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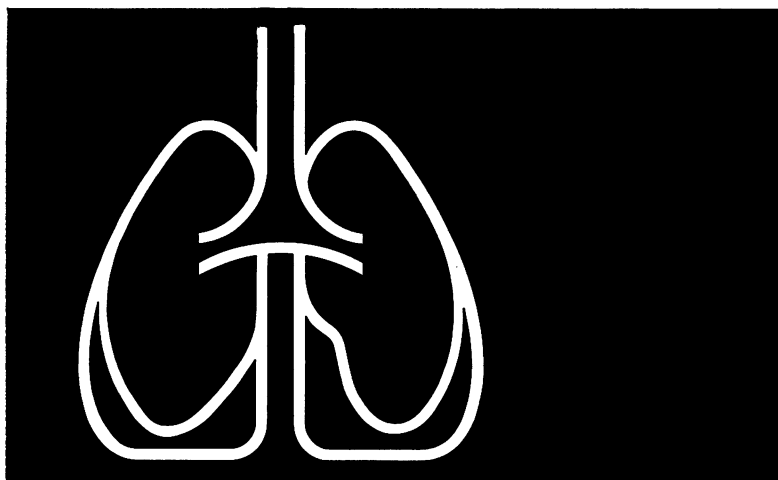
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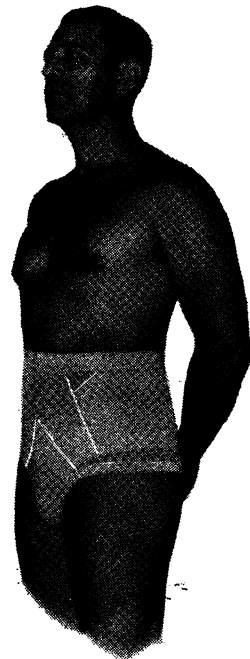
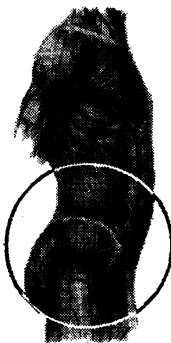
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*Brit.med.J.*, 1964, **2**, 429 (15 Aug)

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*Brit.med.J.*, 1965, **1**, 1329 (22 May)

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# CONTENTS

## No. 1: SEPTEMBER 1965

	PAGE
SOME ASPECTS OF HOSPITAL PLANNING. M. R. Neely, M.B., F.R.C.S.(ED.), F.R.C.O.G. - - - - -	1
ADDRESS AT SPECIAL GRADUATION CEREMONY IN QUEEN'S UNIVERSITY. J. H. Biggart, C.B.E., D.SC., M.D., F.R.C.P. - - - - -	8
FARMER'S LUNG. Helen E. Cairns, B.SC. - - - - -	11
THE HAEMOLYTIC-URAEIC SYNDROME. C. M. B. Field, M.D., D.C.H., F.R.C.P.(E.), and C. Cotton Kennedy, D.M. (OXON.), M.C.PATH. -	13
LEG ELEVATOR FOR CHRONIC OEDEMA. H. C. Dales, M.CH., F.R.C.S., and Sr. E. E. Stevenson, S.R.N., S.C.M. - - - - -	21
A CASE OF SMALL BOWEL PERFORATION. J. Strahan, M.B., D.R.C.O.G., F.R.C.S., and P. J. Sweeney, M.D., F.R.C.P.I., M.R.C.P. - -	22
BLEEDING OESOPAGEAL VARICES IN THE ABSENCE OF INTRAHEPATIC OR EXTRAHEPATIC OBSTRUCTION OF THE PORTAL SYSTEM AND WITHOUT PORTAL HYPERTENSION. George W. Johnston, M.B., F.R.C.S. -	23
OSTEOMALACIA FOLLOWING GASTRECTOMY. J. Piggot, M.B., F.R.C.S.E. -	27
CANCER OF THE BREAST. A. R. Lyons, M.D., M.R.C.P., F.F.R.R.C.S.I. -	33
REVIEWS - - - - -	44

## No. 2: DECEMBER 1965

WHAT OF THE FUTURE? J. S. Loughridge, M.D., B.SC., F.R.C.S. - -	53
RAZORS TO AUTOCLAVES. J. W. S. Irwin, M.B., F.R.C.S.(EDIN.). - -	66
ON NERVOUS DISEASE IN THAILAND. R. S. Allison, V.R.D., M.D., F.R.C.P., D.P.M. - - - - -	74
ACUTE PANCREATITIS. C. J. H. Logan, M.B., F.R.C.S. - - - -	93
A CASE OF CONGENITAL PSEUDO AINNUM. Agnese M. T. Kelly, M.D., D.C.H.	99
OBSERVATIONS OUT OF TIME. Sir John McMichael, F.R.S. - -	103
FORTY YEARS IN CARDIOLOGY. William Evans, M.D., D.SC., F.R.C.P. -	111
ECONOMIC AND SOCIAL ASPECTS OF TAENIASIS. J. S. Logan - -	124
A CLINICAL STUDY OF A SPASMODIC AGENT (CYCLOSPASMOL) IN THE TREATMENT OF ELDERLY ARTERIOSCLEROTIC PATIENTS. P. J. Ward, L.R.C.P.I., L.M., L.R.C.S.I., D.P.H. - - - - -	129
A CASE OF RUPTURE OF THE UTERUS. U. N. Pathak, M.R.C.O.G., M.M.S.A.	137
THE "THIRD COMA" IN DIABETES. Alan P. Grant, M.D., F.R.C.P.I., M.R.C.P.	140
REVIEWS - - - - -	73, 98, 123, 128, 143

# CONTENTS

	PAGE
WHAT OF THE FUTURE? J. S. Loughridge, M.D., B.Sc., F.R.C.S. - -	53
RAZORS TO AUTOCLAVES. J. W. S. Irwin, M.B., F.R.C.S.(EDIN.). - -	66
ON NERVOUS DISEASE IN THAILAND. R. S. Allison, V.R.D., M.D., F.R.C.P., D.P.M. - - - - -	74
ACUTE PANCREATITIS. C. J. H. Logan, M.B., F.R.C.S. - - -	93
A CASE OF CONGENITAL PSEUDO AINHUM. Agnese M. T. Kelly, M.D., D.C.H.	99
OBSERVATIONS OUT OF TIME. Sir John McMichael, F.R.S. - -	103
FORTY YEARS IN CARDIOLOGY. William Evans, M.D., D.Sc., F.R.C.P. -	111
ECONOMIC AND SOCIAL ASPECTS OF TAENIASIS. J. S. Logan - -	124
A CLINICAL STUDY OF A SPASMODIC AGENT (CYCLOSPASMOL) IN THE TREATMENT OF ELDERLY ARTERIOSCLEROTIC PATIENTS. P. J. Ward, L.R.C.P.I., L.M., L.R.C.S.I., D.P.H. - - - - -	129
A CASE OF RUPTURE OF THE UTERUS. U. N. Pathak, M.R.C.O.G., M.M.S.A.	137
THE "THIRD COMA" IN DIABETES. Alan P. Grant, M.D., F.R.C.P.I., M.R.C.P.	140
REVIEWS - - - - -	73, 98, 123, 128, 143

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# CONTENTS

	PAGE
WHAT OF THE FUTURE? J. S. Loughridge, M.D., B.SC., F.R.C.S. - -	53
RAZORS TO AUTOCLAVES. J. W. S. Irwin, M.B., F.R.C.S.(EDIN.). - -	66
ON NERVOUS DISEASE IN THAILAND. R. S. Allison, V.R.D., M.D., F.R.C.P., D.P.M. - - - - -	74
ACUTE PANCREATITIS. C. J. H. Logan, M.B., F.R.C.S. - - -	93
A CASE OF CONGENITAL PSEUDO AINNUM. Agnese M. T. Kelly, M.D., D.C.H.	99
OBSERVATIONS OUT OF TIME. Sir John McMichael, F.R.S. - -	103
FORTY YEARS IN CARDIOLOGY. William Evans, M.D., D.SC., F.R.C.P. -	111
ECONOMIC AND SOCIAL ASPECTS OF TAENIASIS. J. S. Logan - -	124
A CLINICAL STUDY OF A SPASMODIC AGENT (CYCLOSPASMOL) IN THE TREATMENT OF ELDERLY ARTERIOSCLEROTIC PATIENTS. P. J. Ward, L.R.C.P.I., L.M., L.R.C.S.I., D.P.H. - - - - -	129
A CASE OF RUPTURE OF THE UTERUS. U. N. Pathak, M.R.C.O.G., M.M.S.A.	137
THE "THIRD COMA" IN DIABETES. Alan P. Grant, M.D., F.R.C.P.I., M.R.C.P.	140
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## WHAT OF THE FUTURE ?

**By J. S. LOUGHRIDGE, M.D., B.Sc., F.R.C.S.**

Presidential Address to the Ulster Medical Society, 14th October, 1965

I MUST thank you for the great honour which the Council of the Society has done me in asking me to be your President for the incoming session. I appreciate the honour greatly, though it entails certain responsibilities, not the least being this agony of words, usually called the Presidential address. Even the choice of a subject worthy of the occasion gives cause for thought. I could deal with the present and discuss some aspect of surgery in one or more of its rapidly advancing frontiers. The past has been frequently and brilliantly treated by many of my predecessors in the Presidential chair. The third alternative is to talk of the future and I have been so bold and so foolish as to rush in where my betters have feared to tread.

Other attempts at prophecy are not encouraging. Indeed the only really successful example which occurs to mind is that of Jules Verne, who so clearly foresaw the invention of the submarine, but more daringly and with remarkably accuracy in 1865, exactly one hundred years ago, described a journey from the earth to the moon direct in 97 hours 20 minutes. His prophecy is dramatic in that he placed the projection site in Florida, in that the rocket was fired from a shaft sunk in the ground, and in that he was only 30 hours wrong in his estimation of the duration of the flight. He quoted 97 hours 20 minutes; the actual time of Ranger VII was 67 hours 35 minutes. Further, he conceived the idea of a special observatory—the forerunner of the Jodrell Bank of today.

Now that the impossible has been achieved, and rockets have been placed on the moon and, even much more remarkable, in the vicinity of the planet Mars, it is interesting to note how the incredulity of the common man has given way to indifference to the greatest technological achievement of all time, namely the journey of Mariner IV. Such a prophecy must be unique; and for other would-be prophets and myself, I would humbly keep in mind Sam Gee's dictum on pulmonary tuberculosis—"Never to give a forecast, for the only certainty is that you will be wrong." Another discouragement is to think back to my early days in medicine and to note how different the progress has been from what I would then have thought. Thus, up till 1930 the great advances of the previous decades had been largely diagnostic, especially bacteriological, radiological and electrocardiographic.



Biochemistry was just beginning to come into its own as a routine clinical procedure, and that was due in no small degree to one of the two notable therapeutic discoveries of the 1920's, namely the introduction of insulin. One generation has seen biochemistry advance from its humble origin to the routine use of radio-isotopes and to the greatest scientific achievement of this decade, namely the cracking of the genetic code by Crick and Watson. No one then could have seen that the main advances to come would have been in therapeutics, both medical and surgical. Indeed, one well known surgeon in 1927 was so indiscreet as to say that surgery has reached its zenith, and was incapable of further advance; whereas in fact the technique of surgery has made more progress in the last 20 years than at any time except the period which immediately followed the advent of Listerian principles in the operating theatres and surgical wards. A main reason for the sudden advance was the isolation and purification of the active principle of the arrow-poison curare. This and other advances in pharmacology and the application of the basic physiology of respiration have revolutionized surgery and the administration of anaesthetics, and have indeed made factual Moynihan's hope that the patient would be made safe for surgery and that surgery would be safe for the patient.

Within the memory of our elder colleagues a would-be surgeon had to serve a long apprenticeship as an anatomist, and our seniors worked for as many as seven years in the dissecting room as a pre-requisite to an appointment on the surgical staff. Later the emphasis changed to pathology, but now the essential basic science is physiology. Most of the recent advances in surgery have been physiological, and physiological principles and techniques are now applied in many fields. Thus the artificial kidney is an ingenious machine: it has solved the technical difficulty of making a semi-permeable membrane, allowing the passage of metabolites and drugs and retaining the protein and cellular constituents of the blood: it does so at body temperature, keeps the extra-corporeal blood sterile, and returns it to the circulation free of foam and free of clots. With this machine many patients have been safely carried through critical illnesses, and even chronic disease has been held in check by its repeated use.

The anaesthetists now practise true physiology, applying the laws of gaseous exchange and the knowledge of the mechanics of respiration and circulation to the needs of each individual patient. They have improved the heart-lung machine to the point where it is used daily to maintain an extra-corporeal circulation adequate to the needs of the patient during operations on the heart itself. They have also gone beyond the limits of the physiological norm in the induction of the state of hypothermia, and in so doing have made the patient safe for surgery which would otherwise be impossible. All these techniques are really in their infancy and no one can tell how they will develop in the next generation.

Nor must we forget how the ophthalmic surgeon is learning to use laser beams in the treatment of local conditions in the retina, or how the aural surgeon is using a microscope to operate on the auditory ossicles and the semi-circular canals, so that 80 per cent. of patients with certain kinds of deafness can now be made to hear; or how the neuro-surgeon is using a beam of protons to cause localised necrosis in the brain, and is using ultra-sonics as an aid in diagnosis.

The increasing magnitude and duration of operations, particularly of heart operations, require constant critical and skilled supervision of the patient in the

post operative period. This need has given rise to the system of intensive care in which a special ward is used to nurse the patient on his return from the operating theatre. Here a special team of nurses watches the patient and keeps a constant check on his colour, blood pressure, pulse and so on. The Italians have recently introduced an intensive, care monitoring system, patriotically named after Galileo. A recording instrument is situated by each bed in the recovery unit, and all the recorders are connected to a central console at the nurse's station. This console "hunts" each bed in turn, and for 15 seconds it displays the blood pressure, pulse, E.C.G. and temperature of each patient automatically and continuously, but the doctor by pressing a button can concentrate on the records of any one patient. An alarm is included in each monitor, and if the safe maximum or minimum of each single phenomenon is exceeded, a warning light goes up at the patient's bedside and a bell rings. A defibrillator and a pace maker can be included to give automatic control of arrhythmia.

The long list of galenicals which constituted the bulk of the pharmacopoeia down the ages and as recently as twenty years ago has been largely swept away, to be replaced by a wealth of new therapeutic agents, liver extract (already replaced in turn by the isolation of cyanocobalamin), the sulphonamides, antibiotics, tranquillizers and the cyto-toxic drugs. The discovery of penicillin was one of the highlights of the mid-twentieth century; its abuse is one of the tragedies, as its indiscriminate use has led to the evolution of drug resistant mutants. Infectious agents maintain a more or less constant siege of the body and invasion is prevented only by a continuing but fluctuating immunity. Recently the antibiotics have given a temporary advantage to the body, but at a heavy cost. The battlefield is now in a sort of truce which may end at any time in the near future with a resumption of hostilities by more aggressive organisms attacking persons whose immunity has been reduced by disuse atrophy. The best example is the hospital staphylococcus to which patients are exposed in surgical wards or during prolonged operative procedures. It may be that antibiotics will soon prove to be no longer of value, and that we shall have to return to a modern version of Lister's carbolic spray—currently depicted on our postage stamps. A main danger of upsetting the truce between man and his pathogenic bacteria is the use of anti-bacterial drugs either in inadequate dosage or on wrong principles. The anti-bacterial drugs have given a temporary control of the communicable diseases but have been disappointing in the attempt at eradication. The past decade has seen a spectacular decrease in the incidence of tuberculosis but the emergence of drug resistant bacilli render the future bleak unless other means of control are introduced. Malaria has been nearly eliminated, but already it has been shown that monkey malaria can be transmitted to man and it may be that attempts at the eradication of one parasite will make possible its replacement by another more difficult to treat. It is noteworthy that the disease-causing viruses are rarely affected by drugs, except possibly by interferon, but it is fortunate that two of them—smallpox and poliomyelitis are preventable, not by eradication, but by raising the active immunity by vaccination with attenuated virus.

Special mention is to be made of the chlorinated hydrocarbons. Synthesized in the 1880s, the toxic effect of D.D.T. on insects was recognized only in the 1940s, and almost immediately it was used with effect against ticks in Malaya, against

mosquitoes in India, flies in N. Africa and lice and scabies everywhere. At the battle of El Alamein it is recorded that 50 per cent. of the Africa Korps was glued to the commode by dysentery. If D.D.T. had been used by the Germans and not by the 8th Army, the result of the battle could easily have been very different.

But the most recently introduced tool is likely to be the most revolutionary of all. I refer to the computer. Up to 1957 general purpose high speed digital computers had been used in physics and applied mathematics, and were almost unknown in medical research. In 1962 Kendrew & Perutz were awarded the Nobel Prize in Medicine for their studies in the structure of haemoglobin and myoglobin—a problem successfully solved by the use of computers. Already in U.S.A. the computer is being used more in bio-medical research than in pure physics or mathematics. Medical research is particularly amenable to the use of computers and their continued spread is almost certain. The computer is being used in epidemiology, vital statistics, in the analysis of laboratory data and in the processing of continuous physiological data. I see the physician of the future filling in a questionnaire and feeding the items together with a long list of biochemical and other data into a computer and reading off the diagnosis on a cathode ray scheme, or on a punched card. In the storage and retrieval of clinical and laboratory records the Mayo clinic is working out a scheme where the clinical history, physical findings and laboratory data are all recorded on a work sheet, which after a day or a week is sent for key punching. After the cards are verified, edited and checked for errors, all the clinical information is filed in blocks, one block for each patient. Each block represents about 200 items of information and actually occupies about 10 inches of tape. One reel of tape holds information on about 2,900 patients. A printed report can be made when required. The computer has also been used in the storage and analysis of pathology and post mortem examinations. A computer based programme is even developed for automated personality assessment. It is said to be used enthusiastically by physicians of Mayo Clinic, who claim that it is welcomed by patients.

In California, people avail themselves of the Permanente scheme, similar to our British United Provident Association, but at the fee of an extra \$20, the members may have a yearly check. A series of 24 cubicles are arranged in a large circular building. The member, as he enters, is given a computer punched card stamped with his name and particulars. In the first cubicle his retinal fields are photographed and the result is lodged in an analogue computer. In the second cubicle the Achilles tendon reflex is measured as a test of thyroid function. In a third cubicle, the E.C.G., the blood pressure and the pulse rate are all noted electronically and in a fourth the E.E.G. is recorded. In a fifth room the serum lipoids are measured. In a sixth room the member meets his first technician, who takes a sample of blood by pricking the finger. The blood is transferred to an automatic analyser and eight biochemical parameters are measured, blood sugar, urea, sodium, potassium, chloride, bicarbonate, protein and transaminase. This machine can deal with 60 persons per hour. In the next room the individual under test has a second pin prick for haematological parameters. The results from all these tests are fed into the computer. The only non-automatic test is of the urine, a specimen of which is passed through a hatch and planted out for organisms in a quick growth medium. A positive or negative result is obtainable in 30 minutes and a technician

passes the result to the computer. Another cubicle is given over to the determination of height, weight and other anthropometric data. The person under test emerges from this series of cubicles at the end of 40 minutes, when the computer issues a sheet of paper containing all the data appertaining to that individual. He then enters a consulting room where his doctor advises him according to the findings.

The brothers Jungnar are now engaged on a similar project in Varmland for the Swedish Government. They are attempting to measure the biochemical and haematological parameters of 100,000 persons, together with their retinal photograph, urinalysis, blood pressure and a completed questionnaire. The findings are stored on magnetic tape. The scheme is now about to be applied to the whole population of Sweden. The Jungnar equipment handles all the required tests of 400 persons per hour. The British Ministry of Health has taken preliminary steps to carry out a pilot study of population screening in an English town on the Swedish pattern. The scheme will entail the recruitment of staff, the specialized automative machinery and data-processing equipment, for a series of large buildings throughout the country. Every individual will have his own card which will contain a yearly record of these routine tests.

Of the many problems still awaiting solution, mention may be made of a few. From the earliest times man has aspired to graft limbs or organs, but only recently has success been achieved and that in a limited field. The earliest successes were in replacement of the cornea. This is a very delicate operation which is greatly helped by the fact that the cornea has no blood supply. About 80 per cent. of corneal grafts are now successful, though special immunological problems remain to be solved.

The technique of transplanting a kidney is already standardized and is not unduly difficult. The renal artery and vein of the donor kidney are sutured to the iliac artery and vein in the iliac fossa, the ureter being connected to the bladder. The operation has been performed successfully in many patients, in all of whom the donor was an identical twin. In cases other than identical twins the donated kidney works for a limited time. If the problem of the immune reaction can be solved a major breakthrough in transplantation will have been achieved. Living bone or artery, or even heart, will then be used to replace parts damaged beyond repair. In the case of heart transplants it will be technically easier to replace the lungs as well as the heart, as this will entail suturing only of the aorta and both venal cavae; as the pulmonary artery and veins will remain intact. The future of surgery will largely be that of repairing traumatic lesions, transplantation of organs and the repair of congenital defects. The surgeon, like any other good craftsman, likes to do constructive work—a description which applies to most operations, except for those used in the treatment of malignant disease. This group is mutilating by its very nature. Every surgeon will welcome the day when a non-mutilating cure for neoplasia will have been found.

The profession of medicine has been called into being for two great needs, the relief of pain, and the cure of disease. The attention of the profession is therefore focussed primarily on the individual patient. The care and attention which the medical man has given to his patient down the ages is manifest in the high regard for, and the universal trust, of the sick person in his doctor. The good doctor has

one paramount interest, the welfare of his patient, and he has had no cause to consider other factors. But now the very success of medicine is raising problems of fundamental importance to mankind as a whole. These problems refer to the individual, to the genetical influence on future generations, and to the world population.

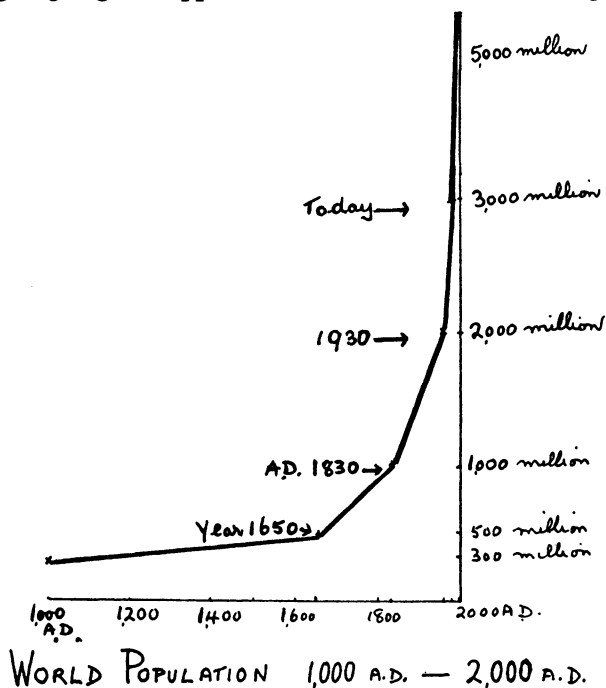
The advantage to the individual cannot be gainsaid. With an adequate diet, improved hygienic living conditions and medical care from birth and the elimination of many of the serious infections, the expectation of life has increased enormously and the majority born may now expect to live healthily for the accepted normal life span. Unfortunately we have discovered no elixir of youth, and our hospital wards will increasingly become geriatric units. We have an increasing number of people living the length of the allotted span, but we still have

"Last scene of all  
That ends this strange eventful history  
Is second childishness and mere oblivion  
Sans teeth, sans eyes, sans taste, sans everything."

I was first made acutely aware of the genetical significance of our work on the day when the late Foster Moore had the tragic obligation to remove both eyes of a baby for glioma of the retina; and on the same day to read in the British Medical Journal of this malignant disease occurring in three members of one family, whose father had survived the removal of a retinoblastoma in his own babyhood. Congenital pyloric stenosis had a high mortality until 1940. Since then surgical treatment results in a recovery rate of nearly 100 per cent. The medical treatment of diabetes not only saves the lives of young people suffering from the disease, but it has allowed them to have children, a state of affairs unknown before the rise of insulin. Pediatric medicine and surgery save the lives and preserve the health of many potentially valuable members of the race, but they undoubtedly contribute to the perpetuation of the genetically unfit.

It is mainly of the increasing world population and the consequences that I should like to speak a little more fully. The near elimination, during the past few decades, of the Captains of the Men of Death, principally tuberculosis, syphilis, gastro-intestinal infections and malaria, has contributed to a notable increase in the expectancy of life. At the same time the scientific production of food and its rapid transport to the large centres of population have caused an unparalleled increase in the world population. Indeed the increase has been called a population explosion, and justifiably so when we look at the figures. Thus radioactive methods of dating indicate that man has lived on this earth for 200,000 years and more. Yet it took 199,000 years, i.e., up till the year 1000 A.D. for the numbers of the human race to touch the 300 million mark, an average increase of 1,500 persons per annum. The birth rate was high, but it was almost neutralized by the high death rate, aided by periodic sharp reduction caused by epidemics. The world population was 500 million in the seventeenth century; it was 1,000 million in 1830 and 2,000 million in 1930. And in the past 30 years over 1,000 million have been added to make a grand total today of 3,000 million. It has been said that one-seventh of all mankind who have ever lived, are alive at this moment. About 17 million more people will be living in Britain in the year 2000, i.e., it will require a new city the size of Belfast each year and every year to accommodate them.

Every biologist knows what a population growth curve of this kind means, whether the curve refers to men or lemmings, to locusts or to bacteria—it means that something is going to happen, and in Nature that something is a crash.



Nature has ensured that in man, as in all other species, the mechanism of reproduction is frighteningly effective. The recent enormous increase in the human population is due, not to an increased fertility, but to the advances in the medical sciences which have caused a sudden and dramatic fall in the death rate, while the birth rate remains high. This fall became acute a decade ago when malaria—the natural controller of the population in the tropics—was largely eradicated. The immediate consequence is a tremendous excess of young people. In some parts of the world half the population is less than 14 years of age and in many other parts half is less than 18 years of age. The reproductive potential of the next 30 years arising from an age distribution of this kind needs no emphasis. Further, the increase is very different in different parts of the world, so we in the United Kingdom constitute a progressively smaller percentage of the human race. The present rate of increase of world population is 2 per cent per year. This does not sound very much but if continued annually for 200 years, the population will be 150,000 million or 50 people to every one now alive. All these will have to be fed, housed, exercised, transported and given amenities, including a health service. It is very evident that in the long term, either birth rate must come down or the death rate will once more go back up. The ability to be fruitful and multiply and to inherit the earth is not, of course, peculiar to man. The prime duty of all species of plants and animals is to survive, and to this end the reproductive capacity is

such that any living creature, able to multiply without hindrance, would soon swamp the world. The fact that this does not happen was first noted by the Rev. T. R. Malthus in his *Essay on Population*. He recognized that the populations of all species are held in check by limiting factors. The main factors are lack of food, disease, and war. In Nature, relaxation of one limiting factor allows a population to increase until it bumps up against the same factor on another level, or against one of the other factors.

In passing it may be noted that Malthus said in 1826 that the indiscriminate doles and bounties upon large families were utterly to be condemned as tending to aggravate the very evils which they were supposed to remedy; also that Darwin on reading his *Essay* was impressed by Malthus's phrase "Struggle for existence" and from it Darwin got the idea of how such a struggle would play a part in the formation of new species.

The population explosion is a direct cause of aggressive imperialistic expansion as in the struggle for lebensraum of pre-war Germany and Japan and now of post-war China. It affects also the living conditions in the world's conurbations. The great wen that is London is now pathologically large with traffic paralysis, and frustration and loss of long hours in commuting.

It is shortly going to affect us in these islands in a way never dreamed of by our forbears. I refer to the colour problem. Smethwick is a borough, famous in the past for James Watt, of the steam engine, and William Murdock, the pioneer in gas lighting. Today it has a population of 60,000 of whom 10 per cent are coloured. These coloured people have migrated from Jamaica and the remote villages of the Punjab. Why? Because at home they are at starvation level and they come here because the post-war boom in the car industry has meant a shortage of labour in the unattractive and unskilled occupations. Thus England is doing what U.S.A. did in the eighteenth and nineteenth centuries and South Africa did in the nineteenth and twentieth centuries. We now criticise S. Africa for apartheid, but I believe we shall see a similar reaction in Birmingham, in Bradford and in Notting Hill within a generation. I see an increase of unhappiness for both white and coloured.

It is evident that if the population is allowed to increase unabated, a check will inevitably be met, in one or more of three ways—war, famine or pestilence. War has always been a means of keeping population down, and its killing power reached a climax only in the past 50 years. Thus in the Great War of 1914-18 this country, France and Germany lost 5 million men; a tragedy all the greater because the deaths were not, as Nature would ordain, of the old and the feeble, but by contrast they were of the young and the fit. I think there can be no doubt but that many of the errors of commission and omission which led directly to the Second World War were due to the fact that many of the best brains of a whole generation were lost in the First World War. The races of mankind were further weakened by lack of food and the pandemics of influenza and of encephalitis lethargica. The number of millions who died in the Second World War will never be known, but the world has been spared any great pandemic such as followed the First World War.

The threat of war is still with us and in even more frightening forms whose power of destruction has completely overwhelmed the means of defence. As we

sit here in this hall at this moment we could be all extinguished in a flash, for Khrushchev has said that with three nuclear bombs he could destroy Britain. Nor are nuclear weapons the only means by which mass destruction could be carried out. The recent death of a bacteriologist in a laboratory in Wiltshire indicated that our own government is working at secret methods of bacteriological warfare. The chemists, too, are active in their search for poison gases. Indeed biological warfare may easily be a powerful factor in the future. Its facts have high priority on the secret list; either for direct killing or indirectly by destroying crops or promoting epidemics. It has been said "Before long it will be the medical establishments which will be surrounded by barbed wire and it will be the biologists rather than the physicists who will be subjected to the most intense loyalty checks."

If we have enough wisdom not to go to war, can we avoid famine? Food supplies can be increased by irrigation, by improved methods of agriculture and by the elimination of plant diseases and pests, but there is a geographical limit to one and drawbacks to the others; though not the least difficulty is the education of the backward, e.g., in the primitive agriculture of India. The large increase in the population of the West consequent on the Industrial Revolution coincided with the conversion of the prairies of U.S.A. and Canada into wheat fields. These fields still produce a surplus which goes but a little way to meet the starvation always present and even extending in the East. No further large areas in the world are available for extension and already large fertile tracts in U.S.A. and China have degenerated into dust bowls through ill-advised husbandry.

A sudden and welcome increase in food productivity followed the introduction of the chlorinated hydrocarbons and other pesticides. Although they were introduced only a few years ago, the enthusiastic advertisements of the great oil companies have already faded from the pages of the scientific journals, for their use has upset the balance of Nature to an alarming extent by their diffusion the world over. Recent investigations in France show that the fatty tissue of 6 out of 10 people tested after death contain an average of 5 p.p.m. of D.D.T.; Americans have also 5, but some people in Sweden are showing levels of 12 p.p.m. Many of the beautiful and useful insects like butterflies and honeybees have been killed as well as the pests. The voices of the insectivorous birds like the cuckoo and the corn-crake are seldom heard in the land. Millions of fish have been killed in the Mississippi River because aldrin was used on the neighbouring farms. The infertility of the Speyside ospreys which feed on sea fish and the finding of D.D.T. in the livers of the Antarctic penguins have proved the widespread diffusion of these poisons throughout the oceans of the world.

I see no prospect of the pressure of population being eased by migration to the moon or one of the planets. Apart from the sheer physical impossibility of transporting a sufficient number of people to have any effect on the congestion here, the few explorers who reach the moon and return will have to tell a dismal tale of lack of water and of air, of intolerable heat and radiation torturing them continuously for 14 days at a stretch, to be followed by an equally long period with the temperature at or near absolute zero. The photographs radioed back to earth by the satellite Mariner IV prove that water is also absent on the planet Mars.

These explorers will be glad to return to Mother Earth, where other problems



will still be waiting for solution. One of these is the problem of pollution of the atmosphere, the rivers and the sea. The pollution of the atmosphere came with the Industrial Revolution. It has taken a constant heavy toll of health and life, with two maxima—one in London in the winter of 1952 and the other in Belgium in 1930. Legislation has recently done much to clear the air, but more could still be done. Our rivers, rising in the hills as gurgling brooks of limpid water, become black and poisonous before they reach their estuaries. It surprises us to read that the Thames was a salmon river in the eighteenth century when its water was taken as low as Greenwich for making beer. Erie, one of the five great lakes of N. America, is dying; its once gleaming sands are now covered with smelly slime and its waters have been poisoned with chemicals and sewage. Even the oceans with their immense reservoirs are being affected. Oil and sewage are the most obvious pollutants, along with radio-active materials, but others are equally serious. For example, two hundred thousand tons of lead are used every year in anti-knock petrol and most of it finds its way into the air and eventually to the sea where the concentration of lead has increased tenfold in the past 50 years.

It is a sobering thought that as the population increases, so will most of these pollutions increase and so will the relative amount of food decrease, also our capital of certain special materials. First amongst these is fresh water. One fifth of the world's land surface is desert, and that area is increasing. By increased personal use but mainly by the demands of industry, the supply of fresh water even in this country is no longer able to meet the demand. Already in New York, the situation is serious and whiskey drinkers have been advised to use imported soda water. Our fossil fuels, coal and oil, are burned wastefully to the extent of many millions of tons annually, and will be exhausted in a century or two. Several hundred tons of the rare metal, tin, go with used food cans into refuse dumps daily. Lead is becoming scarce and silver ever more precious. Recently the U.S. Government has been forced to debase its silver coinage. It is only a matter of time until X-ray films will cease to be made. What will the radiologists do then, poor things? The image intensified has just arrived in time! About one-half of all our mineral resources have been extracted in the past 50 years.

The choice before us for the future is either to restrict the population of the earth to 1,000 million and to allow them to live on steak and pheasant and to have a cottage in the country, or to let the population expand to 100,000 million when it will of necessity become confined to skyscraper tenements with personal freedom reduced to a cruel minimum, and to live on soya beans and seaweed.

If the world's leaders have the wit to avoid all-out war and if we do not have to contend with a serious pandemic, how are we to survive as an intelligent species and how are we to have the space in which to live and move and have our being with sufficient of this world's goods to enjoy life and to satisfy our bodily and mental needs? I see only one answer and that is birth control. But birth control is no easy solution. It suffers from several severe handicaps. None of the methods is completely reliable, and all have one or more disadvantages. There are psychological difficulties and religious prohibitions. Most important of all, it is likely to be practised by those whom we regard as the cream of mankind to their own eventual extinction, while the indolent, the thriftless and the irresponsible will continue to increase. The need for control illustrates the lack of cerebral inhibition

in those who fail to practise, and ignorance and prejudice in those who preach against it.

Within a generation we have seen an unbelievable breakthrough in science and in medicine. Show a diesel engine, a steam turbine or a helicopter to Leonardo or Galileo or Archimedes and they would have no trouble in understanding the principles by which they work; but show them an electronic computer, a nuclear reactor or a television set and they would be entirely at a loss. Röntgen's discovery of X-rays in 1895 was a factor in the break between classical physics and the present day conceptions of radioactivity, the structure of the atom, and quantum mechanics. In only one important subject has progress been tardy, and that is in our knowledge and understanding of our own minds. This is probably to be expected, particularly when we reflect that the chief function of the human brain down the ages has been to seek food and only secondarily to seek truth. Indeed the intellectual qualities have been very unequally divided among the great number of people who have ever lived. "Take 300 men out of history," wrote Sir Arthur Keith, "and we should be still living in the Stone Age." It may be that Keith exaggerated and the number may have been 3,000 or 30,000, but even so it is still true that without an exceedingly small number of uncommon men, the vast mass of humanity would have remained inert.

I have only time to mention the steady and exponential rate of growth of scientific knowledge since 1900. It is said that of all the scientists who have ever lived, three-quarters are alive and working today. Of all the scientific knowledge in the world, two-thirds has been discovered since the Second World War. In the 1920s, the analysis for blood urea took place as single tests in the clinical room beside the ward; now an average of 300 tests are done daily in the biochemical laboratories of the Royal Victoria Hospital alone. Indeed, these laboratories are among the most fully automated in the United Kingdom.

The growth of knowledge has altered profoundly the theory and practice of medicine. At first empirical, it has been influenced in turn by pathology, bacteriology and biochemistry. Now medical physics is playing an increasingly important role in modern medicine, which is recapitulating to some extent what Helmholtz did in his lifetime. You may remember that he started his medical career as a surgeon in the Prussian Army, became interested in the anatomy of the eye and ear, and then in their physiology. Another step took him to the physics of light and sound, and to applied and then to pure mathematics.

The automation in the laboratories is extending into industry. The National Coal Board has now opened the world's first fully automatic coal mine at Bevercotes in Nottinghamshire. The whole operation from winning coal at the face to the final stage of loading it into railway waggons is controlled automatically. The automatic machine in the factory or in the office is the precise economic equivalent of slave labour. It is quite clear that mass unemployment is bound to follow, or a working week of a few hours only. We shall then have the great problem of leisure and a population completely untrained to use spare time interestingly or beneficially. Many will revert to the open air life, some will indulge in passive recreation like the theatre and television. Only a few, even of university graduates, will read anything more than the yellow press. It is probable that the majority will be bored and lapse into alcoholism and gambling, with the more adventurous

taking up a life of crime. Education for leisure is one of the great problems of the future. Recent years have seen an increase in the number of crimes of violence, said to be fifteenfold in the past 20 years. This increase has come as a great shock to those liberals who equated crime with poverty and bad housing; the new violence seems actually to be a product of prosperity and of overcrowding.

It is many years since Pavlov did more to unravel the workings of the human mind than all the introspective writers down the ages. His work on conditioned reflexes has been followed up by himself and his successors in a way unknown to western physiologists and psychologists until the phenomenon of brain washing emerged in recent years.

When students, we all learned something of his work on conditioned reflexes, but neither physiologists or psychiatrists appreciated that Pavlov was a careful clinician, and when he wished to extend his experimental findings to morbid psychology in man, the Soviet Government placed a nearby psychiatric clinic at his disposal. In the United Kingdom and the United States of America prejudice against Pavlov caused many psychologists to neglect his work even though his methods were irreproachably scientific. Pavlov always insisted that experimental facts, however limited in their range, which could be repeatedly tested and checked took precedence over the vaguer psychological speculations. It was only following World War II when great advances in psychotherapy were made by the use of drugs that Pavlov came into his own and his experimental methods were applied to the mechanics behind the historical techniques of human indoctrination, of religious conversion, and of brain washing.

The intense study of neurophysiological problems by the Russians since the Revolution has helped them to perfect the methods now known as brain-washing with astonishing results on their own nationals and in their great state trials, and also on those of other nationalities who had become their prisoners of war, astonishing by reason of the surrender of strongly held beliefs and the adoption of new beliefs often directly opposite to the former. This is not the time and place to consider these recent advances in detail with all their potentiality for good or for evil in the years to come, but it behoves us to consider our own beliefs dispassionately and to remember that many of them have been handed down and accepted uncritically by generation after generation. We must ask "What are the facts? What do they prove?"

The future task of the doctor is to learn how to train the human brain to withstand stresses and strains, how to make it better, able to think and how to learn from experience; and how to redirect it, when disorientated, back into religious and ethical balance. For we are men gifted with religious and social apprehension and with the power of reason. All these faculties are physiological functions of the brain. The brain should not therefore be abused by having forced upon it any religious or political mystic, which stunts the reason, or any crude rationalism which stunts the religious sense.

Can we anticipate a continuation of the idea of progress? The question is not unreasonable when we compare the poetry and prose of today with the fine cadences of the language of the Old and New Testaments, or of "sweetest *Shakespeare*, fancies childe" when he "Warble his native Wood-notes wilde", or when we

compare what now passes for art when compared with the works of the old masters, and even more in the present day bedlam of pop and jazz in contrast with the music of Bach and Beethoven. In his monumental study of the genesis and decay of civilizations, Toynbee has shown that the continual challenge of the environment and man's response afford some explanation of the mechanics of human progress. In the 19th century the triumphs of applied science had caused the idea of progress to be so well established that it was no longer contested by anyone. The twentieth century is realizing that if progress has occurred it is neither simple nor continuous, and that advances in one direction are frequently accompanied by retrogression in another. Recently the belief in progress has been further weakened by the growing recognition that advances in technical knowledge are by no means sufficient to ensure social and moral progress, and also by the fear that the use of scientific knowledge for destructive purposes may out-pace and arrest the growth of its power for good—a situation all the more serious when to the power over nature is added power over the minds of men. We must remember that if science and technology can be used as instruments of oppression and destruction, they can also be used to promote freedom and well being; and also that if they facilitate the concentration of power, they can also show us how to prevent its abuse. Science leaves the path open to progress or to regression. The choice is ours. It remains that knowledge is not sufficient, but it is a necessary condition of progress. It can do something to help man to shape his own destiny before the end is reached.

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# **"RAZORS TO AUTOCLAVES"**

**By J. W. S. IRWIN, M.B., F.R.C.S.(Edin.).**

**OPENING ADDRESS (WINTER SESSION), 1965-66**

**Royal Victoria Hospital, Thursday, 7th October, 1965**

IT HAS for long been the custom in the great teaching hospitals of these islands, at the beginning of each academic year, for a member of the senior medical staff to deliver an address. I have little doubt at its inception this was a method of introducing the new student to his hospital, advising him of its traditions and practices, and instructing him on his new responsibilities and duties towards his patients. This simple introductory lecture has slowly blossomed into an elaborate ceremonial occasion. This morning, on behalf of the medical staff of the Royal Victoria Hospital, I have the pleasant duty of formally welcoming those students who have recently begun to walk the Wards. In addition, I would like to welcome all those who have come here today, and particularly the ladies who now grace this occasion.

My task as spokesman for the medical staff is made difficult by the very high quality of the addresses of previous orators. During the last 30 years I have listened with admiration and awe, first to my teachers, and, more recently, to my colleagues. The depth of their learning and the high content of their orations have left a deep and abiding impression. Last year my colleague, friend and fellow student, Dr. Breen, delighted us all with his oration "Quo Vadis", departing from the traditional historical subject to a more philosophical approach. I find his erudition and scholarship an impossible task to follow.

Every student should know that this hospital and medical school owe their foundation to James McDonnell, a physician, who in 1792 opened the Belfast Dispensary in Factory Row, now Berry Street, with six beds. As Belfast grew and the demands for hospital beds increased, the General Hospital of 100 beds was opened in Frederick Street, off York Street, in 1817. In its early years this hospital was largely filled by fever cases, and it was not until many years later that an operating theatre was equipped. The third move did not take place until 1903, when the hospital moved to its present site. The history of the years 1903-1953 have been recorded with great accuracy and tender care by Dr. Robert Marshall, our admirable historian, consultant physician, and raconteur. To all those who aspire to know their hospital, and follow its traditions, this book is a must.

The Royal Victoria Hospital has been slowly expanding since its inception, adding to its original general wards not only new departments of investigation, but having allied to it in the nineteen-thirties a maternity hospital and a children's hospital. Along with these the Musgrave and Clark Clinic was built for the treatment of private patients, and nurses' homes to accommodate the ever-increasing number of nurses. Since the last war important additional buildings have been erected to house the Medical School in the Institute of Clinical Science. In recent months the Ear and Eye Clinic, the Dental School, the Department of

Microbiology, and a new wing to the Maternity Hospital have been completed. All these new buildings have involved members of the staff in a considerable amount of over-time, attending meetings and planning committees.

Although we now live in the Welfare State where everything is provided, there is much voluntary work to be done. I am a firm believer that despite the length of the medical curriculum, and the vast amount of scientific knowledge and information that the present-day student is expected to digest, there remains a place for extra-curricular activities. Indeed, I believe that these are essential to the proper development of the man, and without them we will tend to produce a narrow-minded scientist rather than an educated doctor.

Some years ago as part of my extra-curricular activities, I was appointed by the medical staff, with some of my colleagues, to assist with the planning of new buildings to house the department of radiology and operating theatres. From this small beginning a team has grown which is now engaged in planning the complete re-building of the Royal. In this exciting project the large, antiquated, noisy, Nightingale wards off the main corridor will be replaced by small modern wards in a multi-storied building. The podium will house all those ancillary services necessary to the welfare of the patient—laboratories, radiology department, operating suites, kitchens and stores.

In this period of rapid change it is well to remember that in 1865, just 100 years ago, Joseph Lister, Regius Professor of Surgery at the University of Glasgow, laid the foundations which made possible the progress and development of modern surgery. Recently we have closed the original four surgical theatres of this hospital, replacing them with a suite of four modern operating rooms which would, I am sure, have met with Lister's cordial approval. The old theatres, where many of us learnt our surgery and took our first faltering steps in operative surgery, are full of memories and it seems worth while to pass on to you some details about them and about operating theatres of the past.

The early years of the 18th century had seen the separation of the surgeons from the barbers and their advance towards an equal footing with the physicians: I say "towards", for it is dangerous to be presumptuous. British surgery slowly progressed under such celebrated names as Percival Pott, John Hunter and Ashley Cooper. The text books of the period, while full of anatomical detail and laborious classifications, deal in a limited way with operative surgery and make no mention of operating rooms or operating theatres. It is clear from these books that such major procedures as lower limb amputations, relief of obstruction from strangulated hernia, and the removal of bladder stones were practised, but successes were few and the majority of patients were carried off by sepsis, fever, gangrene or haemorrhage. Operations were usually performed in the patient's house or in the hospital wards. Little is known about operating theatres in this period as most of them were knocked down or extensively altered during rebuilding in the following century. An early theatre, in its restored state, can be seen to-day in the Chapter House of Southwark Cathedral. In 1821 the Governors of St. Thomas' Hospital, situated beside the Parish Church of the same name close to London Bridge, decided that operations should no longer be carried out at the end of the female ward, but that a new theatre should be constructed by opening a door from the ward into the herb garret above the church. This theatre remained in

regular use until 1862 when the hospital was forced to sell its buildings to the South Eastern Railway to make way for an extension of the line from London Bridge to Charing Cross. The theatre was sealed off and, although many of its fittings were removed, these were carefully listed in an inventory. In recent years this interesting relic has been faithfully re-constructed and remains as a fine example of a surgical theatre of this period. It seems probable that this theatre closely resembled the one built in the Belfast General Hospital in Frederick Street and described at the time as "such a theatre as our surgeons have never seen before". It was a large, sombre room, some 40 feet across, painted in yellow ochre. On three sides from floor to ceiling were raised rows of standings for the medical students, leaving in the middle only a small floor area 14 feet wide. In the centre of this space on its timbered floor stood the strong, low, wooden operating table, 2' 6" in height. Beneath the table was a stout box of saw-dust which was manoeuvred into position by the surgeon or his assistant during the operation to catch the blood. The theatre contained a sky-light and for artificial lighting there was a double pendant gas light suspended from the ceiling. The rest of the sparse furnishings consisted of a wooden instrument cupboard and a small cloth-covered wooden table for the instruments, dressings and sponges. Near the door was a wash-stand with a basin little larger than a soup plate, used by the surgeon more often after than before surgery.

On an operating morning the surgeon would arrive with his assistants and dressers to find the standings packed with a noisy throng of students. Before discussing the operations of the day his frock coat would be changed for an old one, by tradition stained and stiff with the blood and pus of previous operations.

The unhappy patient, blind-folded and sedated with opium, would then be brought into the theatre and securely fastened to the table. In these appalling, unsavoury conditions operations were carried on with great pain and suffering to the sick. It is small wonder that patients were prepared to try anything and everything rather than submit to the surgeon's knife.

The first major advance from these terrible conditions was heralded by the introduction of anaesthesia. Early in the 19th century Humphry Davy had recorded the analgesic properties of nitrous oxide in relieving toothache but this discovery was not followed up. It was left to an American dentist, Dr. Morton, to give the first anaesthetic. In September, 1846, a tooth was removed while he anaesthetised the patient with ether. Within a few weeks he had given further ether anaesthetics in the Massachusetts General Hospital while Dr. Warren removed a tumour from one patient, and then performed a lower limb amputation on another. By the end of the year the good news had crossed the Atlantic and Liston, the celebrated Edinburgh surgeon who had moved to University College Hospital, London, performed the first operation in Europe under a general anaesthetic. An increased observer at this operation was a student of 19 years, one Joseph Lister.

Within a twelve-month James Simpson, a young, progressive, ambitious, Edinburgh obstetrician, finding ether not entirely satisfactory for midwifery, had discovered the anaesthetic properties of chloroform. To those of you with enquiring minds and a bent for research it is worth recording that this discovery was made by the simple process of inhaling a variety of volatile liquids poured on a

handkerchief, the experiments taking place in Simpson's rooms with his friends after a good dinner.

These two anaesthetic agents, ether and chloroform, simple to use, effective and relatively safe, held the stage during the next 80 years. While anaesthesia decreased the horrors and suffering for the patient and made the task of the surgeon easier, it did not at first have any major influence on the design of operating theatres: the apparatus required—a sponge or a cloth on a wire frame with drop bottles—needed no special facilities. More complex methods with elaborate appliances were not to appear until well into the next century.

The eighteen-fifties witnessed two important events which were to influence operative surgery. Florence Nightingale brought to the public notice the squalor and inadequacy of hospitals, first at Scutari during the Crimean War and later at home. Although she is best known as the founder of our modern nursing services, her writings and notes were to have a profound and enduring influence on hospital planning and building. Secondly—Pasteur in France had demonstrated by careful experiments that “fermentation was due to the activity of microscopic particles whose growth was the cause, and the only cause, of this process”.

Advances in operative surgery were still held back by the ever-present and apparently uncontrollable effects of inflammation and putrefaction. These were generally thought to be due to contact of air with the wound and, therefore, unavoidable.

Joseph Lister, a Quaker by birth, had been brought up in a scientific home. His father was a distinguished microscopist and a Fellow of the Royal Society. There can be little doubt that both father and son were early familiar with the work of Pasteur. Joseph had qualified in London and subsequently, on the advice of Liston, had gone north to Edinburgh to work with Syme, then one of the leading surgeons in Europe. Here he carried out researches into inflammation and clotting of the blood and also found time to marry one of Syme's daughters. In due course he was appointed Professor of Surgery at Glasgow. Here he continued his researches into inflammation and began at last to graft the ideas of Pasteur on to his own theories. In 1865, at the age of 38, he was to write in the formal, pedantic style of the period: “In the course of an extended investigation I arrived several years ago at the conclusion that the essential cause of suppuration in wounds is decomposition brought about by the atmosphere on blood retained within them. To prevent the occurrence of suppuration was an object manifestly desirable but until lately apparently unattainable since it seemed hopeless to exclude the oxygen which was universally regarded as the agent by which putrefaction was effected. But then it was shown by the researches of Pasteur that the septic properties of the atmosphere depended not on oxygen but on minute organisms suspended in it which owed their energy to their vitality. It occurred to me that the decomposition in the injured part might be avoided without excluding the air by applying as a dressing some material capable to destroy the life of the floating particles”. Lister, after experimenting with many chemicals for this purpose, finally settled on carbolic acid. This substance, which had been used as a deodorant for sewage at Carlisle, was known to have the ability to kill bacteria. Lister's method involved the spraying of the theatre before and during the operation with mist made from a weak solution of carbolic acid. The same sub-



stance was also used to sterilise the surgeon's hands, the patient's skin and the instruments. At the end of the operation the wound was covered with a dressing soaked in carbolic acid.

His contribution to surgery was not so much the introduction of carbolic acid as a method of antiseptis, but the recognition that infection was due to micro-organisms introduced into wounds from without, and if they could be excluded sepsis would not occur. Lister's principles were at first ridiculed and neglected by most of the leading British surgeons. Their importance was, however, recognised on the continent of Europe and it was here that the major surgical advances were to take place during the next decades. Listerian surgery with its dank spray and the penetrating smell of carbolic was slowly to expand and spread and then, its lessons learnt, gradually to die and be replaced by its cleaner, tidier and more comfortable aseptic successor. During its expanding period the Germans, with Teutonic thoroughness, had gone far beyond the rules laid down by Lister in advocating for the surgeon and his assistants careful douching of the nose and throat and the washing of all exposed parts, particularly the beard, with  $\frac{1}{4}\%$  carbolic. This extreme cleanliness was to bear fruit and in time help advance the aseptic method.

In the General Hospital in Frederick Street in Belfast these new methods had been slowly introduced. Sir John Campbell had operated on and closed a perforated peptic ulcer in July, 1897. Col. A. B. Mitchell, the father of abdominal surgery in Ulster, had operated on a second case in December of the same year, and by 1899 had collected fourteen cases operated on locally with a mortality of a mere 50 per cent., the best figures in the surgical literature of the time.

The move to the new site on the Grosvenor Road was to take place soon and the great plans included four new operating theatres of revolutionary design. These theatres, 26 feet long and 16 feet wide, were large and airy with dazzling white tiled walls and large overhead windows. To prevent the spread of infection they were completely separated one from the other, as advocated by Florence Nightingale. Each served one ward unit so that they belonged to and were under the control of one surgeon, a necessity in those autocratic days. Advances in sanitary science permitted hot and cold water to be piped to basins and sinks, and steam to be laid on to sterilisers for boiling the instruments. Electric generators had started work in 1898 in East Bridge Street and so the new-fangled electric lighting was installed in the hospital. In place of Lister's sprays the air was cleaned and purified by being filtered and humidified in the new plenum system of ventilation. Wooden floors gave way to terrazzo with floor drains to allow cleansing in the best Listerian tradition. One-third of the floor space was occupied by wooden benches for students who had access to them through narrow wooden doors.

When I came to the Royal Victoria Hospital in 1934 I was appointed as a dresser to Mr. Kirk in Wards 9-10. He had been one of the surgeons in the hospital when it opened in 1903, and his methods seemed to occupy a position mid-way between Lister and the more modern techniques employed further down the corridor. Surgeon Kirk, a man with original ideas and unorthodox methods, a true non-conformist, was short of stature with white hair and seemed to us students a solitary, austere figure. In the theatre, after removing his coat, he wore a rubber apron covered by a sterile gown with short sleeves, but no cap or

mask. His rubber gloves were carried in a tobacco pouch and put on before he washed his hands. The gloved hands were then rinsed in a solution of biniodide of mercury. He operated on a narrow low metal table, the top of which was a hollow tank. This was filled with warm water before the operation with the idea that the heat would prevent shock. Above the table hung an ordinary light bulb, as he saw no virtue in the shadowless lamp. The anaesthetic of chloroform or chloroform and ether was skilfully administered by an elderly bearded gentleman, Dr. Fielden. Mr. Kirk used large incisions and few instruments, many of these brown with rust as stainless steel had not yet come into general use. The students sat on the benches without gown, cap or mask to watch the operations. It was not unusual for the operator to pull the table close to the front bench the better to demonstrate some particular point. I remember on at least one occasion, after a perfunctory social wash, at his invitation plunging my bare hand into an abdomen to feel a tumour.

This theatre and its fellows with minor modifications and additions served their day and generation for more than 60 years. Here the great surgical figures of the past welded the girders and built the framework of the surgical revolution. Mitchell, Sinclair, Campbell and Kirk laid the firm foundations on which their successors built so well—Andrew Fullerton, to gain international fame as a urologist; McConnell and Stevenson and many other general surgeons of great skill taught not only generations of students but also the leading surgeons of the future; Cecil Calvert, to advance neuro-surgery from its infancy to full adult status; Barney Purce, perhaps the greatest operator of them all, whose courage knew no bounds and whose skilful technique ranged through the whole spectrum of surgery; he it was who introduced and developed thoracic surgery. My father, S.T. to many generations, played his part in these exciting events with his special interest in the advancement of orthopaedic surgery. In 1939 he persuaded a young Queensman to return from Manchester to Belfast to work in this speciality. Today we mourn the recent death of this man, James Withers, our friend and colleague, who passed away in his prime last June. A man of high intellect with a quick, incisive brain, witty and urbane, he has left to this hospital as a memorial to his genius a first-class Fracture Unit, and to the Province many young disciples, well trained to carry to fruition his plans for an efficient, modern orthopaedic service.

These old theatres, now 60 years of age, carried their weight of years well. Like vintage cars they were interesting but dated and, while still useful, they were not to be compared with the newer models available. Their replacement became overdue as advances in medical science gradually rendered them obsolete. Built as a bulwark against sepsis, they were shown by Dr. Eileen Bartley in a series of well-planned experiments to have a bacterial population well above the safe level. Repeated wound surveys confirmed that the old bugbear sepsis was still a real danger. In 1903 about 800 operations had been carried out in the entire hospital. Recently each of these old theatres was burdened with 1,500/2,000 operations per annum. These were carried out in hot, sticky, noisy surroundings in an area which served not only for the operation but also contained all the paraphernalia of sterilisation, the store for instruments, the scrub-up for the surgical team, and, in recent years, the extensive machinery of the modern anaesthetist. In the immediate post-war years the benches for students had been

removed to give additional space and to take away this likely source of infection. This increased space had long since been filled. After operations there was no place for the patient to recover from the anaesthetic except in the ward—a dangerous hazard especially at night and unpleasant for the other patients. In these cramped surroundings the nursing staff had to clean up from one operation and with great speed lay out the instruments for the next.

Architects in the past have often made the mistake of attempting to fit theatres into an available circumscribed space. In the old St. Thomas' Hospital this was a herb garret. In 1903 the size of the Royal theatres was dictated by the area between the male and female corridors and these in turn by the width of the wards. To some extent this basic error was perpetuated in our new theatre suite which lies one floor above the main corridor, restricted by the line of the corridor on the one side and by the King Edward Building on the other. In this limited space the architects are to be congratulated on a plan which, if not perfect, is at least as good as any of those theatres I have seen in the British Isles, in Europe or on the Eastern seaboard of the United States. In the lay-out each operating suite is self-contained and all the separate functions have been allocated their appropriate places. The theatre is for the operation and the operation alone. Here the anaesthetised patient coming from the quiet induction room meets the already changed, scrubbed, gowned and gloved surgical team. Instruments and equipment are stored outside the theatre. Water boilers have been replaced by the more efficient autoclave and the instruments are laid out by the nurses in spacious, clean surroundings. After the operation all dirty and soiled materials leave by a special door to be despatched well away from the clean areas. The theatre air is automatically filtered, humidified, and heated or cooled to a pre-selected temperature. The terrazzo floor slopes gently to facilitate cleaning by wall hydrants. The windows are double glazed with electrically operated blinds. At the conclusion of the operation the patient is wheeled to a recovery room where, under the care of a team of highly-skilled nurses, consciousness is regained before returning to the ward. Great thought has been given to the comfort and safety of the patient and for the first time some concern has been shown for the well-being of the nursing and surgical staff.

Through all these years there runs the silken thread of progress—progress which has speeded up as the years pass by, so that today surgery has become less of an ordeal and the way to recovery has been made easier.

The dangerous, difficult operation of yesterday is the safe, routine procedure of today.

Changes come, some fast, some slow, the fruits of careful thought, research and experiment. Their adoption may be made difficult or delayed by the rigidity of age and the inflexibility of experience.

You, the students of today, will have to battle to develop your ideas and promote the advances of tomorrow.

This hospital owes much to "the Honorary Medical Staff of Physicians and Surgeons who from 1792-1948 served the people of Ulster by day and by night giving ungrudgingly their knowledge and their skill for no fee or reward apart from the privilege of helping others".

This privilege we still have and you who are students of this hospital inherit it as part of the Royal tradition.

In 1927 my father in his Oration gave this advice to the students. Before I trespass too long on your time I pass it on to you:

“Words are like leaves and where they most abound  
Much fruit of sense beneath is rarely found.”

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## BOOK REVIEW

**ANAESTHETICS, RESUSCITATION AND INTENSIVE CARE: A Textbook for Students and Residents.** By Walter Norris, M.D., F.F.A.R.C.S. and Donald Campbell, M.B., Ch.B., F.F.A.R.C.S., D.A. (Pp. x+253; figs. 118. 30s). Edinburgh and London: E. & S. Livingstone Ltd., 1965.

THE mushroom growth of independent scientific societies and the remarkable advances that have been made in all branches of medicine in the last 25 years has tended to lead to the isolation of the various medical specialities. This isolation of the speciality of anaesthetics and the administrative emphasis placed on the medico-legal hazards of the speciality has led to the complete divorce of the student and the pre-registration house officer from anaesthetic activities. The result is that a mystique surrounds anaesthetic techniques and resuscitative manoeuvres. The reader of this excellent textbook will agree that these procedures are outstandingly simple.

The book sets out to present the outlines of anaesthesia and gives a most comprehensive description of the selection and application of the various anaesthetic techniques.

The mode of action of local and general anaesthetics and the pharmacology of anaesthetic agents contained in the first two chapters would be generally regarded as dull and difficult reading in medical circles. The reader, however, who gets as far as reading these two chapters will agree that the authors have presented the subject in a most interesting, lucid and readable manner. The explanation of the pharmacological action of the various drugs is dealt with by considering their action in relation to the reasons for their use.

No other manual deals with the objects and principles of resuscitation and intensive care in so brilliant and concise a form.

It is unfortunate that the text is marred on Page 30 where Metaraminol (aramine) is described as a potent vasodepressor instead of a vasopressor.

The chapter on pre-anaesthetic examination and preparation of the patient for anaesthesia and surgery is regarded as incomplete, in that no attempt has been made to teach the student to classify his patient according to the operative risk. The classification of physical status used by the American Society of Anaesthesiologists is most useful for this purpose and could have been included with benefit.

The book is strongly commended not only for all medical students, but all doctors. It provides a perfect frame work on which the trainee anaesthetist can assemble his knowledge.

W.B.

We note that Messrs. E. & S. Livingstone of Edinburgh and London have now taken over the United Kingdom Agency for medical books published by Messrs. Williams & Wilkins of Baltimore, three books reviewed in our last issue, i.e., Bailey's 'Textbook of Histology', Milch's 'Surgery of Arthritis', and 'Manual of Gastrointestinal Endoscopy' by Palmer & Boyce are now published by them in Great Britain and not by Messrs. Balliere, Tindall & Cassell. The price of the book by Milch is £5 and not 92s.

This privilege we still have and you who are students of this hospital inherit it as part of the Royal tradition.

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## "ON NERVOUS DISEASE IN THAILAND"

By **R. S. ALLISON, V.R.D., M.D., F.R.C.P., D.P.M.**

Scott-Heron Lecture at Royal Victoria Hospital, May, 1965

UNLIKE BURMA, the Vietnams, Cambodia, Malaysia, Indonesia, Thailand has never at any time been under the domination of a Western Power and it is only in the last quarter of a century that much authentic information about it has become available. Traditionally, of course, it is the home of the white elephant, of Siamese twins and cats, and, to the cinema-going public who remember "Anna and The King of Siam", a romantic land of almost mediaeval splendour.

The country, which occupies some 200,000 square miles, is about the size of France and rhomboidal in shape, with a long narrow tail like a fish of the ray species. High mountain ranges dominate its northern and western borders whilst the central plain is drained and irrigated by many rivers, notably the Chae Phya which flows into the Gulf of Siam. On the north-west it is bounded by Burma, on the north-east by Laos, on its eastern side by Cambodia and South Vietnam, while in the south its frontier joins with that of Malaysia.

Still predominantly agricultural, the economy of Thailand hinges on the production of rice, in this respect its place in the Far East being comparable to that of the United States and Canada in the West. Just as these countries supply the major part of the wheat required for the western style of diet so is Thailand the Canada of the Orient in being the main source of rice in South-East Asia. Other important industries include: tin mining and rubber planting in the southern province, teak forestry in the north<sup>1</sup> and all over the country the manufacture on hand-operated looms of silk, as famous for its quality in the civilized world as is Irish linen.

In the 1960 census the population was 27½ million with a sex ratio of 92.0 for males (13 and 14 million males and females respectively), some 54 per cent being under the age of 20 years<sup>2</sup>. The rapid growth of the capital, Bangkok, and its situation on the direct air route to Japan and Australia has transformed it from the one-time picturesque "Venice of the East" with its many canals or "klongs" and bridges, and a population of some 700,000 before the second great war, to a modern city of 2 million inhabitants which rivals Calcutta, Singapore, Hong Kong and even Tokyo in its increasing importance. Other large cities, however, are few, the chief being the beautifully unspoilt Chiangmai in the north-west province with half a million inhabitants.

Geographically, Thailand lies between the 5th and 20th parallels of latitude so that the climate is tropical, the temperature fairly constant throughout the year and the seasons marked only by dry and rainy phases. During the latter periods extensive flooding of the low-lying central plain, particularly around Bangkok, occurs.

"Thai" means free, and the original Thais were migrants from the Himalayas in India and from Yunnan in China. Ethnically the people are a composite race whose physical characteristics reflect both their places of origin and their mixed Chinese-Indian descent: light-coloured skin like that of southern Europeans, a pyknic build, small stature and the absence of obesity being particularly noticeable, as is their happy disposition and friendly mien towards strangers. No people excels the

Thais in this respect. The original name of the country was pronounced "Shiam", this having been corrupted through usage by the Portuguese, Dutch and British to "Siam". The name "Thailand", which emphasizes the independence and peace-loving propensities of the Siamese, was taken in 1938 after an internal political upheaval which led to the establishment of a constitutional type of Monarchy and Government. The present King and Queen are prominent figures and occupy much the same place in the affection of the people as does our Royal Family. Inheritance is not direct and the advance of medicine in the country owes much to its "father", the previous king, Prince Mahidol, who himself was a doctor and student at Edinburgh and Harvard. The Prasat Institute of Neurology to which it was my good fortune to be attached\* is directly under Royal patronage and at the time of writing is the only one of its kind in Asia.

Although there are some Muslims, especially in the south, Buddhism is the chief religion of the people. There are some 250,000 priests or monks and one sees their profound influence everywhere over the lives of the people as they roam the streets barefooted, clad only in their saffron-coloured robes and carrying the traditional brass bowls to receive the freewill offerings of food upon which they are entirely dependent for sustenance. Temples and pagodas are a constant feature of the countryside, many of these dating back for more than a thousand years and the bas reliefs in bronze with which many of them are decorated indicate that in the Orient as in the West the priest formerly undertook the duties of physician. Even to-day the power of the priesthood is great in this respect for in many parts of the land it has been largely through their co-operation that the authorities have been enabled to procure adequate treatment for lepers. Buddhism, indeed, is as dominant a force in Thailand as is Roman Catholicism in Spain and in the Republic of Ireland.

#### MENTAL DISORDERS

Mental disorder is no more common in Thailand than it is elsewhere, but neither is it less frequent and there are some differences in the pattern it presents as compared to western countries and especially Great Britain and Northern Ireland. In 1953, when the population was 18 million, 3,447 patients were admitted to the five mental hospitals, the bed accommodation of which at that time represented just one half of the total provision made for all kinds of illness, both physical and mental<sup>3</sup>.

I spent a day at the Suanprung Hospital, Chiangmai (Dr. Arie S. Watana) and was impressed by the arrangements for grouping patients according to behaviour and the need for ambulant or bed treatment. There was plenty of space available for recreation and the departments of occupational therapy and physiotherapy were in constant use and well-equipped, the impression received being that the doctors knew their patients individually and that only essential restrictions were placed upon the liberty of the latter. This is remarkable when one considers the statement of one Thai authority that thirty years before such barbarous practices as beating patients or forcibly blowing an irritant up their nostrils were still in vogue for the treatment of depression.

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### *Organic Reaction Types*

It is perhaps with respect to the organic reaction types that the pattern of mental illness in Thailand differs most from that here. General paralysis of the insane and meningovascular syphilis still occur, but in the mental hospitals there are comparatively few old people suffering from presenile or senile dementia and three factors are held to be responsible.

(1) *Structure of the population.* As already mentioned over 50 per cent. is under the age of 20 years, but only 4 per cent. is in the 60 or over age group. The comparable figure for the United Kingdom (Great Britain and N. Ireland) is 17 per cent.<sup>4</sup>.

(2) *Structure of the family group.* Unlike Western countries, in Thailand there is often no scatter of different generations of a family into separate households. It is not uncommon still to find, living under the same roof, grandparents, uncles, aunts, parents and their children, so that a menage may include some 10-30 persons, depending more on the number of survivors than on the size of the house. Great respect is still paid to elders and, because plenty of help is available, dementing and otherwise frail arteriosclerotic patients are treated at home for so long as this is possible.

(3) *Infrequency of atherosclerosis.* Although no convincing statistical information is available, there is a general impression among doctors in Thailand that atherosclerosis has a relatively low incidence, this being attributed to the low animal fat and protein content of the largely vegetarian diet of the population, which consists principally of rice. As already mentioned obesity is rarely seen.

If comparatively few chronic organic brain diseases find their way into Thai mental hospitals, acute toxic hallucinatory reactions are commonly encountered, these states often being induced by drugs, notably cannabis indica or hashish, heroin, opium or alcohol, cerebral malaria, avitaminosis and occasionally cysticercosis. Old ideas die hard and the widely-held belief that the temperament and constitution of western man and of the oriental differ to such an extent that the former seeks relief in alcohol and the latter in opium is not supported by the march of events in recent times. The taking of alcohol is forbidden in the Buddhist doctrine, but in Thailand the import of opium and its derivatives from Laos was prohibited some 15 years ago by Government decree and this may have to do with the fact that over the same period there has been an increase in the misuse of alcohol. Hashish or marihuana, also prohibited, is more difficult to control as it may be grown easily on waste land and is widely used by the peasantry. Thus, in rural districts of the northern part of the country when guests are being entertained, it is the custom to flavour the traditional chicken curry (Thai style) with the drug so that within a quarter of an hour the guests became relaxed to such an extent that what started soberly may well become a hilarious party with much singing and dancing and other manifestations of merriment<sup>3</sup>. Hashish is also often incorporated in native or home-made cigarettes and we sampled these at a party one evening in Lampong, near Chiangmai.

But chronic alcoholism now represents a problem in the country, the kind of alcohol taken depending to a large extent on the social status of the consumer. Labourers, rickshaw coolies, building-site workers drink locally and illicitly distilled rice wine or rum which is comparable to Japanese "Sake". The more impoverished



and psychopathic types use the so-called "Jungle Whisky" or "White Water" which may contain dangerous proportions of methyl alcohol. In common use also is fermented sugar palm juice which, however, is stronger than beer although resembling it in other respects. Finally, there is a liqueur called "Ooh" which is said to have a special flavour and is very potent<sup>3</sup>.

At the Prasat Hospital in Bangkok there is a well-organised and conducted unit of 25 beds devoted solely to the treatment of chronic alcoholics and other forms of drug addiction. There, it is always possible to see examples of the different manifestations of alcoholism, ranging from polyneuropathy and the Korsakov syndrome, Wernicke's encephalopathy, cerebellar ataxia to chronic dementia. One patient I saw, who was demented and had apraxia and other signs of a callosal lesion, may have been suffering from the Marchiafava Bignami syndrome.

#### *Affective Disorders*

These comprise only a small proportion of mental hospital patients but *schizophrenia* ranks high, in one large hospital accounting for 70 per cent. of the total admissions over the period of one year. The simple, catatonic, hebephrenic and paranoid types are all seen but with the last named it is unusual to encounter highly organised delusions leading to anti-social behaviour and, by and large, Thai schizophrenics are said to be quiet and biddable<sup>3</sup>. It is suggested that the emotional reaction of frustration in Thailand is typically one of withdrawal rather than of hostility. In the Buddhist doctrine, if a man acquires true realization of the self, he loses all craving for worldly pleasures and this attitude tends to promote introversion. Indeed, it is normal practice for people all over the country, when faced with an apparently insoluble problem, to retire to a temple where they may remain in solitary meditation for days at a time. A further point of interest in connection with the frequency of schizophrenia among the Thais is the predominance of short, stocky or "pyknic" physical types which is in conflict with Kretschmer's theories on the relationship between body build and character.

#### *Psychoneuroses*

It was the increasing prevalence of psychoneurosis in the population in 1957 that led Dr. Prasop Ratanakorn, now Director of the Prasat Hospital and Neurological Institute, to press for the opening of a hospital in Bangkok, which was the first to provide treatment for this type of patient. At present 40 beds out of the total of 140 are devoted to psychoneurosis and in the outpatient department, where some 100-150 patients attend daily from Monday to Friday, direct observation would suggest that neurotic reactions are very common and affect some 90 per cent. of the patients attending. Neurosis is common among the Buddhist priesthood the asceticism of whose lives places a heavy strain on more vulnerable personalities.

#### ORGANIC NERVOUS DISEASES

The pattern of organic nervous disease in Thailand differs greatly from that seen in western countries, and, as it was with this respect that I was chiefly concerned during my stay there, the subject will be considered in more detail.

There are only three neurological and neurosurgical centres in the country (Table 1). Two of these are incorporated into university teaching hospitals and there is every prospect that the third (the Prasat Institute) may also become so in the next

two years. The great want is a sufficiency of trained medical and nursing staff; ample capital seems to be available for building and for equipment.

TABLE 1  
*Neurology in Thailand (1965)*

<i>Centre</i>	<i>Facilities</i>
Siriraj University Hospital, Bangkok	An old hospital (circa 1879) being rebuilt. Neurological and neurosurgical beds at present scattered but there is a separate neurosurgical theatre and E.E.G. department. A combined unit under the same roof is under construction.
Chulalongkorn University Hospital, Bangkok	Modern 3-storey building housing 33 neurological and 33 neurosurgical beds with 8 psychiatric beds. Laboratories, museum, library, classroom for teaching. E.E.G., E.M.G., operating theatres. Paediatric neurol. affiliated.
Prasat Hospital and Neurological Institute	At present has no university or teaching hospital connections but such are envisaged. 140 beds: 75 neurological, 40 for psychoneuroses, 25 for drug addiction. Buildings modern and beautifully designed and set around enclosed gardens. Cons. neurosurg. visits weekly from Siriraj Hospital. Neurosurgical theatre. E.E.G. and E.M.G. departments with neuro-radiology. Institute contains laboratories for neuro-pathology, chemistry and physiology.
Prasat Hospital, Songkla, South Thailand	A branch of the above with 30 beds, opened in 1965.

Although infrequent I saw examples of many well-known diseases of western civilization such as myasthenia gravis, motor neurone disease, Tay Sachs disease, Friedreich's ataxia, muscular dystrophy, Parkinsonism (Tables 2, 3 and 4). Extra-

TABLE 2  
*Neurological In-Patients Undergoing Treatment*

PRASOP HOSPITAL: a nosological census made on 26.2.65					
Cerebral vascular disease	.....	.....	.....	.....	7
Epilepsies	.....	.....	.....	.....	7
Brain Tumour	.....	.....	.....	.....	7
Sequelae cerebral trauma	.....	.....	.....	.....	5
Parkinsonism	.....	.....	.....	.....	3
Peripheral neuropathies	.....	.....	.....	.....	4
Tuberculous meningitis	.....	.....	.....	.....	3
Other forms of meningitis	.....	.....	.....	.....	3
Friedreich's ataxia	.....	.....	.....	.....	2
Acute encephalitis	.....	.....	.....	.....	1
Motor neurone disease	.....	.....	.....	.....	1
Post-rabies vaccinal myelitis	.....	.....	.....	.....	1
Multiple (disseminated) sclerosis	.....	.....	.....	.....	1
Total					45

TABLE 3

*Neurological Admissions (1964). Chulalongkorn University Hospital*

Cerebral vascular disease .....	218
Acute encephalomyelopathies .....	72
auto-immune (post-rabies vaccination), viral, bacterial, allergic	
Rabies .....	35
Epilepsies .....	52
Intracranial tumours .....	10
Polynuropathies (Beri-Beri) .....	5
Motor neurone disease .....	4
Cerebral cortical atrophy (Presenile) .....	19
Miscellaneous .....	54
multiple sclerosis (7), myopathies (5), myasthenia (3), manganese intoxication (1), etc.	
Total .....	469

TABLE 4

*Neurosurgical Admissions, Chulalongkorn University Hospital (1963). (6 months)*

1. Trauma (cerebrospinal) .....	91
2. Pyogenic Infections .....	18
(brain abscess, epidural abscess, etc.)	
3. Brain tumours .....	24
Spinal cord tumours .....	10
4. Vascular .....	22
Cerebro-vascular insufficiency .....	7
Intracerebral haem. ....	9
Internal carotid occlusion .....	2
A.V. malformations .....	3
Aneurysm .....	1
5. Congenital hydrocephalus and meningocele .....	10
6. Miscellaneous .....	54
Trigeminal neuralgia .....	1
Malignant exophthalmos .....	1
Parkinsonism .....	3
Others .....	49
Total =	229

pyramidal disease is not uncommon and choreoathetosis and Parkinsonism go by the name of "Sanibat"<sup>5</sup>, a Thai word which means jerking, involuntary movements. An hereditary-familial form resembling our Huntington's chorea, and probably having the same genetic characteristics, is also recognised. It affects males more than females and the usual age of onset is between 40-50 years. Sydenham's chorea (Sanibat Luknok) or "little" Sanibat still occurs in children and I saw one

case in a young pregnant woman, but most sufferers from parkinsonism and choreoathetosis in Thailand avoid hospitals and depend for support on the Buddhist priests so that one may see them frequenting the neighbourhood of temples. The local inhabitants treat them with a certain veneration, which is natural because of their belief that they are possessed by evil spirits. But a different kind of evil spirit was responsible recently for the outbreak of 45 cases of parkinsonism in women, all of whom were employed in a flash-light battery factory in Bangkok, where they had been exposed to the inhalation of manganese in dry dust form. No similar cases have been reported in the United Kingdom<sup>6</sup>. Dr. Sombut Sukonthabhand of the Siriaraj Hospital secured the autopsy results in two of these cases and has a paper in course of preparation on their clinical features. Textbooks emphasize that manganese poisoning causes parkinsonism but although signs were present in all of the three patients I examined (impassive, greasy-skinned facies, tremor at rest; bradykinesia and poverty of associated movements; increased resistance to passive stretching of muscles) even more striking were the cerebellar and dementing features. Obesity was also a feature and increased emotional lability, the facile laughter of the patients reminding one of Wilson's disease. Tremor was brought out on attempted action or intention and was coarse in character, at times almost amounting to ballismus and the gait was reeling and ataxic but none of the patients showed nystagmus or dysarthria and there were no pyramidal signs. Treatment had been given by B.A.L. but in all cases the disease appeared to be slowly progressive, the dementing features especially becoming more pronounced with the passage of time. At autopsy changes were found in the cerebellum which corresponded closely to those described by Van Bogart<sup>7</sup> in 1938 as a result of his experimental work with monkeys after poisoning by the inhalation of small amounts of finely sprayed metallic manganese. These changes included degeneration of the Purkinje cells and partial disintegration of the granular layer over a wide area. Changes were also found in the dentate nucleus. When the path of human intoxication is by inhalation, liver and renal changes are not seen, these involving only the nervous system, the earliest signs pointing to cerebellar disturbance. By contrast the effect on the lenticular nucleus may be transient and unaccompanied by any irreversible damage.

There were two other curious features of Thai neurology that may be mentioned and for particulars of which I am indebted to Dr. Charas, senior neurosurgeon at

TABLE 5

<i>Source</i>	<i>% calcified pineal bodies on routine X-ray skull</i>	<i>No. of Subjects</i>
Thumnoon C., Silliawat A., and Charas S., Bangkok (1964)	8.2	500
Vestine & McKinney, U.S.A. (1926)	47.9	616
Dyke, U.S.A. (1929)	51.0	2,724

the Chulalongkorn who, himself, was trained under a former member of our department in Belfast, Dr. Sean Mullan, Professor of Neurosurgery in Chicago. The first is the infrequency among the Thai people of *calcification of the pineal body*.

In the Bangkok series collected by Dr. Charas children were included but the earliest age at which pineal calcification was observed was 15 years. When all persons beneath the age of 20 years were excluded the percentage of patients showing calcification was still appreciably lower than in western countries, i.e., 13.3 per cent. as compared to 49.5 per cent. in N. America<sup>8</sup>.

The other is that when a child is born in Thailand and found to have meningocele or encephalomyelo-meningocele, its situation is not in the posterior part of the skull as in western countries but in the anterior part, giving rise to a *sincipital meningocele*. In most cases Charas<sup>9</sup> found that the site of the persistent cranial opening was at the junction of the ethmoid and frontal bone, just anterior to the cribriform plate and the crista galli. In some patients the signs were so slight as only to cause bulging and flattening of the base of the nose. In others a mass or masses presented, sometimes without skin covering so that brain elements were exposed. The chief differential diagnosis is from congenital and acquired tumours and cysts but in the very young radiograms of the skull will indicate in sinoccipital meningocele that the distance between the orbits is greatly increased and in older children the actual bone defect can usually be seen. Hydrocephalus, epilepsy, mental backwardness, facial deformities and secondary meningeal infection are often associated as complications and operative treatment was only undertaken when these had been dealt with by antibiotics and there was no evidence of considerable brain damage.

### *The Peripheral Neuropathies*

Reverting to more common neurological diseases, one should first refer to the prevalence of the peripheral or nutritional neuropathies, the incidence of which is very great. I saw examples in hospitals all over the country. Usually these cases are classified in admission lists as "Beri Beri" but to relatively few can the term be applied strictly because it refers to absolute deficiency of thiamine in the diet from eating polished rice and this is rarely the sole explanation. In by far the greater proportion the cause is multifactorial and induces a relative rather than an absolute deficiency of thiamine, this often being associated with deficiencies in other essential vitamins, notably B<sub>2</sub>, B<sub>6</sub><sup>10</sup>. Beri-Beri is not a disease which is associated with famine. Cardiovascular beri-beri indeed, occurs in persons who have ample supplies of polished rice and good appetites to eat it<sup>11</sup>. Raw polished rice has a value of only 0.15 mgm. thiamine per 1,000 calories and most fruits, vegetables and flesh foods contain only a little more of the vitamin to raise the content in the diet above the critical level of 0.25 mgm. per 1,000 calories. Whole wheat by contrast is actively protective against thiamine deficiency because it contains as much as 1.2 mgm. per 1,000 calories. It is the poorly-balanced diets taken by most Thai sufferers from beri-beri that accounts for its prevalence and the chief precipitating factors appear to be as follows :

(1) *Hard manual labour*. Although the effect of climate on protein requirements is not fully understood loss of nitrogen in sweat is high when heavy manual labour

is done in conditions of excessive heat<sup>12</sup>. All the patients I saw were young men who had to work 10 hours a day, 6-7 days a week at hard manual labour, digging, shovelling or lifting heavy weights. Most of them were country boys from the north-east part of the country who had migrated to the city for the opportunity of steady employment and the good chance of earning 10-20 Bahts a day, this sum being equivalent in our money to 3s. 4d. to 7 shillings.

(2) *Diet*. Owing to the high cost of living in Thailand, their diet consisted almost exclusively of rice, eaten in the sticky form, that is cold after previous boiling and carried in canister-like bamboo containers or in pots which could be slung to the waist belt.

No statistics of the present day diet of these people are available for comparison against war time figures, but certainly the amount of protein and fat eaten by the patients I saw with neuropathy was very small and consisted only of a little pork, dried or raw fish. The practice of eating raw fish is very prevalent and will be referred to later, but raw fish contains thiaminase, which inactivates thiamine and causes the so-called Chastek paralysis in foxes and cats. It is possible that this may be another factor tending to neuropathy in this type of subject.

(3) *Alcohol*. From what has already been said about alcohol, it will be obvious that more often than not this is a contributory factor to neuropathy. Acetaldehyde, the intermediate product of ethyl alcohol breakdown, interferes with the part played by lipoic acid in enzyme activity and formaldehyde, its counterpart in methyl alcohol drinking, exerts a poisonous effect on cytochrome oxydase.

(4) *Liver disease*. Liver disease is common in Thailand, e.g. amoebic abscess, infestation with trematodes (flukes), e.g., *Schistosoma japonicum* and *S. haematobium*, subjects becoming infected from working in contaminated water in the canals or klongs which abound in the city and countryside or from eating raw fish.

(5) *Gastrointestinal disease* is another important contributory factor interfering with the synthesis of vitamin B in the gut, e.g., bacillary and amoebic dysentery; infestation with tape and round worms. Some notion of the prevalence of parasitic infestation of children in Thailand can be had from the fact that 80 per cent. of children have an eosinophilia, counts up to 20-30 per cent. in the blood not being unusual.

19.2.65. Prasat Hospital: (Male) Thai, aged 17 years, works as labourer in saw mill, Bangkok. Recently moved to city from home in N.E. Thailand. Wages 10 Bts. daily (3s. 4d.), works 10 hours, 6-7 days a week. Diet almost exclusively polished rice with small amounts pork or fish (dried or eaten raw).

Five days before admission became febrile and noticed pains all over with weakness in limbs so that he had difficulty in walking. Feet and hands felt numb and he burned his right hand through its coming in contact with very hot water. No swelling of legs or dyspnoea.

*On examination*: Bilateral foot drop with steppage gait and wrist drop. No muscular wasting but tenderness++, especially in left lower limb. Glove and stocking anaesthesia. Absent tendon reflexes. (Blood count and W.R., C.S.F. normal. Pyruvate tolerance increased).

In all these cases the blood pyruvate level is elevated, but despite its return to normal on intensive vitamin B<sub>1</sub> therapy there is usually little change in the neurological state. Treatment is by a well-balanced diet, rest and physiotherapy and it is only in the long term after several weeks or months that good results with partial or complete restoration of motor and sensory function are seen.

### *Leprosy*

Although rare in Europe and North America leprosy is still common in tropical countries and Thailand is no exception. Not as a rule a direct cause of death, leprosy shortens life and causes incapacity, about 20 per cent. of all patients with the disease showing some physical disability, which is related chiefly to its neurological complications. In Thailand it is estimated that 10 per cent. of all patients who attend dermatological clinics for skin rashes of different kinds are suffering from the disease<sup>13</sup>, but reliable figures as to its prevalence in the country are not available. The W.H.O. and other organizations have conducted many field surveys, teams of observers camping in the vicinity of villages to trace all local cases, and a story is told of one such team who, after they had been on location for some weeks, proudly announced to the head man that they had found some 13 cases of the disease in his district. The head man examined the list politely and complimented the field workers on the thoroughness of their results, but he added two or three other names of patients they had overlooked!

A few miles from Bangkok is the Phra Pra Institute which accommodates 1600 lepers and provides everything necessary for their treatment and welfare from hospital beds, expert medical and surgical assistance, laboratories to well-equipped machine shops, where ambulant patients can work under sheltered conditions.

The skin lesions of leprosy were beautifully demonstrated by the late Dr. Ross in a former Scott-Heron Lecture and I need not refer to them again but there is scope for more extensive study of the neurology of leprosy, especially by electromyography. Monrad Krohn's monograph on its clinical aspects was published over forty years ago<sup>14</sup>. *M. leprae* can attack the cutaneous nerves directly through skin lesions, but in patients with severe leprosy neuropathy it is probable that infection is blood-borne and introduced by insect bites, scratching or abrasions of the skin. The neurological signs depend both on the extent of the infection and the resistance of the host. The organisms lie in the neurolemmal sheaths and Schwann cells of peripheral nerves, and at each neural turn over are liberated to spread infection still further throughout the peripheral nervous system<sup>15</sup>. In districts where the disease is prevalent it is not unusual to see children and even adults who show no other signs of ill health than thickened peripheral nerves, which not only can be felt but seen.

Peripheral loss of sensation is one of the earliest and most constant features, causing anaesthesia and analgesia, but the sparing of joint position sense and other posterior column functions is often equally striking. Nor is the anaesthesia invariably "stocking and glove" in type; a segmental distribution may be simulated. Indeed, seeing these patients with their symmetrically wasted hands it is easy to understand how at one time syringomyelia and motor neurone disease were thought to be *formes frustes* of leprosy.

By and large the clinical pattern, however, is typical of a peripheral neuritis: proximal muscular wasting can occur but is unusual; the V<sup>th</sup> and VII<sup>th</sup> cranial nerves are often attacked, facial paralysis, facial analgesia and hypaesthesia being common, but so far as I am aware trigeminal neuralgia or tic douloureux have never been described. Ulnar, median and radial nerve palsies usually co-exist, causing wrist drop, wasting of the intrinsic muscles of the hands and claw deformity. In the lower limbs bilateral foot drop is common with wasting in both the anterior

and posterior parts of the leg below the knee. Notable in advanced cases is the tendency to ulceration and deformities of the hands and feet, consequent upon fingers or toes sloughing off, so that a patient might only have a pair of stumps upon which to walk and hands so deeply pitted with scars and bereft of all but the proximal phalanges as to render them virtually useless. Undoubtedly (as in syringomyelia) trauma is largely responsible for when patients had been under medical supervision and protected against trauma these effects were not so apparent.

One leper, a man of 60 years, who had been aware of his state for twenty years had marked gynaecomastia, due to leprosy invasion of the testicles leading to residual atrophy. Falling off in sexual libido had been noticed since the age of 40, but he had two grown-up children. Gynaecomastia I believe is of relatively common occurrence in leprosy but in older textbooks<sup>16</sup> is said only to occur when the disease begins before puberty. In this case the evidence was strong to the contrary.

### *The Myelopathies*

Of particular interest in relation to current trends of thought on the aetiology of multiple or disseminated sclerosis is the pattern of demyelinating diseases in S.E. Asia. This differs radically from that seen in northern temperate latitudes, both in Europe and in America and in two chief respects :

1. *Multiple sclerosis can and does occur in Thailand and in Japan but its incidence and prevalence are extremely low in both countries.* McAlpine and his colleagues, who made systematic surveys both in the northern and southern parts of Japan<sup>17</sup> confirmed that the disease is rare in both localities, and during my stay in Thailand I found the same to be true for that country. I was invited to see several doubtful cases but only found two patients in which the signs and symptoms conformed to the clinical picture with which we are familiar.

The first was a schoolgirl of 15 years, a doctor's child, with acute retrobulbar neuritis affecting the left optic nerve. Vision had become impaired in the left eye over the course of a few days and just 3 weeks after the child had had acute tonsillitis, for which she had been treated with one of the tetracycline group of antibiotics. There was a paracentral scotoma in the left visual field with total loss of colour vision in the left eye and some fluffiness of the disc margins, but the fields of vision were full. Subjective sensations of numbness and pins and needles in the lower extremities were complained of at the same time as she had the impairment of vision, but otherwise clinical examination was negative. X-rays of the skull and optic foramina were normal and the W.R. and blood count showed no abnormality. After 3 weeks' treatment by steroids vision was restored although for some weeks later a persistent small scotoma could still be demonstrated with defective colour vision in the left eye and some slight temporal pallor of the disc.

This could be a potential case. Retrobulbar neuritis is, of course, common in tropical countries and is most often the expression of vitamin deficiency but in such instances the lesions are bilateral and in this one the appearances more closely corresponded to the type of unilateral acute retrobulbar neuritis which one finds in multiple sclerosis.

The second case was in a married woman of 40 who had noticed the previous August, 1964, progressive weakness in the left leg and on admission to hospital had shown unmistakable physical signs denoting a Brown-Séquard type of lesion affecting the left half of the spinal cord at the level of T.11. Spinal cord compression was suspected but there was no evidence of a block on manometry or of raised protein in the C.S.F., the only abnormalities in which



were slight pleocytosis (30 lymphocytes per cu.m.) and a slightly abnormal colloidal gold curve 011000000. A provisional diagnosis of multiple sclerosis was made and the patient treated by A.C.T.H. with some subjective improvement, so that she was able to walk again. In January, 1965, however, she had a relapse with weakness this time affecting both legs and on examination was found to have bilateral extensor plantar responses, in addition to paraparesis and the sensory loss previously noted, but there was also some dysdiadokokinesia of the left upper limb and fine nystagmus on lateral gaze to the left. Myelography was performed but showed no abnormality. There were 63 lymphocytes in the C.S.F., protein was not elevated although the colloidal gold curve was now 123332210. All other investigations of the serum proteins, E.S.R., blood, etc., were negative.

In the other cases I saw neither the character of the history nor the physical signs justified a diagnosis of multiple sclerosis. In one, a woman of 40, there had been an obscure illness some 6 months previously with vertigo, vomiting and weakness in the legs but there had never been any convincing neurological signs and when I saw her in March, 1965, she was well. In the other case physical signs were abundant :

In the upper extremities action tremor, dysdiadokokinesia, decomposition of movement, associated with increase of tendon reflexes and voluntary muscular weakness and coarse horizontal nystagmus and dysarthria. This looked like multiple sclerosis but in the lower extremities the picture was quite unlike the disease and more that of a peripheral neuropathy. There was a stocking type of anaesthesia, absent knee and ankle jerks and bilateral foot drop with wasting below the knee. There had been a history of jaundice at the onset with diplopia. The cerebellar signs in the upper extremities had appeared after that and the weakness in the legs had been the last sign to develop. Blood and c.s.f. sugars were elevated and the possibility of a diabetic neuropathy, a collagen disease or carcinomatous neuropathy was considered. It was not felt likely that the case could be one of multiple sclerosis, in which disease signs of peripheral neurological disease are not a feature.

3. *There is a comparatively high incidence of acute disseminated encephalomyelitis, neuromyelitis optica and acute transverse myelopathy in Japan and in Thailand.* All Japanese workers refer to this peculiar feature of their country where multiple sclerosis is notably rare but these other forms of myelopathy relatively common. Today in Japan the incidence of acute disseminated encephalomyelitis has declined and fewer cases are seen, but in Thailand the incidence of acute disseminated encephalomyelitis and of acute transverse myelitis still continues to be high—30-40 cases, for example, being admitted to the Chulalongkorn Hospital, Bangkok, annually.

The connecting link between these curious circumstances probably lies in the prevalence in both countries of another disease of the nervous system—human rabies—which 20 years ago affected Japan and Thailand about equally. Owing to legislation in the former, however, the disease has been brought under some measure of control. But in Thailand human rabies is still prevalent, being invariably fatal and accounting for some 30-60 deaths annually in Bangkok hospitals alone. In England, muzzling and quarantine laws for dogs and cats have been enforced since 1885, since when the disease has become virtually extinct, but in Thailand there are no such regulations. Licences are not required for dogs and a great majority of these animals are ownerless mongrels which roam the streets freely and in large numbers. Religious principle accounts for the tolerance and kindness with which

they are treated by the people—children and adults alike. Motoring accidents are not infrequently caused by drivers swerving to avoid dogs and litters of newly born pups are sheltered and fed even by poor people. After sunset it is not uncommon in Bangkok to see children eating their evening meal of rice, seated on the still warm pavement, and attended by an expectant retinue of dogs. During peripatetic excursions I saw two people being bitten, the incidents, however, causing no great stir. The only official provisions made to cope with the menace are :

First, dog-catching teams which may sometimes be seen at night discreetly carrying out their highly unpopular crusade with the aid of long handled nets, by which any ownerless dogs found wandering are seized and carried away for summary execution in a lethal chamber.

Second, the Saovabna (Pasteur) Institute in Bangkok provides a phenolized anti-rabies vaccine of the Semple type which contains a large amount of neural tissue in its composition. The original strain of rabies virus was brought from the Pasteur Institute in Paris in 1913<sup>18</sup> and thereafter promulgated in rabbit brains. In Thailand since 1946 the vaccine has been given in most instances by subcutaneous inoculation into the thigh in a strength of 5% in doses of 5 ml. daily for 14 days. For deep bites on the face, head or neck 5 ml. are given for 21 days. Between 1913 and 1956 some 84,083 courses of preventive treatment were given.

Not all cases of acute disseminated encephalomyelopathy were related to recent anti-rabies vaccination but the great majority gave a history of a recent dog bite, symptoms appearing within the first 3 weeks of being bitten and after the 4th to the 10th injection of vaccine, thus occurring at a much earlier period than is seen in rabies, where the incubation period may be anything from 1-3 months and is occasionally delayed for a year.

The following two examples which I saw are typical of acute disseminated encephalomyelopathy and acute transverse myelitis respectively :

Male Chinese, aged 25 years. Bitten by rabid dog two weeks before admission to Chulalongkorn Hospital, Bangkok. He had become ill after the sixth injection of Antirabies Vaccine with headache, vertigo, muscular weakness of the limbs and difficulty in micturition. Despite these symptoms he continued to receive "daily shots" until after the fourteenth injection when he developed hyperpyrexia, became delirious and soon after passed into coma.

*On examination :* Comatose, appears to be quadriplegic, all tendon reflexes depressed. No papilloedema. Pupils sluggish. No neck stiffness of Kernig. C.S.F. : clear fluid, cells only, protein normal. Respiratory failure supervened and he died within twenty-four hours of admission despite positive pressure respiration and tracheotomy.

*Post-mortem examination :* Ascending myelopathy in cord with extensive scattered areas of demyelination in cerebral white matter. Cortical neuronal tissue relatively intact, no inclusion bodies seen. Perivascular cuffing.

Male Chinese, aged 33 years. Bitten by dog three weeks before and given daily inoculations from the first day. On 13th day developed coryza-like symptoms and weakness in legs. Weakness progressed so that by the 18th day he was paraplegic and had lost control of his bladder and rectum. (Inoculations of A.R.V. had been discontinued after 13th day).

*On examination :* Absolute loss of motor, reflex and sensory function below the level of T.8-9. Retention of urine with overflow incontinence, faecal incontinence. Paraplegia flaccid. No wasting of muscle. C.S.F. 128 mgm. protein, 38 cells (Neutrophils 75, lymphos. 25%), sugar 59. Queckenstedt negative. Spinal radiograms and myelography negative.

Attention was first drawn to the occurrence of these cases in Thailand by Uchimura and Shiraki<sup>19</sup>, who on post-mortem examination found areas of demyelination in the brain and spinal cord resembling acute multiple sclerosis. It is now known that the post anti-rabies vaccine disease—acute encephalomyelopathy—is identical with its experimental counterpart which can be induced in certain laboratory animals by inoculation with emulsions of homologous brain and spinal cord to which a fortifying adjuvant has been added. In Japan and Thailand, therefore, it is the prevalence of rabies and the need for preventive vaccination or inoculation that has created what is probably a unique and certainly vast natural laboratory for the study of demyelination in man.

I suggested to my colleagues at the Prasat Institute that they should conduct a 10 year follow-up study of survivors from post-rabies vaccinal encephalomyelitis to find out if any of them subsequently developed relapsing and remitting symptoms like multiple sclerosis. Japanese experience suggests that they do not. The follow-up could be both retrospective and prospective and there should be little difficulty in collecting 100 cases and the opportunity of doing this on a significant scale should not be neglected.

Microscopically, the lesions in acute disseminated encephalomyelopathy and multiple sclerosis differ. In the latter, for example, it is always possible to detect age differences in demyelinated plaques, some being of recent origin and others much older. Yet, the autoimmune theory holds such promise that the possibility of there being an immunological connection between the diseases cannot lightly be dismissed. One is reminded of pre-antibiotic days and of acute tonsillitis and quinsy. One attack of tonsillitis predisposed rather than protected the patient from subsequent attacks whereas a fulminating attack of quinsy often left a patient immune to further throat affections.

Much is known about the uneven distribution of multiple sclerosis in the world: its rarity in underdeveloped communities, in the tropics and sub-tropics, and its prevalence in northern temperate regions among highly civilized communities being generally accepted. Collomb<sup>20</sup>, whose work in Central and Equatorial Africa has shown that multiple sclerosis is virtually non-existent among native Africans, suggests that this could be related to the immunological responses of the African differing from the European in some way and this could be true of S.E. Asia also. I must confess that as a theory it attracts me more than do the numerous speculations that have been indulged in as to the possible role in aetiology of climate, sunshine, cosmic irradiation effects, diet and character of the subsoil and its composition as regards trace elements. Natural immunological differences might explain why native-born white South Africans are virtually immune whereas if they migrate to Europe they become as prone to the disease as are Europeans. One is reminded of the plight of the population of Tristan da Cunha who were so subjected to catarrhal respiratory infections after they had been temporarily evacuated and brought to England and of the St. Kildans and other isolated communities in the XIX century who dreaded so much the arrival of ships which could convey "boat fever" to the islanders.

Multiple sclerosis had its origin in the old world. Fifty years ago there may have been grounds for attributing its rarity elsewhere to ignorance of its clinical features. In the mid XIXth century Charcot pointed the finger at English neurologists in

this respected and later we were to do the same at our North American colleagues, where the disease was only infrequently reported before the First Great War. But to-day the features of the disease are too well-known everywhere for it to escape attention and its uneven distribution in the world population has been transformed from the status of an "impression" to that of a fact, proof of which can be found in the many statistically-significant survey reports that have been published. Nowhere, however, has the disease been found to be epidemic and this encourages the belief that there must be two factors involved in aetiology: a fortuitous "contaminating" factor, if I may use the expression, and an environmental factor which lowers the resistance of communities and enable the contaminating factor to affect a greater number of persons. In the Faroes, for example, multiple sclerosis was unknown forty years ago<sup>21</sup> but the prevalence there to-day is still unnaturally low as compared to Iceland, Norway, Denmark, and our own country<sup>22</sup>. The Faeroese, although fast becoming civilised in the sense that they use washing machines, detergents and even packaged foodstuffs, still remain much of their primitive habits and this could be related to differences in their immunological responses as in Thailand. One would like to see serological investigations being made in Thailand of random samples of the population and of patients who have recovered from acute encephalomyelopathy. Samples from children should also be included because it is known that multiple sclerosis has a prolonged preclinical phase and that this most often coincides with the first two decades of life; regarded as the period of maximum susceptibility. The "contaminating" agent may prove to be a virus or a toxin, which interferes with enzyme activity and the metabolism of myelin. Comparative studies of the blood groups and of the results of electrophoresis of the serum and cerebrospinal fluid are also required.

### *Parasitic Diseases of the Nervous System*

Examples of parasitic infections of the nervous system seen in Thailand are amoebic brain abscess and cerebral malaria. In addition to protozoal infections, metazoal forms are common e.g. intestinal flat, round and thread worms, but apart from cysticercosis I saw no cases with neurological complication. In Thailand it is uncommon to detect radiological evidence of calcification in cysts, either in skeletal muscle or in the brain, and this is not due simply to the recency of lesions. I was assured that even in longstanding cases, with pronounced epilepsy or dementing symptoms, calcification is often not seen. The Thais are not uncooked, pork eaters, however, and the disease is probably not so frequent there as it is reported to be in China.

More common in Thailand is the habit of eating raw fish, shell fish and snails. Throughout the country snails are regarded as a delicacy and as the creatures can readily be caught in gardens or in the waters of the "klongs" or canals they are much eaten by poor people. The snails are thought to have therapeutic value and a writer in a Japanese language newspaper<sup>23</sup> actually extolled them as being: "effective against tuberculosis if swallowed alive". As for slugs: these were helpful in improving the voice of "Ballad chanters" and a raw diet in general was recommended for "cleansing the blood". In the tropics slugs and snails often act as intermediate hosts to a nematode. *Angiostrongylus cantonensis*, the natural habitat of which is the lung of the rat. It has been recovered from these rodents all over

the Far East, especially in China, Thailand, Formosa, the Pacific Islands and even Australia. It was first described by Chen in 1935<sup>24</sup>. Rat droppings containing larvae infect wet ground and are taken up by slugs and snails which, like man, play the role of intermediate hosts. Human infection is brought about by consuming them raw, through eating improperly washed vegetables or fruit, or even by walking barefoot over damp ground, where the larvae from the bodies of crushed planitaria are to be found<sup>23</sup>. Between 20-30 per cent. of snails contain the larvae so that human infection is relatively common and several members of the same household may be affected. It is also common in children who can be seen any day rummaging about in the dirty water of the klongs for the creatures.

After ingestion by man the larvae penetrate the wall of the alimentary tract and migrate to the brain where they set up an encephalomeningitis. At post-mortem examination worms of a diameter of 0.13 mm. have been found in the periventricular white matter, in the meninges, cerebellar and cerebral cortices<sup>25</sup>. In one case reported from Bangkok, a worm 13 mms. in length was removed from the anterior chamber of the eye<sup>26</sup>. A somewhat similar worm is found in herrings caught in temperate climates, the eating of which raw may cause intestinal obstruction but not cerebral symptoms<sup>27</sup>. Proof that with *A. cantonensis* the brain is the seat of attack in primates has been obtained from experimental infection of monkeys<sup>28</sup>. In man the incubation period ranges from 2-4 weeks<sup>29</sup> and diagnosis is facilitated by the use of an intradermal skin test made with powdered *A. cantonensis* in saline<sup>30</sup>. Some patients may show only isolated peripheral nerve palsies, e.g. III, VI, VII nerve or musculospiral paralysis, the site of the lesion being indicated by the occurrence in patients with facial palsy of associated loss of taste in the anterior two-thirds of the tongue. In most instances however, headache predominates in association with curious paraesthesiae in the head, body or extremities and dementing features may be prominent. Later, vomiting and drowsiness with clouding of consciousness supervene and there is neck stiffness and then signs of meningeal involvement. The cerebrospinal fluid is under pressure and shows a pleocytosis, counts of 500 cells per cmm. not being unusual and 20130 per cent. of them being eosinophils. The c.s.f. protein is moderately elevated but the sugar content and chlorides are normal.

The following is a brief resume of a case I saw at the Prasat Institute. It is fairly typical:

Thai policeman, aged 25. Admitted Prasat Hospital 6.12.64 complaining of headaches and mental confusion. Headaches paroxysmal, severe throbbing, unrelieved by analgesics; history nine days.

*On examination*: Temperature 37.5°, drowsy, stuporose; neck stiffness pronounced, Kernig +. No skin rash. Fundi normal. Left VI nerve palsy and paresis of right VI, affecting both voluntary and reflex eye movement.

C.S.F.: 246 cells per c.mm. (Neutrophils 9%, Lymphocytes 25%, Eosinophils 66%).

Protein 35 mgm.%.

Blood count: No anaemia; W.B.C. 4,500. Neutrophils 70% Eosins. 5%, Lymphos. 24%.

NOTE—For ten years or more has been eating raw snails all the year round. His family do the same. Catches them by wading in klongs and washes them in vinegar. Will eat one dozen at a time and likes flavour.

Treated by steroids, oral prednisoline 40 mgm. daily by mouth for one month, then dose tapered.

C.S.F. 25.12.64 : 45 cells, Lymphos. 85%, Neutros. 15%.  
12. 2.65 : 32 cells, Neutros. 7%, Lymphos. 93%.  
By 23.2.65, feeling well. No physical signs.

### *Cerebral Trauma*

I have kept cerebral trauma to the end because the subject is of current interest in Britain and the United States, not only on account of its relation to road accidents but to boxing. The former, of course, accounts for the great majority of head injuries in Thailand for, although roads are good and the Thais themselves courteous, capable and quick-thinking drivers, the accident rate per driver, per unit of time and distance driven is many times greater than in the United States. Indeed, one well-known visitor to Bangkok is reputed to have said that "any guy driving an automobile in this city deserves to be awarded The Purple Heart", and this is probably no overstatement. Earlier this year local newspapers stressed the need for reform in traffic regulations and pointed out that the fines imposed for speeding were too lenient and that long-distance bus drivers, when they became tired after lengthy spells of duty, had been known to turn the wheel over to the conductor, who, of course, was not licensed to drive the vehicle. Safety belts, too, appear to be little used.

But if road accidents provide the main source of cerebral trauma, one would think that the yield per boxer (Thai-style), cannot be far behind, yet little is heard of this aspect of that ancient sport, which is unique in its character and most popular with all classes of the community. The contestants not only use their gloved fists to deliver punches chiefly to the heads of their opponents, but they kick, or as they call it "spurn", with the feet, dealing heavy blows either to the head, side of the neck, body or legs. At other times a boxer will try to weaken or knock out his adversary by delivering blows with the point of the flexed elbow or by flexing his knee suddenly and bringing it forcibly into contact with his opponent's upper abdomen or point of the chin.

Quite a classical ritual attends the fights. Entering the ring the boxers first crouch on the canvas covering the floor, facing the direction of the place in which they were born as they pray sincerely for victory. Then they proceed to perform an elaborate mime of the art of fighting, which may last several minutes. Each boxing camp has its own distinctive ritual and the intention is that a good boxer should take pains to pay tribute in this way to his teacher. Some of the miming is traditional and woven into the ancient history of Thailand e.g., "The Elephant Stomp", "The Four-faced Brahma", and "The Making of the Garlands". A sacred cord or thong, known as the *Mongkon*, is worn about the head during the ritual but discarded before actual fighting commences. The boxers, too, usually wear cords or charms around one or both biceps, which are kept on during the contest. A hard sea shell or cup is worn over the genitals, but this is the only protection permitted.

These preliminaries settled, the fight begins to the accompaniment of native music provided by an orchestra of three or four men playing different instruments—the "Pi'charva" or Javanese pipe, the "Ching" which is a percussion instrument of the cymbal type and made of thick metal plates and the "Glaw-ng Khae-K", a long wooden drum<sup>31</sup>.

Fights are of five rounds, each lasting 3 minutes with 2 minute intervals. Knockouts are awarded after the referee has counted ten as in Western boxing and, similarly, points are awarded for superior skill, when both boxers stay the course. The only recognised fouls are wrestling, butting with the head, spitting, biting or kicking one's opponent when he is already down or able to support himself only by holding on to the ropes.

In all the fights witnessed it was evident that, whilst rules were carefully observed and good sportsmanship prevailed, the boxers attacked each other with great energy and with no trace of play-acting. Often they would become locked together, as one tried to kick the other and his foot was caught, and fall violently, still interlocked, to the canvas covering the wooden floor. I counted some 8-10 falls of this kind in a single round. The referee always did what he could to prevent heads striking the floor directly but he could do nothing of course to prevent possible decelerating effects on the brain. On one occasion I noticed that a contestant had a recent scar over the right parietal region of the scalp. He won his fight but I learned that he had been operated upon only three months before at the Prasat Hospital for a subdural haematoma! Five such cases had been treated in that hospital alone in 1964.

However, because of its historic aura and the present interest taken in the sport, both vested and purely sporting in nature, it is difficult to get reliable information as to the frequency of head and other injuries, but that they occur there can be little doubt and one might conclude that the following are the chief risks attendant on the sport:

(1) Traumatic external popliteal palsy causing foot drop from kicking over the head of the fibula, a favourite method of weakening an opponent. In Britain where twenty examples of compression of the nerve have been described by Garland<sup>32</sup> the most frequent causes were sitting with the legs crossed and the wearing of ill-fitting knee pads by coal miners.

(2) Kicks to the side of the neck with the bare foot (only covered with elastoplast around the heel and sole). I saw one man carried out unconscious after such a kick which had clearly set off a carotid sinus reflex. Dr. J. D. Spillane, who was also present at the time, raised the possibility of such direct kicks damaging the carotid artery and leading to its subsequent occlusion.

(3) Direct blows on the head or rapid decelerating effects from falls, causing laceration from contre coup or torsion effects and tearing of veins crossing the subdural space, e.g. subdural haematoma.

(4) Blows delivered to the chin by the fist or knee causing a knockout, or blows to the epigastrium causing sudden syncope from fall of blood pressure.

In conclusion one may perhaps be permitted to quote Dr. Prasop Ratanokorn in the words of a Thai ballad—"You can measure the depth of the water by the length of the stem of the lotus flower<sup>33</sup>". I have been trying to do this in selecting these items to illustrate the extent and form of nervous disease in Thailand to-day. There are other conditions of neurological interest which have not been mentioned but, as I have suggested, the country is a vast natural laboratory and the opportunities for research only await exploration. One would like to see more exchange

arrangements made for promising young Thai graduates to come to our country for training and others, that is to say registrars from this country, taking their places temporarily in Thailand for the first-hand experience they will gain there.

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# ACUTE PANCREATITIS

## A REVIEW ILLUSTRATED BY A SERIES OF CASES

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ACUTE PANCREATITIS is not an uncommon disease but because it frequently presents a varied selection of symptoms and signs, or so closely mimics other abdominal conditions, the diagnosis is often missed. Further confusion arises from an inadequacy of reliable confirmatory tests or misinterpretation of those available. Not only is the disease difficult to diagnose but there is also little specific therapy which one can employ. Finally although many theories have been presented no definite aetiology has been proved. For these reasons a series of cases has been studied retrospectively and the literature on the aetiology reviewed.

### MATERIAL

In the years 1959-1961, 45 patients were admitted to the Leicester Royal Infirmary with a diagnosis of pancreatitis. In 22 this was the first attack of acute pancreatitis and these are the cases reported in this article, the other 23 cases being excluded by either having had previous similar attacks (i.e., relapsing pancreatitis) or by being diagnosed as having chronic pancreatitis.

#### *Age and Sex*

Acute pancreatitis can occur at any age. Pender (1957) has reported an attack in a child aged 3. In this series the youngest case was 23 and the oldest 76. The overall average was 54.6 years, the average for females being 56.6 and for males 52.5. The 22 cases were equally divided between the sexes in contrast to the larger series reported by Pollock (1959) where females outnumbered males in the ratio 71: 29.

#### *Symptoms and Signs*

The two most common presenting features of acute pancreatitis are vomiting and abdominal pain. Of the 22 records examined 19 mentioned vomiting. This usually coincides with the onset of abdominal pain, is frequent and often accompanied by retching. Bile and small intestinal contents are the normal constituents of the vomitus. Classically the pain of acute pancreatitis is described as abdominal radiating through into the back. Back pain was recorded in only 5 of the 22 patients. The precise site of the abdominal pain is most frequently in the epigastrium, but it can be central or even appreciated in the lower abdomen—this, of course, adds to the difficulty in diagnosis and in fact 3 cases in the series were diagnosed preoperatively as appendicitis. Wherever the site of the pain, it is severe, constant (and inevitably requires analgesics at first) but diminishes over the first 24 hours.

Examination reveals a patient who is obviously in severe pain, sweating and generally pale with cyanosis of the lips—a sign particularly worth noting. In only 3 patients in this series was the blood pressure below 120 mm. Hg. systolic, but experience has taught that hypotension is common, especially with haemorrhagic pancreatitis.

Signs typical of peritonitis are elicited in most cases (16 out of the 21 cases in which adequate findings were noted). Bowel sounds were recorded as being present in 10 cases and absent in 8. Peri-umbilical staining (Cullen's sign) and staining the flank (Grey Turner's sign) appear late and indicate a bad prognosis.

One sign not often mentioned is that patients frequently find that crouching or sitting with their heads between their knees eases the pain. Although more common in chronic pancreatitis this is occasionally seen in acute pancreatitis.

### *Diagnosis*

It is desirable that the diagnosis should be made without recourse to laparotomy. Ten cases were diagnosed at operation, 11 clinically and one at autopsy. The preoperative diagnosis in 8 of the cases diagnosed at surgery was—appendicitis (2), cirrhosis, perforated peptic ulcer (2), peritonitis, ? appendicitis ? perforated gall bladder, and intestinal obstruction.

Serum amylase estimation is the most widely used confirmatory biochemical test. However, caution must be exercised in its use. Firstly, elevated levels can be found in other conditions, e.g., cholecystitis, myocardial infarction, and even in perforated peptic ulcers. Unfortunately it is these conditions which the physician is trying to rule out when he is making his diagnosis of acute pancreatitis. Secondly, the serum amylase level falls rapidly after the first 24-48 hours of an attack and consequently estimations should be made early. Thirdly, as in one case in this series, necrosis of the pancreas can take place without a rise in the amylase. The explanation is that early necrosis has destroyed the enzyme amylase. Generally a figure over 1,000 Somogyi units is considered significant. Serum amylase estimations were performed in 13 patients, the average level being 2207 Somogyi units. There was a wide range of levels—from less than 160 to more than 6400 units. Elevated serum lipase levels occur later but persist longer than the raised serum amylase but as they are less sensitive and more difficult to estimate they are not used in routine practice. Plasma benzoyl-arginine amidase has been shown to be raised in pancreatitis (Gullick) 1963) but this test has not yet reached practice. Winstone (1965) has used the presence of methaemalbumen in the plasma for diagnosing acute haemorrhagic pancreatitis as opposed to the oedematous variety. He has shown that when M.H.A. is found in large quantities in the serum the mortality is high.

X-rays are not of help in the diagnosis of acute pancreatitis. A "sentinel loop" of small intestine is sometimes seen over the pancreas on straight X-ray. Calcification of the pancreas itself is rarely seen.

### *Diagnosis at Operation*

This usually presents no problem. On opening the abdomen one frequently finds a considerable quantity of free fluid which can be clear, bile-stained or serosanguinous. Areas of fat necrosis lead to examination of the pancreas which is found to be swollen and oedematous. The gall bladder and common bile duct should be examined to exclude the presence of calculi.

Laparotomy has not been shown to be harmful and it is certainly better performed when there is doubt about the diagnosis. When acute pancreatitis is discovered at laparotomy definitive surgery should be avoided but a concomitant acutely inflamed gall bladder should be drained or an obstructed common bile duct dealt with.

## TREATMENT

### 1. *Supportive*

- (a) *Relief of Pain.* Morphine should be avoided as it causes spasm of the sphincter of Oddi. Pethidine has a similar but less marked action.
- (b) *Reduction of Secretions.* This is achieved in two ways. Firstly continuous nasogastric suction should be instituted. This relieves vomiting and helps to keep pancreatic and duodenal secretion to a minimum. Secondly, atropine and propantheline are used. However these substances cannot affect humorally induced pancreatic secretion but may help by reducing the tone of the sphincter of Oddi.
- (c) *Fluid Replacement.* Hypovolaemia occurs due to vomiting, the secretion of large quantities of peritoneal fluid and oedema of the pancreas. These latter losses also contain protein and many patients require blood and plasma especially in haemorrhagic pancreatitis. Serum electrolytes easily become imbalanced in these circumstances and must be regularly checked. The serum calcium level must also be carefully watched and 10 per cent. calcium gluconate given as required.
- (d) *Corticosteroids.* Steroids are of doubtful therapeutic value in acute pancreatitis but if a patient's condition is worsening or not improving with the usual measures then the use of hydrocortisone intravenously is warranted. Doses of the order of 300-400 mgm., 4-8 hourly should be given.
- (e) *Antibiotics.* Most cases of acute pancreatitis receive antibiotics although the reason for giving them is not always clear. The inflammatory process in this disease is not bacterial and the only reason for giving antibiotics is the prevention of secondary infection. Combined penicillin and streptomycin are adequate for this purpose.

### 2. *Specific Drug Therapy*

The present theories on the aetiology of acute pancreatitis involve activation of trypsinogen with digestion of the pancreas and release of kallikrein and bradykinin. An inhibitor of trypsin and kallikrein was isolated by Frey, Kraut and Werle (1950) from the parotid glands of cattle. It is now marketed under the name of Trasylol—a low molecular weight polypeptide which can be administered intravenously or intraperitoneally. However, despite encouraging reports of its action in experimentally induced pancreatitis, Skyring, Singer and Tarnya (1965) have shown in a double blind trial that the Trasylol treated patients fared no better, or may have fared worse than patients treated without this drug. However, although this finding agrees with Nardi (1963) the figures are very small and many believe the drug to be helpful—consequently its use should be continued until a larger series of cases is published.

### 3. *Surgery*

In early stages of acute pancreatitis, surgery is not indicated. If pancreatitis is diagnosed at laparotomy it may be necessary to deal with an associated condition, i.e., stones impacted in the common bile duct, empyema of the gall bladder, etc. Later the surgery becomes that of complications. The most frequent complication encountered is a pseudo-pancreatic cyst. Early operation in this condition is dangerous as an external pancreatic fistula may result and some of the pseudocysts resolve spontaneously.

Following a diagnosis of pancreatitis, when there is no reason to believe that the pathological processes are active, oral cholecystography should be performed and it may be necessary to follow this with intravenous cholangiography. If these show any biliary abnormality surgical correction should be carried out.

4. Hinton (1962) used propylthiouracil (1500 mgm. intravenously in the first 24 hours and 100 mgm. during each 24 hours for the following two days) in 9 cases of acute haemorrhagic pancreatitis, of whom 8 survived. The rationale is discussed below.

5. On the basis of the view that pancreatic activity is reduced by hypothermia, Wels and Taheri (1962) treated 4 patients with acute haemorrhagic pancreatitis by reducing the body temperature to 33-35°C for 48 to 72 hours. Three patients survived, the fourth dying due to aspiration of gastric contents on the tenth day.

#### MORTALITY

In Pollock's (1959) series there was a mortality of 26 per cent. Skyring *et al.* (1965) reported 5 deaths in 23 episodes of pancreatitis. In the present series there were 6 patients who died out of a total of 22—a mortality of 27 per cent.

#### AETIOLOGY

Grissellius is credited as having described acute pancreatitis in 1681 although he did not recognise the significance of the completely necrosed pancreas (Fitz 1899). Fitz also attributes to Portal the report of haemorrhagic gangrenous pancreatitis given in 1803.

Alcohol and biliary calculi are said to be the two common precipitating factors in acute pancreatitis. There were no alcoholics in this series nor in that of Pollock (1959). This is in contrast to Richman (1959) who states that up to 25 per cent. of cases of acute pancreatitis in America are alcoholics.

Opie (1901) was the first to be credited with the view that calculi in the ampulla of Vater allowed bile to be forced into the pancreatic duct. In this series there was evidence of cholecystitis or biliary calculi in 11 of 17 cases. Pollock (1959) found biliary abnormalities in 50 per cent of males and 75 per cent of females with acute pancreatitis. However, Rich and Duff (1936) found calculi in this situation in only 2 out of 24 cases of acute pancreatitis at autopsy and Pollock (1959) found stones in the ampulla in 5 out of 22 under the same circumstances. To overcome this objection to Opie's theory it has been suggested that spasm or stenosis of the sphincter of Oddi occurs.

Opie's theory also assumes that the secretory pressure of the liver is greater than that of the pancreas. Parry, Hallenbeck and Grindlay (1955) found the opposite in dogs. Elliott, Williams and Zollinger (1957) postulated that pancreatic juice flows into the obstructed common bile duct, mixes with the bile and is incubated in the gall bladder. Later, when the pressures in the two systems become equal the mixed juices flow back into the pancreas and cause pancreatitis.

The main objection to Opie's theory is that it presupposes a common channel between the pancreatic and biliary ducts. The anatomical studies of Opie (1901), Baldwin (1911), Mann and Giordano (1923), Boyden (1947) and McCutcheon (1962) reveal that this is rarely so. Thus although Opie's theory may be correct in a few cases of pancreatitis it is not the main cause of the disease.

McCutcheon (1962) postulates that duodenal enterokinase enters the pancreatic duct and activates proteolytic enzymes within the pancreas. These diffuse across the duct wall and produce the vascular changes which cause pancreatitis, the final process being one of infarction and haemorrhage rather than auto-digestion. No explanation is given by McCutcheon for the duodenal fluid entering the pancreatic duct—could increased intraduodenal pressure be the cause? Pfeffer (1958) tied off a loop of duodenum in a number of dogs and these developed acute haemorrhagic pancreatitis. A similar result was obtained when the experiment was repeated with the bile duct tied off, excluding bile as an aetiological factor. Pfeffer did not postulate reflux of duodenal contents but suggested that increased pressure might interfere with the blood supply in the arterioles with consequent necrosis of the cells of the pancreas.

Safadi *et al.* (1961) injected sterile polyethylene microspheres of 8 to 400 microns into the superior pancreatico-duodenal artery of dogs. They found that the smaller microspheres (8 to 20 microns) caused acute pancreatitis and as the size of the microspheres increased the severity of the pancreatitis diminished. Rapid pancreatic necrosis was thought to be due to release of an intracellular enzyme in response to interference with the blood supply to the individual cells. The necrosis was not related to trypsin or trypsin-like substances acting upon the cells but was due to the intracellular enzymes of the desribonuclease which was obtained from the microsomes. Reid, Paulette and Hinton (1959) isolated canine pancreatic microsomes and these were shown to be the most destructive part of the cell. Reid *et al.* (1957) showed that thiouracil decreased and thyroxin increased the oxygen uptake of pancreatic homogenates of mice. Challis, Reid and Hinton (1957) showed that propylthiouracil given for 7 days reduced the canine serum amylase by 21 per cent. Paulette *et al.* (1958) repeated Pfeffer's closed duodenal loop experiments but gave propylthiouracil intravenously at the same time. Eight of the twelve dogs used did not develop pancreatitis but 12 of 13 control dogs given saline developed pancreatitis.

It has been shown that smooth muscle stimulating and vasopressor substances are liberated from the plasma globulins by pancreatic extracts. Thal, Kobold and Hollenberg (1963) demonstrated that these substances have the properties of plasma kinins and probably represent bradykinin or kallikrein. They produce extreme vasodilation and increased permeability when injected into the vascular bed; they also stimulate pain fibres. It has been postulated that the local oedema, pain, ascites and hypotension of acute pancreatitis may be related to the release of proteolytic kinin-forming enzymes from the pancreas.

Thus, although we can produce acute pancreatitis experimentally by several means and can explain some of the clinical features we still do not know the cause of the disease in humans.

#### SUMMARY

1. If acute pancreatitis is not constantly in ones mind when examining patients with acute abdominal complaints the diagnosis will be missed, incorrect therapy instituted and the patient may die. To remind the physician of the condition a series of 22 cases is reviewed and their signs, symptoms and treatment discussed.
2. Opie's theory for the cause of acute pancreatitis is no longer tenable in

all cases and while the aetiology of pancreatitis is still unknown recent interesting work is reviewed.

I wish to thank the surgeons of the Leicester Royal Infirmary for permission to publish this review, and Dr. A. M. Connell for his help and advice.

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#### BOOK REVIEW

TEXTBOOK OF PHYSIOLOGY AND BIOCHEMISTRY. By George H. Bell, J. Norman Davidson, and Harold Scarborough. Sixth Edition. (Pp. xi+1140; illustrated. 75s.). Edinburgh and London: E. & S. Livingstone, 1965.

THIS book represents a very successful and well balanced collaboration between a physiologist, a biochemist and a clinician. It has been considerably revised in all sections since the last edition four years ago and both text and references reflect not only advances in pure physiology but in clinical science. Even though it covers both biochemistry and physiology it is still a formidable challenge to the average medical student, and the post graduate may better appreciate the many clinical applications, for this is essentially a book of physiology applied to man. It is the best and most readable book in that field and we congratulate the authors on their successful presentation of up to the minute material, and the publishers on the excellence of the format and on the reasonable cost for such a thoroughly revised book.

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# A CASE OF CONGENITAL PSEUDO AINHUM

By **AGNESE M. T. KELLY, M.D., D.C.H.**

Dermatology Department, Belfast City Hospital

THE CHILD referred to in this report was first seen by a surgeon at the age of eleven weeks because of the presence of constricting bands around the base of the right thumb and middle finger, associated with shortening of the left index finger. These features had been present since birth. The surgeon recognised the condition as a form of ainhum and kept the child under review. It was eventually referred to a dermatologist as a matter of interest and was then thought worthy of report because of its comparative rarity. A detailed family history was obtained and a review of the literature undertaken.

The recognised varieties of ainhum appear to be as follows:

- (a) True ainhum.
- (b) Condition simulating ainhum but due to trauma.
- (c) Ainhum-like syndrome.
- (d) Pseudo ainhum.

## *True Ainhum*

This was first described by Clarke in 1860 among natives of the African Gold Coast and it was designated by him as "a dry gangrene of the little toe". In 1867 da Silva Lima together with Wucherer introduced the term "ainhum". It is a disease of unknown aetiology and is seen almost entirely in dark skinned persons. Usually the fifth toes are involved by a painless progressively constricting band. The degree of the constriction varies greatly. It may be slight or it may progress deeply until there is either spontaneous amputation of the little toe, or the toe may have to be removed surgically because of gangrene. In true ainhum there would appear to be a hyperkeratosis deep in the constricting fold. Proust (1889), Doyle (1889), Bergner and Whitfield (1960), Lee, Norton (1957), Newman (1953), Spinzig (1939) all found evidence of this.

From the literature, therefore, it seems that true ainhum has the following features:

1. It affects adult dark skinned races in the prime of life and occurs rarely at the extremes of life.
2. The constricting band is usually around the fifth toe.
3. There is often evidence of hyperkeratosis in the groove or evidence of associated hyperkeratosis palmaris et plantaris.
4. Associated bone changes are often present.
5. The condition runs a variable course of months or years before amputation takes place.

## *A Condition Simulating Ainhum but due to Trauma*

A condition simulating ainhum may be found in malingerers who tie a tight band or insert a tight ring over the digit, and the resultant prolonged pressure then produces the features of the syndrome. Newman (1953) and Heitzmann (1881) favoured the idea of self-induced trauma as the cause of "ainhum" since they had observed cases in which local ligatures or strings were important etiologic factors.



### *Ainhum-like Syndrome*

There are many references in the literature to cases in which a condition simulating ainhum is found in association with systemic disease. It has been described, for example, in association with scleroderma, trophoneurosis, pityriasis rubra pilaris, syphilis, leprosy, osteomyelitis, diabetes mellitus, fungal, bacillary and parasitic infections.

### *Pseudo-ainhum*

This condition is congenital in origin. It is present at birth or is noticed in the early neo-natal period. It varies in severity from a simple groove to complete amputation. This particular syndrome would appear to be rare, and in the literature references have been found to only five such cases: Bluefarb (1948), Johnston (1941), Newmann (1953), Wells and Robinson (1952), Peterka and Karon (1964).

All these cases except the one described by Wells and Robinson were in white children. In all some fingers showed this ainhum-like syndrome and others showed evidence of intra-uterine amputation. Toes were also involved in the cases described by Wells and Robinson (1952) and Johnston (1941). This condition would, therefore, appear to differ markedly from true ainhum and its salient features are:

1. Congenital ring strictures around the digits.
2. There may be associated intra-uterine amputations.
3. Race not an important feature. May occur in the white or black race.
4. No associated bony abnormalities are found.
5. There is no associated systemic disease.
6. There is no hyperkeratosis of the fissures.

In his monograph on intra-uterine amputations Streeter (1930) discusses the aetiology of ainhum. He suggests that it may be of germinal origin. Many cases of intra-uterine amputation are described in this paper. It is pointed out that the defects appear by preference in the mesenchymal tissues and particularly in the subcutaneous connective tissue. The ectoderm, muscle and bone depends partly involved when the defects are extensive. The damage that is done depends partly on the extent and partly on the location of the area involved. In the case of a finger, for example, if the defect is extensive enough, this crease tends to encircle the extremity completely. A lesser defect results in a crease that only partially encircles it; whereas a small defect may leave no mark. According to the classification presented in this present paper, it is felt that some of the cases with congenital ring stricture mentioned in Streeter's work would fall into the group designated here as pseudo-ainhum.

### CASE REPORT

Male infant born of normal parents in hospital on 14th October, 1962. It was a short labour and confinement was said to be two weeks overdue. The mother had no illnesses during her pregnancy and took no medicaments in any form other than iron and a short course of Ancoloxan meclozine, 25 mg. and hyridoxine hydrochlor, 50 mg. for morning sickness in early pregnancy. This drug has no side-effects.

Following delivery the mother noticed that the left index finger was stunted; and both mother and father noticed a small nail a short distance from the tip of this finger. This was shed following the infant's first bath. In addition, tight

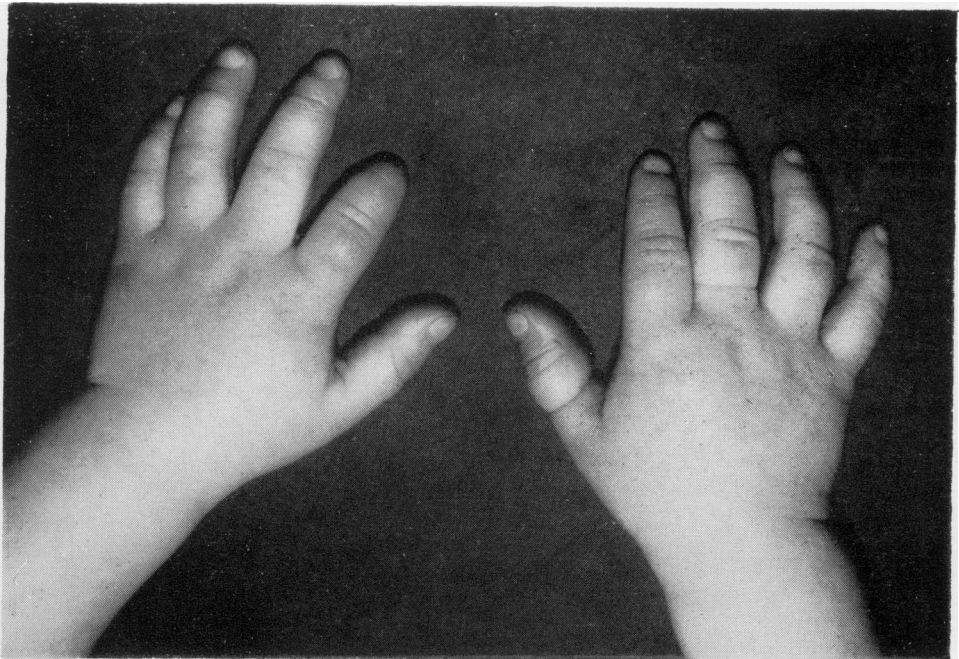
strictures were noticed on the right thumb and right middle finger which have persisted. The mother and child were discharged from hospital ten days after the confinement.

#### *Family History*

No relevant details were elicited on the father's side of family, but there would appear to be many complex deformities on the mother's side dating back to a first cousin marriage in the great grandparents era. Maternal grandfather was blind from birth. Maternal grandmother was normal but she did have a brother with club feet and a cousin with a hump. This patient's baby sister has congenital dislocation of the hips.

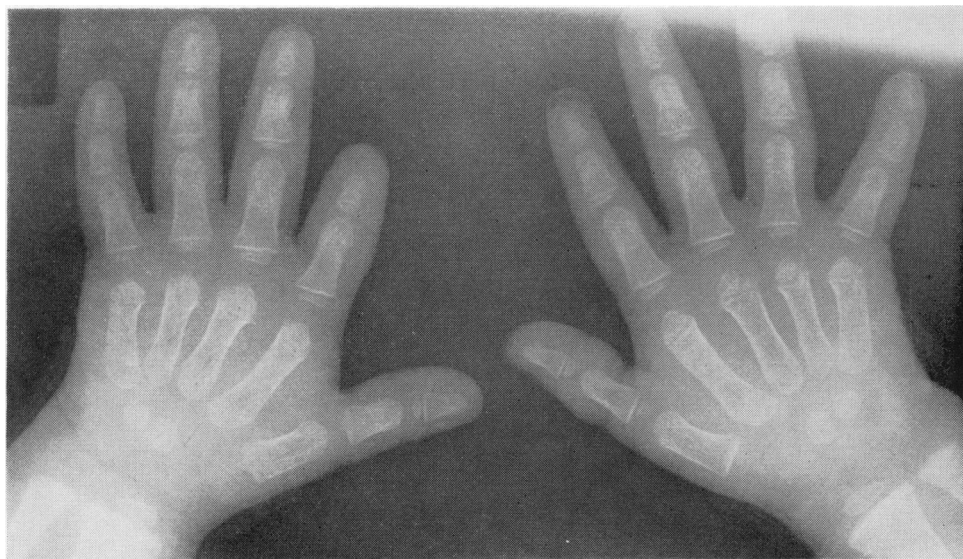
#### *Clinical Details*

On examination in January 1965—The child appeared to be a normal, well developed child of two years three months. He was irritable and bad tempered during examination, but no abnormality was detected in the cardio-vascular, respiratory, gastro-intestinal or central nervous system. His skin generally was good and there were no hyperkeratotic lesions noted at any site. Hair, nails and teeth were perfectly normal.



The left index finger was much shorter than the right index finger and there was no finger nail present on this digit. There were tight constricting rings around the right thumb and middle fingers, but these digits had full range of movements and the circulation was not impaired. Photograph 1 shows these features.

An X-ray of the hands showed the absence of the distal phalanx of the left index finger, but the other phalanges appear normal.



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## OBSERVATIONS OUT OF TIME

By **SIR JOHN McMICHAEL, F.R.S.**

Robert Campbell Memorial Oration to the Ulster Medical Society

11th November, 1965

THE RAPID ADVANCE of medicine in this century has created repeated revolutions in thought and at every turn we have had to discard old ideas in favour of the new. The process can at times be quite painful as we realise the past error of our thinking and the confusion into which we had fallen. Today I shall take up some historical illustrations, finishing up with some personal experiences on some more recent events in the advancement of medicine.

Research in medicine does not proceed in a straight, direct line of logical steps, comparable to those which seem to be employed in the physical sciences and in mathematics, but rather in a sequence of often isolated and apparently unconnected observations which may seem to lead nowhere for the time being until some collateral information or experiment enables the experience to be fitted into place. The build up of biological knowledge is slow and quite often it depends on chance, and until a sufficient number of collateral data have been collected observations may be impossible to explain.

### RESPIRATION

In the early part of the eighteenth century (c. 1720) that indefatigable experimenter, the Reverend Stephen Hales, Vicar of Teddington, measured the blood pressure of a horse using the windpipe of a goose instead of the rubber tubing we should use nowadays to connect his glass manometer to the crural artery. He also made early measurements of the cardiac output of the living heart of various animals. He measured the transpiration stream and the rise of sap in plants and later in his life he studied respiration. He measured the volume of air inspired through respiratory valves and the volume of air expired. He found that the volume of expired air was smaller in volume than that of the air inspired. His observation was obviously correct because, as we know now, the respiratory quotient is normally less than 1, i.e. less  $\text{CO}_2$  is expired than oxygen is taken up. Furthermore as he collected the gas over water no doubt some of the  $\text{CO}_2$  was dissolved. This correct and precise observation mystified him completely as it was inexplicable at that time. Carbon dioxide had not yet been discovered and the realization of the place of oxygen in combustion had not yet been appreciated. Joseph Black and Lavoisier had not yet begun their work. Stephen Hales' speculations naturally led to some confusion in his own mind, but he at least emerged with further useful ideas. He called the expired air vitiated air, realised that something had happened to it, and he became an advocate of proper ventilation and his later practical contribution was the invention of a ventilating pump driven by a windmill to improve the ventilation of the then overcrowded Newgate Prison. In order to regulate his windmill he also invented a wind anemometer to measure the speed of the wind. You will agree that he was a man of singular ingenuity, but with the knowledge of his day he could not be other than baffled by his observation on the diminution of the volume of the expired air. It took in fact more than another 100 years to realise that carbon dioxide was produced

by combustion in the living animal tissues rather than in the lungs themselves, which was finally proved by Pflüger, the German physiologist, following perfusion of the tissues of a living frog and extraction of carbon dioxide by a vacuum pump from the perfusion fluid. This discovery was made only about one hundred years ago. Thus precise observation, enthusiasm and scholarship may all fail for lack of surrounding knowledge. We are in no better case today. "There are more things in heaven and earth than are dreamed of in our philosophy."

#### SCURVY

Let us take another story, the story of scurvy. The cause of scurvy, as we all know, is lack of Vitamin C in the diet. Man and the primates, and the guinea pig, are the only known susceptible animals as the rest of the mammals seem to be able to synthesise the vitamin from carbohydrate.

Jacques Cartier (1535) in the St. Lawrence River had his crew entirely disabled by scurvy and learned a cure from the Indians—probably an extract of pine needles but the identification of the tree was not clear from his writings.

James Lind (1753), taking the hint from the story of a sailor who, unable to walk from the scorbutic bleeding in his leg muscles, had chewed grass to slake his thirst and been cured, tried orange and lemon juice. He studied twelve sailors comparably stricken with the disease. Two got orange and lemon juice and the others, two by two, were given other treatments for the disease. Within a few days the orange juice treated men were on their feet helping with the care of the others who continued crippled: a controlled experiment. Unfortunately, the discovery that lemon juice was curative was muddled and lost after the Napoleonic Wars through substitution of lemons by limes, the vitamin C of which is much lower and deteriorates on storage more rapidly than that of lemons. Scurvy returned on long voyages.

By the end of the century faith in lime juice was understandably lost. Nansen's Arctic voyages were made with no supplies of fruit but his men were free from scurvy because they shot and ate fresh game. In 1900 Lord Lister communicated to the Royal Society experiments by Harley and Jackson on monkeys showing failure to prevent the disease in monkeys by adding a daily apple or banana to a diet of tinned meat. We now know that apples and bananas are poor sources of vitamin C. These unsatisfactory experiments were considered to prove the inadequacy of fresh fruit in prophylaxis and tainted food was considered to be the cause. Tragically this confusion and lack of understanding led to the disaster of Scott's south polar expedition who perished from this preventable disease.

Meantime clinicians were expanding more precise observation well in advance of the laboratory scientists. Sir Thomas Barlow (1883) recognized that scurvy was developing in infants fed on proprietary spray-dried (oxidised) milk, and Dr. George Sutherland in 1906 recognized that the antiscorbutic properties of fresh milk were destroyed by oxidation on boiling.

Accessory food factors (Hopkins, 1909) or vitamins (Funk, 1912) were later recognized and St. Gyorgi in 1928 isolated what he called hexuronic acid, appreciated in 1932 as vitamin C and then called ascorbic acid, responsible for maintaining the integrity of our connective tissues.

In this story we see Lind's great discovery made, lost again by terminological

looseness about limes and lemons, confusion abounding accompanied by successive and appalling human disasters, observations of precision made by clinicians long ages before they could be explained by chemists, animal experiments failing to clarify because lemons and oranges cannot be substituted by apples and bananas, but dependent for its final acceptance on the invention of a word (vitamin) and the final precise chemical identification of the substance, ascorbic acid. It took nearly 200 years.

Here we have observations of convincing and repeatable accuracy made and lost because of lack of precision, such as assumptions that any form of fresh fruit might do, and failure to clear up the mystery of variations in susceptibility of different animals until the exact chemical substance was pinpointed. It illustrates also the enormous contribution which is made by modern organic chemistry.

#### PERNICIOUS ANAEMIA

When I was a medical student, pernicious anaemia was as fatal and mysterious as cancer. Great effort and thought went into attempts to understand its real nature. The bone marrow was profoundly disturbed and became megaloblastic. The blood got thinner and thinner and became macrocytic. All these were known as well as the association with achlorhydria or indeed gastric achylia. The latter was treated by oral hydrochloric acid and oral sepsis was considered to form toxins which in the absence of hydrochloric acid in the stomach poisoned the bone marrow. Arsenic (which we never hear of nowadays) was regarded as the sheet anchor of treatment. A haemolytic process often complicated defective red cell production and haemolysins were also suspected of playing a part. The same blood picture could occur sometimes in relation to pregnancy and though grave this type could recover. Then the whole situation was somewhat confused by the occasional striking occurrence of combined pictures of leukaemia and pernicious anaemia which led to serious discussion as to whether pernicious anaemia might not in fact be a megaloblastic tumour of the bone marrow. One observation stood out, though outside the experience of British physicians, that was the occurrence of a blood picture like pernicious anaemia in Finland where the habit of eating raw fish led to human infestation with *diphyllobothrium*, an intestinal worm, removal of which was accompanied by cure of the blood picture. Although this was an accepted part of the story it simply added to the mystery.

In the year I graduated in medicine, 1927, the B.M.A. meeting was held in Edinburgh, and one of the topics was pernicious anaemia. A paper was submitted by Minot and Murphy announcing the curative effect of half a pound of liver a day. Dr. George Graham, who was then secretary to the Section of Medicine, tells me there were doubts as to whether this paper ought to be read. I remember well the incredulity with which liver treatment was received. Most speakers at the meeting considered it impossible that a dietetic measure of this sort could be effective in such a grave and universally fatal disorder. Within a few months, however, the curative effect of liver was being overwhelmingly proved, although many of the conservative physicians of the day still preferred to give arsenic as well! Precisely what it was in liver that effected the cure remained uncertain and pharmaceutical manufacturers vied with one another in producing better and more effective liver extracts because there always remained a small residue (about

one case in seven) where even liver did not seem to have the desired effect. It took a long time before the inter-related parts played by folic acid and vitamin B<sub>12</sub> were clearly defined and now at long last all the mysterious and perplexing exceptions causing the so-called refractory anaemias seem to be explicable. Folic acid which acts together with B<sub>12</sub> is deficient in both sprue and pregnancy anaemia. Vitamin B<sub>12</sub> is not absorbed in pernicious anaemia and the fish tapeworm uses up any B<sub>12</sub> that may be present in the gut leaving little over for the infested subject. In the mysterious combination of leukaemia and pernicious anaemia proliferating leukaemic cells require large amounts of folic acid for their rapid growth and divert this important factor from red cell maturation. The various baffling observations of earlier days now begin to fall into place. It was always known that the tropical megaloblastic anaemias were much more difficult to treat than those occurring in temperate zones. The African disorder of sickle cell trait in itself makes excessive demands on the bone marrow with the result that in certain parts of the tropics megaloblastic anaemia almost invariably develops in pregnancy. Excessive demands on red cell growth can often outstrip what would otherwise be a normal amount of available nutrient factors. It is perhaps worth recording one other recollection. Somewhere in the interplay of folic acid and B<sub>12</sub> in red cell maturation ascorbic acid is necessary. At the first clinical lecture I attended as a student in Edinburgh in 1924 we were shown a case of scurvy. The physician (Dr. H. L. Watson-Wemyss) told us how this old poverty-stricken bachelor was cured of his disease. He added, "One thing I do not understand was that this patient had a blood picture indistinguishable from pernicious anaemia and this has now got better". Here was one of those baffling observations unexplained at the time of which the good clinician as a field naturalist in disease so frequently becomes aware. The link of pernicious anaemia to nutritional factors was in fact before his very eyes though we cannot of course blame him for his inability to piece the picture together. Nature plays a game in which we are handed little bits of a jigsaw puzzle which we cannot complete until we see the neighbouring picture.

Sir Thomas Browne used the words "little entities still in their chaos". I suppose he meant those observations and awkward facts which do not seem to fit in to any system of knowledge and which may perhaps even appear to add to confusion.

#### SERUM JAUNDICE

I should like to add the story of serum jaundice. Following Ehrlich's introduction of organic arsenicals for the treatment of syphilis, intravenous injections were repeatedly used at weekly intervals over long periods of months in afflicted patients. Jaundice occurred frequently and became a recognised complication of these intravenous regimes. It was also known that some of them might die of acute liver necrosis but the aetiology remained obscure, most people being satisfied with the suggestion that it was a combination of syphilitic damage and arsenical toxicity. The jaundice usually got better and an observation made by Earle Moore that arsenotherapy could be continued in the jaundiced patient without impairing his chances of recovery seemed to rule out arsenic toxicity as an important factor. In the early days of the war, arsenotherapy jaundice was still continuing and following the production of liver damage by Himsworth and others in rats on

protein deficient diets, nutritional factors were suggested as additional possible contributory factors. In 1942 with Professor Dible and later Dr. Shelia Sherlock I became involved in the study of hepatitis by means of liver biopsy and it became quite apparent that the pathological picture of ordinary epidemic hepatitis and arsenotherapy jaundice were identical. One could say quite definitely that there was no histological evidence of syphilis and there was very little evidence of the characteristic features of experimental heavy metal poisoning (with which I was familiar in animal experiment) in those livers from patients who had been subjected to arsenotherapy.

In 1942 several score thousand American soldiers arrived in Northern Ireland and among those who had been inoculated against yellow fever before leaving the home base in the United States there occurred an epidemic of jaundice, several hundred patients with quite a few deaths. The occurrence of jaundice following yellow fever inoculation had already been recorded in this country by Findlay and MacCallum (89 cases of jaundice in 3,100 inoculated). In 1937 there had occurred an incident in which seven mentally defective children had been inoculated with convalescent measles serum for protection against this disease. After an interval of 78 to 83 days these children developed jaundice: three developed rapidly increasing signs of liver failure and died of acute liver necrosis (Propert, 1938). Two of the fatal cases belonged to one family and it was the father who asked for an enquiry which led to recognition of jaundice as a risk from the inoculation of convalescent measles serum. Meanwhile trials of pooled serum for transfusion and shock were recognised as icterogenic after a long incubation period of 2-3 months. The whole business was exceedingly baffling as the yellow fever experience had shown that as little as 0.1 cc. of human serum from a normal subject heated to 60° for one hour would still be capable of producing jaundice after this lengthy incubation period of 90 days. But the facts were there in abundance. At a meeting of the Venereal Diseases Society in 1943, Dible and I presented strong evidence for identity of arsenotherapy and serum jaundice. Minute amounts of serum from one icterogenic subject remaining in the barrel of a syringe would be enough to cause the epidemics. Major M. H. Salaman in the autumn of 1943 introduced in his venereal disease clinic a regime of a fresh autoclaved syringe for each injection and in the following year was able to report that this technique virtually abolished the occurrence of jaundice from arsenotherapy.

The relationship of contamination of syringes with human serum might have been appreciated earlier from the publications on epidemics of jaundice occurring in rheumatism clinics (intravenous gold preparations). An outbreak also occurred in a diabetic clinic from the use of a spring gun skin pricker for blood sampling (Graham, personal communication). I suppose the inhibiting influence was the reasonable view that human blood drawn from the circulation would be sterile. And we are indeed far from understanding why in certain apparently healthy individuals blood should contain an icterogenic agent. The donors seldom give a history of any previous attack of jaundice or other liver disease. Yellow fever vaccine was at first suspended in a minute amount of apparently normal human serum but when it became possible to suspend it in an aqueous solution (after 1943) no instances of jaundice followed its use provided always that the syringes were clear.



There is, however, nothing new under the sun. We may think that the matter of serum jaundice was cleared up in a decade between the mid 1930's and the mid 1940's, under the stimulus of the growing experience of serum jaundice and other forms of jaundice precipitated by wartime epidemics. If we have any pride left in our dilatory recognition of this condition it will be dispelled by the realisation that the experience was documented in 1886 by Hirsch. Here is his description (Handbook of Geographical and Historical Pathology, 1886, New Sydenham Society's translation, Volume 3, page 424).

In consequence of some cases of small pox among the shipyard workers of Bremen, revaccination had been ordered. "Between the 13th August and 1st September 1,289 persons were vaccinated by six doctors with *humanised* lymph in glycerine and of these 191 took jaundice in the course of a few weeks. Other doctors vaccinated 87 of the men away from the yard and of the latter none took jaundice. Among 500 other workmen who were vaccinated at the same time with a different lymph there was not a single case of it. It is remarkable that the incubation period or the time between the vaccination and the appearance of jaundice extended to several weeks."

Hirsch ascribed the jaundice to "bad lymph". But his observation was "out of time", and he could hardly be blamed for failing to recognize that it might have been the addition of *human* serum to calf lymph which was responsible. Pinpointing the culprit in this disorder was indeed not an easy exercise as it was hard to suspect human serum. While we assume the likelihood of a *virus* it would perhaps be safer to talk about a noxious *agent* and make no further mistakes. Precision in medicine is vital. Loosely phrased statements lead to errors.

#### TRAUMATIC ANURIA

Finally, I should like to take up the matter of traumatic anuria. During the bombing of London in the autumn of 1940 we received a number of casualties who had been partially buried or trapped by the limbs under fallen buildings. Often after passing some urine which was smoky or apparently bloodstained these patients became totally anuric. The illness ran a characteristic and intractable course terminating in fatal uraemia after about a week. Dr. Eric Bywaters undertook the task of documenting and investigating such patients. To the naked eye the kidneys, perhaps a little swollen, showed relatively little but on microscopic examination desquamation of tubular cells was noted giving the picture we now recognise as lower nephron nephrosis or acute tubular necrosis. The pigment passed in the urine was identified as myoglobin and the muscles in the compressed or crushed limbs were often pallid and depigmented. We compared the condition to the anuria which followed mismatched transfusion and studies were made to try to define what part was played by necrotic muscle products including myoglobin itself. Following the early reports our team was subjected to a barrage of criticism. Because we took daily blood samples for analysis and catheterised the patients to observe what urine was available, Professor Harris of Cambridge wrote scathingly about our efforts to define this crush syndrome, saying it should be called the "continuous interference syndrome". Professor John Ryle also raised objections at a meeting of the Association of Physicians in Oxford in 1941, saying that what these patients needed was kindness and less investigation! Professor Barnard, who held the Chair of Pathology at St. Thomas's Hospital, wrote to Professor Dible asking him to stop his clinical colleagues making further

publications on this matter as the lesion in the kidneys was completely non-specific and he had in fact seen it in septic abortion. He regarded it as a terminal manifestation in an otherwise fatal disease and of no special significance.

Looking back on this period, one has no regrets. We defined a syndrome which was not previously recognized, but for which effective treatment was subsequently evolved. Beginning with the artificial kidney put into successful action by Kolff, who presented us with one of his models which we began to use in 1949, other methods of control, particularly dietetic, were shown to be effective in the milder cases and after a year or two the artificial kidney came back into use for the more severe cases. Anuria and acute renal necrosis were shown to follow not only severe injuries but other surgical procedures such as unduly long application of tourniquets, gall bladder operations, mismatched transfusion, lesser degrees of renal cortical necrosis and (Professor Barnard was right) septic abortion. Many such patients can now be managed and indeed kept alive over periods of weeks by the application of the artificial kidney and they can be restored to full health. It is interesting to think also of the evolution of our ideas on the need for treatment. A few years ago we thought that one artificial kidney to a population of about ten million would be adequate, i.e. five for Great Britain. There must now be twenty or more such units up and down the country and they are all busy as far as I can learn.

As far as we could find there was very little previous documentation of this condition. A very brief description of it had been made among the buried victims of the Messina earthquake in 1911 and Minami, a Japanese working in Germany in 1920, had studied the kidney taken from soldiers who had been partially buried during the 1914-18 war. The clinical picture was not very clear but a German pathologist had put these kidneys aside for later study. The pathology was as we found it later but no clear recognition of the clinical syndrome was extant until the paper by Beall and Bywaters.

Wilfred Trotter truly said, "There is no more potent antigen known to science than a new idea". Some of the elders of our profession were certainly unsympathetic when we began our descriptive biochemical and pathological studies. We do not know the mechanism of renal shutdown in these patients and there is in fact a vast field of investigative endeavour which must still be pursued, but at least we can feel thankful that much saving of life has stemmed from these early endeavours. I suppose the development of anuria was simply regarded as an ante mortem sign of grave prognostic significance and patients were regarded as moribund. Certainly these patients that we saw in the early days of the blitz could have been saved by our modern techniques. Their blood pressures were often well sustained and they were acutely conscious of the trouble which was developing. It was their very distressing fears and anxieties during the fateful week before death which spurred us to further efforts at comprehension and we should certainly have failed in our duty had we not made the studies which we did.

If young men are making new observations, and particularly if they are using new methods, you can be sure they will be greeted by benign incredulity. They will be criticised for doing something unnecessary and which their predecessors had always been able to get along without, and even weighty authority may come

in to try to put a stop to whatever is being done. No committee can ever understand fully their motives and they will have to rely on no-one but themselves to carry through the new ideas. We may perhaps regard this pattern as a rather sad fact of medical history but there is of course another side to it. It can in fact be dangerous to be unorthodox and our profession rightly applies brakes and so long as the brake is activated by critical thought and scholarship no-one can complain. It is up to the innovator to produce acceptable proof of his ideas.

I have probably said enough about observations out of time. When I was thinking of a title for this talk, which was vaguely germinating in my head, I thought of the title "The Research Spiral". By this I mean that research does not proceed in a straight line of logical steps but rather biological observations are made at first almost at random and perhaps by chance. Even the most perceptive intellect may fail to grasp the full significance of what is before his eyes. When Sir Thomas Lewis heard about myocardial infarction in 1925 he said it must be rare in England. The following year he had one himself. Karl Pearson strongly opposed Mendel's principles, which only gained final acceptance in Britain in the mid 1920's. The approach to each new step in the build-up of knowledge is often made by a somewhat long and circuitous route, often involving other sciences and new technologies, but it finally arrives again at a point where the earlier observations seem to fall into line but we are then one loop higher in the spiral.

I have tried to illustrate my theme from history and also from personal experience. So far as the latter is concerned, I have been endlessly humiliated during my professional life by the thought of my own early and continuing ignorance. Each day, particularly as I attend the post mortem room, my humiliation is renewed as I realise that full comprehension of even the most commonplace disease processes is still beyond our grasp. We look and we say "How very interesting" and come away puzzled. I have no doubt that many of the answers are in fact before our eyes if we could only understand them and we may be as blind as we were over the matter of arsenotherapy jaundice. After all, we are still the same people and advancing years may add to our experience but they do not make us any more quick-witted. But at least we begin to understand what Hippocrates meant when he said:

The Art is long

Life is short

Judgement difficult and the occasion fleeting.

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# FORTY YEARS IN CARDIOLOGY

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ELECTION to this lectureship has brought me an honour which I rank highly, in that I am aware of the acknowledged distinction of my predecessors and which laid claim to their appointment to this office. The invitation has also placed upon my shoulders a heavy responsibility, namely to discharge my duty as creditably as they did, and has planted in me a fear lest I fail to do so. I mean, however, to deal faithfully with my subject, attempting to presage what I believe is to be, in the light of what has already been, and within the limits of my own experience.

To engage in reminiscence is the prerogative of elders. To recite tales is their just entitlement, for they have tales to tell. This exercise, often wrongly regarded as an expression of garrulity is the cult and very spice of a mature life, for as it recounts the feats of yesterday it places them unashamedly on show to compare them with the claims of our today, and match them with the triumphs that may garland our tomorrow.

Cardiology seeped into my blood 40 years ago when I sat at the feet of Sir John Parkinson in the Cardiac Department of the London Hospital, which was the first institute of its kind anywhere to direct its activities exclusively to the study of heart disease. The department had been founded by Parkinson's predecessor, Sir James Mackenzie. To be trained in the right stable gives any horse his best chance in the race he is to run, and I was awarded this good fortune as I graduated in turn to become Parkinson's house physician, registrar, and colleague. Standing at each of these stations I beheld changes in the practice of cardiology which I now mean to recount.

## FRESH NOMENCLATURE

With the march of time it is inevitable that inside any progressive faculty there should be a change of terminology, especially when progress has been profound and swift as in cardiology. In order to understand one another's thoughts we must understand one another's speech. Our conversation needs to be carried out in the same language. Ambiguity in terminology frustrates a true understanding of the subject it purports to portray, and it should not be condoned by any calling which professes to be scientific in its outlook. In my time, many terms have been discarded; most of them deserved this expulsion, but some of them did not, and these have been replaced by less desirous ones. There is need for more weeding, and indeed for more planting, but any change must remain faithful to the principle that the newer version should convey a correct physiological and pathological interpretation. Terms born of conjecture and whims cannot and should not be allowed to survive, for in time they are self-effacing. Before discarding an old term, or accepting a new one, however, there should be good reason for the exercise. Thus, a fashion in terminology should not change just because it is fashionable to change. Certainly, terms should not be cast onside because they are old, for all that is new is not necessarily virtuous. Neither is it virtuous to

supplant a term which has become standard, for another having the same meaning; it is mischievous or worse to supplant it for one having a different meaning.

Terms like *myocardial degeneration*, *athlete's heart*, *tired or strained heart*, *effort syndrome*, *V.D.H.* and *D.A.H.*, which through offering a sham clinical diagnosis, cloaked our incompetence and preserved our ego in earlier years; these vestments have now been shed and rightly cast Lethewards. To change *auricle* into atrium and *auricular* into atrial, has appeared to have bestowed on the cardiologist a certain aplomb; it has even appeared to segregate those within the specialty into the modernists and the archaic, but let no one be deceived by this demonstration of unimpressive conquest. The need to discard *atrial flutter* for atrial tachycardia is real, for that is what it is. Dysrhythmia is a more apposite term than *arrhythmia*. *Extrasystoles* is an endearing term and need not be dislodged provided we regard the prefix "extra" as meaning "external" rather than "additional". If the word were to go out, premature beat would be the best substitute. Certainly, it should not be *ectopic* which should stay in its real home, the gynaecological department.

In the field of auscultation some old terms need changing, and some newer ones need to be expunged before they take hold. With the eclipse of the equestrian era, when the young physician of today is more familiar with the rhythm of his car's engine in the separate gears than with the trotting of a horse, it ill-becomes him to describe the cadence produced by three heart sounds in successive cardiac cycles as *gallop* or *canter rhythm*; rather should he call it triple heart rhythm, and name the added sound which has created it. The murmur of mitral stenosis precedes ventricular, but not atrial contraction, so that we are in error when we name it *presystolic*, and the appellation atrial systolic murmur should take its place. The murmur in early systole may have a sharp quality on occasion, but what makes this sound distinctive is not so much its character, but its place in the cardiac cycle, so that to name it a *click* is both unhelpful and inaccurate. Further recent examples of undesirable terminology are supplied by the prefix *ejection* in the case of some systolic murmurs, and *regurgitant* misapplied to the systolic murmur of ventricular septal defect. Again, why should we opt for complicated expressions when simple ones prove adequately descriptive, and give to the conus (of the right ventricle) the cumbersome name of *pulmonary outflow tract*, or *hypertrophic obstructive cardiomyopathy* in lieu of sub-aortic stenosis? Incidentally myocardial pathology is preferred to *cardiomyopathy*. In that a stenotic valve is an incompetent valve, it is right to substitute aortic and mitral regurgitation for *aortic* and *mitral incompetence*.

Under this heading of fresh nomenclature should be mentioned the pernicious habit of grading from 1 to 6 or more according to their intensity or extent, everything from heart sounds and murmurs to prostatic enlargement and baldness. Surely it is precisely for this purpose that words like slight, moderate, considerable and prominent, were introduced into our vocabulary. In any case the grades themselves have to be defined initially in such terms.

When I plead for uniformity in *bedside terminology* in which to convey a diagnosis to a patient in words that will soothe and not alarm him, I am reminded of one who visited me, greatly disturbed after his discharge from hospital. Seeking an explanation of his illness he said that his family doctor had called it "throm-

bosis", the house physician alluded to it as "a coronary", the registrar said, "a blocked heart vessel", the consultant said "infarction", a patient in the ward said "part of your heart is dead and finished with", and sister quite wisely had said "it is better not to ask". With considerable feeling he uttered, "I am muddled doctor, and I cannot sleep". Is it not better in these cases, which are common, to say when they are visited by the illness, "You have a heart attack that is passing", and later when he has successfully emerged from it, "You had a heart attack which has passed"?

#### HELP FROM RADIOLOGY

When I joined Parkinson in the Cardiac Department I found him restless in his anxiety to know more about the size and shape of the heart in the different forms of heart disease, and the condition of the lungs when heart failure had set in, or was threatening. He had grown impatient of the traditional claim that percussion could delineate the heart's limits. He called percussion a dying method packed with fallacies and imperfections with the token of sterility upon it. Percussion he said had added nothing to cardiology during the past century, and I have been wont to say—neither will it during the next. Inert bones were being X-rayed and ulcers in the stomach were being sought by the same means, but no one in this country heeded the call of the heart for this device to come to its aid, that is, no one except Parkinson. In extolling the virtue of this method of investigation he pointed out that no organ was so well placed for X-ray inspection as the heart, for it was surrounded by translucent lung, and rotation of the patient enabled it to be looked at from all angles. He was already examining patients in this way in his consulting room at home, and he was soon to persuade Lord Knutsford, then Chairman of the Hospital, to provide an X-ray plant for the Cardiac Department and so enable us, as Parkinson put it, to perform as it were a biopsy of the heart. What exciting days they were as we stood behind Parkinson, perched on a high stool when screening his patients, and describing appearances which were familiar to him, and enthusing over a sign not hitherto known. He prepared three diagrams to depict the radiological anatomy of the heart and great vessels so that others might identify the structures as readily as he did; these stand monument to his pioneer work in this field. We had no help from technicians during those early days and we processed our own films to stand as a permanent record of a new finding. Praise for a pretty picture was not expected, but the end-product which usually showed a barium-filled oesophagus portraying the posterior boundary of the cardiovascular shadow in the separate diseased states, was our high reward; through 40 years I have seldom seen them excelled. Successively, we observed the effects on the heart of innocent states like scoliosis, depression of the sternum and bradycardia, learnt the meaning of trespass by certain cardiovascular structures on the lucid areas of the aortic triangle and aortic window, recognised the "ham-shaped heart of goitre", and the "hilar dance" associated with atrial septal defect, as well as the several patterns designed by the separate diseases that affected the heart.

I have taken some time to describe these early exercises in cardioscopy or X-ray screening of the heart, to remind the cardiologist of to-day how barren were the prospects of accurate diagnosis in this field before the advent of this

aid, and to warn them against relinquishing a practice which has proved of inestimable worth through the years. The warning is necessary, for there are signs that screening is being abandoned for films. Films are no substitute for screening. Should the cardiologist lay aside this tool, he forfeits advantages which still-pictures can never provide. These include, the pulsation from a recently formed localised cardiac aneurysm apparent only during systole, the characteristic pulsation seen in mitral regurgitation, the relatively quiet areas in salient cardiac infarction, pulsation of the pulmonary arteries in left-to-right cardiac shunts which supply an estimate of their degree, the progress of a barium-swallow delineating the posterior limits of the cardiovascular shadow, and the height and movement of the diaphragm during the two phases of respiration as well as the effect of such excursion on the position of the heart. Not the least advantage of screening resides with the instruction and training of those who stand to view the changing scene during rotation of the patient, and listen to the remarks of the examiner, either in the examination room or sitting opposite an image intensifier in an adjoining room.

#### THE INCOMPARABLE ELECTROCARDIOGRAM

To operate the Cambridge String Electrocardiograph, one of the first of its kind and acquired for the Cardiac Department by Mackenzie, was a feat in itself. A powerful arc lamp generated unwanted heat and inefficient light, which was enough to fog the plate, but not enough to trace the moving fibre. When optimum favourable photographic conditions prevailed the fibre might snap, and the patient alone remained unfrustrated, and with three limbs immersed in suitably warmed saline solution, he gazed in wonder at this mammoth machine at work. We only recorded three limb leads, and what happy days they were! The fourth standard limb lead IIIR had not then been introduced.

When I was house physician to Parkinson, Evan Bedford had joined him as his registrar, and I shared with them the thrill of discussing the abnormal tracing that told of cardiac infarction situated either in the front or the back of the heart. Soon the apical chest lead was added to the limb leads, and later the posterior axillary lead CR<sub>7</sub> was introduced.

Seventy years of electrocardiography have not seen universal agreement on which leads to record routinely in the investigation of heart disease. Final decision should emerge from a clinico-pathological assay and not from an opinion conjured up in the laboratory, in that the latter, although basing its views correctly on electrophysical laws, discounts the variations inseparable from the complex structure of a viable organ suspended in a variety of positions in relation to its thoracic cage of variable shape.

The addition of the so-called unipolar limb leads VR, VL and VF have contributed no single advantage, and they possess no virtue which justifies their continued inclusion in routine electrocardiography. The contorted lead VR has mystified many and mesmerised some, causing them to believe that it represents some new concept in electrocardiography to be adopted out of hand; instead it should be known for what it is, namely lead I turned upside down most times. Moreover, the so-called unipolar chest or V leads, emphasising as they do the negativity of the electrical potential with diminished wave-amplitude, are inferior to the bipolar CR leads. Thus, the tracing CR<sub>7</sub> in the left posterior axillary line,

so valuable in the detection of small lesions in the lateral wall of the left ventricle, and in the diagnosis of early left ventricular hypertrophy, is vastly superior to the  $V_7$  tracing.

Economy needs to be applied to the number of chest leads now customarily applied. Three stations only are needed, namely 1, 4 and 7. No abnormality ever appears in stations 2 or 3 which is absent in 1 or 4, nor in 5 or 6 which is not apparent in 4 or 7. Thus the 7 leads essential to the electrocardiographic investigation of cardiovascular disease consist of the four limb leads, I, II, III and IIIR, and the three chest lead  $CR_1$ ,  $CR_4$  and  $CR_7$ ; should the R wave be absent or diminutive in  $CR_1$ , lead  $CR_2$  should be added.

Some 40 years have also passed since Sir Thomas Lewis, having satisfied himself with the analysis of the dysrhythmias, said of the electrocardiogram that the cream was off, and he turned away to study ischaemia of the limbs. What remained, has not been skimmed milk, and I have found the electrocardiographic foray in search of islets of myocardial injury to be tremendously exciting and rewarding. Although a study of the tracing has been most informative in cases of constrictive pericarditis, Friedreich disease, amyotonia atrophica, and in some other myocardiopathies, especially the alcoholic variety, I have derived greatest satisfaction from uncovering the lesser faults in the tracing which have pin-pointed the limited kind of cardiac infarction. The reward here has been the secure diagnosis of cardiac pain, and the rescue from unwarranted invalidism of countless patients with cardiac-like pain; a more glittering prize than this can come to no one.

Among the many instruments now in our hands for the readier detection of heart disease, the electrocardiograph has no peer, and we should bend ourselves attentively to interpret aright the language that it speaks.

#### PHONOCARDIOGRAPHY

When I first became curious about the nature of heart sounds additional to the first and second, I looked around for means of recording them. A standard machine was nowhere available, so a make-shift was assembled on the laboratory bench and the noises from the heart were fed into a carbon microphone. This primitive instrument made it possible to identify four kinds of triple rhythm, namely the separately audible atrial sound, the sound in late systole, the snap sound in diastole, and the third heart sound. When this work was concluded, the separate murmurs came under review.

In Mackenzie's old room there had lain two brown-paper parcels and these I had myself carried into the new department, and deposited them tidily under a laboratory bench. It was after concluding the investigation on triple heart rhythm that I eventually became inquisitive about the actual contents of the parcels, and you may imagine my chagrin when I discovered that they harboured the material parts of a phonocardiograph which Mackenzie had acquired 19 years before, but which he had never unpacked. The lesson to which this experience points is that when entering to work in a new post, the first step to take is to become familiar with the equipment and facilities which it offers, and if the lesson were extended, to know the old before proclaiming it anew as if it were new.

At that time, when my experience with phonocardiography had impressed me with its great value in clinical cardiology, it caused surprise that Sir Thomas



Lewis, after recording the murmur of patent ductus arteriosus, had abandoned its pursuance in the case of other auscultatory signs, and in this way to have failed to appreciate the benefit which the science could bestow on cardiology. Indeed, phonocardiography should find a prominent place in the training of every young aspirant in cardiology, for through its agency he will acquire auscultatory discipline, because during his apprenticeship he will test his clinical impression of a sound or murmur through reference to their recording. When Aubrey Leatham joined us in the Cardiac Department he introduced modern equipment to record the high frequency murmurs. He described the characteristic pattern and place of the murmur of aortic stenosis, and later, the significance of the sound in early systole.

It has been a wise observation that the art of auscultation is to listen, not to hear. Such listening should be attentive, freed from any preconceived ideas as to what might be heard, and in company with systematised self-catechism during each consecutive phase of the cardiac cycle. There came to the Cardiac Department one day, that erudite clinician from Boston, Samuel Levine. He was invited to listen to the heart of a patient with suspected mitral stenosis; presently he raised his head to discourse on the quality of the first heart sound. When asked if he had heard a mid-diastolic murmur, he answered rather tersely, "I haven't listened to diastole yet". He also adopts self-catechism as he listens to the successive phases of the cardiac cycle.

#### THE ESSEX SCHEME

More than 30 years ago there came to see me a man of 64 years with an innocent heart murmur, one that had been regarded erroneously as mitral incompetence. He unfolded a story pregnant with pathos, and recounted how he was denied healthy playtime in school, prevented from taking part in games, refused admission for military service, dismissed from tram-driving following a routine medical examination, and rejected for life insurance. As his account drew to its close he added sadly, "Of course, I have always been careful not to keep a big wardrobe". The anguish of that despoiled life, perpetrated through a wrong diagnosis in childhood, made a great impression on me, and when I met with other instances of life-long unwarranted invalidism I resolved to contribute towards preventing it.

The most sure net to trap children that show signs which incriminate the heart is the routine school medical examination, and the Essex Scheme was devised in order to assess accurately at an early age any blemish that might have been apportioned to the heart, so as to prevent the drift of such cases into adulthood with an uncertain knowledge as to what might be wrong.

The scheme operates in three phases. *First*, the School Medical Officer, discovering an abnormality connected with the pulse or the heart during his periodical examination, notifies the County Medical Officer of Health as to his finding, whether a dysrhythmia, displaced apex beat, unusual cardiac pulsation, added heart sound or murmur, or a history of having contracted rheumatic fever in the past. *Secondly*, the child's name and home address are forwarded to a suitably equipped department of cardiology at the Regional Hospital, where the child attends in due course to be specially examined by a cardiologist. The *third* phase

consists of informing three authorities of the diagnosis, whether the signs have been of an innocent character, or arising from congenital or acquired disease. The authorities are the County Medical Officer of Health, the School Medical Officer who informs the Schoolteacher in turn, and the Family Doctor. Naturally, the parents are also informed. The scheme which is simple in its design and inexpensive in its execution, provides a social service of inestimable worth, and its adoption by all County and Borough Councils is long overdue.

#### THE BLOOD PRESSURE DILEMMA

Through most of my forty years, the blood pressure problem has worried me. In earlier years the definition applied to a normal systolic blood pressure, namely 100 plus the subject's age, did not impress me as having the stamp of truth upon it, and later when it was modified to one-third the age plus 111, I became convinced that these were mischievous attempts, based on theory, probability and conjecture, and had no scientific or clinical foundation. Since our conception of the normal springs from such flimsy premises, it follows that a blood pressure value named as meaning systemic hypertension, is equally unreliable.

It appeared to me that a more rational approach to the problem of a raised blood pressure was to establish securely the recognition of systemic hypertension on grounds other than from a consideration of the blood pressure value by itself, a view supported by the knowledge that Nature seldom produces disease exhibiting a single physical sign. I, therefore, assembled for observation over a period of 10 years, four groups of cases, 50 healthy army recruits whose mean blood pressure was 145/85 and mean age was 23 years, 50 healthy army recruits whose individual diastolic blood pressure was 100 or over or systolic pressure 180 or over, and with a mean blood pressure of 160/100, and mean age of 25 years, 50 cases whose mean blood pressure was 220/120 and mean age 61 years, with no other physical sign and with a normal electrocardiogram, and 50 patients whose mean blood pressure was 215/125 and mean age 63 years, with signs of cardiovascular derangement and left ventricular preponderance in the electrocardiogram.

From this investigation it was possible to deduce that, renal, endocrine, and coarctation hypertension apart, subjects with a raised blood pressure of the order of 220/110 or over are in two classes, the one innocent which I have named *hypertonia*, and the other, *systemic hypertension* which is manifestly injurious; the former with the passage of time does not pass into the latter state. Until this differential classification is followed, and with the electrocardiogram as the final arbiter in the diagnosis, so long will unwarranted invalidism be imposed upon the many.

Precisely the same problem has arisen of late in the case of a raised pressure within the pulmonary circulation, and here too the absence or presence of right heart preponderance in the electrocardiogram should be allowed to decide the diagnosis of either the more innocent state of pulmonary hypertonia or the progressive state of pulmonary hypertension, and without recourse to the recording of manometric intra-arterial readings.

In regard to the treatment of systemic hypertension, I have witnessed over 60 medicines introduced for the purpose of subduing the blood pressure, so that I claim entitlement to speak about them. Each entrant on the therapeutic stage

has been hailed with enthusiasm, lauded for a time for its performance, and thereafter withdrawn to be eclipsed by the high praise accorded to its successor. It is a sad reflection that a profession like ours, professing to be scientific in its actions and outlook, should tolerate this dismal parade and overcrowded traffic in proprietary medicines of doubtful therapeutic value, introduced with dubious propriety, and too often possessing undoubted toxicity.

Of course the application of auto-immunisation and homotransplantation of the kidney to hypertensive heart disease, has opened up a prospect which greatly excites me. One day it may become routine procedure, but not yet awhile. In the meantime we should prepare for its coming through a more critical differentiation of the separate forms of an elevated blood pressure.

#### CORONARY ARTERIAL DISEASE

To condense the events of 40 years into an hour's recital is not an easy task especially when such a survey includes reflections on a topic as expansive as coronary arterial disease. The difficulty is not the want of something to say, but to know what to leave unsaid to gain time to say something about other things. I have been as it were with coronary arterial disease from its beginning for as already mentioned I was house physician to Parkinson when he and Bedford assembled 100 cases with cardiac infarction in 1927, and which they described in their monumented paper.

Whenever I am asked why coronary disease should be commoner now than hitherto, I still doubt the inference which the question carries, because two things leap to my mind. First, the *incidence* of advanced coronary atherosclerosis among the population, as shown in routine necropsies at my Hospital, declined rather than increased, during the 40 years, 1910 to 1950. Secondly, Parkinson and Bedford collected their 100 patients with cardiac infarction within a short period and at a time when the clinical diagnosis of the condition was almost never attempted. Moreover, they reported on a further 83 cases examined within 4 years at necropsy.

In this section of cardiology more than in any other I am disturbed by the *terminology* in common usage. The term cardiac infarction has rightly displaced coronary thrombosis, but I greatly deprecate the custom of allocating patients with cardiac pain into three classes, those with angina pectoris, those with so-called acute coronary insufficiency, and those with cardiac infarction. We are told that coronary insufficiency is more serious than angina, but less serious than cardiac infarction. No, not three are these, but one. Such a classification lacks substance, and frustrates a true understanding of the condition in its entirety.

During the first 20 years covered by this survey, we concerned ourselves mostly with the diagnosis of coronary arterial disease, and although my personal interest has not waned in this quest realising that more things need to be uncovered, investigators, especially during the past 15 years, have turned away from it, prematurely in my view, and now pursue intensive and expansive research into the *cause* of coronary atherosclerosis. May I say here that epidemiologists have made known some odd beliefs in this field, and although these have not impressed those who reside at the heart of the problem, namely those who daily manage patients with coronary arterial disease, their pronouncements have been accepted,

and too often acclaimed, in certain quarters as if they were valid and proven, providing a basis for rational treatment. Among these dictates have been that coronary atherosclerosis and its sequelae are commoner in bus drivers than in bus conductors, in sedentary workers than in labourers, among general practitioners than consulting physicians, in those with high blood lipids and who eat dairy rather than vegetable fats, in the obese than the lean, in those who consume much sugar, in those denied breast-feeding during infancy, in those who drink soft than hard water, and in those who smoke cigarettes than those who burn tobacco in a pipe. Need I say more about these unstable predictions propounded so irresponsibly, if not mischievously, by statisticians? It is unlikely that half a century of transgressions on the part of some, matched against restrictions and abstinence on the part of others, will supply the answer to a problem so difficult to plumb, and yet so worthwhile the effort to plumb it.

In the recognition of either cardiac pain or of symptomless cardiac infarction, the *electrocardiogram* has no peer, and clinical examination, laboratory estimation of transaminase or like serum constituents are no match for it. Experience with electrocardiography in coronary arterial disease enables me to make one outstanding observation, which might gain greater emphasis if I presented it in three parts. First, the tracing can presage the onset of cardiac pain by many years. So far it has only been possible to test an interval of 13 years, but it is likely that this period will be extended to 20 years or more. Secondly, it follows from the first truth that in a patient with pain from cardiac infarction, the tracing is abnormal at the very start of the illness. Thirdly, and which is again a corollary of the first dictum, should the electrocardiogram prove to be strictly normal in a patient with chest pain, the source of the pain is not in the heart. This in turn demands a close acquaintance with all the lesser changes in the tracing which tell of cardiac infarction limited at the time to a small area.

Naturally, the *treatment* of coronary arterial disease has not stood still over the 40 years, but the change has taken the form of adjustment rather than advancement, and I mean only to allude briefly to certain trends in therapy. Management of the major episode of coronary occlusion is now under critical review, and occasioned by the formation of intensive care units in hospitals. Decision on whether to treat patients in hospital or their homes is likely to be determined by the dearth of hospital beds. As a rough guide it may be said that in any who show a disturbing dysrhythmia it might be advantageous to gain the service of continuous electrocardiographic monitoring, and provision for artificial pace-making or special resuscitation measures in case of cardiac standstill or the outbreak of a malignant form of dysrhythmia. If on the other hand the patient is in profound shock, to remain undisturbed in the quiet seclusion of his home might be the best course to adopt. In this situation let no-one decry morphine as the premier drug, for to do so would be to deny the one sterling remedy which will bring calm to a patient restless from an unbearable pain. There is no chance of this princely remedy leaving the treatment-tray which stands in the sick-room of a patient visited by cardiac infarction, for a whimsical change in therapeutic fashion will not dislodge a medicine which has no equal in the relief of pain, a need which in the case of cardiac infarction will ever be a first consideration.

The duration of the resting period which has to follow a major coronary

occlusion has been rightly shortened from the one of six weeks initially prescribed and religiously imposed, nor does the regime any longer entail the use of the bed-pan. After a suitable period of convalescence, most now agree to early rehabilitation and a return to customary work, with encouragement and reassurance as necessary refreshment on the journey back to regained health.

I predict that anti-lipid and other fanciful diets, which now place an unnecessary burden on the housewife, and cause disarray in the household, will soon pass Lethe-wards.

Good wine needs no bush, and there is one medicine, namely *digitalis*, whose efficiency in the treatment of heart failure from cardiac infarction or from any other kind of heart disease, has not been in doubt during the 40 years, nor the preceeding 40 years, nor should it surrender its place to shock therapy in the management of atrial fibrillation.

The so-called long-acting nitrites are still being prescribed, although the only thing seen to be long-acting is the gullibility of doctors, and the only indication for their use, that one should have shares in the particular drug house which produces them.

I understand that anticoagulants are going out of fashion in the treatment of cardiac infarction; someone tried to prevent them ever coming in.

How disappointing it is to find patients continuing to be inadequately instructed on the use of the king-remedy for the relief and prevention of cardiac pain, namely glyceryl trinitrate. Patients still dissolve the tablets under the tongue instead of chewing or crunching them. They still take them sparingly and in fear of a sensation in the head, which was never explained to them at the start as an innocent effect of the tablets, tablets whose safety is such that they could be taken in handfuls. Moreover, they remain unacquainted with the benefit which they would gain through taking a tablet just before undergoing any exercise which customarily brings on the pain, and so prevent it setting in.

#### THE ROAD AHEAD

Looking back over 40 years in the specialty of cardiology has been a satisfying exercise, and it has given license to prospect the road ahead. The accomplishments of those years have been considerable, some of them exciting like the giving of penicillin to subdue the infection in streptococcal endocarditis, the surgical repair of so many deformed hearts, and the closer view of cardiac behaviour in the separate diseased states through cardiac catheterisation. Will the Dixon Memorial Lecturer for the year 2005, speaking to the same title, have the same arresting tale to tell? Perhaps the cardiac surgeon will see to that. For the physician at any rate the old challenge remains, namely to discover the cause and treatment of coronary arterial disease and of systemic hypertension and the prevention of rheumatic heart disease. He possesses advantages not available to his predecessors both in regard to equipment and opportunities, and we marvel at their interpretation of the dysrhythmias before the advent of the electrocardiograph, and the heart murmurs before the phonocardiograph, while we remember that James Mackenzie was accoucher as well as cardiologist to the young woman who died at childbirth from auricular fibrillation which he attributed not inappropriately to paralysis of the auricles.

### *The Inroad of Surgery*

The young have a thirst for surgery; conservatism is born of age and is nurtured during the years of accumulated experience. In a small room at the London Hospital some 30 years ago I sat with Tudor Edwards our thoracic surgeon, who 8 years before had performed his first successful lobectomy for bronchiectasis, urging him to operate on cases of coarctation of the aorta which we had begun to recognise was not a rare condition. I invited him to anastomose the left subclavian artery to the aortic ampulla distal to the constriction, but this project was laid aside when Craaford in Sweden showed that resection of the aortic deformity could be effected. As I grew older and along with my patients, I have been known to teach my students in regard to this condition that Nature is the best surgeon to deal with it, and I continue to hold that view. Nonetheless, in other cardiac states the surgeon has wrought marvellous things since Souttar at my hospital in 1925 inserted his finger in the left atrium to stretch a tightened mitral valve in a girl aged 15 years. The surgeon's achievements have been considerable, often spectacular, but this early flush of success should not lead to rash flashes of adventure. He might now pause to reflect on what he has already attained, and improve the procedures which he has meantime adopted as routine. John Hunter once said, "don't think, try", but to those contemplating heroic repairs of faulty heart valves when the ventricles, especially the left, are stiff from hypertrophy, the warning should go out, "don't try, think", for to hazard a guess in surgery is hazardous surgery.

The close partnership now cemented between cardiologist and cardiac surgeon has been a great gain in the management of a patient undergoing cardiac surgery, and the future must ensure that no crack of discordancy ever shows in this newly found unity. A failure to integrate the duties of these two leaders of a cardiological team is not contemplated, for every patient submitted to the risk of heart surgery has a claim to this united care of him.

### *Prospection*

To have stood witness to so many changes, gives brief to inquire if all is well within the specialty, and if not, to disclose the faults and invite the attention of others to the need, if there be one, of setting aright what is wrong.

The first need is for greater precision in the diagnosis of the two common clinical states of coronary arterial disease and hypertension, acknowledging the contribution which the electrocardiogram can make in the recognition of each. In that both states are so common and our diagnosis of them so imprecise, it follows that the unwarranted invalidism imposed during their management is rampant, especially when there has been added in their treatment unneeded drugs which produce symptoms of their own. Precision has been attained in the diagnosis of congenital heart disease, why not the same exactitude also in these two more noteworthy conditions?

In family and hospital practice, conducted respectively by the family doctor and the consultant, the doctor-patient relationship has suffered for more than a decade on account of insufficient time devoted to the consultation. The motor-mechanic names the time he will take over a repair, and the watch-maker stipulates the period it takes to mend a time-piece. To ordain, as is considered proper in

some places, that a cardiological examination, which includes at least electrocardiography and cardioscopy as essential tests, and which necessitates a subsequent talk with the patient, as well as an interview with the spouse, should be conducted during a time prescribed by an appointment system, and to organise the procedure into a sort of conveyor-belt exercise, is a foolish dream and must not be allowed to fructify. Ample time to examine and treat the patient is the real essence of good medicine, and my younger colleagues in the specialty should guard this privilege as if it were their heritage, as indeed it is.

Another question which needs to be placed, is whether in the investigation of known or suspected heart disease, a patient is submitted too often to too many tests, many of them of dubious value to the examiner who conducts them, and of undoubted discomfort to a patient undergoing them. It should not be concealed any longer that the matter causes concern in certain places. When part of a research project, such investigation should be fundamental and never experimental. Parkinson said once that there comes a time when curiosity becomes a sin. To determine *why* such and such a thing takes place is often commendable curiosity; to ascertain *how* it takes place is too often condemnable inquisitiveness. This truth appears in holy writ for in *Ecclesiasticus* we read: "Be not curious in unnecessary matters, for more things are shewed unto thee than men understand".

Lastly, a word for the ear of the research worker in the field of cardiology. The need of him is great, for there is great work for him to do, and the challenge offered by coronary arterial disease and hypertension, is at his door, as well as many another. He should start out with definite aims, and his exertions should always be directed specifically to the advancement of knowledge concerned with either the cause, the readier recognition, or the treatment, of cardiovascular disease; nothing else should distract his attention. In his quest he should on no account spurn the clinical, but he must keep close company with the physical signs exhibited by his patient in the hospital ward, and the pathological findings shown at a necropsy. He should not flirt exclusively among the crucibles and test tubes in the laboratory, nor rely unduly on statistics compiled in a counting house as if they were holy script, for at their best they only indicate a trend, and at their worst they are as fallible as pre-election gallup polls. On the same premises, the claims made on behalf of untried remedies he should oppose and counter with determination, for the might of powerful salesmanship is threatening to outwit scientific therapeutics.

He should court hunches especially drawn from previous factual experience, but he must not announce them prematurely as if they had been proven. He must never wear the cloak of a seer or prophet, and he must be loathe to predict, but equally he must be pugnacious on behalf of a finding which he has shown to be true.

He must readily concede to error as did that great research worker, Sir Thomas Lewis, over the cardiographic patterns of bundle branch block.

He should be insensitive to criticism, but welcome such arrows as are aimed at him by outside judges, for they will test his armour; should this prove impervious to their stings, he will know that he wears the impenetrable breast-plate of truth.

He should persevere in the face of disappointment; patience should be his chief virtue, and he must not construe lack of praise as evidence of failure, remembering that Harvey in his time was regarded as a charlatan, and that medical journals once refused to publish papers from the pen of James Mackenzie.

The journey of the research worker is often a companionless one. His voice raised on behalf of anything that is new is perforce a lone one. It usually provokes opposition and often derisive accusation of unorthodoxy from the many, support from the few, and unreserved acclaim from none, but he should know that uncovered truth cannot be silenced for ever, and draw his comfort from that. Mackenzie once said that the history of medical discovery was in three phases. When it is first announced, people will say it is not true. Later, when its truth can no longer be denied, they will say it is unimportant. Ultimately, when its importance has been established, they will say that anyhow it is not new.

The research worker digs for truth not for gold. He seeks neither profit, promotion nor self-aggrandisement, and earns no reward save the satisfaction of having uncovered something to aid his ailing fellow-man, and what greater reward than this can anyone earn? None.

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## BOOK REVIEWS

THE NATURE OF CANCER. By P. M. Sutton, B.Sc., M.B., B.S., M.C. Path. (Pp. 159, figs. 10, 15s.). London: English Universities Press, 1965.

THIS is one of a series of books intended for the reader with a lively curiosity about the world around him and prepared to make a conscious effort to understand the thoughts and achievements of specialists. It assumes no prior knowledge, and, while the expert may not like the simplified expression of some ideas and concepts, it manages to convey some basic information which may be of interest to many laymen. A really great book of this kind may achieve a simplification which is a clarification of thought and is appreciated by those working in allied field, but this book is for the layman only.

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USED in conjunction with the author's previously published *Illustrated Physiology*, this will aid the junior student in biology, the nurse or other auxiliary to gain some knowledge of physiology. Both are well planned and designed to present basic data at an introductory level.



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# ECONOMIC AND SOCIAL ASPECTS OF TAENIASIS

J. S. LOGAN

Physician, Royal Victoria Hospital, Belfast

*"Atque interdum latos eos, qui peiores sunt, videmus".—Celsus.*

*TAENIA SAGINATA* is a parasite of humans, where its adult form is a large tapeworm in the small intestine, and of cattle, where its larval form is a small cysticercus in the muscles. Man can only acquire the infestation by eating raw beef. Cattle can only acquire the cysticercus by consuming ova from human excreta. Humans, as a rule, are concerned only with their own infestation. They seldom consider the affected cattle and the great epizootic which rages in the herds of Northern Ireland and elsewhere. Cysticercosis bovis is bad for cattle health, and bad in particular for the trade in fat cattle. Any beast with a cysticercosis bovis infestation suffers in greater or lesser degree in health. The loss to milk production cannot be known, but a figure can be arrived at for fat cattle. In 1961 the percentage of cysticercosis bovis in cattle slaughtered in Northern Ireland was 2.3. In 1962 it was 2.5. In 1963 it was 2.8, with a range from 10 per cent. at one abattoir to .1 per cent at another. If we take the gross total output of fat cattle and calves as 438,000, and the rate of infestation as 3 per cent., the number infested will be 13,140. If one reckons the loss per affected beast on slaughter at £10, the total loss to Ulster in 1963/64 on that account is £131,400. If we take the figures for cattle slaughtered in 1963/64—171,000, and cattle shipped—124,267, the total is 295,267. In that case the number infested may be reckoned at 9,000 and the loss at £90,000. In either case this is a substantial national loss. A loss of £100,000 would be .36 per cent. of the gross Northern Ireland output of fat cattle and calves in 1963/64. This is too much to lose because of a single infestation.

This loss of money is unnecessary. The epizootic in cattle can be abolished if the medical profession undertake to abolish human infestation. If that is done, then there would be no ova to contaminate pasture and water, and the cattle could not acquire the disease. Early diagnosis and prompt, efficient treatment are necessary, and both are easy and cheap. Moreover, numerically, it is not difficult. It is doubtful if there are more than 100 adult taeniae saginatae in Belfast. It is doubtful if there are more than 500 in Northern Ireland. To disinfest one case in hospital could not cost more than £15. To disinfest 500 cases would cost £7,500. Once the existing human cases were all disinfect, the charge would not recur. This is much cheaper, and more healthy, than to accept the infestation and share the loss. Let us get rid of it, and share the profit. Eire must do the same, because large numbers of store cattle are imported yearly for fattening in Northern Ireland. In 1964, 127,000 imported cattle, presumably all from Eire, received fat stock certificates.

If a reservation must be made it is this—that the life cycle of *T. saginata* is truly as described in the standard parasitological accounts. There is no real reason to doubt them. Adult taenia saginata is not observed in any host other than man. It has not been observed in cattle. Only a large host could accommodate such a large worm. Segments are not seen in the faeces of any domestic or farm animal.

It is puzzling, however, that pasture should be so heavily contaminated. Transport of ova by birds and rats from sewage outfalls is a possible explanation, especially when so much sewage is discharged untreated into the sea and into rivers. Sewage is also discharged in the country into burns and ditches. Cattle are still watered more from burns and ditches than from main water. These small channels have gained a new importance as sources of ova since the water grid spread about the country. Formerly in the country the contents of the domestic latrine bucket were as a rule buried in the vegetable garden. This minimised the taeniasis risk to cattle (though it increased the ascariasis risk to the children). Many houses in the country now have water closets, and the water-carried sewage is discharged untreated into the fields and ditches. This will lessen the ascariasis risk, but increase the taeniasis risk. Water contaminated with ova is important as well as contaminated grass.

*T. saginata* is the only common tapeworm of man in Belfast. *Taenia solium* infestation with the adult worm is never seen, and seems to be unknown now in the British Isles. It is derived only from eating under-cooked pork. *Taenia nana* is very rare but occurs. The cysticercus stage of *T. solium* is very infrequently seen in men who have been abroad in endemic areas, usually India. Hydatid disease, the cysticercus stage in man of the dog tapeworm, *Taenia echinococcus*, is fortunately rare in Northern Ireland. Since dogs in this country are commonly closely associated with humans, this present fortunate state of affairs is due to mutton and other meat fed to dogs being well cooked, and will only last so long as this is so.

*T. saginata* distresses human hosts not because the hosts are ill but because they do not like the segments migrating actively per anum. Motile segments are found in the bed in the morning, and in the clothes by day. Little or no physical harm comes of the infestation. There is no intestinal obstruction, no malabsorption, no diarrhoea, no anaemia, no abdominal pain. If the host consumes some ova by faecal soiling, a cysticercus stage does not develop in him (though it does in *T. solium* infestations).

Infestation of the human host with a single adult worm is the rule. Multiple infestations are rare. Hindus are not affected because they eat no beef, and vegetarians are not affected because they eat no meat. The worm lives for many years—even, it is said, up to twenty-five years. It is useless to hope that the worm will soon die of old age. It is curious to think that hardly any adult *T. saginata* ever meets another *T. saginata*. The worms, perhaps for this reason, are hermaphrodite, each segment having male and female organs and being self-fertilising. It is difficult to see of what genetic use this can be, unless the worm is a mosaic and the male and female organs belong each to a different element. The worm has no mouth and no alimentary canal. Presumably it absorbs its nutrition, and the drugs we administer to detach it, through its integument. The adult form is capable of little behaviour. Adherence to the mucosa of the host's intestine is active, and the terminal gravid segments are briefly motile from the time of breaking off until the death of the segment.

Infestation with *T. saginata* is a sign of bad hygiene education. Everyone should know that it is only acquired by eating raw or under-done beef. Occasionally in family cooking meat is not well cooked in the centre. Sometimes restaurant beef

is under-done. More often a housewife has had a habit of eating raw sausage and raw minced meat. Occasionally the butcher gives a child a raw sausage because of a primitive feeling that raw meat imparts a magical strength. Sometimes assistants in butchers' shops eat raw meat scraps. If all beef was well cooked before eating, and no one ate raw beef, there would be no *taenia saginata* infestation. This should be advertised constantly to the public by the public health service.

Ascertainment of cases is easy. No mass microscopy of faeces is necessary. It is impossible for a patient to have a tapeworm and not to know it, unless he is insane or mentally defective. The segments will be obvious in the stools or in the clothes. Only a very primitive person such as some itinerants would fail to consult his family doctor. If the patient produces to the doctor a specimen of the worm segment (and he should always be made to do so before the diagnosis is made) it may be assumed in Northern Ireland that the worm is *T. saginata*. Such an assumption would not be warranted in areas where *T. solium* is known to exist.

An infestation of man with the adult *T. solium* is a public health emergency. Such a person is a danger to his associates and to himself, because they and he, if they consume the ova, will become the seat of *taenia solium* cysticercosis (this does not happen with *T. saginata*). This commonly produces brain damage and epilepsy. In areas where *T. solium* is known to exist, the segments should be inspected with a lens so soon as the patient comes to notice, and the worm typed by counting the uterine branches. *T. solium* has about ten or fewer—*T. saginata* has many more. The ova of *saginata* and *solium* are indistinguishable. Typing should also be done if the patient has recently returned from an area where *T. solium* is found. *T. solium* will not be found in Jews or Muslims because they do not eat pork, nor in vegetarians because they eat no meat. A patient who has only the cysticercus stage of *T. solium* is a danger to nobody but cannibals.

A *T. nana* infestation is also a public health emergency because the ova discharged in the patient's faeces are directly infective to other people. No intermediate host is necessary. Faecal soiling, so common, if unsuspected, in households, schools and hospitals, is enough to spread the infestation. Such a patient should be admitted to an isolation block for disinfecting, and the household group should be surveyed by microscopy of the faeces to ascertain all the cases.

It is rarely possible to treat *T. saginata* at home. No patient can be relied on to starve, purge, take the drug, and effect expulsion of the worm when it is detached, as is necessary. Each case should be admitted as an economic emergency so soon as diagnosed. Every day the patient stays at home hundreds of thousands of eggs are discharged, ultimately to infest cattle. The admission should be to a ward where the doctors and nurses are experienced in the details of treatment, and know the difficulties, and where supervision is close.

The segments should always be seen before treatment is undertaken. One does not wish to impose a rigorous treatment on a patient who does not really have an infestation. Anxious patients mistake mucus, for instance, for worms. On the first and second day the patient should have *nothing* to eat, and be allowed only copious *watery* fluids with perhaps some glucose or sugar. Sufficient sodium

sulphate crystals—say two heaped teaspoonsful—are given twice daily, in as much water as will dissolve them, so that the bowels move freely, and watery stools are produced. The dose of sodium sulphate can be adjusted according to the purge produced. On the morning of the third day (the patient still having had no food) 1,000 milligrams of mepacrine hydrochloride are administered in a draught. The dose must be modified for children. The mepacrine is powdered and is suspended in not more than two fluid ounces of water by means of a suspending agent. An hour later a further dose of sodium sulphate solution is given so as to help to evacuate the detached worm. The patient should get up frequently and sit on a commode at the bedside. If the worm is not evacuated by the end of the second hour, a plain water enema should be given, and evacuation of the worm is then usually effected. So soon as the head is seen, the patient, who will be tired, should be given some tea and food.

The worm is usually evacuated in a piece, stained a bright yellow with the mepacrine. The head will be found easily at the narrow end. It is recognised by its shape and size—being a little expanded, compared to the neck, and about two millimetres broad. There is a dark pigmented spot on the centre of the head. The head should be looked at with the low power of the microscope. The presence of the suckers, which are easily seen, confirms that it is the head, and the absence of the hooks assures one that it is *not T. solium*. If the head is inspected at once the suckers may be seen making writhing movements. The worm should be burned.

The usual errors are failure to starve the patient, and failure to purge resolutely. Occasionally the purging is excessive, and an alert nursing staff will give warning of this, so that the sodium sulphate dose can be modified. At the worst intravenous fluids may be necessary if the purging does not cease. This is very uncommon. It is rare for the draught not to be given, but it may be spilled, and a second one should be available. If the patient vomits the draught, a second one, or part of it, may be given through an intragastric tube. If a patient with a gastric tube in place vomits the dose, it can be collected in a dish, and re-instilled down the tube. After administration of the draught the patient must be got up frequently to a commode, whether he feels the necessity or not. If the worm is not evacuated in an hour, efforts must be made to discharge it with more sodium sulphate solution and enemata as described. It is difficult to understand the direction given in old books to sieve the dejecta in order to find the head. In a thoroughly starved and purged patient there will be no faecal material to obscure the worm. The head is always attached to the rest of the worm and, if evacuated, is not hard to find. If it were not attached, it would likely be impossible to find. If the head is not found, it is still possible it has been evacuated. One will soon know if the treatment has failed, for in that case in three or four months segments will appear again in the stools. It is better not to undertake further treatment until segments are seen again. Before the patient is discharged he should be warned against ever again eating raw or under-done beef or indeed any other raw or under-done meat.

#### SUMMARY

*T. saginata* infestation is of considerable economic importance to Northern Ireland because the presence of the cysticercus stage in cattle is common, and this causes a national loss in cattle health and more obviously in meat condemned

and in meat depressed in price. It is a hindrance to the development of the export of cattle and meat. The infestation in men and cattle can be eradicated by:

- (1) Efficient ascertainment of human cases and prompt disinfection in hospital.
- (2) Thorough cooking of all beef and beef products before they are eaten.
- (3) Provision of cattle drinking water from the main supply and not from burns and ditches.

Family and hospital doctors should be active in the first field. Hospitals ought to admit taeniasis cases immediately. Possibly the cases should be concentrated at a few hospitals until eradication is completed.

Public health departments should advertise the second measure to the public, using newspaper, wireless and television announcements.

It is not often given to the medical profession to be able so directly to raise national productivity, and this opportunity should be taken.

I am indebted to Sister J. Montgomery for the nursing of the patients, and to Miss M. Gribbon for typing the manuscript. I am obliged to Mr. W. F. Black for preparing the mepacrine draught.

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For the biology of tapeworms I have referred to the Zoology of Tapeworms—1952. R. A. Wardle, J. A. McLeod, The University of Minnesota Press, Minneapolis.

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#### BOOK REVIEW

ANATOMY FOR STUDENTS OF DENTISTRY. By J. H. Scott, D.Sc., M.D., L.D.S., F.F.D., R.C.S.I., and A. D. Dixon, D.Sc., Ph.D., M.D.S. Second Edition. (Pp. vii+560; figs. 345. 60s.). Edinburgh and London: E. & S. Livingstone, 1966.

THE authors have succeeded here in presenting a book which is both easy to read and follow. One of the outstanding features is the excellent series of diagrams and drawings. The first two chapters give a clear and concise account of the fundamentals.

A large section of the book is taken up with the regional anatomy, etc., of the head and neck. This section is very detailed, and of course must be in that the book is catering particularly for the dental student. The black and white diagrams which have been used extensively throughout I particularly liked, and there is an excellent group of these in the appendix. Chapter X on clinical anatomy deserves special study by the dental student.

The reviewer has nothing but praise for this book and has no doubt that this second edition is a very worthy successor to the first. He is sure it will be adopted by many anatomy departments for their dental students.

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# A CLINICAL STUDY OF A SPASMOLYTIC AGENT (CYCLOSPASMOL) IN THE TREATMENT OF ELDERLY ARTERIOSCLEROTIC PATIENTS

By P. J. WARD, L.R.C.P.I., L.M., L.R.C.S.I., D.P.H.

Bessbrook, Newry, Co. Down

THE progressive arterial deterioration which accompanies ageing, may manifest itself in a variety of symptoms—all causing distress to the patient and increased problems for the physician. Elderly patients with advanced arteriosclerosis usually present one or more predominant signs or symptoms against a background of less obvious mental and physical impairment. Whilst treating a variety of peripheral vascular disorders in the elderly, with the spasmolytic vascodilator, Cyclospasmol, one observed that in addition to its control of the presenting complaint, there was frequently a remarkable improvement in the patient's general mental and physical well-being. Similar observations have been reported by a number of workers, including Ravina 1960, 1964; van der Drift 1961; and Hornstein 1961. A more detailed investigation of Cyclospasmol was made to see if these clinical impressions could be substantiated.

"Cyclospasmol is the mandelic ester of 3-5-5 trimethylcyclohexanol, and is a spasmolytic agent acting directly upon the smooth muscle of the vascular wall in a mode similar to that of papaverine, but with 5 times the activity" (Funcke 1951; Bijlsma et al. 1956). The direct mechanism avoids autonomic effects or interference with circulating adrenaline. The drug has an extremely low toxicity. The approved generic name is cycandelate.

## METHOD

The effect of Cyclospasmol was studied in 27 patients aged from 52 and 82 (mean age 71.8 years), who showed some degree of senility, reflected in physical and mental symptoms. Each suffered several of the manifestations of vascular insufficiency, apart from peripheral complaints such as Raynaud's disease, intermittent claudication and leg ulcers. The vast majority of these patients also showed signs of cerebral vascular impairment. This wide variety of symptoms was also associated with a number of other severe concomitant lesions, some connected with vascular insufficiency and some not. These included 5 cases of coronary thrombosis, 3 cases of cerebral haemorrhage, and 2 cases of peptic ulceration. These conditions were all presented against a background of general senility.

At the commencement of this trial, the subjects were divided into two groups, the first group receiving Cyclospasmol and the second a placebo. The conditions of four patients in the control group deteriorated to such an extent that they were transferred to active treatment after one month. The three groups existing at the completion of the trial are shown in table I.

TABLE I

<i>Cyclospasmol throughout</i>	<i>Identical placebo throughout</i>	<i>Changed to Cyclospasmol after 1 month</i>
16	7	4

TABLE II

SYMBOL KEY:—0 = no improvement + = moderate improvement ++ = good improvement +++ = excellent improvement W = worse

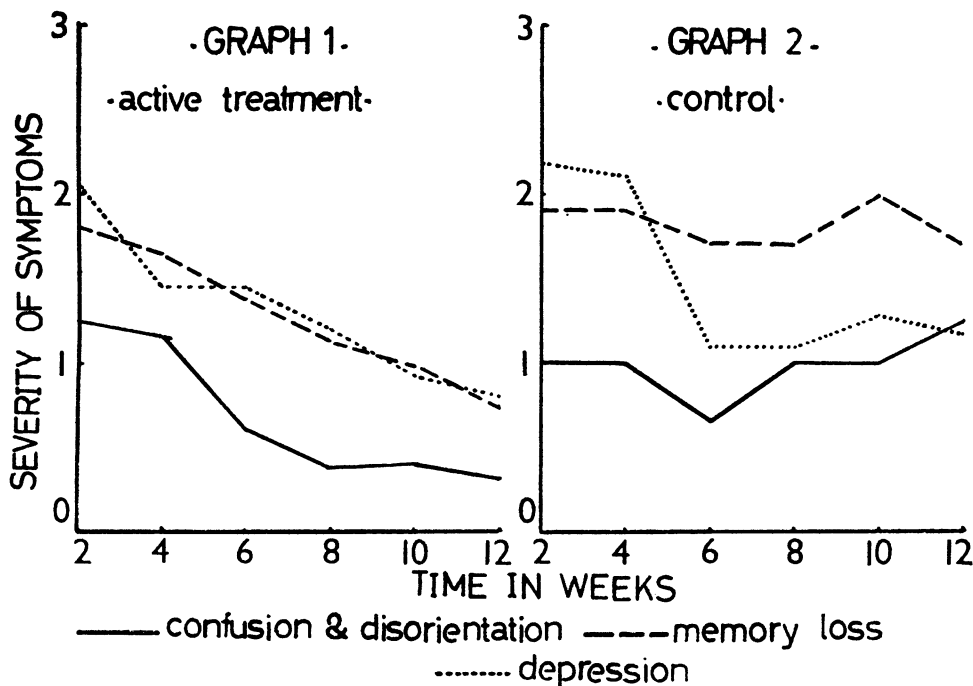
PATIENT			CEREBRAL			PERIPHERAL			CORONARY			DEPRESSION			RESTLESSNESS		
Trial No.	Age	Sex	Memory loss	Confusion/Disorient'n	Vertigo/Dizziness	Interm'tn Claudict'n	Leg Ulcers	Cold hands and Feet	Anginal Pain								
ACTIVE DRUG																	
1	55	F			+	+	+	+				+	+	+		+	
2	85	F		+	+	+		+				+	+	0		+	
3	82	F	W	0		+		+						+		+	
7	52	M			+									W		+	
8	63	M	+		+	0		+	++			+	+	+		+	
9	64	M	+	+	+	+		+				+	+	+		+	
12	65	F		+	+	+		+	+			+	+	+		+	
13	66	F		+	+	+		+	+			+	+	+		+	
14	80	F	+		+	+		+	+			+	+	+		0	
15	63	F		0	+	+		+	+			+	+	+		0	
19	78	M	+	+	+	+		+	+			+	+	+		+	
21	79	M	+	+	+	+		+	+			+	+	+		+	
23	64	F		+		+		+				+	+	+		+	
25	82	M	+	+	+	+		+	+			+	+	+		+	
26	82	F						+	+							+	
27	70	F	+	+				+						+		+	
Change from PLACEBO to ACTIVE DRUG																	
4	77	F			+	+		+				+				+	
10	82	F	+	+	+	+		+	++							+	
11	69	M	+	+	+	+		+	++			+	+	+		+	
18	74	M	+	+	+	+		+	+			+	+	+		+	
TOTAL																	
Number improved			12	8	16	15	6	17	7	15	13	15	13	16			
PLACEBO ONLY																	
5	74	M	0		+	+		+	0			0				+	
6	67	F	0	+				0				0				0	
16	73	M	0	0	0	0		0	0			0				0	
17	79	F		0				+				0				0	
20	76	F	+	W	0	0		0				0				0	
22	70	M				0		W	0							0	
24	71	M	0			0			0			+	+			0	
TOTAL																	
Number improved			1	1	2	1	1	2	3	5	3	5	1	7			

The duration of therapy was three months in each case. The patients received an initial dosage of 800 mg. daily for four weeks, followed by a reduction to 400 mg. daily for the remainder of the course. In some cases the higher dosage was reverted to if considered necessary. Treatment for concomitant disease was continued, and this included sedatives, soporifics, diabetic regimen, topical applications and specific dietary instructions. The subjects were examined at the commencement of the trial and at two weekly intervals until completion.

### RESULTS

Taking the series as a whole, a number of significant points arise. In almost every patient some degree of hypertension was evident, and even on the highest dosage of Cyclospasmol (800 mg. daily) this was not significantly altered. In the series not one patient complained of adverse side effects and tolerance to the drug was excellent.

In the pro-forma clinical information sheet used for each patient, a number of specific headings were used to describe cerebral function as applied to thought processes and a number of headings to describe vestibular function. These are



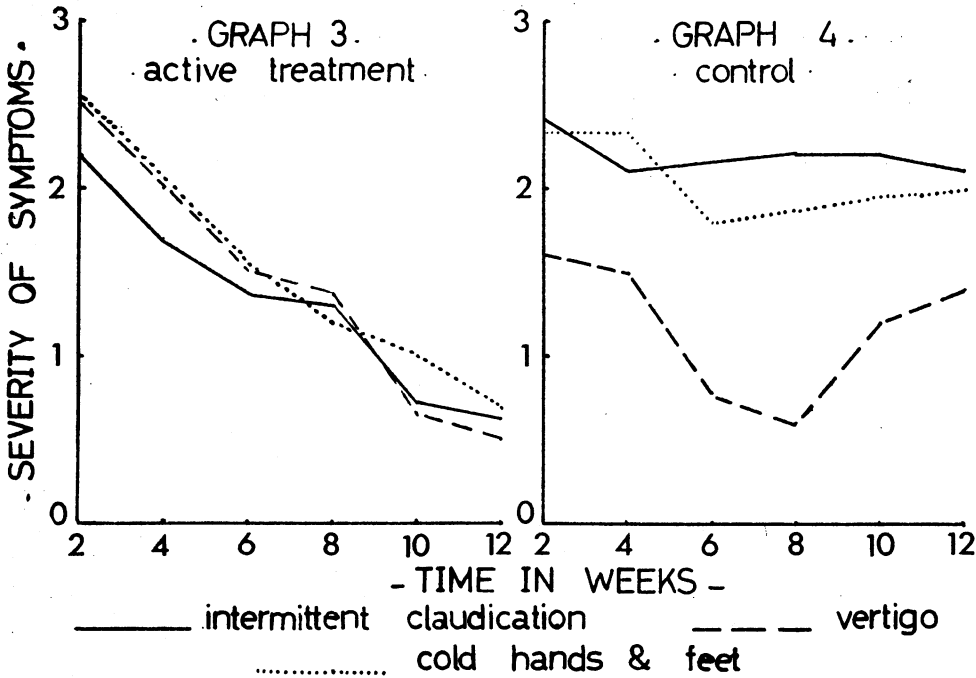
### LEGEND OF TABLE II

Two patients of the control group were treated with Cyclospasmol following completion of the trial; Patient No. 5—male, aged 74 with coronary thrombosis, anginal pain, hypertension and intermittent claudication. Poor response on placebo but changed to Cyclospasmol and showed encouraging improvement. Patient No. 22—male, aged 70 with severe intermittent claudication also showed no improvement on placebo, but changed to Cyclospasmol with good results.

shown in the main result table (Table II), grouped under the following appropriate headings: memory loss, confusion/disorientation and Meniere/vertigo/tinnitus. Graphs Nos. 1 and 2 represent the resultant improvement for each of these headings for the Cyclospasmol and placebo groups respectively. 83 per cent. of symptoms of cerebral origin were relieved.

All 16 patients with vertigo alone, or associated with Meniere's disease, showed a marked improvement on Cyclospasmol—whilst only 2 out of 5 receiving placebo improved.

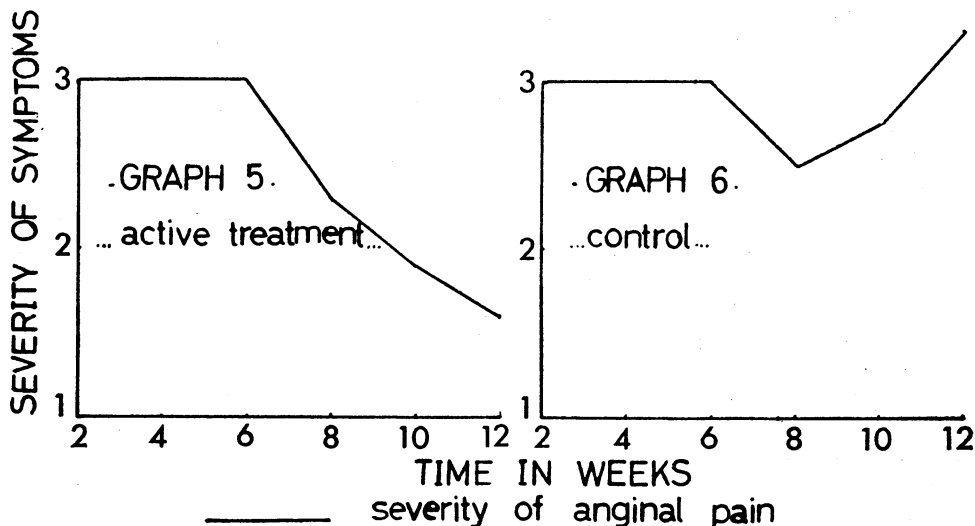
When considering the peripheral vascular symptoms, out of 15 patients with intermittent claudication, 13 receiving Cyclospasmol improved—compared with only 1 out of 4 in the control group. Whilst on the active treatment 16 out of 18 patients presenting Raynaud's phenomenon, or simple cold hands and feet showed improvement in their condition, only 2 out of 7 patients in the control group responded likewise. Graphs 3 and 4 depict progress in this group.



In the trial, 9 out of 27 patients had severe anginal pain as one predominant symptom. Two showed a striking improvement with complete cessation of pain, and 4 recorded improvement which could be classified as good: 1 showed only slight improvement, all receiving Cyclospasmol treatment. Two patients with severe anginal pain who were in the control group showed no improvement, and indeed the severity and incidence of attacks actually increased. It is a remarkable fact that of the 7 patients in the treated group, none showed improvement of any kind for at least a month—whilst the average time taken for reduction in pain to be

demonstrated was 6 weeks. Graphs No. 5 and 6, illustrate the response of the active and placebo groups respectively.

Of 15 patients who were depressed at the commencement, 13 responded well. Out of 27 patients included in this trial, 10 needed whole or partial assistance with dressing and eating; 4 patients receiving Cyclospasmol showed improvement in this respect. It was also noticeable that the majority of patients receiving Cyclospasmol were much less restless, both day and night, than those in the control group.



Two cases are of particular interest:

A 66 year old woman complained of anginal pain and cramps. Diabetes, coronary ischaemia and left bundle branch heart block were all present. Her B.P. was 165/85 with moderate arteriosclerosis. The peripheral and cerebral circulation were also impaired, with a large varicose ulcer, intermittent claudication, cold hands and feet, paraesthesia, and severe headache and vertigo. Treatment commenced with 800 mg. Cyclospasmol daily, reduced to 400 mg. after 1 month. At the end of 3 months, these latter symptoms had practically disappeared. Her hands and feet were only slightly cold, paraesthesia had gone, and the trophic ulcer was clearer. Intermittent claudication, restless legs, and the severe cramps had disappeared, and her cerebral signs of headache and vertigo had also gone; her blood pressure remained constant.

An 82 year old man presented with vertigo and severe leg pain on walking. He was well nourished, with moderate arteriosclerosis, causing a number of cerebral and peripheral symptoms. He was slightly confused, memory loss was severe, and vertigo, intermittent claudication, cold hands and feet, paraesthesia and restless legs were also present. Improvement was slow in onset, but with Cyclospasmol his general condition gradually improved. Memory impairment for recent events decreased, enabling him to be much more useful domestically. His general restlessness was far less, and he slept better than for many years. He could once more dress, and eat, without assistance. Pain might still awaken him, but it soon disappeared on movement. His intermittent claudication was reduced from severe to slight, and he was delighted at being able to walk much further. Cold hands and feet, paraesthesia and cramp was better, in all a marked improvement in his condition.

## DISCUSSION AND CONCLUSION

The general senile background present in these elderly patients is represented by a variety of minor signs and symptoms, each in itself often of small significance, but when grouped together, of major importance. Assessment cannot be by examination of each individual component of the senile background due to the variety of symptoms possible, and the fact that each patient may have a different combination.

The arguments for and against vasodilator therapy are many, but the absence of a simple method giving accurate and reproducible measurements of blood flow in particular tissues, makes substantiations of the various theories difficult. Without a simple objective test, the practising clinician must depend upon his impressions received from a number of semi-objective and subjective observations. Particularly when treating the elderly, the patient's own response and acceptance of the therapy is of prime importance. Therefore, the improvement in this aspect due to therapy must, in practice, be assessed by the general observations of the investigator and the others involved in the care of the patients.

A drug which is to be employed for long term medication should produce a minimum of side effects likely to cause distress. A highly significant factor in the success of the trial was the complete absence of variation in blood pressure, with its attendant risk of irreversible lesions in the cerebral and coronary arteries. Nor was any effect on the heart rate noticed. The importance of this aspect in the treatment of the elderly need not be stressed.

The 27 patients who entered the trial presented a total of 116 symptoms which were directly related to vascular insufficiency. Each subject suffered from at least two such symptoms.

When these results obtained in peripheral vascular disorders are studied, they are found to be very much in line with those reported by previous workers. Of patients with intermittent claudication 86 per cent. improved their walking distance on Cyclospasmol, whilst only 25 per cent. showed improvement on placebo. Similar results were recorded in patients showing Raynaud's phenomenon or suffering from cold hands and feet. My impressions would therefore tend to confirm those of Gillhespy (1959), who considered Cyclospasmol to be one of the most effective drugs in the treatment of serious peripheral vascular lesions.

Of particular interest is the beneficial effect of Cyclospasmol where symptoms of coronary insufficiency exist. All the patients who entered the trial with anginal pain, showed marked improvement at the end, but it is significant that improvement did not become apparent until approximately two months' treatment had been completed. The beneficial effects produced by Cyclospasmol where coronary insufficiency exists coupled with an absence of tachycardial or blood pressure variations, makes it the ideal vasodilator for elderly patients with concomitant coronary lesions.

A significant benefit was obtained in those conditions due to cerebral insufficiency. Both confusion and memory loss showed marked improvement in those receiving Cyclospasmol therapy. Where the symptoms of vestibular insufficiency were present, similar results were obtained. The patient benefits greatly from the alleviation of these symptoms, which tend to cut him off from his normal activities. The effects of cerebral insufficiency, confusion, memory loss, and disorientation, seriously

affect the ability of the patient to care for himself. They may lead to malnutrition, lack of hygiene, and failure to continue treatments as the patient pays less attention to himself and his surroundings. A vicious circle can develop.

A large number of patients entered the trial with symptoms of depression—whether depression can be directly due to cerebral insufficiency is questionable. A more valid explanation would be that the depression reflects the patient's own reaction to the ageing process and the resulting limitation which it puts on his activities, both physical and mental. In the majority of depressed patients, the depression was relieved by Cyclospasmol. It is logical that it is more positive therapy to remove or relieve the basic cause of the depression, than to administer potent anti-depressive agents.

A significant number of patients who previously needed assistance both in dressing and eating, were again able to perform these simple functions, following Cyclospasmol treatment. Such improvement, coupled with relief of confusion and depression, improved sleep and less restlessness, gave marked benefits both to the patients and to those responsible for their welfare.

During the course of this trial, the overall improvement in the treated subjects was so apparent, that a feeling of envy and jealousy was engendered in those not included in the investigation. This reflects the overall effectiveness of Cyclospasmol in treating general senile problems.

It is my conclusion that Cyclospasmol, in addition to producing marked improvement in specific vascular disorders, at the same time has a beneficial effect on the general well-being of the elderly patient. I would echo the remarks of Ravina (1960) "the physical and mental well-being of the elderly is primarily dependent upon the integrity of the vascular system".

In assessing the results, significant improvements have been recorded in a large percentage of patients. Arteriosclerosis is a progressive condition and without treatment the patient's symptoms would normally worsen. Any patient whose regression is halted may be considered as having benefited from the treatment—apart from those showing improvement. Examination of Table II will show such cases in the active treatment group. In the placebo group the deterioration of conditions is apparent.

There can be no doubt that some of the improvement observed during the investigations was due to the increased medical attention which the patients received, but this is probably manifested in the various placebo effects noted—but this must not be allowed to detract substantially from the very marked improvement shown by the large majority of the patients.

The marked absence of side-effects, and the long period of time necessary for the greatest benefit to be derived, demonstrate that Cyclospasmol is a spasmolytic of moderate but sustained activity. Maximum improvement usually becomes apparent within two months.

It is not the purpose of this investigation to discuss the mode of activity of Cyclospasmol, but the question may be raised whether the slow progressive action demonstrated in this trial reflects the promotion of collateral circulation, rather than the questionable dilation of atheromatous vessels. This might also explain the complete absence of hypotensive and tachycardial effects, the body having ample time to compensate for the vasodilation and increased collateral circulation.

### SUMMARY

The spasmolytic vasodilator, Cyclospasmol, was compared with a placebo in a group of 27 patients showing the senile changes attendant in arteriosclerosis. A wide variety of symptoms were present. The dosage employed was Cyclospasmol 800 mg. daily for one month, reducing to 400 mg. daily for the remainder of the three month period of the trial.

1. There were no adverse side-effects reported; Cyclospasmol caused no variation in blood pressure.
2. Cyclospasmol produced improvement in 85 per cent. of symptoms due to vestibular insufficiency.
3. Eighty-three per cent. of peripheral vascular symptoms improved on Cyclospasmol.
4. Seven cases with anginal pain showed marked improvement after a maximum of 2 months' treatment with Cyclospasmol.
5. There was a significant improvement in the general mental and physical well-being of the majority of the patients receiving Cyclospasmol.
6. Cyclospasmol produced a slow but progressive improvement in peripheral, coronary and cerebral circulation. It may be necessary to continue treatment for a number of weeks before improvement is noticed.

My thanks are due to Brocades (Great Britain) Ltd., for their generous supply of Cyclospasmol, without which this trial would not have been possible. I also wish to thank Mr. R. M. Wall, Ph.C., M.P.S., and Mr. D. C. Wren, M.C.S.P., M.R.S.H., for their co-operation and assistance in preparing this statistical analysis.

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# A CASE OF RUPTURE OF THE UTERUS

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BUCCAL PITOCIN as a method of induction of labour is relatively new and a large series of cases have been reported stressing the relative safety of this method of induction (Spence and Chalmers, 1964; Blair, 1964; Dillon et al, 1962; Rice and Benson, 1961). In all these series there was no rupture and only two cases of tetanic contractions of uterus. A point has been made that in "well controlled" series the method is absolutely safe. In spite of close supervision, however, a case of rupture of the uterus occurred with buccal pitocin and is reported below.

## CASE REPORT

Mrs. J. C., aged 32, was booked for hospital confinement because of her unfortunate obstetric career. Her first pregnancy ended in assisted breech delivery of a stillborn baby. There was no post-mortem. The second pregnancy terminated in a spontaneous delivery of an anencephalic foetus at 28 weeks. The third stage was normal. The third pregnancy was successful, the patient delivering a 7 lb. 4 oz. child spontaneously. The placenta was removed manually. There was no difficulty experienced as it was found to be simply retained and not adherent. The fourth pregnancy ended in a 12 week miscarriage followed by a curettage in another hospital.

At her first visit in her fifth pregnancy her general physical examination was satisfactory. The uterus was enlarged to approximately 18 weeks size which corresponded to the period of amenorrhoea. The blood Wassermann was negative. She attended the clinic regularly and remained singularly symptom free. However, at term the blood pressure was noted to be 135/90 with a trace of albumin. She was admitted to hospital on the same day for induction of labour.

A steril vaginal examination revealed only a partially effaced cervix so she was put on a "ripening drip" using 2 units of Syntocinon to a litre of normal saline for 12 hours. The next day the patient was started on a course of buccal pitocin. The detailed chart is attached.

Hours	.....	0	$\frac{1}{2}$	1	$1\frac{1}{2}$	2	$2\frac{1}{2}$	3	$3\frac{1}{2}$	4	$4\frac{1}{2}$	5
Time	.....	2	2.30	3	3.30	4	4.30	5	5.30	6	6.30	7
Right or left cheek		R	L	R	L	R	L	R	L	R	—	—
Dosage Increment (No. of tablets added)		$\frac{1}{2}$	$\frac{1}{2}$	1	1	2	2	3	3	3	3	3
Total Intake (Tabs)		$\frac{1}{2}$	1	2	3	5	7	10	13	16	19	22
Foetal heart rate	.....	144	138	136	136	144	144	144	144	140	144	140
Maternal pulse	.....	96	88	84	88	88	80	80	84	82	84	84
Maternal blood pressure	.....	135/90	130/90	140/90	135/90	140/90	140/90	135/90	140/90	130/90	130/70	130/80
Uterine contractions		—	—	—	—	—	—	B	B	B	M	F
		B=Backache			M=Mild contractions			F=Fair contractions				

By 7 p.m. the patient was having regular, fair contractions. The tablets were discontinued and the patient transferred to the labour ward. At 7.45 p.m. she complained of constant and severe abdominal pain of sudden onset. The uterus was found to be tender and the foetal heart could not be heard. Vaginal examination revealed 2 cm. dilated, cervix and intact fore-waters. Foetal parts could be palpated through the bag of membranes. There was a slight blood loss per vaginum. A tentative diagnosis of mixed accidental haemorrhage was made.

While a blood transfusion was being arranged the clinical picture dramatically changed

over the next half-hour. A supra-pubic prominence was noted. The tenderness over the uterus had increased and the presentation could not be definitely made out. The patient maintained that she was having regular "pains", but none were actually felt. She had started to bleed more per vaginum. A repeat vaginal examination revealed the vagina full of clots. The head had receded and no foetal parts could be felt per vaginum. The cervix was felt to be very posterior and almost "pulled up". It was still 2 cm. dilated. No definite bag of fore-waters could be made out. The catheter specimen of urine did not reveal any blood. It was only now that a rupture of the uterus was suspected. As the general condition was reasonable, immediate laparotomy was carried out under general anaesthesia.

On opening the abdomen the foetus was found in the peritoneal cavity, legs still inside the uterus which had ruptured. The site of rupture was identical to the routine transverse incision of lower segment Caesarean section. The edges were surprisingly clean although there was some extension of the tear into the left broad ligament rupturing a few veins. There was approximately 600 ml. of blood in the peritoneal cavity. The edges of these vessels were secured and ligated. The placenta was still partially attached to the posterior uterine wall and was removed by cord traction. In view of her poor obstetric history it was decided to repair the uterus in the manner of lower uterine segment-caesarean section-closure. She received a total of 3 pints of blood during this procedure. Her post-operative course was quite uneventful, and she was discharged on the 14th day. Her haemoglobin on discharge was 71 per cent. She was seen in the post-natal clinic six weeks later when the uterine involution was found to be satisfactory. The patient had already had a normal menstrual period. A hysterosalpingogram showed a well healed uterus. Both tubes were patent with ample peritoneal spill of radio-opaque material. She has remained well to date, but has not managed to conceive.

#### DISCUSSION

Oxytocin as a method of induction of labour per se or combined with amniotomy has come to stay. The response to the intramuscular method is too erratic and has been largely abandoned. The intranasal induction has been found to be uncomfortable for the patient and is unpredictable as well as difficult to control (Stander, Thompson and Gibbs, 1963). The advance towards "physiological administration" of oxytocin has been accompanied by increasing clumsiness of technique of administration. The time required, the cost of the infusion set-up and the need to subject the patient to constant supervision and immobilisation are a few of the complexities of intravenous infusion. Buccal pitocin came on the scene with this background and was found to be a convenient and safe method of induction. Glowing tributes were paid by Spence and Chalmers (1964), Blair (1964), Dillon and others (1962). These were bound to unleash a spate of enthusiasm. However, the British Medical Journal (1964) in an editorial warned against the risk of "uterine hypertonus with its possible sequence of rupture of the uterus". It has also been commended that the same care should be given to buccal pitocin as to intravenous administration (MacGillivray, 1964; Pinkerton, 1964) pointing that its considered safety and convenience of administration may be a trap in itself. Newman and Hon (1963) demonstrated that the time taken for the uterus to reach 50 per cent. of its mean activity after withdrawal is similar to the time taken after withdrawal of intravenous pitocin, but "the rate of absorption from the buccal mucous membrane is unknown and varies from patient to patient and probably from hour to hour (Theobald, 1965)". Hence the response of the uterus to buccal pitocin cannot be predicted. With increasing stimulation the sensitization increases. With unknown and perhaps uneven absorption, the chances of hypertonic response and consequent rupture of the uterus in unlucky few, must remain a definite possibility.

In the case of Mrs. J.C. it is possible that either the manual removal (even though reportedly of a "retained" rather than adherent) of placenta, or the curettage following the abortion may have resulted in undiagnosed damage to the uterus. But neither of these conditions, per se, are a contraindication to oxytocin induction. The ultimate cause of the rupture must have been increased sensitivity of the myometrium to oxytocin or unusually high rate of absorption from buccal mucous membrane. Neither of these can be predicted or avoided. Once this danger is appreciated and adequate precautions taken, there is no reason why this method should not remain a useful weapon in an obstetrician's armamentarium. With this aim in mind, there are a few suggestions worth considering:

- (1) The regime should be 10 units for the first 4 doses and only then increasing the dose, treating the first 2 hour period as a period of test trial.
- (2) The total dosage should be kept below 2,100 units.
- (3) At the time of insertion of a new batch of tablets the previous ones should be spat out.
- (4) The same strict watch should be maintained as for intravenous administration.
- (5) The tablets should be stopped as soon as regular uterine contractions start.
- (6) Every unit using this method should have a definite routine to be followed if confronted with hypertonic uterine contractions. The nursing and the medical staff should be well drilled in this routine, which should include immediate rinsing of the mouth with warm saline, intravenous pethilorfan (Newman and Hon), and perhaps chloroform by open mask.

Then and only then we can hope to avoid similar accidents.

#### ACKNOWLEDGMENT

My thanks are due to Mr. W. R. Sloan, F.R.C.S., F.R.C.O.G., Consultant, Jubilee Maternity Hospital, for permission to publish this case.

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# THE "THIRD COMA" IN DIABETES

## DIABETIC COMA WITHOUT KETOACIDOSIS

By **ALAN P. GRANT, M.D., F.R.C.P.I., M.R.C.P.**

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THE COMPLEXITIES of the diabetic syndrome are underlined by the fact that diabetic coma may occur without obvious ketoacidosis. The position has recently been summarised in a leading article in the British Medical Journal (1965). To the first two comas met with in diabetes, namely diabetic coma with ketosis and hypoglycaemic coma due to excess insulin, must then be added a third type of coma. The case described below falls into this category.

### CASE HISTORY

A female clerk aged 59 years was admitted as an emergency in "diabetic pre-coma" at 10.00 p.m. on 19th January, 1963. For some months she had been thirsty and she had lost much weight during this time. The patient had stopped work two weeks previously because she did not feel well. She had become very tired and weak, her appetite had failed, her thirst had become excessive and her speech had become slurred. Ten days previously she had vomited for two days only. There was no family history of diabetes nor history of a precipitating infection.

On admission she was extremely dehydrated and very weak. Her blood pressure was 120/80 and the pulse rate 120/minute. The urine was loaded with sugar but only contained a trace of acetone. Her electrolyte block showed the alkali reserve to be reduced to 14 m.eq/litre while the plasma sodium was 150 m.eq/litre and chloride 116 m.eq/litre, plasma potassium was 4.3 m.eq/litre with a plasma specific gravity of over 1030. Her blood sugar level was 800 mg. per 100 ml. It appeared that the patient had severe hyperglycaemia with acidosis and gross water dehydration, but ketonurea was not in evidence.

Initially, therefore, 500 units of soluble insulin were given in a litre of 5 per cent. dextrose by intravenous drip. After two hours following diuresis the plasma potassium had dropped to 2.8 m.eq/litre, suggesting that the total body potassium stores were depleted with transfer from the intracellular to the extracellular compartment. This was corrected by adding 50 m.eq of potassium chloride in a litre of 5 per cent. dextrose to the drip and one hour later the plasma potassium was at the satisfactory level of 4.3 m.eq/litre. The electrolyte block done at this time showed an even higher plasma sodium of 164m.eq/litre and chloride of 116 m.eq/litre. At 5.00 a.m. a further intravenous litre of 5 per cent. dextrose and 30 units of soluble insulin were commenced. At 9.15 a.m. the patient was conscious, although drowsy. Her speech was rather slurred and slight weakness of the right side of the face was noticed. The blood urea was 84 mg. per 100 ml. At mid-day the patient still remained drowsy with slurred speech and the right plantar response was extensor. She could now answer simple questions with difficulty and was able to move all her limbs. She was placed on a salt-free diet of 1,000 calories daily; subcutaneous soluble insulin (10 units) was given, the blood sugar being 285 mg. per 100 ml. She remained dull, listless, and very drowsy for the next week with a right plantar extensor response and a high blood urea. Intravenous 5 per cent. dextrose was continued for two days at three litres daily with a similar amount of fluid by mouth and by the third day her electrolyte block was normal, except that the alkali reserve had slightly dropped again. Blood sugars tended to stabilize and from the aspect of carbohydrate metabolism she appeared to be coming under control. She was able to take her diet and was continued on 10 units of soluble insulin twice daily.

Time	Admission Night				1st Day			Day	
	22.00	24.00	01.00	03.00	04.00	09.00	13.00	2	14
								Fasting Levels	
Alkali Reserve	14		23	28		33	31	30	22
Plasma Sodium	150		164	170	166	170	162	152	235
Plasma Potassium	4.3	2.8	4.3	3.7	4.1	4.8	4.0	4.3	4.0
Plasma Chloride	116		116			124	113	108	98
Specific Gravity	over 1030					1028	1028	1028	1025
Blood Sugar	800	650	465	344	325	205	285	81	220
Blood Urea						84		110	34

Alkali reserve, plasma sodium, potassium and chloride as m.eq. per litre.

Blood urea and sugar as mg. per 100 ml.

After twelve days she was controlled on tolbutamide 0.5 gramme twice daily and had completely recovered, except that convalescence was complicated by a septic lesion due to staphylococcus aureus at the drip site which eventually sloughed and required a skin graft.

Her diabetes has been easily controlled over the past two years on 1,500 C and sulphonylurea. Only over the first ten days was her blood urea elevated and, except for the initial trace of acetone, she remained acetone-free during and after her illness.

### DISCUSSION

The syndrome of stupor or coma with severe hyperglycaemia but without ketoacidosis is likely to meet with increased recognition. Maccario, Messis and Vastola (1965) have recently reviewed the literature and found twenty such cases reported since 1956. They give details of seven more cases of their own, who were admitted with focal epileptic seizures plus coma to a neurological clinic. This type of coma may present in a mild adult diabetic of the type which is later controlled by a sulphonylurea and in whom acetonurea is absent or a very occasional finding. Extremely high blood sugar levels with severe dehydration, haemoconcentration and a rise in the blood urea are the constant features. Shock is frequent on admission and, apart from an epileptiform attack, some evidence of neurological dysfunction, such as a positive Babinski sign, is common. Very high serum sodium levels occur in perhaps half the cases. Lucas, Grant, Daily and Reaven (1963) who report two cases, stress the importance of the great increase in osmolarity. Each increment of 100 mg. per cent. in the glucose level corresponds to 5.5 milliosmols, and if this is combined with a high serum sodium it seems beyond doubt severe neurological disturbances must occur.

Some features of this condition seem worthy of comment. An increase in the blood sugar level will lead to osmotic diuresis and consequently more water will be lost than sodium. Gross water dehydration with reduction in renal function and consequent uraemia may result. It is more difficult to explain why such high levels of blood sugar should occur without ketosis. This fact perhaps underlines the difference in clinical behaviour between juvenile and adult types of diabetes. Little is really known about fat metabolism in the adult type diabetes where it does not seem to be grossly disturbed. To add to the difficulty is the fact that similar comas have been described by Ward (1963) and Davidson (1964) where

autopsy revealed acute pancreatitis. In other instances the post mortem findings have been unremarkable. Lactic acidosis has been reported in three cases of the syndrome by Daughaday, Lipicky and Rasinski (1962). The other big problem is that in ordinary diabetic coma with ketoacidosis focal neurological abnormalities are unusual, while they occur in hypoglycaemic coma and in the syndrome under discussion.

It has long been recognised that ketone bodies may be absent or disappear from the urine in certain patients with ordinary diabetic coma and ketoacidosis. The work of Appel and Cooper (1927) and Coburn (1930) has shown that this occurs with the onset of functional renal failure due to dehydration, and in instances where there is also organic disease of the kidney this is more likely to occur. Adequate intravenous fluids produce acetone bodies in the urine when diuresis is restored, a fact which should distinguish this condition from the syndrome of diabetic coma without ketoacidosis. Furthermore, ketoacidosis is usually a complication of the juvenile type of diabetes. This type of coma with ketosis but without ketonuria was reported in the days when diabetic coma was treated by insulin and glucose without adequate fluids and should seldom be encountered now. It should, however, be remembered in the differential diagnosis.

The main biochemical features of the present case are shown in the figure and correspond well with what has been defined above as diabetic coma without ketoacidosis. They illustrate the initial high blood sugar level, and the high serum sodium level and plasma specific gravity due to severe water dehydration. The elevated blood urea is consistent with temporary renal shutdown due to the dehydration. In addition, the clinical features with a temporary neurological abnormality, including slurred speech, a right facial weakness and right extensor plantar response, are also in keeping with previous descriptions.

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## REVIEWS

**A DIAGNOSTIC APPROACH TO CHEST DISEASES:** Differential diagnoses based on roentgenographic patterns. By G. A. Lillington and R. W. Jamplis. (Illustrated, 116s.). Baltimore: Williams & Wilkins Company; and Edinburgh and London: E. & S. Livingstone, 1965.

THIS is an interesting book and I commend it especially to the postgraduate student who would like to revise his knowledge of chest disease by reading a rather unconventional book. The authors present a series of discussions of the differential diagnosis of commonly seen radiological patterns; what may be the cause of a solitary circumscribed pulmonary nodule, of intrathoracic calcification, of bilateral hilar enlargement, of pleural effusion etc., etc.?

It is an American book and it is biased by American experience, and coccidioidomycosis, blastomycosis and histoplasmosis are more commonly considered in the differential diagnosis than would be appropriate in Ulster—but it is very stimulating. It is a book to read rather than to buy. O.L.W.

**BIOCHEMISTRY.** By S. P. Datta, B.Sc., M.B., B.S., and J. H. Ottaway, B.Sc., Ph.D., A.R.I.C. (Pp. vi+379, 21s.). London: Concise Medical Textbooks, Baillière, Tindall & Cassell, 1965.

THE AUTHORS have written this book as a successor to their popular "Aids to Biochemistry" which ran to six editions. The text is based on a course of lectures to medical students, but the subject matter goes beyond the requirements of the usual medical course and is in fact, a comprehensive survey of general biochemistry.

The format is similar to that of standard biochemical text-books and in spite of the compact nature of the book, structural formulae, chemical equations and diagrams of metabolic pathways are clearly presented. Unusual in a book of this type is the inclusion of an excellent account of preparative and analytical techniques.

The omission of certain clinically important substances is unexpected in a book primarily designed for medical students. No reference is made to the haem pigments, sulphaemoglobin and methaemalbumin, the term protein-mound-iodine is not mentioned and while urinary 17-ketosteroids and 17-ketogenic steroids are described in the text, these well known group names are not included in the index. It would have been preferable to treat steroids and hormones in a single chapter instead of combining steroids with the chemistry of lipids and describing hormones in a chapter on control mechanisms.

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However the book may be useful in departments where there is insufficient time to design a practical course. The book itself should be very useful to teachers of physiology in that it describes well tried class experiments in a clear and simple step by step fashion. This information is not readily gained from other sources. I.C.R.

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## REVIEWS

**A DIAGNOSTIC APPROACH TO CHEST DISEASES:** Differential diagnoses based on roentgenographic patterns. By G. A. Lillington and R. W. Jamplis. (Illustrated, 116s.). Baltimore: Williams & Wilkins Company; and Edinburgh and London: E. & S. Livingstone, 1965.

THIS is an interesting book and I commend it especially to the postgraduate student who would like to revise his knowledge of chest disease by reading a rather unconventional book. The authors present a series of discussions of the differential diagnosis of commonly seen radiological patterns; what may be the cause of a solitary circumscribed pulmonary nodule, of intrathoracic calcification, of bilateral hilar enlargement, of pleural effusion etc., etc.?

It is an American book and it is biased by American experience, and coccidioidomycosis, blastomycosis and histoplasmosis are more commonly considered in the differential diagnosis than would be appropriate in Ulster—but it is very stimulating. It is a book to read rather than to buy. O.L.W.

**BIOCHEMISTRY.** By S. P. Datta, B.Sc., M.B., B.S., and J. H. Ottaway, B.Sc., Ph.D., A.R.I.C. (Pp. vi+379, 21s.). London: Concise Medical Textbooks, Baillière, Tindall & Cassell, 1965.

THE AUTHORS have written this book as a successor to their popular "Aids to Biochemistry" which ran to six editions. The text is based on a course of lectures to medical students, but the subject matter goes beyond the requirements of the usual medical course and is in fact, a comprehensive survey of general biochemistry.

The format is similar to that of standard biochemical text-books and in spite of the compact nature of the book, structural formulae, chemical equations and diagrams of metabolic pathways are clearly presented. Unusual in a book of this type is the inclusion of an excellent account of preparative and analytical techniques.

The omission of certain clinically important substances is unexpected in a book primarily designed for medical students. No reference is made to the haem pigments, sulphaemoglobin and methaemalbumin, the term protein-mound-iodine is not mentioned and while urinary 17-ketosteroids and 17-ketogenic steroids are described in the text, these well known group names are not included in the index. It would have been preferable to treat steroids and hormones in a single chapter instead of combining steroids with the chemistry of lipids and describing hormones in a chapter on control mechanisms.

In spite of these minor deficiencies this is a compact and valuable reference book on biochemistry for students of medicine who are interested in this field. S.G.W.

**EXPERIMENTAL PHYSIOLOGY.** 7th Edition. By B. L. Andrew. (Pp. 244 & vii; Illustrated, 37s. 6d.). Edinburgh & London: E. & S. Livingstone, 1965.

THIS is a manual for use in physiology practical classes. It makes rather dull reading. In the foreword, Professor Bell says that the idea was originally conceived to meet domestic requirements at the University of Glasgow and to avoid the "dreary drudgery of preparing stencilled sheets". With the better secretarial help now-a-days and the great advances in duplicating and photocopying processes this drudgery is not now necessary. It is probably better to tailor practical courses to the resources and aptitudes of individual departments. A published manual imposes a rigidity on the practical course which may not be desirable.

However the book may be useful in departments where there is insufficient time to design a practical course. The book itself should be very useful to teachers of physiology in that it describes well tried class experiments in a clear and simple step by step fashion. This information is not readily gained from other sources. I.C.R.

**"NEED I EVER RETIRE?"** Advice from William Evans, M.D., D.Sc., F.R.C.P. (Pp. 24). London: Chest and Heart Association, 1965.

THIS is a very human document and highly characteristic of the author. William Evans was a classical scholar before he became a combatant in the first World War. His commission was in the Lancashire Fusiliers, and at the end of the war he became Battalion Education Officer. In 1920 he embarked on the study of medicine, and won many prizes in the London Hospital. For the greater part of his life he worked with Sir John Parkinson, and their friendship has always been maintained. This essay on retirement contains many paragraphs which one would be tempted to quote, including one sentence of 116 words which flows with the music of a long cadenza. I feel that I must quote two short paragraphs:

"Those truly appreciative of the dignity of work will not abscond from it in retirement. We should not regard retirement as a rude and unjust interruption of life's journey, but welcome it as one would a friend, for it brings in its laden arms gains and long awaited opportunities that compensate and even outweigh the apparent losses.

Retirement marks the end of gainful employment, but it is the port of entry into a period of rewarding enjoyment; an emergence from the competitive race with its hazards and its hurdles into calm fields which provide for contemplative soliloquy."

In a more homely passage he advocates that the man who has achieved compulsory retirement should undertake a share of the household chores, and quotes the case of the retired rear-admiral who attributed his sun-tanned face not to a recent holiday, but to the fact that the window over the kitchen sink faced south. Such household duties might include the setting of any open fires, attending to the domestic boiler, cleaning boots, sweeping or Hoovering carpets, preparing meals or the washing-up. If these should be exercises he dislikes he should discipline himself to like them, for such regular occupation greatly contributes to his contentment. As might be expected, Dr. Evans' quotations from literature are apt and illuminating, and range from Longfellow, Pope and Milton to Ecclesiasticus.

This is indeed a delightful essay, and may be commended to those who are not yet 65, but who should now be counting the months or years until they achieve this milestone.

R.M.

**CUNNINGHAM'S TEXTBOOK OF ANATOMY.** Edited by G. J. Romanes. Tenth Edition. (Pp. xiv+1014; figs. 1153. 120s). London: Oxford University Press, 1964.

THE tenth edition of Cunningham's Textbooks of Anatomy improves upon the high standard of previous editions. A considerable amount of material has been added, especially in the number of radiographs reproduced in the text.

This book would serve as a complete reference to the structure and functional implications of the parts of the human body, and in these days of shortened courses of anatomy in the medical curriculum the need for a comprehensive and detailed textbook is even more important. The illustrations in the book are all now half tone in character, and 217 new figures have been added. A revised format incorporating two columns of text on a larger page has made the book more readable, and illustrations have been placed close to the relevant references in the text.

This new edition of Cunningham's Anatomy edited by Professor G. J. Romanes will maintain its place in the library of medical students and of those graduates reading for higher degrees in surgery and radiology.

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**EXOTIC DISEASES IN PRACTICE.** By Brian Maegraith, M.B., D.Phil., F.R.C.P., F.R.C.P.Ed. (Pp. ix+361; figs. 31. 50s). London: William Heinemann Medical Books Ltd., 1965.

THIS is a textbook which should find a place in every doctor's library. The speed of modern travel and the greater mobility of individuals and groups of persons has and is bringing into the home countries diseases which were hitherto considered to be purely "tropical". Unless we are alive to the everyday possibility of meeting these the consequences could well be disastrous.

In this book the two aspects of this increasing risk are admirably laid out. Firstly, the geography of disease and secondly, the clinical aspects. The text is clear and concise, the illustrations excellent and the regional maps an innovation which adds greatly to the value of the whole book. The chapters on world distribution of disease and the protection on non-immunes are clearly laid out, readily accessible and contain a fund of easily obtainable and valuable information.

This is a book which should appeal to all classes of medical men and students and prove of invaluable help and interest in an aspect of medicine with which we should and must all become familiar.

W.D.

**CLAYTON'S ELECTROTHERAPY AND ACTINOTHERAPY.** By Pauline M. Scott, M.C.S.P., T.E.T., T.M.M.G. Fifth Edition. (Pp. 390; figs. 205. 35s). London: Baillière, Tindall & Cassell, 1965.

THIS book—laid out in excellent print—is divided into three main sections, covering Electrotherapy (Direct and Low Frequency Currents), High Frequency Currents, Actinotherapy and Other Radiations. Each section progresses naturally towards the next sequence, and the whole work is punctuated with simple line diagrams to illustrate even more clearly the points made.

The chapter on electrical stimulation of nerve and muscle, and on electrical reactions has been brought up to date, and makes a valuable addition to the work, as does the chapter on semi-conductors and transistors and their place in the newer forms of electro-medical apparatus.

The authoress is to be congratulated on producing this accurate, well-balanced and pleasantly written work, which is generally accepted by the Chartered Society of Physiotherapy, London, as a standard textbook for students of physiotherapy throughout their training.

G.G.

**THE SOCIAL EFFECTS OF CHRONIC BRONCHITIS: A Scottish Study.** By Mary C. Neilson and Eileen Crofton. (Pp. 72. 7s 6d). London: Chest and Heart Association, 1965.

THIS small book is a challenge to all who work in chest medicine. The authors report a survey of a sample of men and women suffering from chronic bronchitis in Scotland. It shows the high incidence of severe disability, poverty, misery and despair amongst these sufferers in the midst of an affluent society. It is a picture strangely familiar to those who worked with tuberculosis 25 years ago. After reading this short report of the situation in Scotland, the need for a similar survey in Northern Ireland becomes clear. Such surveys as this are valuable for they indicate the need for a special effort to deal with chronic bronchitis in our community. We must not expect these problems to be solved unless we face up to them and tackle them with determination.

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**CASE STUDIES IN ANATOMY.** By Ernest Lachman, M.D. (Pp. xii+238;; illustrated, 24s). London: Oxford University Press, 1965

PROFESSOR LACHMAN'S BOOK fulfills a long felt need in the pre-clinical course. The dilemma in any teaching programme of gross anatomy is that the student too often fails to realise that much of the mass of anatomical information he acquires is directly applicable to clinical medicine. Too often, if not always, the student finds at the bedside he has forgotten most of the material he assimilated in the dissecting room. This book sets out to correlate anatomical facts with common clinical conditions and does so admirably.

The book consists of thirty case histories in which the physical signs presented in the case are correlated with anatomical and physiological facts. It is difficult to fault the selection of these case histories, which illustrate conditions commonly found in clinical practice. While students in Ireland may sympathise with the 32-year-old geologist who had a vasectomy (excision of a section of the ductus deferens) five years earlier as a contraceptive measure, and on re-marrying found his second wife desired children of her own, they will not come across this condition in their clinical practice here to any extent. On the other hand one feels the study of the clavicle will assume a more vivid mantle after reading that Sir Robert Peel died when a fragment of a fractured clavicle caused a fatal haemorrhage from the subclavian vein. This book is eminently readable and contains fifty line diagrams which contribute to the understanding of the written text.

In recent years in Queen's University an integration between the anatomical course and the wards of the Belfast City Hospital has successfully indicated to students the importance of a sound anatomical knowledge before the clinical years. This paper-back book contains enough anatomical material that it should be compulsory reading for all pre-clinical students as the cases are presented without an overlay of pathological or bacteriological fact but with the emphasis placed fairly and squarely on the anatomy related to the condition.

J.B.B.

**ELIZABETH GARRETT ANDERSON.** By Jo Manton. (Pp. 382; Plates 16. 42s). London: Methuen, 1965.

THIS is a fascinating book; a great deal of research has been done by the author, not only do we have the story of the first woman to qualify as a doctor in England, just 100 years ago in 1865, but we get an excellent picture of the status of women and the state of medicine in that period. Although Elizabeth Garrett was the first woman to qualify in England, there had been women in other countries practicing medicine without registration for many years.

Newson Garrett, Elizabeth's father, was a young ambitious and energetic business man. He believed in education for his daughters, as well as his sons, and Elizabeth and her sisters were sent to a boarding school for young ladies. She had inherited her father's ambition and drive, and as a young woman felt that she must put her energy into some form of work specially for women. After meeting Elizabeth Blackwell, who had graduated in America and had come to London to lecture, Elizabeth decided to be a doctor. Jo Manton gives us a very good picture of the struggle, the many disappointments, and the determination of this young woman to win through. Elizabeth started as a nurse in the Middlesex Hospital; she then attended clinics and classes and got private tuition, as no medical school would register her as a student. After each setback she re-organised her plans and went forward to meet the next hurdle. We see her as a doctor, a licentiate of The Apothecaries' Hall, an M.D. of Paris (Sorbonne), a gynaecologist with her own hospital, working with Sophia Jex-Blake to start a School of Medicine for women, and as a wife and mother.

Miss Manton's research presents the picture of a young woman small in stature, with a lively mind and brusque charm, who in later life became President of the Royal Free Hospital School of Medicine, President of the East Anglian Branch of The British Medical Association and, on the death of her husband, succeeded him as Mayor of Aldeburgh, and was described as a graceful and charming old lady. We are grateful to the author for her interesting biography of one of the pioneers of medicine as we know it to-day.

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O.M.A.



**CLINICAL PHARMACOLOGY (DILLING).** Edited by S. Alstead and J. G. Macarthur. Twenty-first Edition. (Pp. xii+741, 35s.). London: Baillière, Tindall & Cassell, 1965.

For this new edition of Dilling's Clinical Pharmacology extensive revision has been undertaken by the staff of the Department of Materia Medica and Therapeutics of Glasgow University, based in the Stobhill and the Western District Hospitals.

For medical students it is good that so many of the modern textbooks of pharmacology are written by authors familiar not only with pharmacology but also with the use of drugs in current therapy. This is the case with this excellent book. Few books for this price give so much information. There is an interesting section on chemical nomenclature, sensible advice about prescribing and a useful section on immunising agents.

Many students will find this book too detailed; and for its size I would like to have seen included less didactic statement and more critical discussion of modern controversies. It should surely devote more space to the discipline of the controlled therapeutic trial. There is a limited bibliography of useful reference books and textbooks, but I would like to see references to contemporary papers at the end of each chapter. The modern student needs to be persuaded to read journals; it is a necessary discipline if he is to remain an educated doctor throughout his life and in no subject is this more obvious than in modern therapeutics.

O.L.W.

**PSYCHIATRIC NURSING.** By David Maddison, Patricia Day and Bruce Leabeater. Second Edition. (Pp. vi+511, 40s.). Edinburgh and London: E. & S. Livingstone, 1965.

This second edition of a readable text-book for nurses deserves the popularity its first edition achieved. The section dealing with anti-depressant drugs has been revised, but the authors have continued to place more emphasis on trade names for drugs in most instances than on their approved names.

Nurses will continue to find in this book a valuable guide to psychiatric nursing.

J.G.G.

**PHYSIOLOGY OF MAN.** By L. L. Langley and E. Cheraskin. Third Edition. (Pp. 657 and xii; Illustrated, 68s.). New York and London: Reinhold Publishing Corporation, 1965.

AMERICAN medical students often gain a greater knowledge and understanding of physiology in two terms of study than their British equivalents gain in five. There are many reasons for this. One is that most American medical students come to physiology with a superb working knowledge and understanding of the alphabet of medicine; physics, chemistry, mathematics and biology. They rapidly and easily assimilate the concepts of physiology and can discuss them with incredible dexterity. The lack of feeling for the basic sciences in most British medical students is perhaps the greatest weakness in British medicine. It is a weakness which most teachers in British medical schools reinforce continually by their own limitations in the basic sciences.

It would have seemed appropriate, therefore, that the text-book of physiology for people who are ignorant in physics, chemistry and biology should be written in Britain. I regret to say that even here we have been beaten. Langley & Cheraskin in their book "Physiology of Man" have written an excellent account of physiology for those who want to learn rather than understand the subject. It makes practically no assumptions of background knowledge in the reader. It is superficial and provides nothing for the enquiring mind. Nevertheless it is a nicely produced book and is enjoyable to read. It could well be useful as an introductory text for British medical students or as a text for science students taking physiology as a subsidiary subject. But its superficiality is enough to damn it as main text for medical students. It would only compound the intellectual disability which is regrettably fostered by much of the teaching in the British medical schools and stems from an early revolt against the basic sciences.

I.C.R.

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AMERICAN medical students often gain a greater knowledge and understanding of physiology in two terms of study than their British equivalents gain in five. There are many reasons for this. One is that most American medical students come to physiology with a superb working knowledge and understanding of the alphabet of medicine; physics, chemistry, mathematics and biology. They rapidly and easily assimilate the concepts of physiology and can discuss them with incredible dexterity. The lack of feeling for the basic sciences in most British medical students is perhaps the greatest weakness in British medicine. It is a weakness which most teachers in British medical schools reinforce continually by their own limitations in the basic sciences.

It would have seemed appropriate, therefore, that the text-book of physiology for people who are ignorant in physics, chemistry and biology should be written in Britain. I regret to say that even here we have been beaten. Langley & Cheraskin in their book "Physiology of Man" have written an excellent account of physiology for those who want to learn rather than understand the subject. It makes practically no assumptions of background knowledge in the reader. It is superficial and provides nothing for the enquiring mind. Nevertheless it is a nicely produced book and is enjoyable to read. It could well be useful as an introductory text for British medical students or as a text for science students taking physiology as a subsidiary subject. But its superficiality is enough to damn it as main text for medical students. It would only compound the intellectual disability which is regrettably fostered by much of the teaching in the British medical schools and stems from an early revolt against the basic sciences.

I.C.R.

**CLINICAL PHARMACOLOGY (DILLING).** Edited by S. Alstead and J. G. Macarthur. Twenty-first Edition. (Pp. xii+741, 35s.). London: Baillière, Tindall & Cassell, 1965.

For this new edition of Dilling's Clinical Pharmacology extensive revision has been undertaken by the staff of the Department of Materia Medica and Therapeutics of Glasgow University, based in the Stobhill and the Western District Hospitals.

For medical students it is good that so many of the modern textbooks of pharmacology are written by authors familiar not only with pharmacology but also with the use of drugs in current therapy. This is the case with this excellent book. Few books for this price give so much information. There is an interesting section on chemical nomenclature, sensible advice about prescribing and a useful section on immunising agents.

Many students will find this book too detailed; and for its size I would like to have seen included less didactic statement and more critical discussion of modern controversies. It should surely devote more space to the discipline of the controlled therapeutic trial. There is a limited bibliography of useful reference books and textbooks, but I would like to see references to contemporary papers at the end of each chapter. The modern student needs to be persuaded to read journals; it is a necessary discipline if he is to remain an educated doctor throughout his life and in no subject is this more obvious than in modern therapeutics.

O.L.W.

**PSYCHIATRIC NURSING.** By David Maddison, Patricia Day and Bruce Leabeater. Second Edition. (Pp. vi+511, 40s.). Edinburgh and London: E. & S. Livingstone, 1965.

This second edition of a readable text-book for nurses deserves the popularity its first edition achieved. The section dealing with anti-depressant drugs has been revised, but the authors have continued to place more emphasis on trade names for drugs in most instances than on their approved names.

Nurses will continue to find in this book a valuable guide to psychiatric nursing.

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**ESTRANGEMENT AND RELATIONSHIP.** By Francis A. Macnab. (Pp. xix+299, 45s.). London: Tavistock Publications, 1965.

THE existentialist approach to psychiatric problems has gained considerable popularity amongst some groups of European psychiatrists, notably in Western Germany, France, Spain and Italy. In Britain and America the few papers that have appeared on this topic have not always been enthusiastic. The problems of psychiatry and psychology are slowly being formulated in ways that lend themselves to the scientific approach and to begin afresh to re-formulate them in existentialist terms does not seem to be a profitable exercise to most psychiatrists. This does not mean that the existentialist approach is considered to be invalid; rather that it cannot be readily studied by methods at present available.

The present book is a review and shortened version of a Ph.D. thesis. It is an attempt to link clinical psychiatry and theology by building a bridge from the latter to the former. The author has intensively studied a number of schizophrenic patients, and liberally quotes from group sessions to provide the background for an existentialist interpretation of schizophrenia, viz.—estrangement (an accumulating loss of confirmation of being-in-the-world), existence-at-a-distance, decisionless state and loss of the determining Centre (which gives meaning and coherence to the fundamental structures of being). Such terms can be applied to the effects of schizophrenia on the relationships of the individual to his environment, but not so readily as an explanation for its causation.

There is much that is relevant in this book for all who strive to maintain the schizophrenic patients' contact with reality. Perhaps it is best summed up by the quotation from Tillich on p. 187: "Participation is essential for the individual, not accidental. No individual exists without participation, and no personal being exists without communal being".

It is the reviewer's opinion that this book has much to say that is not confined within the limits of Existentialist Philosophy. It is possible that it may eventually reach a growing audience as clergy-doctor co-operation increases. J.G.G.

**NUTRITION AND DIETETICS FOR NURSES.** By Mary E. Beck. Second Edition. (Pp. xii and 232, 21s.). Edinburgh and London: E. & S. Livingstone, 1965.

THE first edition of this excellent and interesting book was reviewed in 1962. The second edition is little changed: a small section on carbohydrate intolerance and a discussion of diets that reduce blood cholesterol levels have been introduced.

I think it is a pity that the title indicates the book is "for nurses" as it deserves a wider public.

Undoubtedly there will be a third edition and when Miss Beck prepares this, perhaps she will include some evidence of the extent to which our patients accept dietary advice. One of the major needs of modern therapeutics, including dietary therapeutics, is operational research. We often know that therapy can do good. We too often do not know whether it is doing good; and if not why not. One of my colleagues had a cynical dictum "If the patient on the reducing diet loses weight, suspect neoplasm". O.L.W.

**ESSENTIALS OF MATERIA MEDICA, PHARMACOLOGY AND THERAPEUTICS.** By R. H. Micks. Ninth Edition. (Pp. xii+509, 36s.). London: Churchill, 1965.

SALUTE to Professor Micks: his book has always been popular with medical students because it is well and attractively written in good English with forceful phraseology and quotable dicta. But how splendid to get to a 9th edition: and what an alert, fresh interesting 9th edition, how up-to-date, how obviously written by a physician in contact with every day problems of therapeutics. This book has increased in stature but not, fortunate student, in girth. I wish, however, a few useful references for further reading were given at the end of each chapter, if only to indicate to students that knowledge is not easily attained and opinions vary, and to inculcate the discipline of reading journals, essential if knowledge of current therapeutics is to be maintained over the years. O.L.W.

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