VOLUME 42 1973

THE ULSTER MEDICAL JOURNAL

PUBLISHED BY
THE ULSTER MEDICAL SOCIETY

CONTENTS

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THE ULSTER MEDICAL JOURNAL

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INSTITUTE OF CLINICAL SCIENCE,
GROSVENOR ROAD, BELFAST BT12 6BJ.

.....19.....

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THE
ULSTER MEDICAL JOURNAL

PUBLISHED ON BEHALF OF THE ULSTER MEDICAL SOCIETY

VOLUME 42 1973 No. 2

DOCTORS' DILEMMAS

by **SIR JOHN PEEL**

THE SIR THOMAS AND LADY EDITH DIXON MEMORIAL LECTURE

Delivered 7th May, 1973

I SHOULD like to begin my talk to-day by quoting some words first written shortly before I was born. "Never has the outlook for the profession been brighter. Everywhere the physician is better trained and better equipped than he was 25 years ago. Disease is understood more thoroughly, studied more carefully and treated more skilfully. The average sum of human suffering has been reduced in a way to make the Angels rejoice. Diseases familiar to our fathers and grandfathers have disappeared. The death rate for others is falling to vanishing point, and public health measures have lessened the sorrows of millions. Vagaries and whims, lay and medical may neither have diminished in number nor lessened in their capacity to distress the fainthearted, who do not appreciate that to the end of time people must imagine vain things, but they are dwarfed by the comparison with the colossal advances of 50 years". If William Osler had been writing in 1973, he could well have used identical language. We tend to think that the progress in our generation has been more dramatic and vital than at any time in history, but the impact on medicine of the triple discoveries of antiseptics, anaesthesia and X-rays, must have been as great in the second half of the nineteenth century as has been the discovery of antibiotics in the first half of the twentieth. What, however, distinguished the present situation from that which existed in the last century and centuries before is the changing pattern in the relationship between the doctor and the society in which he works, and it is on this which I should like to concentrate to-day.

It has been said "the basis of medicine is sympathy and the desire to help others. Whatever is done to this end must be called medicine."

"In the primal sympathy
Which having been, must ever be
In the soothing thoughts that spring
Out of human suffering."

Herein lies the fundamental motivation for most of us into the profession of medicine. To primitive man disease only struck when the individual became possessed of some devil or evil genius. The first task of the medicine man was to drive out the bad spirits by various forms of magic and incantations. Having done that he had to proceed to drive out the physical badness; and I suspect that is why, over the centuries so much of therapy has resided in emetics, purges enemata, diuretics, diaphoretics and venesection. Furthermore in the earliest civilisations medicine was a pre-eminent social force. The medicine man was the one who led his tribe in its struggle against misfortune. Cast in this role he was like the politicians and generals of later years—in order to survive he had to be successful.

The next stage in the evolution of the physician found both patient and doctors looking towards religion and philosophy rather than to science in the endeavours to cure illness. "Physic was early fathered upon the Gods"—and so we find, first Imhotep the Egyptian God of medicine followed by Asklepios in the Grecian cult. He was the son of Apollo whose shrines housed the prophetic serpents, which have remained through the centuries symbolic of supernatural powers, and which to this day characterise so many of the seals and charters of medical organisations. His daughter, Hygiea, was a more cheerful character and in her resided the concept that cleanliness, fresh air and nature's beauty spots were all designed as the natural venues for the prevention of disease. Small wonder then, that it was in one of these beauty spots on the sunny shores of the bright blue Aegean Sea, the island of Cos, that the Father of Medicine was born, reared, practiced and taught. Here for the first time the systematic observation of the natural progress of diseases was practiced and the observations recorded. The effects of treatment and the prognosis of many illnesses were documented for the benefit of future generations. Clinical medicine was born and thenceforward for many centuries the place of the physician was with the individual patient in the sick room. However, success in diagnosis and treatment remained the yardstick whereby he was judged by his contemporaries. The "lex talionis" originating as the code of Hammurabi (2,000 years B.C.) left no doubt of the principle of an eye for an eye and a tooth for a tooth. "If a doctor has treated a gentleman for a severe wound with a bronze lancet and has cured him, or has opened an abscess of the eye for a gentleman with a bronze lancet, and has cured the eye of the gentleman, he should take 10 Shekels of silver. If on the other hand a doctor has treated a gentleman for a severe wound with a bronze lancet and has caused (notice the word 'caused') the gentleman to die, or has opened an abscess of the eye for a gentleman and caused (again) the loss of the eye, then one should cut off his right hand". As late as 1650 a Chinese Physician who lost a royal patient was buried alive with his patient! In the section that deals with fees in the recent report of the Monopolies Commission, it is not without interest and perhaps significance that the suggestion is made that a greater degree of competition within the professions (including medicine) in regard to fees based upon results might not in fact be against the public interest by promoting greater efficiency. How much has Society's attitude to the practitioner of the noble art of healing changed in 4,000 years?

In any society changes can be brought about by either revolution or evolution—and we have seen both in the present generation, in medicine as in other spheres.

In 1948 the introduction of a National Health Service was indeed a revolution in the practice of medicine. It was, I think most people will agree, a bold, imaginative and courageous step, which has, in the event, had more on the credit than on the debit side of the account, in the 25 years of its existence. The political architect of the Health Service said at the time that it would take 25 years for the revolution he was creating to settle down, and for all the teething troubles to be ironed out. That, like many another political prophesy, has proved to be a serious underestimate, and the reorganisation proposed for 1974 bid fair to give the cauldron another good stir. I think there is a tendency to forget just what a revolution this event created for the medical profession, especially as it was introduced on an appointed day with remarkably little preparation. There were three fundamental changes brought about. First of all, although it removed the necessity for any consideration of finance at the time of discharging any item of service, it erected a different sort of barrier between patient and doctor—namely the State, which now became responsible for payment. I shall return to this point later because as time has passed it has caused more rather than fewer problems. The second big change that occurred was to bring medicine within the ambit of politics. It is vain to protest that medicine and politics have nothing in common and are mutually incompatible. They may be strange bed-fellows but nevertheless they are bed-fellows for better or for worse. How much of the national resources are to be devoted to the health service is a political decision, not a medical one. The National Health Service began by costing something over 200 million pounds a year. The designer of the welfare state, "from the cradle to the grave" made what must rank as one of the major miscalculations of all time, when he argued that as the nation became healthier, the cost of the health service would fall, not rise. The rising cost of the health service, 10-20 times more than intially, is due only in a very small part to the inflationary situation in other areas. It is in part due to the much greater degree of sophistication that has developed with technological advances in a wide variety of medical and surgical techniques both of diagnosis and treatment. These are inevitably vastly more expensive than the stethoscope and bottles of medicine of yesteryear. But more and more the rising costs reflect the steadily rising and totally insatiable demand by the public for medical services. It is impossible to foresee any ceiling to this demand. As the more serious diseases recede in both severity and incidence, minor ailments replace them in ever increasing numbers, and who would be brave enough to forecast the disappearance of the thousand and one "malade imaginaires?"

It is no part of the doctor's traditional responsibility to try to restrict these demands. Only Government, by deciding how much of the revenue of the nation can be made available to meet these ever increasing demands, can exercise any sort of control.

The third change that came about in 1948 was the division of the profession into two distinct halves—the general practitioners on the one hand and the hospital doctors on the other. Although both are engaged in the clinical practice of the art and science of medicine, the difference in the relationship that each has with their employer in regard to finance has exercised a subtle influence over the years—an influence that the profession itself has tried to play down. The hospital doctor,

whether he be full-time or part-time is in direct contract with the State as his employer. He has a proper career structure, with the stimulus of competition for promotion and status, the prospects of financial progress by incremental increases based not only on length of service, but also upon merit and quality of service. The general practitioner on the other hand has clung to, and still clings to the 'sacred cow' of being an independent contractor. If one examines the position critically, the family doctor has little real competitive rewards for the practice of good medicine, precisely because of this financial situation. In fact, paradoxically, in some ways the better he equips himself with the wherewithall to practice good medicine by modern standards, the worse off he is. Short of some serious or gross negligence he receives little censure for the practice of poor medicine and even less reward for the practice of good medicine. His main competitive driving force is competition for more patients because more patients mean more money. As a previous Minister of Health has written "The situation of the family doctor therefore combines private enterprise and state service without the characteristic advantages of either—the essence of private enterprise system, competition for gain has been gouged out of family doctoring, while leaving the empty shell". This may seem a harsh criticism, but it is a criticism of a system, not of individual doctors. Because the great majority are dedicated professionals, devoted to the care of their patients, the means that have perforce been introduced over the years to provide the necessary finance for a secure livelihood have created a system of special payments and grants that is surely a financier's nightmare. Apart from disrupting the smooth workings of relationships with patients and other members of the profession, it has created the impression with the public that the only thing the doctor is interested in is money. And in some ways the situation is getting worse rather than better, and at a time when unity within the profession is of paramount importance. Even further schisms are arising with junior hospital doctors, regional consultants and other groups hiving themselves off—and all arguing fundamentally about one thing—money. To those with the best traditions of medicine at heart, it is a scene that inevitably calls for concern and demands some action.

I should now like to turn from the revolution to the processes of evolution that are having such a marked effect upon the practice of medicine in our generation, and which are creating problems as well as solving them. I do not need to remind you of all the technological advances applicable to the care of patients, in diagnosis as well as in treatment, but merely to exemplify my point by a few examples. The application of scientific technology to parturition should in theory bestow great benefit on the next generation. The labour ward with all the paraphernalia of controlled labour and foetal monitoring is an awe-inspiring place. The operating theatre, with advanced vascular or transplantation surgery in progress is demanding the services of large teams of highly trained experts. The intensive care units, whether for newborn babies, for the victims of road accidents or natural disease, are making enormous demands upon the resources of our hospital services. Clinical and laboratory research is becoming the sine qua non of medical practice—even to the point of obsession. There is a tendency to forget that research should be related to the needs of the patient. Research which is not so related may well be research, but it is not clinical research. There is a modern obsession in medicine

to-day that no fact is thought to be a fact until it has been the subject of a controlled trial. I do not want in any way to belittle the enormous contributions that modern scientific technology is making to the control and cure of disease, and the improvement of health, but I do want to emphasise that apart from the enormous costs involved, there is not always enough thought given to long term effects of much that is being done, both on the individual and the community. Where the benefit, actual or potential, to the individual coincides with that to the community, no problems and no dilemmas arise. It is in the interests of both the parent of a child and the society in which it will live that it be born healthy rather than deformed. Any steps therefore, taken to this end are welcome by both, and no limits should be placed upon the resources made available to help achieve this end. But the interests do not always coincide. The doctor by instinct and by training is an individualist and the benefit to his patient is usually paramount to him. But in modern medicine there are many dilemmas arising and I should like to examine some of these briefly.

1. Screening for potential disease. There are two aspects of this problem—which is in fact an enormous one. It has been estimated that there are not less than 5 million in the total population, or 1 in 10 with actual disabilities which are unrecognised and untreated. If we take the figures from the Medical Research Council's Social Medicine Unit, there are upwards of 2 million in the population with untreated and undiagnosed hypertension; half a million with undetected urinary infection; 300,000—400,000 with glycosuria or abnormal blood sugar curves, more than half a million with respiratory tract disorders, and a limitless number with psychiatric morbidity. Well women's clinics and family planning clinics turn up annually a large volume of unsuspected disorders. How far should resources be directed towards efforts to uncover this large submerged iceberg of unrecognised disease? The calculation, whether in terms of economic resources or human wellbeing is an extremely difficult one to make, and because it is so difficult, such efforts as are being made are very half-hearted. But the other side of screening, namely for potential disease, that is, looking among the healthy for the potentiality to develop disease later, is even more problematical. Research has now established that the majority, even if not all, cases of cervical cancer pass through the phase of a pre-invasive lesion or carcinoma in situ. This can be detected in most cases by the application of regular cytological examination. If in the early curable stage the diagnosis is made and the appropriate treatment applied, there is the prospect of nearly 100 per cent cure—and for the individual death from cervical cancer prevented. Why then the doubts about national screening programmes? Apart from the purely scientific problem of whether *all* cervical cancers progress through the pre-invasive stage, apart from the problems of relating costs of screening programmes to the cost involved in treating cases of established disease, there still remains the problem of population motivation to come forward for investigation. So far the impact of our screening programmes in this area have been almost nil in terms of lowering either mortality or incidence, simply because only a small section of the women at risk are being examined, and most of those that are fall into the low risk category. In the years between 1964 and 1971 the total number of women screened rose from 200,000 to 2,000,000, and yet the mortality fell from 2,465 to only 2,417—a figure of no statistical significance. Yet

in British Columbia, where a much more intensive screening programme has existed for 20 years amongst a much more static and homogeneous population, significant lowering of incidence has occurred, and it has been shown that the incidence of the disease is increased 10 times amongst those unscreened compared with those screened by cytology. In spite of this, and because of the British experience, there is a strong feeling among some, that screening programmes are a waste of time and public money, and in the face of the facts even the most optimistic campaigner must often hesitate. At the end of the day, I suspect, it may well be the politician rather than the doctor who will settle the issue by determining priorities.

2. This brings me to a second area of an increasing conflict of loyalties for the doctor—his devotion to the best and most immediate benefit of the individual patient, and his obligation to the public, society, the community—whatever term you may give to his employer. A previous Minister of Health has spelt out this dilemma for the doctor very clearly: "The professional is the servant, albeit specially equipped and endowed, while the layman (albeit often called the client) is the consumer and commands the service, and decides whether to take the advice or no". The doctor is accustomed by tradition and training to receiving patients who come to him with a complaint or a problem seeking his advice. This is being replaced more and more by patients coming to him and demanding a service, to which rightly or wrongly they feel entitled. They are encouraged in this belief because they know that the general practitioner is "contractually obliged to give all necessary care and attention gratis on demand". The ability—indeed the right—for the doctor to exercise his expert clinical judgement, based on knowledge and experience, is being more and more challenged. Better education of the public, itself an admirable development, is partly responsible for this changed approach to medical care, and the sheer pressure of numbers and work load may force doctors into submission to the demand, even against his better clinical judgement. This is not good for the standards of medical practice and of those standards deteriorate in the end, it is inevitably the patient who will be the loser. There are two areas in particular which at the present time exemplify the pressures upon the doctor to conform to an 'on demand' situation, and which in many instances he must find resistance very difficult even though his clinical knowledge and experience must warn him that he is not necessarily considering the ultimate good of the patient—the prescribing of drugs and control of reproduction. Of course it is only a very tiny minority of doctors who are guilty of yielding to the pressures of those addicted to the so-called hard and soft groups of drugs, but the steadily increasing number of cases occupying the time of the Disciplinary Committee of the General Medical Council is disturbing. More widespread, however, is the overprescribing of the tranquilisers, sleeping pills and antibiotics. I have every sympathy with and understanding of the situation that confronts the doctor, but no one can regard it as the practice of good medicine simply to treat a symptom without the time or opportunity to discover the cause. The second area of enormous pressure on the doctor is in regard to demands for contraceptives, sterilisation and abortion. Again in the majority of such instances the demand is doubtless reasonable and right, but what is the doctor's position if a 12-year-old demands the pill or a 16-year-old wants to be sterilised? Rare examples you may say, and extreme, but they are happening, and happening with increasing frequency, and doctors are coming

more and more under criticism in public and in private, if they preserve their traditional right to advise and not necessarily to accede.

3. No one would doubt that it should be society's aim to improve the quality of the life of its citizens. But what do we really mean by the quality of life? To the many it means a bigger paypacket, a better car, or a greater supply of all the paraphernalia of modern technological gadgetry, and then more and more leisure hours. The quality of life is judged in purely materialistic terms. But if you study the catalogue of diseases and disorders that doctors are called upon to treat, affluence does not by any means spell wellbeing or health. Obviously we still have a way to go before poverty and consequent malnutrition and deficiency diseases are eliminated in this country, but by and large we, in common with other societies in the western world are vastly more affluent than our predecessors were, two or even one generation ago. But we are rapidly replacing the diseases which have been eliminated or whose incidence has been greatly reduced, by those which the affluence of society is creating. Malnutrition is being replaced by obesity and diabetes; osteomyelitis by bones broken in road and other accidents; high multiparity by sterility resulting from some of the consequences of sexual permissiveness; pneumonia by bronchitis and lung cancer due to cigarette smoking and other atmospheric pollutants. The list could go on—and what of the enormous volume of stress disorders? In trying to deal with this new fund of clinical material it seems to me that the doctor's role must inevitably change direction, away from the traditional one of curative medicine into the wider field of prevention. Not only is the field wide but it is also very difficult. Enormous strides have of course been taken, in reducing the incidence of so many epidemic and communicable diseases by public health measures such as mass inoculations, mass radiography, improved pre-natal and infant welfare care, better control and prevention of industrial diseases and in many other ways. But medicine is fast coming to the end of that particular road, and the only way in which much progress will be made in reducing so many of the disorders doctors are called upon to treat now, is by influencing human behaviour. Reference to a few figures relative to two disorders currently increasing rapidly in our society highlights not only the problem but also the difficulties involved in trying to deal with it. The exact incidence of obesity in the population is difficult to estimate not least because of the lack of an exact definition. But many figures have been collected by life insurance companies, and one study in 1968 carried out on the employees of the British Petroleum Company revealed that 48 per cent of the males and 46 per cent of the females were significantly above the desirable weight by age and sex. The majority of these individuals are suffering from simple obesity due to over-eating, the wrong sort of eating and often over consuming alcohol. Does this sort of obesity matter—"Let me have men about me that are fat"? But if you look at the disorders that stem from obesity that are taking more and more of the resources of medical time and the country's finance, it seems that it does matter. From the national point of view perhaps the increased mortality does not matter, but the morbidity and suffering arising from hypertension, skeletal disabilities, metabolic disorders and the complications of surgery on the obese must be enormous.

Between 1954 and 1969 there was a 330 per cent increase in the incidence of gonorrhoea; in 1970 the increase over 1969 was a further 20 per cent, and in 1971

a still further 40 per cent. Does this matter? Alexander Fleming is reputed to have said that the discovery of penicillin had made it possible to catch a fresh infection three times a week, and this seems to be the attitude of some sections of the public. But unhappily, with the emergence of an increasing number of drug resistant infections, it is becoming more and more difficult to cure infection three times a week, and many cases in the female are asymptomatic or are associated with other less serious types of infection and so are being overlooked in the acute or subacute stage. Again the increasing volume of the doctor's time, human suffering, and national resources in dealing with the late complications of this and other preventable pelvic infections is increasing every day. Again the steadily increasing numbers of unplanned pregnancies, most of which should be preventable, tells the same story. The diseases and disorders of the human body and mind that are self-inflicted is of course no new problem in society, nor is the contemptuous attitude of many of the public to doctors and others who try to influence behaviour. Plato recognised it when in his Republic we read "They deem him their worst enemy, who tells them the truth, which is simply that unless they give up eating and drinking and wenching and idling, neither drug nor cautery nor spell nor amulet nor any other remedy will avail". Doctors have by and large tended to cold shoulder "Health Education", and it has remained a Cinderella on the fringe of medical practice and often left in the hands of those least equipped to handle it. But I believe it is now gaining the recognition it should surely be given and doctors must become more and more involved. Time is being found in the undergraduate curriculum for introducing study of the behavioural sciences in many medical schools, and it is encouraging to know that in some measure due to the constant prodding from the Society for Health Education and other bodies and individuals, the first Chair in Health Education in this country is to be established in the new Medical School at Nottingham later this year. But apart from the need to study more about the underlying causes of deviations in human behaviour at an academic level, there is also at the practical level the need to study the best techniques whereby to attempt to influence people. In this respect the doctor is still a person of great authority in the community, and perhaps unexpectedly among the lower social classes. One social study in relation to cervical cytology illustrates this point. The study covered a series of women presenting themselves for cervical cytology, and showed that in Social Classes 1 and 11 nearly 70 per cent had been motivated by what they had read in newspapers or heard on television or radio; whereas in Social Class V it was less than 20 per cent. On the other hand in Social Class V over 60 per cent were first informed and motivated to have the test done by family or clinic doctors. There is evidence from more than one direction that as the standards of living—material, cultural and educational—improve, the stature and influence of the doctor in society tends to decrease. He may well regain some of that lost ground if he takes a more realistic and understanding role in regard to public education in the promotion of health.

4. I made reference previously to what is now spoken of and written about with increasing frequency—the quality of life. Are doctors doing all they should to promote that ideal? Are they perhaps sometimes unmindful of the consequences of some lines of therapy made possible only because of scientific progress? Have we become perhaps too obsessed with mortality, the lowering of which has become

the be-all and end-all of our endeavours? To preserve life and to prolong life are of course the long cherished ideals of our profession, and it is only with some considerable misgiving that one should attempt to challenge them. I can well remember an occasion in the United States some 15 years ago, when a particularly massive operation for terminal cancer was under discussion. The speaker was reporting with some pride that he had reduced the primary mortality in his recent series from 50 per cent to 40 per cent, and I was constrained to remark that I was not so much worried by those patients who died, but by those who survived for a few months only and in great pain and distress. Scientific progress is making it more and more possible to look upon the body as an exciting machine, with limitless opportunities to study, examine and research into the way it works. Without such opportunities and the initiative and enthusiasm of doctors to research and to strive to know and to understand progress would cease. Any attempt to obstruct medical research would be disastrous. Nevertheless it is of the utmost importance that those who carry out research involving patients do not offend against the codes of ethical practice laid down and generally accepted by the profession itself, or against the naturally sensitive feelings of the public without adequate communication. How difficult communication can be is well exemplified by the recent revival of the anxieties aroused in some members of the public by the use of the foetus obtained by abortion for research purposes—and this in spite of a report produced last year by a Committee set up by the Department of Health which spent 18 months of intensive study of the problem, and which spelt out all the facts in detail. Nevertheless one can forgive the public if they sometimes wonder what the doctors are really up to, when they see the results of some of the operations for spina bifida and hydrocephalus in neonates, when they see de-humanised automata salvaged from road accidents, and the prospects of even more survivors into old age, stuffed as one writer has expressed it, with an ever-increasing number of other people's unwanted organs. The public has I think the right to be concerned with some of the more elaborate surgical procedures and intensive care designed purely to prolong life. These impinge on many areas—the progress of scientific medicine on the one hand, the ethical and social consequences, priorities in the use of ancilliary staff, priorities in cost allocation and other factors on the other. When as sometimes happens, the whole surgical work of a hospital may be held up for 24 hours or more, with diversion of staff from other duties in order to allow some extensive surgical procedure, often experimental in nature, and often only likely to prolong life for a few weeks or months, one can understand the public when they ask—is this sort of thing necessary, is it desirable, is it right, is it sensible? The need for the profession to communicate properly, in order to allay anxieties and suspicions is vital—otherwise there will be more and more lay interference in decisions that ought to be purely medical ones. And within the profession itself there is a danger of a dichotomy of interests between those dedicated to the progress of medical knowledge to be applied for the benefit of the individual, and those with a more socialogically orientated outlook, whereby the benefit of society as a whole should over-ride those of the individual. Perhaps these devisions are more apparent than real, but they certainly appear very much to exist, and bring me to another point for reference to possible dilemmas. How far should doctors become involved in trying to influence what are fundamentally

political decisions? I was surprised to read recently in a statement put out by the doctors' group on population that "population should rightfully be the concern of Government". Surely it always has been and always will be. It is obviously right that doctors, who have contributed in no small measure to the growing population in the world by lowering mortality and reducing death rates, especially in infants and the elderly, should do all they reasonably can to control excessive birth rates. But equally I do not think that this should be with the object of helping Government to escape their responsibilities for the social and economic progress of the people they govern. The tendency in population statistics is merely to count heads. Even there the population prognosis made in 1960 for this country proved by 1970 to be out by many millions and little research appears to have been published, if indeed it has been done, on the effects that a rapidly falling birth rate will have on the distribution of population in regard to age, social class, religion and race. I believe the doctor's role is still primarily with his or her individual patient, and not to become the tool of Government in trying to interfere with human reproduction. And I say that in spite of firmly believing as an individual that Government should do all that is reasonable to discourage excessive reproduction. I have no anxieties if doctors sterilise women when in reproductive terms they feel they have had enough, but I would be very disturbed that doctors should sterilise women or men simply because Government wants to reduce population, or does not like the colour of the skin of a section of the population or for any other purely political reason. That would put the profession on a very slippery slope.

In conclusion I should like to make reference very briefly to some of the ethical and medico-legal problems that are causing many doctors great difficulty to-day. Attitudes in society are fast changing. It is not for me to argue whether these changes are for better or worse, but the fact that they are changing makes it necessary for the profession itself to examine some of its traditional ethical codes. The fact that it has stood for over 2,000 years in all societies means, I think, that it should not be cast aside too easily, but should not prevent it from being re-examined and perhaps modified in some respect. One of the features of a profession is that it accepts the responsibility for establishing and maintaining its own standards. As a profession we have done pretty well in this area in this country and we have little of which we have any cause to be ashamed. This makes it all the more unfortunate that internal squabbles within the profession have made it necessary for Government to step in and set up an enquiry into how the profession should regulate itself or be regulated. This cannot enhance the stature of the profession in the eyes of the discerning public, most of whom are bewildered by what the doctors are quarrelling about. A complete lecture would be necessary to cover the whole field of ethics and legal responsibilities, and I shall not attempt this here. I merely list some of the more important areas that must be examined and critically reassessed, largely because we have a comprehensive National Health Service in existence, primarily for the benefit of the public. Professional confidentiality, advertising, prescribing, personal relationships between doctors and patients of the opposite sex, human experimentation, and the problems of preserving life at all costs and regardless of consequences, are the principle ethical problems requiring examination. No one would deny the right to compensation for negligence, but in this technological age we need a much more sensitive mechanism than

exists at present to determine continuing competence to practice, and to determine at just what point patient care falls below generally accepted standards.

I began my remarks with a quotation and I should like to end with one—written by the late Lord Brain on the National Health Service. "We for our part should not let ourselves be obsessed by the Health Service, but remember how much medicine has outside it. We cannot live by our traditions alone, but it is vital that our traditional values, embodied in our great institutions should flourish and be seen to flourish in complete independence. Medical research will continue to grow from strength to strength. Moreover in the modern world increasing numbers of issues touching human welfare have medical aspects, which means that doctors have a unique contribution to make to such debates; since no one else possesses the intimate knowledge of the whole man, body and mind. Medicine is, and will remain, a great and growing tree of which the Health Service is but one of its many branches".

"THE CAMPBELL HERITAGE LIVES ON"

by

SIR IAN FRASER, D.S.O., D.Sc.(Oxon.), F.R.C.S., D.L.

THE ROBERT CAMPBELL ORATION
delivered on 8th May, 1973

ROBERT CAMPBELL, if living today, would be well over one hundred years of age. He died in 1920 at the early age of 54 years, and in his 25 years of active work he built up not only for himself but also for this medical school a lasting surgical reputation. It would not be an overstatement if we said that he revolutionized surgery in Ulster

The title of tonight's lecture some fifty years after his death might be "The Campbell Heritage Lives On" for those of us who have practised surgery here since his time are indeed the inheritors of a tradition based on his work. Campbell joined the staff of the Belfast Hospital for Sick Children (then in Queen Street) in 1897 as an assistant surgeon. One of his contemporaries has described him at work there "from nine in the morning until late in the afternoon, examining, treating and operating on . . . children". His work there gave him immense pleasure; he became devoted to children and was in turn beloved by them. I suppose that is why on the back of the Campbell Memorial Medal there appear the words of Hippocrates suggested by the then Vice Chancellor of the university, "Where there is love of man there is love of Art". This motto surrounds a plaque made by Miss Praegar of Holywood which shows a surgeon tenderly dressing the arm of a little child as it sits on its mother's lap.

He is remembered particularly as the pioneer of aseptic surgery in Belfast. He quickly adopted the American novelty of rubber gloves when operating, and he was the first in Ulster to advocate the use of a face mask, which the French surgeons had suggested to keep their beards in check. His surgical interests were wide. He wrote on club hand, on the operative treatment of exophthalmic goitre, on acute appendicitis and on fractures of the radius but his most important contribution was in the field of the operative treatment of hernia in children and in the development of out-patient surgery.

In 1899 Robert Campbell pointed out that the infant should and could have its inguinal hernia repaired at once; up to then it had been customary to wait until the child was 6–10 years of age. During this time it had worn a dirty truss of cotton or rubber, and in many cases the anxious mother had been told that the child must on no account cry for fear of strangulation. He published in 1904 a series of 114 cases and after his death there was found among his papers an analysis of 1500 cases with only one death and this was due to delayed chloroform poisoning. In this series about one-third were aged under three months and almost one-half under six months. Some time before 1909 he began to perform these operations in the out-patients' department. The quantity of outpatient surgery became so great that a special outpatient operating theatre had to be built. This

was much used by Robert Campbell himself but ever more so by Fullerton and those of us who followed on.

Although silent and apparently somewhat inarticulate during the day he seemed to blossom out at 3 a.m. when relaxing after a serious and successful operation. Then he would sit and chat on every possible subject – political, social and medical, all of which he could discuss with his stoic philosophy. This is perhaps a feature of some of the great men whom we have produced in the Belfast Medical School – names such as Purce and Calvert come to mind at once. Although the phrase "The High Priest of Philosophic Doubt" was applied to James Cuming, the Professor of Medicine, yet it embodies Robert Campbell's views on life. In his dealing with the patient he always remembered the remarks made by Florence Nightingale in 1860 – "the first requirement in any hospital is to do the sick no harm". I wish we could say the same about our modern drugs. The patient today has so much to stand up to – at one time it was his disease; today it is his doctor and his treatment.

When the Royal Victoria Hospital opened its doors in 1903 to admit the first patients after their transfer from the old hospital in Frederick Street it was arranged that the first operation would be done with suitable pomp by the then senior surgeon, Sir John Walton Browne, but in the early hours of the morning a patient with a strangulated hernia was admitted requiring an immediate operation. This was done by Robert Campbell; although gloves were available there were no gowns and all that could be found was a shroud from the mortuary. This was looked on by those with a superstitious mind as a bad omen for the future welfare of the new hospital.

At this stage I should like to say how very much I personally appreciate the honour of being asked to give the Campbell Oration. I feel this is a great honour for two reasons – firstly I am one of a group of younger men who were entrusted with the responsibility of carrying on the tradition of Robert Campbell, and if we have gone further and seen further I must say at once, as has been said many times before, "it is surely because we have stood on the shoulders of giants", and our surgical giant was certainly Robert Campbell. My second reason for being grateful for this honour is entirely a personal one; my father and Robert Campbell were in the same year at Queen's and remained close friends throughout life. I have had the responsibility of entertaining the great man on occasions waiting for my father to arrive to take him out for a surgical consultation. Sitting over the fire with my anatomy books I was impressed to find that this apparently old man knew so much anatomy and I so little. Like all great men he was the delightful companion for a young boy, able to put a nervous youngster at his ease. I could easily see why he was described as the "Doctor's Doctor". One incident I remember well was when my father broke his wrist trying to start his Ford car on a frosty winter morning. The car was rather like that old vehicle that one sees in "Dr. Finlay's Case Book." My father came in holding his wrist and I was asked to ring up "Bob" Campbell and ask him to come out and set it. In what appeared a few minutes the great man arrived with his chauffeur in his Chambers motor car, and the wrist was set in the drawing room. Unfortunately all the chairs, sofas, etc., were covered with table mats of pen painting, a rather unattractive table decoration much in vogue at that time, which my mother had prepared for the local church bazaar and which

were yet far from dry. Robert Campbell's bag was put on one, his coat on another, and his hat on a third. I am sure he often wondered afterwards how his clothes got the elegant decorations of pink roses and green leaves.

He married the matron of the Children's Hospital, and his colleague Surgeon Kirk married her successor; in fact for matrons it seemed to be almost an occupational hazard. Whether indeed this was a hazard to be sought after or to be avoided I am not in a position to disclose. Certainly the next matron Miss Knox in her 36½ years avoided this issue and our present matron Miss Hudson has successfully, so far, taken evasive action for twenty-five years.

It is hard to realise the changes that have taken place in nursing and matron's duties with the passage of years. When I was appointed to the hospital the matron was all powerful. She was the only resident and had to take full responsibility both day and night.

While matron, Miss Knox also gave anaesthetics. This was done with the Clover inhaler; a measured quantity of ether was poured into the rubber bag; the face piece was pressed down and held over the face of the struggling child until suffocation took place – periodically the mask was lifted off to allow for a breath of fresh air. This was enough for an operation of the "smash and grab" type – for example, tonsils or adenoids, but it was of little use for longer procedures. The memory of this ordeal remained for ever with many people and even today a person will say, "I have no fear of the operation, but I am terrified of the anaesthetic". This awful feeling of suffocation and being forcibly held down is never forgotten.

I found when I was appointed that there was no dentist at the hospital and, as many of the children had rather infected mouths unsuitable for operations such as hare lip or cleft palate. I provided myself with some second-hand forceps. This was easy as I was sharing No. 1 University Square at that time with my cousin, Marshall Swan the dentist. I thought for a time that I was the first dentist to the hospital until I unexpectedly came across an old pair of rusty forceps which showed that extraction of teeth had also been one of the matron's duties. In a short time, however, we were fortunate to get Mr. Cuthbert McNeill to give up a morning to the hospital on a voluntary basis and today we find some seven dentists are doing the work at one time done by Miss Knox.

Being busy with the anaesthetic Miss Knox was not involved in the technique of the theatre or assisting at the operation. This was often carried out single handed or with the help of a junior nurse. Miss Knox in addition was involved with the cooking and supervision of meals; invariably she did a ward round at 3 a.m. to see that everything was in order and yet at 11 a.m. when we broke off from a busy outpatient department for fifteen minutes for a cup of coffee she was able to grace the proceedings as the lady bountiful at the head of the table accompanied by her Pekinese. The only member of the staff that this dog really approved of was Dr. Malcom Brice Smyth, who smoked a pipe with the strongest and foulest of tobacco. Apparently the dog felt very much at home with him as its previous owner had been a cobbler who smoked the same poisonous weed – black shag, I think. In addition to her anaesthetic, culinary, dental, nursing and administrative duties, Miss Knox had a fine knowledge of the law, and I have been grateful for her help on many occasions.

As soon as a general practitioner was appointed on a part time basis the anaesthetic problem improved and with the employment of another general practitioner as a part time non-resident house surgeon we were able to get a second pair of hands in the theatre. The open Shimmelbusch mask now became the popular method. The metal frame was covered with gauze and with a pad of gamgee covering the face the patient now was given continuous anaesthesia from a drop bottle. The new "rag and bottle" system took over from the Glover's inhaler; the anaesthetic agent was mostly ether. This gave a prolonged and smoother period of unconsciousness, and was the transition period between the early anaesthetic and the modern method. On the anaesthetic trolley was always to be found a bottle of castor oil – a few drops had to be put into each eye at the end of every operation; this was very important as the patient almost always developed conjunctivitis and sore eyes even from the fumes of the ether. Some ointment was also rubbed on to the cheek and chin where often the damp facepiece caused quite a severe burn. There was invariably the mouth gag and finally there was the very nasty instrument called tongue forceps; this crushed the unfortunate tongue almost to pulp. It was much more like pile forceps and would certainly have been better employed at the lower end of the body. It has been long discarded.

Over the years although the matron's duties have greatly changed in character they are today almost as varied and certainly a great deal more complicated. The modern matron must know all about the monitoring of patients and how to run an intensive care unit, understand a heart-lung machine, be an expert in the plumbing of piped oxygen and in modern electronics, and in addition she is expected to understand all sorts of government reports with unusual names like Cogwheel, Salmon and Chambers. It is sad to think that after the modern matron has gained all this knowledge she is no longer to be called "matron"; she becomes an impersonal number such as "No. 9". I remember during the war that a soldier looked on a "No. 9" as something rather drastic, rather unattractive and rather to be feared, which is surely the wrong impression of the modern matron. Built into the regulations for the matrons in the past there was a strong directive against gin; its total avoidance was obligatory. This of course goes back to Florence Nightingale who had to get rid of the image of the Sarah Gamps, all of whom it was said where alcoholics. One doctor wrote of them at that time, "they were all without exception drunkards". Whether with women's lib and modern methods this same strict rule holds good I am naturally not in a position to comment.

Just as the matron's duties have altered so we see similar changes with the sisters and nurses. The sisters, instead of being terrifying middle-aged spinsters set apart from the nurse and creating fear and dimay all around them, are now incredibly young and seem to be in the same age group and very much in competition with the rest of the junior staff. This I am sure is true, and not relative to my own age, when I know it is customary to say that the London Constabulary are getting younger and younger. Reducing the age of the sisters is very important as many of the old girls I am sure could not have dealt with the intricacies of modern dialysis, or understood the un-understandable reports that emanate from laboratories and biochemistry departments.

In the old days the nurses seemed to be on duty all the time; even at a staff dance they appeared in uniform, and if sitting out they sat on the hard stairs

floodlit for all to see. Indiscretion of any sort, even indeed if it had been considered, would have been impossible. In their spare time they were rolling bandages or rubbing dry plaster-of-Paris into crinoline or book muslin to make the plaster-of-Paris bandages for the next day. A helping hand from a willing student or house surgeon was much appreciated, and I am sure it was easier to make the acquaintance of the lady in question on such an occasion than it was at a dance. Another job was the repairing of the rubber gloves; a bowl full of gloves on one side, a bowl of water to find out where the holes were, and a tube of rubber solution – the place smelled like a bicycle repair shop. These repaired rubber gloves were always given to the house surgeon or junior surgeon – the chief was allowed to have an intact pair. These patches were always somewhat insecure and on many occasions I have had to lift a patch out of the wound when it had fallen off; a sharp contract to the expendible gloves as worn today.

Although this might seem primitive it was at that very same time that I paid a visit to Paris and was astonished to find the surgeons there still operating with large thick rubber gauntlet gloves, almost like the gloves used by the motor cyclists of those days. There was of course no finger touch and the French surgeon was entirely dependant upon the Reverdin needle – a needle mounted on a handle which could be threaded, and with it they could do anything from an intestinal anastomosis to the suturing of the abdominal wall.

On one afternoon each week the sisters and nurses were responsible for getting the catgut ready. The plain catgut was bought in bulk but it had to be sterilized and also hardened. Lengths of catgut were rolled around a pair of forceps until a small ball – like a ball of string – was made. This was dropped into a hardening solution, heated in a strong brass container, and the whole thing brought to the boil. This catgut treated in iodine (iodized) or treated with bichromate of potash (chromic) was the only catgut available until America, and later Britain, produced the sealed tubes that are in use today. For the skin one used genuine silkworm gut. This was a long thread which had been pulled from the mouth of a silkworm just when this unfortunate animal was thinking of making its own silk cocoon. It was excellent and more easily knotted than the present nylon but similar in every other respect. It naturally disappeared on the ground of economy with the appearance of the modern man-made synthetic fibre. Barbour's thread from the factory at Hilden was much in use and its general use in many surgical centres in Britain started from here.

In the ward in the early days the nursing duties did not differ much from today. There were no antibiotics and so inflammation, sepsis, suppuration, call it what you may, was treated locally and not by drugs given orally or by injection. In the private home the linseed poultice or the bread poultice was still being used. In hospital the same principle was carried out by applying to the affected area a boracic fomentation. Some boracic powder was put in between two layers of lint. This was rolled up and put into a towel and the whole thing then plunged into boiling water. The excess boiling water was removed by twisting the towel round perhaps the taps of the basin. The boracic lint was removed and quickly (but not too quickly) applied to the inflamed very tender area. Oten it was too hot and roasted the patient but more often it was too cold and did not do any good whatsoever. On a chart one often saw the instruction "apply B.F. four hourly." The

letters B.F. do not mean what they do today, although they might be applied to the man who suggested this method of treatment. Success depended on the infection "coming to a head" and then perhaps evacuation and hope for recovery with the appearance of genuine laudable pus. Vaccines, thanks to the pioneer work of Sir Thomas Houston, were coming into use, but vaccines were too slow if we were faced with a rapidly spreading infection. The septic finger which the pathologist might get at a post mortem or a surgeon at a septic operation, almost always spelt death.

Although the modern nurses have not such chores as fomentations they have to be expert plumbers and understand fully the working of the various tubes which now anchor the unfortunate patient to the bed. These tubes lead to bottles and bags that are surreptitiously hidden away. These tubes are draining from some internal organ his intestine or his pleural cavity. We should also mention the various overhead bottles with different fluids of varying colours which are linked up with his veins. If at the same time he is electrically attached to the monitor indeed the nurse has a maze of pipes, tubes and wires to negotiate before she reaches the product that she is in charge of, which incidentally is the patient. If on top of all this the patient is riding high on the waves of an electrically motivated ripple mattress the game can indeed become an exciting one. The nurses all have to live dangerously as well as the patients for the wrong tube in the wrong place or the wrong fluid can do such harm. There is now much more to go wrong. The modern nurse with her pleasant smile deserves not only the affection of the patient but also of the general public and it is pleasing on an occasion of this sort to have the opportunity of saying how much over the years I have appreciated the value of the help and support of the nursing staff.

It is possibly in ancillary departments that one sees the greatest change. The physiotherapy department was at one time in charge of Joey Boyce, a partially blinded soldier of World War I, and incidentally one of the most loyal friends of the hospital. True physical massage was all that he could do. Now whilst there is still massage and some physiotherapy with the actual laying on of hands yet a considerable amount of treatment in that department is done by plugging the patient into the correct electrical machine, and with an electrical time clock the patient can be as expeditiously dealt with as the Sunday joint in the electric oven. The emphasis of this department has somewhat changed. In the old days it was the patient disabled by poliomyelitis or a fracture who formed the bulk of the cases. Today we find the physicians treating various chest conditions, such as bronchiectasis, are using the department more and more. We can see the growing importance of this treatment when we see that in the North of Ireland we have developed such a large and successful training centre at Jordanstown for the physiotherapists.

In my early times at the hospital the entire collection of splints was kept in a small cupboard and used over and over again – a very different state of affairs exists today.

In Robert Campbell's time to be appointed to the visiting staff of a hospital one had to carry out a large canvass. The day-to-day running of the hospital was in the hands of the management committee with two or three representatives of the medical staff, but it was essentially a lay body. In addition there was a large

group of people called "life govenors" who by virtue of the fact that they had given a large donation to the hospital, or perhaps their parents or relations had done so, were given a life interest in the hospital and also had the power to vote on occasions of this sort.

The entire number of people to be interviewed then was about 60. It took 2–3 weeks to see them all. Professor Sinclair, a contemporary of Robrt Campbell, told me he hired a sidecar and called on each one. Most of the people knew nothing of the ability and skill of the applicant as their questions clearly showed. One important voter always looked to see where the testimonials were printed; he was a printer and owner of an important Belfast newspaper and it was well known that it was hopeless to get his vote unless the testimonials had been printed by his firm. One's religion, one's ability in sport, one's school, one's social position I am afraid all carried weight. At the turn of the century this is what prevailed in Belfast. In London 50–100 years before that the appointment would have been made by patrimony. The applicant succeeded if he was the son or the relation of the great man, or possibly the young man could be taken on as an apprentice at a large fee, perhaps as much as £1,000, but such a sum practically guaranteed a staff appointment at the end of his training. The Belfast system was somewhat better than that although we did have one or two cases where the appointment was influenced by patrimony. One of these was Surgeon Kirk – Thomas Sinclair Kirk – his uncle was The Rt. Hon. Thomas Sinclair, a man of great position and public spirit in the town. At the time of my application for a staff appointment the number of people was reduced to thirty, and I still remember visiting these people in large houses, small houses, dusty flour mills, in an office in the shipyard and in a boardroom in a factory. It was an interesting experience for any young man. I remember borrowing my father's motor car to do my necessary canvassing. Today the appointment is still made by a lay committee but with a strong medical representation and often with an outside adviser so that justice is usually done. I hope this method will continue. With the power of the computer we could see that it could ultimately be used for this purpose; we could imagine the facts of life being fed into it; the age, the sex, the degrees, the research work, the number of operations, the gold medals, the visits to America, etc. etc. The final product I am afraid could very well be someone totally unacceptable to man or beast as the one intangible virtue – the love of mankind – cannot be assessed by any machine.

People forget that before 1948 a staff appointment was totally unpaid. One did get a small fee for teaching the students, but nothing from the hospital proper; this fee was not very large when we remember that each student paid a perpetual fee of £21 which lasted them all their life and this allowed them to visit the hospital for the next 40–50 years.

One of the ancillary departments that I should mention is the X-ray department. When Conrad Röntgen in 1895 invented radiography as a medical help it was quickly taken up by most hospitals throughout the world. With the old Belfast hospital in Frederick Street closing down to prepare for the new Royal Victoria Hospital x-rays had at first to be taken in a photographic shop in Belfast – Lizars. This shop was well geared to deal with this problem, as they had in charge an expert in the person of James Carson. Naturally the patient had to go there. Recently I met a man who remembers taking his father there to locate the

mirror of a laryngoscope which had fallen off its holder and had slipped down his throat.

For many years the Children's Hospital was entirely dependent upon the courtesy of the Royal Victoria Hospital for the necessary radiography. One day in the year 1932 a letter was received by the staff of the Children's Hospital asking them to send out a member to the Cavehill Bowling Club who were giving a whist drive that evening; the proceeds of this whist drive were to be given to the Children's Hospital and it was hoped that a member of the staff would come to accept the small cheque. As I was the junior member it was suggested that I should go, which I did. We played whist all evening and finally I was presented with a cheque for £35. In a small speech of thanks I explained that I would like this to be the nucleus for a fund to buy our first x-ray machine. At 8.30 a.m. the next morning I had not yet read my paper when a lady rang up on the telephone. She had seen a small report of this presentation and the donation. She said, "Do not ask my name but stop the fund; I wish to supply the machine myself in memory of my grand-daughter who died recently". I knew the lady well and this secret was kept for many years although it is now public and one can see the name of Mrs. McNeile McCormick on a tablet in the corridor of the hospital outside the x-ray department. This was indeed a small beginning of the magnificent palace that Douglas Boyd has controlled so loyally for so many years.

The old machines were dangerous and this one was no exception. I remember standing beside it while the nurse was holding a child to have a picture taken of a broken limb. The child gave a jump, the nurse's head moved too close to the tube, there was a spark like lightning and the nurse was hurled backwards across the room striking her head on a radiator in the far corner. I picked her up; I thought she was probably dead but she herself came quickly round and thought she had fainted. There was a pinpoint burn on the top of her forehead where the spark had struck her and there was a very large lump on the back of her head where she had come in contact with the radiator. I would say it did her a lot of good as she is now the wife of a well known consultant and has a grown up family, but at the time I picked her up from the floor I saw very little future for the lady in question.

How the hospital carried on for so long without an x-ray plant is hard to understand as with the inarticulate child we are as much dependant on radiology as are the vets for their animals who cannot speak for themselves.

To revert to James Carson, I should say that he carried on a large and very successful domiciliary practice carrying his machine by side car to the patient's home. For this service he charged ten shillings which compares favourably with today's prices, but one must remember that in those days "inflation" was something small boys did to footballs instead of being as it is today a political war cry.

In the early days of radiography an x-ray of the skull took anything up to forty-five minutes, and so it was not unreasonable that the patient complained somewhat when he found himself completely bald after such an exposure. In even simple portrait photography in the Victorian period the exposure was so long that the head had to be held fixed from behind in an invisible vice. It is small wonder that one's ancestors in the family photograph album appear to be a fairly sour bunch of people whom we show off with very little pride to our children.

The out-patient department in Queen Street was the most interesting part of the hospital. It was a sort of annexe built on behind and jutting out from what I suppose had been the kitchen. Leading off it was a small room which was the out-patient operating theatre. There was too much glass so it was too cold in winter and too hot in summer. There was a very special smell in it, a combination of unwashed mother and incontinent child. It met one at the door and it usually went home with one for the rest of the day. A consultant's wife – I can speak for my own – always knew when one had had a session in the out-patient department so many fleas were brought home. There was a very special staffed couch which was said to be the breeding ground! I am afraid it was not unusual to ask a new student to sit down on it for a few minutes until one explained to him the running of the hospital and the facts of life. There was always a small bet as to when he would start to scratch.

Often for the surgical out-patients the surgeon wore an old pair of trousers, in fact golf waterproof trousers would have been the best. One of my colleagues in London who did a large urological clinic claimed with success each year for two extra pairs of trousers from the Inland Revenue. This was very necessary as it was often easier to take the small patient on one's knee to be examined; something that might have been misinterpreted in an adult hospital.

Lice and their junior colleagues the nits were almost universal, and when the child was admitted to the ward the smell of oil of sassafras and a bathing cap told their own story. It is one of the great features of the National Health Service that this particular problem has greatly disappeared. It was a problem during the war when the women in the services tended to exchange hats and a permanent wave prevented the necessary frequent shampoo. I am told that the modern hairdo of our young men has also brought the problem back, but to a minor extent. Having mentioned fleas and lice and got them out of my system I will not mention them again.

Almost half of the women from the poorer areas came in a black shawl and produced from the hidden depths a pale child. At every out-patient session there were 3 to 6 children with tuberculous glands in the neck in the various stages of the disease; discreet hard lumps, a red superficial so called collar stud abscess, or a frank chronic discharging sinus. It is marvellous to think that almost overnight in 1947 with the advent of streptomycin this problem disappeared almost like the button boots. If we do see tuberculous glands in the neck they are often in the elderly and very rare, at least in Britain. Although most surgeons became very skilled in neck dissection one still sees many adults with the tell tale scars in their necks.

Congenital abnormalities were seen at every clinic – the hare lip and cleft palate were all operated upon, mostly much later than now. Now we have the technical skill of the maxillo-facial surgeons, but we must remember that they have also been fortunate in having intratracheal anaesthesia and antibiotics, which were not then available. Many diseases were seen very late, e.g., congenital dislocation of the hip, which is now detected at birth when early treatment should give a perfect result. Most of us have lived through all the changes in the treatment of club foot. I asked my chief once when one should start treatment and he said, "I have never made up my mind whether one should wash the baby first or not" – meaning

at birth. This was right as far as the correct time was concerned but we had not then the proper method. One tried without success to put the foot into plaster-of-Paris but the baby's bone is so small and the fat around it so large that the plaster-of-Paris splint could not hope in any way to affect any change in the shape of bone or joint. The modern operation is one of the greatest advances that I have seen recently.

We saw every week cases of anterior poliomyelitis. These were either in the acute phase, when the child was ill and almost seemed to be suffering from meningitis, or else the child was well but now had a limp and a wasted leg. With difficulty the mother could sometimes, but not always, remember that the child had had a mild illness like influenza which was ignored at the time but afterwards the weakness was discovered. In some of these cases a tendon transplant was possible but for others a splint or a special boot was the best that one could do. This disease, like tuberculosis, disappeared at once with immunisation. Diphtheria, scarlatina, poliomyelitis, are all scourges that many of us have seen disappear, but are all still found widespread in the underdeveloped countries.

With the absence of antibiotics sepsis was a daily problem. Surface dressings of eusol or hydrogen peroxide were very popular. Pneumonia was a very common sequel to measles and with no specific treatment it had to run its course. An empyema was a very frequent sequel, and drainage of the thorax by either aspiration or by a small tube between the ribs or even by the removal of a small piece of rib was done; this operation took place at least once per week. With the arrival of penicillin the operation for empyema almost disappeared completely.

Congenital abnormalities such as spina bifida and hydrocephalus were a serious problem. Attempts were made to deal with these with limited facilities. On the other hand I think they were in proportion fewer perhaps than they are today because then the very deformed child did not have the same efforts made to save it nor were there the same facilities for resuscitation. Many people today will say that this is survival of the unfittest. I am not going to say whether this is a good thing or a bad thing.

The trauma of the road accident has not changed very much. We in hospital have increased our facilities for salvaging the very ill child with blood transfusions and other intensive care but we must remember that as our methods and facilities have improved so has the traumatizing agent. The motor car goes twice as fast as it did and the overall gain is not very noticeable.

Cancer in children would appear to be on the increase but probably this is not so; rather the case is that other causes of death such as infectious diseases are so much reduced that cancer is now more obvious and noticeable. In the hospital today the three main causes of death among children are (1) cancer, (2) extreme congenital abnormalities incompatible with life, (3) injuries involving the main vital organs – brain, heart, lungs or kidneys. In praising the progress made one must always have the courage to look back with embarrassment on the things we did from lack of knowledge. I used regularly to treat the strawberry birth mark with carbon dioxide snow and hand the patient back to a delighted parent; neither the parent or I knew that this birth mark with patience would in most cases disappear on its own.

Before leaving the out-patient department I should say that this was the main

centre for teaching students. The patient would lie stripped naked gurgling with pleasure, in contrast to the same patient twenty years later. One could show the abnormal condition and one had the full co-operation of the mother as she was so pleased that her child was the centre of such interest, and she herself learned a lot which she would not otherwise have heard. I have always thought that the tummy is much better than the blackboard for teaching students. There was no such thing then as an appointment system and if after three hours the surgeon broke off for a cup of well earned coffee he came back with no feeling of shame as he had at least another three hours before him. Many a young doctor will say that the best clinical teaching that he or she ever got was in the outpatient department of a children's hospital. For the young surgeon also the out-patient department was very important since as he was the junior member of the staff he was only allowed at most four in-patient beds under his own care.

Surgical technique was as today only much more primitive. The scalpels were usually blunt; the replaceable blade had not yet been invented. A retired police sergeant called twice per week to take the scissors and scalpels away to be sharpened. Stainless steel was not in use and so instruments had to be oiled to avoid rust; so had the needles. The word expendable had not been invented. Swabs were used over and over again. The marine sponge was still in use. After an ordinary hand scrubbing the hands were soaked in binodide of mercury or perchloride of mercury depending on whether one liked a red or a blue solution. Both I suspect were useless. The gloves had been boiled and were lying in a basin – it was hoped – of cold water, but one did occasionally plunge one's hand into the glove still with some boiling water inside. The reaction and language used varied with each surgeon.

I must not pass over the disadvantages of the boiled glove without saying that we were at least free from the problem of starch peritonitis which has become quite a problem today when the corn starch, which is used to lubricate our present autoclaved gloves, gets into the peritoneal cavity at an operation. One of my colleagues used the same pair of gloves all day and instead of washing his hands he washed the gloves; his results did not seem much different from the others. Occasionally gloves were not worn at all, and during World War II I had the same problem, when suddenly with the fall of Singapore our source of rubber suddenly stopped, and in the army we were told we had to learn again how to operate with bare hands, rubbing a little antiseptic cream into all the cracks in our hands and fingers.

In the operating theatre the source of light was poor and relaxation was almost non-existent as curare had not yet been invented. Rubber, whether it was a drainage tube or a catheter, was of the red rubber variety which caused such tremendous irritation; so different from the latex or the plastic tubes of today which seem to be totally inert. Anaesthesia was a great problem as almost every child had some chest irritation next day with a running nose, sore eyes and cough. This seemed a very unnecessary price to pay. It was at this time that John Boyd, a general practitioner on the Ormeau Road, was appointed as a part-time house surgeon. He became interested in anaesthetics, became skilled at it, and was a most valuable and willing member of the staff. Almost coinciding with his appointment a new drug appeared on the market. It was Avertin. This solution, in a measured quantity

in proportion to the patient's body weight, when suitably diluted was slowly run into the rectum and in a very short time the patient went quietly to sleep. It was the greatest advance then in the field of anaesthesia. It was, however, only meant to be a basal anaesthetic; in other words it was necessary to supplement it by either ether or chloroform. Dr. Boyd stuck rigidly to the dosage but his chief, Mr. Kirk, gradually increased the dosage until Avertin for him became a full anaesthetic requiring no supplement. However, this is not the place nor have I the knowledge to discuss the advances in anaesthesia which today allow the baby of a few hours old to be put to sleep with safety; a paper could be written on this alone.

Although surgery in the operating theatre was being carried on with relative safety and success there still was a demand for operations to be carried out in the patient's home. I did quite a number but nothing like as many as my seniors had done. I remember going to Larne Harbour in the middle of the night to do an intussusception on the kitchen table; as the father could not describe where I could find the house he said he would be in the middle of the road waving a red lantern, which he did. The child was called Fraser Close afterwards, which at least proves that he did survive. I remember well doing an extra-uterine pregnancy in Pomeroy and I will not readily forget carrying two very heavy bags along the shore at Whitehead to do a strangulated hernia in a cottage. The operation was carried out in the downstairs room with a low window and the chickens kept looking in from the window sill and making rather distracting noises. This all now seems so foolish when the job could have been done with so much better care and facilities in hospital, as well as ensuring an adequate follow up. Daily attention was naturally left entirely in the hands of the family doctor. The family doctor varied in his interests in surgery. Some kept safely away as far as possible from the open wound and some nearly fell into it. One of my senior colleagues dealt with this latter variety by having a retractor with a handle about two feet long. At the beginning of the operation the doctor was given the retractor to hold and he was told not to move, and this did ensure that he did not get nearer to the wound than two feet.

As a junior when I went out on such expeditions, which seemed to be nearly always at night, I found I might have many different tasks to do. Firstly I might have to clear the room, perhaps take up the carpet and clear all movable objects outside. At times I might be in charge of sterilization of instruments, running backwards and forwards with saucepans to the stove. On other occasions I gave the anaesthetic if the local doctor wanted to assist, or I assisted if the family doctor was a competent anaesthetist. I also found I was very popular if I offered to drive the rather tired surgeon home as he found he often fell asleep. On going out on one of these expeditions – a sort of safari – one felt almost as important as Kipling's Gunga Din. These incidents full of excitement no longer exist although a country surgeon who died five years ago told me that he had done 50 tracheotomies on the kitchen table over the years. I suppose Buckingham Palace is the only house in which home operating still persists.

Tracheotomy done as an emergency has changed over the years. At one time it was a life saving measure for the child with diphtheria dying of asphyxia and the operation had to be carried out with any tool that was available – a penknife if necessary. Possibly in this school it was used less than in others as Dr. Gardner

Robb, who was in charge of our infectious diseases hospital, was so skilful with the laryngeal tube. He was able to insert this small tube between the vocal cords blindly and unerringly; the tube was left in situ and easily pulled out with the thread attached to it whenever the obstruction seemed to have abated. It was the forerunner of the intra-tracheal tube invented by another Queensman, Sir Ivan Magill of Islandmagee many years later. With the virtual disappearance of diphtheria the emergency tracheotomy disappeared but it has now reappeared in a different guise and by a different name. The tracheostomy of today is almost synonymous with intensive care. It is interesting how the pendulum swings backwards and forwards.

Although the hospital today has many special departments the first and only one for a long time was the Eye and Ear Department Why these two organs were dealt with by the same man I never knew, as the treatment, the anatomy, the examination and the diseases of each have nothing whatever in common. It is true that territorially they lie close to each other but it would just be as sensible for the gynaecologist to do orthopaedics because the uterus happens to lie hidden in the bony pelvis.

The common surgical operation on the throat was of course the removal of the tonsils, and, if time and the anaesthetic permitted, then there was also a quick scrape to the adenoids. This all had to be a rapid procedure for as yet the throat could not be blocked off and blood could easily get down the open windpipe into the lungs. To ensure that the patient coughed and to avoid the danger of asphyxia in some cases the tonsils were dragged out with the patient sitting up on a chair fully conscious. It was always hoped that the quickness of the hand would deceive the eye. When the operation was carried out under an anaesthetic the tonsils were removed with blunt guillotine. With this the tonsil was pulled out from its bed, whereas if the blade of the guillotine was sharp and the tonsil was only sliced in two with a part left behind and also the operation seemed to be attended with much more bleeding. On many occasions after a tonsil session I have seen one dozen or more children laid along the floor of the out-patient department. The floor had been covered liberally with copies of the Belfast Evening Telegraph – this is not an advertisement – and as soon as the doctor and matron thought they were ready they were moved by their mother, put under a black shawl and taken off home to bed – a contrast to the same operation today when the tonsil is dissected out with meticulous care and the patient remains in hospital for a few days.

With chronic ear suppuration so common and uncontrolled its extension to the mastoid was almost inevitable. At one time the mastoid operation was almost a weekly procedure but this has almost disappeared with antibiotics, as did empyema in the chest We are inclined to forget that all modern throat surgery has been made possible by the originality of Ivan Magill who was the first man to join directly the gas bag to the patient's windpipe and by so doing avoided anything being sucked into the lungs.

The director at that time of the E.N.T. department was Mr. Wyclif Macready, who built up an enormous department. It was quite an experience to see this large man, his sleeves rolled up above his elbow, working with such dexterity with his bare hands. One was always impressed with the tattoo on his left forearm of the

regimental crest of the Royal Irish Rifles in which he had served as a medical officer in World War I.

As you will have gathered by now, part of our problem was that we had not the modern tools or drugs, but we also had not the money. This was a voluntary hospital dependant on voluntary subscriptions. A particular collection day called Alexandra Day, when the Alexandra rose was sold as a buttonhole, like Poppy Day, was a valuable source of income. There were many small whist drives, dances, coffee parties, church functions and small subscriptions from schools, and also door to door collections. In those days a solicitor making up a will might suggest to his client that he might like to leave a few thousand pounds to help the hospital and this was regularly done. I am afraid it was called by some cynics a sort of "fire insurance", presumably thinking of the other world. Quite large sums from this source came in regularly and the hospital was able, just, to live inside its income. Certain big industries like the shipyards arranged for something like one penny per week to be deducted at source from the pay packets of the workmen. The very active ladies' committee was responsible for much of this and one could not praise too much their efforts which went on year in and year out. The ladies' committee not only did a magnificent job in getting the money but they often kept a watchful eye on the spending of it. They were able to say what the money was being spent on and were always willing, if convinced that something was needed, to make a special effort to raise the necessary funds. Much of their work was involved in organising play groups for the children, decorating the hospital and organising the Christmas festivities. Economy was the main order of the day. This was seen by the visiting staff who, although not paid for their services, would bring their own instruments when these were required for a special case. I always brought my own cystoscopes and the replacement of the bulbs was indeed a costly affair. Today with the hospital better equipped than the surgeon, it is the surgeons who borrow from the hospital.

In 1948 when the hospital became state owned this all changed overnight. Voluntary help was no longer needed – flag days ceased, solicitors diverted their clients' money to other charities. The university benefited by some of this money. The cold shouldering of the ladies' committee was a very unfortunate affair as many willing ladies, young and old, tended to lose interest. I feel that the voluntary help should still be maintained although most of the income must naturally come from the State and certainly we must be realistic and understand that with the expense of modern treatment and modern equipment voluntary subscriptions could no longer cover the cost.

To be the junior member of the staff, with no registrar and a non-resident house surgeon who was only present during the day, meant that one had to carry the major part of the emergency care of the patients often during the day and always at night. For many this was a stepping stone for an appointment to the adult hospital when a vacancy arose. It did mean that many men after some years resigned from their children's appointment when the pressure of work on the major hospital got very great. I often felt that this was not very fair to the young child. It meant that some of the most intricate operations in surgery were performed by a young man and often with a rather second rate anaesthetic. Some of us with our love of children's surgery kept our appointment until we reached retiring age

but most people retired after some years. It was clear that someone who would devote his life exclusively to the surgery of childhood and not be involved with adult patients was necessary. We are now most fortunate in that we have two such men in Belfast at the moment. The speciality of paediatric surgery has been slow to be accepted in certain towns in Britain and it is only in the past twenty years that a genuine acceptance of it has taken place.

Time would not allow me to speak of all my colleagues on the staff. This is unfortunate as without exception they were the most devoted team with which I have ever worked. A friend of mine speaking once of a different organisation said that some of the members were more "flowerful than fruitful" – this could be said of no one on the staff of the Children's Hospital.

The two senior surgeons when I was a junior were of such personality and of such contrast that they deserve a special mention. The senior was Thomas Sinclair Kirk whom I have mentioned before. His social background certainly helped in his original appointment both at the Royal Victoria as well as to Queen Street. He was a man full of original ideas but not very willing to see or accept alternative views or suggestions. It is said he once wrote an article to the British Medical Journal which was not accepted so he resigned from the British Medical Association and never read the British Medical Journal again. This may be an exaggeration. He went up for the primary F.R.C.S.; he failed, and he refused to try again. His major degree throughout his surgical career was his M.B. He was the last to call himself Surgeon – Surgeon Kirk; the others were slowly calling themselves Mr., either because they were descended from the barbers who were Mr.'s and not Dr.'s, or possibly because the higher degree of surgery was Master of Surgery as compared with Doctor of Medicine.

To work with, or should I say for, Mr. Kirk was not easy. He had many original ideas. He repaired all hernias with Japanese silkworm gut sutures which, being unabsorbable, I felt went against all the canons of surgery. Many years later I must admit I was burying nylon, equally non absorbable, for the same purpose. Mr. Kirk felt that to sew neatly edge to edge any wound was all wrong; all wounds must be allowed to drain externally and so a few sitches in the abdominal wall and skin was all that was allowed and no linear scar or healing by first intention ever took place. Every wound he felt was likely to be infected from the patient and not the surgeon or from the exterior, and so every wound was filled with at least one tablespoonful of urea crystals. These came in large glass bottles each about the size of a honey jar. Urea looked like sugar crystals and it dissolved at once and produced a profuse clear fluid which drained out of the wound. It certainly did no harm. I saw it used many years later myself in the war and we found it most valuable when it was put into the external ear for chronic infections which were so prevalent with the troops in the Middle East. I remember on one occasion seeing Mr. Kirk putting several ounces of urea crystals in a large cavity left after the removal of a breast. A few months later there were masses of lumps along the scar. These were thought to be recurrences; one or two were removed and they proved to contain bits of glass. It turned out that one bottle had been broken in transit and sister had scooped up the loose urea plus broken glass into another bottle. It was a great relief to the patient and to the students as the case had been

demonstrated to them with confidence as one of the earliest cancer recurrences that the surgeon had seen.

Mr. Kirk had a theory that if a drainage tube was put in the abdomen it was difficult for fluid to drain uphill and so he directed that the patients who were being drained should lie on their face. This they duly did when he was doing his ward round, but they quickly turned on to their back when his car was safely out of sight. I did suggest once to him that drainage was not an inert process like water running out of a handbasin but that the elastic musculature of the abdominal wall had some part to play in it. I even suggested that it made no difference whether one pricked a rubber balloon at the top or at the bottom as it seemed to go down equally quickly either way. My suggestion, like many others I had made, was received with stony silence.

Oxygen from large cylinders was given to many patients, and was more often needed then than now following the many chest troubles produced by ether and chloroform. Mr. Kirk had an idea that oxygen by the mouth did not get quickly enough to the bloodstream and so he gave his patients subcutaneous oxygen. A needle was pushed through the skin and a large bulge like a camel's hump appeared. This process was repeated when the swelling subsided. I saw no cases of air embolism and have no idea whether this method did any good. I certainly did not see it do any harm. With no antibiotics available the patient was entirely dependent on his own resistance. Mr. Kirk felt that this could be boosted by taking serum; this he got from the abattoir. The blood had to be taken from an old animal; "old" was always stressed as the animal had lived a long time and so must have had or at least built up a strong resistance. Having discarded the red cells the plasma was preserved and the unfortunate patient had now to drink this unpleasant fluid, which if it tasted anything like what it smelt like, must have been fairly unpleasant. Later, as it was difficult to keep this liquid protein for any length of time, he got it dried and from this he made compressed tablets. These were large flat brown tablets about the size of one's thumb nail and these were handed out to all surgical patients each day. Being good protein these were dealt with by the gastric juices and were a good supplement to the diet although I am sure few people thought they had any specific protective power. For a time he changed from old cow serum to old horse serum.

He was interested in amputations and he spent a long time trying to devise a working artificial arm and hand. He got for his assistance a Mr. Pringle, a mechanical engineer from Mackie's engineering works. Mr. Kirk made a series of dissectons of the palm of the hand and Mr. Pringle tried to reproduce the necessary tendons with springs and wires. The limb they invented was called the "P.K." arm. They had a showroom just opposite the Ulster Hall – I think this building is now a motor showroom. Mr. Kirk had a very specially trained amputee who was almost a sort of acrobat, who was able to demonstrate this hand. This man could light a cigarette and saw a log of timber and lift a heavy weight, but the arm never succeeded with other people. One of its failures was its weight; all the machinery was in the hand and there was no counterpoise at the elbow. Although Mr. Kirk made several trips to London to convince the Ministry of Pensions of its value it was never accepted. The firm finally closed down and I am afraid Mr. Kirk, who had invested a lot of his own money in it, must have lost heavily.

He was very opposed to emergency surgery and many a young man has gone back to bed very unhappy when, after he had rung Mr. Kirk to say that a patient with perhaps a perforated duodenal ulcer or an acute appendix or a strangulated hernia was in, he had been told, "You will give him an enema and I will see him in the morning." He preferred a short sleeved gown; he varied in his use of gloves, sometimes wearing none at all; sometimes the same pair of gloves would be worn all day, just being washed between cases. He always operated on a very uncomfortable table which had been donated to the Royal Victoria Hospital in 1903. It was said to have been the actual table on which King Edward VII was operated on by Sir Frederick Treves for his appendix abscess, which it will be remembered delayed his coronation for some time. This table is still on view in the Department of Surgery at the Royal Victoria Hospital. He rarely used cap or mask. It was stimulating to work with someone whose ideas were out of his own head and although one could often, and did often, disagree, yet one was always made to think and at least be able to argue.

The other senior surgeon was Andrew Fullerton. He was a complete contrast. The son of a Methodist minister, he had little money and had to graduate through general practice to the consultant status. A keen student, a great reader of all branches of surgery, a pioneer, and a man who although apparently snappy and impatient with people yet could be endlessly patient with a sick patient or a problem. As a pioneer in the use of the cystoscope he used to practise how to use it for hours on end. He got a child's rubber ball, one about the size of a small melon, and made a hole to allow the cystoscope to enter. He would then light up the interior of the ball and then from without push in a pin at different places until he became completely adept at touching this pin with the stilette of the ureteric catheter. Progress in his profession was slow as there was considerable opposition at that time, but his chance came in 1914 when the War Office asked the various Royal Colleges of Surgeons in Britain to nominate a consultant surgeon. The Irish College suggested Andy Fullerton and he went off as Colonel A.M.S. and gained a reputation in France. He made many permanent contacts with the American and French surgeons as well as his English colleagues, and I remember great men like Hugh Hampton Young of Baltimore, Percy Sergeant, Arbuthnot-Lane, Tudor Edwards and many others coming to the Belfast School out of friendship for Fullerton.

Although always interested in general surgery, he made urology his speciality. He was the obvious choice for the Chair of Surgery in Belfast when it became vacant in 1922. He modelled himself on Robert Campbell and did an immense amount of surgery in the out-patient department. He brought to hospital each day his hospital notes, a collection of several boxes of cystoscopes, a few books that might illustrate the case that he was going to operate upon, and if the case needed diathermy he brought from home his portable diathermy apparatus. This large very awkward box which seemed to weigh as much as half a bag of potatoes and was just about as convenient to carry, seemed to travel backwards and forwards from hospital to his home. One of the more cynical assistants said that instead of calling it portable it should be called "shiftable". If there was a trolley it could be wheeled in from his car, but this was not always available. He had a large Morris car which he always told me he had bought out of his war gratuity. I lived through

the last war in the hope of something similar happening to myself, but I am still hoping. Back from the war he also brought Mr. Leman who became the inspiration of the x-ray department and also Miss Mussen, R.R.C., whom he had met in France. She became Matron to the Royal Victoria Hospital and was the pioneer of the modern technique of nurse training in that hospital.

I am pleased to have a public occasion in which to say how much I personally owe to his kindness to me. He died at 3 a.m., and at 8.30 a.m. the same morning Neill, his chauffeur, called at my house whilst I was still at breakfast. He had in his arms some half dozen cystoscopes, some books, and draped over all was his Irish Fellowship gown. Neill told me that Mr. Fullerton had died some hours earlier and his last wish was that these gifts should be delivered at once. This gown I have worn for many years with great pride and finally passed it on to my son some two years ago. After leaving me Neill was going to visit Mr. Purce, Mr. Irwin (Sir Samuel) and some others, all of these being given some token of remembrance.

The two other surgeons in the hospital at that time were Mr. P. T. Crymble and Mr. H. P. Hall. Mr. Crymble succeeded Professor Fullerton to the Chair of Surgery. P.T. was a man of originality and many parts; trained as an anatomist, later in radiology, and finally a surgeon. He had an interest in unusual cars, was a golfer of note, a lover of music, and his speeches were always full of dry humour. Just as he liked his various golf clubs he also liked the unusual and original surgical instruments. He was one of those to pioneer thyroid surgery. In the theatre to keep the students from breathing down the back of his neck he erected a circular barrier of chains and bollards and so seemed to be working inside a sort of play pen. The chains were not too high to prevent the nurses, with the grace of Mary Peters, skipping elegantly over them when necessary and getting into the arena.

The other surgeon was Harry Hall, one of the kindest and most gentle of men, a great friend and one always helpful to his younger colleagues. In the City Hospital, at Queen Street, and at the Craigavon Hospital he did a vast amount of careful surgery, and was a pioneer of orthopaedic surgery before this was a recognised speciality. At his home there was always a welcome for a young man wanting help and advice. I for one appreciated his friendship.

There is no time to deal with the individual physicians. One of these always wrote his notes in shorthand so that a colleague could not read them, but the colleague took a course in shorthand and became more proficient than his friend.

Dr. John McCaw had been a pioneer in the medical diseases of children and his son Ivan McCaw had planned for a surgical career, but a war wound in World War I in the brachial plexus put ideas of surgery to an end. What surgery lost dermatology gained and in Ivan McCaw, one of the most popular members of the staff, this branch of medicine was put on a scientific basis for the first time in Belfast.

Dr. F. M. B. Allen, following in the steps of Dr. McCaw and Dr. Malcom Brice Smyth, devoted his entire life to children's diseases, and when the Nuffield Chair of Child Health was founded Allen was elected as the first professor. He held this chair until he retired; he brought credit to himself and to the province. He built up a great reputation in paediatrics and from his department children's physicians

have been trained and are now scattered far and wide both in the old world and in the new.

Progress I have always found fascinating because as we advance we also discard the useless. I have often found the discarded just as interesting and possibly more instructive than the advances and they are certainly more humbling.

Time unfortunately does not allow me to describe the various surgical operations which over the years I have seen thrown on the scrap heap. I got my hospital appointment just at the time that total colectomy, as advocated by Arbuthnot-Lane for chronic constipation as well as many other ills not even excluding brain tumour, had been discarded by most surgeons although Lane himself was still a strong advocate in its favour. His operation of total removal of the large bowel might now in biblical terms be referred to as the stone which the builders rejected but which since has become the chief corner stone, for indeed in the modern treatment of acute ulcerative colitis it is the keystone of success. Surgery, like ladies' dresses, has popular fashions. In surgery there is often a pseudo-scientific reason given which the ladies in their honesty do not claim.

There was a phase when, if an x-ray showed that an organ was lying perhaps too low or out of position, it was thought it should be hitched up and put where the surgeon insisted, although the patient and his or her Maker may have thought differently. This was the so called "pexy" period. Mr. Fullerton was doing a nephropexy on any low lying kidney and hanging this unfortunate organ to the 12th rib or indeed any other suitable support. Mr. Kirk was doing a caecopexy and fixing this unsuspecting organ, that wanted to be mobile, into the right iliac fossa with many stitches. Fortunately the stitches in a short time disappeared and the organ in the parlance of the farmyard soon became "free range" again. Surgery was then based more on anatomical accuracy rather than on physiological comfort and function.

I myself was much involved with the sympathectomy period. This attractive anatomical exercise was then in vogue for many diseases, e.g., hydronephrosis (Papin and Ambard), gastric ulcer (Wilson-Hay), high blood pressure, the blue hand, the cold foot, spastic diplegia of the infant (Royale), Hirschprung's disease, dysmenorrhoea, to mention only a few. I did the operation on many occasions for all of these conditions and yet today sympathectomy is recognised as the treatment for only two of these diseases. It has been discarded a long time ago for all the others.

Today we are living in the cortisone era. A drug which seems to be looked on as almost a panacea for all ills, or is it the last resort? When this lecture will be given in some years from now cortisone in its present form will certainly be a discard.

We must remember that it was as long ago as 1820 that Napoleon Bonaparte said, "I do not want two diseases – one nature made and one doctor made." As a student when learning my drugs we always used to say, "Give Pot Iod and trust to God". Today our irreverent students are possibly saying "Cortisone can cure all diseases, from wheezy chests to arthritic kneeses."

The various operations for tuberculosis – thoracoplasties, phrenic nerve crush, partial lung removal – almost all disappeared when a medical cure appeared in 1947. This resulted in the emptying of the sanatoria, not to mention unemployment among the chest surgeons.

Mr. Kirk was fond of breaking the legs and re-aligning them for cases of bow legs and knock knees due to rickets – an operation now seldom done. The operation was suggested by Sir William McEwan in Glasgow where rickets being prevalent produced the disease and where the kilt being prevalent exposed the deformity. It is fortunate that the mini skirt is an invention of the post rachitic era.

When we look back on the operations that we no longer do we realise that we were then prisoners of our time. I suppose many ladies looking at their dresses of twenty years ago will say the same. Although I may have included many things in my discards this does not mean that the orator giving this lecture fifty years from now will not have reinstated some of them.

It was Robert Louis Stevenson who in another context once said, "To travel hopefully is a better thing than to arrive." This is very true for those of us who have been privileged to travel along the road of surgical progress. It is fortunate that as far as surgery is concerned there is no finality – each step is nearer the goal of perfection which one never reaches. If we did I suppose we would be like Alexander the Great who is said to have wept because he had "no more worlds to conquer." To complete Stevenson's sentence, "The true success is to labour."

In reviewing the progress of this hospital in the thirty-nine years that I have had the honour and pleasure of being on the consulting staff I find that the changes and advances have slipped in so easily and silently that they almost passed unnoticed, and it is only when asked to write a paper of this sort in my retirement from active work in the hospital that I can stand back at a distance and see and record the progress that has been made.

Of my time on the staff of the hospital I would like to say that in the first half I learned a great deal from my seniors and in the second half I learned even more from my juniors. I suppose for a short time in between – a very short time – I could say I was my own master.

To see a shabby building in Queen Street, now a police station, replaced by the present Royal Belfast Hospital for Sick Children which is part of one of the best teaching complexes in Britain, was one of our first and major advances. General surgery in a children's hospital is now almost a misnomer as it has become so fragmented – each portion is carried out by so many specialists, each a master in his own field, and even the anaesthetists now restrict themselves to the care of children only. The new grouping of diseases into small societies following the American plan seems to increase each year: we have the Cystic Fibrosis Society, the Spina Bifida Society, the Ileostomy Society, etc. Probably the medical profession gains something from it, but if the patient is able to make a social occasion out of his disease it is certainly worth while.

In thanking again the trustees of the Robert Campbell Oration for entrusting me with this lecture, I would like to stress how fortunate we were in Belfast that when the transition from the old to the modern surgical techniques took place we had in Ulster a man of the mental calibre of Robert Campbell who was available not only to lead this revolution but had the personality to carry his colleagues with him. The time was right and the right man was there to match it.

It was Winston Churchill who said once speaking of a close friend, "He banks his treasure in the heart of his friends." Fifty years after Robert Campbell's death we his successors are able to say the same of him.

SUDDEN UNEXPECTED DEATH IN INFANTS
Evidence on a Lethal Cardiac Arrhythmia

by

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THE incidence of sudden unexpected death of infants ('cot death' – 'crib death' in USA – 'sudden unexpected and unexplained death in infants', 'sudden infant death syndrome'), termed below cot death, is 2.0 – 3.0 per 1,000 live births in 'developed' countries of Europe and North America[1], less than 1.0 in Israel[2], while no data are available for underdeveloped countries. In Northern Ireland the 'corrected' figure is 2.8 and represents 10 per cent of total infant, and 33 per cent of postneonatal, mortality[4]. The condition is considered sufficiently homogeneous to constitute a distinctive syndrome and most cases are thought to have an identical —though unidentified—'final common pathway' of death[5, 6]. Despite intensive research the cause (or causes) is unknown; but the consensus holds that victims, mostly healthy throughout life, die because while passing through a period of enhanced physiological vulnerability some critical combination of intrinsic and extrinsic factors proves 'suddenly' and 'unexpectedly' fatal yet produces at autopsy no identifiable abnormality acceptable as being a 'cause' of death. Though certain 'risk factors' have been identified[5—9] it is not known through what 'final common pathway' (or 'pathways') death occurs. Of the many theories adduced that which now commands the widest support and which the data are alleged to favour is that these infants die a *respiratory* death—in the sense that death is mediated through a respiratory (rather than a cardiac) primary mechanism—due possibly to asphyxia secondary to laryngospasm, to apnoea with or without laryngospasm and mediated through some aberrant or immature reflex possibly impeding recovery from 'normal' sleep apnoea, or to respiratory failure as part of an immunological collapse or hypersensitivity on challenge with an appropriate antigen presumed to be a virus.

These explanations are reached mainly by inductive inference: lethal laryngospasm has not been demonstrated; aberrant or immature reflexes have been indicted[10] but their role (if any) in cot death is unknown; no basis for an immunological mechanism has been established. Where deductions as to respiratory death are made either from animal models[11] or from study of selected infants ultimately

being cot deaths[12] the data do not exclude other interpretations. In this article we examine another hypothesis seemingly consonant with the facts—namely, that these infants (or at least a significant number of them) die not a respiratory but a *cardiac* death—in the sense that death is due to a lethal arrhythmia produced by failure or disturbance in the normal electrical activity of the heart. This hypothesis was little considered until 1968[13] and receives only modest attention now despite its plausibility in any form of sudden, unexpected, and 'unexplained' death.

This hypothesis will be examined below as a general theory of causation. Infants sometimes die from documented cardiac arrhythmias and at conventional autopsy no anatomical explanation is found, e.g. the QT interval prolongation syndromes either with[14, 15] or without[16, 17] deafness, but we will not suggest that these or other conditions with *documented* electrical instability of the heart play a major role in cot death though we will draw inferences from them in developing the argument.

Many of the data below are from our own studies, some from other surveys. It is unnecessary to describe these here; full details appear in works as referenced.

Salient Clinical and Epidemiological Facts

We first establish that this cardiac hypothesis is consonant with the data. Salient facts, the consensus of recent work[4, 5, 8, 9, 18], are as follows and as summarised in Table I: (i) death is sudden and silent; (ii) routine autopsy fails to identify a lethal mechanism; (iii) there is no important heritability; (iv) throughout life victims appear healthy and thrive normally; (v) there is enhanced risk in boys, low birth-weight infants, dwellers in poorer urban areas, and winter months—though there is no time/space epidemicity[9]; (vi) upper respiratory, febrile, or coryzal symptoms, usually mild, are frequent (50 per cent of cases) during the week, especially the 48 hours, pre-mortem; (vii) being asleep at the onset of the fatal episode is a presumptive finding in most cases; and (viii) there is a characteristic age distribution with 90 per cent of cases 1 – 6 months and a peak incidence at 2 – 4 months.

Table I

Sudden (Unexpected) Death in Infants—Salient Facts

1. Sudden and silent death
2. Routine necropsy normal
3. No important heritability
4. Infants thrive normally
5. Increased risk in boys, low birth-weight infants, colder months, poorer urban areas
6. Mild systemic or febrile symptoms in 50% cases during 48 hours pre-mortem
7. Sleep
8. Characteristic age distribution

Factors in (i) – (iv) are clearly compatible with a cardiac hypothesis in an otherwise healthy heart, though (iii) will be discussed later. Factors in (v) are general to infant deaths though there is a possible role for cold environment on the hypothesis. Factors in (vi) are, with the seasonal variation, commonly adduced as evidence of a key role for infection in the chain of events leading to cot death and therefore (illogically) as evidence that death itself is ascribable to an infective process. These, together with factors (vii) and (viii), which are crucial findings in cot death (the 'eligibility factors' of Beckwith[6]) are not uniquely explicable on any theory and are discussed later.

The cardiac hypothesis is thus clearly not discredited by the major facts, a prima facie case has been established, and we can now legitimately proceed to consider the theory in detail (including discussion of factors in (v) – (viii) above) recognising that logical inference will only allow one to accept or discard the hypothesis—more strictly to discard a null hypothesis—with a particular degree of certainty and that this is independent of the outcome of testing any other theory.

Examination of the Hypothesis

It is axiomatic that the postulated electrical instability of the heart must be capable of being lethal. Cot death cases however present unique difficulties since there cannot be any *direct* evidence for a terminal arrhythmia: sudden and unexpected death by definition precludes terminal examination. Nor do we know the normal ECG status of these infants: being mostly healthy from birth there is rarely call for medical investigation; and since there is no marked family aggregation of cases[6, 9] there is no demand for family screening to establish any 'at risk' status of members. To examine the hypothesis we must reason inductively—as have those who have examined other theories—and this requires consideration of all relevant data.

Hypothesised nature of the cardiac problem

We first consider possible mechanisms by which a lethal arrhythmia might arise in cot death infants recognising their essentially non-familial distribution, the negative clinical and (routine) autopsy findings, and the thorough neonatal examination and surveillance of most infants (e.g. all the 162 in our series[4, 8, 9] in which 90 per cent were hospital births) which fail to disclose any significant anomalies. We may therefore exclude for the generality: (i) overt heart blocks with or without structural heart defects; (ii) most of the (rare) familial cardiac arrhythmias or conduction abnormalities and (iii) such overt vascular, infective, or myopathic processes, or drug ingestion, which could affect cardiac rhythm lethally. Included *ad interim* is any condition truly or seemingly symptom-free and with clinically and histologically normal cardiovascular system but with a conduction system prone to produce potentially lethal arrhythmias through some mechanism—possibly neural aberration or metabolic disturbance at a cellular level—unidentifiable at autopsy.

Apart from occasional sporadic (e.g. James *et al*[19]) and familial (e.g. Green *et al*[20]) cases of sudden death in healthy young people with or without explanatory histo-pathological changes (demonstrable on special examination of the conduction system as the sole discernible anomaly[21]) QT interval prolongation syndromes are

acceptable for inclusion. These conditions viz. the cardio-auditory[14, 15] and Romano-Ward syndromes[16, 17], are characterised by repeated syncope often in infancy and frequently fatal and due to ventricular arrhythmias—usually ventricular fibrillation though rarely asystole[22, 23]—arising from an innate cardiac electrical instability of uncertain aetiology but involving conspicuously abnormal myocardial repolarisation (Fig. 1) with sinus bradycardia as a frequent salient feature. Their immediate relevance is that the patient until the first syncope appears healthy (he may be deaf but this is unascertainable in an infant) and careful routine autopsy fails to uncover any significant lesion: in fact, the syndromes manifest several documented electrophysiological mechanisms which can produce a sudden cardiac death in infancy and are not immediately incompatible clinically and pathologically with cot death. We must therefore consider whether this mechanism either as part of, or independent of, these syndromes could provide an acceptable model and be consistent with cot death data.

Basis for an aberrant repolarisation model

Given the facts of cot death and postulating aberrant ventricular repolarisation expressed through a prolonged QT interval as the model, we can theorise three main mechanisms of its genesis: (i) inheritance as a Mendelian autosomal trait—as in the QT prolongation syndromes[24, 25]; (ii) arising as an autosomal mutant characteristic (subsequently following Mendelian law); or (iii) origin as an extreme quantitative value of the normally occurring continuous range of QT intervals.

Under (i) above, inheritance may be (in conventional terms) either 'dominant' or 'recessive', the characteristics of which are well-known. Briefly, 'dominant' law requires (a) one or other parent affected, (b) in complete ascertainments about one half of sibs of propositi affected or an equivalent foetal loss, and (c) many other cases among the affected parent's kin. None of these obtain. No parent in our series of 148 (visited) families had a history of pertinent syncopal attacks and the ECGs (238 of a possible 296 were taken) showed neither significant arrhythmias nor an enhanced number with a prolonged QT interval as compared to random (normal) expectation (8 as against an expected of 6.5 at $t=2.0$); and, while ECG tracings on sibs are not uniformly available, sibship aggregation of cot death or of pertinent symptoms, fraternity foetal loss, and suspicious symptomatology in more distant kin, are minimal[9]. 'Recessive' law on the other hand requires (a) increased parental consanguinity, and (b) as (b) above substituting one-quarter for one-half. Again neither of these obtain: (b) is already considered; while under (a) no parents professed kinship whereas random expectation in Northern Ireland for third cousin and closer consanguinity is 2 per cent to 3 per cent[25]. Furthermore, taking cot death as a single and exclusive 'recessive' genotype with population incidence of 3 per 1,000, then on Hardy-Weinberg (with $q^2=3/1000$) and Lenz-Dahlberg (putting $\alpha=1\%$) assumptions first cousin parent marriage should be some 1.4 per cent and total ascertainable cousin marriage perhaps some 3 per cent; and these estimates would increase with the number of postulated genotypes. There is, therefore, no supportive evidence for a Mendelian hypothesis on the pooled sibship data either for cot death or the generating model, though this does not exclude Mendelian segregation in some families or polygenic or other mechanisms.

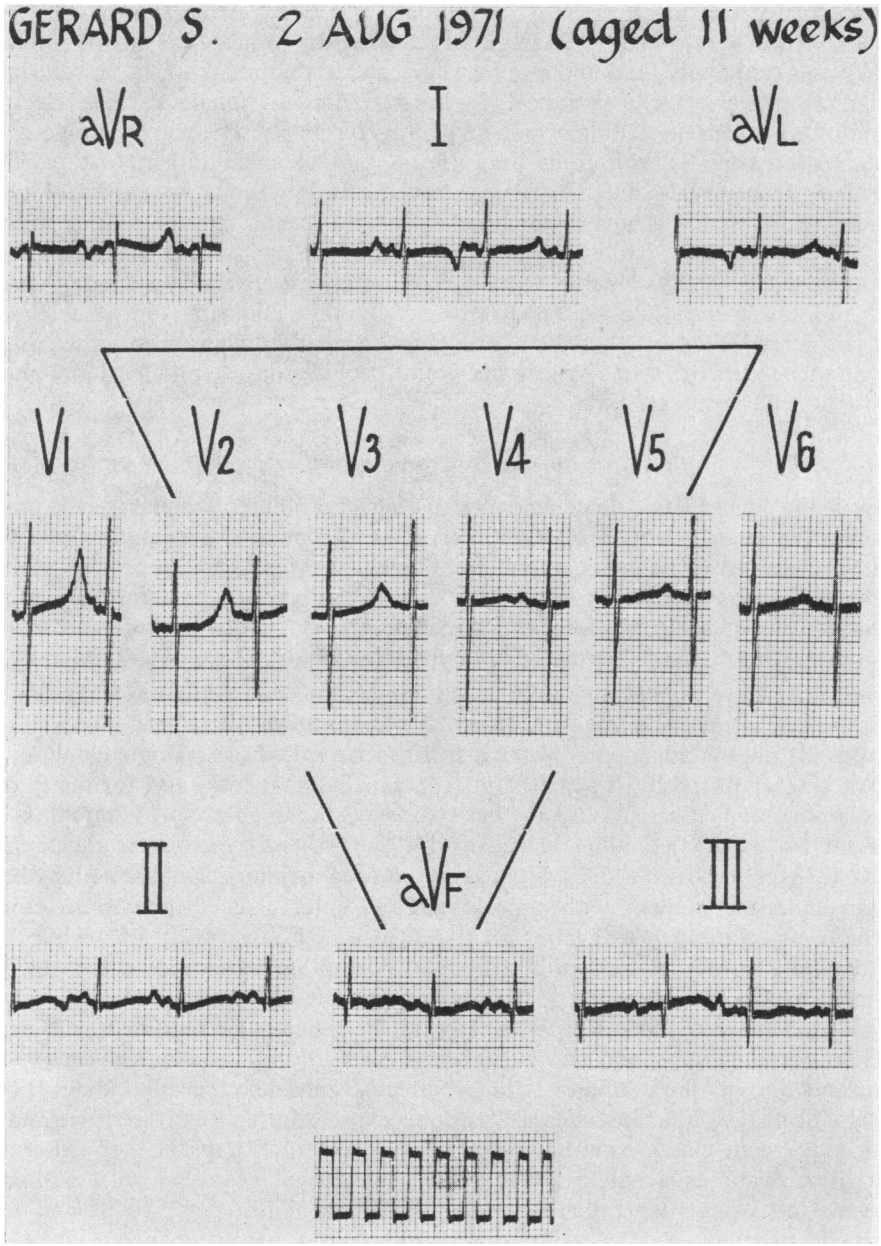

FIG. 1. *Electrocardiogram of an* 11*-week-old boy with unequivocal cardio-auditory syndrome showing prolonged QT interval and TU wave changes. These also occur in the Romano-Ward syndrome and they characterise the two conditions. (Each small square represents* 0.04 *secs.)*

Concerning (ii) above, heritability would not be expected since the genotype does not reproduce. Mutations in both the QT prolongation syndromes probably occur—difficult to demonstrate in the 'recessive' cardio-auditory syndrome but possible in single-case ('dominant') Romano-Ward families (e.g. that of Karhunen *et al*[26]) and probable in the family of Sandra C[27]—a victim of unequivocal Romano-Ward syndrome—where ECG examination of 109 blood relatives and 233 of their spouses and in-laws covering all age groups showed no significant differences especially relevant to QT interval. But if we postulated 'dominant' gene mutation as the exclusive 'cause' of cot death we would have to accept a mutation rate equal to the population incidence since there is complete selection against the genotype, i.e. a rate many hundreds of times greater than any yet postulated for man—an unrealistic assumption.

The third possibility ((iii) above) can be stated as follows. Under (i) and (ii) QT prolongation has been considered as a qualitative change in that, irrespective of degree, it is abnormal and potentially lethal as judged by the resultant clinical stigmata (syncope, ventricular arrhythmias, sudden death) characterising the syndromes. But in the interpretation under (iii) above we are judging whether a QT interval prolongation, which might arise occasionally on population sampling as an extreme value on a continuous scale of QT_c* measurements, could *per se* be potentially lethal. This is now discussed.

Consideration of minimal 'quantitative' QT lengthening in sudden death

We have shown[24] that the QT_c interval among healthy school-children is normally distributed. (This is after the cot death age range when victims have already died: however, there is no detailed information on the form of the distribution in infants —in fact the QT interval in the neonate is very labile[28]—and for the present argument we will accept that the neonatal QT interval is also normally distributed). We would expect therefore about 0.5 per cent of infants to have 'long' QT_c intervals (at $t=2.58$, $P=0.01$)—which is, incidentally, the approximate cot death population incidence. Most will be only slightly prolonged: but even slight statistical prolongation could be *biologically* important—in the two QT prolongation syndromes though there is usually a correlation between degree of QT prolongation and severity of clinical expression especially age of onset[15] nevertheless Tables II and III, compiled from the literature, show that minor or even nil QT prolongation can be associated with lethal arrhythmias in the presumed absence of other heart disease.

Accepting then the credibility of this genesis of the model we would expect three corollaries. *First*, that the QT_c distribution among children over one year would be truncated at its upper bound due to previous removal (by cot death) of infants with the longer QT intervals. Such demonstration would require measurements on very large samples: on our smaller series (random sample of 369 from 82,000

* This is the length of the QT (QT_o) interval corrected for heart rate using one of the many available regression formulae. In random population samples QT_o—QT_c (=QT_d) will be normally distributed so that statistics based on normal theory are appropriate[24].

TABLE II

Romano-Ward Syndrome (QT prolongation without deafness)

*Cases from the Literature distributed by Degree of QT Prolongation**

$\frac{QT_o - QT_c}{SE(QT_c)}$**	*Number of cases (N=62)*	
	with syncope ± VF and/or sudden death	*without symptoms*
0–2.6	16	–
2.6–	16	5
4.6–	11	5
6.6–	4	–
8.6–	1	–
10.6–	3	–
12.6–13.6	1	–

*Compiled from cases with adequate data in 18 families. Facts supplied on request to one of us (P.F.)

**$QT_o - QT_c / SE(QT_c)$ is distributed as t (see text). 99% limits are −2.6 to +2.6: thus 16(25%) – with values $<$ + 2.6 – had "normal" QT_c intervals but had syncopal attacks with or without VF and/or sudden death.

TABLE III

Cardio-Auditory Syndrome

Uniquivocal Cases with Minimal QT Lengthening

Source	*Statistic**	*Syncope*	*Affected Sib*	*Sudden Death (and age)*
Jervell and Lange-Nielsen[14]	4.0	+	Yes	Yes (4)
Fraser, Froggatt and James[15]	3.1	+	Yes	No (20)
Lamy et al[29]	2.4	+	Yes	No (10)
Fauchier et al[30]	3.2	?	No	No (2)
Pernot et al[31]	3.2	+	Yes	No (6)

* $QT_o - QT_c / SE(QT_c)$. Upper range of normality (99% limit)=2.6

children 5 – 15 years in Belfast[24]) truncation is not evident (9 expected against 9 observed with $QT_o - QT_c$ greater or equal to 2 SE (QT_c)) but would in fact be unexpected with this sample size and an incidence of only 3 per 1,000 live births. *Second*, that many infants known to have long QT intervals would themselves have been cot death cases. Though some children with documented or presumed QT_c prolongation have died suddenly in the cot death age range—notably the original cases of Romano *et al*[16]—the majority have been older at death or have survived childhood. And *third*, by postulating lethal arrhythmias in infants with *slight* QT prolongation we must accept *a fortiori* such arrhythmias in infants with *gross* QT prolongation, unless the latter (but not the former) are free of associated factors (e.g. sinus bradycardia and premature beats). The literature shows only a few children under one year with gross QT prolongation and syncope[16, 24, 30-34] but transient potentially lethal arrhythmias could be missed without monitoring. Only one example of QT prolongation syndrome (a boy with unequivocal cardio-auditory syndrome) has been ascertained in the perinatal period and monitored through the first six months[35]. During this time he remained well, had no syncope, but had marked sinus arrhythmia with occasional runs of AV nodal bradyarrhythmia (Fig. 2) and had his first documented syncopal attack ironically just after hospital discharge aged 6 months i.e. within the cot death age range though after its peak. (Monitoring of subsequent syncopal attacks showed tachyarrhythmias including ventricular fibrillation). This slow rate of the escape AV junctional rhythm may be especially important for four reasons: (i) sinus bradycardia is a feature of the disease clinically; (ii) histopathology of the sinus node is one of the distinctive abnormalities at necropsy[15]; (iii) there is normally a consistent mathematical relationship between sinus rhythm and escape AV junctional rhythm[36]; and (iv) AV junctional rhythm is more dependent than is sinus rhythm on intact adrenergic neural tone abnormalities of which may in turn be a partial explanation for the QT prolongation[37].

In summary: the role of this model in cot death cannot be established from the data. But the facts are necessarily limited: e.g. we have accepted the QT interval as an invariant parameter whereas it shows within-person variability even in normal infants[38], and markedly in QT prolongation syndromes (e.g. cases in Fraser *et al*, [15, 24] and in Phillips and Ichinose[39]). If variation approaching this *relative* order (with reference to QT prolongation syndromes) occurred in infants with 'normal' QT intervals then transient prolongations (which may be lethal) are possible without disturbing the form of the population QT_c distribution even in very large samples. Again, it may not be synchronous but *asynchronous* prolonged myocardial refractoriness which predisposes to ventricular tachyarrhythmia and this need not manifest a prolonged QT interval at all. And there are other mitigating factors. (Theories of causation of the QT prolongation are outside the scope of this paper: they are well summarised by James[40]). These, and others, are legitimate variants of the main hypothesis: they further emphasise the difficulty of establishing or discrediting this model by a necessarily inductive approach.

Alternative Mechanism of Sudden Cardiac Deaths

Explanatory histopathological changes in the conduction system in some QT prolongation cases[15] and in sporadic sudden deaths in healthy young people[19] and

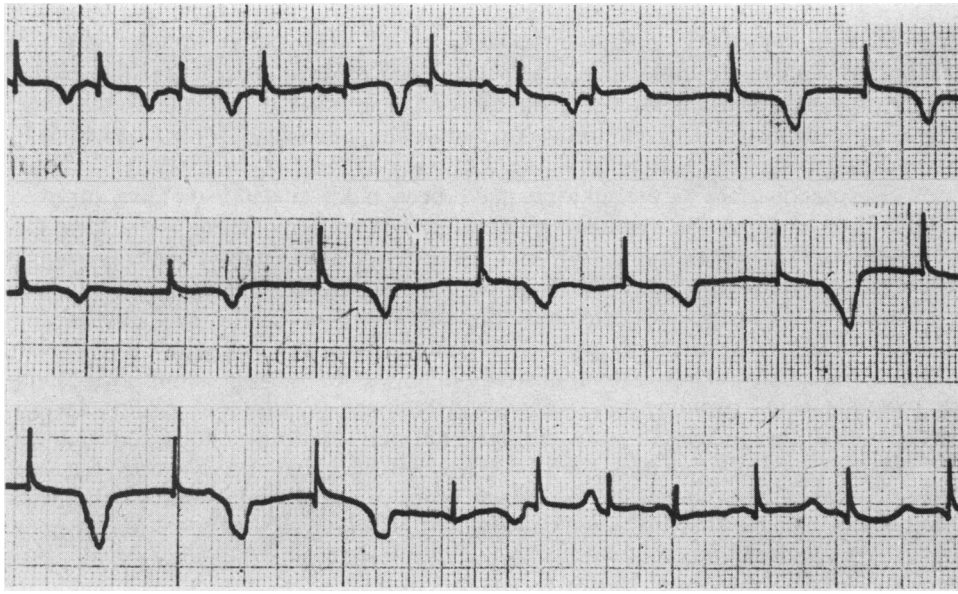

FIG. 2. *Continuous strip monitor tracing of the boy whose ECG is shown in Figure* 1. *Note the run of bradycardia and supraventricular (AV nodal) rhythm before return of sinus rhythm. The relevance of this and associated rhythms to the hypothesis under discussion is considered in the text. (Each small square represents* 0.04 *sec.)*

the clinical facts of cot death, led James[13] to examine the regions of impulse formation and conduction in hearts, and age-matched controls, from the Northern Ireland cot death material. The basic findings, confirmed by Anderson *et al*[41] and Ferris[42, 43] but questioned by Valdés-Dapena *et al*[44] are present in *all* the postnatal hearts including controls but in none of the foetal ones examined. These are a 'quiet', orderly, focal resorptive degeneration of portions of mainly the left part of the undivided His bundle (Fig. 3) and also of the AV node. The process is interpreted as a first step in the production of the thin, smooth, regular, densely collagen-encased 'adult' bundle of older children and adults. There is no associated inflammation, haemorrhage, or massive necrosis. Such orderly cell death is not unusual in morphogenesis: it accompanies digit formation and without it for example all babies would have imperforate ani[45]. James[13] speculates that the relatively large foetal His bundle can allow for some loss of (surplus) tissue during the normal postnatal fibrosing process in the central fibrous body and that the resultant 'adult' bundle is more efficient in maintaining stable longitudinal conduction than is the large, shaggy, 'infantile' bundle—which is electrophysiologically unsafe. The process is postulated to be normal and ubiquitous, to start at or soon after birth, to progress episodically with variation in phase and rate from child to child, and to be more or less complete at about one year of age. James[13] argues that this critically located process could have a dysrhythmic potential: certainly cell death (at least in the myocardium) releases intracellular potassium and other substances—such as adenosine and other nucleosides and nucleotides—with a

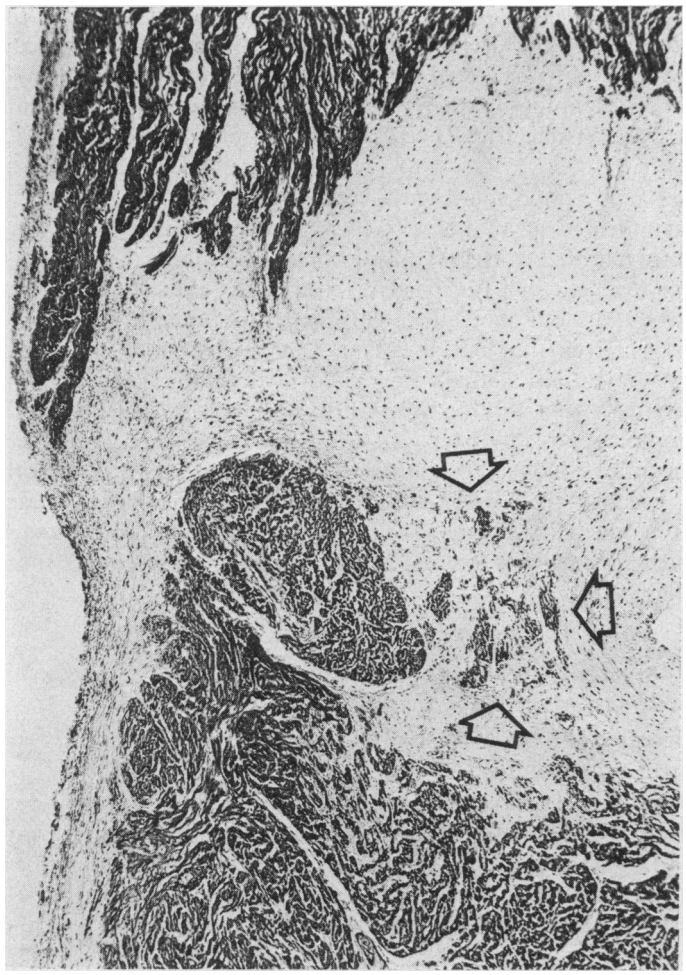

FIG. 3.

Photomicrograph of the His bundle of a 21-week-old male baby from the Northern Ireland series of sudden unexpected death in infants. (Goldner trichrome X 70). The central fibrous body shows the characteristic resorptive degeneration (arrowed) of the left-hand portion (right side as viewed) of the His bundle, the right-hand portion being normal. The interatrial septum is above and the interventricular septum is below. (Reproduced from James[13] by kind permission of the Editor of The American Journal of Cardiology.)

negative chronotropic and inotropic action[46, 47]; produces local acidosis—which can act on the numerous ganglia and nerve endings in the conduction system; and, with other mechanisms, may depress differentially surviving conduction tissue, and all of these could augment the dysrhythmic potential of episodic hyperexcitability of degenerating pockets of tissue. Some specific electrical events may be: longitudinal dissociation of AV conduction, partial block and abnormal re-entry mechanisms, unifocal ectopic tachycardia, and reciprocating tachycardia beginning in, or recycling through, parts of the His bundle and AV node. Thus by maturing to the 'adult' conduction system—which is highly efficient in maintaining stable longitudinal conduction—the infant heart temporarily becomes somewhat electrophysiologically unsafe. These changes occur in *all* infant hearts: cot deaths (on this hypothesis) would be the 2 or 3 per 1,000 in which the above hypothesised electrical disturbances occur *and* prove fatal. By providing an anatomic basis for an enhanced

likelihood of ventricular arrhythmias *in the 'normal' infant in the first year of life* this work provides an alternative to QT prolongation as a model for a cardiac conduction role in cot death. It is to be noted that concomitant delayed repolarisation or other myocardial vulnerability—which would of course compound lethal proclivity especially from 'benign' electrical events hypothesised above—need not be postulated.

Certain facts are immediately supportive of this anomalous conduction model: (i) ectopic rhythms are documented in infants with for example 'breath-holding' or apnoeic episodes[48]; (ii) supraventricular arrhythmias are not uncommon in 'healthy' babies[49]; (iii) asystole[50] and ventricular fibrillation[51] are easily induced in young mammals; and (iv) the nearly random choice of a cot death from among "eligible" (in Beckwith's[6, p.29] term) children—though this is not exclusive to this model. Contrary evidence is that potentially lethal ventricular arrhythmias are seldom documented in normal infants[28]—possibly because only short and infrequent ECG runs are taken on small samples, possibly because such disturbances are themselves brief terminating either in quick recovery or sudden death (either way they would be missed), or possibly because they don't occur. Without further large scale monitoring studies and ongoing surveillance on relevant groups of infants to a standard prospective design, or relevant animal work, additional useful evidence on this hypothesis is unlikely.

Further Testing of the Models

Additional to the above evidence we must consider the following for any general theory implicating cardiac electrical instability in cot death:

(a) why do long QT interval children rarely die or manifest syncope as early as the peak cot death age (2 – 4 months)?
(b) why do cot death infants rarely have a history of previous syncopal episodes given that ventricular arrhythmias in QT prolongation children generally revert spontaneously the child rarely succumbing to the first attack and sometimes surviving hundreds?; and
(c) how successful is the general cardiac hypothesis in explaining factors set out as (5) – (8) in Table 1?

As regards (a), on James's[13] findings we would expect a high mortality in long QT interval syndromes in the first year of life consistent with the dysrhythmic potential of the anatomic changes described. Some such infants do have documented arrhythmias or syncope (see above) or related episodes (e.g. those described by Lipp *et al*[52] and Johansson and Jorming[53]) in the first year, but most do not. Admittedly, cases may die suddenly in infancy before diagnosis; nevertheless we must accept that the initial episode is usually after the cot death age. We have no ready explanation for this.

As regards (b), careful histories will elicit in perhaps 5 per cent of cases[6] evidence of previous suspicious episodes (faints, cyanotic attacks, fits, severe breath-holding etc.) or overt syncope or collapse[4, 6, 8, 9, 54-56]—often termed 'near misses'. Though less common in 'sporadic' than familial cases[4, 9, 12]—whose aetiology may be different—they are not negligible. Their cause is unknown but usually ascribed to severe primary respiratory apnoea, an exaggeration of the apnoeic episodes common

in immature infants[57] though, as discussed below, other interpretations are possible. Even careful history-taking will underestimate their frequency in cot death infants since many episodes must go unnoticed or unrecorded (especially since they are commonest during sleep) even if due to potentially lethal ventricular arrhythmias e.g. a 9-year-old monitored boy with Romano-Ward syndrome had spells of ventricular tachyarrhythmia/fibrillation during sleep unnoticed by ordinary ward staff and without awakening him[53]. Nevertheless we must suppose that most cot death infants die during their first serious attack whereas QT prolongation syndrome cases rarely do. Again, we have no ready explanation for this.

As regards (c), we take the relevant points in order.

Points (5) *and* (6), *Table* 1. The (slight) male excess is unimportant merely patterning the general infant decrement in the male; while the lower birth weight (without obvious smallness for dates) and the evidence of socio-economic disadvantage as measured on the usual parameters and as analysed by single and multi-factor methods[9, 58] are generally unexceptional compared to most other classes of infant death. We need not therefore explain them specifically on our hypothesis: they would be general to most. Increased prevalence in colder months and in crowded homes producing 'season'/'city' contingency—though without demonstrable time/space epidemicity—is however greater than with relevant comparison groups[9]. Together with the clinical facts listed under (6) in Table 1, the pathological evidence of respiratory inflammatory infiltration albeit minor, and the classical interpretation of the intrathoracic petechiae ('Tardieu Spots')—which on Beckwith's[59] evidence may be more dense and widespread than in other infant deaths (but see however Marshall's[60] findings)—these have understandably been adduced by adherents to 'respiratory theory' schools in their own support. This is reasonable; but we can question any exclusiveness. Reasons, admittedly speculative, can be advanced to show consistency of these findings with a theory based on electrical instability of the heart: (a) viraemia and mild general toxicity could influence the functional behaviour in portions of the AV node and His bundle although the infection itself may be innocuous; (b) excess vagal activity caused by coughing or sneezing (though these are not generally recognised as clinical features of the terminal cot death episode) could in an infant disorganise or disrupt normal AV conduction or sinus pace-making or produce a sudden bradycardia which could compound dysrhythmic potential of the actively changing conduction system; and (c) the documented increased frequency of prolonged apnoeic spells during sleep[12]—itself a potentially dysrhythmic factor in normal hearts (see (ii) below) and in post-infarct or ischaemic situations[62, 63]—and with the cardiac impulse originating in an ectopic focus possibly compounding the dysrhythmic potential[48]. (See also argument below).

Point (7), *Table* 1. The presumption that the infant is asleep at the onset of the fatal episode is much emphasised: certainly it is a common[4, 9] or even allegedly a universal finding[6]. With the typical age distribution (see below) it characterises the syndrome and these two data powerfully and independently discriminate cot death from other causes of infant death. Any successful hypothesis must explain them.

Reasoning inductively from the known physiological changes during sleep so as to discriminate between likely explanatory cot death hypotheses is necessary but

unfortunately unlikely to be conclusive due to their pleiotropic and fundamental nature. On the sudden cardiac death model we may note the following phenomena during sleep:

(i) the concomitant decrease in blood pressure and tissue pH[50] may trigger abnormal activity in the infant's (unstable) conduction system;

(ii) the decrease in heart rate may *per se* induce ventricular aberrant rhythms in a normal myocardium[64, 65] and *a fortiori* in a vulnerable one, or permit the emergence of escape rhythms by ectopic pace-making foci;

(iii) the increased accelerative heart rate response to stimuli[66] may precipitate abnormal cardiac rhythm if there is a pre-existing basic conduction vulnerability;

(iv) asphyxia—as frequently postulated in cot death either by external[67] or internal means e.g. nasal blockage in obligate nose breathers[68], or apnoea—as documented in 'near misses' in ultimate cot death victims most markedly in 'rapid eye movement' (REM) sleep and with respiratory tract inflammation[12]—could if not reversed clearly cause sudden death consonant with cot death findings. Beckwith[6] considers that apnoea "with or without myotonic occlusion of the upper airway" could be the "final common pathway" leading to cot death; and others[11] suggest that failure to interrupt a prolonged apnoeic spell, however produced, is crucial. These are reasonable assertions; what is not known, since no terminal episode has been fully monitored in cot death, is whether the apnoea proves fatal *directly* through respiratory failure or *indirectly* through some concomitant lethal mechanism. We have already mentioned the dysrhythmic potential of the concomitant bradycardia (though in monitored prolonged apnoeic spells in monkeys ended by interventionary resusitation French *et al*[11] failed to demonstrate a lethal ventricular rhythm on tachometry); in fact in the so called 'diving reflex'—a complex pattern of apnoea, bradycardia, and vasoconstriction by which diving animals conserve oxygen for vital centres and which can be demonstrated in humans[69]—vagally mediated bradycardia, often severe, is an early and marked finding. This reflex can be easily induced in young monkeys[11] and in man[70] by cold and/or wet non-occlusive facial stimuli; and it may be relevant that mucus on the face is common in cot death, exposure to low ambient temperatures was marked in Steele's[55] first Ontario study, in all surveys cases are commoner in colder rather than warmer months, and in hotter surveyed areas e.g. Israel[2, 3] and California[18] the incidence (respectively 0.3 - 0.73, and 1.55, per 1,000 live births) is less than that from most other comparable North American and European studies[9]. Furthermore, though ventricular arrhythmias in QT prolongation syndromes are classically triggered by emotional shock—which in fact may itself prove lethal in 'healthy' adults[71] and which can *per se* produce the 'diving reflex' changes in man and certain animals[72]—syncope and death while bathing are described in these syndromes[39, 73] perhaps due to the 'diving reflex' changes and an electrically vulnerable heart. Even our own material discloses three instances: a 9-year-old boy with Romano-Ward syndrome and AV dissociation[74] had his first syncopal attack in an outdoor unheated swimming pool in Castlerock, Co. Antrim; Sandra C., an unequivocal Romano-Ward case[27], had her first attack aged 7 years in a YWCA swimming pool; while Paul de la C, with severe cardio-auditory syndrome[35] had his first, and 4 years later his fatal attack, while bathing at sea;

(v) repeated self-limiting attacks of ventricular tachyarrhythmia/fibrillation with syncope have been described in an otherwise symptomless child exclusively on sudden arousal from sleep by auditory stimuli[75]. Resting ECG showed anomalous repolarisation changes (marked U waves) but only equivocal QT lengthening. The auditory stimulus e.g. alarm clock, produced QT prolongation, ventricular premature beats and ventricular fibrillation. In QT prolongation syndromes bradyarrhythmias and AV junctional rhythms[35] and ventricular tachyarrhythmias[53] without patient arousal have been documented; and monitoring would undoubtedly disclose dysrhythms more frequently. We have analysed monitored tracings in three cases and in one (Sandra C[27]) further QT prolongation and therefore enhanced dysrhythmic potential, during sleep was marked (Table IV). (This could either be due to sleep *per se* or as a circadian phenomenon: either would accord with cot death data where most deaths are during the night as well as in sleeping infants). These ((i) – (v) above) and associated data could, on the cardiac hypothesis, imply an important role for sleep in cot death.

TABLE IV

Romano-Ward Syndrome (QT Prolongation without Deafness)

Degree of QT Prolongation while Asleep and Awake: ECG Tracings over Four Consecutive Days (Sandra C., age 8 years)

QT_c—$QT_c/SE(QT_c)$* *mean (and number) of contingent complexes measured*	*range of observations*	*Day, and time of day (24 hour clock)***	*Sleep status*
		Day 1	
10.8 (10)	8.3 – 12.0	1700	Awake
13.3 (10)	11.0 – 16.0	2100	Asleep
13.0 (6)	9.0 – 15.0	2130	Asleep
		Day 2	
12.8 (10)	7.3 – 16.3	0100	Asleep
6.1 (10)	5.0 – 6.5	1100	Awake
		Day 3	
6.1 (10)	4.5 – 7.5	1100	Awake
6.2 (10)	4.0 – 8.0	1330	Awake
6.0 (7)	3.8 – 7.0	1530	Awake
2.5 (9)	1.7 – 3.5	2030	Awake
		Day 4	
11.0 (6)	8.7 – 13.0	0015	Asleep
9.5 (6)	5.2 – 12.3	0030	Asleep
11.6 (4)	11.0 – 12.8	0115	Asleep

Mean of averages: asleep=11.9; awake=6.3

* See Table II, foot-note.

** Tracings taken in the domestic situation in USA by a relative of the patient: this explains the irregular time intervals and numbers of complexes measured.

Point (8) *Table* 1. The age distribution characterises cot death and is grossly disparate to the negative exponential of infant mortality generally where most deaths are earliest after birth. Even allowing for an artifactual underestimate in the first month of life[4, 9] cot death seems commonest during the 2 – 4 month period and is rare after 6 months. No simple explanation for this age distribution is possible because of the number and spectrum of contingency factors producing the critical combination presumed to produce lethality, but on the cardiac hypothesis the His bundle and AV nodal changes in the first year are described[13, 42, 43] as being least marked in the neonatal period (when cot death mortality is lowest) while the same holds for the bradycardia in the 'diving reflex'[69] and for sleep-apnoea spells in immature babies[12]. The age distribution would appear discordant with obligate nose-breathing-induced apnoea[68] which is present *from birth* and may in fact disappear at 3 – 5 weeks[76] rather than at 5 – 6 months i.e. much earlier than the cot death peak incidence. Further argument is on present knowledge speculation and unhelpful to hypothesis discrimination.

Conclusion

In a rationale of this type where inference is inductive and no precise probability can be attached to rejection or acceptance of this or any other hypothesis of cot death put under test, only general likelihoods are possible. Individual preference or experience therefore weigh disproportionately: thus virologists espouse virological theories; immunologists immunological theories; cardiologists cardiological theories. As regards a theory based on electrical instability of the heart we can say that on the evidence it appears neither more nor less likely than a respiratory one—which currently finds general support. All the facts of cot death adduced in favour of the latter may, on the evidence of this article, equally favour the former, and since the logic is identical scientists should not reject (or accept) one at the expense of the other. More data are required from many disciplines before discrimination can be legitimately made, but describing these is beyond the scope of this paper. Epidemiologists and cardiologists are no less human than are other scientists and so we will permit ourselves to say that since cot death infants typically die suddenly and silently without external insult or discernible autopsy anomaly 'causing' death, the credentials of an alternative theory would have to be strong before one should dismiss a cardiac cause for the 'final common pathway of death'.

Summary

The cause of sudden unexpected death in infants ('cot death') is unknown. This article reviews extensively evidence on the hypothesis that an electrical instability of the heart is a component in the 'final common pathway of death' in a significant number of cases. The conclusion is drawn that on available data, much from our own previous work, this hypothesis is no less likely than others currently in favour, particularly those in which cot death is ascribed to respiratory causes. Emphasis is placed on the nature of the evidence and the need for caution in its interpretation.

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OBSERVATIONS ON THE ORIGIN AND EFFECTS OF THE INDUSTRIAL DUSTS OF EAST ANTRIM

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East Antrim Hospitals Management Committee

GEOLOGICAL SCIENCE is responsible for the location of mineral resources, from which are derived end-products that determine the material standards of comfort and wealth in a civilised society. Every facet of technological achievement is totally dependent on raw materials wrested from the Earth's crust. Unfortunately few who partake of the benefits are aware of the origin from which they emanate. This is a regrettable deficiency, particularly in Antrim, which has the richest geological heritage of any county in the British Isles.

The industries on the Antrim coastal strip are compact, modest in scope and output, nevertheless it has been possible to note the effects by inhalation of a variety of dusts on the human organism. The results observed do not invariably correspond with those already published in the literature. It is obviously as desirable to recognise substances that are innocuous, as it is necessary to be aware of the few that represent a serious respiratory hazard if inhaled. Some knowledge of the composition and evolution of the parent rock is necessary for a complete understanding of pathogenic dusts when these present, therefore a brief geological note precedes discussion on the ore or mineral concerned.

Limestone

Limestone contain microscopic traces of belemnites, brachiopods, and other marine exuvia indicative of an era millions of years ago, when Ireland was submerged under the sea, and trillions of these creatures multiplied prodigiously in the warm waters. Their shells and skeletons, pulverised by the action of the waves drifted down to carpet the primeval ocean bed (Lawlor, 1928), to a depth of thousands of feet (Carson, 1953). Small spherical granules with concentric lamellae of calcium carbonate seen in the marine Oolitic limestone suggest that chemical reactions also added to the vast bulk of the calcareous ooze (Trueman, 1963). When the seas retreated for the last time, the uplift of the ocean floor raised these Cretaceous masses above sea-level. They were later inundated by molten lava extruded by the frequent and universal volcanic eruptions of the Miocene era*. This superimposed mantle of tertiary lavas protected and preserved the underlying limestone, and together they form the well-known scenic features of the present-day land mass, the rugged contours of which are mute evidence of the seething climatic cauldron from which they evolved. This magmatic caput extends over an area of 1,550 square miles, the largest single continuous fragment of basalt in the British Isles. It sometimes attains a depth of 1,000 feet (Robson, 1968).

The limestone outcrops are extensively quarried because lime and limestone play an important part in a variety of industries – agriculture, building construction, chemicals, putties, paints, ceramics and abrasives. It is used extensively in blast

* The Miocene era began 23 million years ago, and its duration was 11 million years.

and other furnaces as a flux in fusing steel. Local chalk is exported to Scotland for the manufacture of glass, for which purpose it is said to be the best limestone available. It is an important ingredient in the manufacture of cement. A low moisture content (0.53 per cent) makes Antrim limestone unique. It is consistently harder than the average English chalk, the density of which is 1.95 compared with 2.50 – 2.64 for the local rock. Whether this difference can be accounted for by a variation of the former thermal gradient in the basalt dykes, by compression of the lava load, or a combination of both is a matter for speculation. Perhaps the old geological adage applies, 'the more rapid the cooling, the more compact the stone', (Smith, 1868). This characteristic adds another dimension to the industrial uses of Antrim limestone. It is more resistant to the etching and corrosion caused by the acid solutions of a polluted atmosphere, than other known limestones used for ornamental building and monumental work. It retains its whiteness in the presence of such attack. This durability and resistance to chemical weathering are desirable qualities in building construction in industrialised environments.

A typical analysis of Antrim limestone is:

Lime	55.13%
Magnesia	.25%
Protoxide of Iron	.06%
Alumina	.04%
Silica	.24%
Sulphuric Acid	.05%
Phosphoric Acid	.11%
Carbonic Acid	43.59%
	100
Equal to Carbonate of Lime	98.45%
Sulphur	.02%
Phosphorus	.05%
Iron	.04%

Wherever limestone is crushed or its powder handled a heavy cloud of fine dust pervades the working arena to be inhaled by the workmen concerned. Prior to the operation flints present are culled from the bruised rock, so the residual silica content of the powdered lime is minimal, i.e. 0.24 per cent and this represents no threat to the pulmonary health of the workers, since normal lung silica is reckoned to be 0.25 per cent. (Foweather, 1939).

Free inhalation of limestone dust (calcium carbonate) observed for over 22 years revealed no clinical or radiological insult to the respiratory tract. This may seem at variance with published results. For example, Doig (1955) described eight cases of disabling pneumoconiosis in limestone workers in which limestone was said to have played the principal or sole aetiological role. However, on closer examination of that particular dust it was shown to contain 10 per cent of silicon di-oxide, and this cannot be ignored as the cause of the lung changes in these men.

The inhalation of pure limestone dust (calcium carbonate) is harmless, and does not constitute an industrial hazard.

The regular layers of flints seen in the limestone strata, is yet another geological manifestation of the former submarine existence of the Antrim terrain. Microscopic examination reveals the presence in them of the siliceous skeletal remains of sponges, radiolarii, echini and other primitive forms of sea-life. These rocks are solid and homogeneous in structure and are composed entirely of silicon di-oxide (98 per cent), with a thin cover of calcium carbonate (2 per cent).

A local syndicate crushed these stones to a fine aggregate to sell as poultry grit. The operatives inhaled the fine dust freely, oblivious of its pathogenecity. The disastrous results of this misadventure are recorded fully elsewhere (Scott, 1964). The bulk of the particles were less than 5 microns in diameter, a size calculated to reach and stay in the innermost recesses of the alveoli (Davies, 1949), and being freshly fractured the maximal dissolution of silicic acid was ensured, a factor which proportionately exacerbated the pathological insult to the lungs. (King and Bett, 1938). Acute pneumoconiosis resulted, and of six deaths, the longest period of survival was eight years from initially taking up this occupation. All had massive shadowing on x-ray, and all became respiratory cripples two to three years prior to demise.

It seems to be a popular text-book conception when silica alone is inhaled, unaccompanied by other injurious agents that the disease runs a chronic course, and a long period of exposure is necessary before pulmonary changes take place. From observation there is little doubt that the rate of disability is directly related to the concentration of silica in the dust inhaled, and to the length of exposure. In the most fulminant case seen among the flint-crushers, the interval between initial contact and death, was only three years. The radiological effect on the lungs is shown in Fig. 1, and the autopsy lung analysis was as follows:

Total Silica percentage of dry matter	2.46
Free Silica	1.89
Ash	4.84
Total Silica percentage of ash	50.9
Free Silica	39.1

In cases of silicosis caused by inhaling limestone dust containing 10 per cent silica, a relatively moderate concentration, 18 – 20 years elapsed before partial disability began to appear. This rate of progress is consistent with the findings in series where the concentration of silica inhaled was comparable.

The association between tuberculosis and silicosis is a controversial subject. One view is that silicosis does not ordinarily cause symptoms of pulmonary disability except in the presence of active tuberculous infection (Gardner, 1947), or in rare cases of personal idiosyncrasy, or when there has been excessive exposure to the dust. A peculiar affinity for silica by the bacillus has been postulated (Kettle, 1933), and it has been stated that 75 per cent of cases of silicosis ultimately develop tuberculosis (Christie, 1960). Such statistics are an exaggeration of the position seen to-day. In the autopsies performed in East Antrim tuberculosis had no part in the massive fibrosis encountered. It is appreciated that the dose of inhaled siliceous material was excessive, nevertheless, the periods of

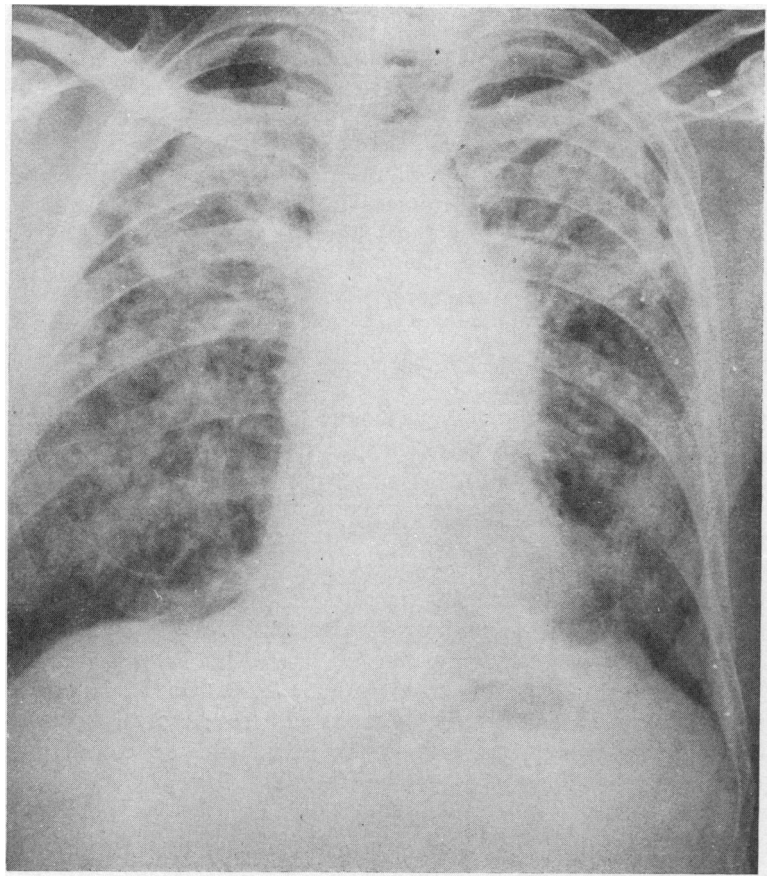

FIG. 1.
Massive and terminal pulmonary fibrosis seen in a 'flint-crusher' after only three years exposure to the dust.

survival ranged up to eight years. This seems ample time for the establishment of 'symbiosis' between the element and the bacillus, if such exists, particularly as the ciliary defences and bronchial peristalis were seriously impaired, and incessant coughing blunted the therapeutic sheet-anchor of pulmonary rest. It seems rational to deduce that silico-tuberculosis was most common when the infection rate was high in the community. The improvement in social conditions and therapeutic control have led to a marked decline in tuberculous infections. In consequence the opportunity for association between the two diseases is greatly curtailed, so the percentage incidence of silico-tuberculosis is much less than formerly. It is also of interest to note that in more recent years where the dose of inhaled silica was not gross, i.e. 10 per cent (Doig, 1955) the onset of pulmonary disability was delayed for 20 years or more, and when fibrosis appeared, it was without the assistance of complicating tuberculous infection.

The size of the inhaled particles has also received considerable attention. It has been suggested that when silica is inhaled in a very fine state of subdivision (20 Angstrom units) it is readily soluble in the pulmonary fluids, and is then eliminated

from the tissues too promptly to do lasting harm (King and Bett, 1938). This point has little application in industry, since industrial machines do not discriminate as regards the particle size, nevertheless this statement is also open to doubt. In Shaver-Riddell disease, a pneumoconiosis specifically associated with the aluminium industry (Wyatt and Riddell, 1949), furnace operators inhaled fumes composed of silica (20-44 per cent), and aluminium (41-62 per cent). These percentages were reflected in the autopsied lungs as follows:

	Silica	Alumina
Dry Weight	6.24%	22.75%
In Ash	26.8%	38.8%

(Shaver C. G. and Riddell A. R. 1947)

Probably influenced by the recorded 'innocence' of finely subdivided silica (King and Bett, 1938) it was concluded that the lethal lung changes were due to the finely divided amorphous alumina. Practical evidence available indicates that alumina is a relatively innocuous inhalant. It has been used extensively as an aerosol of aluminium hydroxide in the treatment of silicosis (Crombie et al., 1944). Carefully controlled trials failed to reveal any therapeutic value of such a regime (Christie, 1960), nevertheless it was significant that no adverse effects were noted on the pulmonary tissues from its use. Again the substitution of alumina for flint to bed china in the pottery industry was wholly beneficial and it reduced the incidence of pneumoconiosis (Bodley Scott, 1961). Experience in East Antrim, and in the aluminium industry in general supports the view that alumina dust is not a pulmonary irritant. If this be accepted the disastrous results caused by the inhalation of bauxite fumes in Shaver Riddell disease must have been due to the silica content, in spite of the fact that it was in the very finest state of subdivision.

Radiological films are recognised to be indispensible in the diagnosis of the pneumoconioses, but alone they are not a reliable index of the degree of incapacity. Heavy shadowing can occur with minimal disability and vice-versa (Kerley and Twiney, 1950). Careful clinical examination is the prerequisite for functional assessment. Fluoroscopic investigation is helpful, as fixation of the mediastinum and limitation of diaphragmatic movement precedes such symptoms and signs as dyspnoea and diminished chest expansion, that precede reduced vital capacity. The accentuation or reduplication of the second pulmonary sound is a late sign, the cri de couer that heralds the advent of terminal cor pulmonale.

It is a recognised fact that a workman may cease to operate in a siliceous atmosphere, when a chest x-ray is still free from radiological evidence of nodular fibrosis. Pulmonary changes may appear after an interval to demonstrate that the patient had been in previous contact with a quartz laden atmosphere. If the dose of silica inhaled is not critical, the tissue reaction may eventually subside, and the partial disability attained at that point may remain static (Gardner, 1947). One workman, for example, was heavily exposed to flint dust for a brief period of two years, and a chest film showed minimal mottling in the right mid-zone, so advice to change the occupation was complied with. Six years later this patient complained of cough and dyspnoea, with a significant reduction in vital capacity. Radiograph now revealed extensive bilateral pulmonary fibrosis indicative of the previous

contact with quartz. This picture (7/9/62) is similar to that taken more recently, Fig. 2 (28/12/72) which shows that the radiological pattern has not altered materially in the ten-year interval, nor has there been further deterioration in the clinical state. The dose of silica inhaled was probably insufficient to perpetuate pathological activity. Whatever the clinical or radiological evidence when the patient is first seen it is never too late to advise his removal from the influence of a suspected dust.

Quartz and silica are the most soluble, and therefore the most pathogenic of the mineral dusts (King, 1947), dissolving to the extent of about 10 mgm of silica per 100 cm. of blood plasma. In spite of the fact that more progress has been made in fighting pneumoconiosis since 1954, than in the previous 200 years (Posner, 1972), one hundred new cases of silicosis are reported in the potteries alone each year. The industry's failure to set up a medical service with research facilities has been criticised, as has the failure to apply properly techniques designed to cut the incidence of the disease. The frailty of the 'human element' is forever destined to be a weak link in the preventive chain.

Silicon di-oxide is a most lethal dust when inhaled. The rate of pulmonary deterioration is determined by the duration, and the severity of the exposure.

Salt

Rock salt or halite (NaCl) is an evaporite deposit precipitated by evaporation of salt water in an arid climate from lakes or lagoons having restricted access to the sea, but with a constant trickle supply of salt-laden water moving in to replace that evaporated. (Robson, 1968). This process took place in the *Triassic era, when centuries of tropical sun relentlessly baked the East Antrim landscape. The nearest approach to such climatic conditions to-day is found only in the Persian Gulf, and parts of China, India, Japan and in the alkali flats of Utah (Carson, 1953). To preserve these crystalline deposits it was necessary for nature to cover them with an impervious material, such as clay or marl, achieved by land-slip or perhaps interred by volcanic activity.

Salt has been exported to all parts of the world for more than a century. The Marquis of Downshire struck salt at Duncrue, Carrickfergus, in the middle of the 19th century, and extracted 20,000 tons of high purity salt yearly. From 1896-1922, 600,000 tons were exported from Tennant's mine at Eden Carrickfergus. These deposits seem likely to extend over a wide area, as recent borings at Larne revealed there that beds of halite reach 1,500 feet in depth, exceeding in thickness the largest known deposits in these islands. The statistical significance of this is reflected in the deduction that a vertical foot over a square mile yields 2,000,000 tons of salt. It is difficult to understand why such resources are allowed to lie fallow. It seems reasonable to hope that a commercial option will be exercised in the not too distant future.

Latterly the salt was obtained by flooding the holdings and piping the resultant brine to the purification plant and the evaporation pans. This process does not

* Triassic Period: began 220 million years ago, and lasted 40,000,000 years.

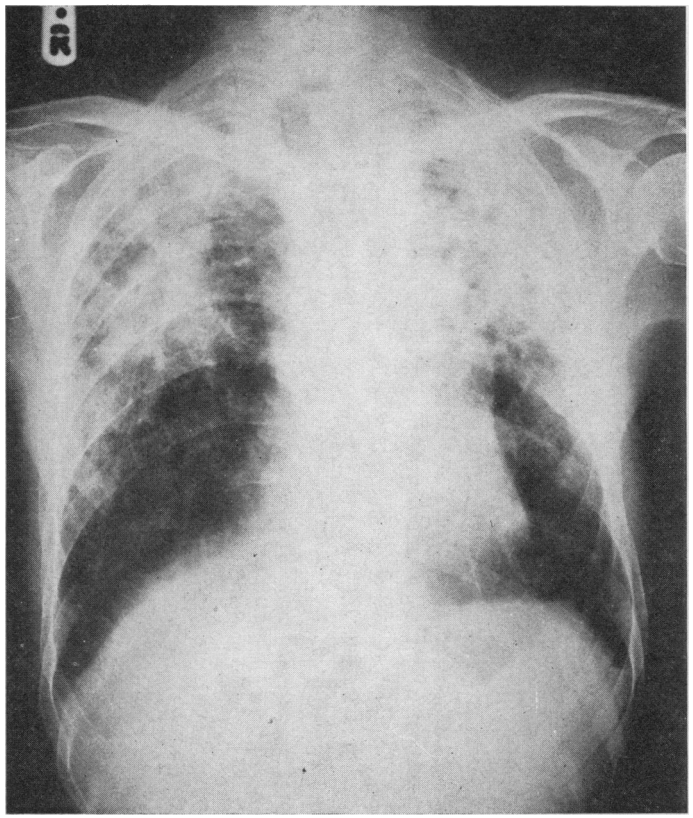

FIG. 2. *Extensive pulmonary fibrosis which developed after a latent period following exposure to flint dust.*

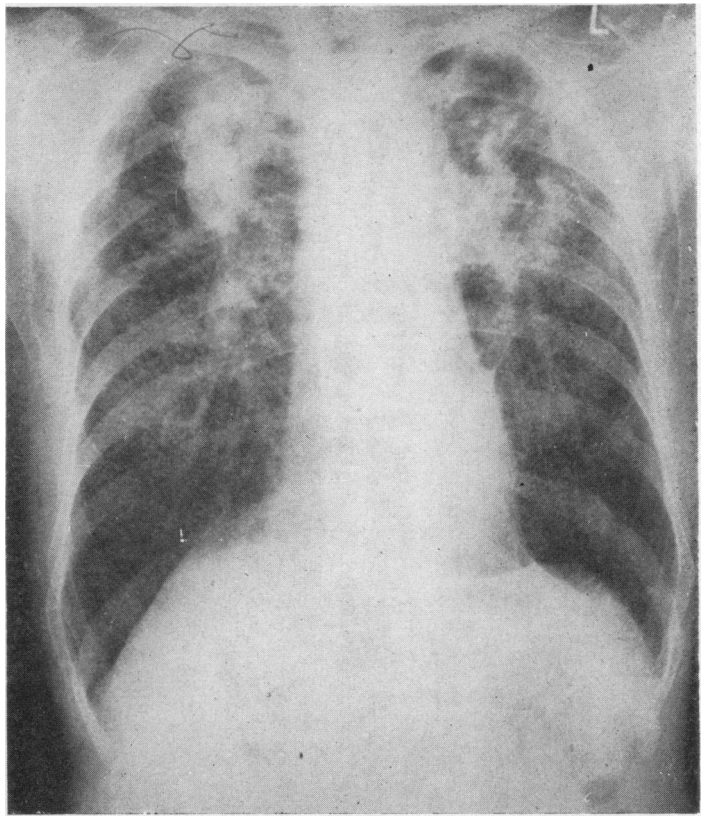

FIG. 3. *Changes of pulmonary fibrosis seen after 30 years exposure to bauxite dust.*

appear to have been associated with any particular health hazard. It is noted in the Factories Act N.I. 1938-1949, under the heading of Prohibited Employment that "Female young persons must not be employed in any part of a factory in which are carried on evaporation of brine in open pans or stoving of salt."

The mining and processing of salt, apart from minor discomforts, does not present an industrial health hazard to the operatives concerned.

Bauxite

Bauxite is the parent ore from which the metal aluminium is derived. It is so-called because it was first discovered at Les Baux, a town in Southern France. A country-wide survey of the British Isles revealed that bauxite deposits are absent except for an area in County Antrim (Edmunds, 1960). Here highly aluminous clays are found to exist between the old lava flows in the Interbasaltic interval. During the last year over 300,000 tons of bauxite were extracted from mines in the hinterland under the managing direction of the British Aluminium Company, and initially processed at their works in Larne. Ample reserves of this ore still remain.

Silica (SiO_2) is the commonest magmatic element, and the key substance in the crystallisation of rocks, comprising 65 per cent of the Earth's bulk. Another 15 per cent is composed of alumina (Al_2O_3), a combined total for both of 80 per cent (Drury, 1964). In nature these elements form a tenacious affinity for each other, the stability of which is extremely difficult to disrupt. Their separation is naturally accomplished, however, by a process known to the geologists as 'weathering'. The principal agents of which are the atmosphere, water, and the sun's energy. The primary lithomarge is exposed to incessant physical, chemical and organic assault in tropical monsoon conditions. As one would expect temperature plays a key role. The difference between night and day temperatures in some tropical areas to-day often exceeds 100°F (Raistrick, 1963). In consequence non-related minerals contained in a rock, by virtue of their different co-efficients of expansion, expand and contract unequally when subjected to the same rise and fall in temperature. Such constantly repetitive internal stresses eventually reduce the crystalline crust to a granular state. Rain has a devastating weathering effect. It is a complex fluid. As it falls through the atmosphere it dissolves small quantities of various gases. On reaching the ground it is a very dilute solution of carbonic acid, and in industrial areas sulphuric acid, and the contained oxygen acts as an oxidising agent. This acidulated solution attacks rocks destructively down their joint planes, and chemically alters existing minerals in the rocks, which in turn may interact with neighbouring substances to form different compounds. Through time rain alters the previous integrity of a rock, so that it may eventually be replaced by a virtually new mineral. (Desaults, 1969). Showers also carry swarms of micro-organisms, Chadothrix, etc., from the surfaces into the crannies of the rock where all catalyst reactions are intensified by the warm climate. When it freezes, water expands by one tenth of its volume, exerting a pressure of 200 lbs. per sq. inch. Decomposing vegetable matter on the ground produces humic acids and these percolate to set up their own individual chemical changes. The winds

carry fine sand and rock particles, to exert a powerful kinetic action capable of eroding the hardest of surfaces.

Chemical weathering breaks the rock down into soluble and insoluble compounds. The bulk of the former is forced into solution, which includes silica, lime, magnesia and alkali of the original rock. These leach out to leave insoluble substances behind to form the new rock, composed of aluminium, iron, titanium and sometimes manganese. This process of desilification is known as 'laterisation'. Should it happen that the insoluble hydrates of iron remain the dominant content of the 'new rock', and of sufficient quantity and purity to make commercial recovery worthwhile, it is termed iron ore or laterite. If on the other hand the residuum is composed mainly of aluminium hydroxide, it is an aluminium ore and is called bauxite. This weathering process is maximal in areas of low latitude, e.g. in tropical Ghana, the Carribean, Southern France, etc., where abundant rainfalls co-exist with warm atmospheres to accelerate the speed of chemical oxidising reactions.

The climatic conditions necessary for the development of laterites and materials rich in alumina are so specific that the occasional presence of these substances in stratified rocks, e.g. in the Interbasaltic Horizon in County Antrim, is regarded as factual evidence of the former existence of tropical weather during the time of their formation. (Kirkaldy, 1962). This was during the *Eocene and *Oligocene eras, when the atmosphere was hot but not arid (Cole, 1912), e.g. warm suns and heavy rains, conditions that prevail to-day in many parts of India and Africa. Proof that such a climate existed in East Antrim is preserved in the volcanic lavas of the Miocene eruptions which enveloped the terrain. Traces of tropical vegetation can be identified in the magma, such as eucalyptus, sequoia and grasses that are found growing to-day in Southern Europe and North Africa. (Charlesworth, 1966).

Weathering is a slow and imperceptible process, and its existence may be doubted by many. It has to be remembered, however, that geological time is measured, not in tens, but in millions of years or more. During these vast periods of time, the agents of denudation have been ceaselessly at work, and the weathering processes of the milennia are continuing at this moment in time. The bauxite beds of the Antrim Lava Plateaux are 20 feet deep, and are said to represent a developmental period of one million years, whilst in Ghana, from whence high grade ore is imported, the 60 foot beds there are computed to have taken 7,000,000 years to form (Cooper, 1936).

Bauxite is chemically an impure form of aluminium oxide (Al_2O_3). It is combined with water, silica, iron oxides and titanium, the residual impurities left with the rock after weathering, and which must be eliminated before the pure metal is extracted. The formula for high grade bauxite is:

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* The Eocene era began 70 million years ago, and continued for 35 million years, whilst the Oligocene era started 34 million years ago, and its duration was 12 million years.

Al_2O_3 (Alumina)	50–70%
Fe_2O_3 (Ferric oxide)	3–25%
SiO_2 (Silica)	1–7%
TiO_2 (Titania)	2–3%
H_2O (Combined Water)	12–40%

(Aluminium Federation).

The ore taken from one of the local mines was exceptional so far as Irish rocks are concerned, in that it had a very low silica content – 1.6 per cent, with a high compensating percentage of alumina – 62.7 per cent. Other sources were not so rich, as silica figures range from 1.6–8 per cent in the holdings worked. The raw material was transported to Larne, and there crushed to a fine powder in the rolling-mills. This was then digested in a hot solution of caustic soda, which dissolved the aluminium oxide. The undissolved impurities, i.e. coarse particles of the oxides of iron, titanium and residual silica were creamed off leaving a clear liquor, which in turn was calcined in rotating kilns at 1,300°F, and a white powder, anhydrous alumina (Al_2O_3) was deposited. This is the intermediate product in the manufacture of aluminium metal. As further reduction depends on ample supplies of cheap electricity which can only be supplied by vast hydro-electric schemes, the alumina was of necessity transported to the Scottish Highlands where these exist. It may, therefore, be of interest to recall that technological methods available in the early part of the last century produced infinitesmal amounts of aluminium. Isolation of the metal on a commercial scale resisted scientific endeavour until 1866, when by a strange coincidence Charles Martin Hall of the U.S.A. and Paul Herault of France, independently discovered the Hall-Heroult electrolytic reduction process, whereby powerful electric currents tore asunder those elements that had been tightly interlocked for billions of years. The alumina is dissolved in a bath of molten flux to allow the hefty current pass. This liberates the oxygen and releases the molten metal to a purity of 99–99.8%, and it is then readily decanted. As a consequence of this discovery cheap electricity became a paramount industrial necessity for the economic production of aluminium. The British Aluminium Company (1894) pioneered the development of powerful hydro-electric schemes in the Highlands of Scotland where ample supplies of surplus water exists. The Fort William project is but one example of engineering ingenuity and skill required to overcome formidable natural obstacles to provide adequate power. Water from a three-hundred square mile area is collected into a complicated catchment system of dams, and conduited by a 15 foot pressure tunnel, for 15 miles through metamorphic rock, schist and granite, through and under the heart of the Ben Nevis mountain range to deliver 6 – 7,000,000 gallons of water a day to the reduction plant. The reafforestation of catchment areas, and the development and stocking of the new pasture lands, with the construction of adequate housing established a balanced environment to achieve an advantageous symbiosis between agrarian and industrial interests all too uncommon where technological development superimposes itself on a rural terrain. The substantial amounts of electricity necessary is reflected in the production statistics of Alusuisse (1888), Zurich, the European pioneers of aluminium production. In 1969 this Company produced a

record output of 1½ million tons of the metal which required 7,500 million kilowatt hours of electricity (15 kilowatt hours per kilogram). This is enough to satisfy the electric power needs of a city of 2,000,000 inhabitants for a full year. It will thus be obvious why it was necessary to transfer the alumina from Larne to the Scottish reduction factories.

The ability of 'aluminium' to cause specific lung disease is debatable. The term 'aluminium dust' appears frequently in the literature, but this term requires careful definition. Such a dust may vary in chemical composition and possible pathogenicity according to the stage reached in processing when the 'dust' presents.

The crushing of bauxite ore is the first step in the eventual production of aluminium metal. The rock is reduced to a very fine powder which heavily pervades the factory atmosphere. It was freely inhaled and preventive measures were not deemed to be necessary. Many were exposed for periods of 30 years or more, and no clinical disability was attributed to the nature of the work. The men exposed volunteered the information that when the rock was being crushed workmates were scarcely visible nearby owing to the density of the bauxite powder in the atmosphere. Examination of all available chest x-rays showed a moderate degree of abnormal shadowing in them all, some more pronounced than others. In Fig. 3 the pulmonary changes developed after 28 years exposure, and at the time the picture was taken the patient had been retired for 28 years, aged 82, was physically well without respiratory embarrassment. Enquiry at the large reduction works revealed that there was little or no incidence of pulmonary disease among bauxite crushers. It may be that the Antrim ore was marginally higher in silica content (1.9 – 8 per cent) than high grade imported ore, and this may be sufficient to cause mild tissue reaction but insufficient to give rise to functional pulmonary change. The record of longevity in the local workmen is testimony to the relative innocence of the inhalation of bauxite dust. At the most it produces a benign pneumoconiosis with the suspected help of a moderate amount of silica.

The second stage in the production of the metal is the digestion of the powdered bauxite with caustic soda, and the resulting liquor is calcined by strong heat to produce a fine white dust or alumina (Al_2O_3). Inhalation of this dust did not produce any adverse effects on the pulmonary system when inhaled over the same periods of time as the fellow workmen above.

It is concluded:

(a) The inhalation of Antrim bauxite dust causes a benign asymptomatic pneumoconiosis.

(b) This inhalation of alumina (Al_2O_3) is innocuous.

It is perhaps appropriate to refer again to Shaver-Riddell disease to clarify its relationship to the aluminium industry. Alumina (Al_2O_3) is a corundum, and other forms of this material occur in nature such as sapphire, oriental ruby, topaz and emerald. It has a basic hardness next to diamond, i.e. 9 on the Moh's scale of hardness. This characteristic has been utilised by industry to produce a commercial abrasive. To do this bauxite was mixed with coke and iron and the mix fused by an electric arc at 2,000°C. The dense fumes evolved were inhaled by the furnace-men who contracted acute pneumoconiosis in consequence. It was postulated that the lung changes were due to the alumina content of the fumes.

This seems unlikely in view of experience in East Antrim, and in the aluminium industry in general. It is likely that the pathological injury in the lungs was caused by the high concentration of finely divided silica inhaled, and that Shaver-Riddell disease was in fact acute silicosis, and not an aluminium lung disease as is commonly supposed.

Cement

Portland cement is 90 per cent alumina, lime and silica, with ratios of SiO_2/Al_2O_3 varying from 2 : I to 5.5 : I (Lea, 1956). The basic raw materials for the manufacture of cements, exist in close proximity on the Antrim coast (Magheramorne). The requisite lime or calcium carbonate is readily quarried from the outcrops, and the siliceous alluvial mud or clay is conveniently obtained by dredging from the bed of the adjacent sea-lough.

Clays are formed from decomposed weathered detritus of argillaceous rocks, felspars and other materials. Mixed aluminium silicate and hydrate is the basis of all clay. These hydrated alumino-silicates are in a state of very fine clastic subdivision, with a particle size of less than 0.05 mm in diameter. (Drury, 1964; Raistrick, 1963; Keikie, 1903). Their fine subdivision was assisted during the *Ice Age by the relentless too and from movement of an ice-cap, up to two miles thick, which covered most of the British Isles. When the seas grew warmer and the glacier melted and retreated, the glacial deposits of alluvial clay were left behind (Lawlor, 1928). Blue mud is the most generally found, and it owes its colour to its content of iron sulphide, arising from the decomposition of organic substances (Gunther and Deckert, 1950).

A typical analysis in per cent of lough clay is:

SiO_2	53.12
Al_2O_3	13.22
Fe_2O_3	5.05
CaO	7.26
MgO	2.76
SO_3	0.24
Sulphide	1.04
Alkalis not determined	4.48
Loss on Ignition	13.22
Silica Ratio	2.91
Alumina Ratio	2.62

(Lee, 1956).

The first step in the manufacture of cement is crushing the limestone, and there is an admixture with flints, so this is a possible focal point for the inhalation of a siliceous dust. This does not in fact occur, because 'damping down' keeps the atmosphere of the working arena perfectly clean. This aggregate is then conveyered

* The Ice Age in Ireland began a million years ago, and the Glacial Maximum was 200,000 years ago. It is 20,000 years since the bulk of the glacier passed on, and 8,500 years ago the last remnants of the ice disappeared (Charlesworth, 1966).

to the wet grinding mills to be mixed with water and lough clay in predetermined amounts, and ground into a homogenous 'slurry'. This mix is passed through great steel rotary kilns, and ignited at a temperature of 3,000°F, and the substance 'clinkered', and then cooled. Clinker consists of complex silicates of lime and aluminium, and it is ground to a fine powder to which gypsum (hydrated sulphate of calcium) is added in specific quantities to control the setting time. This cement is then conveyered to silos for bagging or to fill bulk containers. The entire process is automated, and workmen are not exposed to dust in these terminal stages of manufacture. In addition the silica in the cement is altered to complex silicates mentioned, and these are not injurious if inhaled.

The atmosphere within the factory is surprisingly wholesome and free from dust. The 'smoke' that emanates from the chimney stack, a high level emission, is composed of steam and cement. It causes some comment as it settles in a fine dust film on surrounding property. It is not injurious to health, and the quantity is minimal because the bulk of the dust is removed in transit by an expensive and elaborate system of electrostatic precipitators. Lay opinion is naturally apprehensive of atmospheric industrial dusts, and fears are sometimes stimulated unnecessarily by un-enlightened comment. The factory provides high grade employment without health risk to its employees. Statistics from the huge cement factories abroad substantiate the claim that the health record of the cement industry is second to none. Some 2,278 workers exposed to cement dust for ten years did not develop any pulmonary disability or show radiological changes of pneumoconiosis (Gardner et al, 1939); 250 men engaged in making and 300 using cement showed no respiratory changes on prolonged exposure to the dust (Dervillee and Carrere, 1935); 533 workers in manufacturing cement showed no cases of pneumoconiosis but silicosis was seen in workers who obtained the raw materials, i.e. the quarriers and miners who worked in the marl beds (Parmegianni, 1951).

There are no health risks involved in the manufacture of cement.

The elements described above are but a small proportion of the hundred or more that exist in the Earth's crust. Tempered by the heats, the cataclysms and pressure of climatic extremes they provide the opportunities for the technological scientists to make discoveries beneficial to mankind. The genesis of knowledge, however, down the centuries has been subject to inexplicible 'crescendos and dimuendos' and even phases when the fruits of scientific achievement have been apparently lost. It is fitting that aluminium, the 'youngest' metal in existence to-day should pose this intriguing possibility. According to modern records the first particles of the metal aluminium were produced by a Danish chemist, Hans Christian Oersted in 1825 using a chemical process. Yet it is noted that an ancient girdle found in a third century tomb of a Chinese General Chow Chu (A.D. 265-316) was found to contain on spectrascopic analysis, 10% copper, 5% manganese, and 85% aluminium. There may be occasions when a scientific discovery may in actual fact be a 're-discovery'. The most recent and important scientific advancement, the atomic pile, which produces power, radio-active isotopes so useful in treatment and diagnosis, is completely dependent upon raw materials extracted from the Earth's crust. It can be reasonably argued that the Science of Geology is the handmaiden of technological achievement.

In a journey around East Antrim the trained eye can readily discern the tell-tale signs of the climatic conditions that prevailed in the periods described in the text above, e.g. evidence of the relentless desert heat in the Triassic period, the more pleasant subtropical climes of the Eocene and Oligocene periods, and the snows and blizzards of the Ice Age. Geology is the 'braille' that will open the eyes of the uninitiated into a wider understanding of the topography of the land in which they dwell, and the significance of those features which point to the mineral wealth which may lie below a surface. Furthermore, the enthusiastic amateur geologist has it in his power to make discoveries that have not yet been recorded. It seems that this subject should receive more serious consideration in the curriculum of secondary education.

Summary

The commonest magmatic element, silica, has been one of the most potent causes of pneumoconiosis. The severity of the pulmonary reaction due to quartz dusts depends on the concentration of silica in the inspired air, the length of exposure, and the freshness of the fractured particles. The pharmacological composition of the dust is also important, e.g. heat-treated silicon di-oxide is particularly dangerous, because the modified forms of silica so produced are biologically more active than the parent substance. Wherever a siliceous dust pervades a working arena, stringent precautionary measures are mandatory at all times.

Halite or salt (NaCl) presents no threat to industrial health. The Factories Act N.I. (1938, 1949) does, however, prohibit "female young persons" to be employed in that part of a factory where the brine is evaporated or the salt stoved. In the absence of information for the necessity of such a stricture, it is assumed that there may be local irritant causes, but there is no respiratory hazard in the processing of salt.

Bauxite dust is not regarded in the aluminium industry as a noxious respiratory agent. The relatively benign pneumoconiosis seen in the bauxite workers in East Antrim are likely to have been due to the moderate silica content of the ore, the dust of which when crushed was freely inhaled by the operatives concerned.

Limestone dust (calcium carbonate) can be inhaled in unlimited quantities without damage to the pulmonary tissues. It is necessary, however, to carefully cull the indigenous 'flints' prior to crushing the rock.

Cement dust can be inhaled with impunity. The high level emission of this substance from the factory chimney is a moderate physical nuisance to people and property within its atmospheric range. This has been latterly markedly reduced by sophisticated electrostatic precipitation procedures.

Alumina (Al_2O_3 – corundum), a fine white powder and an intermediate product in the manufacture of the metal aluminium, has no deleterious effects on the pulmonary system when inhaled. Alusuisse, the Swiss pioneers of aluminium production in Europe, founded 1888, and one of the world's principal producers of the metal, "have never heard of any case of health hazard due to alumina." (Swiss Aluminium Ltd. 1973).

Atmospheric concentrations of fumes and dusts can now be monitored and accurately measured. Threshold Limit Values (T.L.V.) have been evolved for individual inhalants. These indicate the levels of atmospheric contamination to

which a workman can expose himself day after day without adverse effects. It has not been found necessary to assign Threshold Limit Values to cement, limestone dust, or alumina. These substances are merely classified as "Inert" or "Nuisance Particulates". (D.E.P. 1971).

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THE ALLERGIC CHILD

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ASTHMA is one of the commonest causes of chronic handicap in childhood, is responsible for a great deal of intercurrent illness in childhood and occasionally has a fatal outcome. It is pre-eminently the concern of the generalist, either general practitioner or general paediatrician – or more commonly both working together. The different views of childhood asthma taken by various specialists remind one of the tale of the blind men examining an elephant. One feels the trunk and exclaims that it is like a rope: another the leg and likens it to a tree: a third feels the ear and says it is like a mat: while the fourth meets the side of the elephant and thinks it is like a wall. All of them are partially right and yet none has any idea of the elephant as a whole: each argues from his own standpoint and is certain that the others are wrong. Thus the allergist sees asthma in terms of identification of the offending allergen and hyposensitization: the psychiatrist as a psychosomatic manifestation: the chest physician as a problem in respiratory function: and so on. Each may be convinced that the others treat asthma inadequately and yet none has a really balanced view of the child and his family. And yet such a global approach is of great importance in a condition which is likely to improve in the course of time whatever treatment is given (Rackemann and Edwards, 1952: Barr and Logan, 1964: Smith, 1971) and in which the potentialities for imposing secondary handicap and iatrogenic complications is immense. I make no excuse therefore for presenting a general paediatrician's view of asthma in childhood which is unlikely to satisfy any of the specialists.

The Atopic Infant

The word allergy originally meant any alteration in tissue sensitivity but its meaning has become restricted to signify only a heightened sensitivity. Anyone may become allergic if the conditions for sensitization are met but certain individuals are unusually easily sensitized. Such people are said to have the atopic constitution, although the precise nature of their difference from their non-atopic fellows is poorly understood. The atopic constitution is inherited and when both parents have a strong personal and family history of atopic disorders, the likelihood of their having an affected child is high, although the precise risk cannot be calculated because the mode of inheritance is not known. In such circumstances it is reasonable to keep the baby under close observation and to consider whether any untoward symptoms might not be allergic in nature. While acute gastrointestinal allergy may be manifest by vomiting, diarrhoea and colic in early infancy, the first indication that the child is atopic is usually the appearance of eczema at the age of a few months. This affects mainly the face, pursues an intermittent course over the next year or so, and then clears up or changes to a flexural type of eczema. While atopic eczema can be controlled with topical

corticosteroid hormones, it may erupt and die down periodically throughout the patient's life, constituting an annoyance by its itching and its unpredictable appearance, and in severe cases a significant handicap. Eczema is readily influenced by anxiety and tension, tending to subside during periods of tranquillity and to reappear suddenly when there is emotional stress.

In the first year food substances are more important than inhalants as allergens and, if there is evidence of hypersensitivity to a food, it is wise to withhold it or introduce it only in very small quantities.

The Atopic Toddler

About the time that the child begins to walk independently, he may begin to experience the first episodes of respiratory allergy. Whenever his upper respiratory tract is infected, he develops obstructive wheezing which may take several days to clear up. At this stage it is not easy to distinguish respiratory allergy from the obstructive type of bronchitis or bronchiolitis commonly caused by the respiratory syncytial and other viruses. A strong family history of atopic disorders, a tendency to wheeze when no acute respiratory infection is present, frequent prolonged attacks or other manifestations of allergy such as infantile eczema, all suggest that we are dealing with an atopic child rather than a non-atopic child with obstructive bronchitis. However, the clinical picture may not become clear until some months or years later, when the child begins to have typical attacks of asthma without obvious precipitating cause.

Unless there are sound reasons for doing so, it is unwise to announce the diagnosis of asthma before this stage. It may generate much anxiety in parents to whom the word conjures up a vision of long-standing disability and this may be quite unfounded, for the child may not develop asthma subsequently, even if there have been suggestive pointers in the history. Once established, the course of asthma is very variable, ranging from slight short-lived attacks which soon cease to occur to severe intractable asthma of long duration, causing disruption of the child's life. When it is clear that the child has asthma, a full explanation of the implications should be made to the parents: this takes time and will usually require to be spread over more than one session. It must be impressed upon them that their child is different only in respect of his allergy and is in every other way a normal child. An analogy can be drawn with the child who has poor eyesight, and must wear glasses, but is perfectly healthy otherwise. They should understand that he has inherited the atopic constitution, that nothing can be done about this and that it may show itself in a number of different ways. Once they fully appreciate that atopy is a part of the child's make-up, they will more readily accept that there is no quick "cure" of asthma and will not be unduly disappointed if other atopic manifestations appear later.

It can then be explained that much can be done to relieve symptoms and that there is no need to consider him as inevitably handicapped or unable to lead a reasonably normal life. It should be especially emphasized that he should not be kept off school when he has slight wheezing, that he should not be allowed to use his asthma to dodge unpleasant but necessary duties or events and that he can be allowed to do anything reasonable which is within his capacity, provided that

undue fatigue is avoided. It is remarkable how one child with sensible parents can play games outside on a cold day, often wheezing audibly but determined to take part, whereas another with lesser symptoms will be in bed surrounded by medicines and over-solicitous attendants. Parents who allow the latter situation to develop live to regret it, because the household comes to revolve round the asthma, which dictates the whole pattern of family life.

Most parents after adequate explanation will accept the reasons why they should be unusually firm with their asthmatic child. At the same time they must show proper sympathy and understanding, and must be taught to recognize when the clinical condition of the child really warrants confinement to the house and suitable therapy.

The Management of the Asthmatic Child

Given sensible, co-operative parents, more than half the battle against childhood asthma is won. In addition to parent counselling, the management of asthma implies environmental control, preventive measures and symptomatic relief.

General Considerations

I have no doubt from my own experience that substantial improvement can be effected in the condition of most asthmatic children if considerable time is devoted to the task. The beneficial effects tend to be in direct proportion to the time spent, but subject to the law of diminishing returns. I am therefore less certain that it is always justifiable to devote a great deal of time to the child with asthma, when medical manpower is limited and there are many other demands on professional skills. Moreover the large numbers of asthmatic children and the likelihood that most will improve and many ultimately recover must influence the amount of time that is spent. Such considerations go far to explain why asthma in childhood is not always optimally treated. Allergists and others can legitimately say that more could often be done but whether it should be done, to the inevitable detriment of other children when resources are limited, is another matter.

The long-term objectives of the physician treating a child with asthma should be to ensure that secondary handicap is not superimposed by faulty management – particularly parental over-protection – and to counter adverse effects on growth and development, for severe asthma can significantly restrict increase in height and weight (Dawson et al., 1969). The effect of the asthma on the lungs and chest wall (McNicol et al. 1970) should be watched closely and measures instituted if there is evidence of increasing damage. The amount of time lost from school and the extent to which social activities are limited must be kept under observation and action taken if the effect on school or social life becomes excessive. Beyond these basic principles, the benefit from treatment must be measured against the cost in time and money and the accompanying discomfort and inconvenience to the patient and his family. It is sometimes difficult to take the long view, especially for the family doctor faced with an acutely distressed child and parental expectations, but I am convinced that he must do so and must try to make the parents understand the reasons.

Recently at a dance my attention was caught by a tall, handsome young couple vigorously enjoying a reel. On enquiring who they were, I realised that I had looked

after both of them during very severe asthma in early childhood. I had spent many disturbed nights with the boy, whose father was a doctor, and had had great difficulty in persuading him not to resort to corticosteroids on such occasions. However, the parents had followed my advice and had been firm with their son and even a little harsh on occasion: as a result he had grown into a tall, healthy and pleasant-mannered young man who no longer suffered from asthma. The girl I had also seen on numerous occasions with severe attacks of asthma, and I recalled many long talks with her over-anxious parents, trying to persuade them to allow her to use her natural initiative and to do what she felt capable of despite her wheezing and breathlessness. My efforts had been successful, the parents increasingly adopted a sensible non-fussing approach to their daughter, and here she was at eighteen – a delightful attractive girl free from all but the slightest symptoms. These are only two striking examples out of many similar instances and I set them in my mind against those many other children who in their teens are no longer asthmatic but have serious personality disorders as the result of mishandling in childhood. I believe that excessive medication, over-scrupulous searching for causes and attempts at hyposensitization, and the imposition of unnecessary restrictions can be far more harmful to asthmatic children than the asthma itself. This is not of course to condemn therapy or to deny that there are some cases of very serious asthma which justify the most vigorous methods of treatment, but simply to urge that in most cases there is more virtue in watchful forbearance than in over-busy interference.

Environmental control

A stable supportive family home is the best environment for the asthmatic child, enabling him to live an equable life without the anxieties and stresses imposed by family friction, excessive parental expectations or sibling rivalries. Other sources of emotional tension outside his home, especially those relating to school, should be identified and removed or reduced as much as is feasible.

A child spends half his time in his bedroom and rendering this as free as possible from allergens goes a long way to improving the environment. House dust is an irritant and also strongly allergenic, usually containing a mixture of protein materials including the mite *Dermatophagoides pteronyssinus;* inspection of the bedroom may reveal many ways in which dust can be reduced – by removing dust-collecting carpets, bedding and toys, by substituting dust-repellent material for curtains and bedcovers, and by banning animal pets from the room. While it is seldom essential to get rid of a pet animal, it is on the whole wiser for atopic children not to keep animals, for their hair or dander is widely dispersed through the house and readily causes sensitization. It is not possible to rid a house completely of dust and extracting equipment of various kinds, apart from being expensive, may defeat its purpose by harbouring allergenic moulds. The house should be sparsely furnished and regularly dusted, the child being out of the vicinity when dusting takes place.

The search for allergens starts with a careful history, when any identifiable cause will usually become apparent or at least suspicion will be aroused. Skin testing can then be undertaken to confirm the suspicion. Random skin testing is seldom

useful and, even if some sensitivity is demonstrated, it does not follow that the protein concerned is causing the symptoms. If the history suggests an agent such as a particular food, animal or plant, and skin testing confirms the suspicion, it may be possible to remove the offending substance from the environment. Failing this, an attempt can be made to hyposensitize the child by a series of injections of the appropriate antigenic extract. If there is no strong lead from history and skin-testing, non-specific or multiple hyposensitization is unlikely to be beneficial.

Other preventive measures

The early treatment of respiratory infections with antibiotics may reduce the frequency of asthmatic attacks in young children, but the value of this is limited since so many infections are caused by viruses unresponsive to antibiotics. Simple breathing and postural exercises regularly carried out at home are of some help in improving posture and preventing thoracic deformity but occasional physiotherapy is of doubtful value and any benefit conferred does not usually justify complex or inconvenient arrangements to attend a clinic.

Antihistamine drugs are of little or no value in preventing or treating asthma. The introduction of disodium cromoglycate, on the other hand, constituted a real advance in the prevention of symptoms. Regular inhalation of the powder two or three times daily reduces both the number and the severity of attacks. The mode of action is not entirely clear but it appears to interfere with the mechanism of histamine release initiated by the antigen-antibody reaction. It is important that parents should realise that cromoglycate does not relieve symptoms but is a prophylactic, and should therefore be taken regularly rather than only when symptoms are present.

Drug therapy

The large number of bronchodilator drugs available makes it advisable to use only a few and become really familiar with their effects. Ephedrine is still a useful drug to start with and may control mild asthma for some time before more potent agents are needed. Thereafter orciprenaline, salbutamol or choline theophyllinate may be used to control wheezing. Aerosols in inhalers should be used with discretion if at all and pressurised inhalers are no longer advised since it seems certain that the recent increase in sudden deaths from asthma was due to the abuse of these. In severe attacks of asthma, adrenaline may be injected subcutaneously but it should be avoided if possible in young children because there is a risk of undesirable cardiac effects. Similarly, the inhalation of a mist containing isoprenaline may affect the heart: salbutamol has much less tendency to do so and is equally effective.

In general, it is unwise to embark on corticosteroid therapy, even in severe attacks of asthma, unless it is deemed absolutely necessary. Steroid dependence soon develops and the long-term nature of asthma increases the probability of eventual overdosage and dangerous side-effects such as osteoporosis or peptic ulceration. Moreover, the prolonged use of corticosteroid hormones results in growth arrest and possible ultimate dwarfing. The intention at the beginning may be to give only short courses at low dosage but the amount and frequency inevitably escalate in response to parental pressure. The risk may be less with ACTH

but here there is the additional risk of sensitization and the need to inject the hormone is a disadvantage in children. Synthetic ACTH (tetracosactrin) or inhaled beclamethasone may not have the same objections as the more familiar hormones, but it is still too early to assess their value fully.

Status asthmaticus

When an acute attack of asthma fails to respond to ordinary therapy and persists for many hours, status asthmaticus is said to exist. Aminophylline by intravenous injection may relieve symptoms but usually it will be necessary to use parenteral hormone therapy, e.g. intravenous hydrocortisone. The presence of pneumonia is often unsuspected in status asthmaticus and if there is any indication of infection the appropriate antibiotic should be given. Treatment with expectorants or nebulized mists is only marginally helpful in most cases and any benefit tends to be offset by the disadvantages.

Hypoxia is commonly present, even when there is no cyanosis, and the need for oxygen should be judged by the pO_2 of arterialised capillary blood, the aim being to prevent it dropping below 60 mm. Hg. If there is increasing retention of carbon dioxide, mechanical ventilation should not be postponed too long, for it is more likely to be effective and less liable to cause harm if it is started early. Modern methods of intermittent positive pressure ventilation by the nasotracheal route avoid the need for tracheostomy with its attendant hazards (Tunstall et al., 1968).

Research

The importance of asthma as a cause of acute illness and chronic disability and the relative inefficacy of treatment indicate the urgent need to find a more effective means of prevention. This implies better understanding of the atopic constitution and the asthmatic process and research is therefore essential. Four main lines of investigation appear to offer promise – the epidemiology of asthma and the characteristics of the asthmatic child: the nature of atopy and its allergic and immunological mechanisms: the metabolism and effects of the active mediators released in asthma: and the ways in which pulmonary function is disturbed. A great deal of work has been and is being done in these and other aspects of asthma: here I shall consider mainly those areas in which my colleagues and I have made some contributions.

Epidemiology of asthma

Hospital admissions for asthma have increased greatly since the earlier years of this century (Sheldon, 1958: Palm et al., 1970). Recent studies of the prevalence of asthma in the child population have shown that it is even commoner than hospital statistics suggest. Thus in the United States, surveys in Michigan and Indiana have shown prevalence rates of 4 to 5 per cent (Broder et al., 1962: Arbeiter, 1967). From Australia, Williams and McNicol (1969) reported a rate of 3.7 per cent. In the United Kingdom, surveys in the Isle of Wight (Rutter et al., 1970) and in Birmingham (Smith et al., 1971) recorded rates of 2.3 per cent: the National Child Development Study of some 16,000 children in England, Wales and Scotland found a rate of 3.1 per cent by the age of seven years (Davie et al., 1972): while our survey in Aberdeen (Dawson et al., 1969) showed that 4.8 per cent

of schoolchildren aged 10 to 15 years had asthma. Although these differences may be due to real geographical variations as well as to different definitions and techniques of case-finding, all the studies clearly indicate that asthma is a common disorder of childhood. It is also a major cause of chronic disability, causing significant handicap in about 25 children per 1,000 of the related population, and heading the list of physically handicapping conditions (Younghusband et al., 1970).

Data from the Aberdeen survey show that boys are more frequently affected than girls – a result in agreement with other studies (Smith et al., 1971: Davie et al., 1972): that over 80 per cent of asthmatic children experience their first attack before the age of five years: and that asthmatic children as a group are more intelligent than their non-asthmatic peers, despite their more frequent absences from school (Mitchell and Dawson, 1973). This survey also showed that children with severe asthma tend to come from larger families in poorer social circumstances: the greater overall prevalence of asthma in Social Class I as compared with Social Class V reported by Davie et al (1972) was not found in Aberdeen.

Allergic and immunological mechanisms

One characteristic of atopic people which has been clearly demonstrated is that they form reaginic antibodies with unusual ease. These antibodies, which have been shown to consist mainly of immunoglobulin E (Ishizaka and Ishizaka, 1970), become attached to the surface of histamine-containing cells – tissue mast cells and basophilic leucocytes. When the specific antigen interacts with two molecules of antibody, an enzyme system in the cell is activated and chemical mediators are released from the intracellular granules. These cause the mucosal swelling, secretion of tenacious mucus and spasm of bronchial muscle which are responsible for the respiratory obstruction in asthma.

The enzyme pathways in the cell have not yet been fully elucidated but may be related to the cyclic adenosine monophosphate system (cyclic AMP). Indeed Szentivanyi (1968) has suggested that the basic inherited defect of the atopic individual is deficiency of the intracellular enzyme, adenyl cyclase, with resultant malfunction of beta-adrenergic receptors in the bronchioles. When active mediators are released, adrenergic imbalance leads to contraction of bronchial muscle. While this theory is attractive and would explain the increased sensitivity of atopic people to bronchoconstrictors such as histamine, it cannot yet be accepted as proven.

One unanswered question about childhood asthma is how symptoms are precipitated by agents which are not allergens, such as emotional stress, cold and mechanical irritation. Some workers postulate that not all asthma in childhood is atopic and that there is a distinct type of psychogenic asthma with a different mechanism of action. While there is no conclusive proof one way or the other, the balance of evidence favours the view that all childhood asthma is mediated through the same pathway. When this has been facilitated by frequent antigen-antibody reaction, it becomes highly responsive to all sorts of stimuli, including a variety of psychological and physical agents, which can then trigger the release mechanism without the need for further participation of antigen. For all practical purposes, I believe that every child with asthma should be considered as having

the atopic constitution, i.e. that all childhood asthma is extrinsic in type, regardless of the fact that it is not always possible to identify the offending allergen or demonstrate an increase in reaginic antibodies (Wood and Oliver, 1972).

Metabolism of active agents

It has been known for many years that histamine is involved in the allergic process and in 1951 Schild and his colleagues proved that it participates in the production of human asthma. Evidence that asthmatic people are unusually sensitive to histamine, that levels of histamine in whole blood vary more in asthmatic than in non-asthmatic people, and that corticosteroid hormones both relieve asthmatic symptoms and cause profound changes in numbers of histamine-containing cells and the amount of histamine in body fluids (see Code et al., 1964: Porter and Mitchell, 1972), all suggested that the study of histamine metabolism would yield the answer to the riddle of asthma. From time to time major alterations in histamine metabolism in asthma have been reported but few have withstood closer scrutiny.

The report by Rose and his associates (1950) that there was a great outpouring of histamine in the urine in asthma stimulated many studies of urinary histamine but the finding was never confirmed (Code et al., 1964). Since only about 1 per cent of extrinsic histamine is excreted in the urine unchanged, only massive alterations in histamine metabolism would be demonstrable in this way. If considerable quantities of histamine were being released in the body in acute asthma, an increase in plasma levels might be expected, but no such increase was found by Porter and Mitchell (1970), who showed that, when very sensitive methods were used, the plasma level remained consistently below 1 ng. per ml.

The catabolic pathways of histamine were elucidated by Schayer and Cooper (1956), who showed that methylation was the principle pathway in man. Subsequently great interest was aroused by the work of Kerr (1964), who reported that end-products of methylation virtually disappeared from the urine in status asthmaticus, suggesting a block somewhere in the degradation process. However, our own recent work (Thom et al., 1973) has not substantiated these results, for we have shown that children with acute asthma methylate histamine efficiently and indeed excrete rather more methyl imidazole acetic acid than do control children.

One major difference in the handling of histamine by asthmatic people is in the histamine-binding capacity of plasma protein (histaminopexy), attributed to the presence of a gamma globulin named plasmapexin I (Laborde et al., 1959). Parrot and his colleagues (1964) showed that histaminopexy is greatly reduced in acute asthma and this has been confirmed in our laboratory (Porter and Smith, 1969), although the degree of reduction was not as great as that reported by the French workers.

There is clearly much still to be learned about the role of histamine in asthma but sufficient is known to indicate that it does play an important part and that there is some fundamental difference in respect of histamine which distinguishes atopic from non-atopic people. Whether this difference is due to abnormal pro-

duction, metabolism, or tissue response is not yet clear but the evidence suggests that more than one of these is involved.

In contrast with the vast amount of research into the role of histamine in allergy, work on slow-reacting substance (SRS-A) in man has been extremely scanty, and in consequence not much more is known now than when Brocklehurst (1960) and Chakravarty (1960) first studied it. This is due at least in part to the difficulty of working with a substance which is very unstable in the laboratory and correspondingly difficult to measure. It is known that SRS-A appears with histamine in response to the antigen-antibody reaction, that its action persists much longer than that of histamine and that it causes a sustained contraction of smooth muscle (Brocklehurst, 1960: Sheard et al., 1967: Ishizaka et al., 1970). It seems reasonable therefore to suppose that released histamine initiates the bronchial changes in acute asthma and that newly formed SRS-A maintains them thereafter (Brocklehurst, 1970). It is possible, however, that newly formed histamine may also play a continuing part (Kahlson and Rosengren, 1968). There is a small amount of evidence that kinins are actively involved in human asthma. Thus Abe and his colleagues (1967) showed that the circulating level of plasma kinins is significantly increased in most patients with severe asthma. Increased kinin-like activity has also been found in the nasal secretions of patients with allergic rhinitis (Dolovich et al., 1970). Whether other substances, such as 5-hydroxytryptamine, acetyl choline, or prostaglandins play any significant part in the genesis of asthma is still uncertain (Collier, 1970) and much more work is needed before their importance can be assessed.

Pulmonary Function

The practical value of pulmonary function tests in asthmatic children has been discussed recently by Weng and his associates (1969). They concluded that measurement of the expiratory flow rate using the Wright flowmeter is the most satisfactory way of assessing the child's response to therapy. Tests on asthmatic children have shown that the degree of impairment of respiratory function as measured by such parameters as forced expiratory volume in one second (FEV_1), peak flow rate (PFR) and maximum expiratory flow volume (MEFV) is directly related to the severity of the asthmatic symptoms (Dawson et al., 1969: Hill et al., 1972). Whereas children with chronic asthma usually have normal pulmonary resistance during symptom-free periods, infants with recurring wheezing show a persistent increase in airways resistance unresponsive to sympathomimetic drugs (Phelan and Williams, 1969). While such studies of pulmonary function are unlikely to lead directly to new preventive methods, by clarifying the mechanisms of asthma and the response to drugs they can be expected to promote that deeper understanding of the disorder which is essential if the approach to prevention is to be soundly based.

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LIVER BIOPSY IN GENERAL MEDICINE
Ten Years Experience

by

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THE taking of liver biopsy is too often confined to specialised units and is insufficiently used in general medical wards. This records experience of 100 cases in a general medical unit over a ten-year period and illustrates its value in diagnosis in that it may sometimes avoid prolonged investigation or even laparotomy. The technique described is now free from significant risk if some necessary precautions are taken.

Technique

Patients should have a prothrombin index at least 70 per cent and it is desirable that their blood group be known. Norris, Singh and Moutuschi (1958) described the technique using the needle developed by Menghini (1957) and the general procedure was described by Sherlock (1963).

On the day previous to the procedure the patient receives vitamin K_1 (Konakion) 10 mg. by injection and one hour before operation diazepam (Valium) 10 mg. In most patients, some difficulty was encountered in penetrating the skin with the cutting needle of Menghini and it was found easier to cut through the skin with a small scalpel. The needle itself requires re-sharpening by the makers after 10 biopsies. A proper syringe with metal barrel and guard is employed to obtain adequate suction. The container for transmission of the specimen must be filled to the top with 10 per cent formalin so that the fragile tissue does not sustain trauma by shaking in transit. These practical points are not perhaps sufficiently emphasised by all workers.

Results

These can be divided into groups where the biopsy provided a useful diagnosis, those revealing only normal liver tissue, those on which no diagnosis could be made and those in which the material was insufficient. These groups are summarised in Table I.

Biopsy material valuable

Diagnostic information was obtained in 55 cases and considering that the technique was without any complications the procedure appears justified. The problems solved saved much unnecessary investigation, hospital time and even laparotomy, and all without significant upset to the patient. The conditions diagnosed are enumerated in Table I and some conclusions can be drawn as to the disease process where biopsy was found of value.

TABLE I. *Biopsy Diagnoses*

MATERIAL VALUABLE (53)			
Liver Diseases			34
Cirrhosis			
Micronodular	8		
Macronodular	3		
With haemolytic anaemia (Banti)	1	14	
Haemochromatosis	1		
Cardiac	1		
Hepatitis			
Active (various stages)	10		
Focal necrosis	3	14	
Toxic (para-aminosalicylic acid)	1		
Obstructive		6	
Carcinoma			14
Reticulosis			5
MATERIAL NOT OF DIRECT ASSISTANCE (47)			
Normal			36
Significance missed			1
Not diagnostic			4
Inadequate or fragmented tissue			6

Liver Disease. A diagnosis of the type of cirrhosis can often be made and the progress and complications anticipated. Various stages of activity in aggressive hepatitis can be assessed in conjunction with other tests as well as a specific diagnosis made. Limitations in the diagnosis of necroses or infections of the liver may be imposed since in many instances the patient is icteric and the prothrombin level too low to allow the biopsy to be performed without risk. However, when possible the procedure was of great help.

Carcinoma. Liver biopsy was extremely successful and established the diagnosis in advanced malignancy. Thus in 14 out of 16 instances the diagnosis of secondary deposits was confirmed preventing unnecessary investigation or laparotomy. An illustrative case may be quoted. A sea captain aged 46 who previously had been in good health had a sudden gastric haemorrhage at sea and was flown home from the Carribean. His liver was palpable and barium meal was negative. The liver biopsy showed carcinomatous metastases consistent with a gastric primary. His wife refused to accept the diagnosis and three months later, after a further haematemesis he was admitted elsewhere. He died after one week and various procedures, such as Wangensteen's tubes, eight pints of blood and numerous

investigations, failed to provide a diagnosis or afford relief. Autopsy confirmed the original diagnosis, a small primary being present in the stomach with secondary deposits in the liver obstructing the portal vein.

Reticulosis. The diagnosis was obtained for a colleague, a haematologist, in five patients out of eight where a reticulosis was suspected and in whom the diagnosis was not obtainable by bone marrow biopsy, blood or x-ray investigations.

Post Hepatic Obstruction. Surgical or obstructive jaundice was proven in six instances at an early stage in their investigation and the appropriate intervention undertaken saved both time and uncertainty. In one a culture of anaerobic streptococci led to the initiation of treatment with the correct antibiotic and a successful outcome. In another the diagnosis of cholangitis and biliary cirrbosis with ascites was confirmed six months later at autopsy.

Biopsy material reported as normal

In thirty-six patients the biopsy was reported as normal. It might seem that the procedure was not directly of clinical assistance. However, in retrospect the minimal risk involved was justifiable, and these cases are enumerated in Table II.

TABLE II. *Liver Biopsy Normal* – Total 36

Carcinoma	3
Reticulosis	3
Idiopathic Anaemia	4
Other Blood Disorders	2
Cardiac Disease + Hepatomegaly	7
Gallstones + Hepatomegaly	3
Portal + Splenic Vein Thrombosis	2
Hepatomegaly + Diabetes	1
Hepatomegaly + Alcoholism	1
Hepatomegaly + Abdominal Inflammation	2
Attempted Diagnosis of Obscure Conditions	5

Carcinoma. Two cases of gastric carcinoma were missed and three instances of carcinomatosis suspected were later proven at autopsy to be of bronchogenic origin. In all three patients biopsies were repeated with negative results. Against this failure the finding of a normal liver in a female with pelvic carcinoma was of help to the gynaecologist who treated the local condition with more confidence and with success by surgery.

Blood Diseases. Six patients with obscure anaemia or thrombocytopenia and polycythaemia were biopsied at the request of the haematologist. These were done as a last diagnostic resort. In three instances the patient later turned out to have reticulosis which was confirmed at post-mortem but missed by biopsy. This, however, must be weighed against the fact that five other patients with reticulosis were diagnosed by this means and treatment instituted.

Cardiac Disease. Biopsy was done on seven patients with what appeared to be a disproportionate enlargement of the liver in long standing cardiac failure due to various conditions. It helped to exclude other causes.

Gallstones. The finding of normal liver tissue in patients presenting with jaundice and later proven to have gallstones in three instances was useful in that it helped to exclude an intrahepatic cause and directed attention towards a correct diagnosis at an early stage.

Portal Vein Thrombosis. Two patients with haematemesis, including one with splenomegaly, had normal biopsies and were later proven at operation to have thrombosis in the splenic and portal veins. The procedure could not be expected to be helpful here.

Hepatomegaly and Alcoholism. A normal biopsy was in one instance a diagnostic failure in that the patient died later from haemorrhage associated with oesophageal varices in presumably a liver cirrhosis. The specimen obtained was poor and fragmented.

Palpable Liver and Diabetes. A normal biopsy was of help in the patient whose many symptoms were eventually found to be on a psychiatric basis and the liver condition proven to have no clinical significance.

Miscellaneous Conditions. Inflammatory abdominal conditions, such as diverticulitis with associated sub-phrenic abscess, tuberculosis, sarcoidosis and a peculiar illness with an erythema multiforme gave normal biopsies. These were performed in an attempt to reach a diagnosis but either there was no actual liver involvement or the biopsy needle did not make contact with the affected area.

Biopsy material abnormal but significance missed

Viewing one case in retrospect the reported presence of large amounts of glycogen in the liver cells might have suggested an islet cell tumour presenting with hypoglycaemic symptoms and hepatomegaly. At laparotomy the condition was malignant and associated with liver secondaries.

Inadequate or fragmented tissue

Six specimens were classified under this label (Table III). It should be stated that the pathologist gave a hint of some toxic condition in one, which showed foamy cytoplasm, later proven to be associated with tuberculous bone marrow, and in another suggested the possibility of a reticulosis, confirmed at autopsy.

TABLE III. *Results of Poor Technique* – Total 6

Specimen	*Suggestion in Report*	*Final Diagnosis*
Poor or Fragmented	Foamy Cytoplasm	T.B. Bone Marrow
,,	Probable Reticulosis	Lymphosarcoma
,,	—	Nodular Hyperplasia
,,	No Abnormality	Portal Cirrhosis
Inadequate	—	Infectious Hepatitis
,,	—	Portal Cirrhosis

Summary

In a general medical unit the absence of complications and the help to diagnosis made liver biopsy in 100 selected patients well worthwhile.

Patients did not complain of discomfort during the procedure, and, when necessary, the rare request for repeat biopsy was met with favourable response from them. The absence of any complications in the series, regardless of age, sex or underlying pathology indicates the relative safety with which the investigation may be undertaken.

An adequate specimen in ninety-four cases and some indication of disease process in three poor specimens may well be considered a reasonable result for the occasional operator and provides encouragement for the procedure to be more widely adopted.

From the biopsy reports and ultimate outcome it is obvious that liver biopsy is of greater value when abnormal rather than when normal tissue is obtained. As a diagnostic aid it is more reliable in diseases which tend to involve the entire liver rather than those with a patchy distribution. However, in the present series a positive diagnosis was reached in 87 per cent of cases of carcinomatosis.

It still remains a diagnostic aid to be used with clinical discernment and not at random when diagnosis is difficult.

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LAPAROSCOPIC STERILIZATION

A Review of 238 Cases

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IN RECENT YEARS laparoscopic sterilization has become a popular method of active birth control. Between 1971 and 1973, 238 patients were treated by this technique in Ards Hospital. This paper reviews these patients, their selection, the operative procedure employed, the results, the complications and the operative failures.

Selection of the Patients

A request for sterilization was furnished by general practitioners and the operations were performed under the National Health Services. The patients were booked and their names placed on the waiting list. A number of surgeons shared the operative responsibility. Of 238 patients, 65 (27.2 per cent) were between 20 – 30 years, 140 patients (60.0 per cent) were between 30 – 40 years and 33 patients were between 40 and 50 years. Most of these patients were taking the contraceptive pill for periods of three to seven years, although a small number of couples were using the sheath for birth control. Many suffered chronic cervicitis. Patients who requested post partum sterilization were operated on six weeks after delivery. Here this replaced post partum tubal ligation as it was thought to reduce the post partum depression frequently met with in newly delivered mothers. It replaced post partum laparoscopic sterilization and avoided risk of injury to the bulky uterus and oedematous tubes (Whiteley, 1971).

Table

Para.	0	1	2	3	4	5	6	7	8	9	10	unspecified
Number	4	9	58	66	42	16	9	1	1	1	1	31

The table shows the parity of the patients. The majority of the patients had two to four children. Four nulliparous patients were sterilised on psychiatric grounds and one of the four had termination of pregnancy at the same time. Patients who suffered chronic cervicitis were treated at operation by cervical diathermy or diathermy conisation at operation.

Procedure

At operation the technique of Steptoe (1967) was followed. An assistant carried out dilatation and curettage and if necessary cauterisation of the cervix. He could

also manipulate the uterus from the vagina. With the patient in the Trendelenberg position, a small transverse preliminary incision was made just below the umbilicus. Pneumo-peritoneum was obtained using de Verres cannula through which 2½ to 3 litres of carbon dioxide were introduced. An incision was then made in one iliac fossa, more often the right. The diathermy forceps were introduced and each fallopian tube was burnt twice and divided. The fallopian tubes were re-inspected and, provided all was well, the instruments were removed deflating the peritoneal cavity in the process. The skin incisions were stitched with braided silk which was removed at a later date in the hospital or by the general practitioner or district midwife. The difficulty that was sometimes met with to build up the pneumo-peritoneum in obese patients was obviated by not lifting the abdominal skin while the needle and the trocar and cannula were introduced.

Surgical Complications

Apart from the two patients who developed complications, all the patients were discharged 48 hours after the operation. They were followed up by their general practitioners, who all replied promptly to a questionnaire, and no minor complications were recorded.

Case 1: *Perforation of the small bowel*

A 34-year-old mother had three normal deliveries. She had laparoscopic sterilization, dilatation and curettage and removal of the intra-uterine contraceptive device. She was discharged next day. She was re-admitted on the next day with acute lower abdominal pain. Bowel sounds were absent. Laparotomy was performed and acute ulceration of the terminal ileum was found. The involved area was excised and re-sutured. She was given Noxyflex saline drip into the peritoneum and Ampicillin post-operatively. She made a satisfactory recovery. The pathologist reported "Acute ulceration with perforation of intestine (ileum). No polyarteritis." The pathologist stated that study failed to recognise any specific features at the perforation site. The patient was discharged on the tenth post-operative day with a haemoglobin 13.2 gm/100 ml.

Case 2: *Acute salpingitis with broad ligament haematoma*

A 24-year-old mother, married, who had had no miscarriages, and had four normal deliveries, all children alive and well. She had laparoscopic sterilization and dilatation and curettage and conisation of the cervix. She was discharged the following day, but she was re-admitted on the seventeenth post-operative day. On admission she was suffering from heavy vaginal bleeding and acute lower abdominal pain. She was examined vaginally under general anaesthesia. The bleeding cervix was burnt by diathermy and laparotomy was performed. A small broad ligament haematoma was found and the appendix was removed. She made a satisfactory recovery. She was discharged on the tenth day with haemoglobin 11.5 gm/100 ml. The appendix showed a few thread worms.

Operative Failures

Case 1: *Ectopic pregnancy*

A 40-year-old mother, who had three normal deliveries, was on the pill for five years. She had dilatation and curettage, diathermy of the cervix and laparoscopic sterilization. She was discharged the following day. She was re-admitted four months later with severe crampy lower abdominal pain. She was pale with weak pulse, a B.P. 90/60 and haemoglobin 9.6 gm/100 ml, and she had a positive pregnancy test. On examination she had rebound tenderness and guarding rigidity of the lower abdomen.

The cervix was very tender and the uterus ill-defined. A laparotomy through a Ffannestiel incision was performed and a ruptured ectopic pregnancy confirmed in the left tube. She had left salpingo-oophorectomy and was discharged after ten days with a haemoglobin of 11.2 gm/100 ml. The pathologist mentioned "Probably the ectopic pregnancy had been implanted in the fimbrial end of the tube and has been expelled. No evidence of predisposing pathology in the fallopian tube."

Case 2: Normal pregnancy

A 29-year-old mother after four normal deliveries had a laparoscopic sterilization. She was re-admitted four weeks later with amenorrhoea dating since operation and a positive pregnancy test. Normal pregnancy was terminated by dilatation and evacuation and a repeat laparoscopic sterilization was carried out at the same time. She made a satisfactory recovery and was discharged with a haemoglobin of 12.6 gm/100 ml. Both round ligaments had been cauterised in the first instance.

Discussion

A series of 238 laparoscopic sterilizations have been reviewed. There were two surgical complications and two operative failures. The method resulted in permanent sterility with two exceptions. Patients required to remain in hospital for only 48 hours.

Neely and El-Kady (1972), in their series of puerperal laparoscopic sterilization, reported two cases who suffered from hypotension, two cases of bleeding from broad ligament vessels and two cases who developed bleeding from the fundus of the uterus due to trauma from the pneumo-peritoneum needle.

Levinson, Schwartz and Saltzstein (1973) reported two cases of perforation of the small bowel which occurred during tubal sterilization by cautery through the laparoscope. Their report indicates the clinical course of this unusual and serious complication, emphasises prophylactic measures to avoid it and recommends immediate operative intervention with small bowel resection as the appropriate therapy. Coagulation necrosis results either from applying the cautery directly or from sparking. It is recommended that all equipment should be checked and must be kept in perfect working condition. It is also recommended that the cautery attachment should be connected only during cauterisation.

I wish to thank Dr. F. G. Grant, F.R.C.O.G., for his encouragement. I wish also to thank Dr. J. H. N. Ferris, M.R.C.O.G., who allowed me to operate on his patients. I wish to extend special gratitude to all the 29 general practitioners who helped with this survey and to the medical and surgical teams of Ards and Bangor Hospitals. Also, I thank Miss A. Cowie, the departmental secretary who dealt with all the filing and correspondence.

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EXPERIENCE OF A CLINIC FOR SEXUAL DISORDERS

by

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THE PURPOSE of this article is to describe a service which has been developed in the Department of Mental Health, Belfast City Hospital, over the last two or three years. The service is devoted to the investigation and treatment of a wide variety of sexual disorders.

Selection of Cases

Some idea of the work of the clinic can be gained from the Table which summarizes the details of the patients seen in the last calendar year. The clinic is "family" orientated and when a patient is married the spouse is investigated as intensively as the person who presents with the problem. This emphasis on assessment of spouse considerably increases the work undertaken by the clinic, but we feel the extra effort is justified both by own experience and the emphasis placed upon the importance of spouses in sexual disorders by other workers (Graham, 1971; Cooper, 1969; and Feldman, 1971).

A number of comments on the Table appear appropriate. Firstly, the rather high number of impotent patients without spouses is due to the fact that, in our sample, twelve of the patients were not currently married (either being divorced, widowers, or single).

Table

Number and diagnosis of patients and spouses seen at a clinic for sexual problems over a one-year period

Diagnosis	*Patients*	(%)	*Spouses*
Homosexuality	20	(22)	—
Frigidity	15	(16)	12
Impotence	37	(40)	22
Other	14	(15)	4
Uneventuated	6	(6)	4

Secondly, in the period from which we have drawn our sample, there has been an unusually low referral rate for homosexuality. Thirdly, it will be noted that only one female homosexual presented at the clinic during this time. This is in line with our own experience from previous years and agrees with the reports in the literature which indicate a low referral rate of female homosexuals. Fourthly,

the "other" group includes trans-sexuals, trans-vestites, exhibitionists and a few unusual sexual disorders.

INVESTIGATIONS

The following investigations are carried out in the clinic:

(1) The patients have detailed psychiatric and physical examinations and the spouse is interviewed by the psychiatric social worker who is a member of the clinical team.

(2) Psychological investigations. Both patient and spouse are assessed, using four kinds of psychological tests:
   (a) standard tests of personality.
   (b) specific tests of sexual interest, orientation and sexual anxiety
   (c) tests of attitude to sexual behaviour and to other important social functions
   (d) measures of marital interaction and adjustment.

(3) Psychophysiological investigations. A number of psychophysiological investigations are also carried out. These involve monitoring the patient's physiological responses to a standard test situation. Heart rate, respiratory rate, skin resistance, E.M.G., and (in males) penile blood flow are monitored, using an 8-channel polygraph, while the patient is either listening to a standard auditory alerting signal or looking at slides of sexual material. From these investigations, two kinds of information are extracted:
   (a) measures of general sexual arousal, orientation and sexual anxiety
   (b) psychophysiological tests of general neuroticism (this test uses the rate of habituation of the altering or orientating reflex).

The psychophysiological tests provide information similar to, but at a different level from, the paper and pencil tests described above. An important theoretical aspect of our work is to investigate what relationships, if any, exist between these two levels of measurement.

It is not intended in this paper to present details of the results of our investigations. The conclusion of our work with homosexuals have been reported elsewhere (Quinn et al, 1973a), but a brief outline of the general results appears appropriate to illustrate the usage of tests which may otherwise be unfamiliar to some readers.

Sexual orientation measures

The Sexual Orientation Method (Feldman et al, 1966) discriminates well between homosexual and non-homosexual groups (such as patients suffering from impotence). Perhaps a useful practical conclusion from this is that homosexual interest as measured by this test is not raised among patients with other sexual disorders.

Personality measures

It would appear from our results that some aspects of personality distinguish between the groups of patients and patients' spouses which we see at the clinic; and that when measures of sexual orientation and personality are combined, using multivariate statistical techniques, the differences between all the groups of patients we see become quite marked.

Psychophysiological assessment techniques

These techniques are much more complicated than the paper and pencil methods, and our confidence as to their clinical use is more limited; however, the psychophysiological measure of sexual orientation described above does discriminate well between homosexual and non-homosexual groups. Again it would appear that at this different level of measurement there is no evidence that people with sexual disorders other than homosexuality have substantial homosexual interest.

It would be possible to present further data about impotent and frigid individuals, but, at the time of writing, the analysis of the data with these groups is less complete and it appears appropriate not to present details of these results.

Treatment Methods

We will now briefly describe some of the treatment methods used in the management of patients referred to the clinic.

Homosexuality

A number of techniques are used in the management of homosexuality. It is not possible in the space available to give more than a cursory outline of the methods available.

Aversion therapy

This is the best known and most controversial method of treatment. Numerous aversion techniques exist, all based on learning principles derived from animal experiments. In general, such techniques set out to form an association between homosexual arousal and a noxious stimulus (such as electric shock). A review of these treatments may be found in a recent book by Rachman and Teasdale (1969). The most extensive series of cases is reported by Feldman and MacCulloch (1971) who claim that over sixty per cent of homosexuals will respond to aversion therapy. However, they emphasise that patients who are exclusive life-long homosexuals do not respond well to aversion therapy. In contrast, we have a particular interest in the use of methods for producing heterosexual interest in exclusive homosexuals, and in fact we rarely use electrical aversion therapy, at least as a treatment of first choice, with any of the patients referred to our clinic.

Desensitisation

This technique is widely used for the treatment of many conditions such as homosexuality, frigidity, impotence and simple and complicated phobias. Its use in homosexuality is described by Bancroft (1970) who claims that about a third of homosexuals respond favourably to desensitisation. It is interesting that Bancroft found no differences in outcome between groups of patients treated with aversion and desensitisation, and his overall treatment results would be therefore less optimistic than those of Feldman and MacCulloch (1971).

Desensitisation attempts to reduce anxiety associated with situations which the patient is assumed to be afraid of. Its use in homosexuality is based on the hypothesis that many homosexuals fear heterosexual relationships (are 'heterophobic').

Techniques for conditioning heterosexual arousal

Two techniques have been developed in this department (Quinn et al, 1973b). One procedure produces or increases heterosexual interest by Pavlovian conditioning; the second is a complicated technique which attempts to 'reward' physiological responses in the presence of heterosexual stimuli. A trial supported by the Medical Research Council is under way, comparing the efficacy of these two techniques. While the results are not complete, it is clear at this stage that some exclusive homosexuals can develop heterosexual interests when treated by either of these two methods.

In view of recent editorial comment (World Medicine 1973), it is useful at this stage to state our policy with respect to the treatment of homosexuality. We do not approach homosexual behaviour with any particular value judgement. Obviously, we have no interest in coercing individuals to change their sexual orientation; but in distinction to some, we believe that there are individuals who find life in their own particular society too difficult because of homosexuality. We believe that these people have the right to be offered an opportunity to learn a new sexual orientation, particularly as methods are now available which do not involve aversion therapy.

Frigidity

We have been treating frigid patients for over eighteen months. The small number appearing in the current figures can be explained by the fact that a colleague, Dr. E. O'Gorman, has seen quite a number of these patients outside the clinic. Her work, however, has been carried out in close association with us and frigid patients are now routinely included in the sexual problems clinic.

Treatment methods in frigidity depend upon the use of one or other of the varieties of systematic desensitisation. As we have already indicated, great emphasis is laid upon involving the spouse in the investigation and treatment. One interesting method used is the desensitisation of the patient in a group setting (O'Gorman et al, 1972). This procedure appears to be very efficient, and appears to be effective in managing some patients with frigidity.

Impotence

Impotence is the most difficult to treat of the three problems discussed in this paper. Two main techniques are under investigation at the moment—the desensitisation of heterophobic responses and positive conditioning of heterosexual interest (using the technique already mentioned above with respect to homosexuality). Our own experience supports the literature in sugesting that approximately one-third of impotent patients are helped by desensitisation. It is too early to say whether or not other procedures – such as positive conditioning – will prove to be more effective than desensitisation in the management of this difficult condition.

SUMMARY

This paper attempts to describe a relatively new clinical development in Northern Ireland. Cases have been referred from all over the province, and by organizing a clinic system, it has been possible to keep waiting lists down to a very short time.

The clinic has also proved very useful for teaching medical students, clinical psychology students and social work students. We hope that, in the future, it will be possible to extend this service, which appears to be valuable in helping people with sexual disorders and also provides a setting for the collection of extensive data for research into these problems.

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ORCHIDOPEXY USING A DARTOS POUCH

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THE undescended testis is more susceptible to trauma (Gross and Jewett 1956) and to malignant change (Collins and Pugh, 1964; Altman and Malament, 1967) than the normally placed testis. It has been shown that degeneration in an ectopic testis begins at about the age of 5 years (Scorer 1967; Cohn 1967). It is therefore generally accepted that orchidopexy should be carried out at around the age of 5 years.

The objects of surgery in this condition are threefold:

1. To secure adequate length of spermatic cord and vessels so as to deliver the testis into the scrotum without tension.
2. To anchor the testis in the scrotum so that it remains there indefinitely.
3. To deal with any associated condition such as an inguinal hernia.

The operation described by Whitaker (1970) and Pryn (1972) of anchoring the testis in a dartos pouch, fulfils these requirements, as well as having some advantages over other techniques.

Operative Technique

Mobilisation of the testis and cord structures is carried out in the usual way through a groin incision. When adequate mobilisation has been achieved, a finger is passed from the inguinal canal down into the scrotum, fashioning a tunnel through which the testis can be passed, and dilating the scrotum. At the apex of the scrotum on the appropriate side, an incision is made about the size of the testis, through skin only. The skin edges are undermined, using blunt dissection, so that a pouch is made between skin and dartos muscle. A pair of forceps is then passed into the scrotum from above, and punched through the dartos muscle underlying the scrotal incision. The testis is then drawn down into the scrotum and through this opening in the dartos. The dartos is repaired around the cord with catgut, so that the testis cannot retract. The scrotal skin is closed over the testis, and the inguinal incision is repaired in the usual way.

Discussion

A number of techniques have been described for anchoring the testis in the scrotum. Some are now mainly of historic interest (Keetley 1894, Torek 1909, Ombrédanne 1910, Browne 1933). At present, the most popular method is to pass a nylon suture through the tunica albuginea at the lower pole of the testis, pass the suture through the scrotum from within out, and anchor it to one or other thigh (Cabot and Nesbitt 1931, Wangensteen 1932). This method has several disadvantages.

1. The anchoring suture must be left in place for at least 5 days, increasing the risk of infection, and requiring a fairly lengthy stay in hospital.
2. The tension on the testis varies with the movement of the patient, and may at times be severe, risking possible damage to the testis and its vessels.

3. Removal of the anchoring suture may lead to retraction of the testis, a situation which will not correct spontaneously.

In addition, the inexperienced surgeon may be tempted to put excessive traction on the anchor suture, in order to make it lie low in the scrotum, leading to possible damage to the testis or vessels.

The dartos pouch technique, where the traction exerted is both gentle and permanent, does not have any of these disadvantages.

TABLE

Case No.	*Age*	*Side*	*Duration of of stay in hospital*	*Length of follow-up*	*Comments*
1	7 yrs	Bilateral	5 days	13 months	Bilateral inguinal herniae
2	8 yrs	Right	3 days	14 months	Right inguinal hernia
3	8 yrs	Left	2 days	8 weeks	
4	8 yrs	Right	2 days	7 weeks	
5	10 yrs	Left	3 days	12 months	
6	9 yrs	Right	2 days	13 months	Testis high in scrotum after operation
7	9 yrs	Left	2 days	14 months	
8	12 yrs	Left	3 days	6 weeks	Right inguinal hernia
9	11 yrs	Right	3 days	7 months	
10	6 yrs	Left	2 days	7 weeks	
11	28 yrs	Right	3 days	12 months	R.I.H. repaired aged 7

The table shows a personal series of 12 orchidopexies in 11 patients using the dartos pouch technique. In all of the cases the testis was well down in the scrotum at follow-up, varying from 6 weeks to 14 months. In case 6, the testis could only be mobilised into the upper part of the scrotum at operation, but at follow-up it was found to be in the lower part of the scrotum. This finding appears to bear out Pryn's contention that the constant contraction of the dartos muscle exerts continued gentle traction on the testis, resulting in further spontaneous descent. Because of this, the technique may also be useful in cases of high undescended testis, where insufficient length can be obtained to bring the testis to the bottom of the scrotum. This situation is usually dealt with by operating in two or more stages. Brender and Wulfsohn (1967) have suggested that sufficient length can be obtained by dividing the spermatic artery, after suitable precautions to avoid ischaemia of the testis. Using the dartos pouch method, it may only be necessary to mobilise the testis into the upper part of the scrotum, relying on the traction of the dartos muscle to complete the descent.

The final advantage of this technique is demonstrated in the table. With the exception of case 1, which was bilateral, none of the patients spent longer than 3 days in hospital after the operation. Using this method, there is probably no reason to detain any patient, including the bilateral cases, in hospital more than 24 to 48 hours post-operatively.

Summary

A technique for orchidopexy using a dartos pouch is described. It is claimed to have several advantages over other techniques.

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A PATHOLOGICAL STUDY OF IDIOPATHIC HAEMOCHROMATOSIS AND ITS RELATIONSHIP TO SIDEROSIS IN LIVER CIRRHOSIS

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HAEMOCHROMATOSIS refers to a general increase in body iron stores with tissue damage. The pathological criteria used for the diagnosis of haemochromatosis were those proposed by MacDonald and Mallory (1960). They were as follows: —

1. Cirrhosis of the liver of a "portal type".
2. Excessive iron deposits in hepatic parenchymal cells, in connective tissue, and in bile duct epithelium.
3. Pancreatic fibrosis and haemosiderosis.
4. Parenchymal iron deposits in other organs of the body.

MacDonald (1964) expressed the view that haemochromatosis was related to portal cirrhosis and was not a specific disease entity. In 1965, MacDonald reviewed the incidence of haemochromatosis in different geographical areas and found the figures to be low in Ireland. As to the aetiology of idiopathic haemochromatosis it had been suggested by Biggs and Davis (1963) that haemochromatosis may be of pancreatic origin as oral pancreatin was supposed to depress iron absorption. The present study was therefore performed to determine the relationship of haemochromatosis to liver cirrhosis with siderosis, and also to study its incidence and presentation in Belfast, Northern Ireland. The role of the pancreas in hepatic siderosis was also reviewed.

Materials and Methods

Three groups of cases of cirrhosis of the liver including idiopathic haemochromatosis were selected from autopsies performed at the Royal Victoria Hospital, Mater Infirmorum and City Hospitals, Belfast, from January 1, 1938 to December 31, 1966 inclusive. During this period 22,050 autopsies were performed. The clinical records were reviewed, and all histological material was re-examined. A control series of autopsies with extrahepatic disease were also studied with regard to the degree of liver siderosis and pancreatic fibrosis. The sections were stained with haematoxylin and eosin (H & E) and Perls' reaction for haemosiderin. Liver cirrhosis was diagnosed according to the criteria postulated at the Fifth Pan-American Congress of Gastro-enterology in Cuba (Pan-American Congress of Gastroenterology 1956). The features described by Baggenstoss and Stauffer (1952) were used to diagnose micronodular cirrhosis of the portal type. Macronodular cirrhosis with the postnecrotic pattern was diagnosed with the criteria postulated by Baggenstoss and Stauffer (1952); and Steiner (1960). Cases were accepted as idiopathic haemochromatosis using the criteria postulated by MacDonald and Mallory (1960). Those cases were excluded from the haemochromatosis group

in which there was a history of blood transfusions or of oral or parenteral iron administration at any time prior to the final admission to hospital.

Incidence of Liver Cirrhosis

The frequency with which liver cirrhosis is found at autopsy varies from series to series. These figures probably depend on available hospital facilities, the frequency of autopsy and whether there is a particular interest in liver diseases. In the present study, there were 640 cases of liver cirrhosis, of which 170 were micronodular cirrhosis, and 40 cases that were not classified. Thus the incidence of liver cirrhosis was found to be 2.9 per cent of all autopsies performed during 1938 to 1966 inclusive. The incidence of idiopathic haemochromatosis was 68 per 100,000 autopsies. The incidence, sex distribution and ages are shown in Table I.

Table I

Incidence, sex distribution and ages in haemochromatosis in 22,050 autopsies

No. of cases	15
Incidence relative to 100,000 autopsies	68
Distribution Male : Female	4 : 1 (12 : 3)
Average age (in yrs.)	56
range (in yrs.)	20–80 – Female
	28–70 – Male

Clinical Data in Cases of Idiopathic Haemochromatosis

The clinical notes of cases with idiopathic haemochromatosis were consulted and some observations may be noted.

Syphilis or a positive Wassermann test had not been noted in any of the cases with haemochromatosis. Syphilis was recorded in 1.2 per cent of the autopsies performed in this Institute. A statement concerning excess intake of alcohol was made in the clinical records of 13.3 per cent (two cases) with haemochromatosis. The alcohol consumed was mainly beer or whisky.

Diabetes mellitus occurred in 53.3 per cent with haemochromatosis. Only 2.6 per cent of the patients autopsied in this Institute had a clinical diagnosis of diabetes mellitus. In Sheldon's (1935) review, diabetes mellitus was found in 59.8 per cent of cases with haemochromatosis. Finch & Finch (1955) observed diabetes mellitus in 82 per cent of their cases, and MacDonald and Mallory (1960) reported that only 30 per cent of their 57 patients with haemochromatosis had diabetes mellitus.

Forty-six per cent of cases with idiopathic haemochromatosis were diagnosed before death to have liver cirrhosis. In patients with haemochromatosis at the Boston City Hospital, a clinical diagnosis of cirrhosis was made during the final admission in 50 per cent of cases. (MacDonald & Mallory 1960).

Pathological Aspects

Hepatic lesions in haemochromatosis

The average weight of the liver was 1,950 g; range 1,300 to 3,200 g. Approximately 86 per cent (13) of the livers weighed over 1,500 g. This was in keeping with other studies of the liver in haemochromatosis. MacDonald and Mallory (1960) found the average weight of the liver was 2,135 g, 60 per cent weighing more than 1,500 g. In the present study 80 per cent (12) of the cases showed the liver cirrhosis to be micronodular or "portal" in type, and 20 per cent macronodular or "postnecrotic" in appearance. The cirrhotic liver had a reddish-brown colour. There was minimal fatty change in 20 per cent (3) of the cases, but no liver showed moderate or severe fatty infiltration. Mild lymphocytic infiltration was observed in all cases. Bile duct proliferation was seen in all cases, but it was moderate in only 60 per cent of the cases. Excessive deposits of haemosiderin pigment were present in all cases. The pigment was present in the parenchymal cells, the interlobular fibrous tissue and the bile ducts. The iron deposits were heaviest in the periphery of the lobules. Iron was also present in the Kupffer cells in 80 per cent of the cases. Figs. 1 and 2 show the micronodular or "portal" and macronodular or "postnecrotic" types of cirrhosis in idiopathic haemochromatosis. A summary of the macroscopic and histological features and other relevant observations are shown in Tables II and III.

TABLE II

Findings at autopsy in idiopathic haemochromatosis

Observations	*No. of cases*	*Per cent*
Average weight of liver	1950g	
Liver > 1500g	13	86.0
Average weight of spleen	340g	
Spleen > 250g	9	60.0
Ascites	8	53.3
Oesophageal varices	5	33.3
Rupture	3	*(60.0)
Peptic ulcer	3	20.0
Primary hepatic carcinoma		
Total	5	33.3
Type: Hepatocellular	5(4R. lobe)	
Cholangiocarcinoma	0	
Mixed	0	
Portal vein thrombosis		
Total	3	20.0
No. associated with liver CA.	3	**(100.0)

*Expressed as a percentage of the total number of oesophageal varices.

**Expressed as a percentage of the total number of cases with portal vein thrombosis.

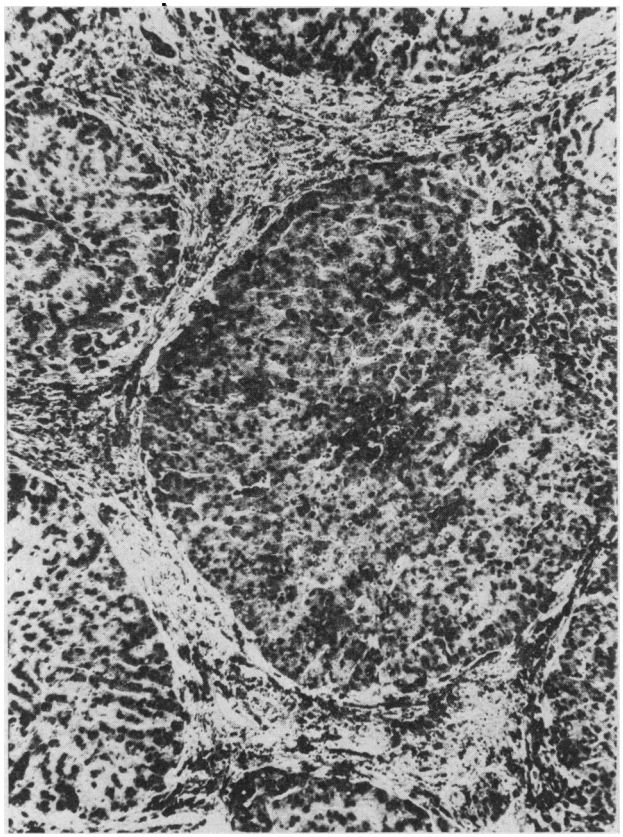

FIG. 1. *Microscopic appearance of liver in idiopathic haemochromatosis showing advanced "portal" or micronodular type of cirrhosis. Small nodules of hepatic parenchyma are enclosed by fibrous bands. Haemosiderin is present in the parenchymal cells, Kupffer cells, fibrous bands and bile ducts.* (*Perls' stain* x 110).

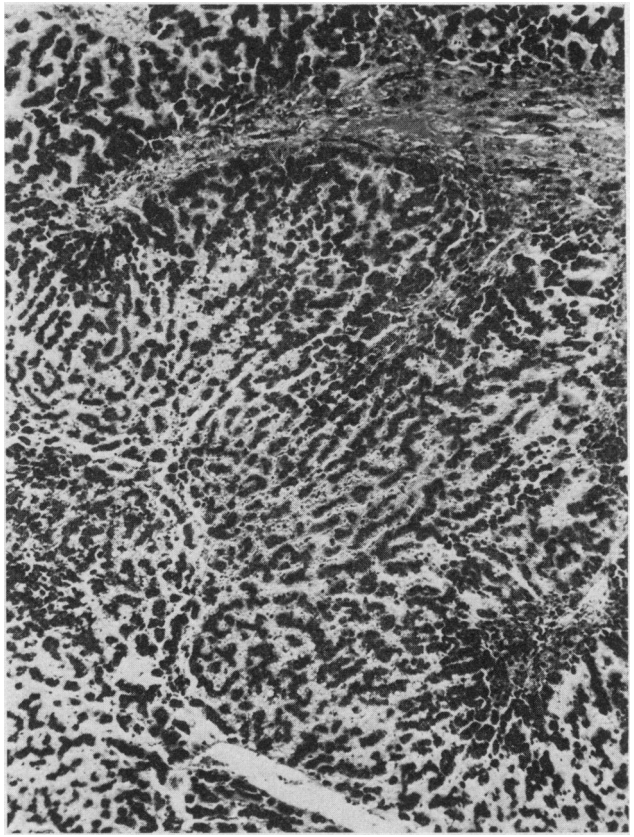

FIG. 2. *Microscopic appearance of liver in idiopathic haemochromatosis, showing "postnecrotic" or macronodular type of cirrhosis. Broad bands of fibrous tissue enclose more than 2 to 3 lobules of liver cells. There are dark masses of iron pigment in the hepatic parenchymal cells and in the connective fibrous tissue.* (*Perls' stain* x 110).

TABLE III

Histological features in the liver in idiopathic haemochromatosis

Observations	*No. of cases* (15)
Morphological appearances	80 per cent "Micronodular" type
	20 per cent "Macronodular" type
Regenerative nodules	80 per cent "Micronodular" type
	20 per cent "Macronodular" type
Infiltration with fat	Mild 20 per cent
Internodular fibrous tissue	80 per cent narrow zones
	20 per cent wide zones
Bile ducts	Mild to moderate proliferation
Leukocytes	Mild – lymphocytes

Evidence of portal hypertension

Splenomegaly (weight above 250 g) was present in 60 per cent of patients with haemochromatosis. Oesophageal varices were demonstrated in 33.3 per cent with haemochromatosis. Ascites was found in 53.3 per cent. Sixty per cent of the varices bled. MacDonald and Mallory (1960) demonstrated that approximately 30 per cent of haemochromatosis had oesophageal varices, and our findings are comparable (33.3 per cent). This is contrary to the findings of Sherlock (1963) who stated that oesophageal varices with haemorrhage were rare in haemochromatosis.

Peptic ulcer

Ulceration was found in 3.7 per cent of autopsies performed in this Institute. Peptic ulceration was observed in 20 per cent with haemochromatosis. MacDonald (1964) reported an incidence of 1.8 per cent peptic ulceration in idiopathic haemochromatosis, which was less than the incidence of 5.5 per cent in the same autopsy population. The increased incidence of peptic ulcer may be due to the more frequent alcohol intake in these cases causing gastric irritation and faulty nutrition. It has been suggested that in liver cirrhosis there is an increased level of circulating plasma histamine, due to decreased breakdown by the liver cells, and it is this increased circulating level of histamine which causes peptic ulcer by increasing gastric acidity; but the exact mechanism is still obscure.

Primary hepatic carcinoma

This was observed in 33.3 per cent of the patients with idiopathic haemochromatosis. Hepatocellular carcinoma was the most common type (91 per cent), and cholangiocarcinoma was found in 5 per cent. The right lobe of the liver was the commonest site for the development of the tumour. In MacDonald and Mallory's (1960) series of 57 cases of haemochromatosis, 12 per cent had primary carcinoma of the liver. Reports of the incidence of primary hepatic carcinoma in idiopathic haemochromatosis have varied in the literature from 5.8 per cent (Sheldon, 1935) to 30 per cent (Willis, 1941), but the majority of reports indicate an incidence

of about 14 per cent. No haemosiderin pigment was detected in the hepatic carcinoma of patients with haemochromatosis.

Portal vein thrombosis

Clot in the portal vein was found in 20 per cent of livers in patients with haemochromatosis. All these patients had primary hepatic carcinoma of the liver. This increased incidence of portal vein thrombosis was related to the high incidence of liver cell carcinoma.

The pancreas

A summary of the findings in the pancreas in control and haemochromatosis patients are shown in Table IV. Twenty per cent of autopsies with extrahepatic disease showed interacinar and inter-lobular pancreatic fibrosis, with minimal lymphocytic or adipose infiltration. Loss of cells in the islets was seen in 7 per cent, and hyalinization in 2 per cent of the control autopsies. No diabetes mellitus was recorded in these cases.

TABLE IV

Findings in the pancreas in control autopsies with extrahepatic disease and haemochromatosis

	Types of cases			
	Controls (100 cases)		*Haemochromatosis (15 cases)*	
Observations	*No. of cases*	*Per cent*	*No. of cases*	*Per cent*
Pancreatic fibrosis	20	20	14	93.0
Leukocytic infiltration	1	1	1	6.5
Islets of Langerhans				
Total involved	9	9	9	60.0
Hyalinized	2	2	6	
Decreased cellularity	7	7	3	
No. with clinical diabetes mellitus	0	*0.0	5	*55.5

*Expressed as a percentage of the total number of islets involved.

In idiopathic haemochromatosis, 93 per cent of the patients showed some degree of pancreatic fibrosis, which was mainly inter-acinar and inter-lobular. Stainable iron was present in all cases, deposited mainly in the acini and connective fibrous tissue. In 6 of the 15 patients, the islets of Langerhans were hyalinized and in 3 there was clinical diabetes mellitus. In three further cases, there was decreased cellularity of the islets, and two of these patients suffered from diabetes. Thus, of the nine patients with hyalinization or poor cellularity of the islets, five had clinical diabetes mellitus. Macroscopically, the pancreas was usually larger than normal and firm, with a brownish-red coloration due to deposition of iron.

Sheldon stated that pancreatic fibrosis was present in at least 90 per cent of cases of haemochromatosis, which is similar to the findings in the present study. MacDonald and Mallory (1960) found that among 57 patients with haemochromatosis at the Boston City Hospital, all the patients had some degree of pancreatic fibrosis with haemochromatosis. In the present study, no definite association between hyalinization and decreased cellularity of the islets of Langerhans and diabetes mellitus was found.

Haemosiderin in various organs in haemochromatosis

Haemosiderin was found in the liver, pancreas and lymph nodes in all 15 cases of idiopathic haemochromatosis. In the adrenal glands the iron was deposited mainly in the zona glomerulosa and haemosiderin was found in the thyroid gland and spleen in 60-65 per cent of cases. Iron was present in the gastric mucosa, skin and kidneys in 50 per cent, and in the heart, bone marrow and pituitary in approximately 40 per cent of the patients. It was found infrequently in the lung parenchyma. The frequency distribution of iron in the various organs is shown in Fig. 3.

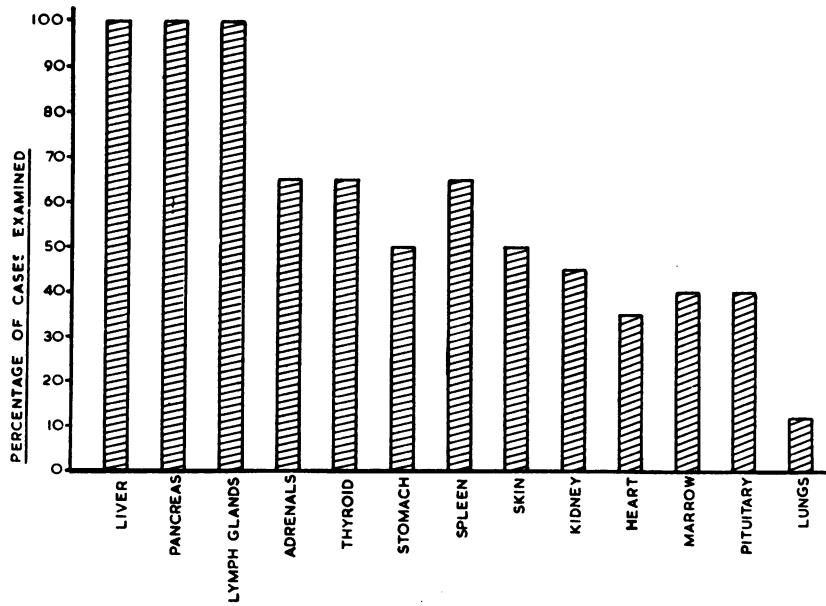

FIG. 3. *The distribution of haemosiderin in various organs in idiopathic haemochromatosis.*

Effect of hepatic cirrhosis on iron deposition in the liver and pancreas

The incidence of siderosis in the liver and pancreas was assessed in a series of 100 routine autopsied patients with extrahepatic disease, 170 with micronodular cirrhosis, 159 with macronodular cirrhosis and 15 with idiopathic haemochromatosis. The degree of iron deposition was expressed as grades 0 – 4, grade 0 being

negative, and grades 1 to 4 representing increasing amounts of stainable iron (Scheuer, Williams and Muir, 1962). All the sections were examined and graded under light microscopy.

There was haemosiderin deposition in the livers of 30 per cent of the 329 patients with liver cirrhosis (micronodular and macronodular), whereas only 5 per cent of the 100 patients with "normal" livers showed haemosiderin (Table V). The difference in the incidence of hepatic haemosiderin between controls and patients with liver cirrhosis was statistically significant (χ^2 test $P<0.005$). The haemosiderin deposits also appeared to be greater in amount in the patients with liver disease than in the patients with extrahepatic disease. Of the 329 cases of liver cirrhosis, 3.6 per cent (12) showed an excess of iron in the liver cells, internodular fibrous tissue and Kupffer cells, which was indistinguishable from the livers of patients with idiopathic haemochromatosis. In the 100 control patients, there was no haemosiderin in any of the sections of pancreas. Of the 329 patients with liver cirrhosis, 5.4 per cent (18) showed excess iron in the pancreas, present as granules in the acinar cells and connective tissue. Of these 18 patients, 10 had grade 1, and 8 had grade 2 iron in the parenchyma, while the patients with haemochromatosis showed grade 3 to 4 iron deposition (Table V). However, there was no significant difference in the incidence of pancreatic siderosis between the cases with liver cirrhosis and extrahepatic disease (χ^2 test $0.10>P>0.05$). Of the 12 cases of liver cirrhosis with grade 3 to 4 hepatic siderosis, there was a history of blood transfusions, iron therapy and excess intake of alcohol in seven instances. But in the remaining five (40 per cent) cases of liver cirrhosis with grade 3 to 4 hepatic siderosis, no exogenous cause for the excess iron in the liver could be found.

Causes of death

Although many factors played a role in causing death in each patient, an attempt was made to estimate from the observations at autopsy the most important cause in each case. The chief causes of death are shown in Table VI. The most frequent causes of death were hepatic insufficiency associated with primary hepatic carcinoma and haemorrhage from bleeding oesophageal varices in 53.3 per cent of the patients. Two of the 15 patients with haemochromatosis died of hypertensive heart disease and myocardial infarction due to a thrombotic occlusion in atheromatous coronary arteries. No deaths due to cardiomyopathy were seen.

Discussion

The incidence of haemochromatosis was reported by Finch and Finch (1955) to be 1 in 7,000 hospital deaths. MacDonald and Mallory (1960) found a high incidence of 1 in 461 autopsies at Boston. MacDonald (1965) reviewed the incidence of haemochromatosis and cirrhosis in different geographical areas. He found that the average incidence in countries other than the United States of America was 180 per 100,000 autopsies, with a range varying from zero in some South American countries, Holland and Hungary, to a figure of 2,770 in France. In the United States of America the average incidence was 178 per 100,000 autopsies. He found that Scotland had one of the highest rates in Europe, with an average of 234 per 100,000 autopsies. MacSween and Jackson (1966) found the

TABLE V

Incidence of hepatic siderosis, pancreatic fibrosis and siderosis in the groups with extrahepatic disease and liver cirrhosis

Disease	*Number*	*Liver iron grade*				*Percentage involved*	*Pancreatic fibrosis*	*Percentage involved*	*Pancreas iron grade*				*Percentage involved*
		1	2	3	4				1	2	3	4	
Control	100	5	0	0	0	5.0	20	20.0	0	0	0	0	0
Micronodular cirrhosis	170	30	11	4	2	27.4	94	55.3	2	2	0	0	2.2
Macronodular cirrhosis	159	27	19	5	1	32.5	96	60.3	8	6	0	0	8.7
		χ^2 test $P<0.005$							χ^2 test $0.10>P>0.05$				
Haemochromatosis	15	0	0	0	15	100	14	93.0	0	4	8	3	100

TABLE VI

Most important causes of death in haemochromatosis

Causes of death	*Haemochromatosis (15 cases)*	
	No. of cases	*Per cent*
Hepatic insufficiency	5	33.3
Associated liver carcinoma	5	33.3
Haemorrhage – total	3	20.0
From varices	3	
From peptic ulcer	0	
Cardiovascular diseases – total	2	13.3
Myocardial Infarct	1	
Hypertensive heart disease	1	
Pulmonary infection	1	6.6
Abdominal catastrophies – perforations, strangulations	2	13.3
No cause determined	1	
Non-hepatic malignant tumours	1	6.6

rate in Glasgow to be just over 200 per 100,000 autopsies. MacDonald (1965) found that Ireland and England with figures of 17 and 40 respectively per 100,000 autopsies were among the lower rates in Europe. However, in the present study the incidence of idiopathic haemochromatosis in Belfast, Northern Ireland, was found to be 68 per 100,000 autopsies. The incidence of haemochromatosis relative to the number of cases with portal cirrhosis and postnecrotic cirrhosis was 1 : 22. All our patients with haemochromatosis were manual labourers or in a low-income bracket, which is similar to the observations of MacDonald and Mallory (1960). The average age at death was observed to be 60 years by MacDonald and Mallory, 55 years by MacSween and Jackson and 56 years in the present study.

Finch and Finch (1955) observed idiopathic haemochromatosis about ten times as frequently in males as in females (90.4 to 9.6 per cent). Sheldon (1935) found that the male sex was twenty times as liable to the disease as the female sex (95 to 5 per cent). In the present study, 80 per cent of the cases occurred in the male. One explanation for this disparity may be the ability of the female to unload considerable amounts of iron through menstruation, pregnancy and lactation. The average woman during her life-time loses from 10 to 15 g of iron through menstruation alone (Finch and Finch 1955). Pregnancy and lactation may account for losses of body iron several times this amount.

Kleckner et al (1955) found that approximately 23 per cent of their 35 cases of idiopathic haemochromatosis were not diagnosed until an autopsy had been done. A clinical diagnosis of haemochromatosis was made during the final admission in 50 per cent of patients at the Boston City Hospital (MacDonald and Mallory 1960), and MacSween and Jackson (1966) found that more than 66 per cent of their 37 patients were not diagnosed clinically as having haemochromatosis. In the present study, 53.4 per cent of the patients were diagnosed as having haemochromatosis only at autopsy. The failure to diagnose more than half the patients with idopathic haemochromatosis has been due to the absence of the classical presentation with the triad of liver disease, diabetes mellitus and pigmentation of the skin being found in 40 per cent of the cases in the present study. In patients with idopathic haemochromatosis, diabetes mellitus was observed in 78 per cent of the patients by Sheldon (1935), in 82 per cent by Finch and Finch (1955), in 27 per cent by MacSween and Jackson (1966) and in 53.3 per cent in the present study. Skin pigmentation was observed in 83.8 per cent of the cases of haemochromatosis by Sheldon, 85 per cent of the patients by Finch and Finch, 55 per cent by MacSween and Jackson and in 53.3 per cent in the present study.

The average weight of the liver in the patients with haemochromatosis was 1950 g – about 500 g heavier than in control groups. Fat infiltration was seldom seen in the liver. The cirrhosis in 80 per cent of the liver was "portal" or micronodular and in 20 per cent "postnecrotic" or macronodular in type. Sheldon in his monograph on haemochromatosis stated that diabetic coma was the most common cause of death (50 per cent). He also found that cirrhosis of the liver caused death in 11 per cent, of which approximately half died from haematemesis and the remainder from hepatic failure. Carcinoma of the liver was responsible for 7 per cent of the deaths, but myocardial failure was not a major cause of death. However, Finch and Finch (1955), Kleckner et al (1955) and MacDonald

and Mallory (1960) found that the most frequent cause of death in haemochromatosis was congestive cardiac failure due to myocardial siderosis. Horns (1949) and Levin and Galum (1953) found that the most important cardiac manifestations were congestive cardiac failure and cardiac arrhythmias. However, in accordance with the findings in the present study, MacSween and Jackson (1966) observed that the commonest cause of death in haemochromatosis was hepatic failure – 33.3 per cent of patients with haemochromatosis died of liver failure. There was an associated primary liver cell carcinoma in many of these patients. A primary hepatocellular carcinoma was found in 33.3 per cent of our patients. Gastrointestinal bleeding from oesophageal varices caused the deaths of 20 per cent of the cases in the present study. This is at variance with Sherlock's (1963) view that portal hypertension is inconspicuous and bleeding from varices rare in haemochromatosis.

Demonstrable haemosiderin pigment was observed in a large proportion of livers from patients with liver cirrhosis, both micronodular and macronodular types. In the control patients without hepatic disease, haemosiderin in the liver was significantly less frequent (5 per cent) and slight in quantity. Thirty per cent of the 329 patients with micronodular cirrhosis and macronodular cirrhosis had haemosiderin in the liver cells, but only 3.6 per cent of the livers contained iron to the same extent as in cases with haemochromatosis (grades 3 to 4). In approximately 60 per cent of these there was a history of multiple blood transfusions, excess alcohol and iron intake to explain the presence of hepatic haemosiderin. Pancreatic siderosis was found in 5.4 per cent of the 329 patients with liver cirrhosis, but the iron deposition was light (grades 1 to 2) and not as heavy as in haemochromatosis. There is some degree of overlap between siderosis in liver cirrhosis and haemochromatosis, but the deposition of iron in the pancreas in the former is not marked. The demonstration of haemosiderin in the hepatic parenchymal cells of patients with liver cirrhosis is in agreement with the observations of other workers (Herbut and Tamaki 1946; Gillman and Gillman 1947; Bell 1955; Dubin 1955; Finch and Finch (1955); Zimmerman et al. 1961).

Finch and Finch (1955) have stated that on biopsy differentiation of idiopathic haemochromatosis from Laennec's cirrhosis with secondary haemosiderosis is difficult. Sheldon (1935) emphasized the similarity between portal cirrhosis with iron and haemochromatosis, but stated "it is true that portal cirrhosis contains more iron than normal, but if haemochromatosis were an extreme development of this process, one ought to find intermediate cases, whereas these appear to be conspicuously absent. The difference in degree is so profound and so sharp that it constitutes a difference in kind". However, the present study showed that the transition from liver cirrhosis with iron to haemochromatosis is a gradual one without a sharp distinction, and differentiation clinically is based on arbitrary features such as the level of serum iron, degree of hepatic siderosis, the presence of diabetes mellitus and skin pigmentation.

MacDonald (1964) expressed the view that the excess iron in the liver and body tissues in idiopathic haemochromatosis was caused by the presence of iron in alcohol, especially wine, cooking utensils and medications or "tonics". MacDonald found that among patients with haemochromatosis at the Boston City Hospital,

85 per cent gave a history of excessive intake of alcohol, while 70 per cent of cases with portal cirrhosis took alcoholic beverages in excess. Thus, he postulated that as portal cirrhosis was accepted to be related to alcohol, and as the frequency of alcohol intake was approximately the same as in haemochromatosis, the two conditions were similar. However, Sheldon (1935) suggested that idiopathic haemochromatosis was an inherited disorder of iron metabolism, and cited family aggregations of cases. Finch and Finch (1955) noted one father-son combination with the disease. Sherlock (1963) postulated that haemochromatosis was transmitted as a "dominant" with incomplete penetrance or expression. Williams et al (1962) suggested that the propositi would represent the homozygous affected, and the relative with raised serum iron and skin pigmentation the heterozygote state. Crosby (1966) defended the position that haemochromatosis is an hereditary disorder of iron metabolism in which several genetically determined faults can produce the pathological changes. Sinniah (1969a) observed raised serum iron levels in the relatives of patients with idiopathic haemochromatosis and there was a familial clustering of cases. Cooking utensils, iron medications or "tonics" and blood transfusions were not contributory causes in the development of haemochromatosis in the propositi studied. In the above study there was excess alcohol intake in 54 per cent of the patients, but the average amount of iron absorbed was approximately 2.61 g, which was much lower than the 20.405 g found in the organs in haemochromatosis (MacDonald 1964). The transition between liver cirrhosis with iron and haemochromatosis may be a gradual one, but the degree of haemosiderosis in the liver, pancreas and other organs is not as severe as in haemochromatosis. The definition and diagnosis of haemochromatosis are not anatomical, the disease being recognized by clinical as well as pathological criteria. Thus, cases of liver cirrhosis with siderosis should be classified as pigment cirrhosis, unless there is a strong genetic evidence for idiopathic haemochromatosis.

The relationship between hepatic parenchymal damage and haemosiderosis is not clear. Walker and Arvidsson (1950) suggested that the haemosiderosis in South African natives was related to the high iron and low phosphorus content of their diets. This view has been supported by MacDonald and Baumslag (1964). Gillman and Gillman (1947) have suggested that the hepatic siderosis of patients with nutritional liver disease may be due to impairment of hepatic enzyme systems involved in iron utilization or storage. Charlton et al. (1964) proposed that alcohol itself may stimulate the production of gastric juice and permit increased absorption of iron. Murray and Stein (1965) observed no increase in iron absorption in normal rats with alcohol supplement to their normal diets. Tuttle et al. (1959) and Tisdale (1961) put forward the hypothesis that the increased iron absorption was related to the presence of collateral channels, for patients with cirrhosis had been reported who had developed haemochromatosis after shunt operations. Williams et al. (1967) conducted iron absorption and hepatic siderosis studies on 76 patients with chronic liver disease, including 29 who had a surgical shunt performed 1 to 11 years earlier. The authors could not correlate increased iron absorption with collateral shunting. Callender and Malpas (1963), Davis and Biggs (1964) and Deller (1965) all suggested that increased iron absorption was a frequent finding in portal cirrhosis. Davis (1961) and Davis and Biggs (1965) suggested that oral pancreatin can depress the increased absorption of iron[59] in liver disease. Biggs and Davis

(1963) even suggested that haemochromatosis may be of pancreatic origin. Van Goidsenhoven et al. (1963) demonstrated a high incidence of abnormal pancreatic function tests in cirrhosis of the liver. MacDonald and Mallory (1960) and Sinniah (1969b) observed marked pancreatic fibrosis in over 50 per cent of patients with cirrhosis of the liver. It has been stated (Davis 1961; Biggs and Davis 1963; Taylor et al. 1931; 1935) that it is the pancreatic deficiency which allows increased absorption of iron. However, Murray et al. (1964) and Sinniah et al. (1973) have not been able to confirm this observation experimentally. They found that in animals with ligation of the pancreatic duct or with pancreatectomy no evidence of liver damage was seen. Pancreatic enzymes in stated doses did not depress iron absorption in these animals with normal livers. Thus the relationship between liver cirrhosis, pancreatic dysfunction and increased iron absorption and storage has not been resolved.

Summary

During 1938 to 1966 inclusive, 22,050 autopsies were performed by the Institute of Pathology, Belfast. The incidence of liver cirrhosis (640 cases) found at autopsy was 2.9 per cent and the incidence of idiopathic haemochromatosis (15 cases) was 68 per 100,000 autopsies. Eighty per cent of the patients were males. A "portal" or micronodular type of liver cirrhosis was found in 80 per cent of the cases and the remaining 20 per cent had a "postnecrotic" or macronodular pattern.

Hepatic insufficiency and haemorrhage from oesophageal varices were the most common causes of death. The incidence of primary hepatic carcinoma was 33.3 per cent and portal vein thrombosis was commonly associated with the hepatic carcinoma. Peptic ulcer was found in 20 per cent of the patients and in 3.7 per cent with extrahepatic disease. Diabetes mellitus was observed in 53.3 per cent of the patients with haemochromatosis and in 2.6 per cent of cases with extrahepatic disease. Approximately 50 per cent of patients with haemochromatosis were not diagnosed until autopsy. Haemosiderin pigment was present in 30 per cent of the 329 patients with portal and postnecrotic cirrhosis, but only 3.6 per cent of the livers contained iron to the same extent as in patients with haemochromatosis. Of these 3.6 per cent patients, 60 per cent had a history of multiple blood transfusions, excess alcohol and iron intake to explain the presence of haemosiderin, but no obvious cause was found in the other patients. There was some degree of overlap between liver cirrhosis with siderosis and haemochromatosis, but the deposition of iron in other organs was not marked in the former. Patients with liver cirrhosis and siderosis should be classified as pigment cirrhosis, unless there is a strong genetic evidence for idiopathic haemochromatosis. The relationship between liver cirrhosis, pancreatic dysfunction and increased iron absorption and storage is not fully understood.

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THE TREATMENT OF PARAQUAT POISONING: THREE CASES OF RECOVERY

by

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THREE cases of recovery from paraquat poisoning are reported. In cases of this sort small amounts of a dilute preparation are not usually fatal. Larger amounts of concentrated preparations are invariably fatal but with very small amounts of concentrated preparations the outcome is often unpredictable. It is suggested that in such cases all measures to prevent absorption, increase excretion, maintain the patient and prevent progressive renal, hepatic and pulmonary damage are justified.

Case Reports

Case No. 1

A 33-year-old man was admitted to an Intensive Care Unit one hour after taking about 30 ml. of "Weedol" (5 per cent paraquat) as well as a mixture of sedatives and anti-epileptic tablets. He was a transvestite with a history of psychiatric treatment. On admission he was given a litre of 7 per cent Bentonite by stomach tube. When seen 11 hours later, he was fully conscious. He was not jaundiced, had no mouth ulcers and was afebrile. His chest was clear clinically. His blood pressure was 116/75 mm Hg. His pulse was 80 per minute and regular. His blood urea was 33 mg%. Paraquat levels in 2 urinary samples the day after admission were 470 ug/100 ml., and 180 ug/100 ml., respectively.

The patient passed no urine for 24 hours after admission, due to retention, but passed adequate amounts after catheterization. He made a full recovery with no evidence of renal or respiratory damage. A chest x-ray showed no active lung lesion although there was a calcified focus in the left lower zone with some calcified left hilar glands. The patient was still physically well five months after discharge when he was readmitted following another overdose; this time he seemed to have avoided paraquat!

Case No. 2

A 56-year-old man was admitted to an Intensive Care Unit 12 hours after taking a mouthful of "Dextrone" weedkiller (a combination of paraquat and diquat) which he spat out at once. Shortly afterwards gastric lavage was performed and after another 4 hours one litre of 7% Bentonite was instilled in a Casualty Department. On admission he was fully conscious and appeared well, although he had begun to suffer from diarrhoea a few hours before arrival. There was no mouth ulceration, no jaundice and no abdominal tenderness. The chest was clear. The blood pressure was 170/80 mm Hg., and the pulse was 80 per minute. There was a low grade pyrexia which persisted for 2 weeks. The day after admission the patient developed a sore throat and dysphagia, later coughing up some blood. He passed only 100 ml. of urine in the first 12 hours but thereafter produced adequate amounts. The blood urea was 170 mg/100 ml. on admission. It gradually fell to a normal level over a period of 3 weeks. The serum creatinine was 1.8 mg/100 ml. 5 days after admission. The serum S.G.O.T. reached a level of 159 K units, L.D.H. 370 W.L. units and alkaline

phosphatase 48 K.A. units 2 weeks after admission. The serum bilirubin was not raised at any time. Serial chest x-rays showed no lung lesion. The serum paraquat was not estimated. Urinary paraquat was measured in samples taken between the tenth and sixteenth days. The highest level detected was only 21 ug/100 ml., and in several samples no paraquat was found.

The patient made a good recovery despite developing thrombophlebitis in the right axillary vein where he had had an initial intravenous infusion. He was discharged eighteen days after admission and when seen 2 weeks later had a normal blood urea and serum creatinine. One month later he remained well.

Case No. 3

A 52-year-old man was admitted to an Intensive Care Unit. He gave a history of splashing his face and mouth with "Gramoxone W" (20 per cent paraquat) from a can of weedkiller about 3 days before. He at once washed his face, mouth and hands. The next day he developed discomfort in his mouth and throat and began to have difficulty in swallowing. He had passed very little urine in the 2 days before admission. On examination he was fully conscious and afebrile. He was slightly cyanosed and had a rapid respiratory rate, but his chest was clinically clear. There was ulceration of the buccal mucosa and severe ulceration of the mucosa over the fauces and pharynx. He had difficulty in swallowing even saliva. The pulse was 120 per minute and the blood pressure 120/80 mm Hg. There was no abdominal tenderness. The blood urea on admission was 70 mg/100 ml. An Astrup test showed a respiratory alkalosis. A chest x-ray showed no lesion. The serum paraquat level on admission was 94 ug/100 ml. The urinary paraquat level was 197 ug/100 ml. The serum S.G.O.T. was 65 K units but there was no other evidence of liver damage.

The patient remained almost anuric for 4 days after admission but thereafter achieved satisfactory diuresis. He was treated with peritoneal dialysis for 6 days, intravenous fluids, sedation and oxygen. His blood urea gradually fell to a normal level. Six days after admission small amounts of paraquat were still present in the urine. No paraquat was found in the dialysate at any stage. A chest x-ray 10 days after admission showed a small patch of consolidation in the right lower zone, with a small left-sided basal effusion. He was given a course of intramuscular penicillin. Subsequent chest x-rays were clear. He was discharged sixteen days after admission. A week later his blood urea was normal and a M.S.S.U. was clear of cells or protein. 3 months later he remained well.

Discussion

Paraquat and diquat are bipyridilium compounds much used in agriculture as surface-contact herbicides. They are believed to be continuously reduced and re-oxidized in the presence of chlorophyll with the gradual accumulation of hydrogen peroxide to toxic levels. They are inactivated by contact with soil, possibly because of the cation-capturing effect of silicates contained in it. There is a minimum dose beneath which dietary paraquat causes no apparent damage and an intermediate dose which on long term consumption produces pulmonary fibrosis in animals (Conning et al, 1969; Daniel and Gage, 1966). Paraquat is poorly absorbed, over 70 per cent appearing in the faeces, and in addition there is evidence that it is degraded by microbiological action in the intestinal tract. It is more rapidly absorbed in fasting than in recently fed animals (Clark et al, 1966) and this may also apply in cases of human poisoning (Greig, quoted by Matthew et al, 1968). It is rapidly excreted in experimental animals (Daniel and Gage, 1966) and this led to the suggestion that it is a "hit and run" poison, since the pulmonary lesions progressed in the absence of further dosage. However, in man, it continues to be excreted for many days in the urine (Tompsett, 1970).

This species variation casts some doubt on the value of animal experiments.

The severe effects of poisoning by bipyridilium compounds are well known. Although small amounts of "Weedol" (5 per cent paraquat) or paraquat and diquat mixtures such as "Dextrone" do not appear to be fatal, herbicides with a higher concentration, such as Gramoxone W (20 per cent paraquat) have a very bad record. The "typical victim" takes a mouthful of 20 per cent paraquat, which he at once spits out, but he later dies, usually of renal or late progressive pulmonary damage, although gastro-intestinal, hepatic and myocardial lesions are also often found. However, the outcome is not always predictable and several patients have recovered fully. Some die in spite of intensive treatment with forced diuresis, and haemodialysis or peritoneal dialysis. Others recover without treatment. (See Malone et al, 1971, for a comprehensive review of their own cases and the literature). In general, the more severe the objective evidence of organ damage, the less likely the patient is to survive. The absence of pulmonary lesions makes survival more likely. Steroids and immuno-suppression have been used in an effort to halt renal and late pulmonary damage, but it is admitted that there is no convincing evidence of their value. Very little paraquat is removed by dialysis (Tompsett, 1970; Carson, 1972), although removal by haemodialysis may be comparable to urinary excretion. Urinary excretion may be increased by forced diuresis (Kerr et al, 1968). In the presence of acute renal failure due to paraquat-induced tubular necrosis, dialysis may of course be essential to maintain life, and it is then the only route of excretion available.

Of the cases reported here, the first two belong to the category in which recovery may be expected, since small amounts of paraquat in low concentration were taken. The third case belongs to the category in which the outcome is very often fatal. Treatment with peritoneal dialysis, although it did not remove detectable amounts of paraquat, will have lessened the systemic effects of the patient's early acute renal failure. However, since toxic effects are related to dose, it is reasonable to assume that *all* possible measures to prevent absorption, increase excretion, maintain the patient and prevent progressive organ damage are justified in cases of this sort. They are unlikely to harm the patient, who may die for the lack of them.

The following measures are therefore suggested in all cases in which the outcome is unpredictable. They are based on what is known of the poison's absorption and fate, and of the response of individual patients to treatment.

1. Immediate ejection of the swallowed dose followed by washing of the mouth and inducement of vomiting.
2. Gastric lavage, although care is necessary to avoid the possibility of perforation of the oesophagus, which may be corroded (Malone et al, 1971).
3. Instillation of 1-2 litres of 7 per cent suspension of Bentonite as soon as possible. Bentonite is a colloidal hydrated silicate, capable of removing cationic substances from solution by a cation-exchange mechanism.
4. Transfer to an intensive care unit.
5. Encouragement of an oral diet, if tolerated, or tube-feeding, unless severe oesophageal damage forbids it.

6. Establishment of diuresis. If possible paraquat urinary excretion should be measured daily.
7. Cyclophosphamide 3 mg./kg., and Prednisolone 1 mg./kg., daily, even though the evidence that they help is inconclusive.
8. Peritoneal dialysis or haemodialysis especially if acute renal failure has developed, when it is the only means of maintaining the patient and excreting the poison.
9. Intensive respiratory care has been used in those surviving long enough or requiring it. Recently, it has been suggested that far from being helpful, oxygen therapy is definitely contra-indicated (Matthew, 1971; Fletcher, 1973).

Only from a survey of a large number of patients treated in this way can it be known whether treatment contributes to survival in cases where the history makes the prognosis unpredictable.

In cases where survival seems likely (such as numbers 1 and 2 in the cases above) the regime may not need to be imposed. In cases where larger amounts of highly concentrated paraquat are consumed, no present treatment is likely to have any effect.

Paraquat has been marketed for 11 years, and the manufacturers record just over 70 cases of fatal accidental poisoning by the concentrated liquid up to 1972. There have been 11 fatal cases reported in Northern Ireland, of which 7 were probably accidental. All the accidental deaths resulted from drinking concentrated solution which had been decanted into unmarked bottles. The farming community prefers to use the concentrated solution, because it is easy to store and is ready for use in herbicidal sprayers. Manufacture of paraquat in a jelly form or as concentrated granules has been considered and is much to be desired if it can be made practicable. If not, the addition of a noxious smell to the concentrate might prevent the unwary quaffing of decanted potions.

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ANENCEPHALUS AND SPINA BIFIDA IN BELFAST (1964 - 1968)

by

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AT the beginning of this century in Belfast, the infant mortality rate was 153 per 1,000 livebirths; by 1970, the rate had fallen to 28 per 1,000 livebirths (Elwood, 1973). On the other hand, the contribution of congenital malformations to the infant death rate has altered only slightly and it is reasonable to assume that as mortality and morbidity continue to fall the relative importance of congenital malformations will increase (Nevin, 1969). The high incidence of neural tube malformations in Belfast has been emphasised by several authors (Stevenson & Warnock, 1959; Stevenson, Johnston, Stewart & Golding, 1966; Elwood, 1970a). A high incidence for anencephalus has been confirmed elsewhere in Ireland, for example, in Cork City and County (Spellman, 1969; 1970), Dublin (Coffey & Jessop, 1955; 1957), and County Galway (Cahalane, Kennedy, McNicholl & O'Dwyer, 1965). Much less information, however, is available about spina bifida in Ireland. Some findings of a study of 350 infants in Belfast having anencephalus and spina bifida have been published (Elwood & Nevin, 1973). The present paper reports additional data and briefly considers some other aspects of neural tube malformations.

METHODS

Since 1957 a register containing biosocial data on all (live and still) births to women resident in Belfast has been maintained by the Belfast Health Department and the University Departments of Social and Preventive Medicine, and of Medical Statistics. These data now are part of the Northern Ireland Record Linkage Project (Cheeseman, 1968). The population studied included all stillbirths of 28 or more weeks gestation and all livebirths irrespective of gestational age delivered to women resident within the statutory boundary of Belfast County Borough during the period from 1st January 1964 to 31st December 1968.

Many mothers living elsewhere in Northern Ireland are admitted to Belfast hospitals for specialist care; births to these non-Belfast residents and to temporary residents were excluded. The at-risk population, so defined, consisted of 41,351 births.

As the study began in 1969, ascertainment was made retrospectively. All infants with anencephalus, iniencephalus, exencephalus, and encephalocele, alone or in combination with one or more additional malformations, including anencephalus with spina bifida, were classified as anencephalus. The group specified

as spina bifida included meningocele, myelomeningocele, and syringomyelocele alone or in combination with hydrocephalus or other defects. Infants with spina bifida occulta, with or without neurological involvement, were excluded.

Infants with neural tube malformations were ascertained from multiple sources including – the birth register, data on all stillbirths and infant deaths collected by the Maternal & Child Care Division of the Municipal Health Department, death certificates provided by the Registrar General for Northern Ireland in which anencephalus or spina bifida was specified, records of the voluntary notification system for congenital malformations in Northern Ireland, data of families with neural tube malformations attending the Genetic Counselling Clinic, and autopsy records of hospitals in the Belfast area. Information from these sources was cross-checked, attention being paid in each case to verifying the diagnosis. Finally affected births, identified by christian names and surname, address and date of birth were linked to the birth register of the population at risk. Cases not successfully matched were discarded. As multiple sources of ascertainment were employed and as the malformations are easily recognizable, ascertainment is probably of the order of 95% or more.

Results

The 41,351 total births at risk were followed until each resulted in either death (stillborn or early death) or survival at the age of ascertainment (from 1 to 5 years). Of this birth population, 151 infants had anencephalus, 185 spina bifida, and 24 both anencephalus and spina bifida (Table I). Females were affected significantly more than males (F/M ratio for anencephalus 2.8: 1, and for spina

Table I

Population studied – Belfast County Borough (1964-68)

Data and Sex	*Observed Number*	*Incidence per 1,000 (live and still) births*
Male:		
Births (live and still)	21,484	—
Anencephalus	41	2.1
Anencephalus with Spina Bifida	5	
Spina Bifida	76	3.5
Female:		
Births (live and still)	19,867	—
Anencephalus	110	6.5
Anencephalus with Spina Bifida	19	
Spina Bifida	109	5.5
Total:		
Births (live and still)	41,351	—
Anencephalus	151	4.2
Anencephalus with Spina Bifida	24	
Spina Bifida	185	4.5

bifida 1.4: 1). The incidence of anencephalus which includes the 24 infants having anencephalus with spina bifida was 4.2 per 1,000 total births, and of spina bifida was 4.5 per 1,000 total births. These figures are extremely high, exceeding those reported for South Wales (Laurence, Carter & David, 1968) and also those for spina bifida in the Irish Republic (Coffey, 1970).

The distribution of the observed cases of neural tube malformations within the electoral wards of Belfast (Table II and Figure) compared with the number expected, based on the population at risk, shows significant variation with respect to anencephalus ($\chi^2=42.2$; d.f.$=4$; $0.30>P>0.20$). Initial inspection of these distributions suggested an association between religious domination and incidence. However, a rank correlation analysis between the percentage of Roman Catholics in each ward and the incidence of anencephalus does not confirm this hypothesis ($r = -0.04$; S error $= 0.27$; $t = 0.15$; $P>0.90$), nor is there a significant association with the incidence of spina bifida ($r = +0.39$; S error $= 0.27$; $t = 1.45$; $0.20>P>0.10$). The data on the proportions of Roman Catholic by electoral ward (Park, 1962) refer to adult residents and not to reproductive mothers. As there is evidence that fertility rates are higher in Roman Catholics than in other religious denominations (General Register Office, 1965), the problem of any association between the incidence of neural tube malformations and religion in Ireland has yet to be satisfactorily answered.

TABLE II

Distribution of Anencephalus and Spina Bifida by Belfast Residential Area (Electoral Ward)

Residential area (electoral ward)	*Births (live and still)*	*Anencephalus*		*Spina Bifida*		*Percentage of** Roman Catholics*
	No.	*No.*	*Rate**	*No.*	*Rate**	
'Inner' Belfast:						
Smithfield	935	10	10.7	2	2.1	91
St. George's	1,004	9	9.0	2	2.0	4
Court	1,101	13	11.8	8	7.3	30
Dock	1,515	4	2.6	6	4.0	5
Sub-total	4,555	36	7.9	18	3.9	44
'Outer' Belfast:						
Duncairn	3,586	20	5.6	13	3.6	13
Falls	5,376	18	3.3	27	5.0	93
Ormeau	3,411	12	3.5	16	4.7	10
Windsor	1,655	6	3.6	2	1.2	15
Clifton	5,123	23	4.5	22	4.3	34
St. Anne's	2,283	10	4.4	16	7.0	41
Shankill	3,145	11	3.5	12	3.8	6
Victoria	3,026	9	3.0	11	3.6	5
Woodvale	3,214	16	5.0	15	4.7	8
Cromac	2,016	2	1.0	14	6.9	24
Pottinger	3,961	12	3.0	19	4.8	15
Sub-total	36,796	139	3.8	167	4.5	24
Total	41,351	175	4.2	185	4.5	29

* Calculated per 1,000 (live and still) births; **See: Park (1962)

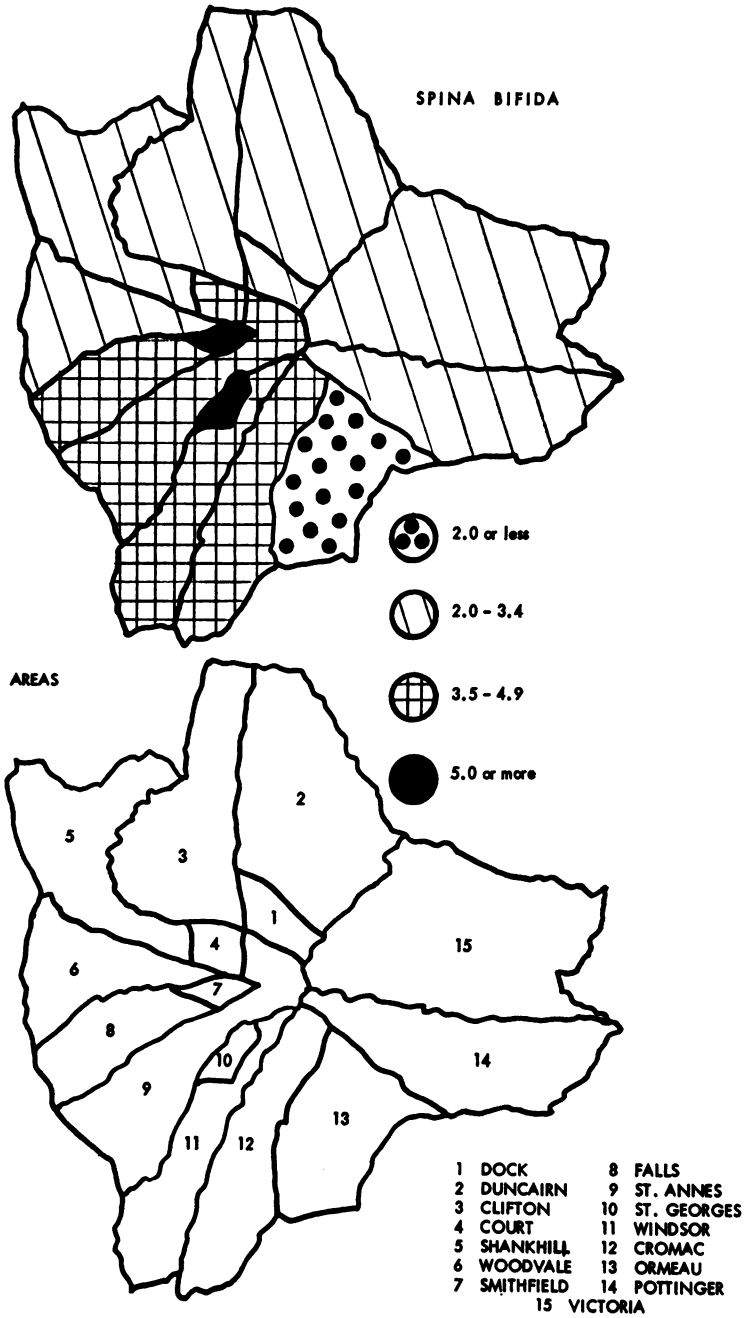

FIG. 1 INCIDENCE OF SPINA BIFIDA PER 1,000 (LIVE AND STILL) BIRTHS BY RESIDENTIAL AREA WITHIN BELFAST 1964-68

Compared with other cities with populations of 250,000 or over in the United Kingdom, Belfast has a high infant mortality rate, 30.6 per 1,000 live and stillbirths (Elwood & Pemberton, 1971). There is considerable variation in both perinatal and post-perinatal mortality rates between the fifteen electoral wards of Belfast. For example, the highest perinatal mortality rate was in Smithfield Ward (53.5), almost twice that for Pottinger Ward (27.3). Significantly, higher rates occurred in the 'Inner' compared with the 'Outer' Belfast areas, 45.9 and 35.3 respectively. Neural tube malformations accounted for 15 per cent of all perinatal mortality in Belfast but the proportion varied considerably by electoral ward. For example, these malformations were responsible for 33 per cent of all such deaths in Court Ward, and for only 12 per cent in Shankill Ward. 'Inner' Belfast fared less favourably than 'Outer'; 21 per cent as opposed to 15 per cent of all such deaths was due to neural tube malformations.

TABLE III

Distribution by index of overcrowding

Data		*Number of persons per room* 1	1–2	2+	*Total*
Total Births	No.	16,668	21,352	3,331	41,351
Anencephalus	No.	77	70	28	175
	Rate	4.6	3.3	8.4	4.2
Spina Bifida (fatal)	No.	32	73	9	114
	Rate	1.9	3.4	2.7	2.8
Spina Bifida (non-fatal)	No.	33	32	6	71
	Rate	2.0	1.5	1.8	1.7
Spina Bifida (all)	No.	65	105	15	185
	Rate	3.9	4.9	4.5	4.5
Both defects	No.	142	175	43	360
	Rate	8.5	8.2	12.9	8.7

For both defects: $\chi^2=7.4$; d.f.$=2$; $0.01>P>0.001$

As housing and socio-economic conditions vary in electoral wards, the relationship between the incidence of neural tube malformations and an overcrowding index based on the number of persons per room was examined (Table III). The incidence of neural tube malformations rises as the degree of overcrowding increases ($\chi^2=7.4$; d.f.$=2$; $0.01>P>0.001$). For spina bifida, the association exists for infants who die early in life but not for non-fatal cases.

The influence of such biosocial factors as maternal age and parity also were examined. Mothers less than 20 years of age had below average rates for both defects (3.6 and 2.5 per 1,000 for anencephalus and spina bifida respectively), mothers aged 40 or more years had average rates (4.4 and 4.5 per 1,000 births); but mothers between 20 and 24 years had the highest rates (4.9 and 5.0 per 1,000 births). A history of one or more previous abortion or stillbirth was associated with an 'above average' risk of an anencephalic or spina bifida infant compared with mothers who had no such previous reproductive experience. A significant trend

with the number of previous livebirths is present in anencephalus ($\chi^2=14.7$; d.f.=7; $0.05>P>0.02$) but not in spina bifida ($\chi^2=6.7$; d.f.=7; $0.50>P>0.30$). The incidence of anencephalus was high in first pregnancies (5.2 per 1,000) after which it declined to 2.5 per 1,000 for the third pregnancy to increase again after four pregnancies.

Finally, the survival of the 185 spina bifida children in Belfast was compared with that of spina bifida children in other parts of the United Kingdom. Of the total cases observed 71 (38 per cent) were alive at the time of ascertainment (Table IV). The survival rate was lower in female than male spina bifida children (34 per cent and 45 per cent respectively). Over the five years studied, survival had not altered significantly. Spina bifida children whose mothers were resident in 'Inner' Belfast fare much worse than those in 'Outer' Belfast, only 18.9 per cent compared with 39.5 per cent respectively being alive (Table V). A greater proportion of spina bifida infants were alive at their first birthday in Belfast than in Liverpool, Birmingham, or South Wales (Table VI). In the Irish studies survival rates beyond the perinatal period are not available, but the proportion of Belfast spina bifida infants alive at the second week, 72.5 per cent, is not very different from Coffey's (1970) finding for the whole of the Irish Republic, 73.6 per cent in 1953-4 and 66.7 per cent in 1961-62.

TABLE IV

Proportions of Spina Bifida Survivors at time of Ascertainment by Sex and Year

Sex	*Year of Birth*					*Total*
	1964	1965	1966	1967	1968	1964-68
Male:						
All	16	18	16	13	13	76
Alive	4	10	6	7	7	34
%	25	55	37	54	54	45
Female:						
All	26	25	16	20	22	109
Alive	9	9	4	5	10	37
%	35	36	25	25	45	34
Both Sexes:						
All	42	43	32	33	35	185
Alive	13	19	10	12	17	71
%	31	44	31	36	48	38

Test of secular trend in number of survivors

Male: $\chi^2=2.97$; d.f.=4; $P>0.50$

Female: $\chi^2=4.15$; d.f.=4; $P>0.30$

Both Sexes: $\chi^2=4.43$; d.f.=4; $P>0.30$

TABLE V

Survival Times of 185 Spina Bifida Children in Belfast

Data	*'Inner' Belfast*		*'Outer' Belfast*		*All Belfast*	
	No.	*%*	*No.*	*%*	*No.*	*%*
Total observed	18	100	167	100	185	100
Stillborn	4	22.2	26	15.6	30	16.2
Death in 1st week	4	22.2	17	10.2	21	11.3
Death in 2–52 weeks	3	16.6	51	30.5	54	29.2
Death in 1 year or over	2	11.1	7	4.2	9	4.9
Alive	5	18.9	66	39.5	71	38.4

TABLE VI

Spina Bifida Survival Rates in Four Communities in the United Kingdom

Area and Period of Observation	*Total*		*Stillborn*		*Died 0–365 Days*		*Alive at First Birthday*	
	No.	*(%)*	*No.*	*(%)*	*No.*	*(%)*	*No.*	*(%)*
Belfast 1964-68 (Elwood & Nevin, 1973)	185	(100)	30	(16.2)	75	(40.5)	80	(43.3)
Liverpool 1960-62 (Rickham & Mawdsley, 1966)	203	(100)	46	(22.7)	84	(41.4)	73	(35.9)
Birmingham 1960-62 (Knox, 1967)	132	(100)	29	(22.0)	71	(53.8)	32	(24.2)
South Wales 1956-62 (Laurence & Tew, 1971)	425	(100)	110	(25.9)	239	(56.2)	76	(17.9)

DISCUSSION

This study, like earlier investigations of neural tube malformations in Northern Ireland (Stevenson & Warnock, 1959; Stevenson et al, 1966; Elwood & Warnock, 1969; Elwood, 1970a) confirms the extremely high incidence of both anencephalus and spina bifida, exceeding those reported from other parts of the world (Stevenson et al, 1966). The explanation for the high incidence of these defects in Ireland is far from clear. The rates of anencephalus and/or spina bifida among children of migrants from Ireland are considerably lower than those reported in Ireland itself but higher than the country of domicile (Naggan & MacMahon, 1967; Leck, 1969). If neural tube malformations were determined only by genetic factors, then the frequency of affected offspring of parents of Irish ancestry would be similar to that of the county of origin.

As with other common malformations, the aetiology appears to be multifactorial with an important genetic factor and a substantial environmental component. The genetic factor is probably polygenic but the mechanism by which it acts is not known. The environmental component is also unknown. Consideration of birth order, maternal age, and the secular and seasonal variation in the incidence has not clarified the environmental factor. Whatever the environmental factor may be, it is important to remember that probably only fetuses that are genetically 'susceptible' are at risk.

There are a number of epidemiological associations which indicate possible environmental factors: there is a marked geographical gradient in the incidence of neural tube malformations in the United Kingdom which steadily increases from the south and east to the north and west. The incidence (per 1,000 total births) in the south-east is about 1.5 for anencephaly and 2.0 for spina bifida, in Wales 4.13 and 3.54, and in Northern Ireland 4.2 and 4.5 respectively. This variation may depend on a variety of factors.

In England and Wales family size is smaller and the incidence of neural tube malformations lower. Differences in regional parity and maternal age between birth populations at risk, however, accounted for less than 5 per cent of the excess of the Northern Irish anencephalic rate over that of England and Wales (Elwood, 1970b). From an investigation of the geographical variation of neural tube malformations in South Wales, Richards, Roberts & Lloyd (1972) also concluded that differences in biosocial factors such as parity and social class did not explain the marked area differences.

An attempt has been made to explain the geographical variation of anencephalus and spina bifida with hardness of water supply which in general, is high in the south-east and low in the north-west (Fedrick, 1970). However, more detailed studies of individual regions do not confirm the association (Fielding & Smithells, 1971).

More recently dietary factors have been implicated in the aetiology of neural tube malformations. Renwick (1972) has put forward evidence supporting a hypothesis that potatoes might be the common factor. He has postulated that the blight fungus, *Phytophthora infestans*, induces a teratogen in certain potato tubers and has suggested that 95 per cent of cases of spina bifida would be prevented if potatoes were no longer eaten in Britain. This hypothesis has been considered elsewhere (Elwood & Nevin, 1973; Elwood, 1972) but an obvious test that has been applied to the hypothesis is that of animal experiments. Poswillo, Hamilton & Sopher (1972) fed female marmosets blighted potatoes and found skull defects in some of the offspring. Details of the skull defect are not yet published but the abnormality apparently differs from the human malformations. Further assessment of Renwick's (1972) hypothesis must await additional animal work and perhaps a potato avoidance trial in mothers who have had a previous infant with anencephalus and/or spina bifida.

The present study indicates that in Belfast, once every five days, a baby is born with either anencephalus or spina bifida. Mothers resident in 'Inner' Belfast and those living in overcrowded conditions are at greater risk. As infants with anencephalus are stillborn or live only a few hours, management is mainly the concern of obstetricians. However, spina bifida presents a more formidable problem, as

patients are usually liveborn and mostly have serious loss of function of the lower limbs, bladder, and rectum. Active surgical intervention has raised the survival rate without unfortunately reducing the proportion of survivors who are seriously handicapped. The present investigation shows a higher survival rate in Belfast children with spina bifida than in any other area in the United Kingdom. An explanation for this is not clear but an important question to be answered is whether the better survival rate is due to less severely affected cases occurring in Ireland compared with England and Wales. In Northern Ireland, as a result of the high incidence and the better survival rate, spina bifida has become a major community problem, greater than for other areas of the United Kingdom. As the environmental component in the aetiology of neural tube malformations remains unidentified, at present, genetic counselling and early detection *in utero* with selective termination of affected fetuses are the only available methods for the control of these malformations. The early diagnosis of anencephalus has been achieved by ultrasound B scan (Campbell, Johnstone, Holt & May, 1972) and by the finding of high levels of alpha fetoprotein (AFP) in amniotic fluid (Brock & Sutcliffe, 1972; Lorber, Stewart & Ward, 1973). As yet spina bifida cannot be diagnosed *in utero* with certainty but high AFP concentrations in the amniotic fluid in early pregnancy may also prove helpful in the diagnosis of a fetus with a myelocele (Brock & Sutcliffe, 1972; Nevin, Nesbitt & Thompson, 1973).

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Requests for reprints to Dr. N. C. Nevin, Human Genetics Unit, Department of Medical Statistics, Institute of Clinical Science, Grosvenor Road, Belfast BT12 6BJ.

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BOOK REVIEWS

THE SEEDS OF TIME, BEING A SHORT HISTORY OF THE BELFAST GENERAL AND ROYAL HOSPITAL, 1850–1903. By R. S. Allison, V.R.D., F.R.C.P., D.P.M. (Pp. xx+318. With illustrations and xvii appendices. £2.00). Belfast: Brough, Cox and Dunn. 1972.

DOCTOR ALLISON has completed with great success his history of the Belfast General Hospital, re-named the Belfast Royal Hospital in 1875, and the Royal Victoria Hospital in 1898. Taken with Malcolm's history of the General Hospital and Marshall's history of the hospital on the Grovenor Road site, this volume puts Royal Victoria Hospital men and women in the fortunate and happy position of being able easily to be familiar with the history of their hospital, its medical school, and the city it has served since 1792. One sees with sincere admiration how Doctor Allison must have laboured to assemble and marshal the material, and yet the Allisonian prose moves as serenely and as lucidly as ever. The triple currents of our history flow through the chapters. Medicine, nursing and administration in turn take the main stream as their successive problems, tasks and difficulties are met, recognised, tackled and solved. There is a vast amount of information, all instructive, and there is a sufficiency of biographical detail and anecdote. Royal Victoria Hospital nurses will value chapter 14 on nursing at the hospital. It is likely that the hospital never gave, and perhaps still does not give, enough attention to public and occupational health, but the work of Malcolm, H. S. Purdon and Henry O'Neill in this field leaves us open to less reproach. O'Neill's work is discussed in chapter 9. Your reviewer has the honour to be one of William Whitla's successors in his wards, and he first pored over Whitla's Materia Medica and Therapeutics as a schoolboy. A delightful chapter (10) amounts to a presentation of Whitla and his work, and is the best account of Whitla available. Chapter 8 recounts the coming of anaesthesia and antiseptic surgery to the hospital with all the blessings that ensued for the citizens. The history of surgery in Belfast cannot be written entirely in terms of the Royal Hospital's experience. John Campbell (1895) reported 22 abdominal operations done between 1893 and 1895 with only two deaths. Four were done at home and 18 in the Samaritan Hospital. They included the first 2 cases of vaginal hysterectomy done in the city.

The paper, printing and design do the Belfast printing trade and Messrs. Brough, Cox and Dunn the greatest credit. The frontispiece is a reproduction of Mr. Frank McKelvey's fine picture of the Frederick Street Hospital. There is a picture of Lady Pirrie facing page 237. We take it that the inscription on Queen Victoria's statue in the quadrangle – *dux femina facti* – really applies to Lady Pirrie. Your reviewer remembers her as an aged lady, president of the Royal Belfast Academical Institution, breaking into gentle tears as she addressed the school and spoke of her husband, the founder with her of the new hospital on the Grosvenor Road, so many years before.

The book has been the victim of a few oversights in proof-reading and of some misprints. Two errors are of some moment. We think that Cuming was appointed to the chair of medicine in the Queen's College in 1865 and not 1858 (page 213), and, if so, he was 32 at the time and held office as attending physician for 34 years. Whitla, we think, presented the *Manual of the Theory and Practice of Medicine* to the members of the British Medical Association at the Belfast meeting of 1909. Osler attended that meeting and must have received the two volumes. We wonder what Osler made of it, and where his copy is now. Page 83 might be misread to mean that Almroth Wright and William MacCormac were medical students at Inst, whereas they were schoolboys there after the medical school of Belfast had been re-established in the Queen's College. Thomas Andrews was at Inst before the medical school there was founded and his first connection with it was as professor of chemistry.

The question of the existence and mosquito-transmission of malaria in Belfast is discussed on page 61. Even granted that the seven cases of ague recorded were malaria, they may have been relapses in patients who had been abroad. (The first case of malaria your reviewer saw

was in a repatriated soldier in Doagh in 1941). An epidemic of malaria was reported in County Cork in the years 1857–1858 (Cummins 1957), but that was before the diagnosis could be made by microscopy of the red cells. It is certainly not possible to understand the social, economic and military history of Ulster without taking into account the epidemic diseases, and any information on the existence of epidemic malaria (or, even more important, epidemic sprue) ought to be recorded. It is interesting that there is no mention of endemic, non-venereal syphilis which was recorded in Londonderry under the name of sibbens (Johnston 1960). H. S. Purdon (1875) mentions a questionable case seen at the Belfast Skin Hospital in 1868 under the name of button scurvy. As for the perpetuation of typhus in the community (page 9) the Brill-Zinsser type of reactivation of a long dormant infection must have been important. Even now it is worth thinking of this in some cases of fever, for example in itinerants, in whom the disease lingered longest.

We see more in this book than the history of a hospital. We see a movement of the national spirit. Here in Ulster we have brought forth a new nation. It was that nation's spirit which first blew life into the charity, which is now the Royal Victoria Hospital, and sustained it. Now that hospital imparts its own spirit to its staff, its students, its patients, and their fellow citizens. Long may it be so. We feel able to offer Doctor Allison the thanks, not only of his hospital, but of his country.

J.S.L.

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THE LIFE AND TIMES OF A VOLUNTARY HOSPITAL. The Royal Belfast Hospital For Sick Children. 1873–1948. By H. G. Calwell, M.A., M.D. (Pp. xiii+138; Plates xxxiv. £1.50). Belfast: Brough, Cox and Dunn. 1973.

IN the second half of the last century due to many not necessary related causes a large number of hospitals appeared throughout Great Britain and Ireland and several this year are celebrating their centenary.

In Belfast at the time two such hospitals appeared both dedicated to the care of sick children—The Belfast Hospital for Sick Children and The Ulster Hospital for Women and Children. Dr. Calwell in his book "The Life and Times of a Voluntary Hospital" deals with the first 75 years of the Royal Belfast Hospital for Sick Children. He did not complete the last 25 years as it is no longer a voluntary hospital but was by then absorbed into the National Health Service.

This is a splendid book and beautifully produced. It is not only the story of a hospital but also the story of the social history of that time. It traces the hospital as it started in King Street, then through that important period in Queen Street until it occupied its present site on the Falls Road. There it is part of what is probably one of the best hospital complexes in the United Kingdom. Our students are indeed fortunate to be able to get their entire medical training and teaching if they wish in the confines of one single campus.

Dr. Calwell does not restrict himself to the obvious advances in medicine that have taken place over the years but he does show how dependent a hospital is on its other aspects – nursing, diet, administration, finance, teaching, epidemics, and its relationship to the major recurring causes of unrest. This hospital has come through three major wars, all of which involved medical staff, nursing staff, food shortage, rationing, not to mention blackouts and bomb raids. It has been hard to isolate it from Belfast's tragic political unrest, all of which has added to difficulties in recruiting of staff.

In World War II Mrs. D. C. Lindsay's gift of her home—Lissue, near Lisburn—now the hospital's convalescent home, was indeed one of the most valuable gifts ever transferred to the Northern Ireland Hospitals Authority.

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In World War II Mrs. D. C. Lindsay's gift of her home—Lissue, near Lisburn—now the hospital's convalescent home, was indeed one of the most valuable gifts ever transferred to the Northern Ireland Hospitals Authority.

It is impossible in a short review to cover all the aspects of this book but no one will be competent to speak on hospital advances in Ulster without reference to this book; it should be in every doctor's library. It is an accurate unbiased survey of the first 75 years of this hospital when finances had to be found and fought for and when as yet the State had no control.

Finally a book is often enhanced by its format, and Dr. Calwell is to be congratulated on the lay out and his choice of illustrations. Messrs. Brough, Cox & Dunn Ltd., the printers, have taken special care that this book will be a credit to them and to the Belfast Medical School.

I.F.

NUTRITION AND ITS DISORDERS. By Donald S. McLaren. (Pp. 280. Figs 15. £1.50). Edinburgh and London: Churchill Livingstone. 1972.

THIS is a pleasant book to read with a good layout and categorisation, though a subindex at the beginning might have been a useful addition. It has the advantage of being a small book, and would be useful for a reference book, rather than a teaching book. It has been written mainly for medical students, but could be useful to others though a preliminary knowledge of the subject is often necessary. The diagrams are clear and useful.

The discussion on the treatment of some diseases is at times a little vague, and therefore it is assumed that the student has a basic knowledge of the treatment concerned, as in diabetes and coeliac disease. There is not enough detail regarding treatment to make the book useful for reference in this respect. However, I do feel the book contains much useful detailed information which is well presented.

D.C.L.

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There is a great deal of interesting and valuable information in this book but it would be unwise to recommend the reader to look up just one contribution – it would be safer for his patients if he read the whole section including the discussion and better still if he read the whole book.

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Finally a book is often enhanced by its format, and Dr. Calwell is to be congratulated on the lay out and his choice of illustrations. Messrs. Brough, Cox & Dunn Ltd., the printers, have taken special care that this book will be a credit to them and to the Belfast Medical School.

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D.R.H.

BRAIN'S CLINICAL NEUROLOGY. Revised by Roger Bannister. Fourth Edition. (Pp. xii+439; figs. 83. Boards. £4.80; paper £3.00). London: Oxford University Press, 1973.

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The cytology service is described in detail. A tremendous effort has been made to evaluate the necessity of such a service, the age at which it should commence and finally to establish the frequency with which the smear should be repeated by a system of recall over and above the usual routine. Many hitherto unknown facts have been observed, e.g., the highest incidence of abnormal smears are found among widows and recently divorced yet the ordinary request form does not include such details so that such people could be classified under the special "at risk" group.

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W.T.

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> "Successful management (of obesity) when it does occur is the result of a knowledgeable sympathetic physician having the time and the interest to meet repeatedly with a patient who has at least a modicum of insight into the condition and a considerable motivation to reverse it."
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> "The patient who has the best chance to diet successfully therefore is a successful business or professional man who has become moderately obese during adult life, is married with children, emotionally mature and no marked tendency to depression."

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Dr. Craddock deals in detail with the treatment of obesity by drugs but puts this subject in its proper perspective in relation to the overall management of the patient. The data from his own general practice will be of considerable interest and his success represents his own considerable interest in the condition. The book can be recommended as an original outlook on a common problem and the information which it contains is conveniently and usefully gathered together. I think that he has fulfilled his aim to produce a comprehensive textbook on obesity and in addition to full clinical coverage he has included calorie tables and various types of diet. It will be useful to physicians both in hospital and outside.

D.R.H.

AUSCULTATION OF THE HEART, WITH NOTES ON OBSERVATION AND PALPATION. By Richard W. D. Turner, O.B.E., M.A., M.D., F.R.C.P., F.R.C.P.E. Fourth Edition. (Pp. vii+122. Figs. 10. £1.00). Edinburgh and London: Churchill Livingstone. 1972.

THOSE of us who remember the first edition of this work, which then appeared as a small pamphlet, will find many improvements in this new edition.

It consists of five sections, viz., Observation and Palpation, Auscultation, Heart Sounds, Murmurs and Summaries of Commonest Disorders. As such it is a short hand book of bedside cardiology and seeks to redress the overemphasis which of late has been placed on instrumental investigation

Many students will find clarification of basic signs which they have failed to understand in the past here and all doctors will benefit from reading this little book. It is excellent value. Unfortunately the binding of the copy which I received allowed pages 91–102 to come adrift.

M.W.J.B.

PRICE'S TEXTBOOK ON THE PRACTICE OF MEDICINE. Edited by Sir Ronald Bodley Scott. Eleventh Edition. (Pp. xiv+1417. Figs. 74. Plates 20. £8.00). London: Oxford University Press. 1973.

IN the seven years which have elapsed since the previous edition of this text book, advances in all fields of medicine have resulted in this new edition being largely re-set and re-written. Seventeen new contributors have joined in this work, making thirty-four authors in all. In spite of this the style is clear and uniform throughout and on this the editor is to be congratulated.

To avoid repetition an important new section has been added on antibiotics, growth and development, involution and senescence, genetic aspects of medicine, immune mechanisms in disease, the general aspects of cancer and its chemotherapy, and the uses of corticosteroids in therapy. The remaining sections have been thoroughly pruned, updated and where necessary the applied physiology introductions have been expanded.

A useful innovation is the incorporation of a section of twenty half-tone plates which are of high quality and will be found useful by students. Each section is succeeded by a list of main references for further reading, and each new chapter is separated by a full page giving the chapter heading in bold print. It is a pity that a list of authors responsible for the section was not shown here. The two column format has been preserved and the text and figures are excellent. For such a thick book it is quite comfortable to handle. There are the usual occasional spelling mistakes such as Butazolidin with an "e" and unfortunately the now almost obsolete term "Collagen Disease" is perpetuated in the text.

The new Price has very much grown in stature in this edition although expanding by only 158 pages. Its increase in price from 90s. to £8.00 is a further indication of the purchasing value of the pound. This is altogether an excellent book of reference and can be thoroughly recommended to the practitioner, consultant and senior and post-graduate student. At present day costs it remains good value.

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D.R.H.

AUSCULTATION OF THE HEART, WITH NOTES ON OBSERVATION AND PALPATION. By Richard W. D. Turner, O.B.E., M.A., M.D., F.R.C.P., F.R.C.P.E. Fourth Edition. (Pp. vii+122. Figs. 10. £1.00). Edinburgh and London: Churchill Livingstone. 1972.

THOSE of us who remember the first edition of this work, which then appeared as a small pamphlet, will find many improvements in this new edition.

It consists of five sections, viz., Observation and Palpation, Auscultation, Heart Sounds, Murmurs and Summaries of Commonest Disorders. As such it is a short hand book of bedside cardiology and seeks to redress the overemphasis which of late has been placed on instrumental investigation

Many students will find clarification of basic signs which they have failed to understand in the past here and all doctors will benefit from reading this little book. It is excellent value. Unfortunately the binding of the copy which I received allowed pages 91–102 to come adrift.

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IN the seven years which have elapsed since the previous edition of this text book, advances in all fields of medicine have resulted in this new edition being largely re-set and re-written. Seventeen new contributors have joined in this work, making thirty-four authors in all. In spite of this the style is clear and uniform throughout and on this the editor is to be congratulated.

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IN recent years there has been rapid progress in the understanding of Hodgkin's disease and improvements in its treatment so that many patients can now be cured. This has not yet been reflected in the attitude of doctors who too often regard the disease with unjustified pessimism and too frequently give treatment which is merely palliative. This book is by one of the pioneers of the present day approach to Hodgkin's disease and its main themes are the importance of clinical assessment of the patient and the potential of adequate treatment to cure even widespread disease. However, the scope of the book is comprehensive and it deals with all aspects of Hodgkin's disease. There is a good account of its pathology with descriptions of its various histopathological patterns and discussion of their significance in prognosis and treatment. Patterns of dissemination of the disease are described and the importance of an awareness of these in the management of the patient is stressed. Other sections are concerned with the vital role of radiology and staging laparotomy in assessing the extent of the disease to determine the correct treatment. Modern megavoltage radiotherapy and combination chemotherapy are very fully described in other chapters. Each chapter deals with its subject exhaustively, discussing its development and giving many references.

This is an excellent book which will surely become a standard text on Hodgkin's disease. It is written in a style which is extremely easily read, an unusual feature of books of this calibre. Dr. Kaplan is an advocate of the very thorough clinical investigation and aggressive treatment of patients with Hodgkin's disease and some of his views are still controversial. However, the evidence gathered from much clinical experience and the logical approach of this book will win him many disciples. This is a book for the specialist and should be read by pathologists, radiotherapists, radiologists and chemotherapists – all members of the team which are nowadays intimately concerned in the diagnosis and treatment of Hodgkin's disease.

J.H.R.

BASIC IMMUNOGENETICS. By H. Hugh Fudenberg, J. R. L. Pink, Daniel P. Stites and An-Chuan Wang. (Pp. vii+214. Illustrated. £2.20). London: Oxford Medical Publications. 1973.

GENETIC polymorphisms or inherited differences among individuals, elucidated by immunological methods, is a field which may be loosely termed immunogenetics. The authors of "Basic Immunogenetics" have not attempted to cover the whole range of immunogenetics but have selected areas where polymorphism seems to be of particular importance and which illustrate the variety and potential complexity of other polymorphic systems. The greater part of the book, chapters 1 to 4, deals with the genetics of antibody diversity. This section is a succint review of the heterogeneity of the immunoglobulin molecule. In contrast to the convention "one gene – one polypeptide' hypothesis which has been found to govern the synthesis of all proteins examined to date, each immunoglobulin polypeptide chain is the product of two different structural genes, one for the variable region and another for the constant region of the chain. Although little is known about the genetically controlled regulatory systems in man, some findings are presented which might be interpreted as evidence for the existence of regulatory systems controlling immunoglobulin synthesis.

The second section of the book, chapter 5, which is concerned with the regulation of immune response, briefly adumbrates the genetics of transplantation and histocompatibility antigens.

The final section, chapter 6, is devoted to the genetics of blood groups. Unfortunately, there is only brief reference to the genetic aspects of the immune deficiency states in man. Although the choice of topics reflects the author's own research interest, it would have been preferable to have had more consideration of the immune deficiency states.

However, the writers present difficult topics lucidly. At the end of each chapter, there is a valuable list of recommended reading. The three appendices are superfluous. The overall impression is that this is a useful synopsis of present-day immunogenetics.

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SYMPOSIUM LIVER DISEASE. Edited by R. F. Robertson and J. I. Hall. (Pp. 149. £2.00). Edinburgh: Royal College of Physicians of Edinburgh. 1972.

THE nine papers read in Edinburgh on 2nd and 3rd December, 1971, including the Sydney Watson Smith, John Matheson Shaw and Stanley Davidson Lectures, together with major points raised in discussion form the text of this Royal College of Physicians of Edinburgh publication No. 41.

In his Sydney Watson Smith Lecture "Liver Function in the Newborn" Professor G. H. Lathe considers in depth the disturbances of biochemical mechanisms which may be responsible for neonatal jaundice. While a primary defect in glucuronyl transferase is probable various aggravating factors such as over-production, defective hepatic uptake and enterohepatic circulation of bilirubin may also be important.

Under the title "Clinical Implications of the Enterohepatic Circulation of Bile Salts" Dr. I. W. Percy-Robb discusses the effects on the absorption of dietary fat of hepatic cirrhosis and of disorders of the small bowel including the stagnant loop syndrome and disease or resection of the terminal ileum.

Dr. Neill McIntyre's paper "Difficulties in the Diagnosis of Jaundice" and the John Matheson Shaw Lecture "The Liver in Systemic Disease" by Dr. J. F. Stokes are full of physicianly wisdom and sound advice and are of great interest and importance to clinicians of many disciplines. The unmistakably authentic clinical setting of the many subjects which are discussed and the narrative style of presentation make them a pleasure to read.

"Virus Hepatitis in Renal Dialysis and Transplantation Units" is a summary of the paper by the late Lord Rosenheim, Chairman of the Working Party, whose detailed report was later published. Professor B. P. Marmion in his Stanley Davidson Lecture "Virology and Epidemiology of Viral Hepatitis" considers that "it is possible to extract from the flood of new information an optimistic and reassuring message about progress with the hepatitis problem." The lack of a simple, widely available laboratory system to detect and assay the hepatitis viruses remains the principal difficulty. The indications are that there are two distinct but similar classes of agents and one of them, SH virus, "is not a unique and sinister entity but is a representative of a particular category of viruses which have a non-cytocidal relationship with the host cell". The mechanism of disease production lies not in the infection per se but in the immune reaction mounted by the host against a virus-infected cell and in this the cell-mediated immune response involving T lymphocytes is crucial. Likewise, viral suppression of the immune response is central to the healthy carrier state.

The paper by Dr. Peter Sheuer "Liver Biopsy in Viral Hepatitis" describes the changes found in the various stages of viral hepatitis and distinguishes them from those caused by other conditions which may have to be considered in differential diagnosis. In patients with chronic hepatitis the most important distinction to be made is between chronic persistent and chronic aggressive hepatitis because of the very different prognosis carried by these conditions.

Professor Niall D. C. Finlayson in his Sydney Watson Smith Lecture, "Immunological Aspects of Chronic Liver Disease", portrays well the confusing picture of hyperglobulinaemia, increased immunoglobulin production and the formulation of various autoantibodies in primary biliary cirrhosis, active chronic hepatitis and cryptogenic cirrhosis. Although autoantibodies appear in the blood in some cases of chronic idiopathic liver disease none has yet been shown to have any pathogenetic significance, but the cytotoxic potential of immune lymphocytes is quite a different matter.

In discussing the management of gall bladder disease, Mr. A. A. Gunn advocates standard surgical practice, emphasizing the necessity for operative cholangiography in every patient submitted to operation for cholecystitis because the "classical" indications for opening the common bile duct are relatively unreliable. Since the mortality rate of choledochotomy is four to ten times that of simple cholecystectomy it is a procedure that should be avoided unless it is necessary

This small relatively inexpensive book brings together current knowledge and clinical experience in several important aspects of liver disease. While those who study the subject know how quickly the ground shifts, there is in this symposium much useful clinical information of lasting value. It will have a special appeal for the gastroenterologist but can also be strongly recommended to the general physician. T.F.

CLINICAL ASPECTS OF DEMENTIA by John Pearce and Edgar Miller. (Pp. 142, plates 12, figures 15. £5.00). London: Baillière Tindall. 1973.

PROBABLY on balance there has been as much failure as success so far in the efforts made by society to come to terms with ageing, and of all the problems involved the most onerous and distressing are those arising from mental disorder. Its prevalence in people aged 65 and over may be at least 30 per cent, and 6 per cent are disabled by primary neuronal or arteriosclerotic dementia. Of all the advances in geriatric medicine brought about by the epidemiological and clinical research of the past 20 years, none hold more promise for the well-being of old people than the diagnostic criteria now defined to differentiate between acute confusional states, depression and paraphrenia which may respond dramatically to appropriate treatment, and dementia which, in the present state of our knowledge, will not. Geriatric terminal care presents enough difficulties without the added torment of misunderstanding and lack of informed management of remediable psychiatric illness. This book, described by Professor John Walton as being written by a clinician essentially for clinicians, will do much to prevent such mismanagement. It is a concise review of research relating to dementia, and its practical application in clinical medicine. Introductory paragraphs on the biology of ageing in the central nervous system and epidemiology are followed by descriptions of the varieties and the differential diagnosis of dementia. Clinical examination is described in detail, including a most useful guide to the assessment of higher cortical function, illustrating particular tests and correlating them with specific disorders. The value and the limitations of special investigations are considered. The proportion of conditions capable of responding to treatment may be no better than 15 per cent, but in absolute numbers the total load of time-consuming and expensive investigation is formidable, and the merits of effective clinical screening are self-evident. Besides the clinical chapters written by Dr. John Pearce, a neurologist, Mr. Edgar Millar, a lecturer in clinical psychology, describes the value of psychological testing, and there is a useful final chapter on management of dementing patients. A psychiatrist might think differently, but to this reviewer this is a book to add to a background of knowledge of mental disorder in old age, rather than one to use as an introduction to it i.e. it is a book for the postgraduate rather than the undergraduate student of medicine. There is little reference to the other main psychiatric syndromes encountered in geriatric medical practice except under differential diagnosis. Paranoid, or persecutory syndromes, are not discussed although they are as likely to be confused with dementia, and are sometimes as responsive to appropriate treatment, as depression. However, this is a minor criticism, and this is a most useful guide to the investigation and care of one of the most perplexing conditions occurring with increasing frequency in clinical practice. It should appeal as much to the psychiatrist as to the physician in general or geriatric practice and the family doctor.

G.F.A.

CLINICAL EXAMINATION. Third Edition. Edited by John Macleod. (Pp. xi+489, figures 125. £4.00). Edinburgh and London: Churchill Livingstone. 1973.

A THIRD edition produced in the space of 9 years indicates the popularity and excellence of this work.

This book is certainly an excellent introduction to bedside and outpatient clinical work and approaches this vital aspect of medical diagnosis with not only clear thinking but also clear concise writing. The new edition is very similar to the previous ones although the section "Examination of the psycological state" and "The examination of the nervous system" have been re-written, the former—because of its importance has been closely integrated with the first chapter on history taking.

It compares favourably with older books of this type, e.g. Hutchinson and Hunter's "Clinical Methods", and it can be recommended whole-heartedly to students in their clinical years and indeed also to all those who continue to deal with patients after they have qualified.

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THERE are several large and expensive medical dictionaries, but only one published some years ago is in English English, and spelling and usage in North America differ considerably from that in Great Britain. This volume whose production and format reflects great credit on the publishers, especially in these days of spiralling prices, meets a very real need. Doubtless the specialist could quarrel about the omission of some words and about the brief definition of others, but consultants, family doctors and students will find it a useful guide to precision, and a help with spelling on those occasions when bad writing cannot hide doubt and uncertainty. The ever-increasing number of those working with the doctor—whether secretaries, nurses or technicians will find it invaluable. The author, who is editor of the Practitioner, has prepared a working dictionary and gives only the derivation of some of the more important prefixes and suffixes. Abbreviations are rarely given since their use can be misleading, dangerous and the ruination of style, and eponyms are also discouraged. When plurals are not made by adding (s) they are given. This is a last rearguard action against such Transatlantic usages as "serums", but the retention of sarcomata and teratomata and the acceptance of a plural with "s" for other tumours is less useful.

It is doubtful if the 70 pages giving tables of arteries, muscles, nerves and veins with anatomical details are really sufficiently useful for inclusion. Conversion factors for metric and imperial measures are given, but tables or graphs facilitating rapid conversion would be more welcome.

MEDICINE IN SOCIETY by Henry Miller (Pp. 87. £0.80 paper: £2.25 boards). London: Oxford University Press. 1973.

ANYTHING written by Henry Miller, physician and now Vice Chancellor of Newcastle University, is certain to provoke thought and probably a mixture of agreement and disagreement, perhaps even violent disagreement. This book is intended for discussion by an informed general public and it clearly and briefly outlines many of the serious defects in medicine today and takes a hard look at our priorities and resources. The author's clear and vivid writing sometimes tends to overstate the many theses presented, but medical men and our political masters should read this book and ponder over the conflicting issues outlined. It must be realised that medicine alone cannot solve these problems, but that in the future many hard and difficult decisions must be taken calling for informed political thinking in its highest sense.

LIVER BIOPSY INTERPRETATION by Peter J. Scheuler. Second Edition. (Pp. x+171; 110 illustrations and 59 in colour. £6.00). London: Baillière Tindall. 1973.

NEEDLE biopsy of the liver is a well established aid to diagnosis, but the interpretation of the small amounts of tissue can be extremely difficult. Large textbooks on liver disease do little to prepare the histologist for this task. Dr. Schueler's book, first published in 1968, has been invaluable in the laboratory and a new edition is very welcome.

A new chapter deals with practical problems of biopsy diagnosis and the interpretation of fibrosis, necrosis and cholestasis. Rewritten sections with considerable changes deal with toxic and drug induced disturbances, acute viral and chronic hepatitis and there are significant and valuable changes throughout the text. The book promises to be even more useful when consulted, as in the past, in the laboratory and when the pressure is on the pathologist to come to some diagnosis. All the useful facts are presented, histological findings are well illustrated in black and white and in colour and relevant technical methods are given. The reviewer would like more emphasis on the safe transport of friable specimens, and finds the technique of the container completely filled with fixitive and without airlock, learnt from the embryologists, useful. The author wisely avoids discussion of liver disease in its many aspects, but some indication as to how he allows his report and decision to be influenced by biochemical findings would be useful. J.E.M.

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THOMSON'S CONCISE MEDICAL DICTIONARY by William A. R. Thomson, M.D. (Pp. vii+439. £1.50). Edinburgh and London: Churchill Livingstone 1973.

THERE are several large and expensive medical dictionaries, but only one published some years ago is in English English, and spelling and usage in North America differ considerably from that in Great Britain. This volume whose production and format reflects great credit on the publishers, especially in these days of spiralling prices, meets a very real need. Doubtless the specialist could quarrel about the omission of some words and about the brief definition of others, but consultants, family doctors and students will find it a useful guide to precision, and a help with spelling on those occasions when bad writing cannot hide doubt and uncertainty. The ever-increasing number of those working with the doctor—whether secretaries, nurses or technicians will find it invaluable. The author, who is editor of the Practitioner, has prepared a working dictionary and gives only the derivation of some of the more important prefixes and suffixes. Abbreviations are rarely given since their use can be misleading, dangerous and the ruination of style, and eponyms are also discouraged. When plurals are not made by adding (s) they are given. This is a last rearguard action against such Transatlantic usages as "serums", but the retention of sarcomata and teratomata and the acceptance of a plural with "s" for other tumours is less useful.

It is doubtful if the 70 pages giving tables of arteries, muscles, nerves and veins with anatomical details are really sufficiently useful for inclusion. Conversion factors for metric and imperial measures are given, but tables or graphs facilitating rapid conversion would be more welcome.

MEDICINE IN SOCIETY by Henry Miller (Pp. 87. £0.80 paper: £2.25 boards). London: Oxford University Press. 1973.

ANYTHING written by Henry Miller, physician and now Vice Chancellor of Newcastle University, is certain to provoke thought and probably a mixture of agreement and disagreement, perhaps even violent disagreement. This book is intended for discussion by an informed general public and it clearly and briefly outlines many of the serious defects in medicine today and takes a hard look at our priorities and resources. The author's clear and vivid writing sometimes tends to overstate the many theses presented, but medical men and our political masters should read this book and ponder over the conflicting issues outlined. It must be realised that medicine alone cannot solve these problems, but that in the future many hard and difficult decisions must be taken calling for informed political thinking in its highest sense.

LIVER BIOPSY INTERPRETATION by Peter J. Scheuler. Second Edition. (Pp. x+171; 110 illustrations and 59 in colour. £6.00). London: Baillière Tindall. 1973.

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