VOLUME 44 1975 No. 1

THE ULSTER MEDICAL JOURNAL

PUBLISHED BY
THE ULSTER MEDICAL SOCIETY

CONTENTS

Hon. Treasurer

N. C. NEVIN, B.SC., M.D., M.R.C.P.

Hon. Editors

J. E. MORISON, M.D., D.SC., F.R.C.PATH., The Laboratory, Belfast City Hospital, Lisburn Road, Belfast.

D. A. D. MONTGOMERY, M.D., F.R.C.P., Metabolic Unit, Royal Victoria Hospital, Grosvenor Road, Belfast.

Fellows and Members of the Ulster Medical Society receive the Journal Free. Details as to subscriptions on back page.

This publication is available in microfilm from Xerox University Microfilms, 300 North Zeeb Road, Ann Arbor, Michigan 48106

CONTENTS

Hon. Treasurer

N. C. NEVIN, B.SC., M.D., M.R.C.P.

Hon. Editors

J. E. MORISON, M.D., D.SC., F.R.C.PATH., The Laboratory, Belfast City Hospital, Lisburn Road, Belfast.

D. A. D. MONTGOMERY, M.D., F.R.C.P., Metabolic Unit, Royal Victoria Hospital, Grosvenor Road, Belfast.

Fellows and Members of the Ulster Medical Society receive the Journal Free. Details as to subscriptions on back page.

This publication is available in microfilm from Xerox University Microfilms, 300 North Zeeb Road, Ann Arbor, Michigan 48106

THE ULSTER MEDICAL JOURNAL

NOTICE TO CONTRIBUTORS

1. Authors are reminded that concise and clearly expressed papers are those most welcomed by readers and by the Editorial Board.

2. Manuscripts should be typewritten with double spacing and with wide margins. They should be fully corrected, and contributors will be responsible for the payment of any sum charged for alterations in printer's proof in excess of 50p per sheet (16 pages).

3. References should be restricted to those really necessary, and useful and cited as in the publications of the British Medical Association and in most modern British journals. Either the full title of a journal or its correct abbreviation as given in *World List of Scientific Periodicals* or *World Medical Periodicals* should uniformly be employed.

4. Tables and illustrations should be reduced to a minimum, and should be sent detached from the typescript of the paper. Line drawings should be used whenever possible. All illustrations must be in a finished form ready for reproduction. Authors may be charged for all blocks at cost price.

5. Orders for reprints must be given when the author returns the printer's proof. The cost of these may be obtained from the printers in advance.

6. Editorial communications should be sent direct to the Editor, Professor J. E. Morison, D.Sc., M.D., The Laboratory, Belfast City Hospital. The Editor will be glad to advise authors on the preparation of their manuscripts.

DATES OF PUBLICATION

It is hoped to issue a Winter and Summer Number each year in February and September.

THE ULSTER MEDICAL SOCIETY

P.O. Box 222,
Belfast City Hospital,
Belfast 9.

If you are not a member of the Ulster Medical Society, we would appeal to you to give the question of joining your consideration. The Society has been in existence since 1862 (and is the direct descendant of the Belfast Medical Society founded in 1806), and has always been active in keeping its members interested in the advances in medical science. Meetings are held at intervals of a fortnight during the winter months, and papers are contributed by members and distinguished guests. Facilities are provided for doctors to meet informally afterwards and have a cup of tea. *The Ulster Medical Journal, the official organ of the Society, is issued to all Fellows and Members free of charge.* The Society will soon be rehoused in its own Rooms (in the new buildings at the Medical Biology Centre) which will replace the Whitla Medical Institute which had to be vacated in 1965.

May we, therefore, appeal to you to join the Ulster Medical Society, and so enable us to widen its influence and sphere of usefulness still further? A proposal form is appended: your proposer and seconder must be Fellows of the Society. If you do not know any Fellows please contact the Honorary Secretary. All persons registered as medical practitioners under the Medical Acts shall be eligible for election as members of the Society (Constitution, Section VI). Temporary membership may be allowed at the discretion of the Council.

If you do not wish to become a member of the Society, will you consider entering your name as a subscriber to THE ULSTER MEDICAL JOURNAL? The subscription is £2.00 per annum, payable in advance to the Honorary Treasurer.

J. E. MORISON, *President.*
D. R. HADDEN, *Hon. Secretary.*
N. C. NEVIN, *Hon. Treasurer.*

MEMBERS **£1.5.** (A Member is one who is less than seven years qualified. He or she will automatically become a Fellow seven years after qualification and be liable to the higher subscription rate.)

FELLOWS—1 (a) Annual subscription of Fellows resident, practising or holding an appointment within ten miles of Belfast, **£3.15;** (b) husbands and wives in the above category who are both Fellows will be entitled to pay a combined subscription of **£4.20;** 2 (a) annual subscription of Fellows resident, practising or holding an appointment outside the above area, **£2.10;** (b) husbands and wives in the above category who are both Fellows will be entitled to pay a combined subscription of **£3.15;** 3, annual subscription of retired Fellows, provided that any Fellow who, by reason of retirement either through age or illness, is no longer engaged either in private practice or in salaried employment, shall be entitled, *on application,* to pay an annual subscription of **£1.15** only, and provided always that such Fellow has previously paid to the Society a subscription at the current rate for an uninterrupted period of at least ten years, or during such time has been in practice or service abroad.

All Fellows and Members of the Society who have paid subscriptions for 40 years or alternatively having been a Fellow or Member for 20 years and reached the age of 65, or more, shall be exempt from any further subscription.

LIFE MEMBERSHIP—Fellows and Members shall be eligible to become Life Members, **£31.50.**

To DR. N. C. NEVIN,
DEPARTMENT OF MEDICAL STATISTICS,
INSTITUTE OF CLINICAL SCIENCE,
GROSVENOR ROAD, BELFAST BT12 6BJ.

.....19.....

Dear Sir,

We nominate for $\frac{\textit{Membership}}{\textit{Fellowship}}$ *of the Ulster Medical Society—*

Name of Candidate .....

Postal Address .....

.....

Year of Qualification and Degrees .....

.....

Signature of Proposer .....

Signature of Seconder .....

EXCHANGES: Exchange journals and all relevant correspondence should be addressed to:
QUEEN'S UNIVERSITY MEDICAL LIBRARY,
INSTITUTE OF CLINICAL SCIENCE,
GROSVENOR ROAD, BELFAST BT12 6BJ,
NORTHERN IRELAND.

BOOKSELLERS: All correspondence, orders and payments for institutional and private subscribers, through booksellers, should be sent to:
THE HONORARY TREASURER,
ULSTER MEDICAL JOURNAL,
c/o QUEEN'S UNIVERSITY MEDICAL LIBRARY,
INSTITUTE OF CLINICAL SCIENCE,
GROSVENOR ROAD, BELFAST BT12 6BJ.
NORTHERN IRELAND.

SUBSCRIPTIONS: Individuals who are not members of the Society wishing to take out a direct subscription should send a banker's order for £2.00 payable to the Ulster Medical Society (Northern Bank, Shaftesbury Square, Belfast), Ulster Medical Journal Account, to Dr. N. C. Nevin, Department of Medical Statistics, Institute of Clinical Science, Grosvenor Road, Belfast BT12 6BJ. This covers one volume (two numbers) of the Journal.

THE
ULSTER MEDICAL JOURNAL

PUBLISHED ON BEHALF OF THE ULSTER MEDICAL SOCIETY

VOLUME 44 1975 No. 1

ONE ENTRANCE INTO LIFE

by

PROFESSOR J. EDGAR MORISON, M.D., D.Sc., F.R.C.Path.

Presidential Address to Ulster Medical Society 10th October 1974

"For no king had any other first beginning;
But all men have one entrance into life
And a like departure."

The Wisdom of Solomon—The Apocrypha

OVER three-hundred and thirty years ago, just when England was about to be rent apart by the Civil War, Thomas Browne, a student of Padua and Montpellier and a Doctor of Medicine of both Leiden and Oxford, wrote *Religio Medici*. This contributed little to religion, but in the stately prose of a bygone age ranged far and wide with protestations of piety and a gentle irony. One of the best known passages is where he writes " . . . . and every man is some months older than he bethink him, for we live, have a being, and are subject to the action of the elements, and the malice of disease, in that other world, the truest microcosm, the womb of our mother". Tonight I would like to consider a few of the ways by which "the action of the elements and the malice of disease" may affect a man, be he future king or future beggar, before he is born and again while he is making the first adjustments to breathe air, that breath of life which in primitive animistic thought represented the beginning of his life.

In the older civilisations of the world, and even in recent times, men thought little of the miracle of normal development, but when a malformed and monstrous being was born reacted with admiration, awe or terror. Other disturbances of foetal and neonatal life were scarcely considered at all. Apart from a few descriptive studies it was only late in the last century that even malformations were studied in any scientific manner and the science of teratology developed and became integrated with the study of normal development. Until recently theories of causation were largely futile speculations over mere coincidences. Preyer in 1885 did report

acute physiological experiments on the animal foetus, but available studies made no attempt to determine how the foetus lived in utero or could be exposed to the malice of disease before birth.

About the beginning of this century J. W. Ballantyne of Edinburgh with prodigious energy and dedication ranged far beyond descriptive studies of malformations and studied many intra-uterine diseases. Before the First World War the descriptive pathology of Germany excelled in the anatomical minutiae of malformations and also gave some useful descriptions of a few foetal diseases, such as congenital syphilis, and of the injuries and haemorrhages due to physical trauma at birth. In the decade before the Second World War careful surveys of foetal and neonatal deaths were started in Edinburgh by Dr. Agnes Macgregor, in Chicago by Dr. Edith Potter and in Boston, in the department of my former teacher, Dr. Sidney Farber.

In the published work before 1930 there is little of value for the understanding of disease in the foetus or newborn child and certainly little which even tries to go beyond the anatomical recognition and description of a few disease conditions. Almost the whole development of foetal and neonatal pathology has occurred during the years since I qualified, and it has been made possible by advances in foetal physiology pioneered in the thirties and forties by Sir Joseph Barcroft in Cambridge and by his disciples now scattered over the world, and more recently by the studies of Geoffrey Dawes in Oxford. Concepts from the general biology of development have increasingly helped and developmental immunology and biochemistry is beginning to help. Despite the belief still mistakenly held in some centres, pathology is much more than the description and recognition of changes of structure in dead bodies and tissues. It is the recognition of the whole sequence of such disturbances as constitute disease, and to this the traditional techniques of tissue pathology have still much to contribute, but only if integrated with continuing advances in other disciplines. The advances made throughout the world in the pathology of this period of life have sometimes come from the thinking of men I have met and sometimes from those whose friendship I cherish. I have always looked backward over the territory conquered and forward to the frontier with a very special interest. For me the detailed story of these advances illustrates real co-operation in the world of science which transcends all national barriers.

Congenital Malformations and Abnormalities

In the world of our forefathers, and up to at least the nineteenth century prayers for deliverance from pestilence and sudden death expressed a real and ever present fear. It was accepted as normal that about half of all children born alive should die in early infancy. The death of children before birth, the birth of malformed

Fig. 1. *White marble figurine of double headed twin goddess from Anatolia approximately* 6000 *B.C.* (*Mellaart, J.* (1963) *Archaecology,* **16**, 29 *by permission.*

Fig. 2. *Dicephalus dibrachius* (*Ahlfeld Atlas,* 1880).

Fig. 3. *Janus from a silver Roman coin of the third century B.C.*

Fig. 4. *Cephalothoracopagus twin* (*Ahlfeld Atlas,* 1880).

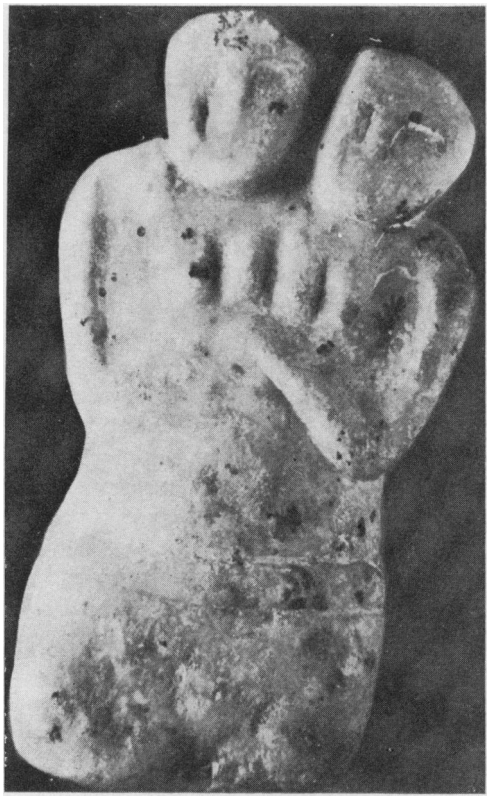


FIG. 1

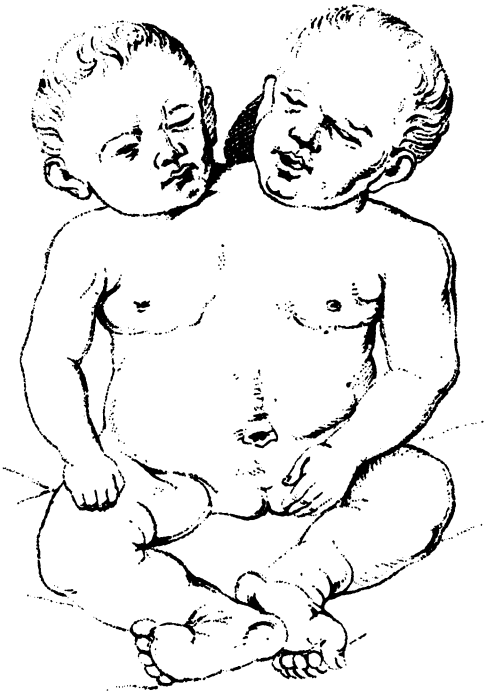


FIG. 2

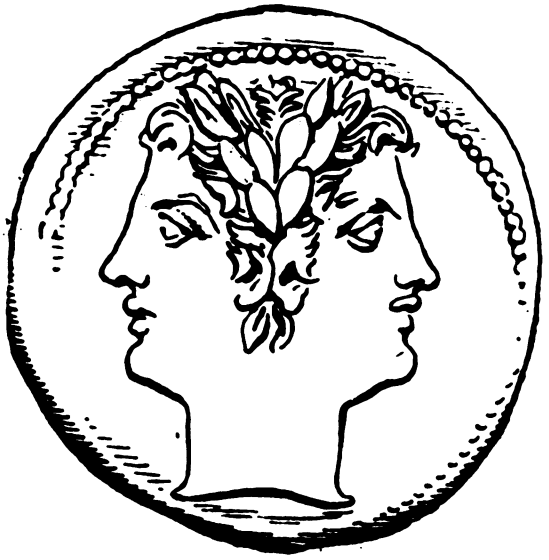


FIG. 3

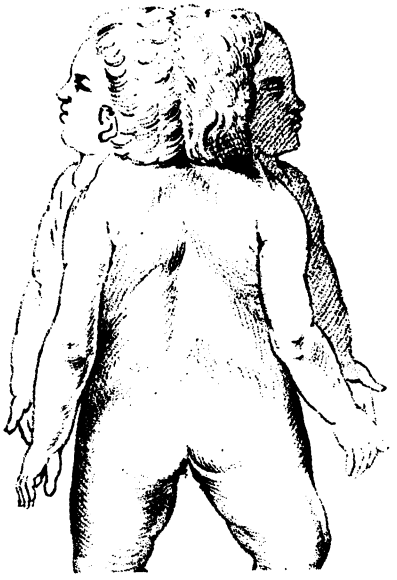


FIG. 4

children who were almost certain to die, and the death of many children in the early days of life were thought inevitable. However, many views were held, especially about the more unusual and curious malformations. In ancient pre-Christian civilizations deformed children were often held to reveal the power and intentions of the gods, and the term monster means to show forth. Monsters were sometimes worshipped, and, if men made gods in their own image, they also often made them in these monstrous forms. A figurine (Figure 1) in white marble from a neolithic site in Southern Turkey dates from 6500 B.C. and, like a chalk figure from New Ireland in the South Pacific and pre-Columbian sculptures from Mexico, shows a dicephalus dibrachius (Figure 2). These were not figments of the imagination. Janus was one of the oldest and most important of the native Roman gods. He had two faces (Figure 3). He presided over all beginnings in public and private life and was the god of all doors and gateways and portals, including the womb, and even Heaven itself. As the god of the opening of a new year he could look forward into the new and backwards into the old. The form of this twin faced god may be based on a variant of a cephalothoracopagus or diprosopus twin (Figure 4). The fearful Cyclops, blinded by Ulysses died at birth and had his nose above his single eye (Figure 5), a single cerebral hemisphere and an abnormal chromosome pattern. Atlas (Figure 6) with his crushing burden of the firmament of the Heavens was probably modelled on an occipital encephalocoele (Figure 7). Prometheus with his liver exposed to be torn by vultures may have been an exomphalos or more likely a gross gastroschisis. The great gods it was thought also liked to play, and they made monsters in fun or jest. In more recent times botanists have described the production of variants in nature by the term 'sport'.

In many civilisations malformed infants were venerated by astrologists as being sent from the gods to reveal the future. In the clay tablets of an Assyrian king ruling in Ninevah almost four thousand years ago there are long lists of malformations and their significance. Great calamities were foretold by the absence of nostrils, lips, tongue and anus, and great prosperity followed the birth of a child with three legs or an absent penis. In various forms other supernatural beliefs have persisted up to the present time, and deep within the minds of afflicted parents you may still find hidden fears and doubts, premonitions of disaster and ideas of punishment by an angry god.

In the Christian era, and especially when Christianity and the Church fought for the souls of men against residual beliefs in the old pagan gods and against witchcraft and devils, there was a greater tendency to ascribe malformations to evil spirits, to parental sin and even to bestiality. There are many painful episodes where good and scholarly men blinded by superstition acted unjustly. The learned anatomist Bartholin recorded objectively and without disapproval how in 1683 an unfortunate girl who gave birth to a child with a 'cat's head' was burned in the public square of Copenhagen.

The theory of maternal impressions represented a more humane belief. It flourished, especially in the seventeenth and eighteenth century and was accepted in some medical textbooks in America as late as 1889. An anencephalic child occurred because the mother saw a frog or a toad, a hare-lip followed a fright from a hare, and multiple bony deformities occurred because a mother watched a

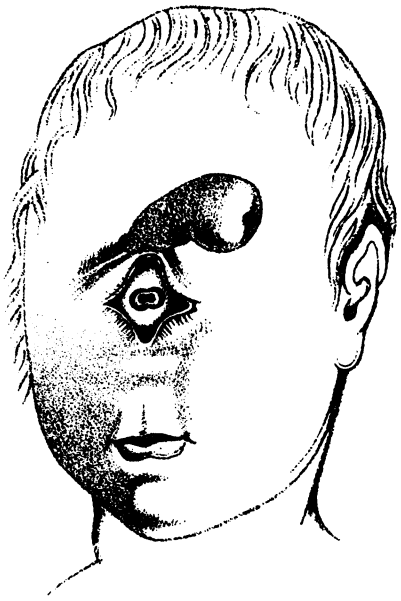


FIG. 5

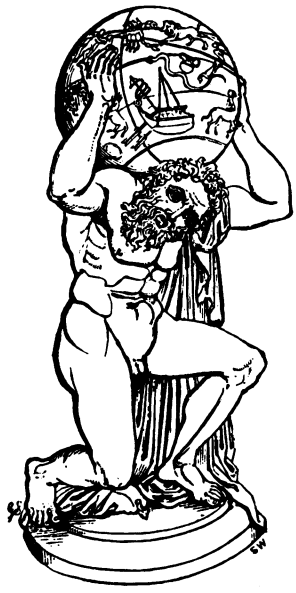


FIG. 6

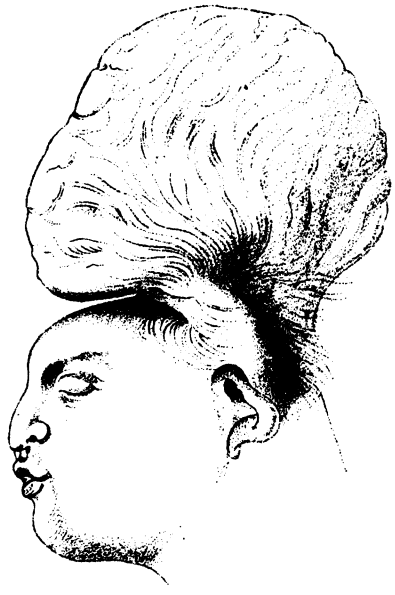


FIG. 7

FIG. 5.
Head of a cyclops monster (*Ahlfeld Atlas*, 1880).

FIG. 6.
Atlas carrying the Heavens. A drawing from a statue in Naples.

FIG. 7.
An occipital encephalocoele (*Ahlfeld Atlas*, 1880).

criminal broken on the wheel. This enormous and useless literature is a warning against retrospective study and the failure to observe controls, and yet wise and scholarly men discussed it in learned terms and believed in it, and perhaps it lingers still in the minds of some of our patients.

What conclusions can be drawn from the enormous volume of scientific work which up to now has been carried out on congenital anomalies? Certainly there is no single cause. Some are due to an inherited or genetic basis and sometimes Mendelian inheritance is evident. Dominant inheritance is usually manifest in trivial disorders often skeletal. Recessive inheritance is seen in a multitude of little known metabolic anomalies. These are rare except in inbred populations. Some conditions appear more frequently in the general populations when the recessive gene involved has a high incidence. This occurs in cystic fibrosis of the pancreas where a gene carrier incidence of 1 in 20 gives an nicidence of 1 in 1600 on chance mating. Since there is high penetrance the usual recurrence rate for a Mendelian recessive of 1 in 4 is found in sibs. In many anomalies, such as congenital pyloric stenosis, hare lip and anencephaly and spina bifida a statistical study will show clustering in kindreds suggesting a contribution from multiple genetic factors. This is multifactorial or polygenic inheritance. However, to have the genetic inheritance expressed requires a large contribution from unknown environmental influences. Even like twins with identical genetic inheritance and apparently very similar intrauterine environment may show one affected and one normal baby. Such lack of concordance in like twins shows how subtle may be the environmental influences modifying any genetic inheritance. Gross anomalies of chromosomes recognisable by existing methods are, as will be suggested later, relatively much more important in causing foetal loss early in pregnancy.

Many different agents, mostly chemical and physical, have produced malformations in experimental animals and often in doses far in excess of what the human foetus would ever encounter. Rubella and thalidomide are the best known agents in man, but even with all other known environmental causes they are numerically unimportant. The problem is far more complicated than the production of an arrest of development by the agent acting at a period and stage critical for the development of the region or part affected. Agents may produce anomalies in one strain of animals and not in another, and many environmental agents, known and unknown, may be powerless on their own, but may act if the genetic background is favourable. We must search carefully for any such environmental factors as can determine the expression of defects which are preconditioned by genetic factors. We can at present perhaps hope to control some environmental factors, but not our genetic inheritance. This search for facilitating or conditioning factors in the environment is the only present hope of reducing the toll of congenital defects. It is also not realistic to demand a guarantee that any drug is entirely safe and inert and will not influence the expression of some hidden genetic trait in some individual. The relationship between certain skeletal defects and such environmental influences as those exerted by thalidomide was relatively direct and the drug and not the genetic background was important. The disasters produced by this drug received disproportionate and unbalanced publicity. Let us hope that any discovery of other and less direct relationships will be treated by the lay press and pressure groups with

more appreciation of the whole tragedy of congenital disease in general. These great human problems go far beyond medicine but are not advanced in courts of law or by clever legal and journalistic minds pleading special cases.

Wastage Before Birth

Basic to all understanding of disordered reproduction is an appreciation that from the very beginning the developing ovum or embryo may be malformed, and whether malformed or normal often dies. In this study of unsurpassing difficulty tribute must be paid to Arthur Hertig of Harvard University. Though a pathologist, he was also trained in the classical school of embryology of the Carnegie Institute of Washington. With the gynaecologist, Dr. Rock, he studied uteri removed from women of known fertility where the clinical history suggested that opportunities for conception immediately before operation were highly favourable. By irrigation of tubes and uteri and by searching with the binocular microscope he found eight ova before implantation and of these only four were adjudged normal. Implanted in the uterus before the time of the next menstrual loss he found 26 early ova and considered 9 were abnormal. He considered it probable that in any one menstrual cycle, and with 100 previously fertile women exposed to optimal conditions for conception, 42 failed to fertilise or failed to implant a fertilised ovum and 16 implanted a recognisably abnormal ovum which would often be lost without the women being conscious of anything but a slightly delayed period. Forty-two women missed a period because they implanted an apparently normal ovum. It is accepted that 15 to 25 per cent of recognised pregnancies abort in the first trimester. Many of these, and all abnormalities recognisable at birth, are derived from those implanted as apparently normal ova. Hertig's figures cannot be precise but are illustrative of early pregnancy wastage and comparable with observations in animals.

It would be interesting to discuss possible causes of this high loss of ova and embryos. Possibly the age of the female sex cell at ovulation is, as suggested by Hertig, one factor. Undoubtedly chromosomal and genetic factors are important even from the earliest cleavage stages. They are certainly important in abortions in the early months of pregnancy. At birth chromosomal anomalies cause only 3 or 4 of every 1000 abnormalities, but they cause about 4 of every 10 spontaneous and recognisable abortions occurring in the first three calendar months. The distribution of this relatively high incidence of abnormal chromosome patterns in abortions is illustrated in such data as is given in Table 1. Only a few of the less severe chromosomal anomalies escape abortion and are born as malformations.

This evidence from chromosomal studies of a high loss of abnormal embryos is interesting because we suspect that a major proportion of all embryos abnormal for any cause are lost in the early months of pregnancy. Spontaneous abortions rarely yield material suitable for the recognition of these malformations, but there is another piece of evidence. In Japan legalised abortions have been permitted since 1952, and a dedicated group in Kyoto University have been able to obtain embryos of the second and third month which are less damaged than they usually are. The numbers are small, but for the anomalies studied the incidence of malformation in early pregnancy is considerably higher than at birth (Table 2). There

TABLE I

The incidence of various chromosomal anomalies in early abortions and in live births and showing the high abortion rate. Table from Smithells, R. W. (1971). *The prevention and prediction of congenital malformations in* Scientific Basis of Obstetrics and Gynaecology *by permission of the publishers Messrs. Churchill, London.*

Karyotype	*Frequency per 1000 in spontaneous abortions*	*viable infants*	*% Aborted (assuming 20% abortions)*
XO ('Turner's syndrome')	55	0.4	97
Triploids and tetraploids	55	0	100
Trisomy G (mongolism)	25	$\leqslant 2$	80
Trisomy E	33	0.5	95
Trisomy D	30	0.25	97
Trisomy A, B, C, F	20	0	100

TABLE II

The ratio of malformations found in legal abortions to those present at birth. Calculated from data of Nishimura and others (1968). *The numbers involved do not allow of any statistical significance.*

	Embryo/Infant Ratios
Exencephaly/anencephaly	3 : 1
Myeloschisis	9 : 1
Cyclopia	40 : 1
Hare lip	9 : 1
Polydactly	9 : 1

must be a high wastage rate for abnormal embryos, and they must contribute largely and disproportionately to spontaneous abortions. The apparent excessive loss of those with minor anomalies, such as hare lip and polydactly, suggests that often minor structural anomalies are linked to other less evident defects highly detrimental to intra-uterine life.

There are maternal causes for spontaneous abortions and for apparent infertility, and these may cause much distress to many families, but it is fortunate that so many malformed products are eliminated by abortion. Recently pre-natal diagnosis in the early months of gestation has allowed recognition in high risk families of a few other infants with congenital anomalies, some with chromosomal anomalies such as the Down syndrome, others with various rare metabolic anomalies, and now even anencephaly. For some it may be a moral question whether these should be electively aborted. Even if they were all to be so destroyed it would be only a tiny fraction of those eliminated spontaneously.

Other Aspects of Intra-Uterine Life

I have dwelt too long on congenital anomalies, but they are the largest single problem in the pathology of reproductive failure. There are many other aspects of intra-uterine life we might discuss. There is the central question of how the placenta, which immunologically is wholly foreign to the mother, is not rejected like any other foreign organ. There lies a secret central to the whole problem of kidney, heart and other transplants. There is the problem of how the placenta so different in structure in different animal species oxygenates and nourishes the foetus and of how disturbances in this may be recognised by histological or biochemical techniques. There are the fascinating studies of the complex factors which determine intra-uterine growth retardation. In the Western world this is not, as some of our social reformers would have us believe, a question of deficient maternal nutrition. It is very complex and in our society today it is an interesting fact that many more babies are underweight because their mothers have smoked than because their mothers have not had an adequate diet. Twins, like and unlike, are for the biologist a subject of increasing importance, and with like (one egg) twins there can be a wide difference in birth weight and the possibility that one twin may steal the life blood of the other. Before and after birth there is the fundamental study of how infections reach the foetus and how the whole complex immune system matures and reacts against what is foreign. There is the unsolved problem of what determines the time of birth. From those babies born prematurely we are learning that they do not all develop at the same rate and that organs and tissue activities do not always mature in the same order. Ashley Weech was a stimulating leader of the group in the Children's Memorial Center in Cincinnati in the forties. He studied individual variations in the maturation of enzyme systems responsible for the post-natal elimination of bilirubin through the liver cells. He appreciated the significance of individual biochemical differences in liver cell function among infants of apparently the same maturity for the occurrence of so-called 'physiological jaundice'. We have long looked for individual variations in structural maturity of the lungs and hoped they might explain why some infants of a given maturity survived and others died. It is only in recent years that the biochemists are showing us that here also the variation is biochemically mediated. Tissue and biochemical maturation and the factors influencing it are important as we pass on to consider the initiation and maintenance of respiration.

The Breath of Life

With backward glances into development during intra-uterine life I want to look briefly at the greatest adventure of every mammal—the attainment of extra-uterine respiration, and the co-ordination of development in the respiratory, nervous and circulatory systems which makes that possible. Survival into post-natal life is dependent first on a development of lungs sufficient to maintain air breathing, on nervous mechanisms controlling this breathing, and on profound changes in the circulation from a foetal to a post-natal pattern. Many other activities and adaptations are required later, but the breath of life is the first necessity for life outside the womb.

Anatomically the lungs in utero are fiilled with fluid and are often expanded to a degree very comparable with that after breathing air. Lung tissue can develop without a communication with the surface, as when the trachea is absent. For a long time pathologists have recognised that a large amount of amniotic sac debris, squames and fat from the foetal skin, are sometimes present in the air spaces in stillborn and newborn babies. This is taken to indicate inspiratory gasping strong enough to draw fluid through the air passages and to indicate an episode, or episodes, of serious foetal distress. However, an episode of anoxia occurring after the membranes have ruptured and when the amniotic fluid has drained away will not be revealed in this way. There has been a long debate as to whether the foetus normally makes other respiratory movements before it is born. There is now good evidence that rapid movements involving the diaphragm and the intercostal muscles occur for long periods before birth. They have been extensively studied in sheep and in the human by Dawes and his team in Oxford. Undoubtedly, despite previous scepticism, they have been felt by some women and recognised by some obstetricians. The muscular apparatus of respiration is well exercised before birth. These rapid movements of the respiratory muscles, and even irregular single and stronger movements superimposed on them, do not move the fluid filling the air space system through the dead space of the trachea and bronchi. They are not related to anoxic conditions in the foetus, but in severe asphyxia they are replaced by strong gasping movements which may draw liquor and debris into the lungs.

There must be debate as to how far any movements occurring in utero correspond to respiration. They must lack the reflex controls of post-natal respiration. An important factor in initiating and maintaining rhythmic breathing after birth is a mature nervous system responsive to the massive new inflow of stimuli from the external world and especially from the lungs and other receptors controlling the rhythm of respiration. We may recently have attained some new insight into physical and chemical conditions in the lung making aeration possible. A new challenge is the study of the nervous control of breathing and especially the pulmonary reflexes. We will never understand lung reflexes adequately until the complex of the brain stem respiratory centres has been unravelled, but at present we know little even of the lung receptors and of the peripheral and central chemoreceptors.

Fish make do with a cardio-vascular system by which blood passes in parallel circuits through the gills and through the body tissues. Even in amphibians and reptiles there is no complete separation in the heart of blood from the body from that from the lungs. The body tissues can thus never receive fully oxygenated blood, but the rapid movements of most fish suggest the system is moderately efficient. It has to suffice for the mammalian foetus, where the placenta can be equated with the gills, though there is a beautiful adaptation by which the foetal brain receives the best oxygenated blood. Normally the foetus in utero does not suffer from oxygen want, and we now know that terms such as 'Mt. Everest in utero' were based on measurements which emphasised only the variable but narrow margin of reserve of the placenta to any disturbance. With warm blood the birds and mammals attain the more efficient system by which all the blood after passing round the body is then passed to the lungs and oxygenated before being recirculated through the body. The newborn attains this perfected system virtually at the moment of birth by

closing the ductus arteriosus by a mechanism still debated and by certain haemodynamic pressure changes, consequent to this and to the opening up of the blood vessels of the lung.

We must now come to the preparation of the lungs for the breathing of air and for nearly thirty years this has seemed to hold the secret to what I regard as the central problem of perinatal pathology. Can findings in the lungs explain why many infants are born alive with a beating heart but fail to establish respiration, or more often establish respiration for a time, but in hours or at most days die with progressive respiratory distress and yet show no primary anatomical lesions in the lungs or other organs? Clinically this is the respiratory distress syndrome, and, with or without associated hyaline membranes in the lungs, it is responsible for nearly 40 per cent of neonatal deaths and now shares with congenital malformations major responsibility for neonatal death. I could weary you with how the simple branching tubules of the air spaces become increasingly complex and could illustrate this with histological sections or neoprene casts. I might describe how elastin develops in the air space walls and may help to prevent over-expansion of some spaces and resultant collapse of others. I would have to admit that in the walls of the terminal air spaces the development of elastin only becomes significant in the weeks and months after birth. We could discuss the lining cells of the air spaces and how increasingly blood vessels come into close contact with the potential air spaces. Some babies, usually under 28 weeks maturity, are obviously not structurally mature enough for independent life. Nearly thirty years ago I satisfied myself that structural maturation of the lung was not to be correlated closely with foetal age, weight or length. However, I think all would now agree that despite enormous study and research no recognisable structural deficiency and no anatomical immaturity can serve as the basis for these deaths, many of which occur around 35 weeks.

In the late 1950's it became increasingly apparent that lung structure alone was not adequate for air breathing if the surface tension forces usual at air-fluid interfaces operated without modification in the terminal air spaces (Figure 8). Surface tension forces would resist the expansion of these small spaces by air, but as they expanded the force would weaken. Tissue structures, such as elastin, would be inadequate to prevent the resultant over-expansion of some air spaces and the further collapse of any poorly expanded neighbours. Again towards the end of expiration the walls of the spaces opened by air would be pulled together by surface tension forces and each new inspiration would require the effort of the first. A physically unique substance, designated surfactant, was discovered which reduces the force of surface tension in minimally expanded air spaces and allows them to expand readily. As spaces expand with air the surfactant in their air-fluid film increases the surface tension and so prevents over-expansion. It also prevents them collapsing completely as they again become smaller on expiration. It is the presence of this substance which makes air breathing possible, and in all air breathing animals it develops in the lungs only as term approaches. In man it develops probably by at least two chemical pathways, one appearing early but markedly subject to depression by adverse influences such as anoxia, and the other developing rapidly around 35 weeks. Certain inclusions in the cells lining the air spaces

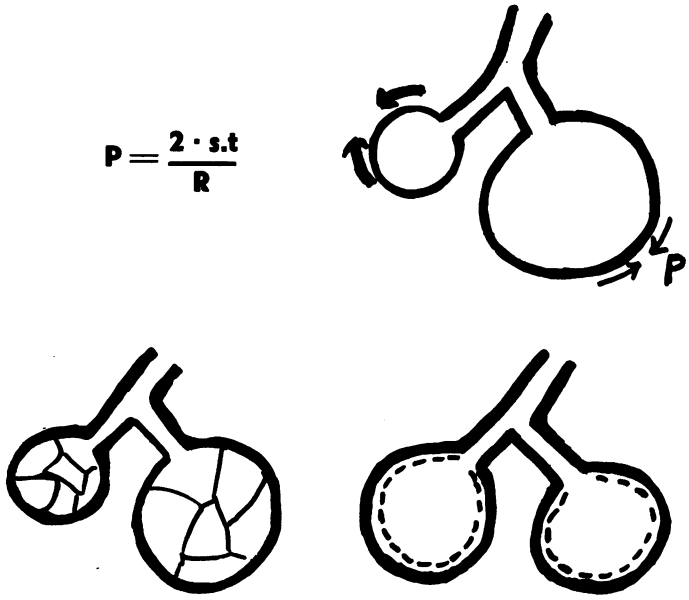


FIG. 8. *If surface tension remains constant the formula shows that the pressure resisting expansion of the air spaces is high when the spaces are collapsed; as they expand it diminishes and allows over expansion. Elastic or other structures in the wall are insufficient to control this. A surfactant film alone allows uniform expansion.*

may indicate its manufacture, but its study is still essentially a biochemical one. In the foetus it leaks into the amniotic fluid and the level there gives some indication of the preparedness of the foetus for extra-uterine life. The obstetrical department of this school developed one of the methods used to assess this. There is evidence that it reaches critical levels earlier under certain conditions, as in toxaemic babies and in those with prolonged rupture of the membranes. Its appearance is retarded in other states such as erythroblastosis and in the babies of most diabetic mothers. It thus seems that its delayed maturation is not simply a genetic or inborn biochemical immaturity, but is dependent at least in part on environmental factors operating on the foetus. Continued production is necessary and factors such as anoxia before, during and even after birth can reduce surfactant levels. Deficiency results in the respiratory distress syndrome. When there is deficiency of surfactant the pressure required to re-open air spaces during each fresh inspiration is raised approaching that of the first inspiration. Perhaps, because of the high negative pressure created within the air spaces as the infant struggles to aerate them fluid of high protein content escapes from capillaries and sometimes forms hyaline membranes. Many small air spaces remain collapsed and non-aerated and in these anoxic areas of lung the production of surfactant remains depressed and blood passing through them is not oxygenated. Whether maturation of surfactant can be usefully accelerated in man by glucocorticoid administration to the mother may still be debated. It does seem that synthesis is rapidly stimulated by birth, and if the infant with a deficiency can be kept alive for four to five days adequate levels will

appear, and here the techniques of continuous positive pressure to the airways (C.P.A.P.) are proving valuable.

There are many other problems about the initiation and maintenance of respiration, and the recognition of surfactant and its mode of production is only one very significant advance in an area where for years little or no progress appeared to be made. Immediately after birth the lining of the lung air spaces is in direct contact with the highest oxygen concentration reached in the body. Especially when the infant is in an oxygen enriched atmosphere the lining cells may sustain direct damage. We have still the problem of how the flow of fresh stimuli from all over the body following birth immediately starts the well oxygenated infant to breathe and what chemoreceptors and reflexes maintain and control breathing. Some asphyxiated babies only gasp as chemical influences operate directly on lower medullary centres or through peripheral receptors, and almost with their dying gasp some of these fight their way back to life or are resuscitated after prolonged failure to breathe. What are the consequences, immediate or remote, of such severe asphyxia especially to the highly sensitive human brain? Much depends on how long oxygen deficiency has lasted in utero and on the maturity of the foetus. For many years large groups of workers have been studying this, and endeavouring to distinguish it after birth and throughout later life from the effects of prematurity itself and of toxic levels of circulating bile pigment and the outcome of developmental deficiency. Debate continues on its relative contribution to the heavy load of mental and nervous deficiency in the community.

The baby whose breathing is established is now ready to face other hazards which we as pathologists must study. Hazards of adaptations to post-natal nutrition and to metabolism independent of the mother present problems very different from those of adult pathology. The pattern of infection is distinctive with some organisms assuming a different importance from later life and with cellular and humoral immune mechanisms developing rapidly. More clearly than in the adult, pathology appears not as a rigid self-contained discipline but linked to all studies of life and living matter.

Lough Gill in County Sligo is the site of the lake isle of Innisfree. The Irish mystic and poet William Butler Yeats wrote of his wish to find peace there.

"I will arise and go now, for always night and day
I hear lake water lapping with low sounds by the shore;
While I stand on the roadway, or on the pavements grey,
I hear it in the deep heart's core."

Not far away on his tomb in the churchyard of Drumcliff there is the inscription written by him before he died—

"Cast a cold eye
On Life, on Death,
Horseman pass by".

The pathologist must study with cold detachment both life and death, and he of all men is constantly reminded that

" . . . all men have one entrance into life
And a like departure."

Bibliography

The literature is very extensive. It may be entered through references given in the following books and papers. A few sources of historical interest are also included.

Ahlfeld, F. (1880). *Atlas zu die Missbildungen des Menschen.* Leipzig: Grunow.

Avery, Mary Ellen and Fletcher, B. D. (1974). *The Lung and its Disorders in the Newborn Infant.* Third Edition. Philadelphia: Saunders.

Ballantyne, J. W. (1902). *Manual of Ante Natal Pathology and Hygiene: The Foetus.* Edinburgh: Green.

Ballantyne, J. W. (1904). *Manual of Ante Natal Pathology and Hygiene: The Embryo.* Edinburgh: Green.

Barcroft, J. (1946). *Researches on Pre-Natal Life.* Oxford: Blackwell Scientific Publications.

Carter, C. O. (1969). Genetics of common disorders. *British Medical Bulletin,* **25**, 52.

Davis, J. A. and Dobbing, J. (1974). *Scientific Foundations of Paediatrics.* London: Heinemann.

Dawes, G. S. (1968). *Fetal and Neonatal Physiology.* Chicago: Year Book Medical Publishers.

Dawes, G. S. (1973). Revolutions and cyclical rhythms in prenatal life. *Pediatrics,* **51**, 965.

Hertig, A. T. (1968). *Human Trophoblast.* Springfield, Ill.: Thomas.

Morison, J. E. (1970). *Foetal and Neonatal Pathology.* Third Edition. London: Butterworth, also as *Patologia Fetal y Neonatal,* Barcelona: Editorial Pediatrica, 1972.

Morison, J. E. (1974). Perinatal Pathology in *Clinical Perinatology* edited by Aladjem, S. and Brown, A. St. Louis: Mosby.

Morison, J. E. (1974). Birth defects and congenital disorders. *Encyclopaedia Britannica.* Fifteenth Edition. Chicago: Benton.

Nishimura, H., Takano, K., Tanimura, T. and Yasuda, M. (1968). Normal and abnormal development of human embryos. *Teratology,* **1**, 281.

Potter, Edith L. (1961). *Pathology of the Fetus and Infant.* Chicago: Year Book Publishers.

Warkany, J. (1971). Congenital Malformations: Notes and Comments. Chicago: Year Book Medical Publishers.

WILLIAM BAIRD McQUITTY—CLINICIAN

by

H. W. GALLAGHER, M.B., F.R.C.S.(Ed.)

Ards Hospital, Newtownards, Co. Down

IT IS SAID of the Irish that our memories are far too long and instead of preparing for the future we live in the past. This may apply to our socio-political outlook but we are all too ready to forget the giants on whose shoulders we stand. The only advantage in looking backwards is to prepare for the future and by examining the life and work of one of those giants, whose name is better known than his career, we may be able to learn something for our own improvement and to the advantage of our students in the future. The man to whom I refer is, of course, William Baird McQuitty, whose name is remembered in the McQuitty Scholarship of the Royal Victoria Hospital, Belfast. This scholarship is unique. It is the only prize, awarded by that hospital, to be established by public subscription.

The initial subscriptions were given at a public meeting held under the Chairmanship of the Lord Mayor of Belfast in January, 1911. The sudden death of Dr. William Baird McQuitty on the 30th December, 1910, after an illness of only a

few hours duration, had evoked such sorrow throughout all classes and creeds that leading articles in local papers suggested that some permanent memorial should be created to perpetuate the memory of a beloved physician.

In my student days I do not think a single one of us knew why prizes named the Malcolm and Coulter Exhibitions and the McQuitty Memorial Clinical Scholarship were awarded on the results of separate examinations, or who the various gentlemen were, or why they were remembered in such a fashion. Since 1940, through the initiative of Dr. Robert Marshall, a short history of the creation of each prize and a description of the person it commemorates, is given to each successful candidate. Not until the publication in 1954 of Dr. Marshall's book "Fifty years on Grosvenor Road" did I learn that the McQuitty of the Scholarship had been Senior Honorary Assistant Physician to the Royal Victoria Hospital when he died suddenly at the zenith of his career at the early age of 48 years. His age at death is wrongly given there and in all later records. It was 47 years.

Family History

The McQuitty sept of the Buchanan Clan, whose territory abuts Loch Lomond in lowland Scotland emigrated to Ulster in the late seventeenth century. According to the book, written and recently published by Dr. Ian Adamson, a member of this Society, the McQuittys were descendants of the Cruthin, the ancient kindred, the oldest race of Irishmen. They were returning to their homeland after an exile of 1,000 years. They fled from Scotland to escape religious persecution. They were non-conforming protestants—Covenanters—who would not bow the knee to any Bishop be he Anglican or Presbyterian. They were of that breed of Ulstermen who a century later tried to destroy all political and religious discrimination in this island by armed revolt against established order and religion. We are still looking forward to such a Utopia and after 200 years of intermittent violence we should surely have learned that violence can never produce tolerance.

In the early years of the nineteenth century some of the McQuitty family forsook the faith of their fathers and joined the established church and a generation later, about 1860, a James McQuitty who had business interests in Larne and Belfast married Alicia Ann Courtney Baird who was also a member of the Church of Ireland.

Early Life

William Baird, the second of four children of this marriage, was born in 1863. The mother of this young family died in 1872, and the father in 1876, leaving the four children in the care of relatives. William went to the home of his uncle, William Savage Baird, who a few years earlier with his brother, George Courtney Baird, had founded the Belfast Evening Telegraph. The business in those early days demanded the re-investment of most, if not all the profits, so there was very little money available for the education of adopted children. Fortunately William was a bright pupil and the Charters Prize carried him from the Belfast Model School to the Royal Belfast Academical Institution for free tuition for two years. Because of his outstanding academic success and continuing financial need, the bursary was extended for another year. At "Inst", in successive years he gained exhibitions

in the Junior, Middle and Senior Grades of the Intermediate Board for Education and in 1881 he entered Queen's College, Belfast, with an Entrance Scholarship and the Porter and Tennant Exhibitions.

Undergraduate Years

His undergraduate record in Queen's College and the Royal University of Ireland has probably never been equalled. He won over 30 prizes, scholarships or exhibitions, about a third being first places. In 1884 he was first of First Class Honours in Experimental Science in B.A., winning a University studentship valued at £500. His other scholastic awards totalled £300. Money then had almost the same value as a century earlier when Goldsmith's parson was passing rich on £40 a year. A third of a century later my father, also a parson, was able to get married when receiving a stipend of £1 per week, with the addition of £1 per month for his wife.

The value of the prizes awarded by the Royal University was remarkably high. The policy was to encourage academic excellence by intense undergraduate competition for a few very valuable studentships. I do not think that it was a good policy, in fact the winning of the studentship probably had a bad effect on McQuitty's academic career. He never again achieved the peak performance of first of first class honours. In 1885 he passed the hurdle of M.A. with first class honours —not first of first—and both the number and value of his money prizes after 1884 diminished. Perhaps the economic drive was no longer present, perhaps the effort required to achieve the Studentship was too much for the indefinable something which had kept him not only on the crest of the wave but also at the leading edge. Whatever the reason, in 1887 he suffered further disappointment. In final medical he obtained first class honours in obstetrics, second in surgery and only a pass, albeit with a recommendation for honours, in his favourite subject—medicine. This comparative failure was mentioned by the anonymous writer of his obituary in 1911 in the British Medical Journal . . . "he was considered easily the best man of his year, and took the degrees of M.Ch. and M.A.O. with honours, but even his immense capacity and steady nerve for once played him false, and he was only recommended for honours in M.D. instead of getting first place with first class honours, which was considered his due".

He was lucky in his misfortune in that his first class was in obstetrics so that his entry in the Medical Directory could quite legitimately read: —"McQuitty, Wm. Baird, M.A., R.U.I. (1st Honours and Exhib.) 1885, B.A., (1st Honours and Exhib.) 1884, M.D., M.Ch., M.A.O. (1st Honours) 1887". Perhaps not the whole truth, but certainly not a lie.

The practice of obtaining references from as many of one's teachers as possible, immediately on qualification has long since ceased. McQuitty obtained references from 20 clinical and pre-clinical teachers and from the Rev. J. L. Porter, D.D., Th.D., D.Lit., President of Queen's College. All predicted a brilliant career, none more clearly than Professor Cuming who wrote: —"His success in the examinations has been most exceptional, and he seems equally strong in theoretical and practical work. He is a gentleman of rare ability, who will distinguish himself in his profession".

The Royal University of Ireland, awarded as primary qualifications what we now recognise as higher degrees. I do not know the historical reason for this but it meant that the graduates were eligible without further evidence of proficiency for hospital appointments. In fact most of the consultant physicians and obstetricians in Belfast at that time had only primary degrees. It was left to the surgeons, most of whom were fellows of a Royal College, to blaze the trail for post-graduate education and higher degrees. McQuitty did however obtain the post-graduate Diploma in Public Health from Cambridge in 1890, thereby making himself one of the best qualified practitioners in Belfast, when, in the same year, he set up his plate in College Square East. He had spent the three post-graduate years working at the Royal Hospital, Belfast; Rotunda Hospital, Dublin; The Great Ormond Street Hospital for Children and the London Hospital where he had clerked for Hughlings Jackson, the world famous neurologist, still remembered in the term "Jacksonian Epilepsy".

General Practice

Setting up in practice was always a gamble, although for good doctors it was usually successful, and McQuitty, even at that early stage seems to have been, at least, better than average because he soon obtained two appointments, one as Medical Officer to the Royal Irish Constabulary and the second to the Staff of the Ulster Hospital. For the appointment to the R.I.C. he had all his 21 references printed for distribution to the equivalent of the Police Authority. A surviving specimen is in the Public Records Office and a photostat copy is in the archives of the Royal Victoria Hospital.

Many years after he set up in practice, in fact not long before he died, a Mrs. Glendinning of Balmoral Avenue came into premature labour with her first child. Mr. Glendinning set out on his bicycle to summon medical help. It was dark and he had no lamp. On the way to the nearest telephone situated on the Lisburn Road opposite Marlborough Park he, himself, almost received a different type of summons when he was stopped by a policeman. However, when the circumstances were explained, and especially when it transpired that it was his "own" Dr. McQuitty who was being sought, the policeman sent the distracted expectant father safely on his way. Dr. McQuitty duly attended Mrs. Glendinning who was safely delivered of a girl. I know that the story is true because the only person still alive who took part in the drama—the infant—is the sister-in-law of Professor George Adams, C.B.E.

This story, along with the family tradition that the treatment of ingrowing toenails in policemen was his bête-noire, shows that his practice was truly general although at the same time he was a consultant on the staff of a teaching hospital. There was nothing strange in those days in combining general and specialist practice, indeed the custom only died out at the inception of the Health Service 26 years ago and now we are trying to devise methods of getting general practitioners back into hospital.

Honorary Surgeon to the Ulster Hospital

In September, 1890, Dr. Strafford Smith resigned his appointment as Honorary Physician to the Children's Department of the Ulster Hospital. The medical staff

agreed to Dr. Calwell's request that he be permitted to transfer from the surgical to the medical side and they also recommended that W. B. McQuitty be appointed to the vacancy of Honorary Surgeon. The Hospital Management Committee agreed and the Minutes of the next monthly meeting of the Medical Staff duly record the presence of Dr. McQuitty. There is nothing to suggest that he was welcomed to the staff nor is there any indication to suggest that there had been any other applicants for the position.

In 1891 he examined in surgery for the hospital gold medal, but because of the unfortunate loss of hospital records during the war we know nothing about his surgical work or what operations he performed. There is a photograph in the archives of the Royal Victoria Hospital showing him about to operate. His black coat and striped trousers are protected by apron and detachable sleeves but his hands are of course uncovered. He is holding a long amputation knife and the patient has had a tourniquet applied above the elbow. The assistant, who is holding the arm with one hand, has a stop watch in the other. The anaesthetist is using a Clover inhaler and two stalwarts are ready to re-inforce his efforts if he loses the battle for oblivion. This phrase "The Battle for Oblivion" has been used by Betty McQuitty as the title of her history of the discovery of anaesthesia. She is the author-wife of the internationally famous photographer and author, William Baird McQuitty, so named in memory of his uncle, our Dr. McQuitty.

Honorary Physician to the Ulster Hospital

In 1891 there was another defection from surgery to medicine on the Ulster Staff, this time by Dr. McKisack. Dr. Dill, Professor of Midwifery in Queen's College and Chairman of the Medical Staff Committee of the Ulster suggested that this should not be taken as a precedent, but in 1893 McQuitty followed the example of McKisack and Calwell and transferred to the medical side to replace Calwell who resigned.

We know even less of his work as a physician in the Ulster Hospital than of his surgery. There is not even a photograph to help us. But he had a way with children who were not intimidated by his presence. His nephew, William, remembers many happy episodes but when 6 years old he stumped his uncle by asking "Why does paper become black when it burns and coal becomes white?" The only answer he got was "It's a good question!" He resigned in 1900 shortly after his appointment to the Royal Hospital. The Minutes of The Ulster Hospital Staff Meeting for November, 1900, are interesting—"Hon. Sec. read letter from McQuitty resigning his post. As he had been connected with the Hospital for more than ten years, Staff recommend that he be appointed to the Consulting Staff and vacancy advertised in usual manner.

"Dr. Mitchell gave notice that at the next meeting he would move that in future, all appointments be made on the distinct understanding that the Staff should not be asked to change any one appointed to a surgical vacancy to a medical vacancy at a subsequent date and vice versa . . . "

This Dr. Mitchell was the famous A. B. Mitchell. He had been appointed to the staff of the Ulster in 1894 and as a career surgeon he obviously did not want surgical jobs to be used as stepping stones to medical consultancy as had happened

at least three times in the previous ten years. His proposal was accepted at the next meeting.

The method of appointment to the staff and the power of the Medical Staff Committee of The Ulster Hospital at that time were remarkable. The usual method of appointment to the other hospitals in Belfast, and probably throughout he three kingdoms up to the inauguration of the Health Service 26 years ago, has been well described by Sir Ian Fraser in his Robert Campbell oration (1973). It involved a printing of references in the same manner as McQuitty had prepared for his appointment to the R.I.C., and a canvass of all the members of the management committee. The resulting appointment was often a matter of patronage rather than a choice of ability.

McQuitty's resignation from the Ulster Hospital was caused by his decision to concentrate his hospital activities to the Royal Hospital to which he had been appointed as Honorary Assistant Physician. He was a regular attender at staff meetings and took his turn in examining for the Coulter and Malcolm Exhibitions and in 1902 he gave the introductory lecture at the commencement of the teaching session. That function then did not have the importance or publicity which it has to-day and there is no record of either the subject or the content of his address.

Contributions to the Literature

Soon after his appointment to the Royal he made his first recorded appearance on the rostrum of this Society. In 1901 he demonstrated three cases of myxoedema and in 1902 a case of aortic stenosis. This was followed in 1904 with a demonstration of muscular dystrophy and also of general paralysis of the insane, followed four years later by the demonstration of a case of general paralysis in a juvenile. In the same year, 1908, he showed a case of splenomegalic polycythemia to the Ulster Branch of the British Medical Association. Advice on examination for life assurance in 1903 is the only formal address of which we have records. Each contribution is interesting and useful but only that dealing with life assurance has not been overtaken by subsequent scientific discoveries. In it he tries to hold the balance evenly between the applicant and the insurance company. His description of the hypochondriac is apt and his advice on how to deal with those who would conceal all damaging facts is valuable. But let him speak for himself: —

> "Two classes of applicants give trouble to the examiner:
>
> (1) The hyper-conscientious proposer who magnifies all the trivial ailments he has ever had into serious and important illnesses, as, for example, referring to a common cold as congestion of the lungs, a few twinges of muscular pain as an attack of rheumatism, a diminished secretion of urine as an affection of the kidneys. Fortunately those who belong to this class are few in number, and easily recognised; their statements therefore can be discounted.
>
> (2) The second class is a much larger and more troublesome one, in which I place all those who see no harm in representing unpleasant facts as to personal or family history in the most favourable light possible to themselves, who think it undesirable to place too much information at the disposal of an insurance company for the same reason that they preserve a discreet reticence when confronted with the Income Tax Commissioners.
>
> An applicant in this class is in much the same position as a hostile witness in a law court, and it requires a certain amount of tact to extract the necessary information without appearing to cross-examine him too closely".

His case reports show the acute observation and attention to detail for which he was renowned and which were noted in the obituary notice in The Lancet—"He appeared at times to the greatest advantage at the local medical societies, when, with the keenest powers of observation, he showed rare cases, and at the same time indicated by a few words his complete knowledge of medical literature". His love of music could perhaps have had an effect on his choice of language and when describing aortic stenosis he preferred the euphony of the Latin "Pulsus rarus, parvus, tardus", to the English "infrequent, small, slow pulse." His description of myxoedema was his most lengthy and important contribution and apart from being an excellent description of the disease he records two clinical signs which had not previously been described. One is the reversibility of colour change of the hair when proper treatment is commenced and the other is profuse sweating of face and scalp which may persist when the rest of the skin is dry, hard and cracked. This sweating which he observed in two patients got worse in both on exercise and in one also on eating. I must admit that I have never heard of this persistence of sweating of the head and it does not appear in modern descriptions of the disease. Treatment with thyroid extract had been introduced in 1891 but the patients in whom he observed this sign had obviously been grossly myxoedematous for many years before being seen by him.

Physician to Out-patients

His appointment as assistant physician carried only the duty of attendance at out-patient clinics. There were no beds in which he could, as a right, treat his patients except during the prolonged absence of a senior physician. Like all other staff appointments the position was purely honorary although there was a small honorarium for teaching—presumably a bit more than the few pounds, even at times as little as thirty shillings, which were distributed at Staff Meetings of the Ulster. To look at the emoluments of the professors of this school up to 1945 makes one realise what Hippocrates meant when he enjoined us to honour our teachers. In 1940 when I joined the Army as a lieutenant I was paid far more than any clinical professor in the University. As the war continued and inflation started, army pay increased but not that of the professors. Their annual emoluments from 1939–1945 were £300—considerably less even than they had been 30 years earlier.

The out-patient department was where he made his name. He was careful, thorough, painstaking, acutely observant and meticulous in note-taking, and had a way with patients and students, both of whom flocked to his clinics. His teaching of students, was so good that when they became general practitioners in the province they called him out in consultation in increasing frequency although Calwell, McKisack and Professors Lindsay and Sir William Whitla were the more senior physicians also available. He had very cold hands and usually asked for hot water in which to wash before examining a patient. This became well known and water was usually ready for his visit, but he was also known to have warmed his hands by playing on the household piano before entering the sick room.

Until recently a case book of some of his private patients was still in existence. Its neatness, line diagrams and shorthand notes demonstrated his clarity of thought and attention to detail so often remarked of him.

Sir William Whitla had a very high opinion of him, high enough for him to ask W.B. to become his personal physician. His hospital patients loved him because not only was he clever but he was humane and more than that, he treated his patients not only as human beings but as ladies and gentlemen. On one occasion a young woman obviously the "worse for drink" maintained that she had only had one small whiskey that day. "I hate to doubt the word of any patient, but I believe that this young woman is not telling the truth" was his characteristic comment to the students.

His diplomacy was also an attribute which helped in many a difficulty. I am sure that all of us have seen many patients to whom he would like to have said "Go away home and have a good bath". Perhaps this does not happen as often as it once did, but what would you do if called upon to treat a high society lady whose only treatable condition was filthiness? In these circumstances McQuitty prescribed and probably dispensed a supply of sugar coated pills whose only constituent was white bread. The accompanying instructions were that one was to be taken daily after a hot bath. No wonder he was a popular physician and no wonder his fame spread far and wide—wide enough to attract an American couple to come from New York specially to consult him. They arrived in Liverpool on January 1st, 1911, and when they learnt that he had died two days previously they returned to New York on the next available ship. His success as a physician does not seem to have given him any false notions as to the efficacy of the medicines he prescribed. If he kept a common-place book it has not survived but he thought sufficiently highly of this quotation, attributed by him to Drake, to copy it out in his own hand: —"Medicine has been defined to be the art or science of amusing a sick man with frivolous speculations about his disorder and of tampering ingeniously till nature either kills or cures him". I have not yet traced the source of this wisdom but I presume it is from the pen of Daniel Drake born in a log cabin in the Kentucky wilderness in 1785. He became a noted medical educationalist and his writing style and eloquent lectures made him famous. It certainly suggests that McQuitty shared the therapeutic nihilism of Sir William Osler and Oliver Wendell Holmes.

By 1910 his consulting practice was large enough for him to give up general practice completely and he moved to 12 University Square, Belfast. This was to have been not only the centre of his practice but also his house and home to which he hoped to bring his fiancée, a Miss Bowden of Plymouth, whom he had met on one of his annual holidays.

Recreation

These holidays must have been a source of continual enjoyment in prospect and retrospect to W.B. as he was affectionately called by his contemporaries and students. Every year, usually with his brother James, he visited a foreign country. France, Italy, Switzerland, Scandinavia, U.S.A. and even Russia were all visited. They were a musical pair and were much in demand for ship-board concerts—James as a singer and W.B. as accompanist.

Although completely self-taught, W.B. had become an accomplished church organist. During his student days he had been honorary organist and choirmaster, as his brother George before him, in St. Jude's Church of Ireland in Belfast, and

he maintained his interest in and membership of that church till he died and often trained the choir for special services. Characteristically he made himself available to deputise for organists who were ill and in a period of Church Extension he was much in demand to "open" new organs—if that is the correct word to use in association with the dedication of a new church and organ.

Medicine is more than a profession. It is a way of life which pervades all our activities—we look at life through medical spectacles and often our recreation and leisure pursuits are but different facets of our medical personalities. So it was with McQuitty. He was Medical Officer to the National Society for Prevention of Cruelty to Children and valued this appointment so highly as to have it listed in the Medical Directory before his other attainments. His practical philanthropy was not confined to children and this is an opportune time to tell, probably for the first time, a characteristic act of kindness.

We as a Society are looking forward to occupying some time in the near future a new home which is being built in the grounds of Queen's University where we are to-night. In a place of honour there will be the stained glass window first erected in the Medical Institute in 1901 by Sir William Whitla as a memorial to Dr. William Smyth and to commemorate the tragedy in which he lost his life. Some fellows and guests may not know that when all others had refused help, he, William Smyth, had continued providing material and medical help to the islanders of Arranmore who were stricken with typhus. Smyth succumbed to the disease leaving behind a widow and daughter. McQuitty created a fund to help them face their future which was spent in Bangor where they lived for many years.

Learned Societies

He joined this Society in 1888 and was a regular attender at the monthly meetings but does not appear to have taken part in any discussion following presentation of cases until 1904. In the 90's a recurring phrase in the Minutes is that the Paper or presentation was *criticised* by various members. With the new century, either our predecessors became less pugnacious or the word criticism took on a different shade of meaning because the papers were *discussed* at their conclusion. McQuitty became a fairly frequent contributor to these discussions.

In 1892 he voted against the proposal that Belfast City Council be recommended to adopt the Notification of Infectious Diseases (Ireland) Act. This seems to be a frightful admission to have to make about a leader of the profession. When we realize that there was no hospital for infectious diseases, and that this was probably an attempt to make the city authorities wake up to their responsibilities, we can more readily understand the apparent obstructionism.

From 1893–1895 he was Joint Secretary for Pathology with John Campbell, F.R.C.S. The office lapsed in 1904 but judging by its occupants it must have been important and certainly it was no sinecure. Their immediate predecessor was Henry Burden, Pathologist to the Royal Hospital. They were expected to provide a clinical-pathological service for the members and fellows of the Society on an honorary basis and I wonder if any two surgeons in the province to-day would feel capable of following in their footsteps, and if capable would any be altruistic enough to do so? In the session 1893-4, 33 specimens were presented to them for

microscopic examination and in addition 16 specimens of urine were examined qualitatively and quantitatively for albumen and urea. Their report for the session ends . . . "During the session the Council authorised us to spend a sum not exceeding two pounds on re-agents and appliances; we have availed ourselves of this permission, and have derived great benefit from having a free supply of re-agents. Formerly such expenses fell upon us personally". In the following year they reported on 38 specimens of tissue, 6 of sputum and 15 of urine. They then thought they had done their stint and who could blame them? They were succeeded by James Lynas, M.B., and J. Lorrain Smyth, the first Musgrave Professor of Pathology in Queen's College.

He was appointed Honorary Treasurer in 1902. He relinquished this on being appointed to Council in 1905, and was appointed Vice-President in 1906. During his treasurership he was responsible for collecting the subscriptions for a bust of Sir William Whitla which was commissioned at the cost of £150. The sculptor requested a further allowance to cover his travelling expenses from Dublin, but the majority of Council members did not think it was a good likeness and refused to pay any more. Indeed they had no more money available and it would appear from the Minutes that the £150 target was never attained, and presumably McQuitty made good the deficit from his own pocket.

The Association of Physicians of Great Britain and Ireland was founded in 1908. McQuitty and James Alexander Calwell were the only two Belfast physicians to join the two professors—Sir William Whitla and James Alexander Lindsay—in the select band in the foundation of that noted society.

He did not take a very active part in the local British Medical Association but in 1909 he played an important role in the annual conference held that year in Belfast. One would think that his position of Senior Honorary Assistant Physician to the Royal would have entitled him to the secretaryship of the Section of Medicine. His appointment as Vice-Chairman to Professor Lindsay, M.A., M.D., F.R.C.P., must indicate the esteem in which he was held by his colleagues.

Early Death

On the 31st December, 1910, all Belfast, in fact all Ulster was stunned by the news of the sudden death from cerebral haemorrhage on December 30th of this beloved physician at the early age of 47 years, after an illness of only 15 hours. The obituary notices in all the Belfast papers were long and laudatory. The Belfast Evening Telegraph, of which his brother James was now a director, asked several of W.B's. colleagues to give appreciations of his life and work. Of these, that by Sir William Whitla is representative and part is worthy of repetition . . . "he had the rare genius for taking pains with the problems submitted for his solution, unravelling each intricacy by a careful determination of the condition of every organ of the body, before forming or pronouncing any opinion upon the nature of the disease under investigation. The most needy sufferer coming under his care invariably received from him of his best, and never less than did the wealthy who called upon him for advice . . . "

The sorrow of his colleagues and fellow citizens was demonstrated by the vast crowd that accompanied him on his last journey—this time past the Royal Victoria

Hospital to the City Cemetery. The esteem in which he had been held was manifested by the groundswell of public opinion that something should be done to perpetuate his name. The Belfast Evening Telegraph, in a leader of 27th January, 1911, suggested that the institution of a Clinical Scholarship and the erection of a bronze bust or plaque, both in the Royal Victoria Hospital, would be fitting memorials.

On the same evening the Lord Mayor chaired the meeting to which I have already referred. At least 86 people attended and a further 23 took the trouble to apologise for their absence. A representative committee was elected to receive subscriptions for a memorial whose nature was to be determined by the committee. W. W. D. Thomson, later Professor Sir William Thomson, D.L., M.D., F.R.C.P., of this school was specially elected to the committee to represent the students.

We know nothing of how the committee did its work but in a few months £750 was presented to the Medical Staff of the Royal. At a staff meeting on 6th June, 1911, it was decided that the McQuitty Memorial Clinical Scholarship should be awarded annually on the results of a clinical examination in medicine, surgery, gynaecology, ophthalmology and pathology to be held at the termination of a student's third winter session in the Royal Victoria Hospital. The scholarship was and in spite of inflation remains £30. The first winner in 1912 was H. P. Malcolm who became a consultant surgeon on the staff of the Royal and who died only a few months ago.

Neither bust nor plaque was erected but a physical memorial does exist. It is a stained glass window, made in Belfast, and erected in St. Jude's Church in 1914 in memory of the two brothers, W.B., and George Henry and their sister, Ellie S. The three had all been associated with the choir of St. Jude's, each of the brothers as honorary organist and choir master and sister Ellie as a leading member of the choir. The window was erected by their brother James who had accompanied W.B. on many of his holiday tours. He was well known in the printing and journalistic worlds, being joint proprietor and director of the Telegraph. He led the campaign for the betterment of conditions of the workers in the printing trade, showing, I think, that W.B's. humanitarian instincts were a family characteristic.

Each year the McQuitty scholar is given a scroll which records his name as the winner and which outlines the life of McQuitty and the founding of the Scholarship. It reads . . . "Of all those who have been Physicians on the Staff of the Royal Victoria Hospital none had a more brilliant academic record than William Baird McQuitty whom this scholarship commemorates. He became an Honorary Assistant Physician in 1900 and died in 1910 aged 48 years. He is remembered for his unfailing gentleness and kindness to all who came in contact with him. The scholarship was created by his friends and colleagues". The age is inaccurate and I suppose it could be argued that all who subscribed to the Scholarship were in fact his friends.

The first edition of this sketch was written over 30 years ago by Dr. Robert Marshall who is probably the only person still alive who remembers McQuitty as a teacher and physician. He also had the distinction of following McQuitty on to the staff of both the Ulster and Royal Victoria Hospitals.

So great had the impact of McQuitty been on the young student that 63 years later Robert Marshall could produce in his own inimitable style, within 24 hours of its request, an appreciation of his teacher. I am indebted to him for this, part of which reads . . . "I was then (1910) a third year student and at the beginning of clinical instruction. I cannot remember who it was that advised me that on Saturday mornings I should go to McQuitty's extern. I did so, and thus began a kind of hero-worship which has lasted for some sixty-three years. I was too raw to appreciate the clinical acumen, based on 'an infinite capacity for taking pains', for which he was already famous. It was the man himself and his approach to his chosen task which won for him my youthful devotion. Hospital patients were, for the most part, of a poverty-stricken class, and personal hygiene was of a low standard; but W.B. never showed any distaste for unclean bodies or soiled clothing. His manner was gentle and his compassion was so deep that it didn't show. He was never either patronizing or condescending. He addressed them as he would ladies and gentlemen, and I remember thinking at that time that he felt that they were indeed ladies and gentlemen. His early death was mourned by his colleagues in hospital and outside it, by his patients rich and poor, and, perhaps as keenly, by those students for whom his out-patient room had become a kind of shrine".

In my opening remarks I said that a biographical lecture such as this should not only be of interest, it should also be of benefit. I think the lesson McQuitty's career tells us is so obvious it hardly needs underlining. He was a great physician not only because he had a first class brain. No doubt that was a help but ordinary folk like myself can draw comfort from the fact, often stressed, that a first class doctor does not need a first class brain but he should have the three other qualities so clearly exemplified by McQuitty, the capacity for hard work, the willingness to work hard at times for no financial reward and most important of all—compassion. In this present crisis, no matter who becomes our paymaster, we should retain the willingness and facility for doing some work for the love of the art rather than the love of money, otherwise we will lose completely and for ever, the right to call ourselves a vocational profession, and with that loss it would be very difficult to retain any of these qualities.

Acknowledgements

This lecture could never have been compiled without the help and co-operation of many people to whom I am very grateful. They include Messrs. W. B., and J. L. McQuitty, Dr. Robert Marshall and Miss Glendinning for personal recollections, Dr. R. S. Allison and Dr. R. L. McCorry for access to the archives of the Royal Victoria and Ulster Hospitals, Dr. D. A. Pyke for searching the records of the Association of Physicians, Miss Webster and Staff of the Medical Library of Queens University, Belfast, and Miss Jean Fletcher who patiently typed many pages before the manuscript attained its final form.

References

Primary Sources

Glendinning, Marjorie (1973). Personal communication.
Marshall, Robert (1973). Personal communication.
McQuitty File. Public Records Office of Northern Ireland.
McQuitty Papers, in possession of J. Lloyd McQuitty, Q.C., and W. Baird McQuitty, M.A.
Minutes of Medical Staff Meetings, Royal Victoria Hospital, Belfast.
Minutes of Medical Staff Meetings, The Ulster Hospital, Dundonald.
Minutes of the Ulster Medical Society and its Council.

Secondary Sources

Allison, R. S. (1972). *Seeds of Time.* Belfast: Brough, Cox and Dunn.
Jamieson, J. (1959). *The History of The Royal Belfast Academical Institution,* 1810-1960. Belfast: Mullan.
Marshall, R. (1954). *Fifty Years on the Grosvenor Road.* Belfast: Royal Victoria Hospital.
Marshall, R. (1973). *The Story of the Ulster Hospital.* Belfast: Ulster Hospital.
Moody, T. W., Beckett, J. C. (1959). *Queens, Belfast.* London: Faber & Faber.
Strain, R. W. M. (1967). A History of the Ulster Medical Society. *Ulster Medical Journal,* **36**, 73.
Strain, R. W. M. (1969). University Square. *Ulster Medical Journal,* **38**, 1.
Transactions of The Ulster Medical Society 1893–5.

References

Adamson, I. (1974). *The Cruthin.* Conlig, Newtownards: Nosmada Books.
Fraser, I. (1973). The Campbell Heritage Lives On. *Ulster Medical Journal,* **42**, 116.
McQuitty, Betty (1969). *The Battle for Oblivion.* London: Harrap.

MEDICAL STUDENTS AND THEIR EDUCATION

by

T. B. SMILEY, M.C., M.B., F.R.C.S.

ANNUAL ORATION AT OPENING OF TEACHING SESSION

ROYAL VICTORIA HOSPITAL

LADIES AND GENTLEMEN, may I first say how gratified I am to see so many of you here, and especially my senior colleagues. It is always a pleasure to see them, and it must always be so at the Royal Victoria Hospital. However, I hope that you will forgive me if I address myself principally to the younger generation. I would like to associate myself with Mr. Irwin's welcome to those of you who have just come to hospital. It is a very important step in your education. We all hope that your expectations will be fulfilled, and that your time spent in clinical studies will be both pleasant and rewarding.

You will find many of us willing, indeed eager, to help. Numerous clinical tutorials and ward rounds are at your disposal. Too many lectures have been arranged, but someone, or some people thought that they would be good for you. It was not always so.

At the beginning of the last century, many who wished to study medicine were largely self-taught, and only learnt from their teachers in return for much menial work and a very handsome fee. Not only medical education, but medicine was in a chaotic state. The healing art was practiced by the physician, the surgeon and the apothecary. The physician was described in an Act of Parliament, as "Profound, sad, discreet, groundedly learned and deeply studied in Physic." They may have been sad; but profound, discreet and as regards medicine, learned, of these I have found little evidence. The Royal College of Physicians was founded in 1518. To become a physician one had to have a degree in the humanities, from either Oxford or Cambridge. Three terms of lectures from the Professor of Medicine were then necessary before they could be accepted by the College as a licentiate. This was theoretical, since it was later discovered at Cambridge that no lectures had been given in medicine for over 100 years. After being accepted by the College, some went abroad to study, usually in Paris, but many merely associated themselves with a practising physician, and after learning the pharmacopeia, set up in practice. Scotland and Ireland had their own Colleges and medical education, especially in Edinburgh, was better organized.

The surgeons had just recently separated from the barbers and established the Guild of Surgeons, shortly to become the Royal College of Surgeons. They were not so well educated. A university degree was unnecessary. The first step was to attend a private school for anatomy. These schools abounded, especially in the larger cities, and were usually run by young surgeons before they had established themselves in practice. It was also necessary to walk the wards. After a variable time, and often at the whim of the surgeon, the pupil could apply to become a member of the College. Like the apothecary, he was forbidden by law to prescribe

drugs. He was allowed to treat external swellings, syphilis and diseases of the skin. He was supposed to operate under the direction, and sometimes the supervision of the physician.

The apothecary owned a shop. His official function was to dispense the prescriptions issued by the physicians, but because of the high fees asked by the physicians, and the fact that frequently when required they were not available—in times of plague and epidemics they were wont to leave town—the apothecary became the poor man's doctor. The laws were relaxed and they were permitted to visit and prescribe. They could not ask a fee for the visit, but only for the medicines supplied. This may have been the origin of the still common practice—the doctor must always prescribe something. As the result of a famous judgement in the High Court by Lord Tenterden in 1830, their position was further strengthened, in spite of the most strenuous resistance by the physicians. They were permitted to visit and ask a fee for it. This established the apothecary as the general practitioner, a term first used that year in the new medical journal, The Lancet. To become an apothecary it was necessary to serve an apprenticeship of five years. The conditions were very strict. Some apprentices, as the century progressed, were allowed "time off" to study anatomy, and later to walk the wards. Thus they were able to get the double qualification, and were known as surgeon-apothecaries.

Medical knowledge was in its infancy. It was described as "The withered arm of Science." Treatment was directed towards the symptoms, seldom to cure the disease. As one doctor said to his new apprentice "There seems to you to be a great variety of medicines here, and that it will take you long to get acquainted with them. Most of them are unimportant. There are four which equal all the rest; Mercury, Antimony, Bark and Opium"—or as another said: "At one time I used a dozen bottles for every ailment, now I use a single bottle for a dozen ailments." Edward Jenner, of smallpox fame, writing to his friend Finch said: "For it is by appearances, my dear friend, not a real knowledge of things, that the world forms a judgement." The hospital patients were medical and surgical. Medical patients suffered from the endemic diseases. The surgical patients were largely the outcome of trauma, with some superficial tumours, bladder stones and gangrenous limbs. As a result the students mostly attended the surgical wards. In any case, there was little the physicians could do. The surgeons had acquired great dexterity. Amputations were usually performed in one minute and bladder stones removed in a similar time, all without anaesthesia. If the student had money, he could become a dresser or a ward clerk, or better still become the apprentice of a surgeon, in which case he helped at operations. Most of the students were only able to walk the wards with the surgeon, and with a large number of others crowd in to see the operations.

Students were a rough, rumbustious and dirty lot. Bob Sawyer and Ben Allen were not exaggerated by Dickens. Henry, later Sir Henry Ackland, when he went to join the students at St. Georges', wrote "Everything wears the air of low man, of low habits, such as I have never hitherto come in contact with," and he had just returned from two years in a man of war. William Dale tells the same story—"Drinking, smoking and brawling were the very rational occupations of the dissecting room." It was not only the students, many of their teachers used filthy

language. The kind of indecency would be unprintable, but as an example of the cynicism of the time—at an inaugural lecture such as this—the orator began "You are about to begin your medical studies. The sole objects of such studies are two—first to get a name—secondly to get money." There were many reasons for these low standards. The student was a product of his time. The industrial revolution was beginning, the cities and larger towns were rapidly expanding. One of their problems was that the expanding population was trying to bury its dead in the already over-populated church yards. The stench which overhung the churchyards of London, or any other large city, could only have been rivalled by the foetid dissecting rooms. The mortality rate was so high from cholera, typhoid, typhus, small-pox, as well as all the other prevalent diseases such as puerperal sepsis, gangrene, erysipelas and tuberculosis, for all of which it seemed nothing could be done, that the students and the doctors must have been very disheartened and cynical.

It is an astonishing fact that up to this time, and in spite of Hipprocrates, physical examination of the patients seldom took place. The doctor listened to the patient's description of his symptoms, he observed him, he looked at the urine, the faeces and the vomitus, but he did not auscultate, percuss or palpate. The case records of the London Hospital in 1823 make interesting reading in this respect. Only the very occasional case report does other than describe the patient's symptoms. It was not until the 1850's that all case notes contained a description of the physical signs. The physicians did very little teaching. In any case, most medical information could be gleaned from the library, and the occasional lecture. The physician was: —

"Anon a figure enters, quaintly neat
All pride and business, bustle and conceit
With looks, unaltered by the scenes of woe
With speed that entering, speaks his haste to go".

Henry Ackland, giving an account of his student days in 1843, writes of lectures on botany, medicine, anatomy, insanity, chemistry, and later practical pharmacology in a druggist shop, but only once a week did he attend the hospital and then to see operations. Twenty years later another dedicated diarist, Shepard Taylor, was constantly attending outpatients for experience in the new science of clinical medicine.

The change was started by Laënnec. In 1819 he published a book describing the stethoscope and its uses. The physicians began to ausculate, then to percuss and palpate. Very soon they were relating the physical signs to those found at post-mortem. As their experience increased, though they were unable to cure, they were able to prognosticate. Many famous names are associated with the development of clinical medicine: Bright and Addison in London, Stokes and Graves in Dublin, though according to Newman, it was principally the students to whom most of the credit must go.

With the growth of clinical medicine pathology was developing. Its growth coincided with the introduction of the microscope in 1843 into medical teaching, though it was not until 1869 that the General Medical Council recommended that

microscopy should be included in the curriculum. Students now began attending the medical wards as well as the surgical. Throughout the country there was a re-awakening of interest in medicine. It was not confined to clinical medicine. As a result of the work of Walker, Chadwick and others great strides were made in public health. They met with much opposition from manufacturers and others. Even the public was lukewarm, but from a small beginning public health made vast strides in the latter half of the century.

This reawakening of interest meant more students, and as a result new hospital medical schools throughout the British Isles were opened and the old established ones became reinvigorated. The private schools could no longer compete. They were in any case only equipped to teach anatomy, with some botany, and chemistry. The Belfast General Hospital, the forerunner of this hospital, was opened to students in 1820 following a recommendation of the Management Committee:

"The hospital, we trust has now attained such a state of permanence, and promises to be conducted on such an extensive scale, that the advantages flowing from it should not be confined to the "mere objects" who are relieved within its walls. The physicians and surgeons of Belfast should be invited to place their pupils there, to acquire experience by observing its practice, and in the course of a few years it might become a School of Physic and Surgery."

At the same time an anatomy school was opening at Inst, and though the teachers there tried to start a new hospital, in an old barrack block behind the school, it failed, and the students continued to attend the General Hospital. Between 1821 and 1850 four hundred students attended the hospital, though there was no official connection between it and the Medical School at Inst.

In 1845 ether and three years later chloroform were discovered and, though anaesthetics were slow to be generally accepted, they did bring untold relief. It was not, however, until Lister published his paper in 1867 that the full effectiveness of anaesthesia was apparent. There had been, up to this time many heroic operations both by the surgeons and the patients, only for the patient to succumb later to sepsis. Six months after Lister's paper the Belfast Royal Hospital, as we had now become, was using carbolic acid. In 1868 the accounts show that six pounds was spent on carbolic acid and in the following year twenty-five pounds. Up to the end of the century it continued to be an appreciable item of expenditure. As a result surgery was progressing rapidly. It became more precise and consequently slower, but the rewards were greater. Medicine however was lagging behind; physicians could still examine and prognosticate, but they had very few curative drugs.

Pari passu with these advances medical education was changing and the name of Thomas Wakely, the founder of The Lancet, cannot be omitted from these changes. He had come up from Devon after an apprenticeship of two years to study surgery. He had only eighty pounds; thus he was unable to buy himself a favoured position and within a few years had antagonised the surgeons at St. Thomas's. He was forbidden to enter the hospital. He appears to have had little scruple, and used the Lancet for many scurrilous attacks, particularly on the surgeons. Referring to the Royal College of Surgeons he wrote "This sink of

infamy and corruption. This receptacle of all that is avaricious, base, worthless and detestable in the surgical profession . . . . They take our money. Give us ex post facto laws. They lock up our property. Insult us with mock-orations. Live at our expense, and refuse to call us by our proper names." There was a great deal of truth in what he wrote. The surgeons did extract large fees from the students and were not always meticulous about teaching. Post-mortems were carried out at odd times. The organs removed without comment. And if the student did get into the post-mortem room, a further fee was demanded.

Possibly, as a result of Wakely's attacks, teaching did improve, though it was more likely that it was the result of the increase in medical knowledge and the agitation of the medical students. The Royal College of Physicians was still a small aloof reactionary body. The apothecaries continued to be very nervous and sensitive of their professional status, and were wont to over-react. There had been a plethora of medical Bills before Parliament. Some, to recognise the power of the colleges; others to strengthen the apothecaries. All seemed to recognise the differences between the physician, the surgeon, and the apothecary. All failed, often because Wakely who was now a Member of Parliament, objected on the ground that none of them curbed the power of the colleges. One of these Bills is, at least, interesting—that of Sir James Graham in 1845. He suggested three colleges—The Royal College of Physicians, The Royal College of Surgeons, and a new college—The College of General Practitioners. The Bill was amended so that it would have been obligatory for all who wished to practice, first to take the examination of The College of General Practitioners, and then, if they wished, those of the other colleges. This would have provided a single registerable degree, but Wakely objected since it did not curb the physicians or the surgeons, and by various political machinations he succeeded in stopping it.

The Medical Act of 1858 was a compromise. It aimed at a "high standard of qualification which would be valid throughout the United Kingdom." It established the General Medical Council which among its duties was to 'appoint examiners and to inspect the standards of examinations.' The Act did not make it illegal to practice medicine without a degree or a licence. It merely stated that you could not claim to have a degree if you did not have one. Quacks still abounded and the public was prone to seek their help. But who could blame htem? Many of those registered had only studied surgery, others were apothecaries, and it was still possible to become a physician at the whim of the Archbishop of Canterbury or the Dean of St. Paul's.

Some people state that the medical profession really started to progress as a result of the Act; but the wind of change was already blowing. Medical education was taking shape. The practice of the doctors charging the students individual fees had stopped. All fees were now paid into the common teaching fund. The medical schools were rising to their responsibilities at last.

There were, however, still vast differences in standards, and of these the G.M.C. through its extern examiners, were well aware. Rivalry between medical schools was intense. Large advertisements appeared in the papers praising the virtues of a particular school and hinting that it was not too difficult to pass the preliminary examination, that is—the examination required to be registered as a medical

sudent. This preliminary examination, if Rivington in 1878 is correct, must have been farcical. After quoting the G.M.C. requirements, which in themselves were very basic, a proviso was added "provided always that an examination may be accepted as satisfactory, that secures on the part of the candidate passing it, a sufficient grammatical knowledge of English." A report by the G.M.C. extern examiners the following year on the preliminary examinations in Ireland and its three Colleges reported "That Belfast was better than Cork or Galway, but that the examinations were scarcely sufficient in any of the Colleges to ensure that the successful candidate should have even a moderate school education, and in two of the colleges was, in some respects, little more than a farce." The initial progress in education which had started in 1850 slowed down. Laffin in 1870 writes "The real key to the indolence of many, and the incorrigible idleness of most students, is to be found in the selfish timidity of many school authorities." He was referring to the fact that the students fees still reached the pockets of the teachers. They were unwilling to discipline the students lest they transferred to another school, but only too glad to receive those fees. But who could blame the students? There was so little that could be done for the patient. Those with infections lived or died as a result of their own body reactions and with the help of devoted nursing—frequently by a relative, and depending always on the patients will to live. The good doctor could help with advice on nursing. He could give the patient encouragement, but ultimately it depended on the patient. Some doctors realizing their limitations did a great deal and became family counsellors and friends. Many just paid their visits and accepted their fees. It must be stated, however, that the reward was not great. A comparison may make it easier to appreciate. In the British Medical Journal January 1876 there is an account of a doctor's life in Scotland. He had to travel up to thirty miles to visit patients; in the same area there were four clergymen, the worst paid of whom received more for doing less. It was a lonely life and in spite of the romantic tales the discerning general practitioner cannot have had too much job satisfaction. Modern surgery was in its infancy, and for cases other than trauma was confined to the centres of population. But as the century neared its end there were changes on the horizon. The peritoneal cavity was being opened. Spencer Wells in 1878 resected the intestine. Billroth in 1880 had resected the pylorus for a cancer and Wolfer had introduced the operation of gastroenterostomy.

There was another factor which influenced medical education—the ladies. Elizabeth Garrett, Elizabeth Blackwell and Sophia Jex Blake qualified with others after 1858. This statement of fact gives no idea of the commotion and changes that followed the registration of women as medical students. The antagonists of women doctors came from many quarters—some, like Sir Henry Ackland were genuinely too embarrassed to lecture on some subjects to a mixed audience. Some teachers apparently objected because they could not use filthy mnemonics to instill anatomical facts into the minds of the students. Others were just pompous reactionaries. Sir William Jenner—"I have only one daughter, and would rather follow her bier to the grave, than see her become a medical student." Dr. Charles West—"There is a grave risk of gravely modifying the mental and moral characteristics of women." But, as always the ladies won, and the Medical Act of 1876 removed the restriction on the granting of qualifications on the grounds of sex. Two years

later London University unconditionally accepted women as undergraduates.

The admission of women students to medicine did nothing but good. It cleaned up the lectures, and it cleaned up the male students. The women were more assiduous in their studies, and began doing better than the men, who now began to work and to live down the bad reputation they had had. The admission of women to medicine was responsible for another change unforseen by the G.M.C. "Nursing," asserted Florence Nightengale in 1860," was undertaken by those too tired, too weak, too drunken, too stolid, or too bad to do anything else." Under her influence it all changed. Not only did the standard of nursing improve out of all recognition, but the medical students and young doctors had little chance of escaping matrimony with the lovely and well educated young ladies, who now joined the profession. The appearance of the female medical students now meant that the nurses had competition!

Thus there was another surge forward in medical education. Surgery had extended its scope and its benefits. Diseases of the peritoneal cavity were better understood and many of these could be cured if diagnosed early. In 1896 appendicitis and appendectomy first appeared in this hospital's records .It was an exciting time. More could be done for the patients. There was more for the students to learn. Their teachers were stimulated and a great deal of discussion took place about the medical curriculum. It was felt that the medical student should have a good working knowledge of all clinical subjects. The controversy was principally about when he should study physics, chemistry, botany and materia medica. It was concerned about when he should first attend hospital, rather than how much physics, chemistry and botany he should learn. An interesting example of this point—the G.M.C. in 1896 recommended that whilst chemistry was desirable for making pathology, physiology and pharmacology more comprehensible, it was thought that the student should learn physics "so as to be able to advise on common domestic questions of nuisance preventing, warming, ventilation and the like." In other words the aim of the medical education was utilitarian—to produce the safe general practitioner. In this, for the first part of the century, it was successful.

Progress in all branches of medicine was being made. Even the physicians could now cure some diseases; they had insulin for diabetes, liver for pernicious anaemia, digitalis for cardiac conditions, iron for anaemia, alkalis for peptic ulceration and iodine for thyrotoxicosis and even blood transfusions when a suitable relative could be found; and in the late thirties there was the introduction of the sulphonamides. Progress in surgery had been steady and sound. Roentgen discovered x-rays in 1896 and they were used in this hospital six months later, but in 1914 only 100 plates were taken. In 1920 the number was 3,000. As a result of all these advances, the role of the general practitioner was becoming more important and satisfying. He had to diagnose the condition more accurately and quickly. It was not enough to diagnose cancer, it had to be diagnosed early and precisely. If a patient with intestinal obstruction was to survive, the diagnosis had to be early. The present post-operative electrolytic care was not understood. For the first half of this century the student did get a fairly comprehensive education. Many of the routine laboratory tests, the blood counts, the crystals in the urine, the fractional test

meals and so on were done in the wards by the students. The student, whether he was resident or not, felt that he was part of the team, especially in casualty and extern where he spent a good deal of his time. He had then only a fraction of the lectures, which it is now obligatory to attend. It is unnecessary to tell you anything about the advances which have occurred in the past twenty-five years. Practically every aspect of medicine has been revolutionised and several new branches have been born. Into these the poor student has been inexorably drawn, whether they have any relevance to clinical medicine or not. So much time is allocated to the study of these esoteric subjects that the student spends less and less time with the patient and often fails to learn how to observe him or to communicate with him. The faculty of observation is weak in the medical student. Most clinical teachers know this, yet the student's preliminary training does nothing to enhance it. What is likely to help? Certainly not physics and chemistry, which he is expected to continue studying as an undergraduate, when he already knows enough. What then? Perhaps some form of sociological project. It is a matter which certainly merits serious consideration. At the same stage of his career it would benefit the student to learn to express himself with fluency and accuracy. Since the medical curriculum is now largely the responsibility of the University it follows that it must accept most of the blame for its shortcomings, though the clinical teachers are not innocent. Over the past number of years there has been a proliferation of professors and of course professors must have lecturers. Helped by an embarrassingly large grant from the Universities' Grants Committee, it is planned to increase these even further. In a recent forecast, I noticed that one department, which was nonexistent not so many years ago, hopes to appoint a new lecturer in each of the next four years. I have no objection to the university increasing its staff. Its purpose is not only to teach, but to advance knowledge. My concern is that every new appointee considers it a duty to lecture the students, who have already too many lectures on too many subjects, most of which are of little importance in the primary aim of producing a young medical practitioner.

There are many things that cannot be taught—other than by example. Lectures and even ward rounds cannot teach you the small courtesies, or rapport with the patients. What may appear as trifling acts of nursing care may be all important to the patient. How are we to communicate with the dying. Too often the screens are drawn and we tip-toe past. There is loneliness in dying. The feeble squeeze of the hand has often indicated appreciation of a visit. The nurses and especially the sisters can teach you a lot about your relationship with patients.

You must be receptive. I feel sure you have come to hospital with high ideals. It is imperative—not only for your patients—but for you and your job satisfaction that you maintain these. As your experience increases you will be less personally affected by the tragedies, just as your successes will be accepted with less elation. But your standards must never drop. There is only one sure way to maintain these. Keep your conscience sensitive. We have all, and you will all, make mistakes. Usually you should admit these. Sometimes, it is advisable not to do so but then it must always be for the benefit of others. What you must never do, is to fool yourself. It is easy to find all sorts of reasons as to why you took a certain action. Unless you keep a sensitive conscience—this can lead to self delusion. Once on this path

your standards will inevitably drop. In your self criticism be harsh with yourself, and resolve not to make the same mistake twice. But to develop these qualities you need time. Time in the wards, and if possible in the homes, and time to think.

Here, I should like to congratulate the university on recently appointing several consultants to personal chairs. These appointments of experienced and distinguished doctors with their interest in this medical school and its teaching could be a great help to the faculty. Another appointment which gives great pleasure is that of Professor George Irwin, in the newly created chair of general practice. We wish him well, but hope that he will not lecture too much and will remember the words of Osler that "a true knowledge of medicine is learned at the bedside." Although the subjects we, the clinicians, teach are relevant, is it necessary for the student to know all about the nerve of Laterge or the technique of a thoracic operation? There are obscure and rare diseases in the medical wards, the diagnosis of which may be a triumph, often for the laboratories rather than the clinician. Is it necessary that he should learn all these when there are so many important gaps in his knowledge? Surely our teaching should be directed towards the young doctor seeing the patient in the home, the surgery or sometimes more critically, by the roadside. He should first be taught those things which he will be called upon to recognise and treat when his is alone. Greater stress could also be put on the early symptoms and signs of disease. It is indisputable that the general practitioner can now do more for the patient than ever before, yet the externs are as full as ever. A high percentage of these visits is unnecessary. Many of the complaints are trivial and could be treated by the general practitioner. An increasing number are functional, and could have been aborted if the doctor had been aware of and sufficiently interested in some special strain or marital upset.

There is a vast number of illnesses which the student will not see in hospital, and which he is unlikely to see in the few weeks he now spends with the general practitioner. Is there not great virtue in apprenticeship? To quote Sir Henry Ackland again—writing about his experiences as an apprentice. "Many things of great utility in after life could be thoroughly learned. Things of which the ignorance is now a frequent hindrance to success . . . . There was ample opportunity for observation in practice without being confused by a crowd of cases, in which it is for a student equally difficult, either to study the whole or to make a good choice." It would help, not only the student, but also the doctor. Would some months spent with carefully selected general practitioners not be more useful than a good deal of the pharmacology, bacteriology, medical jurisprudence and pathology, and even some medicine and surgery? But this is the nub of the problem. Throughout our history we have been frustrated by our vested interests. Any change which threatens these is always strongly resented and resisted. In the past we muddled through, often somewhat late with modifications of the curriculum.

Medical education was probably at its best between the wars. The face of medicine was not changing so rapidly and there was not so much to learn. Since the war electrifying changes have occurred and are still occurring. Scientific advances have been made, which would then have been inconceivable. What is conceivable, is that before another decade the computer may well play a major role in hospital diagnosis. The medical student and the young doctor will be expected to know

something about it. Yet the computer threatens to take over not only many aspects of observation, but the analysis of it. We are in the age of scientific medicine, but is science all that matters? Does it help when a man comes to a doctor's surgery with some vague complaint and you know that his wife has left him and the family? He is looking for help—not science.

I drew your attention earlier to the poor image of the doctor in the middle of the last century. In this country our image has fluctuated. Of its waxing and waning we are aware. What to some is not so obvious is the cause. Lord Moran once said "when culture has gone from the leaders of our calling—we shall no longer remain a profession." Can this really be so? Surely our image is influenced less by our culture, not even by how much good we do, but above all by how hard we try. Even this is not enough, if our efforts are impersonal. The doctor should have a favoured place in the community, but if he cures in an impersonal way he could be likened to a ship builder or a scientist. If you mix humanity with your skill your image will be good and most probably your patients will make better progress.

There are those who believe my aim is wrong. They hold the view that young doctors should be so trained that they can readily enter any branch of medicine with a good background of knowledge and the implication is usually that they should have a scientific background. We are not providing this at present. The field is too vast and more important things suffer as a result of this quest. In any specialty the student will always start at the beginning under supervision. Those of you who are specialists know that is so. It may eventually be the path to general practice. I believe the general practitioners' scheme envisages this, but it is unlikely that it could happen in the foreseeable future. Should it occur it will be necessary to alter our aim. In the meantime we flounder. It is imperative that we state our aim in the training of students. In a recent report "Career Preferences of Pre-registration Doctors in N. Ireland (1972)"—Rafausse shows that 50 per cent of graduates hope to go into general practice. Surely some knowledge of a general practitioner's problems would be good for all of us. I believe Higgins was correct when a few years ago he wrote: "medical schools are still turning out practitioners equipped to treat diseases they never see, using facilities they do not possess." If we so define our aim, it will be necessary for many of us to forget our vested interests and to remember, even in this age, that the patient first seeks help in the doctor's consulting room, where it becomes obvious that medicine is still largely an art and that experience, patience and compassion may be more important than science.

BIBLIOGRAPHY

The following books, amongst others, have been consulted in the preparation of this address.

ALLISON .... "The Seeds of Time"
FAY .... "The Diary of Richard Fay"
HOLMES .... "Medical Essays"
KRUIF .... "Microbe Hunters"
LAFFAN .... "The Medical Profession in 1879"
NEWMAN .... "The Evolution of Medical Education in the 19th Century"
REFAUSSE .... "Career Preferences of Pre-registration Doctors in Northern Ireland (1972)"
RIVINGTON .... "The Medical Profession in 1879"
RIVINGTON .... "The Medical Profession in 1887"

CHILDREN CONVICTED OF HOMICIDE

by

K. S. WALSH-BRENNAN, M.R.C.Psych.

Consultant in Child and Family Psychiatry, Sale, Cheshire

THERE has been an increase in crimes of violence in Britain during the past two decades (Sparrow, 1968). With this change there have also occurred variations in the pattern of homicide by both sexes and of all ages in England and Wales, particularly since the introduction of the Homicide Act in 1957 as shown in the Figure and a growth in murders committed by children as shown in the Table.

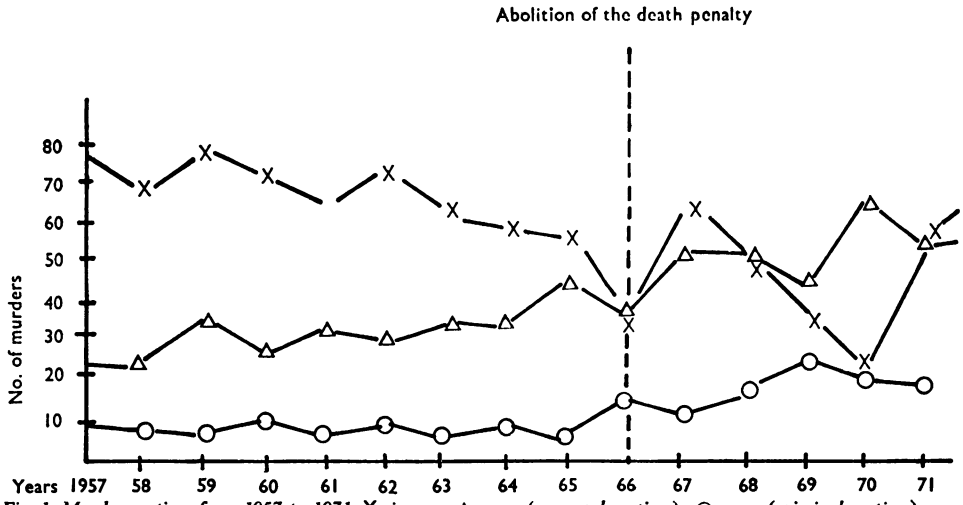


Fig. 1. Murder motives from 1957 to 1971. X, *insane;* △, *sane (personal motives);* ○, *sane (criminal motives).*

Before the abolition of the death penalty for homicide the Children and Young Persons Act 1933 defined 18 years as the minimum age for execution, the last teenager to be hanged being "Flossie" Forsythe in 1960 at the age of 18. Prior to 1966 a murderer could "hang by the neck until dead" and due to this courts were more ready to allow a culprit to be termed "insane". Since then the number of "insane" murderers of both sexes and all ages has fallen from four times the figure for those classed as "normal" or "sane" to a nearly equal number as shown in the Figure. Due to this people are now going to prison who would formerly have gone to Broadmoor or Rampton, an unforeseen development of community psychiatry (Walsh-Brennan, 1973).

Regarding factors associated with the development of child killers it has been stated (Home Office, .1968) that "there are many influences on the behaviour of children and that of the family is particularly important." In his Sing-Sing Prison

THE TABLE

Boys found guilty of murder in England and Wales between 1957 *and* 1972 *who were younger than* 18 *at the time when the offence was recorded as known to the Police. One girl was involved in* 1971

Year	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72
Number	1	1	1	4	1	2	1	1	1	3	5	4	9	8	8	8

Survey Gleuck (1954) related psychopathic behaviour to home background. So also did Johnston (1955) at the Mayo Clinic, and as a result of 10 years of study of parent and child there she concluded that children who are aggressive, homicidal, set fires or exhibit sexual deviations "are usually doing what their parents subconsciously wish". She believed that "the child's defective conscious is traceable to a like defect in the parents' own poor resolution of unconscious impulses to similar anti-social behaviour".

Burt (1944) associated childhood violence with the parents and he concluded "to lose respect for one's parents is to lose respect for oneself, for one's fellows, and for the whole basis of morality". It is noteworthy that poverty was not considered a cause by Burt, in which sense he quotes Seneca (Epist. XVI) "Si ad naturam vivas, numquam eris pauper; si ad desiderium, numquan dives" (If you live in accordance with Nature, you will never be poor; if you live in accordance with your desires, you will never be rich). Spock (1969) considered that "A child acquires his basic standards from his parents. If they are decent people and love him, he loves them deeply too, and patterns himself after them".

It was thus decided to investigate a group of 11 child and adolescent murderers, one girl and ten boys, under the following three aspects: —

1. Family and social history.
2. Adverse factors in family background.
3. Previous criminal records, psychological, psychiatric aspects and treatment.

The age of the group ranged from 10 to 15½ years when the offence was recorded.

FAMILY AND SOCIAL HISTORY

Two boys were in Social Class III. The girl's parents fulfilled the criteria of Social Class IV as did five of the males. Three were in Class V while doubt existed as to the remaining two boys. In contrast to the observation by Burt (1944), who noted a high proportion of only children in this context, none of the children belonged to this category. Five were the eldest in their families, one of the youngest and the remainder in intermediate grades. The five eldest could be associated with the Gleucks' survey (Gleuck & Gleuck, 1950) who reported a deficiency of only and youngest children in their group. While there was only one female in the group it was noteworthy she was the eldest in keeping with the work of Ming Tse-Tsuang (1966) who found eldest girls more aggressive and emotionally more unstable than their siblings. None of the eleven was adopted and all were legitimate.

Personal relationships between the girl and her mother were normal. In eight of the ten boys the maternal role was aggressive and overdominant as illustrated in the following case histories: —

Case 1

This boy was convicted at the age of 12½, of murdering a subnormal girl, aged 11. He was the product of an intact home background with no marked material deprivation. The home background was disturbed, however, in that the father was a weak passive figure who left not only the running of the house but other responsibilities to his wife. The female parent gradually assumed a dominant and aggressive role to the extent of bringing into the house at different periods two male companions with whom she had sexual relations.

Case 2

Norman was aged 11½ when he drowned a boy. His father, a postman, spent little time at home and left familial discipline to his "14 stone wife who came from the Isle of Man." Norman's mother was a demanding, attention-seeking and "mannish type" woman who ruled Norman and the rest of the family rigidly. In the family Norman had an intermediate position.

Adverse Factors in Family Background

Parental promiscuity existed in at least three cases. Alcoholism was not found in any one of the parental groups; but as alcoholics lack insight, and are unreliable, information may not have been disclosed to the investigating social workers.

The father of the girl was the only parent with a criminal conviction although this was suspected in three other cases. Only one family had a member with chronic physical illness, a spastic child causing inter-personal stress: the remainder were physically fit. There was also no record of parental neuroses nor psychoses. The girl came from a slum area in Newcastle-on-Tyne, five boys came from congested industrial regions, one lived in a National Park in North Wales, the rest in rural or suburban areas.

Poniatowski (1973) in an address to a Conference of European Ministers of Health at the Council of Europe proposed payment of a "social wage" to mothers with children at risk with anti-social traits. Investigations were, therefore, carried out into the proportion of working mothers. Five of the female parents went out to earn money, but for varying periods of time alternating with illness and redundancy. In view of statistical difficulties in establishing criteria, and the observation by Stolz (1960) that "one can say almost anything one desired about children of employed mothers and support the statement by some research study," this research has been left for a later occasion. Difficulty was experienced in attempting to establish criteria to assess "The Cycle of Deprivation Theory" put forward by Joseph (1972). While there were indications in the girl and four of the boys of possible applicability of the Cycle of Deprivation, the eight overdominant maternal relationships appeared more noteworthy.

"The Cycle of Deprivation" means the way in which those parents of all social classes who have been themselves emotionally, intellectually or culturally deprived and therefore "hurt" in their own youth, tend to "hurt" their own child in exactly the same way. This is by repeating the actions and attitudes which initially damaged

them as children, or by exaggerating those same actions. The estimated amount of children affected is between 10 per cent and 15 per cent of the total child population. To date, the role of a Cycle of Deprivation has not been the subject of wide research, although the fraction of the national child population suffering should be easily identified.

Previous Criminal Records, Psychological, Psychiatric, and Neurological Aspects

The girl had no criminal record. Three of the boys had, but it was merely of a minor nature. (Here it is perhaps noteworthy that occupational therapy staff found the homicidal children more co-operative generally than other boys and girls with non-capital offences).

The psychological tests of Burt, Weschler and Cattell were applied to each of the eleven children. Normal intellect was found in all 33 examinations with no indications of mental handicap.

All the subjects were physically fit and although "blackouts" had been reported in several cases, nothing abnormal was found on routine examination including Wassermann test, X-ray skull and E.E.G. Three of the boys had anxiety reactions but no other neuroses or psychoses. Child Psychiatry Aids (Walsh-Brennan, 1973) were not required for incontinence. Contrary to expectation none showed attention seeking or demanding behaviour. This facilitated rehabilitation as shown by Gosney and Walsh-Brennan (1969).

Treatment

Treatment varied considerably. One boy aged 11 examined by the author in October, 1973, had killed a man of 47 by fracturing his skull with a brick, but was sent home for Christmas. The girl at one time spent a short period in a paediatric ward after conviction. Four received Borstal sentences and the rest transferred to community homes: their further behaviour showed no abnormalities.

Discussion

Various reason are advanced for the increase in the number of child killers. TV violence for example was considered by Belson (1973) who did fieldwork on 1,565 London boys in the 12-17 year old age group. The increase coincides with the 1968 peak of childrens' drug abuse recorded by Boyd (1972). It may be related to the concept of "Social Deprivation" put forward by Eisenberg (1973) which tends to conform with the animal behaviour research of Tinbergen i.e. "deprivation of parental, perhaps primarily maternal love" (1973). A theory that better detection of battered babies leads to more who live and who themselves later batter and kill has been put forward by Andrew (1974) to explain the growth. In addition there is "The Permissive Society" described by Whiteley and Whiteley (1964).

In the group studied the figure of eight overdominant mothers appears noteworthy. Adoption agencies may take encouragement from the fact that none were adopted and all were legitimate.

In view of the relatively large number of abnormal maternal relationships, further research is indicated on two aspects—(a) Role of the working mother as

defined by Stolz with particular reference to maternal dominance and (b) "The Cycle of Deprivation" theory put forward by Joseph.

Summary

An analysis of 11 children convicted of homicide, one girl and ten boys, indicates a maternal over-dominant relationship in eight of the males studied.

The murderers were found to have more co-operative personalities than other children found guilty of non-capital offences and showed both normal intelligence and personality factors. Despite a history of 'blackouts' in several cases, all were found on investigation to be free from epilepsy and all were healthy.

Difficulty was experienced in determining the presence or absence of parental alcoholism, promiscuity and criminal convictions. All of the 10 boys and the girl came from relatively normal homes and apart from minor offences none were involved previously in serious anti-social behaviour.

Future research is indicated on two aspects: (a) Role of the working mother with particular reference to maternal dominance, and (b) The 'Cycle of Deprivation Theory'.

References

ANDREW, J. M. (1974). *Personal communication.*

BELSON, W. A. (1973). *Address to the British Association for the Advancement of Science,*

BOYD, P. (1972). *Brit. med. J.*, **4**, 540.

BURT, SIR CYRIL (1944). *The Young Delinquent.* London: Univ. of London Press. 23.8.1973 and *personal correspondence,* 18.12.1973.

EISENBERG, L. (1973). *Lancet*, **2**, 1371.

GLEUCK, B. C. (1954). *Psychiat. Qtly.*, **28**, 1.

GLEUCK, S. and GLEUCK, E. (1950). *Unravelling Juvenile Delinquency.* Cambridge, Mass.

GOSNEY, K. G. and WALSH-BRENNAN, K. S. (1969). *Health Visitor*, **42**, 10.

HOME OFFICE (1968). *Children in Trouble, Cmnd* 3601. London: HMSO.

JOHNSTON, ADELAIDE (1955). *Amer. J., Dis. Child*, **84**, 27.

JOSEPH, SIR KEITH (1972). *Lancet*, **2**, 774.

LENG, ANNE and WALSH-BRENNAN, K. S. (1973). *The Criminologist*, **8** (No. 28) 31.

MING-TSE TSUANG (1966). *Brit. J. Psychiat.*, **112**, 1131.

PONIATOWSKI, MICHEL (1973). *Address to Conference European Ministers of Health, Council of Europe,* 11.9.1973 quoted from *The Irish Times,* 12.9.1973.

SPARROW (1968). *A Probe into the Changing Pattern of Crime.* London: Feature Books.

SPOCK, B. (1969). *Baby and Child Care.* London: Bodley Head.

STOLZ, L. M. (1960). *Child Development*, **31**, 749.

TINBERGEN, N. (1973). *Personal correspondence.*

WALSH-BRENNAN, K. S. (1973a), *Brit. med. J.*, **3**, 628.

WALSH-BRENNAN, K. S. (1973b), *J. Roy. Inst. Pub. Health*, **5**, 169.

WHITELEY, C. H. and WHITELEY, W. M. (1964). *The Permissive Morality.* London: Cox and Wyman.

DERMATOPHYTE ISOLATIONS IN NORTHERN IRELAND 1967-1973

by

W. A. FLEMING,

Department of Microbiology and Immunobiology,
The Queen's University of Belfast,
Grosvenor Road, Belfast BT12 6BN

THIS is the second retrospective survey of the work of the Mycological Diagnostic Service since its establishment in 1959. Its purpose is to review the isolation of dermatophytes (ringworm fungi) of both human (anthropophilic) and animal (zoophilic) origin in Northern Ireland over the period 1967 to 1973, and to compare the findings with previous reports for the province (Mackenzie and Rusk, 1964), and with the situation in the United Kingdom as a whole.

Specimens and Isolations

During the period 1967–1973, investigations were made on 13,864 specimens from 9,999 patients. Dermatophytes were isolated on 1699 (12.3 per cent) occasions and there was microscopic evidence of fungal infection in a further 246 (1.8 per cent) cases, although no fungus was isolated on subsequent culture. Of these microscopically positive specimens, 122 (49.6 per cent) were identified as *Malassezia furfur*, the cause of *Pityriasis versicolor*. The frequency of isolation of different dermatophyte species from human sources is shown in Table 1. The table does not include 3 isolations of *Trichophyton equinum* made from clippings of infected horse hairs.

Table 1

Dermatophyte Species Cultured from Human Sources 1967–1973

Species	*Number of isolates* 1967	1968	1969	1970	1971	1972	1973	*Total no. of isolates*
Trichophyton verrucosum	105	96	55	71	73	59	32	491
T. rubrum	36	54	35	64	44	33	32	298
Epidermophyton floccosum	36	36	26	34	29	31	19	211
T. mentagrophytes var *interdigitale*	11	5	39	21	31	45	50	202
T. mentagrophytes	25	23	37	33	34	27	24	202
Microsporum canis	36	38	27	16	21	23	24	185
T. sulfureum	11	12	23	14	15	7	23	105
T. violaceum	—	—	—	—	—	1	—	1
Unidentified	—	1	—	1	—	—	2	4
% Animal ringworm	63.8	60.6	49.2	47.4	51.8	48.2	39.2	51.8

Sites of Infection

Scalp Ringworm

Table 2 shows the species of dermatophytes isolated from ringworm of the scalp from 1967 onwards. The findings confirm the report of Mackenzie and Rusk (1964) that the majority of such infections are zoophilic in origin, but also show a further decrease in the isolation of *T. sulfureum*. This organism was responsible for 42 per cent of cases of scalp ringworm diagnosed in 1959 (Mackenzie and McArdle, 1960), but was isolated in only 14.5 per cent of cases during the period of this report. Although several 'hairbrush' surveys were carried out between 1967 and 1973, no outbreaks of *T. sulfureum* were detected in the children tested.

Table 2

Ringworm of the Scalp

Causative organism	*Number of isolations in* 1967	1968	1969	1970	1971	1972	1973	*Total no. of isolations*
M. canis	23	10	9	6	13	14	15	90
T. verrucosum	5	10	9	12	5	10	5	56
T. sulfureum	4	10	2	4	1	—	5	26
T. mentagrophytes	2	—	—	1	—	1	3	7
% Animal ringworm	88.2	66.6	90.0	82.6	94.5	96.0	82.1	85.5

Ringworm of the Feet

The dermatophyte species isolated from cases of ringworm of the feet are shown in Table 3. *T. rubrum* is now the organism most frequently isolated from foot lesions, and toe-nail involvement was found in 63 instances. *T. mentagrophytes* and *T. mentagrophytes var. interdigitale* were isolated on rare occasions from nail clippings, but we have recorded no case of nail infection due to *E. floccosum*. The only significant incidence of zoophilic infection was due to *T. mentagrophytes*, which accounted for 21 per cent of isolations from this site.

Table 3

Ringworm of the Feet

Causative organism	*Number of isolations in* 1967	1968	1969	1970	1971	1972	1973	*Total no. of isolations*
T. rubrum	28	30	19	39	23	15	14	168
T. mentagrophytes var *interdigitale*	11	19	3	13	21	23	34	124
E. floccosum	7	8	6	14	7	5	9	56
T. mentagrophytes	9	10	14	17	19	12	10	91
% Animal ringworm	16.6	20.8	33.3	20.5	27.1	21.8	14.9	20.7

Ringworm of the Trunk, Limbs and Face

Zoophilic dermatophytes were the most common isolates from lesions of the trunk, limbs and face (Table 4), accounting for 73 per cent of the total, and *T. verrucosum*, in particular, accounting for 49 per cent. Although the distribution of isolations was fairly stable until 1971, a pronounced downward trend in the number of zoophilic isolates occurred thereafter, particularly noticeable in 1973. In that year, however, the total number of dermatophyte isolates was the lowest recorded by the Mycological Diagnostic Service since its establishment in 1959, and the figures may not represent the true incidence of zoophilic infection in the community.

TABLE 4

Ringworm of the Trunk, Limbs and Face

Causative organism	*Number of isolations in* 1967	1968	1969	1970	1971	1972	1973	*Total no. of isolations*
T. verrucosum	88	65	37	44	54	47	25	360
M. canis	28	24	19	9	7	9	6	102
T. mentagrophytes	10	11	18	15	10	9	6	79
T. rubrum	12	12	12	7	5	8	8	64
T. sulfureum	7	6	7	6	8	7	12	53
E. floccosum	12	5	6	6	4	5	5	43
T. mentagrophytes var *interdigitale*	1	2	6	2	4	15	8	38
% Animal ringworm	79.7	80.0	70.5	76.4	77.2	65.0	52.9	73.2

The isolation of *T. violaceum* from scrapings from an arm lesion on a six-year-old child was somewhat unexpected. This organism is not endemic in the United Kingdom, and is most commonly found in Africa and Eurasia (Rebell, Taplin & Blank, 1964). However, further investigation showed that the child had recently holidayed in India, and the lesion had developed shortly after her return.

Ringworm of the Groin

E. floccosum was the infecting agent in 90 out of 159 cultures from patients with *tinea cruris*, and *T. rubrum* was isolated in 48 cases. *T. mentagrophytes* var. *interdigitale* was isolated on 21 occasions, and no zoophilic infections of this region were recorded.

COMMENTS

This survey confirms previous reports that Northern Ireland has a high incidence of infection due to zoophilic dermatophytes, and, in particular, that *T. verrucosum*, the cause of cattle ringworm, is the dermatophyte most frequently isolated from patients (Mackenzie & McArdle, 1960; Mackenzie, Corkin & Bell, 1961; Mackenzie, Corkin & Rusk, 1962, 1963). Between 1967 and 1973, *T. verrucosum* accounted for 29 per cent of all dermatophyte isolations in Northern Ireland, a figure not far removed from the 34 per cent incidence reported by Mackenzie and Rusk (1964) for the period 1959-1963. Northern Ireland differs markedly from the rest of the

United Kingdom in this respect. The incidence of *T. verrucosum* isolates in the United Kingdom and Republic of Eire during the three year period 1967-1969 was 7.8 per cent and the total incidence of zoophilic infections for the same period was less than 25 per cent (British Medical Journal, 1970). In a recent survey of dermatophyte infections over a ten-year period in South-East England, English and Lewis (1974) report a 16 per cent incidence of *T. verrucosum* infection, and an overall zoophilic isolation rate of 52 per cent.

Although zoophilic dermatophytes are the predominant isolates in Northern Ireland, there has been a marked increase in the incidence of anthropophilic infections as judged in the laboratory. This applies in particular to the isolation of *T. rubrum* and *T. mentagrophytes* var. *interdigitale* which now account for 18 per cent and 12 per cent of isolations respectively. Between 1959 and 1963, Mackenzie and Rusk (1964) reported incidences of 9 per cent and 5 per cent respectively. In the United Kingdom as a whole, *T. rubrum* accounts for 55 per cent of dermatophyte isolations, and *T. mentagrophytes* var. *interdigitale* for 12 per cent (Gentles, 1974), and English and Lewis (1974) reported a 42 per cent incidence of *T. rubrum* infection in South-East England.

Although the findings of the Mycological Diagnostic Service may not reflect the true incidence and distribution of different dermatophytes in Northern Ireland, they should provide an accurate representation of dermatophyte infections in patients referred to dermatological clinics in the province. Although zoophilic dermatophytes are the most common isolates, over the past seven years there has been a definite trend towards a higher incidence of infection passed by human to human transfer. In fact, if the high incidence of *T. verrucosum* isolations is ignored, the relative incidence of other dermatophyte isolations differs little from that reported by English and Lewis (1974) and Gentles (1974). Presumably, the high incidence of cattle ringworm reflects the strong agricultural bias of the Northern Ireland economy, and it would be of considerable interest to compare these findings with observations in areas with a similar economy in other parts of the United Kingdom.

References

British Medical Journal (1970). **1**, 185.

English, M. P. and Lewis, L. (1974). *British Journal of Dermatology*, **90**, 67.

Gentles, J. C. (1974). Personal communication.

Mackenzie, D. W. R. and McArdle, Maura (1960). *Ulster Medical Journal*, **29**, 70.

Mackenzie, D. W. R., Corkin, D. L. and Bell, Hilary (1961). *Ulster Medical Journal*, **30**, 29.

Mackenzie, D. W. R., Corkin, D. L. and Rusk, Lesley (1962). *Ulster Medical Journal*, **31**, 93.

Mackenzie, D. W. R., Corkin, D. L. and Rusk, Lesley (1963). *Ulster Medical Journal*, **32**, 197.

Mackenzie, D. W. R. and Rusk, Lesley (1964). *Ulster Medical Journal*, **33**, 94.

Rebell, G., Taplin, D. and Blank, H. (1964). *'Dermatophytes: Their Recognition and Identification'*. Miami: Dermatology Foundation.

HL—A TYPING IN NORTHERN IRELAND 1971-74

by

S. D. NELSON, F.R.C.P.I., M.R.C.Path.,

Consultant Haematologist, Craigavon Area Hospital

and

D. MIDDLETON, B.Sc.,

Senior Scientific Officer, The Laboratories, Belfast City Hospital

INTRODUCTION

FOR the past few years the policy in most transplantation centres has been to allocate cadaver kidneys to recipients whose tissues are antigenically similar to the donor's. Tissue similarity has been assessed by comparison of the HL-A antigens identifiable on lymphocytes (not kidney or other tissue cells) from donor and recipient. The technique of HL-A typing is not in itself difficult. Briefly, lymphocyte suspensions are prepared from freshly drawn peripheral blood by flotation on a Triosil-Ficoll solution (Harris and Ukaejiofo, 1969). After washing with buffered saline, the suspensions are added to tissue typing plates which have been primed with sera and covered with liquid paraffin to prevent evaporation. Each plate has spaces for up to 72 sera. After incubation, complement, in the form of a mixture of rabbit and human serum, is added to each test and a further incubation carried out. In those tests where lymphocyte antigens have reacted with the sera, complement activation results in cell death. Microscopic examination after the addition of trypan blue (which stains the killed cells but is excluded from living ones) enables positive tests to be identified.

In common with most of the tissue typing laboratories in Great Britain, we receive our sera from the National Tissue Typing Reference Laboratory (N.T.T.R.L.) in Bristol. This has the advantage that donors and recipients throughout Britain are, in the main, typed with the same sera. The HL-A antisera in use are mainly obtained from women during pregnancy who become immunised to HL-A antigens inherited by the foetus from the father. Antibody-containing sera are identified by the same basic method as for HL-A typing, except that cells of known antigen content from a panel of volunteers (members of staff) are tested against sera of unknown antibody content. Most tissue typing laboratories, including our own, carry out a screening programme on pregnancy sera as part of their routine work. Potentially useful sera are submitted to N.T.T.R.L. who carry out further tests, and may request further supplies of the test sera.

In parallel with the antibody screening programme, serum samples from prospective kidney recipients are also tested. This is of importance, since antibodies in a recipient's serum may cause immediate rejection of an incompatible transplant. They are in general weak antibodies, and are difficult to characterise.

The work of the tissue typing laboratory thus comprises three parts, namely HL–A typing for transplantation, serum supply, and transplant recipient screening for HL–A antibodies. We present below some of our findings during the three year period, September 1971–August 1974.

HL–A Typing

During the three year period 64 potential kidney recipients were typed. A further 48 patients, potential kidney donors, were also typed; and in the establishment of the antibody screening programme cells from a staff panel numbering 108 were tested, most of them during late 1973 and early 1974. We were, therefore, able to type the staff panel with an improved range of sera for antigens in the W19 complex, earlier tests being relatively insensitive for these factors. Since there is at present much interest in the distribution of the HL–A antigens in various diseases and conditions of stress, we have compared the antigen frequencies in our prospective kidney recipients and potential donors, and in our staff panel with the Bristol blood donor panel reported by Nelson, Darke and Tovey (1974). Table I shows the antigen frequencies in the four groups.

TABLE I

HL–A antigen frequencies in kidney recipients, donors, and hospital staff, compared with a blood donor panel (Nelson et al, 1974). Chi squared values greater than 8.0 (with Yates' correction) are indicated

HL–A	*Kidney Recipients (Actual + Potential)* N=64		*Kidney Donors (Actual + Potential)* N=48		*Staff Panel* N=108		*Bristol Blood Donor Panel* N=1036	
	No.	%	No.	%	No.	%	No.	%
1	25	39	20	42	42	39	348	34
2	38	59	24	50	52	48	536	52
3	14	22	14	29	25	23	265	26
9	11	17	13	27	15	14	190	18
10	6	9.4	4	8.3	6	5.6	87	8.4
11	6	9.4	2	4.2	12	11	106	10
W28	0	—	2	4.2	9	8.3	38	3.7
W19	10	5.6	2	4.2	26	24	175	17
5	3	4.7	3	6.3	9	8.3	87	8.4
7	19	30	19	40	32	30	265	26
8	22	34	16	33	23	21	260	25
12	16	25	13	27	†46	42	254	24
13	1	1.6	1	2.1	3	2.8	45	4.3
W5	8	13	6	13	6	7	114	11
W10	8	13	6	13	15	14	116	11
W14	5	7.8	4	8.3	3	2.8	72	7
W15	9	14*	1	2.1	11	10	50	4.8
W17	7	11	4	8	11	10	79	7.6
W18	5	7.8	3	6.3	2	1.91	35	3.4
W21	1	1.6	1	2.1	1	0.9	18	1.7
W22	2	3.1	1	2.1	3	2.8	55	5.3
W27	5	7.8	2	4.2	10	9.3	77	7.4

*Chi squared=8.39; $0.005 > p > 0.001$; after correction $0.115 > p > 0.023$
†Chi squared=15.56; $p < 0.0005$; after correction < 0.015

When the same population samples are compared several times, the chance of finding a "statistically significant" difference increases with the number of comparisons. Accordingly, in assessing the significance of inter-sample differences, the p value obtained must be corrected by multiplying it by the number of comparisons (Grumet et al, 1971). In this instance where we have made 23 comparisons, statistical significance will only be maintained if p before correction is less than 0.002; (Chi squared greater than 9.548).

Under these criteria, the antigen frequencies in our patients and staff showed few differences from the Bristol blood donors. Surprisingly, the expected reduction in W19 antigens of the kidney recipients and donors did not achieve statistical significance; the only finding of significance was that HL–A12 occurred more frequently in our staff panel than in the Bristol blood donors (Chi squared=15.56). The fact that our staff panel is, by definition, a selected population sample and not a random one is the most obvious explanation of the increase in HL–A12, particularly since population sampling errors tend to be more striking in relatively small samples.

Pregnancy Serum Testing for HL–A Antibodies

Since October 1973 we have screened samples of ante-natal sera kindly supplied by the Northern Ireland Blood Transfusion Service, and by the Laboratory, Craigavon Area Hospital. The sera are obtained from blood grouping specimens taken routinely during pregnancy, and the test for HL–A antibodies does not involve taking extra blood from the patients. The frequency with which HL–A antibodies are found in the serum increases with maternal parity, from approximately 5 per cent in primigravidae, to around 40 per cent in women who have had five or more pregnancies. Antibodies formed during a first pregnancy are usually weak, although often of narrow specificity. In subsequent pregnancies, the antibodies may be of higher titre, and are often directed against more than one antigen. Sera in which antibodies are found are re-tested in an attempt to define their specificity and titre. When the antibody is of good titre and monospecific, a further sample (30 ml) is requested through the courtesy of Col. Field (Northern Ireland Blood Transfusion Service). The sera from these larger samples are submitted to the National Tissue Typing Reference Laboratory for confirmation of our findings. If suitable, the sera are used as HL–A typing reagents. Table II presents a brief statistical summary of the ante-natal serum screening programme.

Antibody Testing of Kidney Recipients' Serum

A small proportion of patients awaiting a transplant already have, or may develop, HL–A antibodies following blood transfusion. Transplantation of an incompatible kidney into these patients is usually followed by hyper-acute rejection. In many cases the antibodies are weak; indeed they may become detectable only after a pyrexial episode (Nelson et al, 1971). It is therefore important to test recipients' serum regularly and to carry out a "cross match" using patient's serum and donor lymphocytes prior to transplantation. By this means, the possibility of a hyperacute rejection reaction can be avoided.

TABLE II

Results of Pregnancy Serum Screening
October 1973 – *August* 1974

Number of Pregnancy sera tested				3,700
Number with HL–A antibodies				460
Per cent with HL–A antibodies				12.4
Larger sample requested for further investigation				50
Samples sent to N.T.T.R.L.				36
Specificities:	HL–A1	(5)	HL–A2	(5)
	HL–A5	(2)	HL–A7	(8)
	HL–A8	(4)	HL–A12	(6)
	W5	(2)	W15	(1)
	W10	(2)	W32	(1)

During the three year period under review, serum samples from 58 patients were tested for HL–A antibodies. Eleven (19 per cent) were found to be positive, and of these, seven were awaiting a second transplant. No positive cross matches have been found and nine of these eleven patients have now received a transplant without evidence of hyperacute rejection.

COMMENT

The place of HL–A matching for transplantation has not yet been fully assessed; and while recent reports have suggested that HL–A identity between donor and recipient confers some benefit (Oliver et al, 1972; Van Hooff et al, 1973) there is no doubt that many kidneys transplanted to recipients of widely different HL–A types will function for a long time (Belzer et al, 1974). It may be that the emphasis should be placed on ensuring that kidney recipients are immunised by their transplants only to low frequency antigens. This policy would have obvious benefits in the event of a second transplant becoming necessary, because a second donor would be unlikely to present the recipient with an antigen to which he had already been immunised.

In the pregnancy serum screening programme our experiences have been similar to those of Stastny (1972). So far we have identified sera with activity against the more common HL–A antigens, but we hope in due course to uncover also examples of the rarer antibodies. Attempts to provide useful sera for our own or for national use have become more important following the demonstration by Brewerton et al (1973) of a striking relationship between ankylosing spondylitis and the presence of the antigen HL–A27. This antigen, present in about 7.5 per cent of healthy people, is found in more than 90 per cent of sufferers from ankylosing spondylitis; its presence or absence may be a helpful diagnostic clue, and we can now provide tests for the presence of this antigen when requested. The use of HL–A typing tests in various disease states will almost certainly increase during the next few years, but we hope also for an increase in the number of potential (and actual)

kidney donors, since successful transplant operations are of benefit not only to the recipients but may also permit new patients to receive dialysis treatment more readily.

Summary

The Tissue Typing Laboratory deals mainly with the immunological tests carried out in relation to renal transplantation. These include HL–A typing of prospective recipients and donors and testing of recipients' serum for the presence of antibodies which might cause hyperacute rejection of a transplant. The antisera used for HL–A typing are usually obtained from pregnant mothers, and most tissue typing laboratories also test pregnancy sera for potentially useful antibodies by observing their reactions with cells of known HL–A type.

Between September 1971 and August 1974, 64 potential kidney recipients and 48 possible donors were typed, as were 108 members of staff at the Belfast City Hospital whose cells were used in antibody detection and identification. The HL–A antigen frequencies in these three groups were compared with each other and with a large population of blood donors from the Bristol area. HL–A12 was identified more frequently in members of staff than in the other groups. This finding is attributed to the sampling error inherent in selected and relatively small population samples.

HL–A antibodies were found in 460 (12.4 per cent) of 3700 pregnancy sera; 36 of these were potentially valuable as typing reagents and aliquots were sent to the National Tissue Typing Reference Laboratory for confirmation of our findings. The urgency of the task of serum procurement is made more acute by the increase in requests for tissue typing which has followed recognition of the association between HL–A27 and ankylosing spondylitis.

Acknowledgements

We are indebted to Col. T. Field and his staff at the Northern Ireland Blood Transfusion Service for their help with the provision of serum samples from pregnant mothers. Thanks are also due to Miss D. Calvert who typed the manuscript.

References

1. Belzer, F. O., Perkins, H. A., Fortmann, J. L., Kountz, S. L., Salvatierra, O., Cochrum, K. C., and Payne, Rose (1974). *Lancet*, **1**, 774.
2. Brewerton, D. A., Hart, F. D., Nicholls, A., Caffrey, Maeve, James, D. C. O. and Sturrock, R. D. (1973). *Lancet*, **1**, 904.
3. Grumet, F. C., Coukell, A., Bodmer, J. G., Bodmer, W. F. and McDevitt, H. O. (1971). *New England Journal of Medicine*, **285**, 193.
4. Harris, R., Ukaejiofo, E. O. (1969). *Lancet*, **2**, 327.
5. Nelson, S. D., Darke, C., and Tovey. G. H. (1974). *Tissue Antigens*, **4**, 361.
6. Nelson, S. D., Selwood, N. H., White, H. J. O., and MacKenzie, J. C. (1971). *Lancet*, **2**, 1424.
7. Oliver, R. T. D., Sachs, J. A., Festenstein, H., Pegrum, G. D. and Moorhead, J. F. (1972). *Lancet*, **2**, 1381.
8. Stastny, P. (1972). *Symposia Series in Immunobiological Standardisation (Karger, Basel)*, **18**, 48.
9. Van Hooff, J. P., Schippers, H. M. A., Van der Steen, G. J. and Van Rood, J. J. (1972). *Lancet*, **2**, 1385.

SPINAL BRACING IN CHILDREN WITH ATONIC CEREBRAL PALSY

by

W. V. JAMES, F.R.C.S.,

Consultant Orthopaedic Surgeon,
Musgrave Park Hospital, Belfast

FOLLOWING a survey of mentally subnormal patients with orthopaedic abnormalities at Muckamore Abbey (James 1971), a group of children were found who were unable to sit unaided. These children were suffering from a mainly atonic form of cerebral palsy. Due to poor muscle tone their spines tended to "collapse" when sitting, and some had developed a fixed kyphosis or kyphoscoliosis. Due to their inability to sit they tended to lie in their cots and to have a very restricted view of the world. Attempts were made to sit them up, but they tended to sag and fall over. It seemed logical to fit these children with a spinal support that would hold their spine in a corrected position, so that the fixed spinal deformity could be prevented.

Some fifty children were found that would benefit by a support. The production of fifty standard braces was beyond the capacity of our usual orthotic services at that time. Miss G. Morris, of the Northern Ireland Orthopaedic Service, designed a support made of plastic that was produced in the Plastics Workshop at Musgrave Park Hospital, and later was also produced in the Plastics Workshop at Muckamore Abbey. The aim of the support was to correct the spinal deformity when the child was sitting, and that it could be easily, quickly and cheaply produced. The design has undergone changes as a result of experience. The main change is the abandoning of the chin support for those children that are unable to support their heads, and the substitution of a soft foam neck support.

The Children

Those selected were children with atonic cerebral palsy who were unable to sit unaided due to a "collapsing spine." Whilst the atonia was primarily responsible for the inability to sit, these children also had degrees of athetosis and spasticity, and the children were also mentally subnormal. All the spines were fully correctable when the children were suspended by the head.

The Support

Casting

The aim was to produce a cast of the trunk of the child with the spine straight. This position could be achieved either by manually suspending the child by the head, or applying neck and pelvic traction when the child was lying. While the child was held with the spine in the corrected position, three or four rolls of plaster of Paris were wrapped round the trunk and well moulded. If warm water was used

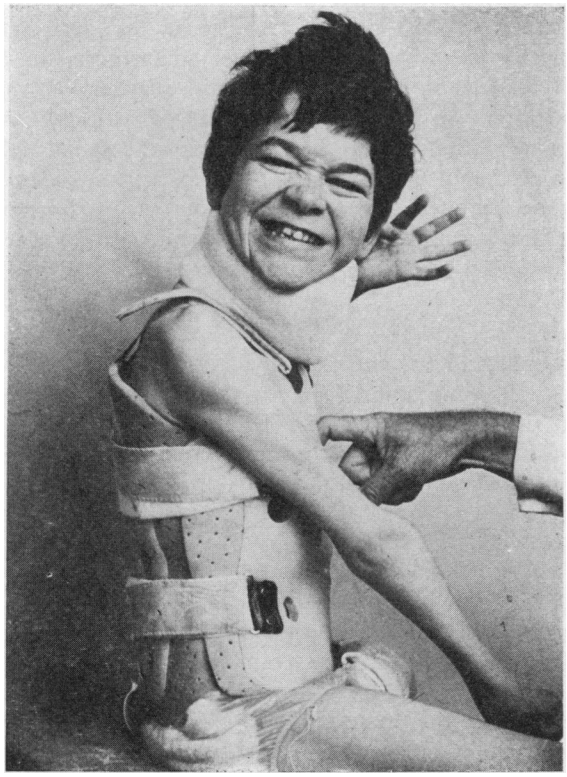
the plaster set rapidly. The cast was then removed with a plaster saw or shears, and was then reconstituted by closing the saw cut with a plaster bandage.

Production of the Support

Normally a positive cast of the trunk would be produced by filling the cast with Plaster of Paris. This step was eliminated by using a thin cast, and the plastic was moulded on to the outer surface of the cast. The slight increase in the circumference was allowed for when cutting the plastic. The support was made of polyethylene lined with Plastazote. Most of the supports consisted of an anterior and posterior shell united by Velcro straps, and shoulder and crutch straps were sometimes added.

Results

Over sixty children have been fitted with this type of support over the last four years. The benefits of the support in preventing fixed spinal deformity have not as yet been proved, for this will take many years to demonstrate. Other benefits have become apparent, that make the fitting of the support justifiable.



Balance

With their supports on the children can sit upright—many of them for the first time. Some of them have learned to balance their bodies and to sit unaided, which is the first step to some form of independance. Others, whilst unable to sit unaided, can manage to be propped in a vertical position and to avoid falling sideways or forward, although they do not have the capacity to correct their position if they do actually fall sideways or forward.

It was also noted that with the spine held in the extended position, that the tone of the neck muscles improved in some children, so that they were able to hold up their heads without support. In those children where the head was still difficult to control, a soft-foam neck support was used.

Nursing

Both parents and nurses found that these children were far easier to handle. The atonic child is like a "rag doll" and tends to slip out of the grasp. With the support on they are more easily held, especially when being fed. When sitting up in a chair without the support on, it was a constant worry that the child would fall across the arm of the chair, and this would cause injury or pain due to the inability of the child to move. With the support on, this is less likely to happen, and if it does, the child can sometimes correct itself, and if it cannot, the trunk is protected by the support itself.

Mental State

There is no doubt that these children benefit by external stimulation. Before wearing these supports there was a natural tendancy to leave these children in a cot, where external stimulation was limited and there was little of interest. With the support on they could sit in groups, see the world around them, play with toys lying before them, and generally take an interest. This was noted by Dr. Calvert, Consultant Psychiatrist at Muckamore Abbey, who conducted an experiment in intensive stimulation upon the children, and confirmed that they appeared to benefit. He has produced a film of the experiment and also of the method of production of the support.

Summary

A body support was produced for children with atonic cerebral palsy in order to prevent the onset of fixed spinal deformity. While the capacity to prevent spinal deformity has yet to be proved, other benefiits have become apparent. The children are now able to sit upright, are far easier to nurse, and due to more intensive stimulation appear more alert and contented.

Reference

James, W. V. (1971), *Ulster Medical Journal*, **40**, 54.

My thanks to Miss G. Morris, M.S.C.P., late of the Northern Ireland Orthopaedic Service, and to Mrs. G. Mills, Senior Physiotherapist at Muckamore Abbey. Those wishing instruction in the production of the support should contact the Plastics Workshop, Musgrave Park Hospital.

FENFLURAMINE IN THE TREATMENT OF HYPERTENSIVE PATIENTS WITH REFRACTORY OBESITY

by

M. E. SCOTT, M.D., M.R.C.P., B.Sc.

and

P. G. NELSON, M.B., M.R.C.P.

Royal Victoria Hospital, Belfast

M. E. Scott now at Cardiac Unit, Craigavon Area Hospital, Craigavon, Northern Ireland.
P. G. Nelson now at Diabetic Department, King's College Hospital, London.

INTRODUCTION

OBESITY frequently co-exists with hypertension (Epstein et al, 1965) and the combination carries a higher mortality than either obesity or hypertension alone (Kannell et al, 1967). Weight reduction per se may lower the blood pressure (Fletcher, 1954; Salzano et al, 1958) and is therefore an essential part of any therapeutic regime for obese hypertensives (Chiang et al 1967).

The majority of obese patients can lose weight satisfactorily by dieting, provided regular visits to a dietitian or physician for advice and encouragement are arranged. However some patients require additional help in adhering to a reduction diet and to this end appetite suppressant drugs are widely prescribed (Duncan and Munro, 1968). Appetite suppressants of the amphetamine type have central nervous system stimulating properties, and antagonise sympatholytic antihypertensive agents (Day and Rand, 1962). Fenfluramine is an appetite suppressant which is claimed to be devoid of central nervous system stimulating properties (Oswald et al 1968), and to lower the blood pressure in hypertensive patients, including those on sympatholytic anti-hypertensive agents (Waal-Manning and Simpson, 1969; Stiglich, 1970; Bolodeoku et al, 1972). The present study was designed to evaluate the effect of fenfluramine on the appetite, weight and blood pressure of hypertensive patients with obesity which had proved refractory to serious attempts at dieting.

PATIENTS AND METHODS

During a six-month period 450 patients attended the hypertension clinic of the Royal Victoria Hospital, Belfast. One hundred and fifty-four (34 per cent) were 11 per cent or more above their standard weight (Metropolitan Life Insurance Co., 1960). These patients were placed on a 1000 calorie diet and reviewed at the clinic four weekly for 12 weeks by the doctor and dietitian. After this period most patients had lost at least 2 kg. The 26 patients who had lost less than 2 kg were invited to take part in a double blind cross-over trial of fenfluramine versus a placebo. The nature of the trial was explained to each patient and his general practitioner. Twenty-three patients agreed to enter the study. None was diabetic but six had

clinically stable ischaemic heart disease. All had been overweight for many years and had tried unsuccessfully to lose weight on at least two occasions.

Each patient received the active tablets (fenfluramine 20 mg) and the identical placebo tablets for consecutive 12 week periods, the order being determined randomly. The tablets were prepacked in labelled boxes which were coded in such a way that the patient, the doctor and the dietitian did not know which was being administered first. The key to each patient's code was kept in the hospital notes. The master code was held by the hospital pharmacist. Patients were instructed to take one tablet 1½ hours before the mid-day meal and two tablets 1½ hours before the evening meal. The patients were told to continue to diet and were seen every four weeks by the same doctor and dietitian. The weight was recorded and the erect and supine blood pressures were measured.

Of the 23 patients entering the trial, 3 attended poorly from the outset. Four patients withdrew during the first half of the trial because of symptoms which they attributed to the tablets; 3 of these had been taking the placebo. Fifteen of the remaining 16 patients completed the trial. One patient who died during the second half of the trial while on the placebo was included in the analysis.

An analysis of variance technique was employed to isolate independently the main sources of variation in the response to treatment, defined as weight change (kg) in each four week period. The sources of variation investigated were treatment, order of treatment, period of treatment (1-4, 5-8 and 9-12 weeks) and patients. Data relating to alterations in weight, blood pressure and serum biochemistry and details of the statistical techniques employed are available in the form of an appendix which can be obtained, on request, from M.E.S.

During the trial, alterations in the dosage of hypotensive drugs were avoided where possible. The occurrence and degree of anorexia (desired effect) were elicited at each visit and the patients were asked if they had developed any undesired effects. Estimations of serum electrolytes and liver function tests were performed at the start and end of each 12 week period. At the end of the trial each patient was exhorted to continue on the reduction diet and to return for review 12 weeks later.

Results

The average age of the nine females and seven males participating in the trial was 52 years. Their initial weights ranged from 77.4 kg to 123.2 kg. Their mean weight was 90.2 kg, which was 36 per cent above their standard weight. All received cyclopenthiazide plus potassium chloride throughout the trial. Six were receiving guanethidine, three methyldopa and three more received both these drugs. Two received debrisoquin and one, hydrallazine. The eight patients receiving fenfluramine first showed a mean fall in weight of 2.39 kg in the first 4 weeks and 3.41 kg in the full 12 weeks on the drug.

However, over the next 12 weeks, while receiving the placebo, the patients gained weight again so that at the end of the trial period the mean weight loss was 0.49 kg.

The eight patients receiving the placebo first showed a mean weight loss of 0.55 kg in the first 4 weeks and of 0.72 kg in the full 12 weeks on the placebo. Both these values are significantly less than the corresponding fall shown by the patients

receiving fenfluramine first ($P<0.01$). On switching to fenfluramine there was a further mean fall in weight of 1.43 kg in the first four weeks but thereafter there was an insignificant mean gain so that after the full 12 weeks on fenfluramine the mean weight loss was 1.19 kg. Both fenfluramine and placebo were significantly more effective when given first ($P<0.01$). In addition to this order effect there was a significant period effect for both fenfluramine and placebo, with progressive diminution in effectiveness in the second and third four week periods on each treatment. The rate at which the effectiveness of fenfluramine diminished in successive periods was significantly greater than that for the placebo ($P<0.05$).

The dosage of hypotensives was altered in 4 of the 16 patients. The dosage was reduced during fenfluramine therapy in 3 and increased slightly in one. Two of the patients whose dosage was reduced while on fenfluramine had it increased again when switched to the placebo. The degree of postural fall in blood pressure noted before the trial did not differ during treatment with either fenfluramine or the placebo.

In the 13 patients whose hypotensives were unchanged or reduced during fenfluramine therapy the mean fall in recumbent pressure was 15 (± 7) mmHg systolic and 9 (± 3) mmHg diastolic. For those receiving the placebo the mean fall was 1 (± 5) mmHg systolic and 2 (± 3) mmHg diastolic. In the former case the fall is significantly different from zero for systolic blood pressure ($P<0.05$) and also for diastolic blood pressure ($P<0.05$), while in the latter it is not. The magnitude of the fall in pressure tended to be greater when fenfluramine was given before the placebo (20/12 mmHg) than when given after it (+4/-6 mmHg).

The three patients who had to have their dosage of hypotensives reduced showed a mean fall in pressure of 38/22 mmHg. One patient whose hypertension had proved resistant to therapy, only came under reasonable control while taking fenfluramine and control was lost again on changing to the placebo. All 6 patients showing falls in systolic blood pressure of more than 20 mmHg while taking fenfluramine, were amongst the 8 patients being treated with guanethidine and methyldopa, or guanethidine alone. No striking changes in blood pressure were observed in the 2 patients on debrisoquin nor in the single patient on hydrallazine.

Anorexia was reported by seven of the eight patients receiving fenfluramine first and also by seven of the eight patients receiving it second. In 10 of the 16 anorexia was sustained throughout most of the 12 weeks on the drug. Five of the eight patients receiving the placebo first reported anorexia compared with one out of seven receiving it second: in only three cases out of fifteen was it sustained.

Side effects were given as the reason for withdrawal from the trial by four patients who are therefore included in the analysis of side effects. Among nine patients receiving fenfluramine first, one left the trial because of severe diarrhoea which returned with each re-exposure to the drug, and five others experienced: –weakness (3), drowsiness (1) and mild diarrhoea (1). Of the 11 patients receiving the placebo first, three withdrew early in the trial, partly because of alleged weakness (1), dizziness (1) and diarrhoea (1), and partly because of the discouragement occasioned by their failure to lose weight. Two patients felt mildly depressed for a few days after switching from the active tablets to the placebo.

The serum sodium, potassium, chloride, carbon dioxide, specific gravity, urea and six measures of hepatic function were estimated in participating patients before and after fenfluramine therapy. Hotelling's T^2 test of the null hypothesis of no alteration in each of these measurements simultaneously yielded a non-significant result ($P<0.05$). Furthermore, no individual patient, including two who had initially mild elevation of their SGOT and SGPT levels, showed any clinically important change in hepatic or renal function.

Discussion

In the management of obesity the role of anorectic drugs, including those possessing additional glycolyptic activity is unclear. The fact that 83 per cent of our hypertensive patients lost more than 2 kg with diet and encouragement alone indicates that most obese patients do not need drug therapy, at least initially.

To merit prescription for obesity a drug should be effective in patients who have proved incapable of losing weight without drugs, should not rapidly lose its effectiveness and should not aggravate or interfere with the treatment of common co-existing conditions such as hypertension. It should also be free from unpleasant subjective and dangerous metabolic side effects and from the risk of abuse. In this study fenfluramine met some but not all of these criteria.

Fenfluramine did help our patients to lose weight. As in earlier studies (Traherne, 1965; Munro et al, 1966; Brodbin and O'Connor, 1967; Gaind, 1969; Stunkard et al 1973), fenfluramine performed significantly better than a placebo. This superiority was especially marked during the first four weeks of treatment. The progressive diminution in the rate of weight loss indicates that tolerance occurred (Stunkard et al 1973). The magnitude of the weight loss over the 12 weeks was disappointing, though other anorectic drugs studied under carefully controlled conditions have given similarly disappointing results (Stunkard et al 1973; Silverstone et al 1970; Follows, 1971). The fact that the patients' mean weight was as great 12 weeks after the end of the trial as at its commencement indicates that fenfluramine did not have the lasting beneficial effects found by Lambusier (1965) and Hähnel (1973).

Fenfluramine had a significant overall hypotensive effect on our patients. The mean fall was not marked and no patient became hypotensive. However, patients on hypotensive drugs, particularly guanethidine and methyldopa, should have their blood pressure checked regularly on being given fenfluramine and again on its withdrawal. Waal-Manning and Simpson (1969) found a similar hypotensive effect in patients on guanethidine and methyldopa and also those on reserpine. They suggested that these three hypotensive agents may partly counteract the anorectic effects of fenfluramine. In spite of the possibility of such an effect, our patients reported sustained anorexia more frequently with fenfluramine than with the placebo.

Side effects were commoner during consumption of fenfluramine than with the placebo, but as in most other studies they were relatively mild. In the only patient to withdraw because of a side effect (diarrhoea) while on fenfluramine, the reappearance of the same side effect on subsequent exposures indicated a true cause and effect relationship. In contrast the three patients who withdrew because of side effects which they attributed to the placebo and who would not sample it again,

may have been influenced as much by disappointment at not losing weight as by the severity of the side effects. The incidence of side effects in patients on fenfluramine was comparable to that found by Gaind (1969), Silverstone et al (1970) and Lawson et al (1970) but less than that found by other authors (Stunkard et al 1973; Hollingsworth and Amatruda 1969). The absence of any alteration in renal or hepatic function in our patients is reassuring, though more exhaustive evidence would be required before the safety of fenfluramine in patients with substantial impairment of renal or hepatic function could be established.

The mild depression noted by two patients at the time of switching from fenfluramine to placebo agrees with experimental observations made in the sleep laboratory (Oswald et al 1971). No episodes of serious depression were observed on withdrawal of fenfluramine but it would seem prudent to use fenfluramine cautiously in patients who have been depressed and to withdraw it gradually (Anderson 1972; Harding 1972).

We conclude that the administration of fenfluramine to hypertensives with intractable obesity is helpful in initiating weight loss. A course of treatment lasting not more than four weeks may help to convince such patients that weight loss is possible. However since tolerance develops rapidly prolonged treatment with fenfluramine does not appear to be indicated in their longterm management. In view of its relative freedom from side effects its hypotensive action merits further study in patients with mild hypertension.

Summary

A double blind cross-over trial of fenfluramine and placebo tablets, each given for 12 weeks, was performed on 23 hypertensive patients with refractory obesity. Weight loss with fenfluramine was significantly greater than with a placebo, especially in the first four week period, but the absolute weight loss was disappointing. A statistically significant order effect was noted in that both fenfluramine and placebo resulted in greater weight loss when given first. Twelve weeks after the trial the patients had returned to their original weight.

There was a significant fall in blood pressure with fenfluramine therapy but not the placebo. Fenfluramine therapy was associated with more anorexia and a slightly higher incidence of side effects than the placebo. It produced no alteration in renal or hepatic function.

Acknowledgements

This work was done while MES held a Royal Victoria Hospital research fellowship. We are grateful to Professor J. F. Pantridge for allowing us to study the patients under his care; to Miss B. E. Eakins for dietetic advice and assistance, and to Servier Laboratories for supplying the fenfluramine and placebo tablets. Our particular thanks go to Mr. Gilbert Mackenzie for his help with the statistical analysis.

Requests for reprints should be addressed to Dr. Michael E. Scott, Cardiac Unit, Craigavon Area Hospital, Craigavon, Northern Ireland.

References

ANDERSON, J. (1972). *British Medical Journal*, **1**, 560.

BOLODEOKU, J. O., KWAKU ADADEVOH, B., PALMER, E. O. (1972). *Nigerian Medical Journal*, **2**, 199.

BRODBIN, P., O'CONNOR, C. A. (1967). *Practitioner*, **198**, 707.

CHIANG, B. N., PERIMAN, L. V., EPSTEIN, F. H. (1967). *Circulation*, **39**, 403.

DAY, M. D., RAND, M. J. (1962). *Lancet*, **2**, 1282.

DUNCAN, L. J. P., MUNRO, J. F. (1968). *Practitioner*, **200**, 167.

EPSTEIN, F. H., FRANCIS, J. JR., HANER, N. S., JOHNSTON, B. C., KJELSBERG, M. O., NAPIER, J. A., OSTRANDER, L. D. JR., PAYNE, M. W., DODGE, H. J. (1965). *American Journal of Epidemiology*, **81**, 307.

FLETCHER, A. P. (1954). *Quarterly Journal of Medicine*, **23**, 331.

FOLLOWS, O. J. (1971). *British Journal of Clinical Practice*, **25**, 236.

GAIND, R. (1969). *British Journal of Psychiatry*, **115**, 963.

HAHNEL, J. (1973). *Therapiewoche*, **48**, 4692.

HARDING, T. (1972). *British Journal of Psychiatry*, **121**, 338.

HOLLINGSWORTH, D. R., AMATRUDA, T. T. (1969). *Journal of Clinical Pharmacology and Therapeutics*, **10**, 540.

KANNELL, W. B., LEBAUER, E. J., DAWBER, T. R., MACNAMARA, P. M. (1967). *Circulation*, **35**, 734.

LAMBUSIER, P. (1965). *La Vie Medicale*, **46**, 679.

LAWSON, A. A. H., ROSCOE, P., STRONG, J. A., GIBSON, A. (1970). *Lancet*, **2**, 437.

METROPOLITAN LIFE INSURANCE CO. (1960). *Statistical Bulletin*, **41**, 4.

MUNRO, J. F., SEATON, D. A., DUNCAN, L. J. P. (1966). *British Medical Journal*, **2**, 624.

OSWALD, I., JONES, H. S., MANNERHEIM, J. E. (1968). *British Medical Journal*, **1**, 796.

OSWALD, I., LEWIS, S. A., DUNLEAVY, D. L. F., BREZINOVA, V., BRIGGS, M. (1971). *British Medical Journal*, **2**, 70.

SALZANO, J. V., GUNNING, R. V., MASTOPAULO, T. N., TUTTLE, W. W. (1958). *Journal of the American Dietary Association*, **34**, 1309.

SILVERSTONE, J. T., COOPER, R. M., BEGG, P. R. (1970). *British Journal of Clinical Practice*, **24**, 423.

STIGLICH, G. M. (1970). *Tribuna Medica*, **25**, 8.

STUNKARD, A., RICKELS, K., HESBACHER, P. (1973). *Lancet*, **1**, 503.

TRAHERNE, J. B. (1965). *Practitioner*, **195**, 677.

WAAL-MANNING, H. J., SIMPSON, F. O. (1969). *Lancet*, **2**, 1392.

BOOK REVIEWS

THE EPILEPSIES. MODERN DIAGNOSIS AND TREATMENT. By J. M. Sutherland, H. Tait and M. J. Eadies. Second Edition. (Pp. 149, figures 30. £2.50 (soft back)). Edinburgh and London. Churchill Livingstone .1974.

EPILEPSY is a common symptom and about 6–8 persons per 1000 of the population suffer from some form of this distressing disorder. Few doctors are likely to escape the responsibility of management of patients suffering from epilepsy. This is an up-to-date sensible and practical guide to the subject for senior medical students, postgraduates and practitioners. The tables and summaries at the end of each chapter should be particularly useful for examination candidates. The illustrations are clear and numerous and the text easy to read.

The chapter on anticonvulsant drug therapy is outstanding and the authors emphasise the value of estimating the plasma levels of hydantoins and barbiturates in the management of patients.

Strongly recommended and good value for money!

J.H.D.M.

References

ANDERSON, J. (1972). *British Medical Journal*, **1**, 560.

BOLODEOKU, J. O., KWAKU ADADEVOH, B., PALMER, E. O. (1972). *Nigerian Medical Journal*, **2**, 199.

BRODBIN, P., O'CONNOR, C. A. (1967). *Practitioner*, **198**, 707.

CHIANG, B. N., PERIMAN, L. V., EPSTEIN, F. H. (1967). *Circulation*, **39**, 403.

DAY, M. D., RAND, M. J. (1962). *Lancet*, **2**, 1282.

DUNCAN, L. J. P., MUNRO, J. F. (1968). *Practitioner*, **200**, 167.

EPSTEIN, F. H., FRANCIS, J. JR., HANER, N. S., JOHNSTON, B. C., KJELSBERG, M. O., NAPIER, J. A., OSTRANDER, L. D. JR., PAYNE, M. W., DODGE, H. J. (1965). *American Journal of Epidemiology*, **81**, 307.

FLETCHER, A. P. (1954). *Quarterly Journal of Medicine*, **23**, 331.

FOLLOWS, O. J. (1971). *British Journal of Clinical Practice*, **25**, 236.

GAIND, R. (1969). *British Journal of Psychiatry*, **115**, 963.

HAHNEL, J. (1973). *Therapiewoche*, **48**, 4692.

HARDING, T. (1972). *British Journal of Psychiatry*, **121**, 338.

HOLLINGSWORTH, D. R., AMATRUDA, T. T. (1969). *Journal of Clinical Pharmacology and Therapeutics*, **10**, 540.

KANNELL, W. B., LEBAUER, E. J., DAWBER, T. R., MACNAMARA, P. M. (1967). *Circulation*, **35**, 734.

LAMBUSIER, P. (1965). *La Vie Medicale*, **46**, 679.

LAWSON, A. A. H., ROSCOE, P., STRONG, J. A., GIBSON, A. (1970). *Lancet*, **2**, 437.

METROPOLITAN LIFE INSURANCE CO. (1960). *Statistical Bulletin*, **41**, 4.

MUNRO, J. F., SEATON, D. A., DUNCAN, L. J. P. (1966). *British Medical Journal*, **2**, 624.

OSWALD, I., JONES, H. S., MANNERHEIM, J. E. (1968). *British Medical Journal*, **1**, 796.

OSWALD, I., LEWIS, S. A., DUNLEAVY, D. L. F., BREZINOVA, V., BRIGGS, M. (1971). *British Medical Journal*, **2**, 70.

SALZANO, J. V., GUNNING, R. V., MASTOPAULO, T. N., TUTTLE, W. W. (1958). *Journal of the American Dietary Association*, **34**, 1309.

SILVERSTONE, J. T., COOPER, R. M., BEGG, P. R. (1970). *British Journal of Clinical Practice*, **24**, 423.

STIGLICH, G. M. (1970). *Tribuna Medica*, **25**, 8.

STUNKARD, A., RICKELS, K., HESBACHER, P. (1973). *Lancet*, **1**, 503.

TRAHERNE, J. B. (1965). *Practitioner*, **195**, 677.

WAAL-MANNING, H. J., SIMPSON, F. O. (1969). *Lancet*, **2**, 1392.

BOOK REVIEWS

THE EPILEPSIES. MODERN DIAGNOSIS AND TREATMENT. By J. M. Sutherland, H. Tait and M. J. Eadies. Second Edition. (Pp. 149, figures 30. £2.50 (soft back)). Edinburgh and London. Churchill Livingstone .1974.

EPILEPSY is a common symptom and about 6–8 persons per 1000 of the population suffer from some form of this distressing disorder. Few doctors are likely to escape the responsibility of management of patients suffering from epilepsy. This is an up-to-date sensible and practical guide to the subject for senior medical students, postgraduates and practitioners. The tables and summaries at the end of each chapter should be particularly useful for examination candidates. The illustrations are clear and numerous and the text easy to read.

The chapter on anticonvulsant drug therapy is outstanding and the authors emphasise the value of estimating the plasma levels of hydantoins and barbiturates in the management of patients.

Strongly recommended and good value for money!

J.H.D.M.

A PRELIMINARY EXAMINATION OF GENERAL MEDICAL ADMISSIONS TO BELFAST HOSPITALS IN 1973

by

A. P. GRANT, F.R.C.P.

Belfast City Hospital

INTRODUCTION

THERE have been so many changes—political, social and technical which have altered the practice of general medicine in less than a professional lifetime that confusion and bewilderment affects many physicians. In Belfast the introduction of the Emergency Bed Service on 1st October 1969 combined with civil disturbances have intensified the problems of the general physician. Private and domiciliary practice have been decimated and personal contacts with general practitioners and colleagues have diminished. A responsibility to an impersonal system of community medicine rather than to patients referred by their family doctor seems to have arisen. It is appropriate to commence an examination of trends in general medicine in Belfast with a study of such figures as are available. An analysis of how the development of specialist subgroups, such as neurology, cardiology, rheumatology and geriatrics has affected it would require a much more detailed study. This preliminary study must determine where general medicine is being practised and what is the work load and its distribution. It is now possible to access the size of the emergency problem which is accepted by physicians on the Bed Service Rota where there is an unspecified clinical responsibility, an open commitment, and no rights to transfer. The statistics for general medicine in 1972–73 will be examined to ascertain the facts.

THE MEDICAL EMERGENCY SYSTEM IN BELFAST

The Input

The decision as to what constitutes an emergency is made by the general practitioner or in many instances at night by his locum, who is often a practitioner employed by a deputizing service. The factors which influence this decision are often largely social and only in part medical. The demand is infinite and increasing, while the pressures to pass on an insoluble problem become greater as society organization breaks down. Having made the decision on the data provided by the patient and his relatives, an assessment of the domestic support and sometimes the civil disturbances in the neighbourhood, and having made an examination or accepted the evidence of hearsay, the practitioner contacts the Emergency Bed Service (E.B.S.). The E.B.S. then has to find a bed and places the primary responsibility for providing it on the general medical unit on "take in" for the 24 hour period. If full, a back up hospital (Mater Hospital (M.H.) or Ulster Hospital (U.H.)) may be utilised, but if the system is overloaded the "take in" unit is again faced with making a bed available somewhere. This is accomplished by boarding out

patients in surrounding units, with not unreasonable complaints by the specialities thus involved. The input to a "take in medical unit" is, therefore, unspecified.

The Duration of Stay

A space of 6 days elapses before the same unit is again on "take in". Theoretically sufficient beds have been made available to deal with the expected input, which means approximately half the beds should be vacant in most units, with a service time or duration of stay of 14 days for each patient and 100 per cent bed occupancy.

The Output

Unfortunately, this is where the bottleneck seems to occur. Social long stay and geriatric problems have to be maintained in the unit as well as psychiatric patients. All these services claim an overload and the right of selection. There is no authority to pass on the responsibility of care for a patient who has received adequate medical treatment and investigation for his acute illness. Geriatric units work on a geographical basis of districts. They are not responsible for patients admitted to their own hospital group who may have come from another district except to make a geriatric assessment. Contact with geriatricians outside the district of the hospital concerned is on the whole unsatisfactory.

TABLE I

General Medical Accommodation in the City of Belfast 1973 (*E.B.S.*)

Hospital	*Beds*	*Take-in Medical Units*
Emergency Bed Service Rota:		
Royal Victoria (R.V.H.)	134	3
Belfast City (B.C.H.)	132	3
Musgrave Park (M.P.H.)	58	1
	324	7
Back Up Hospitals:		
Mater Infirmorum (M.H.)	66	
Ulster (U.H.)	48	
	114	
Total General Medical Beds	438	

Figures obtained from Emergency Bed Service

THE RESOURCES

The hospitals in the City of Belfast with their complement of general medical beds are shown in Table I. It will be seen they fall into 2 groups:

1. Hospitals on the Emergency Bed Rota which include the 2 major complexes

of the Royal Victoria Hospital (R.V.H.) and the Belfast City Hospital (B.C.H.). These, together with Musgrave Park Hospital (M.P.H.) provide 7 medical units each covering a take in for 24 hours every week and provide 324 beds.

2. Back up hospitals which do accept emergencies but are not under a specific responsibility in this respect are able to operate with greater selectivity. They provide 114 beds.

The Responsibility

Table II shows the population served by the hospitals. It will be noted there is a difference of 118,685 between the census figure and the population supplied by the

Table II

Population Statistics

City of Belfast (Census 1971)	362,400
New Health and Social Services Districts on 1st October 1973 (Department of Finance)	
North and West Belfast	228,511
South Belfast	105,754
East Belfast and Castlereagh	146,820
	481,085

newly defined Health and Social Services Districts for Belfast and Castlereagh. A difference which is only partially explained by the inclusion of Castlereagh Rural District with an estimated population of 64,406. An official explanation was not forthcoming but it was suggested that population transfers of major proportions could be a factor. It seems likely that the population of 481,085 is a more accurate assessment of the demand. To serve this population there are 0.91 general medical beds per 1,000.

The Workload and its Distribution

Table III shows the workload for 1973. Column 1 gives the total medical patients admitted to the hospital and includes both the medical units and observation unit. Column 2 gives the patients admitted to the care of medical units only and includes transfers from the observation unit. The difference may also include medical patients boarded out in surgical and other units during peak periods. The exact figures for these would be difficult to obtain under the present accounting methods. Column 3 shows the "Medical Emergencies" admitted via casualty on request of the E.B.S.

In Table IV these gross figures have been analysed as percentages for the purpose of comparison. As could be predicted from the system, the following facts emerge: –

TABLE III

General Medical Admissions and Their Distribution for the Year 1973 (*E.B.S.*)

Hospital	*Column* 1 *Total Admissions*	*Column* 2 *Total Admissions to Wards*	*Column* 3 *Medical Emergencies*
R.V.H.	3,930	3,421	3,197
B.C.H.	4,882	3,739	4,407
M.P.H.	944	944	767
M.H.	1,450	1,450	424
U.H.	1,480	1,480	337
	12,686	11,034	9,132

Figures from weekly statistics of Emergency Bed Service Cols. I, IA & 4

TABLE IV

Analysis of Medical Emergency Admissions during the Year 1973

Hospital	*Distribution of emergency load* *Percentage*		*Ratio emergency/Total in each hospital* *Percentage*	*Proportion*
R.V.H.	35.03		81.34	10 out of 12
B.C.H.	48.25		90.27	10 out of 11
M.P.H.	8.39	91.67%	81.25	10 out of 12
M.H.	4.64		29.24	10 out of 34
U.H.	3.69	8.33%	22.97	10 out of 41

1. The "medical emergencies" were overwhelmingly the responsibility of the hospitals on the E.B.S. rota which dealt with 91.67 per cent of them. These consist of the two major teaching complexes and 3 out of the 7 units are professorial.
2. The problem of dealing with the "medical emergencies" completely dominated the work of the medical units in these hospitals so that 10 out of 11 or 12 admissions were "emergencies". Each medical unit has to gear its whole activity to coping with a weekly input of unpredictable proportions at this level. To this end other responsibilities and commitments have of necessity been pruned by most of the consultants concerned. The input at times overwhelms the resources.
3. The back up hospitals show a very different pattern being able to cut their involvement in "medical emergencies" to a third or a quarter of the admissions to their general medical units. It may be reasonably concluded that the more traditional methods of consultant medical practice still apply. The physician accepts personal responsibility for the care of patients he has seen at the request of a general practitioner he knows. He is able to fill his beds on his own criteria of need for his skills. He can continue to see domiciliary and private patients knowing he is able to use facilitties for treatment and investi-

gation. His out-patients decisions are backed up by the knowledge he can admit patients for investigation without anxiety as to the bed state.

The Emergency Bed Rota as a Geriatric Admissions and Disposal Unit

Criticisms have been made by casualty consultants as well as physicians that the Emergency Bed Rota Units are being used for social and geriatric patients. An examination of such allegations would be complex but has been commenced. It would require analysis of the intake of patients and a critical determination of how much of the demand was for social reasons and how much of their medical need could be met by the provision of less costly accommodation than wards in a general hospital. Table V does, however, demonstrate that half the intake to the

Table V

Comparison of Age Statistics in General Medical Wards—B.C.H. & R.V.H.

		Under 40	41-65	65 + *years*
B.C.H. (1972)	2791 patients	13%	37%	51%
R.V.H. (1973)	1044 patients	12%	39%	49%

R.V.H. data from "Report of Working Party on the R.V.H." Page 7 which analysed the admissions to General Medical Units 1st January—1st April 1973.
B.C.H. figures extracted from Hospital Activity Analysis of patients in General Medical Wards during the whole of 1972.

major hospital medical beds are senior citizens over 65 years. The objectives of the general physician have not been clearly spelled out and it seems probable that financial stringencies may soon require a drastic reappraisal of the roles of the general physicians, the geriatricians, the general practitioners and the welfare authorities.

Summary and Conclusions

The workload of general medicine and its distribution among the Belfast hospitals has been analysed for the year 1972. To deal with these patients, beds are supplied at an apparently reasonable rate of 0.91 per 1,000 population. The influence of the Emergency Bed Service (E.B.S.) upon the practice of hospital medicine is predominant—out of a total 12,686 admissions 9,132 were "medical emergencies". The hospitals on the emergency rota had to accept 91.67 per cent of this load into 324 beds while the remaining hospitals only accepted 8.33 per cent into 114 beds. "Medical emergencies" are designated by the outside practitioners. The E.B.S. undertakes to arrange their admissions and the medical unit on duty in the emergency rota is made ultimately responsible for providing a bed. This label provides at present the only unrestricted access to hospitals and 50 per cent of such patients are senior citizens. "Medical emergencies" may be largely social, geriatric or even psychiatric problems as there are long waiting lists for these services. Their admission is unrestricted and their disposal from medical units is difficult.

Two types of hospital practice may be identified: –

1. The seven medical units on the E.B.S. rota have already all their patients admitted as "medical emergencies". These units are in the major hospital complexes with a heavy teaching programme and include three professorial units. Their work is dominated by the burden of accepting and disposing of "medical emergencies".
2. The back up hospitals which have approximately a quarter of the available beds have only a third or a quarter of their patients admitted as medical emergencies. It must be presumed that the majority of their patients are selected either by arrangement, by consultation or after a domiciliary visit. They would appear to practice more traditional medicine.

ACKNOWLEDGMENTS

My sincere thanks to Mr. A. Kelly, Unit Administrator, and Mrs. M. Stockman, Patients' Services Officer, Belfast City Hospital, without whose co-operation and advice on statistics this article could never have been written.

BOOK REVIEWS

DIVERTICULAR DISEASES (CLINICS IN GASTROENTEROLOGY Vol. 4, No. 1). Edited by A. N. Smith (Pp. 224. Illustrated. £6.00). London: Saunders. 1975.

THIS latest volume in the 'Clinics' series is devoted to papers on diverticular disease edited by Adam Smith, and with contributions from both sides of the Atlantic and both sides of the Irish Sea. Many aspects of this disease have been studied in the last two decades and these have thrown new light on the aetiology of this curious disorder of colonic function. There seems little doubt that dietary variation is correlated with the prevalence of the condition and that a high residue diet seems to protect against the development of the basic disorder. Denis Burkitt makes a cogent case for this theory with the touch of an evangelist, who regards a low residue diet as leading to the gates of vesico-colic fistula, if not quite to Hell itself. The precise mechanisms by which these changes are brought about are explored in papers by Alastair Connell, George Parks and Basil Morson and, in the last paper, John Hodgson attempts to convince us that animal models are appropriate for further research; not all of us will be convinced.

There is not as much that is new in the papers dealing with clinical management which has changed very little except in the assimilation of the fact that a high residue diet lowers colonic pressures, and we remember how, in the past, low residue diets were prescribed without any logical basis. These papers give a sound account of both medical and surgical management with a paper by Michael Reilly and Adam Smith discussing the place of sigmoid-myotomy in the management of early disease. This remains controversial and most clinicians suspect that the case that will respond to myotomy could be equally well managed by dietary measures and that if operation is really indicated resection is required. The case is also well made that resection before major complications arise should be considered.

This is an excellent book, well balanced and informative, bringing us up-to-date in this common disease which requires care and judgment in its management. The editor, the contributors and the publishers are to be congratulated.

D.R.

Two types of hospital practice may be identified: –

1. The seven medical units on the E.B.S. rota have already all their patients admitted as "medical emergencies". These units are in the major hospital complexes with a heavy teaching programme and include three professorial units. Their work is dominated by the burden of accepting and disposing of "medical emergencies".
2. The back up hospitals which have approximately a quarter of the available beds have only a third or a quarter of their patients admitted as medical emergencies. It must be presumed that the majority of their patients are selected either by arrangement, by consultation or after a domiciliary visit. They would appear to practice more traditional medicine.

ACKNOWLEDGMENTS

My sincere thanks to Mr. A. Kelly, Unit Administrator, and Mrs. M. Stockman, Patients' Services Officer, Belfast City Hospital, without whose co-operation and advice on statistics this article could never have been written.

BOOK REVIEWS

DIVERTICULAR DISEASES (CLINICS IN GASTROENTEROLOGY Vol. 4, No. 1). Edited by A. N. Smith (Pp. 224. Illustrated. £6.00). London: Saunders. 1975.

THIS latest volume in the 'Clinics' series is devoted to papers on diverticular disease edited by Adam Smith, and with contributions from both sides of the Atlantic and both sides of the Irish Sea. Many aspects of this disease have been studied in the last two decades and these have thrown new light on the aetiology of this curious disorder of colonic function. There seems little doubt that dietary variation is correlated with the prevalence of the condition and that a high residue diet seems to protect against the development of the basic disorder. Denis Burkitt makes a cogent case for this theory with the touch of an evangelist, who regards a low residue diet as leading to the gates of vesico-colic fistula, if not quite to Hell itself. The precise mechanisms by which these changes are brought about are explored in papers by Alastair Connell, George Parks and Basil Morson and, in the last paper, John Hodgson attempts to convince us that animal models are appropriate for further research; not all of us will be convinced.

There is not as much that is new in the papers dealing with clinical management which has changed very little except in the assimilation of the fact that a high residue diet lowers colonic pressures, and we remember how, in the past, low residue diets were prescribed without any logical basis. These papers give a sound account of both medical and surgical management with a paper by Michael Reilly and Adam Smith discussing the place of sigmoid-myotomy in the management of early disease. This remains controversial and most clinicians suspect that the case that will respond to myotomy could be equally well managed by dietary measures and that if operation is really indicated resection is required. The case is also well made that resection before major complications arise should be considered.

This is an excellent book, well balanced and informative, bringing us up-to-date in this common disease which requires care and judgment in its management. The editor, the contributors and the publishers are to be congratulated.

D.R.

PANCREATIC ISLET-CELL TUMOUR ASSOCIATED WITH CUSHING'S SYNDROME

Report of a case with Estimation of Tumour ACTH Content

by

IAN D. CRAIG and **PETER G. NELSON**

Institute of Pathology, The Queen's University of Belfast,
and Royal Victoria Hospital, Belfast

INTRODUCTION

CUSHING'S SYNDROME as a result of ectopic ACTH production has been recognised for several years. Many tumours arising in tissue thought to be derived from the primitive foregut appear to be capable of elaborating a variety of hormones, of which ACTH is the most completely documented. These include tumours of the lung, pancreas, bile ducts, thyroid, thymus and also from other sites such as colon (Crooke, 1946; Hallwright, North and Reid, 1964; Sasano, Fukuda, Saton and Tohoku, 1969; Bartholomew and Schutt, 1971; Anderson and McHugh, 1971; Rosai and Higa, 1972; Schteingart, Conn, Orth, Harrison, Fox and Bookstein, 1972). However, it is only recently as a result of improvements in radioimmunoassay techniques, that comparison of measurements of ACTH content of these tumours has become practicable. Pancreatic tumours, after bronchogenic tumours, are the entodermal derived tumours most frequently associated with ectopic ACTH production. Very few reports exist in the literature of cases where ACTH content of the pancreatic tumour has been determined using radioimmunoassay techniques (Sasano, Fukuda, Saton and Tohoku, 1969). It therefore seemed appropriate to record the following case report: —

HISTORY

A 59-year-old male was admitted to the Lagan Valley Hospital in 1972 (Dr. Jean Langlands) with a 4-week history of polydipsia, and recent excess alcohol intake. Apart from mild chronic bronchitis he had been in good health prior to this illness. A tentative diagnosis of diabetes mellitus was made which did not respond to treatment. His muscular weakness increased and he developed severe hypokalaemia (2.1 mmol. per 1). Adrenal overactivity was suspected and urinary steroid excretion was found to be raised. He was transferred to the Metabolic Unit, Royal Victoria Hospital (R.V.H. U.N.932311). His appearance was now more suggestive of Cushing's syndrome, with considerable proximal muscle wasting and weakness but no obesity, hypertension or skin striae. His face was not unduly florid. He complained of pain over the left lower rib margin consistent with a collapsed 6th dorsal vertebra. Straight x-ray of abdomen suggested a pancreatic tumour or cyst but on examination no abdominal mass could be palpated.

Investigations were curtailed due to his poor general condition. Cortisol secretion rate was 122 mg per 24-hours. Plasma cortisol at 11 p.m. was 44 μg per 100 ml. 2 mg dexamethasone was then given by mouth: the plasma cortisol at

7 a.m. next morning was 49 μg per 100 ml, confirming the absence of a circadian rhythm and showing non-suppressibility of adrenal cortical function. Urinary 17-oxosteroid excretion was 21.5 mg in 24-hours and 17-oxogenic steroid excretion was 42.8 mg in 24-hours. An oral glucose tolerance test had been mildly abnormal. The highest blood sodium was 141 m mol/l, the lowest potassium 2.1 m mol/1, and the CO_2CP was increased to 39 m mol/l. Haemoglobin was 14.0g percent. Radiological examination showed extensive osteoporosis with collapse of the sixth dorsal and second lumbar vertebrae. Barium meal showed a large space-occupying mass displacing the stomach downwards and forwards.

At operation on 4th October, 1972 (Mr. T. L. Kennedy) a large malignant tumour was found involving the tail of the pancreas. It was possible to remove most of this tumour. There was also bilateral adrenal hyperplasia and a total adrenalectomy was performed. The blood pressure was low during the operative procedure. He did not recover consciousness presumably due to this hypotensive episode and he eventually died on the fifth post-operative day.

Biopsy Specimens: Both glands were enlarged. The left gland was received intact and weighed 17g., the right was in several pieces and weighed 12g. Histologically there was bilateral cortical hyperplasia involving primarily the zona fasiculata. Zones of lipid depletion alternated with zones of high lipid content.

The specimen of pancreas and tumour was received in two pieces. The tumour which arose in the tail of the pancreas consisted of an infiltrating carcinoma, the cells of which were arranged in sheets and cords and in areas resembling islet cells, being oval to spindle in shape with small round hyperchromatic nuclei and lightly staining cytoplasm. Mitotic figures were rare. In some sections the tumour was divided into imperfectly formed lobules by bands of hyaline stroma. No capsule was observed and invasion of the peri-pancreatic fat was seen in most sections taken. Granules could not be demonstrated in any of the sections examined, using Gomori's chrome alum haemotoxylin and Gomori's aldehyde fuschin.

ACTH estimation was by radio-immunoassay using the Amersham Radiochemical Centre kit. ACTH level was 0.772 ug/g wet weight. No ACTH was found in normal pancreatic control material.

At autopsy the tumour was found to have been completely excised. The head and part of the body of the pancreas were intact but at the site of the operation an acute inflammatory process was seen. A few fragments of the right adrenal gland remained and showed a similar appearance to the biopsy specimens.

The pituitary was not enlarged but Crooke's hyaline change was found. Proximal limb muscles showed diffuse fibre involvement with no evidence of group atrophy. Sarcolemmal proliferation with marked fibre degeneration and occasional fibres showing abortive regenerative changes were observed. Peripheral nerves however showed no abnormality. The spinal cord was not available for examination.

Discussion

The rapid onset of Cushing's syndrome with severe hypokalaemia in an otherwise healthy adult is highly suggestive of inappropriate ACTH secretion by a tumour. Histologically the tumour in this case showed the generally accepted appearances of an islet cell-derived carcinoma of the pancreas, the inability to demonstrate granules histologically being well-recognised. The findings in the adrenal and

pituitary were typical of Cushing's syndrome secondary to excess ACTH production. The proximal muscle wasting was most probably a direct cortisone effect; as it was not possible to examine the spinal cord, CNS involvement could not be definitely excluded although the muscles did not show fibre group atrophy.

The association of adrenocortical overactivity and "non-endocrine" tumours was actually suspected before Cushing's original monograph was published (Brown 1928). The ectopic ACTH syndrome was first defined by Meador *et al* (1962) who showed elevated ACTH (bioassay) in the tumour and plasma, and decreased pituitary ACTH content. This syndrome is the best documented model of ectopic hormone production and at least 94 cases with positive tumour levels by bioassay or radioimmunoassay have been published (Rees and Ratcliffe, 1974). Tumours associated with ectopic ACTH production can be divided into four main groups—(i) oat cell carcinomas of bronchus; (ii) tumours of foregut origin (islet cell pancreatic tumours, carcinoids, thymoma and medullary carcinoma of thyroid); (iii) phaeochromocytomas and related tumours; and (iv) certain ovarian tumours. Many of these tumours are rather pleomorphic.

The amount of ACTH determined by radioimmunoassay in this pancreatic tumour was in the mid-range of ACTH content in reported cases of ectopic ACTH production by all types of tumour tissues (.001 to 1000 μg/g wet weight). This very wide range is confirmed for both bioassay and radioimmunoassay techniques, and presumably represents wide variation in the peptide struction of these ACTH-like compounds.

Summary

A case of ectopic ACTH production in an islet cell tumour of the pancreas associated with Cushing's syndrome of rapid onset is reported. The ACTH content of the tumour was determined by radioimmunoassay.

Acknowledgements

The authors are grateful to Dr. D. R. Hadden, Dr. D. A. D. Montgomery, Dr. Jean Langlands and Mr. T. L. Kennedy for their encouragement to report this case and to Mr. J. S. McKay and Mr. B. Sheridan, Metabolic Laboratory, R.V.H., for carrying out the ACTH estimations and other endocrinological measurements.

References

ANDERSON, A. E. and MCHUGH, P. R. (1971). *Journal of Nervous and Mental Diseases*, **152**, 427.

BARTHOLOMEW, L. G. and SCHUTT, A. J. (1971). *Cancer*, **28**, 170.

BROWN, W. H. (1928). *Lancet*, **2**, 1022.

CROOKE, A. C. (1946). *Journal of Pathology and Bacteriology*, **58**, 667.

HALLWRIGHT, G. P., NORTH, K. A. K. and REID, J. D. (1964). *Journal of Clinical Endocrinology*, **24**, 496.

MEADOR, C. K., LIDDLE, G. W., ISLAND, D. P., NICHOLSON, W. E., LUCAS, C. P., NUCKTON, J. G. and LEUTSCHER, J. A. (1962). *Journal of Clinical Endocrinology*, **22**, 693.

REES, L. H. and RATCLIFFE, J. G. (1974). *Clinical Endocrinology*, **3**, 263.

ROSAI, J. and HIGA, E. (1972). *Cancer*, **29**, 1061.

SASANO, N., FUKUDA, T., SATON, E. and TOHOKU, J. (1969). *Journal of Experimental Medicine*, **99**, 361.

SCHTEINGART, D. E., CONN, J. W., ORTH, D. N., HARRISON, T. S., FOX, J. E. and BOOKSTEIN, J. J. (1972). *Journal of Clinical Endocrinology*, **34**, 676.

AN UNUSUAL CASE OF ANAEMIA

by

W. G. HUMPHREYS, F.R.C.S.

Belfast City Hospital*

LYMPHANGIOMATOUS cysts of the greater omentum are uncommon. They are seldom diagnosed prior to surgery. They may be discovered incidentally at laparotomy or when complications ensue.

This case is reported to emphasise the importance of omental lesions in the differential diagnosis of intra-abdominal abnormalities and because of the unusual mode of presentation.

Case History

A two year old boy was admitted to the Belfast City Hospital on 11th November 1972 with a one week history of anorexia, listlessness and increasing pallor. He had been well until one week prior to admission when he had had a 'flu-like illness. There was no relevant past or family history.

On examination, the child was normally developed with no evidence of recent wasting. The most striking feature was marked pallor. He was apyrexial and there was no generalized lymphadenopathy. The cardiovascular and respiratory systems were normal. The abdomen was distended with umbilical eversion. No discrete masses were present. The liver was palpable at the right costal margin but there was no splenomegaly. Bowel sounds were normal. There was dullness to percussion consistent with the presence of ascites.

Haematological investigations revealed the haemoglobin concentration to be 2.8 gm/100 ml with a normal differential white cell count. The direct Coombs test was negative. A paracentesis abdominis was not carried out. Straight x-rays of the abdomen demonstrated bilateral loss of renal and psoas shadows, with an overall ground glass appearance suggestive of ascites. The bowel was displaced upwards and to the right without evidence of intestinal obstruction. An intravenous pyelogram was normal. A provisional diagnosis of an intra-abdominal malignancy with ascites was considered.

The child was transfused with packed cells, leading to a general improvement, though the abdominal distension increased and began to embarass respiration. An exploratory laparotomy was carried out on 14th November 1972 through a right paramedian incision, when the abdominal cavity was found to be completely filled by a huge, thin walled cyst originating by a narrow pedicle from the omentum of the upper third of the greater curvature of the stomach. No other pathology was present. The cyst was easily removed by ligation and division of the pedicle. It was multilocular, containing 2 litres of heavily blood-stained fluid, of both old and recent origin.

---

* Now Department of Surgery, Institute of Clinical Science

Histologically the lesion was considered to be a lymphangiomatous cyst. The post operative course was uncomplicated and when reviewed 8 weeks later, the child had completely recovered.

Discussion

Since the first lymphangiomatous omental cyst was described by Gairdner (1852), approximately 170 cases have been recorded in the literature. This does not represent the true incidence of the lesion, the more unusual cases only being reported. Most cysts are incidental findings at laparotomy and in their series, Montgomery and Wolman (1935) noted that only a small proportion of cases present with acute symptomatology. The most frequent complications were torsion and infection. This was confirmed by Oliver (1964) who stated that of the cases presenting as an "acute abdominal crisis" more than 90 per cent were misdiagnosed as acute appendicitis. Only one of Oliver's 17 cases presented with haemorrhage into the cyst necessitating surgical intervention and this is the trend in other reviews.

This case is unusual in exhibiting a profound anaemia with abdominal distension as the only physical sign.

The need for exploratory laparotomy in any case of undiagnosed ascites is stressed, even in the presence of a bloody tap on paracentesis abdominis. This is particularly so where the history is short and the patient's general condition does not suggest malignancy.

Pathologically, true cysts of the omentum lined by endothelium are five times more common than all the others together, and of these 52 per cent are lymphogenous (Horzan 1935). Most cysts are considered to be congenital though only 30 per cent occur in children below the age of 10 years (Montgomery 1935). The clinical presentation of an acute surgical abdomen caused by omental cysts is almost exclusively a disease of children (Walker 1973). Symptoms are occasionally preceeded by a viral infection.

The treatment of the cysts is simple excision, carrying a very low morbidity and recurrence rate.

Hertzler (1919) referred to the omentum as "the Good Samaritan of the abdominal cavity, always ready to render aid but seldom becoming sick itself". Although rare, abnormalities of the omentum must be considered in the differential diagnosis of intra-abdominal swellings or "ascites".

I wish to thank Mr. R. C. Curry, Consultant Surgeon, Belfast City Hospital, for permission to report a case under his care.

References

Bearhs, O. H. and Dockerty, M. B. (1950). *Surgical Clinics of North America.* **302**, 1073.
Gairdner, W. T. (1851). *Transcations Pathological Society, London.* **3**, 374.
Hertzler, A. E. (1919). *The Peritoneam*, St. Louis: C.V. Morby Company. Vol. 1 and 2.
Horzan, J. (1935). *American Journal Surgery*, **29**, 343.
Montgomery, A. M. and Wolman, I. J. (1935). *Surgery Gynecology and Obstetrics*, **60**, 695.
Olivier, G. A. (1964). *Surgery*, **56**, 588.
Walker, A. R. and Rutman, T. C. (1972). *Annals Surgery*, **178**, 13.

HYPERTHYROIDISM, RESULTS OF TREATMENT — AN APPRAISAL*

by

D. A. D. MONTGOMERY

Sir George E. Clark Metabolic Unit, Royal Victoria Hospital, Belfast, Northern Ireland

"WHENEVER you find that for a particular disease there are many remedies, you may know that there is something doubtful about the action of these remedies, and that none is particularly efficacious."

Introduction

We have come a long way since Mackenzie wrote these words in 1905, and yet in one sense they are still true. It is not that the modern modes of treatment are of doubtful value; all are effective, but the ideal treatment for hyperthyroidism still eludes us. Neither do we have reliable methods of selecting the best treatment for the individual patient. This could be arranged more rationally if it was possible to predict which patients would undergo spontaneous remission without therapy and which would suffer protracted and serious illness.

The aim of treatment is to reduce the secretion of the thyroid gland to a level which supports normal metabolic processes, to prevent complications and to correct those already present. Specific measures which reduce the secretion of the toxic gland effectively are antithyroid drugs, subtotal thyroidectomy and radioactive iodine. Opinions differ about their relative merits and no well-controlled comparisons of the three methods appear to have been made.

The purpose of this paper is to report the experience gained in the Metabolic Unit of the Royal Victoria Hospital in treating patients with hyperthyroidism and to make an appraisal of their advantages and disadvantages. Table I shows how some of our patients have been managed over the last 14 years. All these have been subject to special analysis and study. Some have had more than one form of treatment. Antithyroid drugs and surgery have, of course, been continued since 1967, although not analysed for the purpose of this presentation.

Antithyroid Drug Treatment

Many different forms of medical treatment have been used over the years to treat thyrotoxicosis but all have been superceded by the use of modern definitive antithyroid drugs and beta-adrenoceptor blockade.

---

* Based in part on a lecture delivered at the Royal College of Surgeons in London in 1970 and revised.

TABLE I

Treatment of Hyperthyroidism and Methods Employed 1960–1973
Metabolic Unit, Royal Victoria Hospital, Belfast

	Medical—antithyroid drugs	*Surgical*	*RAI—conventional dosage*	*RAI—small dosage with propranolol*	*Propranolol alone*
1960–67	153	128	—	—	—
1961–66	—	—	254	—	—
1968–73	—	—	—	247	—
1970–71	—	—	—	—	25

Antithyroid Drugs

These are of two types: (1) those which interfere with the synthesis of thyroid hormones (methyl and propyl thiouracil, methimazole and carbimazole, and (2) those which inhibit the trapping of iodide by the thyroid gland (perchlorate). Definitive treatment of hyperthyroidism with antithyroid drugs is undertaken in the hope that the disease will undergo spontaneous remission, or that the gland will alter in such a way that the hyperthyroidism will not recur when therapy is stopped. Earlier writers on the thyroid (see Wilson 1966) claimed remission in nearly a third of their patients. Recent knowledge of the natural course of thyrotoxicosis is unknown since few patients are permitted to go untreated. Perhaps the easiest way of studying the natural history of the disease is to block its peripheral manifestations with propranolol. Results achieved using this method (see later) confirm the view that remissions of the order of 30 to 40 per cent probably occur naturally. On the other hand, in a study of 50 untreated patients (in terms of specific antithyroid therapy) with fully developed exophthalmic goitre, Kessel and his colleagues (1923) found only one patient in full remission at the end of a year's observation, although many had improved with non-specific measures. It must be accepted then that, for the present, we do not know how antithyroid drugs "cure" the patient in whom a remission has been obtained. A possibility is that antithyroid drugs induce remissions by virtue of reducing the level of thyroid hormone which, in turn, may have an effect on the production of LATS and LATS protector. In other words, the return of the euthyroid state may reduce the tendency of the body to synthesize antibody directed against the thyroid gland (McKenzie 1967). Others (Alexander et al 1965; Harden et al 1966) have shown that depletion of the body's store of iodine increases the likelihood of achieving a remission. However, the remission rates achieved by us with antithyroid drugs and propranolol alone (see below) are not much better than the chance of obtaining a natural remission. This must make us ask: Are these drugs doing anything more than making the patient comfortable while a natural remission takes place?

The response of a series of 153 patients treated with carbimazole is shown in Table II. All had continuous treatment for at least 18 months and more than half had had it continued for over two years. The results show that only 43 per cent achieved a remission and that 51 per cent relapsed and required other therapy.

TABLE II

Antithyroid Treatment (Carbimazole) for Hyperthyroidism (153 patients) 1960–67

Clinical status	*Number*	*Percentage*	
Euthyroid (follow-up ½–8 years)	64	43	
Remaining on therapy at time of review	6	4	
Untraced	4	2	
Relapsed—treated surgically	75	49	51
Relapsed—treated with RAI	4	2	
Total	153	100	

Indeed, a remission rate of 43 per cent may be optimistic because a few patients were observed for less than 12 months after the withdrawal of treatment. Since the majority of relapses occur within a year of this the relapse rate might have been higher if all had been observed for a minimum period of a year.

TABLE III

Incidence of Remission achieved with Antithyroid Drug Treatment (from Astwood, E. B. 1967)*

Authors	*No. of patients*	*Years after treatment*	*Remission (percentage)*
Solomon et al	101	4–10	55–70
McCullagh and Cassidy	60	4–6	66
Douglas and McKenzie	187	?–5	45
Manson	70	>1	71
Goodwin et al	94	¼–1	41
Aspenstrom	120	>1	70
Trotter	157	10	45
Wilcox	152	1–12	72
Revens and Rosenbaum	167	4–19	57
Hershman et al	176	6–20	54
Metabolic Unit, R.V.H.	153	½–8	43
Total	1,437		56

*Reproduced by permission of Churchill Livingstone

The reported remission rate achieved by other workers in the field (Astwood 1967) is shown in Table III. Such reports are difficult to compare with each other. However, if one takes a crude average, the overall rate of remission is over 50 per cent. This is probably too high and the best that can be expected for medical treat-

ment will be between 40 and 50 per cent. This means that definitive treatment with antithyroid drugs will often be ineffective, unless the patient and doctor are prepared to continue treatment for an almost indefinite period.

Recently it has been fashionable to try and forecast those patients who are likely to respond to a course of medical treatment from those who will not. Empirical criteria include a small smooth gland, young patient, short history and a reduction in the size of the goitre during treatment, but none are very reliable. Another method involves the identification of patients in whom thyroid suppressibility returns during treatment (Alexander et al 1966). The test is useful in distinguishing between hyperthyroid patients and euthyroid patients with a high ^{131}I neck uptake. Failure of the radioactive iodine uptake (RAIU) by the thyroid to be suppressed by thyroid hormones (eg, triiodothyronine 100 mg daily for seven days) is characteristic of hyperthyroidism (Werner et al 1952; Werner 1955). A positive response (suppressibility) is defined as a fall of 50 per cent or more of the pre-treatment RAIU or a 20-minute uptake of less than 8 per cent (Alexander et al 1967). The test has been used to try and separate patients who will obtain a prolonged remission with antithyroid drugs from those who will not. Lack of suppressibility is said to be followed by relapse and the return of thyroid suppression during treatment means that a remission will follow the withdrawal of the drug. Proponents of this view (Alexander et al 1967) believe that if thyroid function remains unsuppressible at the end of six months' medical therapy it should be abandoned in favour of subtotal thyroidectomy or radioactive iodine treatment. Unfortunately, the test has not proved to be sufficiently reliable upon which to base a programme of treatment, for it does not indicate clearly those patients who will eventually relapse or remain in remission (Lowry et al 1971; Table IV) and for these reasons it has largely been abandoned. Similar hopes were expressed for the TRH test, which correlates well with the T_3 suppression test (Ormston et al 1973), but experience has shown it to be no more reliable.

TABLE IV

*Thyroid Suppressibility in Relationship to Remission and Relapse in Hyperthyroid Patients treated with Antithyroid Drugs**

Clinical status 2 years after completion of treatment		*Suppressed*		*Non-suppressed*	
		Number	*Percentage*	*Number*	*Percentage*
Remission	35 (55%)	20	57.1	15	42.9
Relapse	29 (45%)	8	27.6	21	72.4
Total	65	28	43.8	36	56.2

*Lowry et al (1971)

Despite the drawbacks mentioned, antithyroid drugs play an important part in the overall management of many thyrotoxic patients. They are helpful in the preparation of patients for surgery and have a place in the treatment of hyperthyroidism in special circumstances; for example, in pregnancy, childhood, for those wish-

ing to avoid an operation and for the young patient with mild symptoms and a small smooth gland. Toxic effects of carbimazole are rare and mostly mild and were noted in three of the 153 patients described; an incidence of under 2 per cent. The advantages of antithyroid drug treatment for hyperthyroidism are summarised in Table V.

TABLE V

Antithyroid Drug Treatment for Hyperthyroidism

Advantages

1. No damage is done to the thyroid gland.
2. No irreversible changes are induced.
3. Lasting myxoedema does not occur.
4. Hyperthyroidism can be corrected uniformly in a short time.

Disadvantages

1. High incidence of relapse of hyperthyroidism after treatment.
2. Inconvenience of frequent and prolonged (1–2 years) attendance at hospital or health centre.
3. Small incidence of toxic side-effects.
4. Goitre does not diminish in size.
5. Few physicians attain sufficient expertise in their administration.

Iodine and Iodides

Iodide increases the storage of colloid in the thyrotoxic gland and reduces the height of the epithelial cells. It thus induces the changes characteristic of involution, diminishes the vascularity of the gland and reduces thyroid hormone synthesis and release. The effect is transient, however, so that iodides have no place in the treatment of hyperthyroidism, apart from the preparation of patients for thyroidectomy and in the management of a thyrotoxic crisis (Havard 1974).

Sympathetic antagonists

Many of the clinical features of hyperthyroidism resemble the effects of increased activity of the sympathetic nervous system and two types of sympathetic antagonists are helpful in the relief of symptoms and signs. Drugs such as reserpine and guanethidine, which deplete the tissues of their catecholamine content, improve symptoms without affecting the concentration of the circulating thyroid hormones. However, their delayed action and side effects have precluded their general use. More effective in controlling the heart rate and some of the peripheral manifestations of thyrotoxicosis is the beta-adrenoceptor blocking drug propranolol. Since propranolol does not influence thyroid activity (Hadden et al 1969) it can be given in combination with radioactive iodine or as an adjunct to antithyroid medication. It has been used successfully alone or with iodine in preparing patients for thyroidectomy (Vinik et al 1968; Pimstone and Joffe 1970; Lee et al 1973; Michie et al 1974). Propranolol has greatly simplified preoperative management. The peripheral manifestations of the disease are brought under con-

trol quickly and the patient's apprehension of operation is rapidly allayed. Those with mild or moderate disease are ready for operation in 10 to 14 days when given iodine and propranolol together, while those with severe hyperthyroidism, given antithyroid drugs simultaneously, are ready in three or four weeks. Propranolol is given orally in a dose of 40 mg six-hourly during the period of preparation and for several days after operation. If it is withdrawn prematurely, at or before surgery, rebound tachycardia or cardiac arrhythmia may develop and be mistaken for a thyroid crisis. Some surgeons (Lee et al 1973; Michie et al 1974) omit iodine pre-operatively and depend solely on propranolol for the preparation of their patients. It remains to be seen whether other thyroid surgeons will follow suit. Iodine is so safe, cheap and effective in reducing the activity of the hyperthyroid that it seems unwise to abandon it altogether.

Propranolol alone in the management of hyperthyroidism

With increasing experience of the successful management of thyrotoxicosis using smaller and smaller doses of RAI and propranolol (see later) it seemed logical to try the effect of propranolol alone in treating the milder cases. Pimstone and others (1969) suggested that this might be an acceptable form of definitive treatment. Accordingly, 25 selected patients have been given 160 mg of propranolol daily for up to one year as the sole method of treatment. The results are shown in Table VI

TABLE VI

Treatment of Hyperthyroidism with Propranolol Alone

Number of patients treated	25	
Euthyroid at 1 year	10	(40%)
Remaining thyrotoxic at 1 year and requiring additional treatment (RAI, antithyroid drugs or surgery)	12	(48%)
Withdrawn from trial before 1 year (miscellaneous reasons)	3	(12%)
Total	25	

(Lowe et al 1975). Those who responded (40 per cent) became euthyroid between two and nine months after commencing treatment. Since propranolol does not affect the intrinsic function of the thyroid it is likely that these are naturally occurring remissions of the disease process to which allusion has been made already. It may or may not be significant that the remission rates for antithyroid drug treatment and propranolol are so close. No difference could be found clinically or biochemically between those who responded to propranolol and those who did not. Ten euthyroid patients have now been followed for up to four years. Two have subsequently relapsed after being euthyroid for three and two years respectively. In the remaining eight patients the TRH test was positive in two and negative (unsuppressible) in six 18 months after they went into remission. Unfortunately,

propranolol alone cannot be recommended as a definitive form of antithyroid treatment because it is impossible to select prospectively patients who are likely to respond; a view supported by McLarty and others (1973).

Surgical treatment

Subtotal thyroidectomy has a long and honoured place in the management of hyperthyroidism since the operation was introduced towards the end of last century and perfected by Sir Thomas Dunhill in the first decade of this century. The results achieved in a series of 128 patients treated surgically (1960–67) are shown in Table VI.

TABLE VII

Hyperthyroid Patients Treated Surgically 1960–67

Clinical status	*All cases* (128)		*Subtotal thyroidectomy–initial treatment* (53)		*Subtotal thyroidectomy–after failed medical treatment* (75)	
	Number	*Percntage*	*Number*	*Percentage*	*Number*	*Percentage*
Euthyroid	108	84.3	41	77.3	67	89.4
Hypothyroid	12	9.4	7	13.3	5	6.6
Relapsed	8	6.3	5	9.4	3	4.0
Dead	0	0	0	0	0	0

Thyroidectomy was performed as first treatment in 53 patients and as second treatment in a further 75 who had relapsed after antithyroid drug therapy (Table VII). It is of interest that slightly better results appear to have been achieved for those who relapsed after antithyroid drugs than for those whom surgery had been selected as initial treatment. However, the numbers are too small from which to draw valid conclusions. Thyroidectomy is equally successful in Graves' disease and toxic nodular goitre. Unilateral lobectomy for the solitary toxic adenoma ("hot nodule") removes the pathological lesion and allows the normal, but suppressed, thyroid tissue to recover.

Complications of surgery in this series are listed in Table VIII. Most are not serious but the morbidity associated with the operation still gives cause for concern. Hypocalcaemia occurs frequently enough for all patients to be screened carefully for three months after thyroidectomy. It has been suggested that "partial" or "latent" hypoparathyroidism may sometimes follow thyroidectomy and cause vague symptoms, which can be relieved by calcium supplements (Fourman 1967). This view has not received general support (Billis and Montgomery 1967; Stowers et al 1967). Deficiency of calcitonin as the result of thyroidectomy does not appear to affect calcium homeostasis to any extent. McIntyre (1969) has suggested that this may be due to extra thyroidal sources of calcitonin. Conversely, hypocalcaemia is not found in the presence of medullary cell carcinomas of the thyroid secreting calcitonin in excess (Montgomery and Welbourn 1975).

TABLE VIII

Complications of Subtotal Thyroidectomy for Hyperthyroidism

(128 *cases*)

	Number	*Percentage*
1. HAEMORRHAGE		
(a) Requiring surgery	3	2
(b) Extensive bruising	5	4
2. SEROSANGUINEOUS EFFUSION		
(a) Requiring aspiration	1	1
3. CHEST INFECTION OR PULMONARY COLLAPSE	7	5
4. WOUND INFECTION (serious)	4	3
5. RECURRENT LARYNGEAL NERVE PALSY		
(a) Bilateral	0	0
(b) Unilateral – Temporary	10	8
Permanent	0	0
6. TETANY (Hypoparathyroidism)		
(a) Temporary	7	5
(b) Permanent (requiring continuous therapy)	4	3
7. HYPOTHYROIDISM		
(a) Temporary	2	2
(b) Permanent (requiring continuous therapy)	12	9
8. UNSATISFACTORY SCAR		
(a) Fibrosis	0	0
(b) Keloid	3	2

From these results and essentially similar figures published in several other British surveys (Wade 1960; Riddell 1962, 1970; Green and Wilson 1964; McNeill and Thompson 1968) it may be concluded that subtotal thyroidectomy offers the patient a better than 80 per cent chance of a remission and that the incidence of major surgical complications, such as recurrent laryngeal nerve damage or permanent hypoparathyroidism, while not great, still occur and must continue to challenge thyroid surgeons to produce even better results. The 9 per cent incidence of hypothyroidism might increase with a longer period of observation. On the other hand, we were impressed with the rapidity with which hypothyroidism developed in this group. Most were diagnosed within 12 months of operation. The early onset of hypothyroidism has been confirmed by Olsen et al (1970) and Michie et al (1972). All but one of the latter's patients who became hypothyroid did so within the year following thyroidectomy. They concluded that if a sufficiently high degree of suspicion of hypothyroidism is maintained during the early postoperative months the *late* diagnosis of hypothyroidism is rare. In Britain, the incidence of hypothyroidism after thyroidectomy has ranged from 3.3 to 49 per cent (Riddell 1962; Michie et al 1972). In America, for example, a figure quoted for the development

of hypothyroidism following surgery for Graves' disease is 42.8 per cent (Beahrs and Sakulsky 1968) and Olsen and his colleagues (1970) quote an incidence of 25 to 50 per cent.

The causes of postoperative hypothyroidism are not fully understood. Neither the age or sex of the patient, the size of the goitre or the amount and duration of preoperative antithyroid drug therapy appear to be involved (Michie et al 1972). On the other hand, Michie found that the size of the thyroid remnant was the most significant aetiological factor. When a policy of increasing the size of the thyroid remnant was adopted the hypothyroid rate fell although it was not abolished. However, the policy of leaving a larger remnant increases the risk of recurrence of the hyperthyroidism. Wilson (1967) observed that with the removal of a smaller amount of thyroid there is a diminished incidence of hypothyroidism and a higher recurrence rate, while with the more radical excision the reverse holds.

Variations in iodine intake and surgical technique may reflect the differing incidence of postoperative hypothyroidism in certain parts of the world. The level of thyroid antibodies in serum appears to be important and where these are high the incidence may be of the order of 25 per cent or more (Irvine and Stewart 1967; van Welsum et al 1974). The former authors suggest that a high level of circulating thyroid autoantibodies is a relative contraindication of thyroidectomy and that if it is performed the patient should be kept under regular supervision. Possibly in these cases the operation should be less radical than usual. In contrast to surgery, serological tests seem to be of little value in predicting the development of hypothyroidism in patients treated with RAI or of any prognostic value in determining the outcome of the patient's response to antithyroid drug therapy.

Radioactive iodine treatment (RAIT)

Radioactive iodine has been in use since 1941 but it was not until the early 1950's that large numbers of patients received this form of therapy. RAIT although much slower in correcting hyperthyroidism (8 to 12 weeks or longer) than subtotal thyroidectomy or antithyroid drugs seemed, at first, to be an ideal method of treatment. For the patient it is the most convenient as it involves only a drink of tasteless water. However, there were some initial difficulties because no satisfactory way of estimating the correct dose of RAI, in relation to size, activity or nodularity of the thyroid gland could be evolved. Too small a dose did not cure the hyperthyroidism, whereas too large a dose caused early and permanent hypothyroidism. The most serious objection to RAIT, however, has become apparent only with the passage of time. In the 1960's, reports of a disturbingly high and progressive incidence of hypothyroidism began to appear from Scandinavia, Great Britain, America and elsewhere. These showed a relentless increase in the incidence of hypothyroidism each year after treatment which reaches a level of about fifty per cent or more at 10 years (Beiling and Eindhorn 1961; Green and Wilson 1964; Nofal et al 1966).

From 1961 to 1966, 254 patients were treated in the Metabolic Unit (Bhatia et al 1968) using conventional doses of RAI (150 μCi/g thyroid tissue). Adequate information about their thyroid function was obtained in over 98 per cent subsequently, and 232 were re-examined in 1967 and 1968 (Table IX). For the group

TABLE IX

Therapeutic Radioactive Iodine 1961–66
Thyroid Status at Review (1967–68)

Year of first treatment	*Mean dose mCi*	*Number of patients*		*Euthyroid*		*Hypothyroid*	
		Treated	*Reviewed*	*Number*	*Percentage*	*Number*	*Percentage*
1961	8.2	36	31	13	42	16	51
1962	8.6	62	55	24	43	18	33
1963	8.1	40	35	14	40	16	45
1964	5.1	43	39	22	56	9	23
1965	4.2	48	48	22	45	7	15
1966	4.8	25	24	14	58	4	16
Total		254*	232	109	47	70	30

* 158 patients had no previous treatment.
81 patients had failed antithyroid treatment.
8 patients had a previous subtotal thyroidectomy.
7 patients had both drug treatment and subtotal thyroidectomy.

as a whole the remission rate, i.e., the achievement of euthyroidism was 47 per cent, while 30 per cent were hypothyroid. However, the longer patients were observed the greater was the incidence of hypothyroidism. For example, 51 per cent of the original 36 patients treated in 1961 were hypothyroid six years later. From 1964 onwards, the dose of RAI was reduced substantially and the incidence of hypothyroidism diminished slightly. Nevertheless, 23 per cent of the 1964 group were hypothyroid in three years. If to this figure is added a yearly cumulative incidence of about 4 per cent of hypothyroidism, which these results suggest, this 23 per cent becomes 35 per cent at six years; an incidence which is still very discouraging.

TABLE X

Effect of Age at First Treatment on Subsequent Incidence of Hypothyroidism

Age group (years)	*Total patients treated* 1961–66	*Mean dose of RAI (mCi)*	*Total percentage hypothyroid at review*
40–49	89	6.57	38.2
50–59	92	6.70	27.1
60+	73	6.24	15.1

The effect of age on the development of hypothyroidism is shown in Table X. The youngest age group had the highest incidence of hypothyroidism regardless of the year of treatment. Differences in the size of the goitre, dosage and turnover rates of RAI do not appear to explain this difference and it is probable that the "younger" the thyroid gland is the more sensitive is it to the effects of ionizing

irradiation. The incidence of hypothyroidism in those who had previously received a course of antithyroid drugs was 26 per cent, less than for the whole group but not statistically significant. For those who had a thyroidectomy previously the rate soared to 62 per cent (five out of eight subjects).

It must be clear to all that the late results of RAIT are most disappointing Patients require regular follow-up for sooner or later many will require permanent treatment with thyroxine. For these reasons some clinicians felt that such results could not be tolerated and have sought methods that would exploit the advantages of RAIT (using smaller doses) while at the same time diminishing the risk of hypothyroidism. These carry the risk, however, of incomplete control of the disease and usually necessitate the administration of an antithyroid drug as well (Smith and Wilson 1967; Smith et al 1970; Rapoport et al 1973). While these methods reduce substantially the risk of hypothyroidism developing (a reduction from 30 per cent to 8 per cent at two years according to Smith et al 1970), the long period of antithyroid drug treatment makes it less acceptable from the patient's point of view. It can be argued that if RAIT is to be extended over several years using antithyroid drugs, it might be preferable to accept the incidence of hypothyroidism with conventional RAIT alone and administer thyroxine if and when it is needed.

In 1968, we reduced the treatment does of RAI by about half from that employed earlier, to a level of about 70 μCi/g thyroid tissue. With an average size goitre this meant a therapeutic dose of about 2.5 mCi and this amount was prescribed routinely for all patients. Subsequently the dose was reduced by a further 50 per cent to 1.25 mCi. At the same time 160 mg of propranolol was given daily to control symptoms until the intrinsic thyroid abnormality was brought under control.

Table XI summarises the results obtained with this form of combined therapy in patients given a single dose of RAIT (those given two or more doses have been omitted for the purpose of this presentation). The incidence of hypothyroidism at one year with 2.5 mCi is not far short of that achieved with larger doses but at four years it is much less. For the 1.25 mCi dose the hypothyroid rate is very much less and, although the number of patients achieving euthyroidism at one year is slightly fewer the difference is not pronounced.

The management of patients who have not responded to treatment with a small dose of RAIT at three or four months poses a number of problems. Although a few may become euthyroid over the succeeding months, the majority are likely to

TABLE XI

Small Dose RAIT 1968–73

Dose RAI (mCi)	*No. of patients given a single dose*	*Euthyroid (%)*		*Hypothyroid (%)*	
		1 year	*4 years*	*1 year*	*4 years*
2.5	63	41	43	13	17
1.25	32	35	39	0	3

remain hyperthyroid, although protected, to some extent, from the effects of the thyroid toxicity by propranolol. However, adrenergic blockade is unlikely to prevent all the metabolic consequences of protracted hyperthyroidism—for example, the possibility of progressive osteoporosis (McLarty et al 1973). For these reasons, a second dose of 2.5 or 1.25 mCi of RAI is given at three or four months to non-responders. Third or even fourth supplemental doses may be required in an attempt to titrate the amount of RAI required to provide the optimum dose to control thyroid toxicity without inducing hypothyroidism. As might be expected, more (55 per cent) of the 1.25 mCi group than the 2.5 mCi group (38 per cent) required additional doses of RAI to achieve euthyroidism. The long-term effectiveness of this method remains to be worked out fully and will be the subject of a subsequent report but the early results are encouraging. Nevertheless, the criticism levelled at the combined regime of small dose RAIT with antithyroid drugs can be made equally against RAI and propranolol. The only point of difference is that the control of treatment is easier with the latter, for achievement of euthyroidism is specifically related to the RAI, whereas in the former it may be due to either the RAI or antithyroid drug.

Summary and Conclusions

This review has attempted to show what can be achieved with the available methods of treating hyperthyroidism. None alter the underlying cause of the disease; a possible exception being the removal of a single toxic nodule. Antithyroid drugs and propranolol suppress thyroid hyperfunction or its peripheral manifestations; a lasting cure probably depending on a natural remission which we are powerless to influence. Surgery and radioactive iodine destroy part of the gland and the eventual outcome depends on the balance between the amount of tissue destroyed and the function of the remainder. Until more is known about the fundamental mechanism of hyperthyroidism so that it can be prevented or its causal factors removed, we must apply existing methods in the most efficient way.

Effective treatment can nearly always be provided and the advantages and disadvantages of each method are set forth below: –

Antithyroid drugs

1. Limited value as definitive treatment.
2. Useful in special circumstances.
3. Morbidity minimal and reversible.
4. Remission in selected cases between 40 and 50 per cent.

Surgery

1. Remission rate between 80 and 90 per cent.
2. Hypothyroidism variable but often considerable; high antibody titre significant.
3. Morbidity still important and serious for the patient.

Radioactive iodine

1. Remission rate of just under 50 per cent.
2. High cumulative incidence of hypothyroidism.
3. Of value in controlling persistent hyperthyroidism.

All these factors must be considered in relation to the age, clinical findings, nature of the goitre and the patient's emotional make-up and responsibilities. There are many in whom the choice of treatment is not easy. Problems arise, for instance, when the gland is of moderate size or causing minimal compression of the trachea or when the patient is a few years under the age of 40. A planned policy for treatment must be selected from the start. Where the diagnosis is in doubt, symptomatic

TABLE XII

*

Type of Goitre and Clinical Features	*Treatment recommended*
I. *Diffuse Goitre*	
1. Under 40 years	
(a) Small gland and mild or moderate toxicity	Antithyroid drugs
(b) Large gland and moderate or severe toxicity	Subtotal thyroidectomy
2. Over 40 years	Radioactive iodine
II. *Nodular Goitre*	
1. Under 40 years	Subtotal thyroidectomy
2. Over 40 years	
(a) Small gland without obstruction	Radioactive iodine
(b) Large gland with obstruction	Subtotal thyroidectomy
III. *Recurrent Thyrotoxicosis*	
1. After antithyroid drugs	
(a) Under 40 years	Subtotal thyroidectomy
(b) Over 40 years	Radioactive iodine
2. After operation	
(a) Under 40 years	Antithyroid drugs
(b) Over 40 years	Radioactive iodine
(c) Large obstructive goitre at any age	Subtotal thyroidectomy
3. After radioactive iodine	Radioactive iodine
IV. *Special Circumstances*	
1. Childhood	Antithyroid drugs
2. Pregnancy	Antithyroid drugs or subtotal thyroidectomy
3. Neonatal thyrotoxicosis	Antithyroid drugs
4. Infirmity (heart failure, old age, intercurrent disease, etc)	Radioactive iodine
5. Hyperophthalmopathic Graves' disease	Antithyroid drugs until eyes stabilized and special measures
6. Solitary toxic adenoma	Partial thyroidectomy
7. Thyrotoxic crisis	Special measures

*Reproduced by permission of the publishers, Arnold, London.

control of the hyperthyroidism can be achieved with propranolol, while investigation proceeds unhampered by treatment. The best results are achieved by the close collaboration of physicians and surgeons and the provision of a careful follow-up system.

Table XII summarises the general policy for treatment hyperthyroidism in the Metabolic Unit, Royal Victoria Hospital, which has evolved over the last decade.

ACKNOWLEDGMENTS

I would like to thank my colleagues, Dr. J. A. Weaver and Dr. D. R. Hadden, for help in the management of many of these patients. It is a pleasure to record my appreciation of the skill of Mr. W. Wilson and Mr. R. H. Livingston who performed the thyroidectomies. Dr. S. K. Bhatia and Dr. Daphne Lowe (who respectively held an R.V.H. Fellowship and an M.R.C. Grant) helped with much of the work and most of the results recorded here. My thanks are also due to Miss Bridget Bassett and Miss May Weller for secretarial assistance.

REFERENCES

ALEXANDER, D. W., HARDEN, R. McG., KOUTRAS, D. A., and WAYNE, E. (1965). *Lancet*, **2**, 866.

ALEXANDER, D. W., HARDEN, R. McG. and SHIMMINS, J. (1966). *Lancet*, **2**, 1041.

ALEANDER, D. W., HARDEN, R. McG., SHIMMINS, J., McLARTY, D. and McGILL, P. (1967). *Journal of Clinical Endocrinology and Metabolism*, **27**, 1682.

ASTWOOD, E. B. (1967). In *Thyrotoxicosis*, ed. Irvine, W. J., p. 85. Edinburgh: Livingstone.

BEAHRS, O. H. and SAKULSKY, S. B. (1968). *Archives of Surgery*, **96**, 512.

BEILING, U. and EINHORN, J. (1961). *Acta Radiologica*, **56**, 275.

BHATIA, S. K., HADDEN, D. R., MONTGOMERY, D. A. D. and WEAVER, J. A. (1968). *Irish Journal of Medical Science* (7th series), **1**, 449.

BILLIS, A. and MONTGOMERY, D. A. D. (1967). *Irish Journal of Medical Science* (*6th series*), **No. 495**, 105.

DUNHILL, T. P. (1909). *British Medical Journal*, **1**, 1222.

FOURMAN, P. (1967). *Thyrotoxicosis*, ed. Irvine, W. J., p. 192. Edinburgh: Livingstone.

GREEN, M. and WILSON, G. M. (1964). *British Medical Journal*, **1**, 1005.

HADDEN, D. R., BELL, T. K., McDEVITT, D. G., SHANKS, R. G., MONTGOMERY, D. A. D., and WEAVER, J. A. (1969). *Acta Endocrinologica*, **61**, 393.

HARDEN, R. McG., ALEXANDER, D. W., KOUTRAS, D. A., HARRISON, M. T., and WAYNE, E. (1966). *Journal of Clinical Endocrinology and Metabolism*, **26**, 397.

HAVARD, C. W. H. (1974). *British Journal of Hospital Medicine*, **11**, 893.

IRVINE, W. J. and STEWART, A. G. (1967). In *Thyrotoxicosis*, ed. Irvine, W. J., p. 111. Edinburgh: Livingstone.

KESSEL, L., HYMAN, H. T., LANDE, H. and LIEB, C. C. (1923). *Archives of Internal Medicine*, **31**, 433.

LEE, T. C., COFFEY, R. J., MACKIN, J., COBB, M., ROUTON, J. and CANARY, J. J. (1973). *Annals of Surgery*, **177**, 643.

LOWE, DAPHNE, HADDEN, D. R., MONTGOMERY, D. A. D. and WEAVER, J. A. (1975). *In preparation.*

LOWRY, R. C., LOWE, DAPHNE, HADDEN, D. R., MONTGOMERY, D. A. D. and WEAVER, J. A. (1971). *British Medical Journal*, **2**, 19.

MACKENZIE, H. (1905). *British Medical Journal*, **1**, 10.

McINTYRE, I. (1969). In *Proceedings of the Third International Congress of Endocrinology*, ed. Gual, C. and Ebbling, F. J. J., p. 717. Amsterdam: Excerpta Medica.

McKENZIE, J. M. (1967). In *Thyrotoxicosis*, ed. Irvine, W. J., p. 97. Edinburgh: Livingstone.

McLARTY, D. G., BROWNLIE, B. E. W., ALEXANDER, D. W., PAPAPETROU, P. D. and HORTON, P. (1973). *British Medical Journal*, **2**, 332.

McNEILL, A. D. and THOMPSON, J. A. (1968). *British Medical Journal*, **2**, 643.

MICHIE, W., PEGG, C. A. S. and BEWSHER, P. D. (1972). *British Medical Journal*, **1**, 13.

MICHIE, W., HAMER-HODGES, D. W., PEGG, C. A. S., ORR, F. G. G. and BEWSHER, P. D. (1974). *Lancet*, **1**, 1009.
MONTGOMERY, D. A. D. and WELBOURN, R. B. (1975). *Medical and Surgical Endocrinology*, pp. 326, 335. London: Arnold.
NOFAL, M. N., BEIERWALTES, W. H. and PATNO, M. E. (1966). *Journal of the American Medical Association*, **197**, 605.
OLSEN, W. R., NISHIYARIE, R. H. and GRABER, L. W. (1970). *Archives of Surgery*, **101**, 175.
ORMSTON, B. J., ALEXANDER, L., EVERED, D. C., CLARK, F., BIRD, T., APPLETON, D. A. and HALL, R. (1973). *Clinical Endocrinology*, **2**, 369.
PIMSTONE, B. L., JOFFE, B., PIMSTONE, N., BONNICI, F. and JACKSON, W. P. U. (1969). *South African Medical Journal*, **43**, 1203.
PIMSTONE, B. L. and JOFFE, B. (1970). *South African Medical Journal*, **44**, 1059.
RAPOPORT, B., CAPLAN, R. and DEGROOT, L. J. (1973). *Journal of the American Medical Association*, **224**, 1610.
RIDDELL, V. (1962). *British Journal of Surgery*, **49**, 465.
RIDDELL, V. (1970). *British Journal of Surgery*, **57**, 1.
SMITH, R. N. and WILSON, G. M. (1967). *British Medical Journal*, **1**, 129.
SMITH, R. N., MUNRO, D. S. and WILSON, G. M. (1971). In *Further Advances in Thyroid Research*, ed. Fellinger, K. and Hoffer, R. Vol. 1, p. 611. Vienna: Verlag der Wiener Medizinischen Academie.
STOWERS, J. M., MICHIE, W. and FRAZER, S. C. (1967). *Lancet*, **1**, 124.
VAN WELSUM, M., FELTKAMP, T. E. W., DE VRIES, M. J., DOCTOR, R., VAN ZIJL, J. and HENNEMANN, G. (1974). *British Medical Journal*, **4**, 755.
VINIK, A. I., PIMSTONE, B. L. and HOFFENBERG, R. (1968). *Journal of Clinical Endocrinology and Metabolism*, **28**, 725.
WADE, J. S. H. (1960). *British Journal of Surgery*, **48**, 25.
WERNER, S. C., HAMILTON, H. and NEMETH, M. (1952). *Journal of Clinical Endocrinology and Metabolism*, **12**, 1561.
WERNER, S. C. (1956). *Journal of Clinical Investigation*, **35**, 57.
WILSON, G. M. (1966). In *Symposium on Thyroid Disease and Calcium Metabolism*, p. 51. Edinburgh: Royal College of Physicians.

BOOK REVIEWS

OBSTETRICS ILLUSTRATED. By M. M. Garry, A. D. T. Govan, C. Hodge and R. Callender. Second Edition. (Pp. 538. Illustrated. £3.75). Edinburgh and London: Churchill Livingstone. 1974.

THE second edition of this book, coming only five years after the first (which went to three reprintings), must speak of its popularity. The combination of line drawings and simple text produces a method for easy assimilation by the ever-pressed medical student. The rapid changes in many aspects of the specialty have been coped with by extensive rewriting of chapters dealing with fetal monitoring, early diagnosis of immaturity and dysmaturity, induction techniques and planned labour and delivery; the chapter relating to the newborn infant is particularly well presented. The remaining subject matter is covered adequately having sections on physiology and anatomy as well as dealing with the most common, and a good few not so common, pathological states of pregnancy. One obvious error appears on page 186 relating to the estimation of H.S.A.P. The authors rightly point out that this test has now been shown to have little clinical use as it is not sufficiently discriminating; however the estimation of the enzyme is not carried out on a sample of amniotic fluid.

This book (500 pages) is very reasonably priced at £3.75 and I would recommend it to the undergraduate.

W.T.

MICHIE, W., HAMER-HODGES, D. W., PEGG, C. A. S., ORR, F. G. G. and BEWSHER, P. D. (1974). *Lancet*, **1**, 1009.
MONTGOMERY, D. A. D. and WELBOURN, R. B. (1975). *Medical and Surgical Endocrinology*, pp. 326, 335. London: Arnold.
NOFAL, M. N., BEIERWALTES, W. H. and PATNO, M. E. (1966). *Journal of the American Medical Association*, **197**, 605.
OLSEN, W. R., NISHIYARIE, R. H. and GRABER, L. W. (1970). *Archives of Surgery*, **101**, 175.
ORMSTON, B. J., ALEXANDER, L., EVERED, D. C., CLARK, F., BIRD, T., APPLETON, D. A. and HALL, R. (1973). *Clinical Endocrinology*, **2**, 369.
PIMSTONE, B. L., JOFFE, B., PIMSTONE, N., BONNICI, F. and JACKSON, W. P. U. (1969). *South African Medical Journal*, **43**, 1203.
PIMSTONE, B. L. and JOFFE, B. (1970). *South African Medical Journal*, **44**, 1059.
RAPOPORT, B., CAPLAN, R. and DEGROOT, L. J. (1973). *Journal of the American Medical Association*, **224**, 1610.
RIDDELL, V. (1962). *British Journal of Surgery*, **49**, 465.
RIDDELL, V. (1970). *British Journal of Surgery*, **57**, 1.
SMITH, R. N. and WILSON, G. M. (1967). *British Medical Journal*, **1**, 129.
SMITH, R. N., MUNRO, D. S. and WILSON, G. M. (1971). In *Further Advances in Thyroid Research*, ed. Fellinger, K. and Hoffer, R. Vol. 1, p. 611. Vienna: Verlag der Wiener Medizinischen Academie.
STOWERS, J. M., MICHIE, W. and FRAZER, S. C. (1967). *Lancet*, **1**, 124.
VAN WELSUM, M., FELTKAMP, T. E. W., DE VRIES, M. J., DOCTOR, R., VAN ZIJL, J. and HENNEMANN, G. (1974). *British Medical Journal*, **4**, 755.
VINIK, A. I., PIMSTONE, B. L. and HOFFENBERG, R. (1968). *Journal of Clinical Endocrinology and Metabolism*, **28**, 725.
WADE, J. S. H. (1960). *British Journal of Surgery*, **48**, 25.
WERNER, S. C., HAMILTON, H. and NEMETH, M. (1952). *Journal of Clinical Endocrinology and Metabolism*, **12**, 1561.
WERNER, S. C. (1956). *Journal of Clinical Investigation*, **35**, 57.
WILSON, G. M. (1966). In *Symposium on Thyroid Disease and Calcium Metabolism*, p. 51. Edinburgh: Royal College of Physicians.

BOOK REVIEWS

OBSTETRICS ILLUSTRATED. By M. M. Garry, A. D. T. Govan, C. Hodge and R. Callender. Second Edition. (Pp. 538. Illustrated. £3.75). Edinburgh and London: Churchill Livingstone. 1974.

THE second edition of this book, coming only five years after the first (which went to three reprintings), must speak of its popularity. The combination of line drawings and simple text produces a method for easy assimilation by the ever-pressed medical student. The rapid changes in many aspects of the specialty have been coped with by extensive rewriting of chapters dealing with fetal monitoring, early diagnosis of immaturity and dysmaturity, induction techniques and planned labour and delivery; the chapter relating to the newborn infant is particularly well presented. The remaining subject matter is covered adequately having sections on physiology and anatomy as well as dealing with the most common, and a good few not so common, pathological states of pregnancy. One obvious error appears on page 186 relating to the estimation of H.S.A.P. The authors rightly point out that this test has now been shown to have little clinical use as it is not sufficiently discriminating; however the estimation of the enzyme is not carried out on a sample of amniotic fluid.

This book (500 pages) is very reasonably priced at £3.75 and I would recommend it to the undergraduate.

W.T.

THE NORTHERN IRELAND COUNCIL FOR POSTGRADUATE MEDICAL EDUCATION

PSYCHIATRY SPECIALITY COMMITTEE

The Committee looks forward to an easier task in arranging suitable training for junior doctors with the centralisation of senior house officer appointments from August, 1975. It is hoped that a smoothly planned training covering Senior House Officer and Registrar years will be arranged for most trainees. Early in 1975 all current trainees will be invited informally to discuss their training plans and needs with two members of the Committee. These members will be consultants from hospitals other than the one where the trainee is working.

In recent meetings a major task has been to provide the Department of Health and Social Services with realistic figures for establishments in Psychiatry and of doctors actually in post.

W.O.McC.

ANAESTHETICS COMMITTEE

The Anaesthetics Committee of the Northern Ireland Council for Postgraduate Medical Education pursued its usual activities during the course of the year. Two intensive courses for the Primary and Final F.F.A.R.C.S. were held during the year and were well supported both by local trainees and also by some not working in Northern Ireland itself. Apart from this, weekly tutorial classes were maintained throughout the academic terms.

The rotation of trainees was supervised satisfactorily and at present each trainee has the opportunity of acquiring experience in all branches of anaesthesia while in the training programme. The Department of Anaesthetics also supervised several overseas graduates working in research for higher qualifications.

During the course of the year representatives of the Joint Committee for Higher Professional Training visited Northern Ireland and went to hospitals in each of the Area Boards. They returned a satisfactory report on the higher training programme as organised in Northern Ireland and there are now 16 approved Senior Registrar posts on an agreed rotation.

J.W.D.

SURGICAL TRAINING COMMITTEE

The members of the Committee are:–Professor A. D. Roy (Chairman), Mr. T. G. Parks (Secretary); Mr. J. H. Balmer, Southern Area; Mr. H. M. Bennett, Western Area; Mr. R. C. Curry, Belfast City Hospital; Mr. C. Gilligan, Mater Infirmorum Hospital; Mr. N. C. Hughes, Plastic Surgery; Mr. G. W. Johnston, Royal Victoria Hospital; Mr. T. L. Kennedy, Royal Victoria Hospital; Mr. A. McCalister, Ulster Hospital; Dr. J. E. McKnight, Secretary, N.I. Council for Postgraduate Medical Education; Mr. N. McLeod, N.I. Orthopaedic Service; Dr. R. P.

Maybin, Central Services Agency; Mr. J. D. A. Robb, Northern Area; Mr. H. M. Stevenson, Thoracic Surgery; Mr. R. I. Wilson, N.I. Orthopaedic Service.

The death of Mr. G. W. V. Greig in August, 1974, was much regretted by the Committee. He had been a most useful member for a number of years and had contributed much to postgraduate education and the training of young surgeons.

During the past year representatives of the Specialist Advisory Committee in General Surgery made their second visit to the Province. They visited the Waveney, Altnagelvin and Craigavon Hospitals and met senior and junior staff from various hospitals in the Northern, Western and Southern Areas respectively. In the Eastern Area they visited the Ulster and Mater Infirmorum Hospitals, and met administrative and senior and junior medical staff from a number of hospitals in the Area. They have now made their recommendations as to the suitability of various posts for higher surgical training. In addition, the Advisory Committees dealing with Higher Training in the Surgical Specialties have, for the most part, completed their assessment and made their recommendations.

For some time the Advanced Course in Postgraduate Surgery had been held on Monday evenings from 6.30 p.m. to 8.30 p.m., with additional ward rounds and Radiology and Surgical Pathology lectures at 5 p.m. on a number of afternoons during the winter session. In response to numerous requests and after consultation with the surgical consultants throughout the Province it was agreed to hold the 1974/75 course on a half-day release basis instead of Monday evenings. It was felt that Friday afternoons, 2.00 p.m.—4.15 p.m., would be the most suitable, especially for those coming up from the peripheral hospitals who might then attend the surgeons' meetings normally held at the Royal Victoria Hospital at 4.45 p.m. on Fridays.

Over the years some of the surgical trainees have kept a log of the surgical operations which they have undertaken personally or with the assistance of a senior colleague. The committee felt that it would be helpful for all surgical trainees to keep such a log of their work and to this end a preliminary pilot scheme has been introduced to assess the usefulness of such records.

OTOLARYNGOLOGY COMMITTEE

The Committee which consists of: Mr. J. H. A. Black, Mr. R. S. McCrea, Mr. R. Harvey, Mr. G. D. L. Smyth, Mr. A. G. Kerr, has advised the Department of Health and the Northern Ireland Council for Postgraduate Medical Education.

In March 1974 a meeting was held with the Joint Committee for Higher Surgical Training concerning the future organisation of training programmes during the next decade. At present, rotational training exists between the Eye & Ear Clinic, Royal Victoria Hospital and the ENT Departments of the Belfast City, Tyrone County and Altnagelvin Hospitals. Advanced lectures in para-otological subjects are given each week during the Christmas and Easter terms by consultants in other specialities and by guest speakers from other ENT centres. Lectures and demonstrations in micro-anatomy of the temporal bone and the ENT region generally are presented at weekly intervals by one of the consultant staff. Intensive

tuition and case presentation is available preparatory to the final ENT FRCS, and a journal club is held weekly in the Eye & Ear Clinic, Royal Victoria Hospital.

Expansion of the activities of the Department of Otorhinolaryngology with development of the work of the research laboratories and augmentation of our audio-visual facilities continues.

G.D.L.S.

BOOK REVIEWS

MEDICAL AND SURGICAL ENDOCRINOLOGY. By D. A. D. Montgomery and R. B. Welbourn. (Pp. 615, tables 74, figures 73. £27.00). London: Arnold. 1975.

IN 1963 these authors published a highly practical textbook of Endocrinology entitled "Clinical Endocrinology for Surgeons" which was widely acclaimed. Progress in endocrinology in the intervening twelve years has demanded the production of a revised version, but the present volume is much more than just a second edition. It is deliberately aimed at a larger market, including physicians, physiologists and laboratory workers as well as surgeons.

Much of the original has been eliminated, including almost all the clinical photographs and the rather charming, almost anecdotal, "Belfast series" of clinical experiences. Removal of this type of material is in keeping with current practice, but it does perhaps make the remaining text just a little drier. Progress in endocrinology has been so explosive that the size of the book is doubled—to a total of some 600 pages. Every clinical aspect of endocrinology is covered in detail, including clear descriptions of biochemistry, easily comprehended even by the amateur.

The "Belfast" flavour of the work is preserved by Dr. McGeown's excellent chapter on the parathyroid glands, and Professor Ivan Johnston's lucid contribution on the endocrine response to stress. Each clinician will probably choose a different chapter as the most interesting and useful to him, but my personal choice includes those on the adrenal cortex and the alimentary tract, which is rightly recognized as the largest endocrine organ in the body.

The book is encyclopaedic in its information content and remarkably up-to-date (in view of the delays in publication) with many 1973 references. References are not included in the text, but given at the end of each chapter; a system with advocates, but also with disadvantages. The index is excellent and the layout of individual chapters is clear, greatly helping the busy doctor who dips into the book to find information quickly.

I do wish that I could give the hackneyed advice to "every clinician to buy a copy" but unfortunately inflation has intervened. In 1963 the cost was £4.00; today, all the expensive photographs have been omitted and the quality of the paper having deteriorated, the price has increased more than six-fold! It is perhaps not within the remit of the reviewer to criticize the publisher, but this fantastic price, together with repeated delays in publication, really is disappointing.

I predict that this book will be in great demand, so that libraries and those with A+ awards are advised to keep their copies on the end of a chain.

T.L.K.

tuition and case presentation is available preparatory to the final ENT FRCS, and a journal club is held weekly in the Eye & Ear Clinic, Royal Victoria Hospital.

Expansion of the activities of the Department of Otorhinolaryngology with development of the work of the research laboratories and augmentation of our audio-visual facilities continues.

G.D.L.S.

BOOK REVIEWS

MEDICAL AND SURGICAL ENDOCRINOLOGY. By D. A. D. Montgomery and R. B. Welbourn. (Pp. 615, tables 74, figures 73. £27.00). London: Arnold. 1975.

IN 1963 these authors published a highly practical textbook of Endocrinology entitled "Clinical Endocrinology for Surgeons" which was widely acclaimed. Progress in endocrinology in the intervening twelve years has demanded the production of a revised version, but the present volume is much more than just a second edition. It is deliberately aimed at a larger market, including physicians, physiologists and laboratory workers as well as surgeons.

Much of the original has been eliminated, including almost all the clinical photographs and the rather charming, almost anecdotal, "Belfast series" of clinical experiences. Removal of this type of material is in keeping with current practice, but it does perhaps make the remaining text just a little drier. Progress in endocrinology has been so explosive that the size of the book is doubled—to a total of some 600 pages. Every clinical aspect of endocrinology is covered in detail, including clear descriptions of biochemistry, easily comprehended even by the amateur.

The "Belfast" flavour of the work is preserved by Dr. McGeown's excellent chapter on the parathyroid glands, and Professor Ivan Johnston's lucid contribution on the endocrine response to stress. Each clinician will probably choose a different chapter as the most interesting and useful to him, but my personal choice includes those on the adrenal cortex and the alimentary tract, which is rightly recognized as the largest endocrine organ in the body.

The book is encyclopaedic in its information content and remarkably up-to-date (in view of the delays in publication) with many 1973 references. References are not included in the text, but given at the end of each chapter; a system with advocates, but also with disadvantages. The index is excellent and the layout of individual chapters is clear, greatly helping the busy doctor who dips into the book to find information quickly.

I do wish that I could give the hackneyed advice to "every clinician to buy a copy" but unfortunately inflation has intervened. In 1963 the cost was £4.00; today, all the expensive photographs have been omitted and the quality of the paper having deteriorated, the price has increased more than six-fold! It is perhaps not within the remit of the reviewer to criticize the publisher, but this fantastic price, together with repeated delays in publication, really is disappointing.

I predict that this book will be in great demand, so that libraries and those with A+ awards are advised to keep their copies on the end of a chain.

T.L.K.

CEREBROVASCULAR DISABILITY, AND THE AGING BRAIN. By G. F. Adams. (Pp. xi+151, figures 13. £4.50). Edinburgh and London: Churchill Livingstone. 1974.

PROFESSOR GEORGE ADAMS is an established international authority on cerebrovascular disease in old age. This little book is not a textbook but a distillate of 25 years experience in Wakehurst House, Belfast City Hospital. The book is dedicated to the late Dr. Louis Hurwitz, who is widely quoted and is responsible for two chapters, one on aphasia and the other management of major strokes. This is a human document, clearly written and produced; the quotations at the head of each chapter are particularly apposite.

There is an historical introduction of great interest. Chapter 1 reviews the pathogenesis of neurological disability in old age, with an excellent section on vascular disorders. In chapter 2 the author deals chiefly with various simple tests of mental capacity in the elderly and makes due acknowledgement to Dr. R. S. Allison. The clinical aspects of mental disability in old age are discussed in chapter 3, with a particularly good section on the chronic brain syndrome. Posture and movement is the title of chapter 4 and there is a review of the different gaits and types of tremor encountered in disease of the nervous system. The remaining chapters are concerned with various clinical presentations of cerebrovascular disease, their treatment and management, subjects on which Professor Adams and his colleagues have made many important contributions to the literature.

It is very valuable to have his mature views now in book form, and he is to be congratulated in achieving his aim in producing a book which will be of great interest to all who have to look after the elderly and patients of all ages who suffer from cerebrovascular disease.

J.H.D.M.

OPHTHALMOLOGY. By K. C. Wybar. Second Edition. (Pp. 347, figures 76 and plates 8. £2.50). London: Bailliere, Tindall & Cassell. 1974.

THIS compact and concise survey of ophthalmology now in its second edition is directed particularly towards the medical student, the general practitioner and the specialist in other branches of medicine. The author presents a short but reasonably comprehensive account of ophthalmology in a well organised and systematic fashion.

The arrangement of the eighteen chapters is conventional, beginning with the basic methods of examination and ending with a short but pertinent section of the care of the blind.

Disorders of the eye are discussed in an anatomical manner and in considerable detail considering the size of the volume. A brief discussion of the form and function of each ocular structure preceeds the clinical descriptions. The text is well organised, lucid and illustrated by carefully selected diagrams. The sections on disorders of the extrinsic ocular muscles, neurophthalmology, and endocrine disturbances of the eye are particularly well presented, reflecting the author's particular expertise in these fields.

The book will be particularly appreciated by medical students, not only for its clear and succinct clinical descriptions but because of its convenient size and relatively low price.

D.B.A.

PSYCHIATRIC ILLNESS. By H. Merskey and W. L. Tonge. (P. 292. £2.80). London: Bailliere, Tindall & Cassel. 1974.

THIS is the second edition of a medium-length book directed more to general practitioners and students than to specialists.

It is easy to read and refreshingly unorthodox in much of its approach. Instead of producing a cut-down mince of major systematic texts the authors tackle most of the subject

CEREBROVASCULAR DISABILITY, AND THE AGING BRAIN. By G. F. Adams. (Pp. xi+151, figures 13. £4.50). Edinburgh and London: Churchill Livingstone. 1974.

PROFESSOR GEORGE ADAMS is an established international authority on cerebrovascular disease in old age. This little book is not a textbook but a distillate of 25 years experience in Wakehurst House, Belfast City Hospital. The book is dedicated to the late Dr. Louis Hurwitz, who is widely quoted and is responsible for two chapters, one on aphasia and the other management of major strokes. This is a human document, clearly written and produced; the quotations at the head of each chapter are particularly apposite.

There is an historical introduction of great interest. Chapter 1 reviews the pathogenesis of neurological disability in old age, with an excellent section on vascular disorders. In chapter 2 the author deals chiefly with various simple tests of mental capacity in the elderly and makes due acknowledgement to Dr. R. S. Allison. The clinical aspects of mental disability in old age are discussed in chapter 3, with a particularly good section on the chronic brain syndrome. Posture and movement is the title of chapter 4 and there is a review of the different gaits and types of tremor encountered in disease of the nervous system. The remaining chapters are concerned with various clinical presentations of cerebrovascular disease, their treatment and management, subjects on which Professor Adams and his colleagues have made many important contributions to the literature.

It is very valuable to have his mature views now in book form, and he is to be congratulated in achieving his aim in producing a book which will be of great interest to all who have to look after the elderly and patients of all ages who suffer from cerebrovascular disease.

J.H.D.M.

OPHTHALMOLOGY. By K. C. Wybar. Second Edition. (Pp. 347, figures 76 and plates 8. £2.50). London: Bailliere, Tindall & Cassell. 1974.

THIS compact and concise survey of ophthalmology now in its second edition is directed particularly towards the medical student, the general practitioner and the specialist in other branches of medicine. The author presents a short but reasonably comprehensive account of ophthalmology in a well organised and systematic fashion.

The arrangement of the eighteen chapters is conventional, beginning with the basic methods of examination and ending with a short but pertinent section of the care of the blind.

Disorders of the eye are discussed in an anatomical manner and in considerable detail considering the size of the volume. A brief discussion of the form and function of each ocular structure preceeds the clinical descriptions. The text is well organised, lucid and illustrated by carefully selected diagrams. The sections on disorders of the extrinsic ocular muscles, neurophthalmology, and endocrine disturbances of the eye are particularly well presented, reflecting the author's particular expertise in these fields.

The book will be particularly appreciated by medical students, not only for its clear and succinct clinical descriptions but because of its convenient size and relatively low price.

D.B.A.

PSYCHIATRIC ILLNESS. By H. Merskey and W. L. Tonge. (P. 292. £2.80). London: Bailliere, Tindall & Cassel. 1974.

THIS is the second edition of a medium-length book directed more to general practitioners and students than to specialists.

It is easy to read and refreshingly unorthodox in much of its approach. Instead of producing a cut-down mince of major systematic texts the authors tackle most of the subject

CEREBROVASCULAR DISABILITY, AND THE AGING BRAIN. By G. F. Adams. (Pp. xi+151, figures 13. £4.50). Edinburgh and London: Churchill Livingstone. 1974.

PROFESSOR GEORGE ADAMS is an established international authority on cerebrovascular disease in old age. This little book is not a textbook but a distillate of 25 years experience in Wakehurst House, Belfast City Hospital. The book is dedicated to the late Dr. Louis Hurwitz, who is widely quoted and is responsible for two chapters, one on aphasia and the other management of major strokes. This is a human document, clearly written and produced; the quotations at the head of each chapter are particularly apposite.

There is an historical introduction of great interest. Chapter 1 reviews the pathogenesis of neurological disability in old age, with an excellent section on vascular disorders. In chapter 2 the author deals chiefly with various simple tests of mental capacity in the elderly and makes due acknowledgement to Dr. R. S. Allison. The clinical aspects of mental disability in old age are discussed in chapter 3, with a particularly good section on the chronic brain syndrome. Posture and movement is the title of chapter 4 and there is a review of the different gaits and types of tremor encountered in disease of the nervous system. The remaining chapters are concerned with various clinical presentations of cerebrovascular disease, their treatment and management, subjects on which Professor Adams and his colleagues have made many important contributions to the literature.

It is very valuable to have his mature views now in book form, and he is to be congratulated in achieving his aim in producing a book which will be of great interest to all who have to look after the elderly and patients of all ages who suffer from cerebrovascular disease.

J.H.D.M.

OPHTHALMOLOGY. By K. C. Wybar. Second Edition. (Pp. 347, figures 76 and plates 8. £2.50). London: Bailliere, Tindall & Cassell. 1974.

THIS compact and concise survey of ophthalmology now in its second edition is directed particularly towards the medical student, the general practitioner and the specialist in other branches of medicine. The author presents a short but reasonably comprehensive account of ophthalmology in a well organised and systematic fashion.

The arrangement of the eighteen chapters is conventional, beginning with the basic methods of examination and ending with a short but pertinent section of the care of the blind.

Disorders of the eye are discussed in an anatomical manner and in considerable detail considering the size of the volume. A brief discussion of the form and function of each ocular structure preceeds the clinical descriptions. The text is well organised, lucid and illustrated by carefully selected diagrams. The sections on disorders of the extrinsic ocular muscles, neurophthalmology, and endocrine disturbances of the eye are particularly well presented, reflecting the author's particular expertise in these fields.

The book will be particularly appreciated by medical students, not only for its clear and succinct clinical descriptions but because of its convenient size and relatively low price.

D.B.A.

PSYCHIATRIC ILLNESS. By H. Merskey and W. L. Tonge. (P. 292. £2.80). London: Bailliere, Tindall & Cassel. 1974.

THIS is the second edition of a medium-length book directed more to general practitioners and students than to specialists.

It is easy to read and refreshingly unorthodox in much of its approach. Instead of producing a cut-down mince of major systematic texts the authors tackle most of the subject

from the viewpoint of the practitioner facing the clinical problem. Presenting problems are discussed, rather than categorised psychiatric disorders. A particular strength of the book is the emphasis given to the doctor's own reactions and feelings when faced with difficult emotional problems.

This reviewer finds a number of points of disagreement but this is inevitable in this subject. For example the authors seem rather over-sold on the value of some drugs and over-alarmist about the risk of death and need for immediate in-patient treatment in anorexia nervosa.

A further criticism is the ambitious (but unsuccessful) aim to cover child and adolescent psychiatry in 19 pages. However, useful chapters are included on the particular problems of sex and marriage, old age, emergencies and suicidal behaviour.

This book is recommended for general practitioners and clinicians in other non-psychiatric fields, for whom it will give more useful guidance than most short text-books.

W.O.McC.

PHARMACOLOGY. By R. G. Penn. Second edition. (Pp. 328+figures 14. £2.50). London: Bailliere, Tindall & Cassell. 1974.

THIS brief text is presumably written for medical students in those medical schools where the teaching of pharmacology is still kept entirely separate from clinical reality. It is a lucidly written book well illustrated by simple graphs and diagrams. It is unfortunate that many of the illustrative examples of drug action chosen have no clinical relevance and that the notes on the therapeutic aspects of most drugs described bear little resemblance to current practice.

P.C.E.

THE JOURNAL OF PSYCHOLOGICAL RESEARCH IN MENTAL SUBNORMALITY. Volume 1. No. 1. October 1974. (Twice yearly. £3.00 private individuals, £6.00 libraries and institutions). Muckamore, Co. Antrim: Department of Psychology, Muckamore Abbey. 1974.

It is with great pleasure that we welcome this new journal produced and printed in Ulster and edited by Donald MacKay, Ruth Elliott and Gerry McDonald of the Department of Psychology, Muckamore Abbey Hospital. This issue contains articles from the active unit at Muckamore Abbey and will doubtless stimulate contributions from further afield. The articles are necessarily of a somewhat specialised interest but one by MacKay, McCoy and Mulligan on the possible connection between long-term emigration and subnormality must be of general interest and concern.

The journal shows careful editing and proof reading, and especially we in Ulster will look forward to its continued success and will wish it well and an honoured place in the future.

from the viewpoint of the practitioner facing the clinical problem. Presenting problems are discussed, rather than categorised psychiatric disorders. A particular strength of the book is the emphasis given to the doctor's own reactions and feelings when faced with difficult emotional problems.

This reviewer finds a number of points of disagreement but this is inevitable in this subject. For example the authors seem rather over-sold on the value of some drugs and over-alarmist about the risk of death and need for immediate in-patient treatment in anorexia nervosa.

A further criticism is the ambitious (but unsuccessful) aim to cover child and adolescent psychiatry in 19 pages. However, useful chapters are included on the particular problems of sex and marriage, old age, emergencies and suicidal behaviour.

This book is recommended for general practitioners and clinicians in other non-psychiatric fields, for whom it will give more useful guidance than most short text-books.

W.O.McC.

PHARMACOLOGY. By R. G. Penn. Second edition. (Pp. 328+figures 14. £2.50). London: Bailliere, Tindall & Cassell. 1974.

THIS brief text is presumably written for medical students in those medical schools where the teaching of pharmacology is still kept entirely separate from clinical reality. It is a lucidly written book well illustrated by simple graphs and diagrams. It is unfortunate that many of the illustrative examples of drug action chosen have no clinical relevance and that the notes on the therapeutic aspects of most drugs described bear little resemblance to current practice.

P.C.E.

THE JOURNAL OF PSYCHOLOGICAL RESEARCH IN MENTAL SUBNORMALITY. Volume 1. No. 1. October 1974. (Twice yearly. £3.00 private individuals, £6.00 libraries and institutions). Muckamore, Co. Antrim: Department of Psychology, Muckamore Abbey. 1974.

It is with great pleasure that we welcome this new journal produced and printed in Ulster and edited by Donald MacKay, Ruth Elliott and Gerry McDonald of the Department of Psychology, Muckamore Abbey Hospital. This issue contains articles from the active unit at Muckamore Abbey and will doubtless stimulate contributions from further afield. The articles are necessarily of a somewhat specialised interest but one by MacKay, McCoy and Mulligan on the possible connection between long-term emigration and subnormality must be of general interest and concern.

The journal shows careful editing and proof reading, and especially we in Ulster will look forward to its continued success and will wish it well and an honoured place in the future.

from the viewpoint of the practitioner facing the clinical problem. Presenting problems are discussed, rather than categorised psychiatric disorders. A particular strength of the book is the emphasis given to the doctor's own reactions and feelings when faced with difficult emotional problems.

This reviewer finds a number of points of disagreement but this is inevitable in this subject. For example the authors seem rather over-sold on the value of some drugs and over-alarmist about the risk of death and need for immediate in-patient treatment in anorexia nervosa.

A further criticism is the ambitious (but unsuccessful) aim to cover child and adolescent psychiatry in 19 pages. However, useful chapters are included on the particular problems of sex and marriage, old age, emergencies and suicidal behaviour.

This book is recommended for general practitioners and clinicians in other non-psychiatric fields, for whom it will give more useful guidance than most short text-books.

W.O.McC.

PHARMACOLOGY. By R. G. Penn. Second edition. (Pp. 328+figures 14. £2.50). London: Bailliere, Tindall & Cassell. 1974.

THIS brief text is presumably written for medical students in those medical schools where the teaching of pharmacology is still kept entirely separate from clinical reality. It is a lucidly written book well illustrated by simple graphs and diagrams. It is unfortunate that many of the illustrative examples of drug action chosen have no clinical relevance and that the notes on the therapeutic aspects of most drugs described bear little resemblance to current practice.

P.C.E.

THE JOURNAL OF PSYCHOLOGICAL RESEARCH IN MENTAL SUBNORMALITY. Volume 1. No. 1. October 1974. (Twice yearly. £3.00 private individuals, £6.00 libraries and institutions). Muckamore, Co. Antrim: Department of Psychology, Muckamore Abbey. 1974.

It is with great pleasure that we welcome this new journal produced and printed in Ulster and edited by Donald MacKay, Ruth Elliott and Gerry McDonald of the Department of Psychology, Muckamore Abbey Hospital. This issue contains articles from the active unit at Muckamore Abbey and will doubtless stimulate contributions from further afield. The articles are necessarily of a somewhat specialised interest but one by MacKay, McCoy and Mulligan on the possible connection between long-term emigration and subnormality must be of general interest and concern.

The journal shows careful editing and proof reading, and especially we in Ulster will look forward to its continued success and will wish it well and an honoured place in the future.