eventually still be the case.

One of the most thrilling things in science is the cross-fertilisation which can often occur between the different branches of learning. In the last few years enormous progress has taken place in genetics and especially in the studies on the way in which genes transmit the instructions according to which inheritable features of an organism are determined. This has now centred on studies on deoxyribonucleic acid, the now famous DNA, and much of this work has really been a study in bacterial genetics. One of the most eminent workers in this field has been F.H.C. Crick of the Medical Research Council Unit for Molecular Biology at the Cavendish Laboratory, Cambridge and most of his work was done by the use of bacteriophage T4, which acts on *Escherichia coli*. The story is too involved to deal with in this essay, but it is clear that the story of genes is shedding an enormous amount of

light on the intimate structure of viruses and perhaps the chapter which is now being written will be the most important one of all. Who knows but that it may be not only a chapter in virology but also a most vital one in the history of the human race? Reverting to the problem of the origin of new growths, we can point out that Rubin, of the California Institute of Technology, suggests that virus entering a cell can unite with the cellular material, distort it, but go on dividing with it. By this theory, which receives support we believe by the work of Crick and others, the necessity is avoided of choosing between theories of neoplasia which depend on a change of a non-infectious character in the cells and those which attribute the change to viruses.

It is probable that the rate at which progress in virology has gone on will decrease, but certainly the end is not yet for the subject still has many growing points. So far it has been a chapter of history which many have found fascinating. Like so much else in the history of medicine in general, and unlike so much in general history, it is a chronicle the contemplation of which affords mankind nothing to be ashamed of and a great deal to spur it on to ever nobler achievement.

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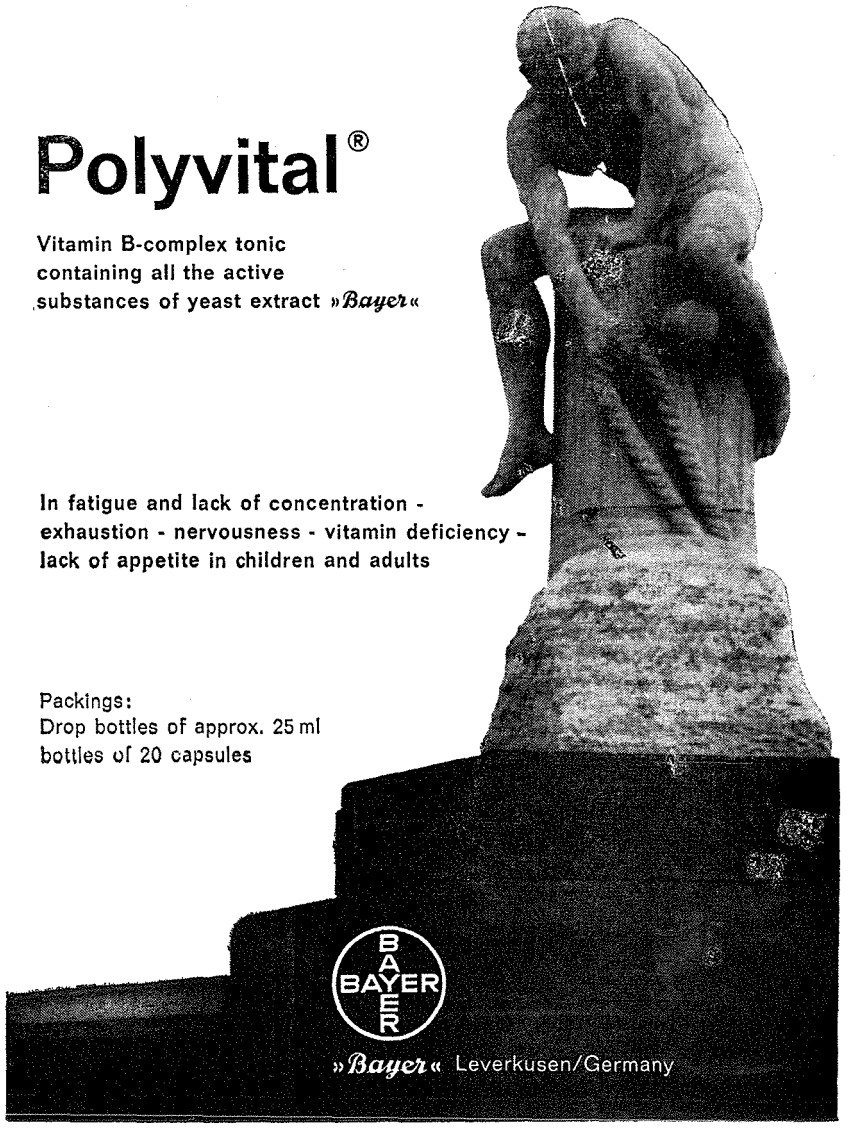

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A PSYCHIATRIST LOOKS AT ADOLESCENCE

Paul Cassar, B.Sc., M.D., Ph.C., D.P.M., F.R.Hist.S.

The Royal University of Malta.

One of the disturbing features of our times is the so-called teenager or adolescent. Many parents think that the teenager is a phenomenon of our age but nothing could be further from the truth. In fact only the name of "teenager" is modern but the human being so labelled and his difficulties are as old as mankind itself and will always be with us as long as humanity exists. It may well be asked: "If adolescents are not a new phenomenon why are they vexing our minds?" There are several reasons for this concern on our part:

1) The population of our Islands is increasing in numbers. Infantile mortality has been reduced considerably and, therefore more children are surviving to reach adolescence now than in the past.

2) Owing to the increased competition for jobs, parents are taking more interest in the educational upbringing of their children than formerly and, therefore, the conduct of our young people has become of paramount importance to us.

3) Stimulation of the physical and psychological needs of the adolescent is today more frequent and more intense than formerly through such media as books, advertising, television, films and the stories about the personalities of the world of entertainment. There is also more exploitation of these needs by commercially interested adults who tempt young people with suggestive literature and music through magazines, pictures, fan clubs of film stars and gramophone records.

4) We are providing our children with dangerous and expensive toys, so that when they reach adolescence they are accustomed to the use of quite harmful means of expression. For instance, instead of fists and stones, they are using knives and guns; instead of the bicycle they have the motor bike and the car. Adolescents, therefore, are getting into more serious trouble than in the past.

5) The chaotic economic and political situation of the adult world, the constant threat of war, our ideological conflicts and our declining standards of honesty and sincerity are all influencing our adolescents in an unfavourable manner by undermining their confidence in our moral code and by increasing the feelings of insecurity and perplexity to which their period of life makes them unduly liable.

What is Adolescence?

Life is a continuous process of change in body and mind from birth to death. This change, however, is so gradual that we become aware of it only at certain stages of our life when it reaches a sufficiently high intensity of development or decay. Thus we speak of the periods of infancy, childhood, adolescence, adulthood, middle age and senility.

Adolescence is that period of transition from childhood to adult age extending roughly between the ages of 14 and 20 years. It is a time of growth of body and mind, a phase of adaptation from the unrestraint of childhood to the social and psychological maturity and responsibility of the adult. It is a period of trial and error characterised by the emergence of new desires and needs, new feelings and new drives resembling those of the adult but lacking the personal and material means of satisfying them because the boy or girl is still without experience, is still economically dependent upon his parents and is still without a mate for satisfying the incipient sexual urges. It is, therefore, a time of stress which the adolescent tries to neutralise by striking some sort of balance between the drives within himself and the opposing pressures of the adult environment that impinge upon him. This process of adjustment is not always smooth and, when unsuccessful, may lead to frustration, resentment and rebellion. In the majority of cases these disturbances are only of a temporary nature and disappear as maturity sets in.

What are the main characters of adolescence?

1) There are outward changes in the appearance of the body, especially of its sexual features. With these changes goes awareness of sexual feelings, curiosity and interest in the body which are shown by the desire for personal adornment, dresses, etc. There may be fear of menses in the girl and of nocturnal emissions in boys because they do not understand the nature and the harmlessness of these natural manifestations.

2) There is a feeling of physical well-being and power and, therefore, a craving for activity and adventure; hence the zest for life and the restlessness of the adolescent.

3) There is a craving for independence and for new experiences which makes the adolescent resent advice and control regarding his conduct.

4) The adolescent imitates the behaviour of adults and is attracted by their temptations such as drink, gambling, sex, cars, etc.

5) He feels the desire to belong to a group because this gives him a sense of security and strength in his budding independence from his parents and also support against the restrictions of the adult world.

6) He strives for recognition and acceptance as an important person. In his attempts at self-assertion he uses awkward and irritating methods such as cheating (to show his cleverness), opposing for the sake of opposing, bullying, bravado, snobbery, defiance, extravagance and even the earning of an unsavoury reputation.

7) He criticises his parents because he starts realising that adults (and, therefore, his parents) are not always the ideal beings he thought they were in his childhood and because he discovers that they are not always truthful and right in their dealings with him. In this way his parents cease to be the idols of his childhood and to command the blind obedience and respect of former days.

8) He rebels against authority and convention; he enjoys flaunting the social and moral codes of adults and takes pride in being vulgar, noisy and destructive.

Management of the adolescent

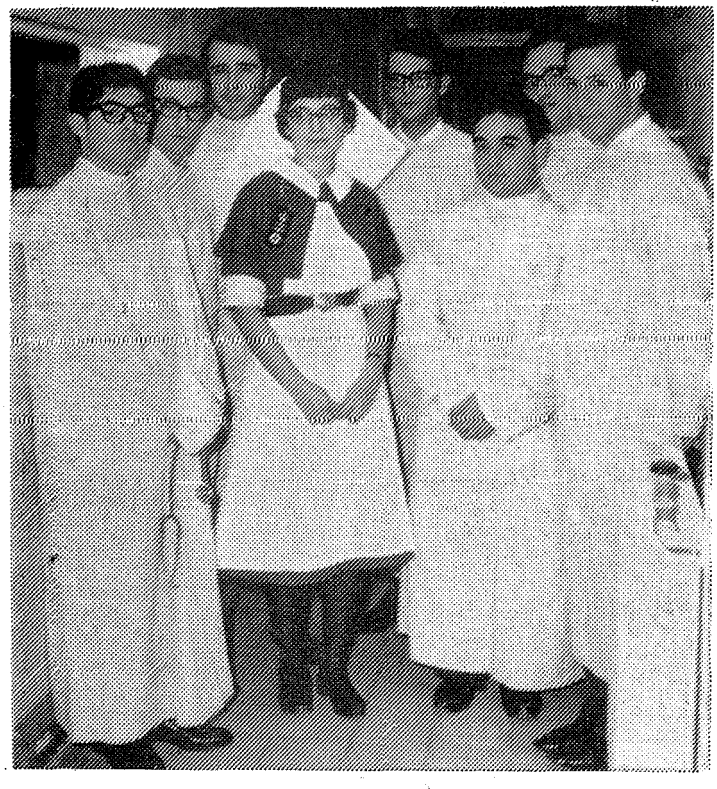
Since adolescence represents a phase of the growing up process we must accept the inevitability of this period of development but we must take care to guide it along rational and harmless channels. We must, therefore, allow that measure of freedom to the adolescent which would enable him to follow his talents, to experiment and even to make mistakes. We must, however, check his freedom when he tends to depart from socially and morally approved ways of conduct to show him that there are limits to one's liberty not only during adolescence but also later on in life. We have also to encourage stability and reliability in him by enforcing regularity in the performance of certain activities such as a time-table for study, meals and recreation.

When we have to correct his behaviour, we should try to talk straight but to avoid arguing and sermonising because arguing creates ill feeling and resentment while preaching is boring to the young. We have to base our authority on wisdom and friendship and not on dogmatic and sneering domination.

Do not ignore his point of view and his opinions but listen to them and show him why you have other ideas. Remember that as we reach middle age we tend to form rigid patterns of thought and behaviour, to resent change and to become intolerant of anyone who tries to disturb our opinions and way of life. We must make an allowance for the change in the customs of society since the days when we ourselves were boys and girls. Society is not a static organization but a dynamic and constantly changing one. We must, therefore, not expect the adolescent of to-day to conform to all the standards that were applicable in our own adolescence. Let us remember that we, too, have had to abandon certain standards that prevailed in our parents' time and to accept new ideas and new conditions. We must keep in mind that the world of to-morrow belongs to the adolescent of to-day and not to us. Our duty is to place at his disposal the wisdom and the results of the experiences we have gained throughout our life but we must not expect him to accept them unconditionally or to apply them in all circum-

stances. After all we adults do make a mess of things sometimes in spite of our experience and the warnings of our elders. It seems that in certain respects each generation has to start from the very beginning in learning the lessons of life — hence the repetitions of the same blunders and fallacies by one generation after another.

As I have already said, adolescents imitate adults. In the long run, therefore, it is we adults who provide them with a pattern and standard of conduct to which they try to conform. That is why they want to read adult papers and magazines, to see adult films, to go to dances and to meet in clubs and cafes. They imitate us in our quest for power, in our sexual code, and in our efforts for social prestige. They also imitate us in our blunders and in our stupidities. We must, therefore, take care to provide the adolescent with high moral and religious ideals and examples, to serve him as a stabilising force in moments of stress. But we must do so in childhood before he reaches adolescence. If we succeed in doing so, then we can feel sure that he will not go seriously astray not only in adolescence but later on in life as well.



Since December 4, 1973 the group of Final Course Medical Students doing practical obstetrics for the month at St. Luke's Hospital are visiting the Mtarfa Services' Maternity Hospital. Cases are demonstrated to the students by the resident staff and points of obstetric interest are discussed. The series of visits has been arranged by Professor A.P. Camilleri together with Lt.-Col. G. Gavourin, Consultant-in-Charge at the hospital. and has proved of great value to the students. Photo shows the first group of students to visit the hospital — (R. to L.) G. Abela, W. Cassar Demajo, A. Busuttil, G. Attard, R. Bencini, A. Agius, F. Bonello — with Miss G. Gamble, at the hospital's Premature Unit.

(photo: UNION PRESS).

DRUG TREATMENT IN PSYCHIATRY

Abraham Galea, M.D., B.Pharm., F.R.F.P.S., M.R.C.P., D.P.M.

Modern drug treatment in psychiatry dates back only ten years when Delay and Deniker in France introduced Chlorpromazine. This followed the observation of the anaesthetists that patients under the influence of this drug, though fully conscious of the surroundings, became indifferent to the surgical procedure. In 1952, Swiss scientists analysed and synthesised Reserpine, a drug which had been used for centuries by Indian physicians for the relief of high blood pressure and insanity. Berber introduced Meprobamate in 1954 and Kuhn observed the euphoriant effect of Imipramine in spite of the drug's structural resemblance to Chlorpromazine. In 1957 Kline reported his observation that tuberculous patients put in Iproniazid, a substance related to I.N.A.H., became very elated irrespective of their clinical condition. It will be noted that these break-throughs were due to keen clinical observations. The physician, by the bed-side, and not the research worker in the laboratory, deserved most of the credit. The advent of these drugs created a new interest in the mental patient. The 'therapeutic frustration' was dissipating and the main symptoms of disease were being controlled. The patient could be treated at home, while at work and without the 'stigma' of hospitalization. Vast reforms in the mental hospital followed, chief among which one could mention the 'open ward system', the general hospital psychiatric unit, and the rehabilitation and occupation centres. The follow-up out patient clinic, the Psychiatric Social Workers, and the participation of the General Practitioner made Community Care a working possibility.

CLASSIFICATION OF PSYCHIATRIC DRUGS

"The burgeoning flood of reports on drugs almost defies analysis; the physician, unfortunately, has difficulty finding adequate guide lines and objective information and the only good method to date for identifying a new drug type is skilled clinical observation." Wortis Jean Delay has classified psychiatric drugs into: —

GROUP I. DEPRESSORS OF MENTAL ACTIVITY (PSYCHOLEPTICS)
- a) Depressors of Vigilance (Hypnotics)
- b) Depressors of Affect (Tranquillizers)

GROUP II. STIMULANTS OF MENTAL ACTIVITY (PSYCHO-ANALEPTICS)
- a) Stimulants of Vigilance (Dexamphetamine)
- b) Stimulants of Affect (Anti-depressants)

GROUP III. DISTURBERS OF MENTAL ACTIVITY (PSYCHO-DYSLEPTICS)
Hallucinogenic Drugs.

HYPNOTICS

Hypnotics may be Barbiturates or non-Barbiturates. The former are the most commonly used drugs in psychiatry. When prescribing a barbiturate preparation the physician should keep in mind: —

i) The real danger of addiction, and one uses them for the shortest possible time.

ii) The real danger of suicide amongst depressed patients, and one should trust them in the care of a responsible relative after explaining the reality of the danger.

iii) Side effects like rashes, confusional states, vertigoes, peripheral tremors, ataxia and double vision are all rare, but one takes the precaution of advising the patient not to drive on the first few days of taking the drugs.

iv) In the elderly the barbiturates may stimulate instead of sedate and can give rise to a confusional state. A preparation containing Chloral is usually preferred.

v) The effect of the barbiturate is often enhanced by simultaneous administration of Phenothiazines, Antidepressants and Alcohol.

TRANQUILLIZERS

MINOR TRANQUILLIZERS

Chlordiazepoxide (Librium) and Meprobamate (Equanil) are the two most widely used drugs of this group. Chlordiazepoxide in doses of 10 to 20 mgms t.d.s. has been used in Anxiety states, Obsessive Compulsive Neurosis and Psycho-Somatic disorders. It has claimed a place in the attenuation of alcoholic craving. It is a very safe drug and the reported side effects of ataxia and rage reaction have been encountered very rarely. Its use with antidepressants has been favourably commented upon especially in the hysterical type of depression. Valium (2 & 5 mgm tablets) has recently been introduced but the effects are quite similar to Chlordiazepoxide. Meprobamate (Miltown, Equanil) is a muscle relaxant which has had explosive vogue in the U.S.A. following its introduction. Various side effects like rashes, purpura and bone marrow depression have been reported but they must be extremely rare. The dose is in the region of 400 mgm, t.d.s. Both these drugs may lead to habituation.

MAJOR TRANQUILLIZERS

i) The Rauwolfia Alkaloid Group

ii) The Phenothiazine Group

Piperazine Group (Trifluoperazine-Stelazine)
Promazine Group (Chlorpromazine-Largactil, Thioridazine-Melleril, Promazine-Sparine).

iii) The Butyro-phenon Group

Haloperidol-Serenace.

The Rauwolfia Alkaloids (Reserpine 1 to 4 mgm tabs) have been superseded by the phenothiazines.

The Phenothiazines are very widely used drugs. They do not cure diseases but they reduce agitation and tension. Probably they diminish the 'hold' which delusions and hallucinations have on the patient. Possibly they remove apathy and make the patient more cooperative. Their use is mainly confined to the psychoses. Chlorpromazine (Largactil) is the drug of choice in restless and aggressive patients because of its added soporific or sedative effect. It is the best studied drug and has withstood the test of time. It calms the patient while leaving him fully conscious and

thus claims the name 'tranquillizer'. Where there is agitation, whether schizophrenic, depression or organic psychotic state, Chlorpromazine has been found useful. Dosage ranges between 25 to 200 mgms t.d.s. Promazine (Sparine) in equivalent dosage is probably milder and has fewer side effects and is indicated in the elderly psychotic Thioridazine (Melleril) in the same scale of doses has little effect on blood pressure and is suitable for outpatient practice. In fact one often uses them quite interchangeably. Whenever we use these drugs we take the following precautions:

i) Check the blood pressure especially on initiation of treatment.

ii) Routine W.B.C. every 15 days and emphatic warning to the patient and his relatives to report any fever or sore throat.

iii) to report at once in case of abdominal pain and icterus.

Trifluoperazine (Stelazine) in doses of 1 to 5 mgm t.d.s. is a very effective and potent phenothiazine and is probably the drug of choice in the withdrawn apathetic schizophrenic and the Paranoid type. In actual fact because most of its side effects are not serious and all are reversible it is the first to be prescribed in all forms of Schizophrenias in the young. It has a high failure rate and if there is no response in ten days of adequate dosage one thinks of alternative therapy. Thiopropazate (Dartal) in 5 to 10 mgms t.d.s. has the same spectrum of activity but is reputed to work satisfactorily in Huntington's Chorea and Obsessive Compulsive Neurosis.

Haloperidol (Serenace) in doses of 1.5 mgm to 10 mgm/day is mostly used in Manias but it has proved its worth in the Schizophrenias, diminishing the delusions and hallucinations.

When prescribing the above drugs one should anticipate extra-pyramidal syndromes and one may give anti-parkinsonian drugs beforehand.

Side Effects of Tranquillisers

On the whole the tranquillizers are relatively safe drugs, but like all potent drugs they carry therapeutic hazards which make the physician measure up the benefit from the drugs as against the risks. In spite of the side effects the Tranqillizers have proved themselves to be effective therapeutic devices to combat the miseries of mental illness.

The chief side effects can be grouped into three categories: —

i) Those that are due to idiosyncrasy and independent of dosage:

a) skin manifestations—papular rashes, erythemas, desquamation, light sensitization.

b) blood dyscrasias, chiefly leukopenia which might lead to agranulocytosis.

c) liver damage in the form of ball thrombi in the bile canaliculi leading to obstructive jaundice.

ii) Those which depend on dosage and/or the physiological action of the drug:

a) Autonomic disturbances—dryness of mouth, micturition difficulties, visual blurring, constipation, sexual difficulties and hypotension.

b) Extrapyramidal Syndromes—akinesia, dyskinesia, akathisia, Parkinsonism.

iii) Alleged effects on the foetus in animals.

As a rule, the more potent the phenothiazine the commoner and more persis-

tent are the extrapyramidal effects but the less the autonomic or blood or liver damage, and vice-versa. Thus while Trifluoperazine (Stelazine) if given in adequate dosage will invariably produce extrapyramidal symptoms, but will not produce hypotension or leukopenia, Promazine (Sparine) will, though rarely, produce hypotension and marrow depression, but only with massive doses will it produce extrapyramidal effects.

1) Agranulocytosis:

This is the most serious complication estimated as occurring in 1 every 100 cases and carrying a 36% mortality. It is an extremely rare complication in our practice, never encountered with Trifluoperazine. It is said to be more frequent in women beyond the age of 40 and manifests itself in the 40th to the 70th day of treatment. It may occur as a progressive leukopenia (and a white count of less than 4000 calls for revision of treatment) or as an 'agranulocytosis out of the blue'.

2) Obstuctive jaundice:

Occurs in 1 to 2 per thousand of cases on Chlorpromazine or Promazine after the first month of treatment and usually clears up spontaneously in 4 weeks. It is heralded by chills, fever, abdominal pain, persistent nausea with occasional vomiting, and pruritus. In hospital practice this complication has been seen only rarely.

3) Hypotension:

Likely to occur with large doses of the weaker phenothiazines or with parenteral administration of the drug. The patient feels dizzy and may collapse. This is particularly dangerous in the elderly, as a cerebral or coronary thrombosis might be precipitated. The patient should be nursed flat in bed but may have to be given a Noradrenaline-Saline drip. Contrary to previous belief, Mephentermine in large doses is found effective.

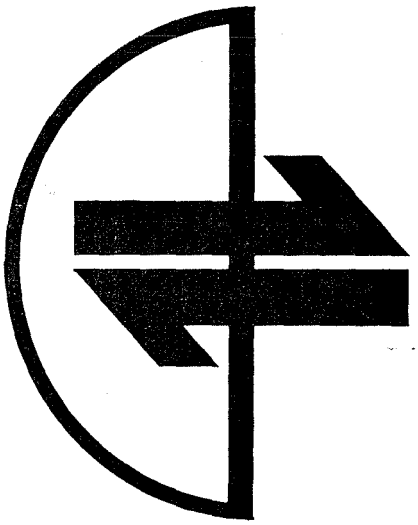
4) Parkinsonism and Extrapyramidal Syndromes:

i) Akinesia: The patient is aware of feeling very tired whatever he does. He complains of weakness and muscular fatigue in a limb used for any activity.

ii) Dyskinesia: This takes the form of torsion spasms, myoclonic twitchings, torticollis, speech and swallowing defects and involuntary protrusion of the tongue. Usually a transitory phenomenon appearing in the first 5 days of treatment and responds to lowering of dose.

iii) Akathisia: the patient complains of jitters, and is compelled to pace the floor, smack his tongue and perform all sorts of bizarre chewing movements. It is common in females in the first 15 days of treatment. Antiparkinsonian drugs will help.

iv) Parkinsonism: The usual triad of cog wheel rigidity, tremors and autonomic disturbances (salivation, oculogyric spasm and difficulty in accomodation) occur in the elderly group (over 50) and respond well to antiparkinson drugs (Artane, Disipal, Akineton) In patients over 60 iatrogenic parkinsonism may be very resistant to any form of treatment. With the strong Phenothiazines (Trifluoperazine) and also with Haloperidol it may be forestalled by initiating a combination of antiparkinsonian drugs together with the Phenothiazines from the start.



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1 Prytz, B., *et al.* American Chemical Society Meeting, Cincinnati, Ohio, Jan. 13-17, 1963
2 Morani, A. D., J.med.Wom.Fed., 1960, *42:* 12
3 Cowan, A. B., Med. Press, 1961, *246:* 453

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5) Effects on Human Foetus

These are deduced from animal experiments. Reserpine and Chlorpromazine can cause foetal death in experimental animals and can significantly affect birth weight. Chlorpromazine can retard embryonic growth in salamanders; it depresses both foetal and maternal brain oxygen in gravid guinea pigs. All these suggest caution in the use of tranquillizers during pregnancy. As a rule one uses drugs which are compatible with safety and which yield the best therapeutic results. One realizes that in pregnancy the risks to be reckoned with include the vulnerability of the foetus and one cannot condemn too strongly the use of any drugs unless there is adequate indication; but if there is (and a schizophrenic or depressive episode can be really serious) one should not hesitate to take this calculated risk.

STIMULANTS

Amphetamines and Allied Substances

Dexamphetamine Sulphate (Dexedrine) in 5 mgm tables is widely used as a stimulant and an appetitie suppressant. Often it is combined with a barbiturate (Drinamyl or Purple Hearts) and as such it is widely used. Recently it was found that large quantities of the drug were being consumed by youngsters in search of excitement or an easy way out of the problems of life. It is a drug of addiction and its prolonged use gives a clinical picture very much like that of paranoid schizophrenia (ideas of reference, paranoid ideas, auditory hallucinations and facile affect.) Dexedrine should be used under medical supervision as a short term treatment in transitory depressive reactions. When prescribed to inadequate persons the danger of psychological dependence should be kept in mind. In children Dexamphetamine is a sedative and has been used successfully in behaviour disturbances. In enuresis it is said to help.

Antidepressants

Antidepressants fall into two groups:

(i) Iminodibenzyl group — Imipramine (Tofranil) 25mgm. tabs.
Amitriptyline (Tryptizol, Laroxyl, Saroten) 25mgm.
Nortriptyline (Aventyl, Allegron) 25 mgm. tabs.

(ii) Monamino-oxidase-inhibitor group—
Nialamide (Niamid) 25mgm.
Phenelzine (Nardil) 15mgm.
Isocarboxazid (Marplan).
Tranylcypromine (Parnate).

It is usual (though admittedly very difficult) to divide the depressive syndrome into Endogenous and Neurotic depression. Endogenous group (which includes the M.D.P. and Agitated Depression) is characterised by disturbances in *mood* (depression which is persistent, usually unprovoked, unmodified by changes in the environment), *behaviour* (retardation or agitation, insomnia, loss of appetite and refusal to eat, somatic effects like bradycardia, constipation and fatigue), and *thought* (hypochondriasis, ruminations, ideas of unworthiness, suicidal ideas, and phobias.)

Quite characteristic of endogenous depression are the following features: past history of mood swings or frank manic episode; depression worse in the morning with slight improvement towards the afternoon; late insomnia.

The Neurotic group is said to have the following features: good previous personality which has broken down under stress; fluctuation in mood; preoccupation with the lack of emotional control; cannot fall off to sleep; very irritable, with a tendency to exaggerate the symptoms. Probably the drugs of Iminodibenzyl group (Imipramine, Amitriptyline) are the more effective in the endogenous type of depression, while the Monamino-oxidase inhibitor type are to be preferred in the neurotic type. These drugs are believed to be "mood lifters" as they relieve the depression, but the agitation is not well controlled. For this reason they are very often combined with a phenothiazine.

a) When using the Iminodibenzyl group (Tofranil or Amitriptyline) we keep in mind: —

(i) Start with small dosage and work smartly up to a maximum e.g. 25 mgm t.d.s. up to 50 mgm t.d.s. within a week (if one starts with maximum dosage the patient will not cooperate owing to side effects).

(ii) These drugs take 2 to 3 weeks to exert maximum effect and if the patient is actively suicidal this point will work in favour of hospitalization or the more rapidly acting Electric-Convulsive Therapy.

(iii) These drugs do not cure the depression but alleviate symptoms — early withdrawal or sudden stoppage of the drugs by the patient may precipitate an acute psychotic episode.

(iv) Imipramine works well in M.D.P. but in 30% of cases the patients are pushed into the manic phase.

(v) Always check for urinary obstruction (prostatism) or glaucoma because these two conditions constitute the only contraindication at outset.

(vi) The two groups of drugs are never to be used together (i.e. never use Imipramine with any of the M.A.O. inhibitor drugs).

(vii) If these drugs are taken for suicidal purposes, they are highly toxic and so far no antidote is known, therefore one must never trust a suicidal patient with them but they should be entrusted to the care of a responsible relative.

Amitriptyline is said to have caused paralytic ileus in a few cases. On starting treatment the patient will often complain of drowsiness (especially with Amitriptyline), some dizziness, dryness of mouth, constipation, difficulty in starting micturition, blurring of vision, tachycardia, hot flushes and heavy sweating.

b) When using the M.A.O. inhibitor group of drugs one should remember:

(i) These drugs have been subjected to a torrential amount of criticism and one hesitates to use them until one hears more about their effects and side effects (e.g. the drugs Catron, Monase and Drazine have been withdrawn from the open market for further study owing to alleged toxicity).

(ii) Maximum effect is reached within 2 to 3 weeks, a fact which should be borne in mind in dealing with suicidal patients.

(iii) Never couple them with drugs of the Imipramine series (3 weeks must pass before a patient who was having these drugs can be safely put on Imipramine or Amitriptyline).

(iv) Patients on these drugs should be warned that they are not to have any drugs of the pethidine, morphine group and they are to tell the doctor before 'any injections'.

(v) Sympatheticomimetic amines like adrenaline, ephedrine, caffeine, benzedrine may have untoward reactions owing to blod pressure changes.

(vi) Serious side effects may follow the use of these drugs—toxic hepatitis occurring on the 30th to 40th day with 20 to 30% mortality has been reported. There is considerable controversy at the moment. Rees says that toxic hepatitis in U.K. never occurred with Nialamid or Isocarboxazid. Definitely there are no cases reported with Tranylcypromine. Sargant believes that the hepatitis is in fact due to viral infection and the drugs have nothing to do with it or if they do they just lower the patient's resistance.

(vii) Blood pressure changes and headaches like those due to subarachnoid haemorrhages have been reported with Tranylcypromine (Parnate), especially if cheese containing tyramine is ingested (Camembert and Stilton cheese).

THE PSYCHODYSLEPTICS

We have no experience with these drugs like Lysergic acid, Mescal, Phencyclidine, etc. They produce hallucinations, skinesia, distort the sense of time, remove the customary inhibitions in respect of speech, fantasy, feeling and action or may induce a state of perplexity or confusion.

Phencyclidine (Sernyl) has been used in the management of Obsessive Compulsive Neurosis and mixed neurotic conditions; it is alleged that Lysergic Acid Diethylamide deepens insight by the patient into his illness during therapeutic sessions. Psilocybine has been utilised for diagnostic purposes.

CONCLUSION

There is no doubt that the advent of psychotherapeutic drugs has marked a step forward for the mental patient. As soon as they appeared the ever increasing hospital admission and overcrowding have been halted and the trend reversed. The patient came to expect control of symptoms while still in the community and even if admitted his stay in hospital became shorter. We notice that mental ill-health became very much the concern of the research worker as well as the legislator. There is hope that in the future the psychoses as we know them today will be entirely the business of the general practitioner, and the mental hospital will tackle the thorny problem of the psychopath, the juvenile delinquent, the addict and the degenerative conditions like the senile dementias and even senescence itself. However that may be, these drugs are potentially dangerous and should be accorded the respect we usually attach to potent therapeutic agents. At a symposium in New York marking the 10th anniversary of the coming of the tranquillizers, Dr. F. Ayd estimated that 200 million people around the globe have been given tranquillizers. In the U.S.A. tranquillizers compete with antibiotics and barbiturates as the fastest selling pharmaceutical compound. We should however be very much on the alert lest "the milder tranquillizers are used sort of like vitamins. If the doctor can't quite pin a person's problem down, he's apt to write a tranquillizer prescription." Nothing could do greater harm to psychiatry than this attitude, rightly condemned by Dr. Greiner of Bailer University,

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OTITIS MEDIA IN CHILDREN

W.A. Sultana, M.D., B.Sc., D.L.O., F.I.C.S.

Otitis media in children is one of the more important problems of the diseases of the ear. So much of the future well-being of these children depends upon accurate diagnosis and prompt treatment, and so much harm may result from bad treatment that the condition should be familiar to every doctor. Indeed, many of these cases, if treated promptly and energetically by the family doctor, may not come to the otologist at all, except perhaps to assess if any damage has resulted from the disease or to treat a known causative factor.

In considering otitis media one should not think of the disease as limited to the tympanum, but as involving the whole middle ear cleft, viz, the tympanum, attic, antrum, and mastoid air cells. Moreover, in infants, this cleft extends from the pharynx to the mastoid, because their Eustachian tube is short, wider than in the adult and the isthmus does not exist. The mastoid antrum in infants is also comparatively larger than in the adult and, as Paul Bernard demonstrated radiologically, air cells may be present even at birth.

This intimate connection between the middle ear and the upper respiratory tract obviously plays an important role in the aetiology of otitis media. In fact, it can be said that the middle ear is involved to a greater or lesser extent in most conditions affecting the respiratory passages.

The commonest single cause of acute otitis media in children, especially in infants, is undoubtedly acute rhinitis. Next come the acute fevers, influenza, diphtheria, measles and scarlet fever, the latter two being especially prone to produce a virulent type of infection, often passing on to a mastoiditis, or, if inadequately treated, leading to a chronic suppurative otitis media. Whooping cough may also produce an obstinate type of infection.

Tuberculous otitis media was formerly regarded to be quite common in children, but is now rarely seen.

Trauma to the tympanic membrane, especially by foreign bodies or by ill-guided attempts at removal, is a frequent cause of otitis media in children.

Infection may also spread inwards from an otitis externa, especially from a furuncle.

Allergic reactions involving the nasal mucosa may involve the mucosal lining of the Eustachian tube and of the tympanum producing an intractable type of otitis media. Such cases are said to be especially common in young children and infants.

Chronic infection in the nasopharynx is by far the commonest predisposing factor in children; adenoids are undoubtedly the most important single cause. Septic tonsils are other causes, but less so than adenoids, especially in infants in whom obviously diseased tonsils are hardly ever encountered.

The relation of the sinuses to the middle ear is not definitely established, and it is debatable whether they should be investigated in all cases of otitis media if they are not causing any symptoms of their own. When obviously diseased, they should be treated not merely for their own sake but also on account of the ill-effects they have on the pharynx, lungs and ears.

All weakening conditions, such as anaemia, nephritis, diabetes and severe malnutrition are predisposing causes of otitis media.

The commonest organisms encountered are the Streptococcus haemolyticus (beta) and the Staphylococcus aureus. Others are Pneumococci, especially the Pneumococcus mucosus, the Staphylococcus albus and rarely Friedlander's bacillus.

The pathology of the disease is fortunately well known, and in a typical case follows a definite pattern. In the beginning, due to obstruction of the Eustachian orifice in the nasopharynx by an inflammatory oedema, the air in the middle ear is slowly absorbed and a negative pressure develops which causes dilatation of the blood

vessels of the tympanum and of the tympanic membrane; the latter, therefore, will appear congested and indrawn. This vasodilatation brings about a transudation of a clear, somewhat yellowish liquid containing lymphocytes and monocytes, but no, or only few, polymorphs; culture is sterile. In allergic cases, eosinophiles will be present. The mucous membrane of the middle ear will be intact and there will only be some oedema of the submucous layer. This stage has been given various names, viz., catarrhal otitis media, non-suppurative otitis media and various others.

If the obstruction in the Eustachian tube subsides, the fluid in the middle ear will drain out, equilibrium between the outside air and that in the tympanum will be established and the condition will resolve. But if the obstruction persists and infection reaches the middle ear, which it generally does via the lymphatics, but also rarely by direct continuity or by the blood vessels, then acute suppurative otitis media results. The pathology then is that of inflammation in general. Marked hyperaemia is followed by submucous infiltration with round and polymorphonuclear cells, and thickening of both mucous and submucous layers. There is exudation of fluid into the middle ear, rich in pus cells, mucus and fibrin. The drum is intensely hyperaemic, thickened and bulging from the pressure of the fluid in the tympanum. Culture of the fluid will reveal the causative organism. This process in children involves the whole of the middle ear cleft, and it is because of this that the disease may now take one of several courses. Resolution may occur once the inflammatory process is stopped and drainage established either via the Eustachian tube or via the drum through a perforation or a myringotomy incision. But if the inflammatory process is not checked, fluid will continue to accumulate which will press on the blood vessels and eventually cause pressure necrosis and ulceration of the mucosa. This will immediately expose the underlying bone to infection. The further evolution of the process depends on several factors, such as type and virulence of the invading organism, type of mastoid bone (well-pneumatised or sclerotic), resistance of the child, and several others. Briefly, the disease may either lead to an acute mastoiditis, to a chronic suppurative otitis media or to a complication, either extra or intra-cranial.

The signs and symptoms of otitis media differ markedly according to whether they occur in a child or in an infant, for while in the former the disease will show signs and symptoms referable to the ear, in the latter, because the Eustachian tube is comparatively wider and in more direct continuity with the nasopharynx, spontaneous perforation is less frequent and the condition may easily pass undiagnosed because the symptoms may be general and systemic and not aural.

In children, pain in the ear is the first and may be the only indication of the otitis media. It comes on suddenly, is located deep inside the ear and is generally described as throbbing in character. This pain is at first due to the negative pressure inside the middle ear, but later it will be due to the pressure exerted by the accumulated fluid on the drum. The temperature at this stage may or may not be raised. The otological signs will be either bulging or indrawing of the drum, according to whether fluid is present or not in the middle ear, but in either case there will be some loss of lustre of the membrane with injection of the blood vessels around the handle of the malleus. Mild deafness will be present, and there is often some mastoid tenderness, generally over the mastoid antrum, but it may also be present over the tip.

When suppuration occurs, the pain becomes more severe owing to the increase of fluid in the middle ear. The general condition of the child deteriorates somewhat; he becomes listless, cries out in pain and goes off his food. The temperature will be raised. The drum will now be uniformly red and bulging and the normal 'landmarks' cannot be made out. Rarely one can see a yellowish spot, generally in the antero-inferior quadrant of the drum, indicating the site where perforation will take place. Deafness is marked, and mastoid tenderness is almost always present. When perforation takes place, and this occurs as a result of pressure necrosis of a part of the drum, the pain suddenly dis-

appears and the condition of the child improves.

The character of the discharge is important because it may reveal how far the process has advanced, and may also give an idea of the causative organism. The Pneumococcus mucosus, for instance, will produce scanty but thick discharge, while the Streptococcus haemolyticus will produce thin but slightly haemorrhagic discharge. When a mastoiditis is developing, the discharge will be thick and creamy. Examination at this stage will show the site and size of a perforation and, if the process is still active, the discharge will be seen to pulsate. The size of the perforation is important because it will give an idea as to whether it is sufficient by itself for adequate drainage.

If the ordinary tuning fork tests are carried out, Rinne's test will be negative and Weber's test will be lateralized to the affected ear.

When resolution begins, the discharge will diminish and its character will alter, becoming thinner in consistency. The temperature rapidly returns to normal and the general condition of the child will improve considerably. The drum will either regain its natural position or be slightly indrawn; the 'landmarks' begin to show up and only a few injected blood vessels will be seen coursing through the membrane. The first 'landmark' to appear is generally the short process of the malleus followed in a short time by the handle. Next will be seen the so-called 'cart-wheel' injection of the membrane, which is a large blood vessel coursing round the periphery of the drum with smaller blood vessels radiating to it from the umbo. Injection of the posterior segment of the drum and of Shrapnell's membrane may persist for some time after the attack has subsided.

Deafness normally disappears entirely once the acute process has ceased, and this fact is important because persistence of deafness means either that the negative pressure in the middle ear is still present (if the drum is intact) or that adhesions have formed within the middle ear, or, more important, that there is still an active process going on, most probably within the mastoid process.

In infants, the otitis is frequently associated with some other disease which is in many instants the etiological agent. The otitis may remain latent for a long period, and it should be suspected when:

1. there is a febrile condition whose cause is not known;
2. although the cause of the febrile condition is known, yet the general condition of the infant does not improve with the subsidence of the local signs (e.g. in pneumonia);
3. the treatment of a digestive condition brings only partial relief;
4. the infants appears to be in pain or cannot sleep.

Marriot stated as early as 1927 that otitis media in infants was the most frequent infection responsible for nutritional disorders. An investigation carried out in 1947 on 880 children under 3 years suffering from acute otitis media, showed 238 of these to be suffering also from gastroenteritis. This shows the importance of examining the ears in all cases of infants suffering from diarrhoea or vomiting. On the other hand, the ears should not blamed for all cases of diarrhoea whose cause cannot be found, and the indiscriminate myringotomy sometimes advocated for such cases is not justifiable.

The temperature in infants suffering from otitis media is not reliable because it may be normal or even subnormal.

More reliable signs are uneasiness, rubbing of the ears, chewing and certain localised (especially ocular) or generalized convulsions.

The drum will be injected but its contour should not be decided on a first examination because, owing to the patency of the Eustachian tube, bulging of a normal drum may be seen when an infant is crying. If discharge is present, the diagnosis is of course obvious.

The treatment of otitis media should be divided into two parts: 1. Treatment of the attack; 2. prevention of recurrences.

The antibiotics have greatly simplified the treatment of an acute otitis media since the vast majority of cases are produced by organisms sensitive to them. Adequate doses of penicillin (or other broad spectrum antibiotic) should be given as soon as the diagnosis is made. In most cases the temperature rapidly returns to

normal, the pain subsides and the discharge stops. The deafness does not clear up so quickly but takes about a week to return to normal. This is important and, when possible, hearing should be tested frequently and regularly, because, when using an antibiotic, the hearing is a useful guide as to whether the disease has subsided or not. The pain, temperature and discharge may all disappear, but the deafness will still be present in those cases where the disease is still active, and so long as this is so, treatment should not be stopped. The so-called "masked mastoiditis" is often due to failure to detect this important sign.

The drum does not generally return to normal before 4 or 5 days, but in antibiotic-sensitive cases where the membrane was red and bulging, it will be seen that 24 to 48 hours after starting the antibiotic, the bulge will have completely disappeared and the injection will be limited to the posterior segments of the drum. It will also begin to move slightly on 'seigelization', indicating that the liquid in the middle ear is diminishing.

General nursing measures should not be neglected, and if there is temperature the child should be put to bed. If pain is present, aspirin should be given for the first 12 hrs. If there is discharge, the meatus should be cleaned out and wicks soaked in plain glycerin inserted, not merely because of a soothing effect, but also because of the hygroscopic action of glycerin, thus facilitating drainage. The use of local antibiotic drops are unnecessary and often harmful, especially if not combined with systemic antibiotics, since they may bring about resistance to these drugs. Moreover, allergic reactions are common.

Measures to diminish congestion in the nose and throat should be started without delay.

When the antibiotics are started early in the disease and the organisms are sensitive, all operative procedures are unnecessary in the treatment of acute otitis media. Certain surgeons maintain that a myringotomy should be done in all cases where the drum is bulging when first seen, but the results obtained by the use of the antibiotics alone are so good and resolution so rapid, that it is worth trying their effect first, rather than subjecting the child to an anaesthetic and an operation which in a large number of cases can be avoided.

Myringotomy should be considered:

1 When the pain in the ear persists for 12 hrs. after starting the antibiotic;
2 When the drum is still bulging after the antibiotic has been given for 24 hours.
3 When there is an increase in the deafness notwithstanding the use of the antibiotic.

Cases caused by antibiotic-resistant organisms present a greater problem, because in these the pain and temperature will still be present 24 hours after starting the antibiotic and, if the drum was bulging, it will either perforate, and in these cases the discharge will be pulsating, or if the drum is merely injected, the redness will still be present after the use of the antibiotic. In these cases, if there is no discharge, a myringotomy should be done. In either case, a swab should be taken for culture and sensitivity and the appropriate antibiotic started without delay.

Cases which do not respond to any of the antibiotics will require surgery as part of the treatment, generally a cortical mastoidectomy, because in these cases the process has usually gone beyond the middle ear and has localized itself in the mastoid process.

When the attack subsided, measures should be immediately taken in hand to prevent a recurrence of the condition. The child should be encouraged to lead an open healthy life. Decongestants should be continued and about a week to 10 days after all signs and symptoms have disappeared, politzerisation and auto-inflation of the middle ear should be started and continued for several days in order to prevent the formation of adhesions in the middle ear.

If adenoids are present, they should be removed at the earliest opportunity. Adenoid remnants should likewise be dealt with. If during the operation adenoid tissue is found to be present in that part of the Fossa of Rossenmuller just posterior to the opening of the Eustachian tube in the nasopharynx which cannot be removed surgically, consideration should be given to irradiation. Good results are said to be obtained in 60% of cases.

(*References on p.* 49).

ANATOMICAL TRIANGLES

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Anatomical description is given of certain areas in the human body which have a triangular shape and which are of anatomical or surgical importance.

There are at least 30 described anatomical triangles, many of which receive eponymous names. Some are of marked importance and well known e.g. Scarpa's femoral triangle, Hesselbach's inguinal triangle, and Petit's lumbar triangle; others are of relatively minor importance and not so well-known e.g. Elau's, Friteau's and Assezat's triangles.

Anatomical triangles are described in various regions of the body e.g. Macewen's and Trautmann's in the head region, Beclaud's and Pirogoff's in the neck region, Hesselbach's, Henke's, Petit's and Grynfeltt's in the abdominal wall region and Scarpa's and Weber's in the lower limb region. Their size varies, some being large e.g. Scarpa's triangle, others being very small e.g. Macewen's triangle.

The boundaries of these triangular areas may consist of muscle borders e.g. the triangle of Lannier and the various triangles of the neck; of muscle borders and bony surfaces e.g. Petit's triangle, the triangle of Marcille and the triangle of Auscultation; of muscle borders and blood vessels e.g. Hesselbach's; of imaginary lines drawn between fixed bony points e.g. Macewen's, Bryant's and Assezat's triangles; and others have boundaries seen only on X-Ray pictures e.g. Ward's and Codman's triangles.

The contents within these anatomical triangles vary. Some contain numerous anatomical structures including arteries, veins, nerves and lymphnodes e.g. Marcille's and Scarpa's triangles. Most, usually those of surgical importance, enclose no contents at all.

A few of these triangles are primarily of anatomical importance as they contain or are related to a host of important structures. Such are Scarpa's femoral triangle, Marcille's lumbosacral triangle, the six triangles of the neck, the anal and urogenital triangles and, amongst the less common, Elaut's and Trautmann's triangles.

Other triangles are primarily of surgical importance. Some are potential sites of weakness where a hernia or diverticulum may form e.g. Hesselbach's inguinal triangle, Petit's lumbar triangle and the Triangle of Lannier (Killian-Jamison dehiscence). Others are of importance as surgical markings for easy localisation of anatomical structures at operation e.g. Macewen's suprameatal triangle for localising the mastoid antrum and Langenbeck's triangle employed in arthrotomy of the hip. Others are made use of in surgical clinical diagnosis e.g. Bryant's ileofemoral triangle for diagnosing fractures of the neck of the femur, Sherren's triangle which marks the site of tenderness in acute appendicitis and the Triangle of Auscultation which is of no importance nowadays but which was made use of in pre-X-Ray days for diagnosing cases of oesophageal obstruction.

Other triangles are of use in other branches of medicine e.g. Assezat's triangle is of use in comparative craniology.

Scarpa's femoral triangle was named after Antonio Scarpa (1747-1832) an Italian surgeon and anatomist who was a pupil of Morgagni and a friend of Volta and Spallanzani.

Situated in the upper third of the front of the thigh, the femoral triangle is bounded laterally by the Sartorius, medially by the medial border of the Adductor longus and superiorly by the inguinal ligament; its roof consists of the fascia lata and cribriform fascia, and its floor is formed from the lateral to medial side by the Ileopsoas, Pectineus, and Adductor longus.

Its contents are the femoral artery, the femoral vein lying on its medial side (but behind it lower down) and lateral to the artery, the femoral nerve above and the saphenous nerve and nerve to Vastus medialis below.

The Triangles of the Neck

The side of the neck is quadrilateral in shape being bounded above by the base of the mandible, below by the upper surface of the clavicle, in front by the anterior median line and behind by the anterior margin of the Trapezius. The Sternomastoid divides this quadrilateral space into anterior and posterior triangles. The anterior triangle is sub-divided by the Digastric and the superior belly of the Omohyoid into 4 triangles viz. muscular, submental, carotid and digastric. The posterior triangle is sub-divided by the inferior belly of the Omohyoid into 2 triangles viz. the occipital and the supraclavicular. Within these, smaller triangles are delimited which are of no importance e.g. Beclaud's, Farabeuf's, Malgaigne's and Pirogoff's triangles.

The most important contents of the carotid triangle are the common, external and internal carotid arteries with their branches and corresponding veins, the hypoglossal nerve and its descending branch and the external and internal laryngeal nerves.

The chief contents of the digastric triangle are the accessory nerve, the cervical plexus, part of the brachial plexus and numerous cervical lymphnodes.

The supraclavicular triangle contains the subclavian vessels, the external jugular vein, the transverse cervical vessels, the brachial plexus and some lymphnodes.

The Urogenital and Anal Triangles

The urogenital triangle is contained between the ischiopubic rami and the line passing between the anterior parts of the ischial tuberosities. This line forms the base of the anal triangle, the sides being formed by the sacrotuberous ligaments.

The contents of the urogenital triangle in the male are the root of the penis and its muscles and the bulbo-urethral glands and in the female the openings of the vagina and urethra as well as the bulb of the vestibule and the vestibular glands. The contents of the anal triangle are the anal canal and the ischiorectal fossae with their contents .

The Triangle of Marcille (the lumbosacral triangle).

Nothing is practically known of Maurice Marcille (1871- ?) after whom this triangle is named.

The boundaries of this triangle are the side of the body of the 5th lumbar

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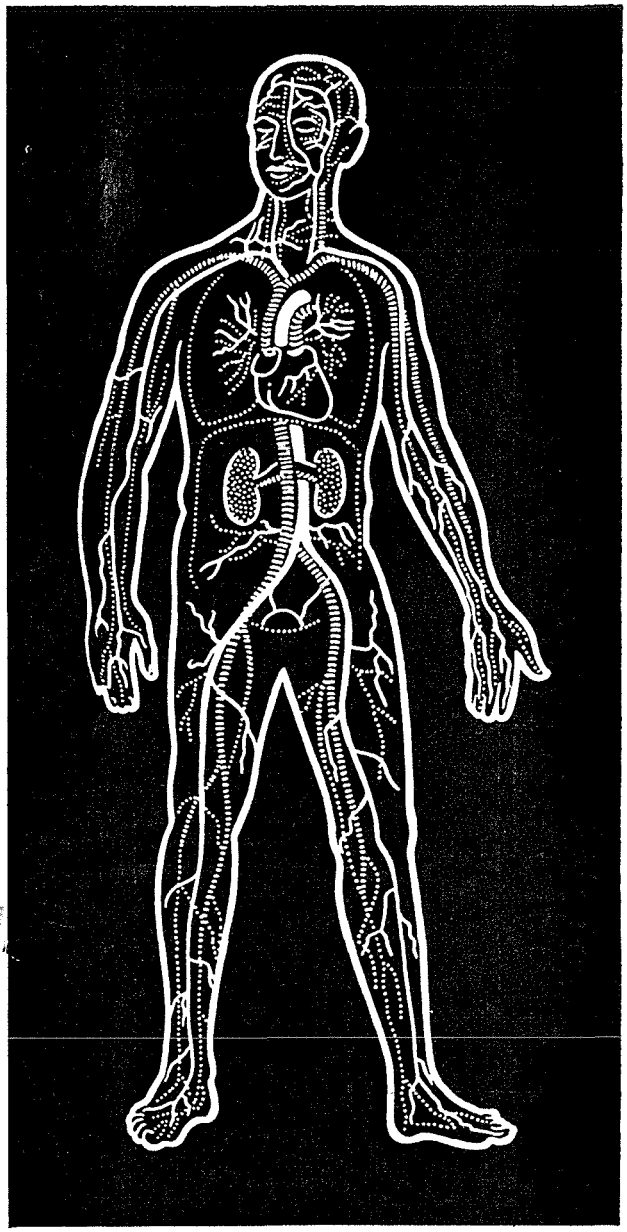

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Tablets and Ampoules

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vertebra medially, the inner border of the Psoas major laterally and the upper surface of the ala of the sacrum below, its posterior wall consisting of the transverse process of L. 5 and the ileo-lumbar and lumbosacral ligaments.

The triangle is related to several important structures. The left common iliac artery crosses the triangle and divides into internal and external iliacs at its distal angle where it is crossed by the ureter. The iliac veins follow the arteries. The inferior mesenteric artery crosses these vessels from left to right and becomes the superior haemorrhoidal. The testicular (or ovarian) vessels pass along the outer border of the triangle. The common iliac lymphnodes lie deep in the triangle medial to the vessels. From the medial to the lateral side of the triangle are the sympathetic trunk, the lumbosacral trunk (L. 4-5) hugging the body of L. 5 and joining S. 1 nerve just below, the ileolumbar artery, the obturator nerve and the genitofemoral nerve on the Psoas just outside the triangle. On the right side both common iliac veins and the inferior vena cava overlie the triangle, the inferior mesenteric vessels being present only on the left side.

Hesselbach's Inguinal Triangle.

Franz Kaspar Hesselbach was a German surgeon and a Professor of Surgery at Wurzburg.

This triangle is situated in the lower part of the anterior abdominal wall, being bounded laterally by the inferior epigastric artery, medially by the outer border of the Rectus abdominis and below by the inguinal ligament. It is divided into medial and lateral halves by the lateral umbilical ligament (obliterated umbilical artery).

As the inferior epigastric artery is medial to the internal inguinal ring only a *DIRECT* hernia can push through the triangle of Hesselbach.. The direct hernia may leave this triangle through its outer part (lateral direct hernia) or through its inner part (inner direct hernia).

Petit's Lumbar Triangle.

Jean Louis Petit (1674-1750) was a French surgeon and anatomist. He learned anatomy from Littrè at the age of 7, attended lectures at the age of 12, became, Littrè's demonstrator at the age of 14 and by the age of 16 was already a surgeon!

This triangle is bounded in front by the posterior border of the External oblique, behind by the anterior border of the Latissimus dorsi and below by the iliac crest, its floor being formed by the lumbodorsal facia and the Internal oblique.

This triangle is also known as the 'triangle of lumbar hernia' because, rarely, a hernia, the so called 'upper lumbar hernia', may occur here. In such a hernia the gut escapes at the anterior border of the Quadratus lumborum and appears at the surface through the triangle of Petit just above the highest point of the iliac crest. The hernia therefore pushes before it the floor of the triangle which therefore forms the coverings of the sac.

Triangle of Lannier (Killian - Jamison dehiscence).

This triangle is found only in upright animals and is due to descent of the larynx which occurs in these animals.

The base of the triangle is formed by the transverse fibres of the Cricopharyngeus and its sides by the oblique fibres of the Thyropharyngeus which ascend slightly from the anterior cornu of the thyroid cartilage and the fibrous band which covers the Cricothyroid muscle, and pass upwards and backwards to reach the apex of the triangle in the posterior midline.

This triangle is a potential source of weakness in the posterior pharyngeal wall. Weakness of the triangle gives rise to pharyngeal pouch or diverticulum.

Macewen's Suprameatal Triangle.

Sir William Macewen (1848-1924) was a Scottish surgeon who was interested in the growth of bone and in bone lesions. Macewen described the suprameatal triangle in his book, *Pyogenic Infections of the Brain* (1893) in these words: "Roughly speaking if the orifice of the external osseous meatus be bisected horizontally the upper half would be on the level of the mastoid antrum. If this segment be again bisected vertically, its posterior half would again correspond to the junction of the antrum and the middle ear, and immediately behind this lies the supra meatal fossa".

This small depression just above and behind the external acoustic meatus marks a point, 1 cm. medial to which is the mastoid antrum of the tympanic bone. The triangle corresponds to the uppermost part of the concha of the auricle.

Triangle of Auscultation.

The upper border of the Latissimus dorsi is overlapped by the lateral border of the Trapezius. This angle is converted into a triangle by the medial border of the underlying scapula. The floor is formed by the Rhomboids, which are superficial to the 7th rib and the 6th and 7th intercostal spaces.

The triangle is so named because deep to it on the left side is the cardiac orifice of the stomach where the splash of swallowed liquids was timed in cases of oesophageal obstruction in pre-X-Ray days.

Other Triangles.

Assezat's triangle is situated between the nasal point, the alveolar point and the basion and is used as an index of prognathism in comparative craniology.

Triangles which are related to abdominal wall structures are:

a. Grynfeltt's fascial triangle (Grynfeltt and Legshaft) is bounded by the posterior border of the Obliquus internus abdominis, the anterior border of the Quadratus lumborum and above by the 12th rib.

b. Henke's triangle. This is situated between the descending part of the inguinal fold, the lateral part of the fold and the lateral border of the Rectus abdominis.

c. Labbè's triangle. This is a triangular area included between a horizontal line along the lower border of the 9th rib, the line of the false ribs and the line of the liver. It is the area where the stomach is in contact with the abdominal wall.

Two triangles are seen only on X-Rays viz. Ward's triangle which is an area among the trabeculae of the cancellous tissue of the neck of the femur and Codman's

triangle which is a deposit of new bone in the angle where the periosteum is stripped up from the surface of the bone by the swelling of an osteogenic sarcoma.

Other triangles are Elaut's (between common iliac arteries and promontory of sacrum), Friteu's (an area of cheek devoid of facial nerve), Calot's (cystohepatic triangle), Sherren's (bounded by lines joining the umbilicus, right anterior superior iliac spine and symphysis pubis) and Weber's triangle (between the heads of the 1st and 5th metatarsals and the midpoint of the plantar surface of the heel).

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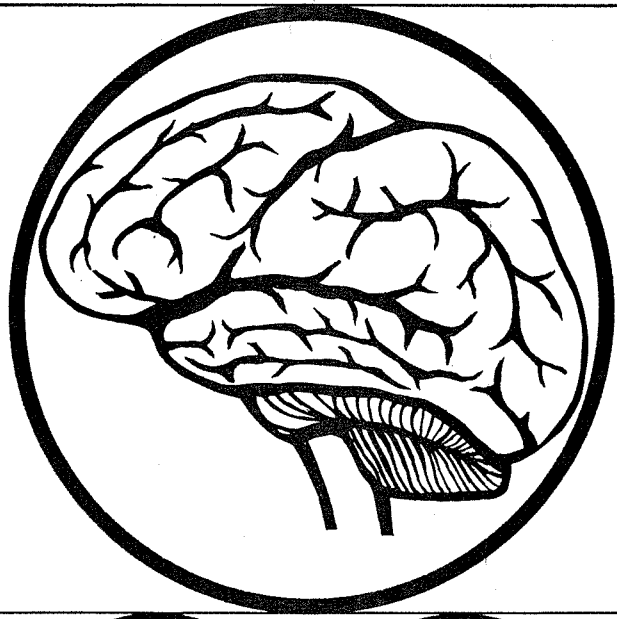
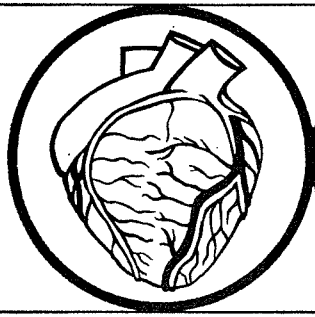
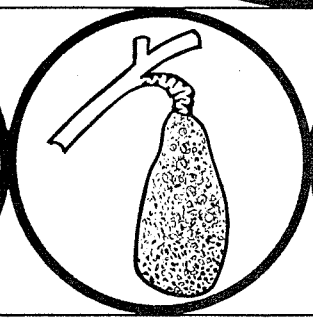
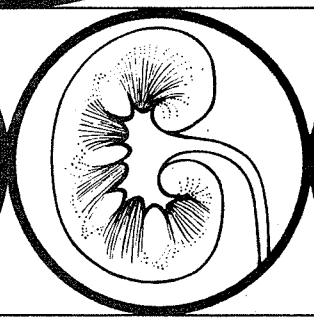




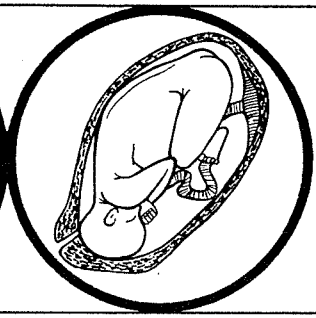
Dilation of the coronary vessels



Relief from biliary colics



Relief from renal colics



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Indications:

1) **Colics of the biliary and urinary tracts.**

Gall-stones (or calculi) developing in the gall-bladder or in the bile-ducts may give rise to attacks of biliary colics. Intravenous injection of 1 ampoule AVAFORTAN will promptly relieve spasm and pain and facilitates or accelerates the passage of stones to the intestines from where they are excreted with the stools.

The same applies to renal calculi located either in the renal pelvis or the ureters. These calculi will pass, after smooth muscle relaxation of the associated organs, to the urinary bladder and then through the urethra. The passage of the calculus is generally not painful to the patient.

It has been proved that AVAFORTAN produces peristaltic-like motility in the walls of the ureter.

2) **Painful spasm of the abdominal organs,** such as congestion of the liver, stomach cramps, and intestinal colics due to diarrhoea.

3) **Acute pancreatitis.**

A very rare but nevertheless interesting indication of AVAFORTAN in acute pancreatitis. Spasticity of the sphincter of Oddi may produce biliary reflux into the pancreatic duct. This will cause agonising pain. Morphine and its derivatives enhance spasticity of the sphincter and thus prolong the very painful condition. AVAFORTAN, however, relaxes the sphincteral spasm and may thus be regarded as a real therapy of acute pancreatitis.

This condition is caused by an acute inflammation due to infection through the pancreatic duct, or by the blood stream in pyaemia, infective endocarditis, or complicating an acute infectious disease, especially mumps.

4) **Tenesmus,** whether rectal or vesical.

5) **Myocardial infarction.**

Intravenous injection of 1 ampoule AVAFORTAN—the injection may be repeated after 10-20 minutes—will bring relief from pain and sedation of the patient, an essential prerequisite of management of infarct patients.

Sedation is a psychological by-effect of AVAFORTAN therapy.

6) **Angina pectoris.**

AVAFORTAN does not only relax smooth muscle spasticity of ducts and tracts, but also of the coronary vessels. It is therefore indicated to control attacks of angina pectoris, which is insufficient blood supply to the heart muscle due to spasm of the coronary arteries.

7) **Hiccough (Hiccup).**

This condition, which sometimes produces a very painful spasm of the diaphragm, can be satisfactorily controlled by the injection of 1 ampoule AVAFORTAN. Repeated injections of AVAFORTAN may definitely cure this condition.

8) **Obstetrics.**

Primary or acquired rigidity of the lower uterine segment and of the cervix uteri in particular, may delay child-birth. Intravenous injections of AVAFORTAN during the expulsion period will accelerate parturition significantly. AVAFORTAN was shown to be absolutely innocuous to mother and child.

9) **Migraine.**

AVAFORTAN injections as well as tables and suppositories have also proved their value to control *spastic migraine*. It is suggested to inject 1 ampoule intravenously and to maintain relief from pain with repeated doses of tablets or suppositories.

10) **Dysmenorrhoea.**

11) **Jaundice (spastic),** when due to obstruction or spasm occuring in the biliary tract—the jaundice generally subsides within one week.

12) **Spastic constipation.**

This is a form of constipation induced by neurasthenia, or by the effect of lead poisoning—there is constrictive spasm of part of the intestine. The type of constipation can also be associated with chronic and ulcerative colitis and after the abuse of cathartics and enemas.

Treatment should be initiated with AVAFORTAN injection, and the patient maintained on AVAFORTAN suppositories.

13) **Peptic ulcer**

An injection of AVAFORTAN brings symptomatic relief after 20 minutes. The patient is maintained on the suppositories.

Administration and Dosage.

In severe cases intravenous injections of 1 ampoule (5 ml.) is advisable—it may be repeated after 2-3 hours if necessary; in the case of heart attacks after 10-20 minutes. Intravenous injections should be given slowly at the rate of 1 ml per minute, with patient lying down. Generally the pain disappears almost immeditely, but does not take more than 4-5 minutes after completion of the injection.

In less severe cases the injection can be given intramuscularly.

Coated tablets and suppositories are recommended for milder conditions, and as maintenance following parenteral therapy.

ACTIVITIES OF THE I.F.M.S.A. STANDING COMMITTEE ON LIAISON 1964-1965

By ARTHUR G. MERCIECA (DIRECTOR 1964/1965)

At the General Assembly of the International Federation of Medical Student Associations, held in Gdansk, Poland in August, 1964, the Malta Medical Students Association was honoured by being appointed member of the Executive Board of I.F.M.S.A. and entrusted with the directorship of the Standing Committee on Liaison.

This appointment was given to the MMSA after it had successfully organised the Executive Board. and Exchange Officer's Meeting of the I.F.M.S.A. in Malta in December 1963 — January 1964. The I.F.M.S.A. was greatly impressed by the fact that the smallest member association of the federation. was able to organise a medical student International Conference so efficiently and with such a success.

THE I.F.M.S.A. EXECUTIVE BOARD

The Executive board of I.F.M.S.A. is elected yearly at the General Assembly, and consists of the President, Vice-President, Secretary. Treasurer. 3 members, and Directors of the I.F.M.S.A. Standing Committees. which are the Standing Committees on Liaison, Medical Education, Publications, Professional Exchange, and Student Health.

The directors of the Standing Committees are entrusted with the carrying out of the work for the current year. which the Executive Board plans out at the General Assembly and at the Executive Board Meetings.

THE WORK OF S.C.O.L.

The main activities of the Standing Committee on Liaison were:—

(a) Correlating the work and correspondence of the various members of the Executive Board.

(b) Promoting the organisation of various activities and enterprises by both member and nonmember associations, and also advising them on the various problems encountered in the organisation of such activities.

(c) Establishing new contacts with non member countries, and inviting them to apply for membership to the I.F.M.S.A.

THE ACHIEVEMENTS OF S.C.O.L.

The achievements of the Standing Committee on Liaison during the past year were very satisfactory.

Soon after the M.M.S.A. committee appointed me as director, one of my first duties was to attend the 39th Executive Board and Exchange Officer's Meeting of I.F.M.S.A. in Stockholm. There some of my most profitable work was getting the other delegates interested in the importance and value of the work of S.C.O.L. This proved most rewarding, because some of these delegates subsequently helped me to establish very good contacts with non-member associations, as a result of which a number have applied to the I.F.M.S.A. for membership.

Medical Student Associations from 9 different countries have applied for membership.

At the I.F.M.S.A. General Assembly held in Edinburgh in August-September 1965, Full Membership was granted to Costa Rica, Ireland, Congo, and Czechoslovakia. Associate membership was granted to Singapore, Panama, and Belgium. Ghana and Iran were not granted membership this year.

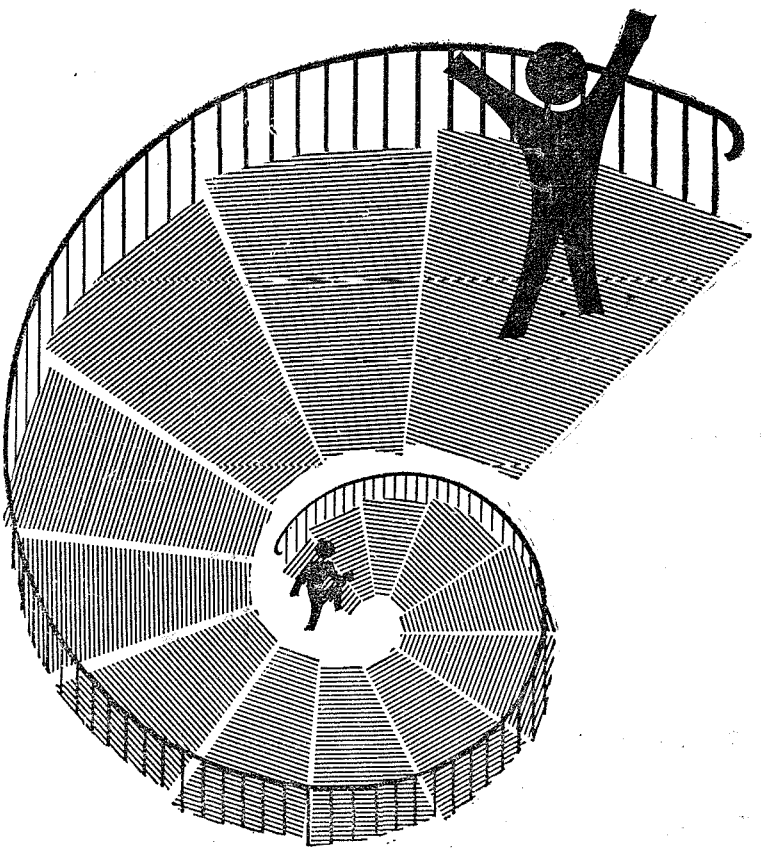
Other countries, including Ethiopia, Bulgaria and Korea, although very interested in I.F.M.S.A., were unable to apply for membership this year. They will probably do so in the next.

During my term of office, I have also tried to encourage the establishment of a National Medical Student Association in Ceylon, by promoting the amalgamation of the two main Medical Students Associations in that country. Advisory help and encouragement was also extended to the Medical Student Association in Tanzania, who intend to organise a Tropical Health Conference in 1967.

CONCLUSION

Although the work involved in S.C.O.L. was vast, it proved to be a great and worthwhile experience, both for me, personally, and also for the M.M.S.A. We have proved our reliability, and also shown that we can successfully take up responsibility attached to such high offices as that which the Federation had given us, namely that of member of the I.F.M.S.A. Executive Board, and Directorship of one of the Standing Committees.

BAYER



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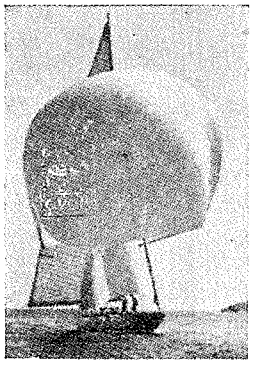

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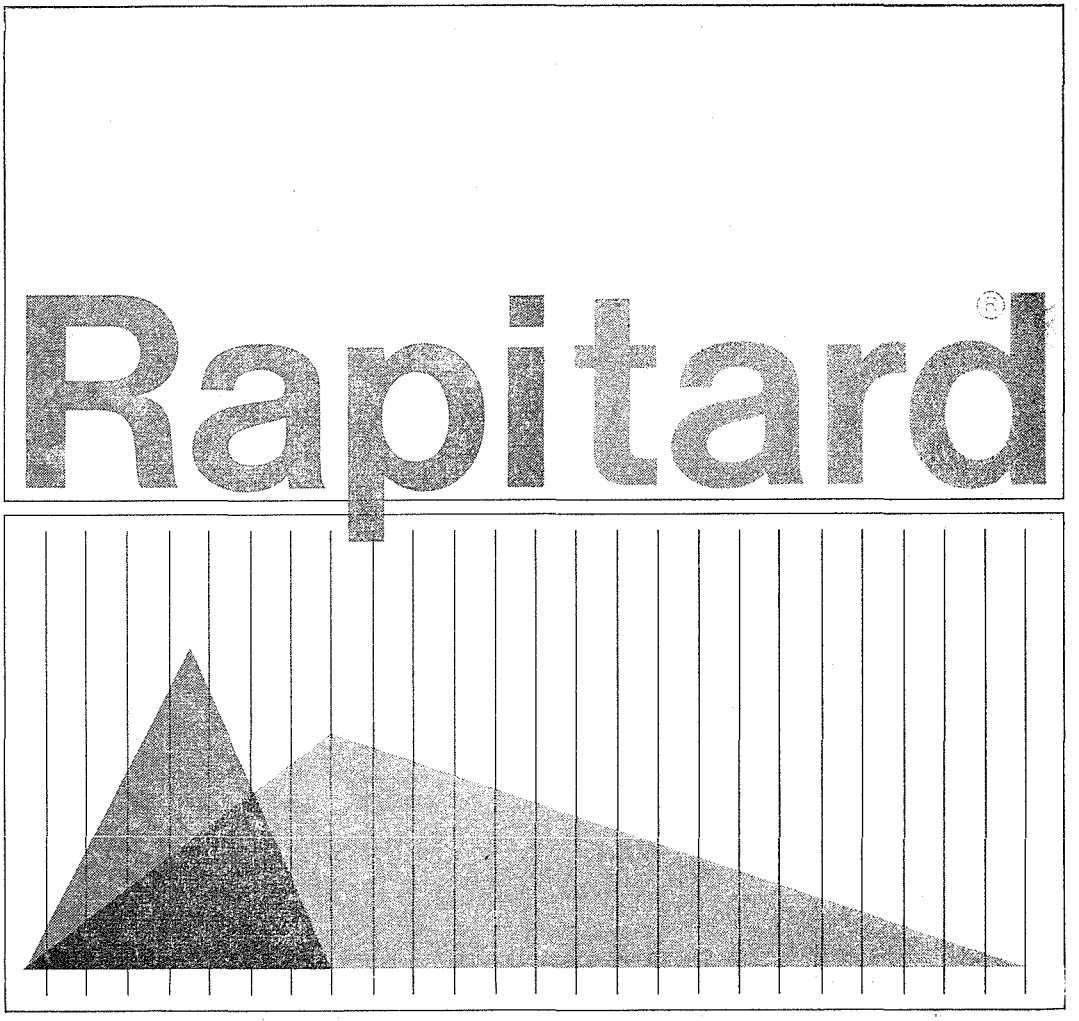

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