VOLUME 45 1976 No. 1

THE ULSTER MEDICAL JOURNAL

PUBLISHED BY
THE ULSTER MEDICAL SOCIETY

CONTENTS

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2. Manuscripts should be typewritten with double spacing and with wide margins. They should be fully corrected, and contributors will be responsible for the payment of any sum charged for alterations in printer's proof.

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4. Scientific measurements should be given in SI units, but blood pressure should be expressed in mmHg and haemoglobin as g/dl. Traditional units may usefully be given in parenthesis and conversion factors may be stated, especially with tables and illustrations.

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THE ULSTER MEDICAL SOCIETY

P.O. Box 222,
Belfast City Hospital,
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If you are not a member of the Ulster Medical Society, we would appeal to you to give the question of joining your consideration. The Society has been in existence since 1862 (and is the direct descendant of the Belfast Medical Society founded in 1806), and has always been active in keeping its members interested in the advances in medical science. Meetings are held at intervals of a fortnight during the winter months, and papers are contributed by members and distinguished guests. Facilities are provided for doctors to meet informally afterwards and have a cup of tea. *The Ulster Medical Journal, the official organ of the Society, is issued to all Fellows and Members free of charge.* The Society will soon be rehoused in its own Rooms (in the new buildings at the Medical Biology Centre) which will replace the Whitla Medical Institute which had to be vacated in 1965.

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

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To DR. J. D. BIGGART,
THE LABORATORIES,
BELFAST CITY HOSPITAL,
BELFAST BT9 7AD.

.....19.....

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.....

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THE
ULSTER MEDICAL JOURNAL

PUBLISHED ON BEHALF OF THE ULSTER MEDICAL SOCIETY

VOLUME 45 1976 No. 1

THE ULSTER MEDICAL SOCIETY. QUO VADIS ?

D. A. D. MONTGOMERY

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

PRESIDENTIAL ADDRESS TO ULSTER MEDICAL SOCIETY, SESSION 1975–76

EACH YEAR at this time the incoming President is given the opportunity of addressing the Society on some theme of his choosing. My duty is clear enough—I have to give a talk! Equally clearly, your work is set before you. *You* have to listen! I trust we will finish our work at roughly the same time and as well disposed to each other as when we started.

This session will prove to be an important landmark in the life of our Society. Early next year we will take up residence in our new home in the extension to the Biology building. Over the years we have had several homes. The most famous, of course, was the Whitla Medical Institute, a building of great elegance and comfort, with which many of you were familiar and loved greatly. Dr. Allison recalls in "The Seeds of Time" that, "Sir William's great affection for the Society led him to donate a permanent home or Medical Institute to the Society in College Square North, which was then the University Square and College Gardens of the period. He spent £6,000 on its building and furnishing before it was declared open in 1902". Earlier meetings were held, first in a rented house in High Street and then in rooms in the basement of the new wing of the General Hospital in Frederick Street. In 1884, the Society moved again to the Museum buildings in College Square North. From there it was but a short step across the road to Sir William's magnificent new Medical Institute. Here the Society remained at home for the next sixty years or so. Alas, in the sixties, the rising cost of its upkeep, the threatened imposition of rates and the decreasing use made of the premises by Fellows who could no longer find parking space for their cars in the vicinity, forced council to relinquish the property and it was sold to the governors of the Royal Belfast Academical Institution. This sad chapter in our history is vividly retold in Dr. Strain's excellent paper on the "History of the Ulster Medical Society". Since then we have been most generously

housed by the University, first in the Keir Building and more recently in the Institute of Biology. Through their further consideration and help, permanent accommodation has been provided for the Society in the extension to the Biology Building and we hope to take up residence early next year. Then we shall have the opportunity of thanking the University authorities properly, for their kindness.

In 1967, Dr. Strain wrote these prophetic words: "Perhaps too in days to come, at some focal point dedicated to the purposes of the Ulster Medical Society the stone faces of Gordon, Andrews, Redfern and McCormack, with the portrait of Sir William himself, may look down on a new generation of their professional colleagues and not be left to stare in vain into the traffic-turmoil of College Square North where the Hippocratic tradition no longer prevails". All this has come to pass and these splendid men, the "immortals" of the Society, have returned to their proper setting in a medical environment. The Society must be for ever grateful to the trustees, the University and successive members of Council who, with wisdom and dedication, have made all this possible.

The new session, 1975–76, upon which we are now entering, opens the fourth quarter of the twentieth century and it seems an appropriate time to think about our Society, its place within the field of medicine, and the role it is to play today and in the future. We all recognize, I think, that we have received a goodly heritage from our founders, and the acquisition of a new home provides the impetus for the Society to regain some of the vigour of its earlier years. No organization like ours can rest on past achievements alone and hope to flourish. If the Society is unwilling to change as the needs of medicine alter, it will perish. While I see no signs of instant demise I wonder do I detect a little hardening of the arteries; some middle-aged complacency; perhaps an unwillingness to recognize the extent of the change that is taking place in medicine and contemporary society. As I thought about this I recognized that we would have to ask and try to answer some searching questions about our Society. I expect some of the younger Fellows and Members have been concerned with the same sort of problems. And so I thought that I would share my questions with you and see if we could assess the Society's present state of health and try to reach some conclusions which may possibly give us guidance for the conduct of our future affairs and development.

My questions are:

What is the Ulster Medical Society?

What has it done in the past?

What does it stand for today?

What should it do in the future?

Who speaks for medicine in Northern Ireland today?

To answer my first two questions certain points of reference and historical facts are needed. At first I turned to our constitution but to my surprise I obtained no help. Indeed, this document, which was readopted in 1972, is strangely silent on the purpose and object of the Society. As you know, it is the boast of the British people that they have no written constitution. Perhaps, unconsciously, our founders

felt there was wisdom in this attitude, and decided not to be too definite as to what the aims and objects were to be. This reluctance proved costly because subsequently the Society was unable to prove that its purpose was principally scientific and educational. As a result, legislation was introduced to compel us to pay rates from which we had previously been excused on the mistaken assumption that we were entitled to exemption. Thus the answers to my first two questions can only be found by looking back to our foundation and the subsequent growth and development of the Society. By analysis of the evidence it is possible to discover some of the answers. But before doing so it is helpful to look at historical developments and the reasons which drove medical men to combine together into groups for their mutual learning and advancement.

The precursor of the medical societies in the United Kingdom was the Royal College of Physicians of London, founded in 1518 by Thomas Linacre and incorporated by Henry VIII. In 1540, the Barber-Surgeons were incorporated and the Apothecaries followed in 1606. However, none of these was then, or subsequently, anything like a medical society as we understand it. In fact, we have to wait for over a century for the birth of the earliest strictly medical society. This was founded in Edinburgh in 1741. London followed soon afterwards in 1752, and several more were formed in the second half of the 18th century. In America, a similar pattern evolved. A medical society was reportedly in existence in Boston in 1735 and survived for a number of years. However, it was not until after the revolutionary war and in the new climate of independence that medical societies started to flourish.

Belfast did not lag far behind the others, for in 1806, "the most respectable physicians, surgeons and apothecaries, not merely of the town but of the vicinity likewise" . . . . enrolled under the designation of the Belfast Medical Society. A. G. Malcolm says that those responsible were activated by a spirit for mutual improvement in their common profession and that they were united for the purposes of affording to each an equal opportunity of obtaining professional information, by the contribution of all to a common purpose. This was the guiding principle of the Society which half a century later, in 1862, to be precise, joined with the Belfast Clinical and Pathological Society, a relative newcomer founded in 1853, to form the Ulster Medical Society. Clearly these men were activated by a desire to meet, to talk about medicine and to widen their knowledge. Education and unity seem to have been their watchwords and yet, as I said earlier, no hint of this was evident in their articles of association. No doubt the Society was a means of fostering friendship between members of the profession but the primary purpose seems to have been this desire for collective education and mutual self-help.

We may well ask what was responsible for the remarkable growth of medical societies during the latter part of the 18th century and the first part of the 19th? Largely it coincided with increasing knowledge of natural sciences and the first flowering of the scientific method in medicine and surgery, together with the decline in empiricism. As new discoveries were made and improvement in methods of treatment arose, inter-change of views and opportunities for discussion of new ideas became a necessity. It was the age of revolution and revival. Medical men, no

less than others, were shaking off the shackles of a dead past and the dogmatism of previous centuries. The ancient tradition by which doctors profited from secret remedies, of which the midwifery forceps of the Chamberlens was a prime example, was no longer acceptable. Medical men as members of a liberal profession were now eager to be the first to share new knowledge with their colleagues. With the rapid dissemination of new ideas it is not surprising that our founders were so concerned with education and the development of the art of medicine. This aspect excited the interest of Sir William Osler and formed the theme of his centennial address in 1903 to the New Haven Medical Association, a society which is our senior by a mere three years. Osler underlined the importance of education of the doctor after graduation and emphasised the place of the medical society in furthering this aim. "No class of men", he said, "need to call to mind more often the wise comment of Plato that education is a life-long business". The doctor's further education comes from patients, from books and journals, from association with colleagues and from thoughtful observation and reflection on life itself. He went on: "The well conducted medical society should represent a clearing house in which every physician in the district would receive his intellectual rating and in which he could find out his professional assets and liabilities. It keeps his mind open and receptive, and counteracts that tendency to premature senility which is apt to overtake a man who lives in a routine".

There is no doubt that our Society fulfilled this role effectively. It provided a library, some of the most important medical journals of the day, a reading room and regular well-conducted meetings. Over the years the educative role of the Society was outstanding. Additionally, the Whitla Institute provided many of the amenities of a club which, in the leisurely days up to the Second World War, added greatly to the enjoyment of the Fellows.

As knowledge increased in the 19th century more and more practitioners became specialists. These men had to cultivate their own postgraduate education for their very livelihood compelled them to keep abreast of the times. In those days the simple law of the market place demanded the regular up-dating of their knowledge. The practitioner, on the other hand, had no such strong incentive to increase his knowledge and, indeed, might have become sadly out of date without the stimulation of meeting keen minds and cultivating the new learning that the developing specialties were providing. The Society supplied opportunities for both to learn but it also offered a convenient place for specialist and practitioner to meet. Circumstances made it essential for the young specialist making his way to be on view. It provided him with a forum to show his wares with a contribution or discussion on his specialist subject.

It was during the session 1873–74 that the Ulster Medical Society first published its transactions. These were printed in the Quarterly Journal of Medical Science in Dublin, but in 1884 they were published separately in Belfast. Volume one of the Ulster Medical Journal as we know it today was issued in 1932. Council has always believed in its importance and felt that it should be recognized as the journal of the Belfast Medical School. Many a young medical writer has had the pleasure of

seeing early work printed in its pages. As well as providing an outlet for local research, the journal acts as a repository of local medical history. Each Presidential Address to the Society, the Annual Oration at the opening of the hospital year at the Royal Victoria Hospital, named lectures and biographical papers on prominent members of the Medical School are afforded space. Within its pages a rich harvest awaits the sickle of a future medical historian.

Thus, the Society evolved over the years providing unity of purpose, friendship and the opportunities for professional education.

In what I have said so far I have attempted to answer briefly my first two questions, viz, what is the Ulster Medical Society and what has it done in the past? Now I want to spend a little time considering what the Society stands for today.

The easy association between practitioner and specialist to which I have drawn attention and the happy equilibrium on which this was based, could not last for ever. As long as medicine, surgery and midwifery did not advance too quickly the balance was maintained and members were largely in touch with each other. Indeed, until World War Two the inscription physician and surgeon was found on many a brass plate and the all-round competence of the provincial surgeon was legendary. The rapid advance of scientific medicine in the second and third quarters of this century and particularly in the years following the last war changed all that. Scientific medicine has created the need for the specialist in ever-narrowing fields. As each specialty and sub-specialty has developed it has demanded a place in the academic sun. Lord Brain put it neatly when he said: "that as each specialty came of age it demanded a front door key to medical education and a roof of its own in the curriculum and examination hall". "The curriculum," he went on to say, "should not be that of a honeycomb in which individual bees add cell to cell, but rather that of the cerebral cortex in which all the cells are functionally inter-related."

Nonetheless, for the very reasons that drove the founders of our Society to join together for support and education, the newer specialty groups have felt the urge to band together to promote their own developing interests. So widespread has this become that in Northern Ireland today, there are no less than eight specialist societies as well as a host of local medical societies and clubs throughout the Province. I make no mention of National or European specialist societies nor those confined to Ireland as a whole. This development has tended to fragment the profession and the Ulster Medical Society has suffered in the process. The specialist society has its part to play in maintaining the thrust of scientific medicine but there is a real danger that they will flourish to the detriment of our own membership. Some of these organizations, however, maintain links with the Ulster Medical Society. One, for example, the Ulster Society for Internal Medicine, insists that its members must be fellows of our Society. Others, while not demanding co-membership hold joint meetings with us and contribute usefully to the programme. While the growth of the specialist society is understandable it carries with it the risk, it seems to me, of creating groups of doctors so specialized and devoid of contact with their fellow specialists, that they are quite out of touch with developments outside their own sphere of interest. Divisions are widening because communication between

specialities is becoming more difficult, due, as Mr. Kennedy reminded us in 1971, to their excessive use of jargon and neologisms. As a result, we are perilously close to the situation described so graphically in the book of Genesis: "And the whole earth was of one language and speech . . . . And the Lord said, Behold the people is one . . . . Go to, let us go down, and there confound their language, that they may not understand one another's speech".

Where is this process to end? Can it be halted? Should it be halted? Whatever one may say, specialization is here to stay and no one would contemplate a retreat from the remarkable benefits that it has conferred. Somehow, we must provide a means to integrate the new learning so that it can be made intelligible to the widest audience. Here our Society has an important role to play. Firstly, by providing a platform where specialists can speak to each other and those of us with a more generalized training. Secondly, our audience with its wider perspective can demand simplicity and a sense of proportion in the presentation and discussion of even the most obscure subject. It is excellent discipline for the specialist to be compelled to explain his subject to an audience unfamiliar with its technicalities. Often by doing so the specialist gains fresh insights into his own problems. Sir Geoffrey Vickers advanced this idea amusingly when he wrote: "Even the dogs may eat the crumbs which fall from the rich man's table, and in these days when the rich in knowledge eat such specialised food at such separate tables, only the dogs have a chance of a balanced diet". Our Society can and does provide the medium whereby we may obtain a balanced diet of learning and where we can enjoy the titbits from the exotic dishes prepared by those working in specialized fields. While recognizing the danger of over-specialization, we must not fail to appreciate what the specialist is trying to do, nor must we ignore them. Let us borrow some of their enthusiasm so that we may enlarge our own horizons. I believe that the dangers of over-specialization can be contained. All of us, I think, are realizing that the totality of medicine is greater than the sum of all its individual parts. Its strength lies in a proper amalgam. Only within a society like ours can this be achieved. We provide the opportunity for each branch of medicine to bring their skills and new knowledge to the notice of their colleagues and the chance to maintain contact with experts in other fields.

After the last war, Dean Acheson, the United States Secretary of State was severely criticised for daring to say that Great Britain had lost an Empire and was seeking a role for itself. Wordsworth's lines describe the setting:

> "Whither is fled the visionary gleam,
> Where is it now, the glory and the dream?"

Are we, today, in the Ulster Medical Society, facing the same sort of situation? Our pioneering role in postgraduate education is being taken over by the new postgraduate centres which have the advantage of receiving financial support from Government sources. The resurgence of interest in postgraduate education by the older Royal Colleges and the creation of newer colleges full of enthusiasm and drive have created facilities for specialist training to an extent never seen before. Nowadays, so much more is being demanded of the profession. More scientific

knowledge, more heroic surgery, more sophisticated medicine entail higher standards of qualification and specialist training. As a consequence, the programmes offered by these institutions far surpass anything that our Society could offer. Nevertheless, I detect a danger in the present situation in which the emphasis on technology and expertise is getting out of proportion. In our attempt to become masters of the science of medicine we are in serious danger of becoming illiterates in the art and forgetting that our primary purpose is caring for the sick. The recognition of the proper balance between the art of medicine and the science of medicine must be the aim of us all. Our Society, while partly shorn of its educative role, is uniquely placed to cherish and foster the art. Here is one of our essential tasks. If we fail to grasp our opportunity it is unlikely that the postgraduate centres, with their narrower perspective and concentration on the newer technologies will do it for us. The hard won art is easily made to look archaic. Don't let the technologist fool us for the true art of medicine is our most prized possession.

While I accept that a society like ours has largely lost out in specialist training programmes, we still have an important part to play in the education of the doctor. In a recent article, Murphy reminds us that medical education is made up of three separate strands. First there is the transmission of fact and routine methods. A more difficult step is education which is concerned with the structure of thought and inference, and the synthesis of knowledge into a coherent pattern. Lastly, the most elusive object is the cultivation of mature scholarship which requires that not only knowledge and organization be imparted, but that perspective and critical analysis develop as well. The first two can be acquired without great difficulty. The third is more elusive but it can be found and fostered in the company of minds, wiser and more mature than our own. A venerable society like our own can provide the necessary atmosphere in which our minds develop and ripen. Here too, we can learn that the best men in the profession are those who rate wisdom more highly than cleverness, who value compassion as much as efficiency and integrity more than expediency. Scholarship, the art of medicine and the cultivation of the highest codes of the practice of medicine for the wellbeing of our patients are ideals that our Society is best equipped to keep alive. If we fail they will be in real danger of being lost.

Earlier, I mentioned how the Ulster Medical Journal came into being. What then is its purpose today? The maintenance of a progressive medical journal is one of the most important tasks facing the Society. Its upkeep is expensive and costs of production continue to rise steeply but its value to the Society and to the medical school is more than can be quantified in monetary terms. While this is true there is a tendency for more senior authors to feel that papers printed in the Ulster Medical Journal do not find as wide an audience, as when they are published in the national journals or in the Irish Journal of Medical Science. This is true, and while I can understand their reasons, I think that Fellows who are publishing regularly have some obligation to support their own journal from time to time. There is sufficient material being produced in Northern Ireland today to double the size of the Journal. By increasing the quality of the papers printed, the Journal's influence will be greatly enhanced. A great deal of research is being done in the

province, the results of which are finding their way into specialist journals elsewhere. This, too, is understandable, but isn't it a pity that workers elsewhere often know more about discoveries made here than those of us working close at hand? I recognize that in an age of specialization the Ulster Medical Journal must retain a general role if it is to fulfil the purpose for which it was created. However, I think we would be well served if some of our younger colleagues would consider writing brief reviews of their work for inclusion in the Journal. This would help us all to keep up with new ideas and to follow the progress of research which is exciting attention elsewhere. The Journal is an important asset and we must keep it afloat and try to increase its prestige. I urge Fellows and Members to recognize its worth and support it wholeheartedly. I believe a journal like ours forms an important part of any societies' survival kit.

Osler stressed the importance of well-conducted meetings for the prosperity of a medical society and in recent years the quality of our meetings and their scientific content has not been excelled. Local communications are of a high standard while distinguished scientists are happy to appear before the Society as Guest Lecturers. The membership stands at over six hundred and is in positive balance by about two hundred in comparison with the years when I was Secretary. However, there are more than two thousand seven hundred qualified doctors in the province so that less than a quarter of those eligible are members of Ulster's oldest and most influential medical society. This must give us cause for concern and I believe that Council must consider methods of stimulating recruitment. All of us must adopt a positive attitude to attracting new members and encourage our colleagues, senior and junior, to join.

This, then, is the state of the Society today. I believe we are coming to terms with the challenge of specialization and recognizing the need to adapt ourselves to the changing pattern of medicine. The Society is fulfilling an integrative role for a divided profession and striving to maintain the highest ideals of the art and practice of medicine. The Journal is maintained and I have suggested ways in which it might be developed. Our move next year into permanent accommodation will give us fresh hope for the future and provide a real stimulus to meet the challenge of the next twenty-five years.

I hope from what I have said that the picture of your Society is emerging more clearly. I do not need to apologise for reminding you of our past or present. The present depends on the past, and thus it is essential for every society to recall former days lest they forget their origins. This has been a recurring theme from man's earliest years and forms the basis for many ceremonies of remembrance. It is well to recall from time to time our "famous men and our fathers who begat us". Their names are all recorded in our history. "And some there be which have no memorial"—these were the faithful commoners whose support has sustained the Society since its foundation. If you seek their memorial, look around you, it is here in a living and active organization. In a society like ours it is important to cultivate a sense of the historic past and to seize the opportunity to inform new members of the unbroken links that bind them to our origins.

And what of the future? Mankind has always been attracted to devination and the desire to look into the future. This practice was actively pursued in ancient Greece, where at the temple of Apollo at Delphi devotees submitted their questions to the oracle. The prophesies were uttered by a female medium known as the Pythia. Apollo was believed to speak through her while she was in a state of trance. The oracular replies were unintelligible to the uninitiated so that the anxious enquirer had to seek the help of holy men or priests who acted as interpreters. This ancient practice has now become a cult word in medicine and medical "delphination", as it is called, means the attempt at defining futuristic trends in the development of medicine. Generally this involves serious men, in committee, trying to resolve the unresolvable and attempting to forecast trends without the necessary information upon which wise decisions are normally based. While it is easy to poke fun at delphination, it is necessary for all of us to try in some measure to look ahead and extrapolate into the future trends that are becoming apparent now. Having said that, I shall tentatively try to look ahead and consider how our Society might conduct itself.

One of the "in-words" at present is "medical audit" and we ought to make our own audit of the Society. Are we satisfying the needs of Fellows and giving them what they want? What exactly are our resources? How best can they be employed? To this end, I hope that Council might conduct a survey of Fellows' opinions and seek advice from the regulars as to how they think the Society should operate in the future. Is the content of the meetings and the time at which they take place satisfactory? Perhaps more attention should be paid to meetings to which our wives could be invited? Formerly their involvement with the surgery and consulting room kept them in close, sometimes too close, contact with medicine. Now the trend is the other way and wives, greatly to our detriment, are being isolated from our working lives. Professor Symmers' lecture earlier this year which was preceded by a buffet supper was a great success. Admittedly, the entertainment was sponsored by a drug firm but if we had something similar within the hospital environment I believe that members might be prepared to meet the modest cost. This session we hope to hold such an evening at the Ulster Museum as an experiment.

For my own part, I feel that Council should form a Programme Committee. For too long the programme has depended primarily on the Secretary and to a lesser extent on the President elect. It is too heavy a task for one man, and each President can have only a fleeting influence on the selection of meetings and papers. On the other hand, a Programme Committee could develop a more co-ordinated policy of papers, discussions and symposia, over several years. The one-day symposium held early this year was a success and serious consideration should be given to whether something of this nature should be repeated on a yearly or biennial basis. Such a venture imposes too great a burden for one pair of shoulders to bear and a committee could deal more effectively with the detailed planning and organization required for a successful outcome.

Some consideration must be given to the Presidential Dinner. Are formal occasions of this nature right for our present Society? They were certainly satis-

factory for the age of elegance, now passed, and suited the life style of doctors of a different era. But how many of us now are accustomed to regular formal dining in our own homes? Most of us help with the washing up and the evening meal is often taken on a tray in front of the television set. Would a more informal buffet type meal, and the opportunity of moving around to speak to friends, be more appropriate? Do we want to hear formal speeches or would some form of entertainment be more acceptable? No doubt there will be many views on this subject. The traditionalists will want to maintain the status quo but all of you will realise that the cost of a traditional dinner may soon render it unrealistic. Others will want to experiment and I hope we will soon be able to get your views.

How are we and the other specialist societies to work together? It has been suggested that the Ulster Medical Society should develop the role of an academy of medicine to which they could become affiliated. This has some attractions, but I fear it will perpetuate our divisions instead of healing them. There is little evidence that members of different sections of such organizations cross the specialty fences—indeed, they often become more entrenched. The broad basis of our Society does not need defending. The principle is, I believe, right and is being increasingly recognized to be so. Greater recruitment to our membership from within the ranks of the specialist societies and mutual co-operation is probably the correct approach.

In this modest attempt at delphination I have not arrived at any definite conclusions. Rather, like the suppliant at Delphi I have put the questions and you, dear audience, will have to play the oracle. All of you support the Society loyally and I feel sure that Council will be glad to hear your views, and I hope they will interpret them correctly.

One of the symptoms of the malaise that affects society is the attitude of disinterest. To say that no one cares about anything is, of course, a gross exaggeration but there is a degree to which this is true. It is an expression of people's disenchantment with our times. The attitude can only be corrected by people like us caring passionately for the right things and this should extend into our support of our Society. In his inaugural address to the nation, President Kennedy said: "And so, my fellow Americans, ask not what your country can do for you; ask what you can do for your country". This seems to me to be the right approach for all of us in our dealings with our Society today.

And now, who speaks for medicine in Northern Ireland today? I have already commented on the divisions in medicine and the sectional interests that are fragmenting our frail fabric. No single organization, other than our own Society, can give expression to the authentic voice of medicine. Certainly not the B.M.A. with its increasing involvement with medical politics, nor the postgraduate centres, nor the specialties. Only we, who hold all the strands together in the manner of the skillful coachman holding the reins, are capable of giving the right lead. In recent years we have not been consulted on the big issues, as we were formerly. I wonder why? Have we lost our prophetic role and failed to recognize the authority that we possess? When the Government consults the profession we are excluded. It should not be so because we, with our unique blend of family doctor, specialist, community

physician, laboratory worker, academic and many others, are better placed to give the opinion of all the forces that maintain and foster the best that is in the profession. We possess the real voice of medicine today. Let us hope that in the future it will be heard.

In conclusion, Fellows and Members, if our Society is to realize its potential as a unique integrating force in medicine it must continue to provide a platform where clinician and specialist can communicate with each other. It must continue with its broad educative role which the specialist societies cannot emulate. It must continue as keeper of the historical archives. It must remain an active, integrated, eclectic society concerned with and informed of all aspects of medicine as it is practised today.

Fellows and Members, the continued success and vitality of our Society is in your hands. May you discharge this honourable task faithfully. Some of you who are here tonight will be able to greet the year two thousand with most of your faculties intact. I hope you will find our Society in as good heart then as it is now. When you look back I hope you will be able to say that in our brief span of service here we have fulfilled our responsibilities. If we are truly men and women of vision, if we are truly men and women of integrity, if we are truly men and women of dedication, we shall not fail to hand on a Society worthy of those who will follow us. It is to them that we pledge ourselves tonight.

Acknowledgments

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THE FIRST THREE PROFESSORS OF SURGERY

by

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THE Roman orator and philosopher Marcus Tullius Cicero wrote in 75 B.C. that not to know what happened before you were born is always to remain a child. It is true that there are present tonight relations of each of the three men about whom I am to speak and also others who know something of their lives and work either by tradition or personal encounter, but 'old men forget and all shall be forgot', and it therefore behoves us to set down on paper what we know about our predecessors before it is too late.

The surgical school in Belfast has always had a high reputation, much of which is based on the work of three great men, the first three professors of surgery. They were the pillars but each was an interesting personality and as they gave so much to the school I feel that a short note on each might be of interest.

TABLE I

The Professor of Surgery: Queen's College and University

1847 Inst.			
1849	1849 B. 1818 (31) 37 years 1886 Age 69 D. 1887	Prof. Alex Gordon, MD, ED, LRCS ED. "Old Alick", "Jasus"	1. Irish Famine 2. Crimea 3. Anaesthesia 4. Fractures (No Radiology
1909 Queens University	1886 B. 1858 (28) 37 years 1923 Age 82 D. 1940	Prof. Thomas Sinclair, CB, MD, MCh, FRCS, MP "Tommy"	Antiseptic Surgery Pathology Abdominal Surgery Two Wars
	1923 B. 1868 (55) 10 years 1933 Age 66 D. 1934	Prof. Andrew Fullerton, CB, CMG, MD, MCh, FRCSI, FACS "Andy"	Urology War, Surgery Blood Transfusion ±
	1933 B. 1880 (53) 14 years 1947 Age 90 D. 1970	Prof. P.T. Crymble, MB, FRCS Eng. "P.T."	Anatomy Radiology Abdominal Surgery Antibiotics
	1947 B. 1907 (40) 26 years 1973 Nigeria	Prof. H.W. Rodgers, OBE, FRCS Eng. "Stuffy"	Surgical Research Blood Chemistry
	1973 B. 1925 (48)	Prof. Douglas Roy, MD, MCh, FRCS Eng. FRCS ED, FRCS Glas.	Surgical Research Tropical Diseases

To make the picture complete it is worth mentioning that since Queen's was opened in 1849 it has had in all six professors of surgery. Table I gives in a tabulated form their length of service, the situation and status of the Belfast School when they were in office, as well as the main interests of each individual man. The thin line half way through Professor Crymble's term of office indicates when the Chair became a full time appointment with the salary changing from £1,200 per annum to £1,500. The thick line in 1947 not only is the date of the arrival of Professor Rodgers but it is also the date when a real Department of Surgery was founded with full research facilities—laboratories, animal rooms etc.

Before Professor Gordon was appointed the first professor of surgery in Queen's there had been some teachers who had been given the title of Professor. In the fourteen years from 1835, while the Medical School was at Inst. there had been three professors of surgery. The first was appointed in 1835; he was John McDonnell, son of the great James McDonnell, who later went off to Dublin. He was succeeded by Dr. Thomas Ferrar who in fact never took up the appointment but went off to Sligo. His successor was Dr. Robert Coffey who was appointed early in 1837 and would appear to have given ten years of most excellent service; it was on his death that Professor Alexander Gordon was appointed.

The Irish Medical Schools

As some people may be as much confused as I am myself about the origin of the various medical schools in Ireland I may be excused if again in tabular form in Table II I put down the origin of the early schools and the changes and evolution that took place before our own Queen's University of Belfast became an independent university. Although Trinity College, Dublin is shown by its charter to have been

Table II

SCHOOLS OF MEDICINE IN IRELAND

1592	Trinity College Dublin School of Physic			
1654	King's College suggested, never functioned			
1784	Royal College of Surgeons Ireland			
1791	Apothecaries Hall—ceased 1972			
1845	Enacted	Queen's Colleges	Belfast	Queen's University of Ireland
1850	Established		Cork	
1879	Ceased		Galway	
1879	Established	Colleges	Belfast	Royal University of Ireland
1908	Ceased		Cork	
			Galway	
1908	Established	Queen's University of Belfast		
		University Colleges of	Dublin	National University of Ireland
			Cork	
			Galway	

founded in 1592 when Henry Ussher requested Her Majesty Queen Elizabeth I "to give her assent to the foundation of a college which would give a blessing on to the whole realm and would plant religion, civilitie and true obedience in the hearts of this people"—at times like the present we wonder if this succeeded. It was not, however, until 1711 that the main medical buildings were built although Dr. John Stearne, who had been appointed as Public Professor of Medicine, had already been giving his lectures from 1654. It should be remembered that Trinity College Dublin Medical School is always described as a "School of Physic". I suppose the Barbers filled in this gap which was later taken over by the surgeons. In 1654 a King's College for all Ireland was suggested but it never functioned. In 1784 by Royal Charter the Royal College of Surgeons in Ireland was founded and it has flourished ever since. It was thought to have been suggested for two reasons; firstly with the imminence of the Napoleonic wars it was felt that further and urgent surgical education was necessary and this although naturally more needed for the welfare of England yet could be given in Ireland. A second reason for the origin of the Royal College of Surgeons in Ireland was that Trinity was still a school of Physic and the surgeons were able to give a more balanced education. In 1791 the Apothecaries Hall was founded. It led a chequered career with at times a doubtful reputation until it finally closed down two years ago mostly through pressure from the General Medical Council.

Coming up to modern times we find that an act of Parliament in 1845 established Queen's Colleges in Belfast, Cork and Galway; Dublin was excluded. They became constituent colleges of the Queen's University in Ireland in 1850 (Figure 1). This new body had a short life of thirty years as it ceased to exist in 1879, it was succeeded by The Royal University of Ireland, an examining body with no constituent colleges. This new university also had a short life of 29 years until 1908. Most of its examinations were held in Dublin which was in many ways inconvenient. It was said that "the parents did not like their sons at this most critical period of their lives to go far from home and be exposed to the damnations of a large city without proper oversight". There is a very different outlook in the world today. The link up of these three colleges never had been a very happy marriage so in 1908 the Royal University of Ireland ceased to exist and the new National University of Ireland came into being, with colleges in Dublin, Galway and Cork and at the same time the Belfast College now was given the status of a university proper as the Queen's University of Belfast. The Government of the Republic has a plan for the creation of a new university of Dublin embracing Trinity College and University College, Dublin and new universities in Cork and Galway.

When the Royal Belfast Academical Institution (Inst.) was founded in 1810 it was primarily intended to have a collegiate and school department. There are many people who do not realise the extent of the medical school in Inst. before the opening of the Queen's College in 1849. For fourteen years a full medical training had taken place at Inst., and during those years some 600 students had been trained with on occasions as many as 70 students in one year. There were seven professors doing full duty when the change took place. One of these, Professor Drummond, had reached the age of retirement, three of the others were

not re-appointed and went into retirement with the help of a golden handshake of £350. One of these was the famous Dr. Henry MacCormac, the other three professors, all men of exceptional ability, moved up to the new college. They were Professor Thomas Andrews, F.R.S., the Professor of Chemistry, Professor Burden, Professor of Midwifery and Gynaecology, the pioneer of that speciality in Belfast, and Professor Alex. Gordon, Professor of Surgery. The golden handshake in today's currency may not sound a great deal but we must remember that a professor's annual salary was only £50 per year.

Inst. did all it could to retain the medical school; it bought a disused building on the north side to be a hospital so that the practical and clinical work for the students could all be carried out on the same campus. This did not succeed. In the latter part of the fourteen years it was clear following a Government investigation that the writing was on the wall. The Presbyterian Church was withdrawing its students and this reduced the value of the institution for collegiate instruction. Physical defects were found in the fabric of the building itself and it was pointed out that as it had been built on swampy ground it was sinking. In fact in the centre it had sunk to the extent of one foot with perhaps six inches or so near the perimeter. This defect was pointed out by Sir Charles Lanyon, the leading architect of that time, but it must be remembered that he was later chosen as the architect of the new Queen's College which, he had been instructed, had to be built on higher ground. We hope that there was no wishful thinking in his criticism. With the disappearance of the Arts, Medical and Divinity Schools Inst. lost for ever its collegiate status and became a secondary school, achieving a position in the first rank of Irish schools which it has retained ever since.

On the opening of the new college all classes moved up to the Malone Road but although an anatomy lecture room was provided for there was no dissecting room and students had to dissect at Inst. for another eighteen years until an anatomy department was built. During that time Queen's had to pay the Inst. Board of Management £25 annual rental. It was a great nuisance for the students who had to waste about one hour per day going from Queen's to Inst. and back.

Professor Gordon

When Alex. Gordon was appointed to the Chair of Surgery in Inst. in 1847 he was a young man of 31 years of age (Figure 2). He succeeded Professor Coffey whose portrait and an illuminated address given to him by his students are in the Department of Surgery. In his reply to this address he says he is indeed very honoured and mentions that this is the sixth illuminated address that he has had, so presumably he must have been considered to be a very good teacher. Alex. Gordon was the son of Dr. Gordon of Saintfield; he had a younger brother who later became a general medical practitioner in that town and succeeded his father there (Figure 3). Professor Gordon himself had been a prize winner as a student. We see that in 1838 he had won class prizes—one was on "the osteology of the human cranium and its variations in different nations and different individuals". He also won a chemistry prize when his subject was "The Changes produced in the air and blood during respiration". In 1845–1846 we find he was a demonstrator

FIG. 1. *The crest of the old Queen's College which existed for 29 years only.*

FIG. 2. *Professor Gordon—a young man at the time of his appointment.*

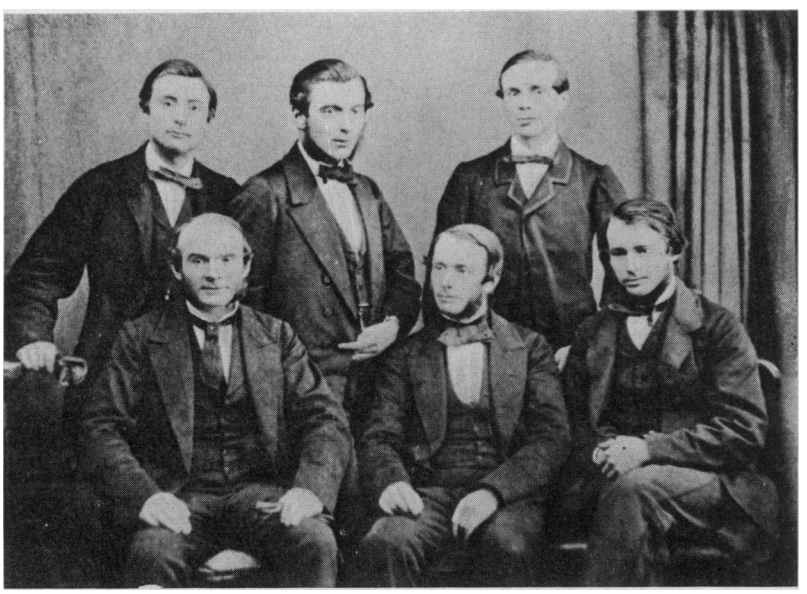

FIG. 3. *Professor Gordon and his brothers. Left to right in back row: Craigie, Dr. Williams and John, and front row: Rev. David, Professor Alexander Gordon and Robert Wilson.*

in anatomy; he there made a great reputation for himself as a teacher and it was from that post that he was elected Professor of Surgery. Although he took some of his undergraduate classes in Belfast he actually qualified in Edinburgh obtaining the degrees of the University and the licence of the Royal College of Surgeons of Edinburgh in 1841.

On returning to Belfast he took up practice at once. In those days the most convenient consulting area was near Inst. His first address was Upper Arthur Street, later he moved to 2 College Square North almost next door to the house which was later occupied by William Whitla when he qualified in 1877. Finally Professor Gordon moved to 1 Howard Street where he practised until he retired. His successor Professor Sinclair moved into this house and lived there for a time and later when he moved to University Square he still retained the Howard Street consulting rooms. It is easy to see why Sir William Whitla was to choose College Square North for the Medical Institute that he built for The Ulster Medical Society as it had long been a medical focal point. It also had an easy approach to the General Hospital in Frederick Street and the Childrens' Hospital in Fisherwick Place as well as the railway terminus. We can now see with the college moving later to Malone Road, and also with the building of the new Royal Victoria Hospital, that it was natural that those people of Harley Street status should move up to University Square, College Gardens and neighbourhood—the centre of gravity had changed to the new Queen's area.

In judging a man's ability we must relate him to the time in which he was living and the medical facilities and advances then available. The Irish famine was still in progress and the Crimean war had not yet taken place when Gordon was appointed professor. This war was useless from a military angle but it did perhaps give a start to modern British nursing and it gave the new invention of anaesthesia a successful field trial under difficult conditions. In this respect the French got much more benefit from it than the English. It also showed that plaster-of-Paris even in a crude form was an excellent splint; the Russians used it over thick woollen stockings. Of course Pasteur and Lister were still twenty years away. This was the world into which Alex. Gordon entered as a young professor at the age of 31. He had a first class knowledge of anatomy and also an inventive and creative type of mind, and so he enjoyed the challenge presented by the many fractures he encountered in his practice. He made many ingenious devices and his splint, the Gordon splint, for fractures in the region of the wrist, soon had an international reputation (Figure 4). Without x-ray control the idea then naturally was to make the fracture fit the splint—today with careful radiography of the bones we make the splint to suit the fracture. Splints—named after the inventor—hardly exist today, the light plaster-of-Paris splint has replaced them nearly all. Many people invented their own splint and as a student even in my day a question in the final examination always was to name splints and bandages! Gordon's splint had a great reputation for many years yet I remember well Professor Fullerton pointing out to me all its faults and carefully explaining to me that the only way to avoid them was to use the Fullerton splint.

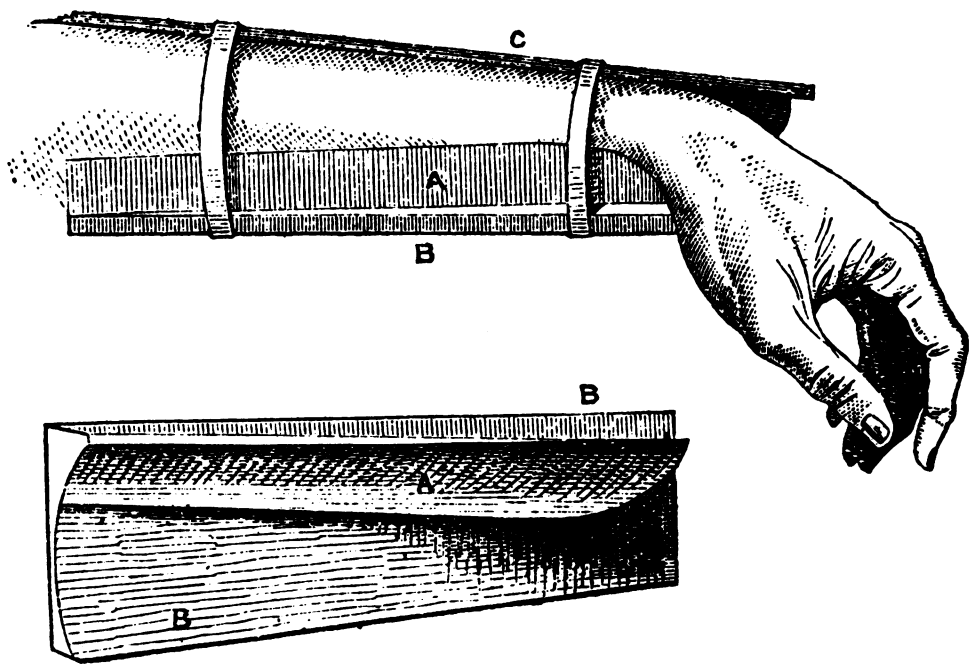

FIG. 4. *The Gordon splint for Colles' fracture.*

Gordon was no ordinary man. He is not easy to describe as in many ways he was a contradiction in himself. He was careless yet painstaking. He was amiability itself yet could be vindictive to a degree. While totally careless of his own person he would give meticulous attention to those under his care. His brusque manner and blunt speech concealed a rare kindliness of heart. He had no graces of oratory and sadly was not adept with the pen. His teaching was simple, thorough and entirely practical. He hated trappings and outward show and was oblivious of worldly honours. He was one of those men who was so brilliant that he could afford to be eccentric. Students as a rule always like something out of the ordinary; the nickname of "old Alick" given to him by his students was a term of endearment. His other nickname was "Jasus" given by his less reverent students. It is said that on one occasion a rough farmer having a deep and painful abscess opened used this expletive as the knife went in; Gordon at once reprimanded him and said "It is only the students that are allowed to call me that". Notwithstanding all this he had a large practice extending to distant parts of Ulster. As a surgeon he was neither dashing nor brilliant but his patients did well. It was always said that he never made much money. It was also said that his fees indicated his humility rather than his merit. He left behind quite a modest sum when he died. As a consultant he was most obliging and always ready to help his colleagues, but sometimes his doctor friends wished that he was a little more polite and presentable. The story is often repeated of how he was asked to see one of Belfast's notabilities of that time. The

family doctor, Dr. Purdon, called to convey Professor Gordon who appeared at once in his famous old tweed hat. Dr. Purdon suggested that as the patient was a man of such importance perhaps Professor Gordon could put on a better hat, perhaps even a top hat. Gordon went inside at once, closed the door, and sent out a top hat on a tray by his manservant with a note which said "I see it is the hat you want and not the man". He could when provoked have a fiery temper and his language to the students on such occasions was far from parliamentary. He could swear like a trooper but once his temper had settled he would end up pathetically by saying "Gentlemen, if you only listened you might commence the practice of medicine where I am leaving off". He treated all patients alike. On one occasion he was asked to go to Clandeboye to see a member of the Dufferin and Ava family on a Saturday afternoon; he said he was too busy cleaning out the byre to go but would hope to find time some time later.

He was an indefatigable worker and an enthusiastic teacher. Right to the end it was said that each day he would spend one hour in the anatomy department before giving his surgery lecture. He is remembered most of all for his success in the treatment of fractures. Sir William Whitla in his usual flowery language said of Gordon "he transformed the treatment of fractures from being a stagnant pool into being a clear crystal spring". His published works were, alas, too few, but he left behind an unrivalled collection of mounted specimens showing healed fractures of almost every bone. These are preserved in the anatomy department of Queen's today.

When the British Medical Association held its first annual meeting in Belfast in 1884 his demonstration of fractures was the outstanding exhibit of the meeting. It is hard today to know how he obtained them. Whitla thought a great deal of him; in fact one edition of Whitla's Treatment of Medicine is dedicated to Professor Gordon. Whitla described him as "the most illustrious of Irish surgeons, a man of worldwide fame—an original genius—a man with an inventive creative mind". Whitla I am afraid was always willing to use hyperbole.

When Sir William Whitla generously donated the Ulster Medical Institute as a gift to the doctors of Ulster in 1902 he ornamented it on the outside with four carved heads. He selected the two whom he thought had done most for the school during the Inst. period—they were Professor Thomas Andrews, F.R.S. and Dr. Henry MacCormac. The other two were Professor Peter Redfern and Professor Gordon, whom he considered to be the most illustrious of those who were in the Medical Faculty when it moved to the Malone Road site. No one could disagree with his choice. It is hoped that these heads will be safely rescued from the old Whitla Institute to get a permanent place of honour in our new building.

I feel that like Hugh Owen Thomas of Liverpool, famous for the Thomas splint, Gordon could have been regarded as one of the early medically qualified bone setters, something that without x-ray control required a third sense. When he died someone said "he belonged to a past generation which we hope will never become extinct" so even 100 years ago he was an interesting eccentric character.

As I said his town house was at No. 1 Howard Street but he was a countryman at heart and finally as he grew older he felt he needed a weekend house to get away from it all. He decided that a house beyond Comber with fields running down to Strangford Lough would suit him and so he bought an old farm house called Ringneill (Figure 5). He had there a pleasant orchard of seven acres and kept some cattle. He also put a new front on this house copying the frontage of his house in Belfast. On one occasion he decided to build a wall by his own hands to keep the lough from flooding the fields. In this he made two mistakes; firstly he did not dig

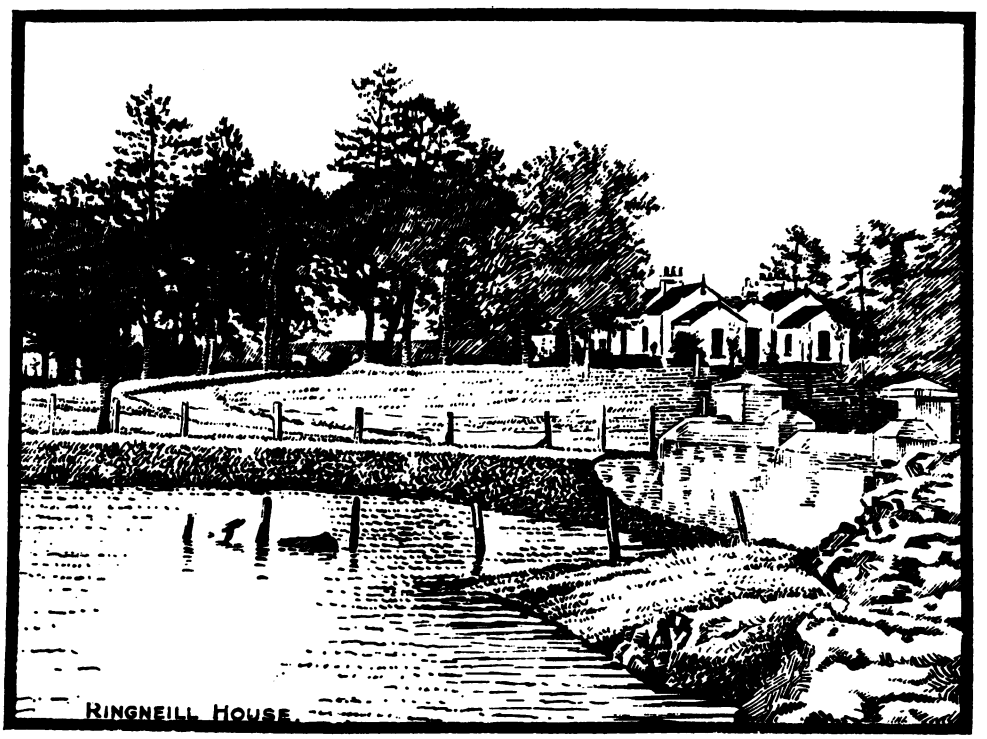

FIG. 5. *Ringneill, Comber.*

foundations—incredible for a man with some knowledge of engineering—but just built it on the surface of the field, and secondly and more serious still he built it on a Sunday. When it collapsed, as it did not long afterwards, there was great satisfaction among the Presbyterians in that area as it proved that any work done on the Sabbath was bound to fail.

Although a man highly successful in his professional life his home life was a disaster. He did not get on at all with his wife; there was constant friction. His son Alex. was a great disappointment, ran away from home, became a ne'erdowell and was missing for many years. His one solace was his daughter Winnie to whom he was greatly attached and on whom he had to depend greatly in his later years when

he lost his sight. His wife had died some years before. His only disagreement with Winnie was on the occasion when she wanted to marry a Mr. David Lowry; her father refused to allow this. One is not sure of the reason for this but one theory is that possibly David Lowry was held slightly responsible by Gordon for the young Alex's bad behaviour. However, Winnie did get married in 1893 to Dr. Harrison Stallard, M.R.C.P., London, and they emigrated to America.

I was fortunate in getting from the University of California San Francisco an interesting reference to Professor Harrison Stallard who was at that time Professor of Medicine in the Post Graduate Medical Department. He was very much older than Winnie and must have died round about 1895. In the history of the San Francisco Medical Society 1850–1900 the following report on him is worth quoting:

> "Dr. J. H. Stallard was another Englishman and it occurred to him to send home for a Hansom. It was a unique vehicle and resembled an upright coffin on trunnions. Instead of having a coachman perched high in the rear over the roof of the carriage it was driven by the doctor himself, the reins passing through a slit in the front of the coffin. When the doctor with his white flowing sidewhiskers, his black frock coat, his stove pipe hat, and his saucy lapdog sitting beside him, drove forth in his peculiar showcase he was one of the sights of the town."

Professor Gordon died intestate and his estate therefore went to his two children, but at that time Alex., his son, could not be found and Winnie became the sole legatee. On her husband's death she returned to Ulster and in her will she left Ringneill to her former lover, Mr. David Lowry, if her brother did not turn up within five years. If he did turn up after that time he was to be given an annuity of £1 per week for life. Many years later the young Alex. came back; he lived on a very small pittance near his old home—£1 per week from Mr. Lowry and one or two other small sums. He died in 1945 in the Ards District Hospital and is buried in the City Cemetery, Belfast although Professor Gordon is buried in the old churchyard in Saintfield. One retired lady living at Comber told me that she remembers well young Alex. then an old man with a beard like his father, and she said always with the appearance of being a gentleman, coming often, looking in to Ringneill from the side gate, standing there for a short time and then walking away, a very sad old man.

It is pleasing to think that Ringneill still has medical connections. The late Dr. Maitland Beath and his wife bought it in 1927 and Mrs. Beath spends still much time there each year enjoying the freedom of Co. Down.

One story that Professor Gordon used to enjoy telling about himself was that when at Comber he wore even more shabby clothes than usual, and on one occasion he began to talk to a man sitting on the roadside breaking stones. After a time the man said he had a very painful shoulder. Professor Gordon thereupon said he would like to have a look at it and gave him some advice. Some months later Professor Gordon on his way to Belfast well dressed for an important occasion stopped his gig and asked the old man how he was. The old man not recognising him said he was a great deal better thanks to an old tramp who had given him very good advice some months before.

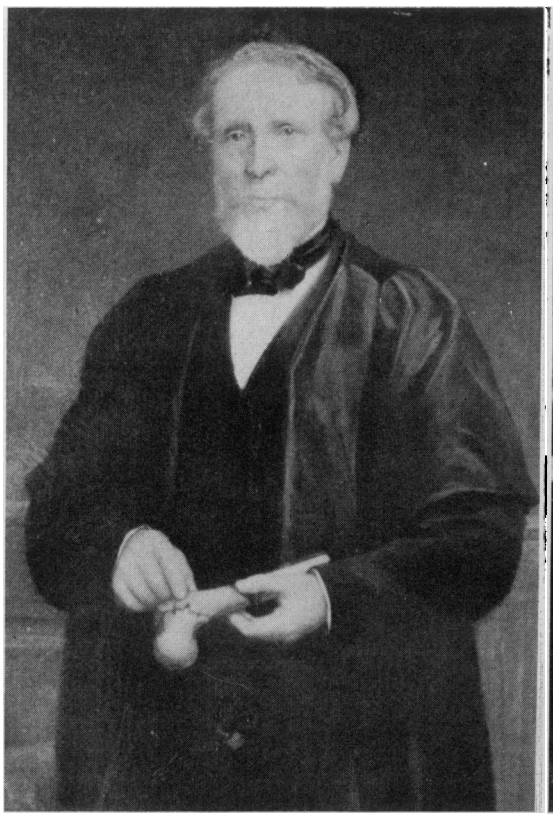

FIG. 6. *Professor Gordon—oil painting almost certainly from the photograph (figure 7).*

FIG. 7. *Professor Alexander Gordon—photograph*

There are two portraits full length oil paintings of Professor Gordon at the university (Figure 6). One of these, given by the students, shows the professor demonstrating a fracture through the neck of the femur and naturally beside him can be seen on the table an example of the famous Gordon splint. The other oil painting was given to the university in 1904 by his daughter Winnie, who called herself Mrs. Gordon Stallard. Winnie died that very same year at the age of 40 having been born in 1864. The second painting is not unlike the first one; this time he has some notes in his hand, and in fact I think both of these portraits were painted after his death from a photograph (Figure 7).

His family tree is an interesting one and shows what influence this family had in Ulster affairs (Figure 8). His father and brother were much respected doctors in Saintfield, another brother was a minister, and another brother somewhat mentally backward, it was said after a fall out of his pram. One often wonders in cases of this sort which came first, the mental retardation or the fall? Another brother John became an important linen merchant and was the father of Malcolm Gordon a man

who had great influence in the town in later years; in fact members of this family still play an important part in Ulster affairs. There were five sisters; they do not appear in the portrait with the six brothers. Of the five sisters one got married and was immediately disinherited, the others remained single—I do not suggest that there is any inference to be drawn from this!

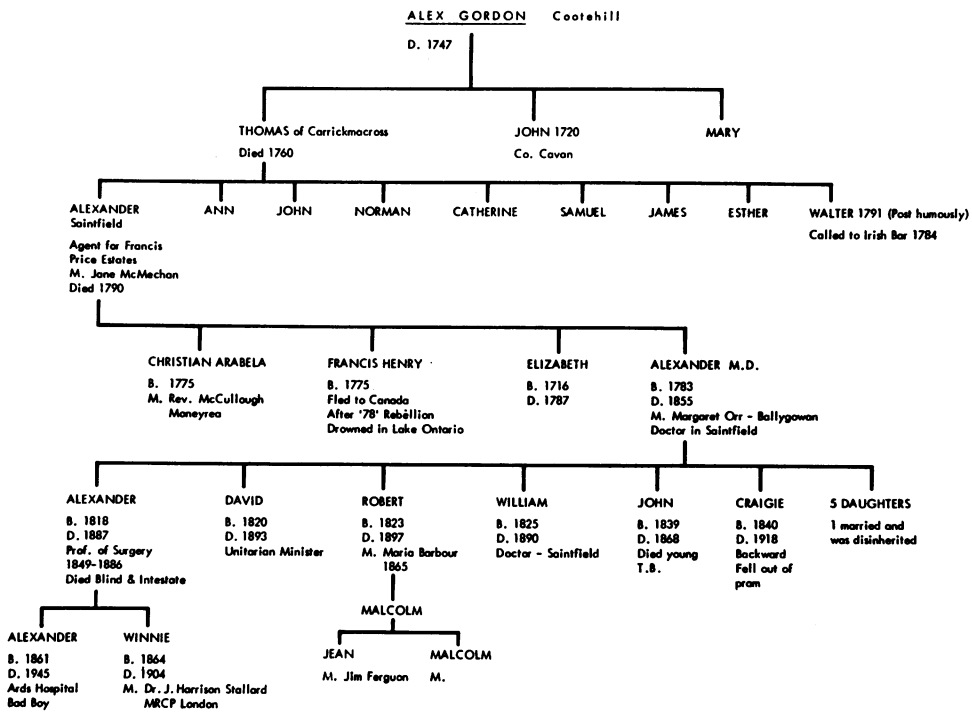

FIG. 8. *The Gordon family tree.*

Towards the end of his life he must have been a sad man; it is said that he threw his books into a pond in one of his fields and certainly none of them exist. Ringneill, a pleasantly situated and partially secluded house with its seven acres, was a very suitable house to be used on the famous night of the gun running in April 1914 when a consignment of arms for the U.V.F. arrived and suitable places had to be found where they could be hidden before being distributed. In 1914 gun running was looked on as almost an honourable pastime. The Public Records Office files show that Alexander Gordon was the occupier of Ringneill from 1866 and after his death, since his son was missing and his daughter was in America, it was let furnished to several different tenants. In 1907 the property came into the hands of the Lowry family. It will be remembered that David Lowry was one of Winnie's early suitors, and he lived there until 1923. He had a very well known ladies' outfitters in Belfast at that time. After 1923 there was a short interval of four years before it was bought by Dr. and Mrs. Maitland Beath.

At the age of 68 Professor Gordon with failing health and failing eyesight resigned from the Chair which he had held for 37 years. Sadly only a few months later, when staying in the old homested at Saintfield, one morning after breakfast he took a severe headache, developed a serious stroke, and fortunately did not survive. He died in the very same room in which he had been born 68 years before. The funeral at Saintfield was a very large one attended by his colleagues and students. He had been President of this society in 1856, and at the time of his death his younger brother William was in general practice in Saintfield. William himself died in 1890 at the age of 65. Their father who had started this practice died in 1856 at the age of 72.

It was Gordon's ardent wish that when he retired he should be succeeded by his favourite student, Thomas Sinclair. Supporting this was the most powerful man then in the Medical Faculty Peter Redfern, who had come to Queen's from Aberdeen in 1860 as Professor of Anatomy and Physiology.

Professor Thomas Sinclair

Thomas Sinclair was born in 1858. He was the eldest son of Samuel Sinclair a business man of some importance and one of a family much respected both in industry and for its charity. The family consisted of four sons and two daughters. Several of Thomas Sinclair's brothers took a prominent part in the affairs of Belfast and as can be seen from the family tree (Figure 17) the next generation produced politicians, professors and medical consultants, all of whom gave vital service to the province as well as to their country both in peace and war. Thomas himself was always thought to be delicate and so was educated privately before entering the medical school in Belfast in 1877. The medical curriculum covered four years in those days and throughout this period we find he was a prize winner, an exhibitioner and a gold medallist, and so it was no surprise when in 1881 he qualified M.D., M.Ch. with First Class Honours and a Gold Medal in the final examination in Dublin of the Royal University of Ireland (the M.D. and M.Ch. were still the primary qualifications).

At that time behind the scenes and virtually the 'eminence grise' of the medical school was Professor Redfern a man who it was said could always pick a winner. It was he who insisted that the young Sinclair should get the best surgical degree possible and that he should go to London, which he did, to work in the London Hospital, and from there to obtain the F.R.C.S. England. This he got in 1885; he was in fact the first in Belfast to have this diploma. Professor Redfern also insisted that he should go to Berlin and Vienna for further post-graduate study before coming back to settle in Belfast. In doing so Sinclair was a man well before his time.

This knowledge of pathology—there was not as yet a professor in this subject—gave his surgical lectures a scientific basis. Sinclair brought back with him the most modern ideas. Anaesthesia was now fully established, Pasteur and Lister had made surgery safe by the antiseptic carbolic spray, rubber gloves had just been invented in America made by the Goodyear Tyre Factory, modern surgery was

just being born and Sinclair was the right man to bring this new child to Ulster. He was not long back to Belfast and had already gathered a small practice, but was still an assistant surgeon in the Belfast Royal Hospital, when the Chair of Surgery became vacant with the resignation of Professor Gordon. Sinclair applied for the post and with the backing of Professor Redfern (Figure 9) was successful. This caused a regular bombshell as there were many more senior people who had expected to get it and it did not make the young professor's life an easy one for some time. He was then a young man of 28 years. John Walton Brown, later Sir John, was one of the disappointed applicants—he was then a very senior and very important person. Sinclair at that time was on the staff of the Belfast Royal Hospital in Frederick Street as well as The Ulster Hospital for Women and Children in Fisherwick Place. He soon had other appointments—at the Forster Green Hospital, Belfast and the Antrim Infirmary in Lisburn. In fact he soon had a

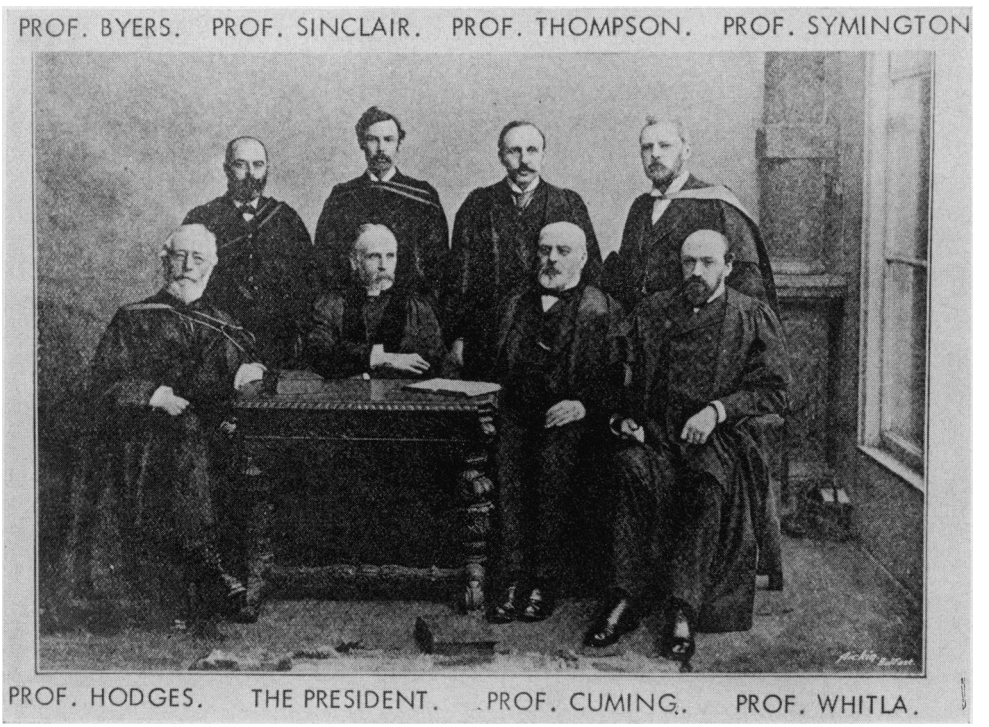

FIG. 9. *The Medical Faculty in* 1894.

loose attachment with most of the outlying hospitals, since many of these were staffed at that time by general practitioner surgeons glad to avail themselves of a second opinion from the professor. It was said of him that if he had not been the leading surgeon of his time he would have been the leading physician. I remember him saying one day in class that "a surgeon is a physician doomed to the knife" and occasionally looking at a patient he would say "I think this patient requires

a little tincture of steel in the surgical sense". Iron of course in that period was a very popular medical drug.

Appointed to the Chair in 1886 at the early age of 28 he held the post for 37 years—by a coincidence exactly the same length of time as his predecessor. No two men could have been more dissimilar (Figure 10). With Sinclair correctness

FIG. 10. *Professor Thomas Sinclair on appointment as professor.*

of dress, careful speech, politeness, good manners and tranquility were the outstanding features. He is said never to have lost his temper but there was a certain coldness and aloofness about him. When appointed he did resemble Gordon in that he had a flowing well trimmed black beard and a bow tie. This may have been the style of dress of that period.

As Gordon died very shortly after Sinclair was appointed he was able to take Gordon's house in No. 1 Howard Street and he lived there for many years before moving in 1900 to University Square, but even then he still retained Howard Street as his consulting rooms. In his early years, in fact from 1886–1914, he was a very busy man. His mornings were spent in hospital and each afternoon he gave his lectures at Queen's as well as having a very busy consultant practice. It was always said that he had the reputation of charging large fees. Many of the operations that he did were done for the first time in Belfast. He did the first short circuit for duodenal ulcer in Belfast and for fear the new opening would close he inserted some bone plates to keep the passage open—an idea that was very soon discarded.

When the British Medical Association paid its second visit to Belfast in 1909 Professor Sinclair was president of the surgical section, and he pointed out that in the operating theatres in the Royal Victoria Hospital each morning there were at least three short circuit operations being performed. Today this operation without the present modifications is very rarely performed.

It is sad that with such a vast experience of over 37 years he wrote very little, and one would have thought that a man who liked speaking would have enjoyed writing. It is perhaps just as well for he was such a master of detail that often the main subject might be missed or forgotten. In a hospital alphabet dealing with members of the staff of the Frederick Street Hospital in the 1890's and written by R. J. Johnstone, later Sir Robert, it is said "S is for Sinclair professor profound, if you give him the chance he will talk the day round". He remained a bachelor living in great comfort and cosetted by his unmarried sister Nell. I often wondered whether the alleged ill health was really true when it is realised that he hunted with the hounds each Saturday during the hunting season. He was a skilful fisherman and enjoyed this sport very much; he played an adequate game of golf, perhaps slightly sub-standard, but probably skating was the sport that he enjoyed most. It was said that on one occasion with the sudden onset of a hard frost he cancelled his lectures at hospital—perhaps giving the general impression that a sudden operation of importance had arisen requiring his services; however, there was no recrimination on either side when he found when he reached the lake that most of his class were already skating there long before he arrived.

He took a great interest in the university and in fact at some point or another he had been president of almost all the student societies. He was a member of the Academic Council and a member of the Senate and in 1919 was Registrar of the university. This close attachment to Queen's meant that as soon as he retired from the Chair in 1923 he was at once appointed Pro-Chancellor. He also became a member of Parliament representing the university at Westminster. He held this post for seventeen years in succession to Sir William Whitla and during those

seventeen years there were five elections and he was returned unopposed on each occasion. During the same period he was also a member of the Senate at Stormont. Notwithstanding his alleged ill health he offered his medical services in 1914 to the Army Medical Service and was commissioned with the rank of full Colonel as consulting surgeon to the 4th Army in France (Figure 11), which was then commanded at that time by Sir Henry, later Lord, Rawlinson.

Last year in the hairdressers I picked up the usual two year old magazine, a copy of Time. In it was a long detailed article on the life and death of the famous German Air Ace Baron Manfred von Richthofen (Figure 12) whose death created quite a stir and a bitter controversy. The Germans said that he had made a forced

FIG. 11. *Col. Sinclair and niece.*

FIG. 12. *Baron von Richthofen—the German air ace.*

landing behind the British lines and had been machine-gunned as he sat in the cockpit of his plane. Other views were that he had been killed in aerial combat, and there was even a suggestion that from jealousy he had been shot by members of his own air circus. In this article the writer finished by saying that the answer will never be known. In actual fact Colonel Sinclair was the one called in to do the important post-mortem examination, and was able from this to prove conclusively that the famous airman had been shot in the air in aerial combat. He often told us this story during his hospital ward rounds.

For his service in France he was appointed in 1917 a Companion of the Order of the Bath and was mentioned in despatches. Apparently during his time in the army he developed social qualities which many people did not think he possessed. Later in the war he went as consulting surgeon to Egypt as advisor to General Allenby. He must have enjoyed his army life and he was always very pleased afterwards to be addressed as Colonel Sinclair. This retaining of the war time temporary army rank seems to have been much more prevalent after the 1914–1918 war than after World War II. Andrew Fullerton also liked to be known as Colonel Fullerton.

One physical alteration that the war made for Professor Sinclair was the removal of his flowing black beard which had to go when 'he first put this uniform on'. I was a student in his class in his last year just before he retired. His classes were well attended, I am afraid mostly because he was the professor and also an examiner and we were likely to meet him later in other places. His lectures were too diffuse—there was not enough meat in them to help us to pass our final examinations. We preferred the younger men like S. T. Irwin who gave the information in tabloid form. Even Professor Lindsay with his list of 27 causes of vomiting or his 33 causes of headache at least gave us material which would fill an examination paper.

I thought in appearance at that stage that Professor Sinclair was the perfect prototype of a professor—somewhat different perhaps from today's models (Figure 13). He was cultured in speech and immaculately dressed with a dark suit, white shirt, stiff collar, stiff cuffs with gold cuff links and grey tie with pearl tiepin; he appeared just ready for a garden party or for Ascot. There was a white inset to the waistcoat and across his waistcoat there was his watch chain with a gold revolving signet that he could play with—which he did. He kept it spinning round all the time that he was lecturing which at times was somewhat offputting. He was then cleanshaven with his white hair neatly trimmed with a gentle wave in it. He had a pale somewhat grey face and certainly looked frail. He walked with a slow dignified air, but having said all this we must remember that he lived another seventeen busy years after his retirement. He did not operate much in his last few years on the hospital staff but left most of this to his No. 2 S. T. Irwin, later Sir Samuel. As with many others that we can think of the No. 2 has often been left to do most of the work.

I always felt the Professor enjoyed best looking back to the surgery of the past although this was not necessary as he kept himself well abreast of all modern advances. I suppose many of us as we get older think the past more exciting than the present. Before an operation he sat down with his eyes closed for a few minutes —whether this was to revise his anatomy or to make a short prayer is uncertain; he was a religious man attending fairly regularly his church in Rosemary Street. Another suggestion was that he was having a rest before the ordeal of the operation. It was said that he was very weary after an operating session, in fact he often sat when operating when such was possible. What he did was done with meticulous care for detail. His work always had logical background and with his knowledge of anatomy and pathology he was able to tackle most problems with confidence.

As he always looked solemn I never knew if and when he was joking. He used to say the word "abdomen" comes from the latin "Abdo—I hide"—which even I knew it did not. He would then say "Gentlemen, you never can be sure what is hidden inside that box". As he bridged the pre-and-post x-ray period of 1895 he used to describe how to diagnose a stone in the bladder when cystoscopy and x-rays were not yet available. One had to pass a hollow metal sound into the bladder and when the tip touched the stone it produced a metallic bell like ring. He used to remind us that if this instrument were to touch our own gold cuff links (not that we had any) a similar sound might be produced and this might mislead us! This was just a reminder that in the old days the surgeons did not even roll up their sleeves before carrying out this interesting manoeuvre. I do suppose they did have a slight social hand wash first of all. These stories all told with great solemnity were very interesting but it was the junior surgeons who supplied us with the necessary material to help us to pass the final examination. On another occasion I remember the professor asked me what material I would use to sew up a wound in the face to leave the least visible mark. I knew the answer he wanted was horse hair—naturally this was long before our modern fine nylon was invented. The next

FIG. 14. *Professor Sinclair—portrait at Queen's.*

FIG. 13. *Professor Sinclair—photograph.*

question was what part of the horse, the mane or the tail; I risked tail which was right and then in a typical Sinclair way he said "would it be better to come from a horse or a mare?"—to which of course I had no answer. At the end of the class he called me over and asked me to consider the different methods that the two animals had in passing their water and that I could report next day—which I did not do. Many students got tired of this folk lore type of surgery feeling at times that it was a sort of pose—a great contrast to Gordon. It was all very unnecessary as he was the pioneer of modern abdominal surgery. Many of his operations are too technical to recount in a short lecture of this sort.

The professor of surgery was entitled to have an assistant who was paid by the university the princely sum of £200 per year. In Sinclair's time the late Mr. H. P. Malcolm held this post and as Professor Sinclair did not like fractures it was Harry Malcolm's duty to give a university lecture each Friday covering the whole field of fractures. Harry—debonair, perhaps somewhat lazy, was the most sought after bachelor surgeon in Belfast at that time. A hospital alphabet compiled by Hugh G. Calwell, a medical student in the 1920's, summed him up very well—"M is for Malcolm the elegant Harry, so eager to work but so willing to tarry".

I think in retrospect that Sinclair did not get enough recognition for his work. He should have had an honorary degree from his own university or indeed further honours for his seventeen years of political service. He is commemorated by the Sinclair medal which was founded for competition among the members of the surgery class. His portrait in oils was painted by George Harcourt in 1931 and presented to the university by his students and friends (Figure 14). The students were very courteous throughout Sinclair's lectures; I never saw any rowdyism. On one occasion he entered the room to find no one there so he went out only to be recalled to find every student in his seat. They had all hidden behind the high benches and were quite invisible—indeed a harmless prank. This was in marked contrast to what was happening to some other lecturers. I remember when a donkey and cart was brought into a certain class (Figure 15). The lecturer took the cart to push it through the door—he did not realise that we had spent half an hour or more taking off the wheels, bringing the cart in sideways, re-assembling it and setting the donkey into the shafts. Professor Sir John Byers for a time used to send up his chauffeur some time before the lecture with a bag containing some interesting organ that he had removed earlier that day rather like a fisherman showing off his morning catch. He hoped with this to interest and illustrate his talk to the students. When he found that the specimen was often removed and all the bag contained was perhaps an old pair of football boots or a bottle of Guinness he brought the bag into the class himself (Figure 16).

In 1922 the Association of Surgeons of Gt. Britain and Ireland—quite a young body formed out of the 1914–1918 war—decided as its third visit to come to Belfast. It had already met in London and Edinburgh and now was due to come to Belfast. It shows the high regard that there was at that time for the Belfast School. A. B. Mitchell had been chosen to be president—he was better known, more flamboyant and perhaps a better mixer than Thomas Sinclair who should have been by virtue

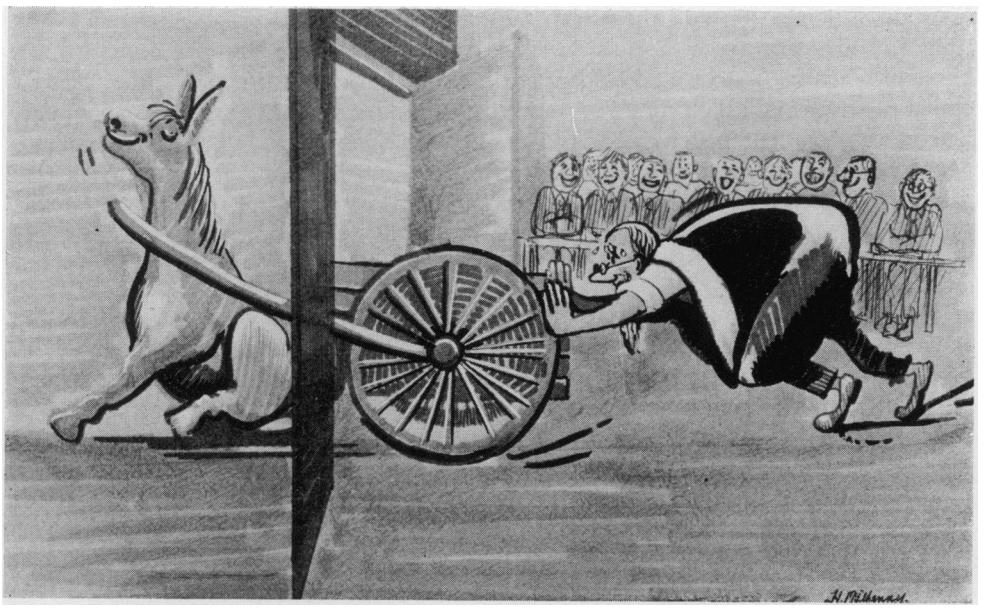

FIG. 15. *Dr. V. G. L. Fielden tryingto do the impossible.*

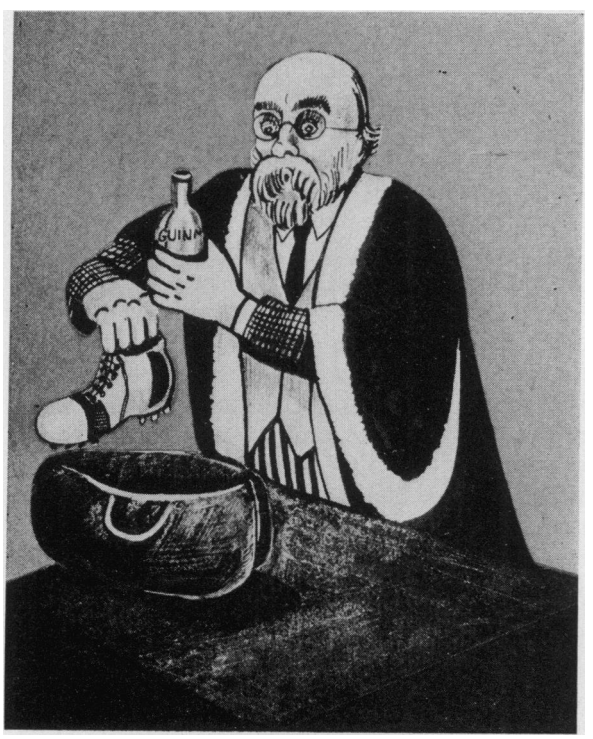

FIG. 16. *Sir John Byers—"Someone has changed the surgical specimen".*

of the position he held the right man for the job. However, as it happened this meeting never took place. It was postponed "on account of the unsettled state of Belfast"—sadly we can say the same today, 53 years later. The postponed meeting took place in 1931 with Professor Andrew Fullerton as president. This meeting was an outstanding success. I always felt that Sinclair did not make enough of overseas contracts. He did not realise that surgery was now international and not parochial; the opposite must be said of his successor because Andrew Fullerton was probably better known and more highly valued in England and America than in his own Ulster. A short family tree of the Sinclairs shows how much this family have given to Ulster as professors, industrialists, soldiers and politicians as well as medical consultants (Figure 17).

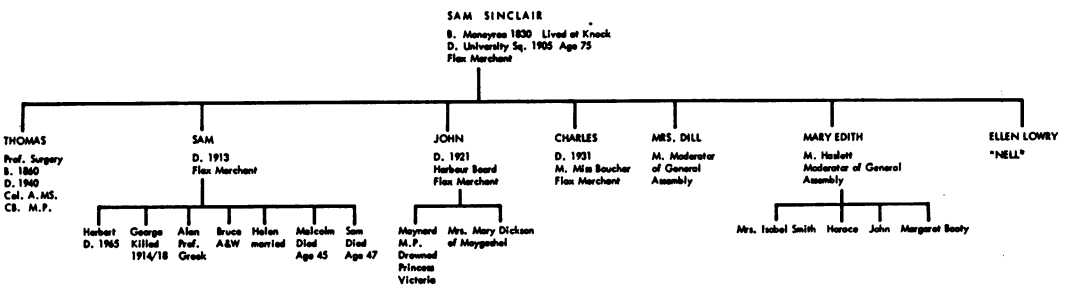

FIG. 17. *The Sinclair family tree.*

Professor Sinclair was President of this society in the session 1895–1896.

PROFESSOR FULLERTON

In 1923 when the Chair of Surgery became vacant it was just over four years after World War I. The young men who had come back were not yet equipped for the position and so an established surgeon had to be elected. It must be remembered also that the salary for this Chair—it was a part-time post—was in the region of £233 per annum. Anyone applying for the Chair must have had already a large practice and an adequate income, since to fill the post honourably he was likely to lose money if doing it properly. One young man did apply but the two really serious candidates for the Chair were S. T. Irwin and Andrew Fullerton. Irwin would have been the students' choice as he was an excellent teacher and had been giving special coaching classes for years. Fullerton on the other hand had come back from World War I much decorated and with almost an international reputation, having made so many valuable contacts while in France with the English, French and American surgeons. The Queen's Senate in its wisdom appointed Fullerton—it had to take into consideration the fact that he was then 55 years of age and had at most only ten years to offer, but they had to assume and hope that he was not a man who had reached his peak and was over the hill. In retrospect their choice was the correct one. Andy Fullerton in those next ten years became President of the Royal College of Surgeons in Ireland—the first ever to be chosen from Ulster since the college was founded in 1784. He was made an Honorary

Fellow of the American College of Surgeons—the first from Ulster, and he was elected President of the Association of Surgeons of Great Britain and Ireland when it made its first and postponed visit to Belfast in 1931.

During his ten years in the Chair Belfast was visited by many surgeons of world fame like the Mayo brothers, and even in his last years he was keeping up his research into urological problems and had several papers lined up to work upon after he retired but these were never completed. He left an incredible selection of mounted kidney and bladder stones all fully analysed and documented as well as the detailed results of some 3,500 cystoscopies.

Andrew Fullerton was the third youngest son of Rev. Alex. Fullerton, Methodist Minister of Dalkey, Co. Dublin, and was born in 1867 in Cavan (Figure 18). In his early life, because of his father's peripatetic profession his education must have been somewhat irregular, but his final school was Lurgan College and it was from there that he entered Queen's College in 1885. He qualified from the R.U.I. in 1891 with First-Class Honours, Gold Medals and Exhibitions (Figure 19). It will be seen from the family tree that his brothers all held very important positions. There was always on his mantlepiece a photograph of one of his brothers—this brother had joined the IMS where he had done some remarkable work in the eradication of plague in India. For this work he was rewarded with the Kaiser-1-Hind medal a much valued decoration; sadly later this same brother pricked his finger while doing a difficult operation, got septicaemia and died. The same brother it will be seen left two sons both of whom reached high rank in different regiments in the Indian Army.

Having qualified in Dublin and before settling in Belfast Andrew Fullerton spent two and a half years in England in two different hospitals in Kent. As soon as he had obtained the diploma of F.R.C.S.I. he returned to Belfast but he had to do a spell of general practice to make some money before he could get his foot on the first rung of the surgical ladder. His progress was slow, his manner was against him, and he was sharp of speech which gave the impression of him being snappy. This was not really so; he could be extremely patient and could be very sensitive. I remember assisting him at one operation to remove the tongue because of advanced cancer; it was indeed a hopeless case. We both had to work from below the table with the patient's face downwards because there was then no way of blocking off the windpipe and no blood must be allowed to flow back into the lungs. The patient died on the table. Fullerton was so upset that I had to drive him home, and he went straight to bed. This is a very different picture from the one he gave to the students and to the public. I remember the deep emotion that he suffered on the death of his first wife. She was undergoing an abdominal operation in a nursing home and he was waiting down below. He was called up to the theatre expecting to be told that the operation was over; instead it was to be shown the open wound and to have pointed out to him that nothing could be done. To me this was an unforgiveable act for any surgeon to do to a colleague.

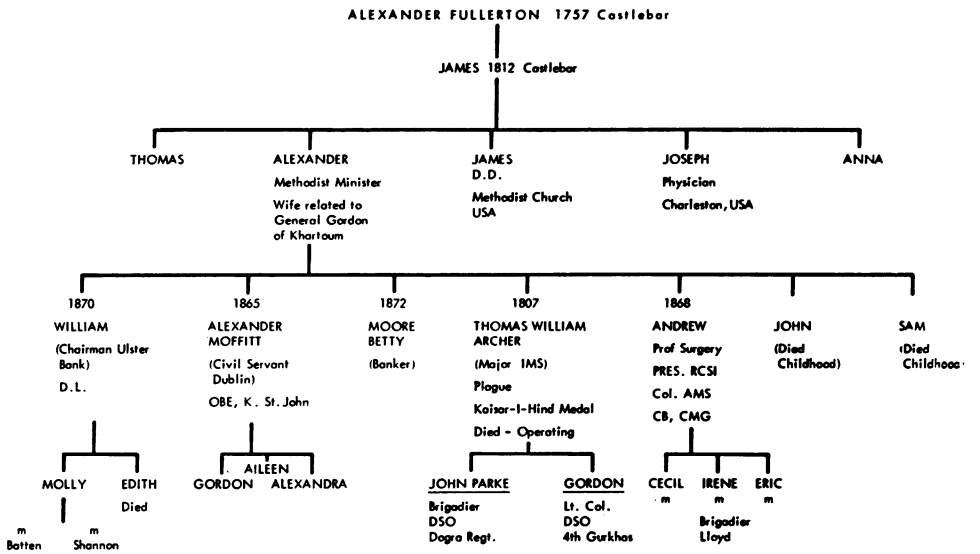

FIG. 18. *The Fullerton family tree.* (The date for Thomas William Archer should be 1867).

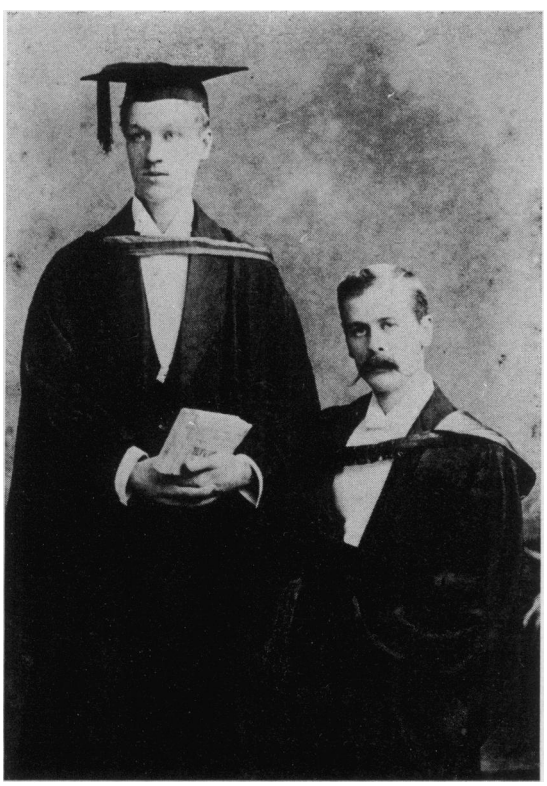

FIG. 19. *Dr. Andrew Fullerton and his brother on Graduation Day.*

He never had a large practice and on his death left a very modest amount in his will. Research permeated all that he did, he was always trying new methods. In those days research, it must be remembered, was a one man show. At one time he felt that patients died if allowed to be under an anaesthetic too long and so he developed an operation for the removal of the prostate which he could do at very great speed. I have on occasions stood by with a stop watch. On one occasion when he was particularly rapid and I was able to record the time as 57 seconds he at once remarked with a wry smile "Fraser, where did we lose time today?"

A man must be judged by what facilities are available; blood transfusion was virtually non-existent and new anaesthetics and antibiotics were not yet available. He was one of the early pioneers with the new electric cystoscope which many of his colleagues still thought was just a new and interesting toy. Edison had just brought in the new cold lamp so one no longer ran the risk of burning the patient with the hot bulb. On a child's rubber ball about the size of a bladder he would practise for hours at home, having passed the cystoscope through a small hole into the interior of the ball, until he could see every corner of its lining clearly. He had a large collection of cystoscopes all bought by himself, and these he brought each day to hospital to use on his hospital patients. He quite rightly asked the hospital to replace the bulbs which were easily blown and were very expensive. On one occasion he was trying to impress one of his cynical colleagues with the great value of this new instrument. He passed it into the bladder and began to look for an artery or vein to show his colleague. Finally he saw one and said "Ah, I see a vessel on the right" to which his friend at once replied "I suppose I am now expected to say "Ship Ahoy". The hospital was not fully equipped then with a diathermy apparatus; he had one at home which he also brought each day to hospital when there was a case likely to require it, such as a tumour of the bladder. This large, so called portable, apparatus had to be carried from his car to the ward either in one's arms or on a trolley. My pupil at the time, and now a retired consultant, who often had to carry it suggested that the machine should not be called portable but rather shiftable. Finally each day he brought back two, three or four bound volumes of hospital notes—he kept at home a duplicate copy of all his hospital cases of urological interest. These were illustrated by his own personal sketches; this enabled him to have the material at home available to write his various papers. On his death he had 77 monographs to his credit—a copy of these he left to the Ulster Medical Society library. One must remember that in those days a paper was usually a one man effort with acknowledgments in the appendix; today there may be six or eight authors with apparently everyone taking part—at times it is difficult to know who the main author is.

He was a fast and neat operator; he took great care, often preferring his fingers to instruments but his cases often did not do as well as they should have done. He had a tendency to be always trying new methods—not all of these were advances and often they were too experimental. Although not interested in fractures he did as a younger man write a short book on fractures of the forearm, and, as I said before, he felt that his splint was able to correct deformity which the Gordon splint was unable to do (Figure 20). Unfortunately his little light wooden splint never

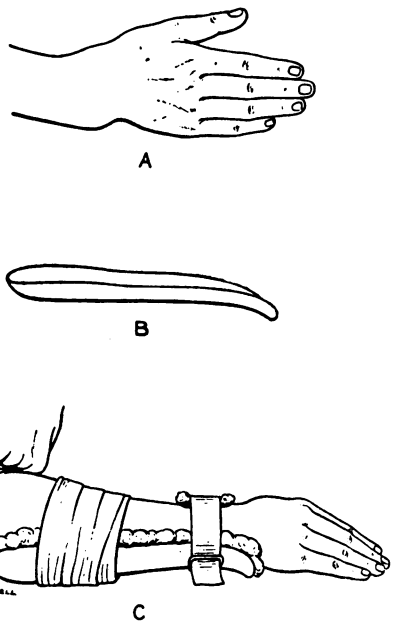

FIG. 20. *The Fullerton splint for Colles' fracture. In A the marked displacement to the radial side is show, in B the Fullerton splint and in C the splint as applied.*

won any popular appeal. Although always a general surgeon—as indeed a professor should be—he tended in later years to see mostly cases of urological interest. He did a great deal of work at home in his small consulting room; how the thick red carpet stood up to so much soiling with water, urine etc. I never understood. It was quite a sight to see him holding the cystoscope in position in the patient's bladder with one hand and answering the telephone with the other. He must have wondered at times whether it was easier to pull the patient over to the 'phone or the 'phone over to the patient. On occasions I have been asked to go to help but he usually had a nurse from a nearby nursing home who came in for two hours each afternoon.

The professor of surgery, as I said earlier, was entitled by the university to have an assistant. I held this appointment for a few years and the salary was still £200 per year. I felt that part of the job was rather like being a verger or a sexton; my function was to see the great man into the lecture room and close the door, and after that I got back to my consulting rooms in University Square. The only difference from being a verger, as far as I could see, was that the latter was never expected to give the sermon. I on the other hand had always to go with the possible lecture in my pocket lest the professor should be detained or should not turn up. Of course one had to deputize for him on holiday as well as helping to organise the examinations.

One thing I always admired about Andrew Fullerton was his honesty. If things went wrong he always took full blame. He never pandered to popular appeal but he did like praise. He could have had a larger practice with just a little more tact. He could be foolish also—I remember him telling a doctor with a very large prac-

tice not to call him Dr. Fullerton, he was Mr. Fullerton. That doctor never sent him another case.

From the time he got his FRCS in Dublin he kept up a close contact with the Irish College of Surgeons. He had been born in the South of Ireland and still had some relatives there including an older brother who now had an important position in the Civil Service in Dublin. It was therefore no surprise when in 1926 he was

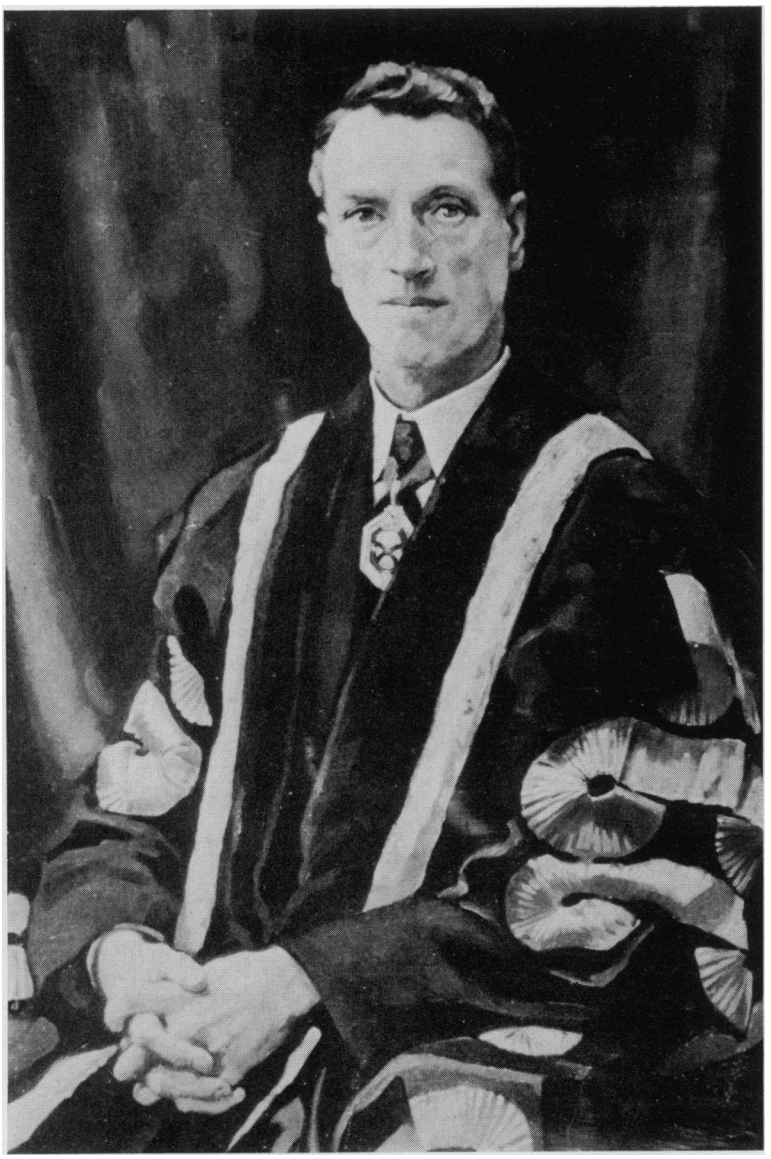

FIG. 21. *Professor Andrew Fullerton, President of the Royal College of Surgeons in Ireland. Painted by William Conor.*

elected President of the Royal College of Surgeons (Figure 21). He filled this position with great success, the first Ulster man to be President. Andrew Fullerton on a meagre income was a very generous man and each year took many of his colleagues in Belfast to the famous annual Charter Day Dinner in the College. He was such a success as president that when his successor died while still in office Andrew Fullerton was chosen unanimously to fill the vacancy. Few people have filled the presidential chair twice.

It was just by coincidence that in 1923 both the Chair of Medicine and Surgery in Belfast fell vacant at the same time and so Professor W. W. D. Thomson and Professor Fullerton were both appointed on the same day. It gave the students a chance to celebrate (Figure 22). The new incumbents were both forced to wear pyjamas over their suits, drink some champagne and be anointed with oil over a laurel crown. I think they had been warned not to wear their best suits. W. W. D.

FIG. 22. *Students' Rag. Installation of Professor Fullerton and Professor W. W. D. Thomson.*

Thompson many years later was knighted and it was a bitter blow to Andy Fullerton that he was not similarly recognised; in fact to be President of the Royal College of Surgeons in Ireland prior to 1922 automatically carried this honour. It is popularly believed that this did not happen in Fullerton's case because at a certain dinner in Dublin in a speech he had said among other things "in the field of surgery there should be no border". In the Northern press next day there appeared the notice "famous Belfast surgeon says there should be no border", leaving out the vital first part of the sentence. It is said that Lord Craigavon got out his 'blue

pencil' at once. Fullerton's multiple public appointments and his position in the world of surgery certainly warranted recognition. He made one or more trips to Canada and later was elected an Honorary Fellow of the American College of Surgeons, the first Ulsterman to be so recognised. After the ceremony Willie Mayo gave him his own personal gown and later when the Mayo Brothers came to Dublin and Belfast some years later, each to get the Honorary FRCS Ireland Willie returned to America wearing Fullerton's gown—rather like what now goes on at rugby football matches. Andrew Fullerton after his visit to the Mayo clinic decided that we must all wear white trousers and shirts in the operating theatre. He was the first to bring this new idea to Belfast. On the first day in which he appeared on the corridor thus attired the students kept calling after him "off to play tennis, Sir?" In a Hospital Alphabet in the 1920s, it said "A is for Andy of Cystoscope Fame, In far Minnesota they've heard of his name". When the Association of Surgeons finally paid its already mentioned visit to Belfast in 1931 Andrew Fullerton was the obvious choice for President. In those days all the surgeons were expected to put on an operating list to show their expertise. Andy, expert in removing the kidney. decided that this would be his party piece and as his registrar at the time it was my duty to assist. Unfortunately the case had not been fully investigated; it turned out to be a horse shoe kidney with both kidneys joined together at the lower end. We had a whispered conversation and decided we could do what had now become a difficult and risky job with less embarrassment if the audience were to fade away gently on to the corridor. A hint was made that they might like to have a cigarette, and being an understanding bunch of people—possibly something similar had happened to them—they packed their tents like the Arabs. Although this was upsetting, in fairness one must mention that certain x-ray tests now available were not in existence then.

On a Saturday morning Andy always arrived in plus fours to do a hasty ward round before he was driven to the County Down Railway Station to get the 12 o'clock train for Newcastle, Co. Down. With a game of bridge on the train, lunch at the club house and eighteen holes of golf it was for him indeed a very different atmosphere compared with the tight regime in which he lived for the rest of the week. His bridge was more gallant than scientific—I played with him on many occasions, and he was an equally good loser and winner. He enjoyed his golf and was indeed a very different man on the golf links. Few golf prizes came his way but he was immensely proud to be elected Captain of the Royal Co. Down Golf Club, a prestige position in 1922–23 (Figure 23). It was indeed a very happy coincidence that the Prince of Wales—later Edward VIII—should pay a visit to Ulster that year, and it was naturally the captain's privilege to partner the Prince on that occasion.

He occasionally came to hospital on Sunday on his way home from church. He now had joined the Church of Ireland and attended St. George's; I do not know when and why this conversion took place from Methodism.

Andrew Fullerton never looked robust; he suffered from indigestion and blamed a great deal of this on Lord Moynihan, the then Sir Berkeley, who had operated

FIG. 23. 1923—*Andrew Fullerton Captain Royal County Down Golf Club, entertaining H.R.H. Prince of Wales (Edward VIII).*

on him many years before doing a short circuit for a suspected duodenal ulcer. This operation never gave him much comfort. He liked a party and a glass of wine, and one felt that the short circuit allowed the wine perhaps to have more effect than it should have done. In all he was a temperate man but enjoyed the social occasion. On one such occasion after a public dinner he was asked to go and see a rather difficult old lady. Having examined her she said "Mr. Fullerton, do I smell drink?" He said at once "Why yes indeed, would you rather that I smelt of food?".

One of the great men to visit Belfast was Hugh Hampton Young of Baltimore who had perfected his own method of removal of the prostate from below by the perineal approach (Figure 24). To me it seemed the obvious way of making an easy operation difficult and dangerous, but he was a man of world-wide fame with an international reputation. He did two of his own operations in Belfast—both patients died. Fullerton tried a few further cases later using the same technique and we were all very glad indeed when he went back later to the old method.

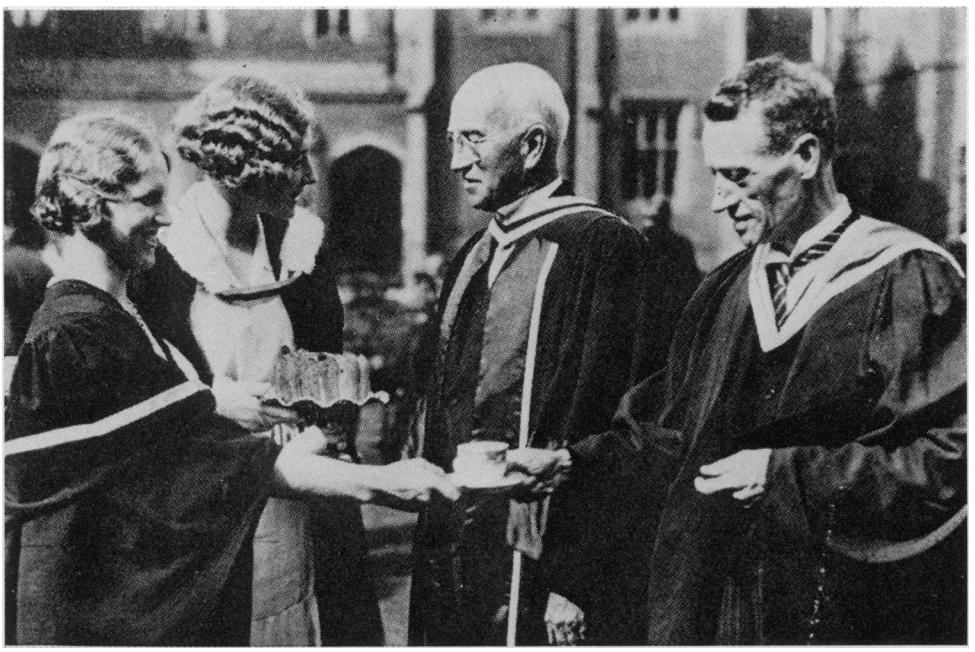

FIG. 24. *Garden Party at Riddell Hall. Professor Fullerton and Hugh Hampton Young of Baltimore after an Honorary Degree Ceremony.*

In his last year Andy himself developed prostate trouble. He went over to London to have a new technique performed. This was being done with great success by Terence Millin—"Transurethral resection". He came back but never regained his old strength and in fact he seemed to get weaker. We all thought it was just a slow recovery from the London operation, but in fact an unsuspected malignant growth was then just appearing.

Just after he retired it could be seen that Andy Fullerton was losing his energy and drive, and it was no surprise when an acute illness supervened, and an immediate operation was necessary. This was carried out by two of his Belfast colleagues but he asked one of his best friends from England Sir Geoffrey Jefferson from Manchester to come over. He insisted that under no circumstances would he accept a colostomy. He died fortunately a few hours later.

At 8.30 a.m. on May 22, 1934 when I was at breakfast a car came up to my home; I recognised Neill, Professor Fullerton's chauffeur. In his hands he carried a few books, a few cystoscopes, and draped over them all was the professor's own gown of the Royal College of Surgeons in Ireland. Neill said the professor had died at 3.30 a.m. and his last wish was that certain presents should be given to his colleagues at once. This gown like its master had seen much service but I have kept it ever since and worn it on all suitable occasions in pride and in happy remembrance of a great man, a great teacher, and a close personal friend (Figure 25).

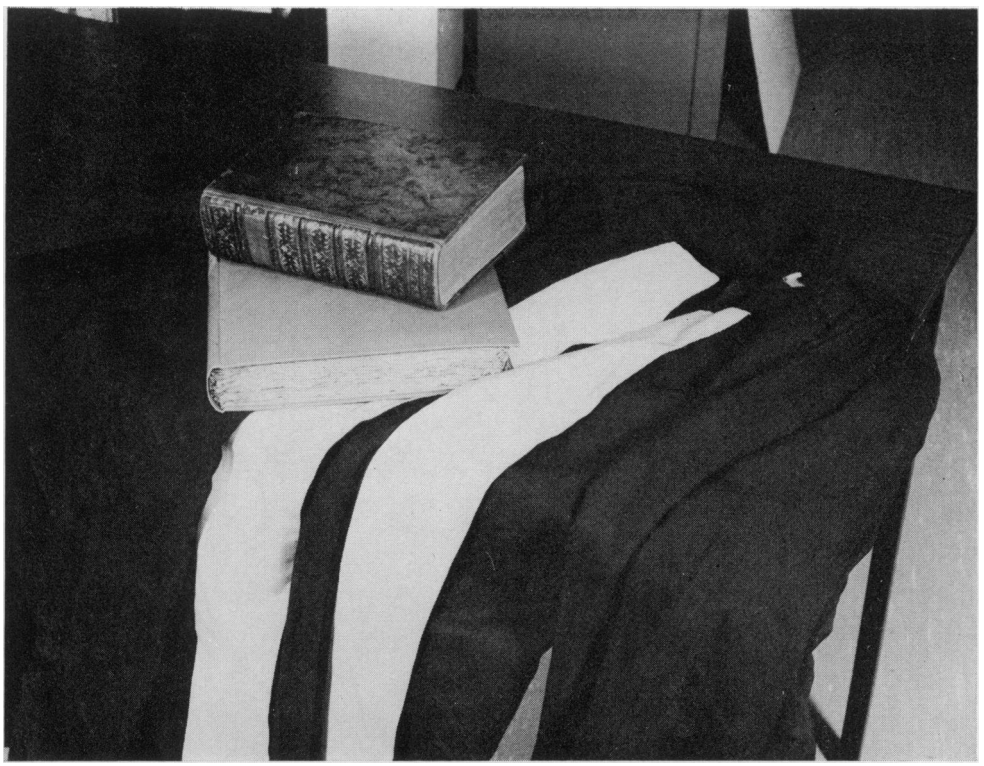

FIG. 25. *The gown and the books.*

When World War I broke out each Royal College of Surgeons was asked to nominate a consultant who would be willing to join the Army Medical Service. The Irish College suggested Andrew Fullerton, and he was appointed at once consultant to the army with the rank of full colonel (Figure 26). He was in France from 1915–1919, stationed at the Base Hospital near the coast. This was a hospital complex of British/American (Harvard and Yale) and French hospitals. It was a most stimulating centre for surgery and research. The cream of American surgeons and scientists were there—Crile, Harvey Cushing and others as well as the senior London consultants such as Sir George Makins. This was the turning point in Fullerton's career; he got unlimited scope and facilities and was able to make use of conditions that he had never had before. At first it was chiefly general surgery, the study of infection and the problem of surgical shock and many other general problems which came his way, but soon he became the recognised master in genito-urinary surgery. He produced some very valuable original work treating men with a paralysed bladder following injury to the spine, but gunshot wounds to kidney, ureter and bladder were his main forte. He wrote many papers on this subject and was also called to the forward area for genito-urinary injuries. At the end of the war he was responsible for writing the section on gunshot wounds of kidney, ureter and bladder in the History of War (Medical Service).

When in France at a party in the Officers' Mess Colonel Fullerton's party piece was to stand on his head and drink a bottle of beer, naturally uphill. Although this may at the time have been an item of great physiological interest yet in his day to day life afterwards it proved to be a skill of little practical value. This was reported to me by Alfred Webb Johnston, later Lord Webb Johnston, who was one of his brother officers.

FIG. 26. *Col. Andrew Fullerton*—1915.

FIG. 27. *Andrew Fullerton as President of the Ulster Medical Society*—1919.

In 1916 he was appointed C.M.G. and in 1919 C.B. as well as being mentioned three times in despatches during these valuable three and a half years. In 1919 when he returned to Belfast he was at once made President of the Ulster Medical Society (Figure 27). As one might expect his presidential address was on Shock and Haemorrhage, a paper based on experience. He made lifelong friends when in France and in the ensuing years we in Belfast were fortunate to be visited by people such as Percy Sergeant, Sir William Arbuthnot Lane, Ernest Miles and Tudor Edwards, all of whom were willing to operate and show us the latest advances in brain surgery, chest surgery, rectal surgery, as well as the 'no touch

technique in bone plating'. Close to the base hospital where he worked there was a fracture centre at Wimereux where H. P. Malcolm was working with Maurice Sinclair, and so when Andrew Fullerton returned to the Royal Victoria Hospital after the war a certain number of beds especially for fractured femurs were reserved in his ward under the care of Harry Malcolm. I was his dresser when he came back and had to carry out the techniques that he brought back with him. One of these, the Carrel-Dakin continuous irrigation of compound fractures, was a technique which it was quite impossible to carry out successfully.

From France Fullerton brought back to Belfast two people who gave wonderful service to the Royal Victoria Hospital. One was a Queen Alexandra Nursing Sister, Miss Mussen, who became Matron of the Royal (1922–1945). She brought a new look to the corridor where her predecessor of stately appearance seemed to us all a constant reminder of Florence Nightingale (Miss Bostock, 1901–1921). The other was R. Leeman. Andy had realised his value as a radiological technician in France and had suggested he came to Belfast. No one has served Ulster better or longer than Ralph Leeman.

In World War I blood transfusion was a question of trial and error. Four methods were tried, the first although rejected ultimately became when modified the basis of our present blood transfusion technique. One of the others was the Bazett-Fullerton method. Captain Bazett from Oxford and Andy Fullerton suggested a direct transfusion method in which a needle was put into the donor's artery, another needle into the recipient's vein. The two needles were joined by a short piece of rubber tubing with a small piece of glass to act as a viewing chamber to see that the blood was flowing. A successful series of cases treated this way was written up in the Lancet in 1917. Naturally of course there was no way of measuring the amount given; I suppose one went on until the patient looked better and the donor looked worse.

Andy always looked back with great pleasure to his army life. He was one of the founders of the University Services Club; his lectures were often illustrated by incidents from his war experience, and to the end he was very pleased when people called him Colonel. In his early life his papers were often on general subjects—fractures, injuries of the knee joint as well as the many surgical conditions of childhood. He enjoyed greatly his attachment to the Belfast Hospital for Sick Children, in fact he only resigned from it when he became deeply involved with university teaching.

In addition to the Fullerton splint for fractures of the wrist he also invented a special pair of forceps still in daily use to hold up the ureter. He was one of the first to put an inflated bag into the bladder to stop bleeding after removal of the prostate. Many of his inventions have not stood the test of time, but he was interesting, stimulating and always had the entire loyalty of his staff, medical and nursing, and they would have done anything for him. He will be best remembered as a small figure, barely visible under a large black sheet with his eye at the end of the cystoscope. As he emerged after half an hour with his hair tousled, his face wet (we hope with sweat)—if he had been able to show that one kidney was able

to produce one teaspoonful of urine more than the other kidney in the same time—he went home as satisfied as a cricketer who had made a century. It was his hobby horse to show that the earliest sign of disease in a kidney was when it produced more urine of a weaker quality. At that time this test gave invaluable information before the modern x-ray excretory tests were invented which have made the problem today so much easier. His patience in pioneering work of this sort was remarkable and not at all in keeping with his quick and brusque manner of speech. It is sad that this man, a pioneer in urological surgery with an original mind, an inventive brain and endless energy as well as being a meticulously careful recorder of facts, never received the recognition that he deserved. There is no medal or lecture to his memory nor was he recognised by his own university or by the state. I suppose for him the words of William Blake would be particularly apt "Energy is an eternal delight".

Conclusion

I have tried to give a fair appraisal of the value of these three great men who in my opinion were the foundation stones upon which the present surgical school now stands. It was Cromwell who said "paint me warts and all" and if I have painted in the warts it is merely to accentuate the underlying greatness of the man. All had something different to offer and perhaps they each had a different method of approach. Each was the leader at a different stage of medical progress and the school was fortunate to have men of this type as the pioneers. I hope someone will in time put on paper the work of their successors; men who have carried and are carrying on the torch that they lit.

I have been fortunate in being able to contact members and distant relatives of all three families and I am most grateful for their interest and the help that they have so willingly given to me.

THE MEDICAL LIBRARY

by

J. H. D. MILLAR, M.D., F.R.C.P.

ANNUAL ORATION AT THE OPENING OF THE 1975–76 TEACHING SESSION, ROYAL VICTORIA HOSPITAL

MY pleasant duty is to welcome the new students to their first term in hospital and to wish them every success at this exciting time in their career. They have one great advantage that I and others of my vintage did not have, and that is an excellent medical library close to the wards. This gives them unrivalled opportunity to examine patients and then to compare their observations with what they might or should have found. Learning in medicine, of course, doesn't end with qualification. It is a continuing education and hence the importance of understanding how to make the greatest possible use of the library. Such is the flood of medical literature, journals and books, that it is very important for the student to have guidance, as well as being able to follow his own inclinations in his reading.

I quote Dr. Peter Mann who carried out a survey on the use of the library at Sheffield University in 1972. "It has been said that lecturers do not actually explain anything to their students, but leave them at a higher level of confusion. This certainly appears to be the case with the purchase, borrowing and reading of books. Of course, when they leave school most students have never had experience of using a library as big or as complicated as that of a university, and very few have been accustomed to spending thirty to forty pounds a year on books. All the more reason for us, the lecturers, to see that they receive guidance on how to use books properly, because if we don't help them no one else can take our place." However the students here to-day have been 2 – 3 years already at university and know how to use books and a library, so perhaps this advice does not apply to them but it certainly does to their teachers. In Sheffield Medical School 26 per cent of medical students had never borrowed books from the library, although the university library has a very liberal scheme of book borrowing which permits an undergraduate to have five books out at any one time. But the students stated that the supply of medical texts on the general shelves was lamentable. There were inadequate duplicate copies and the vast majority of the popular books were out of date. I am sure that these criticisms do not apply to our medical library.

The medical library has played an important part in the great advances in medical knowledge. It is the link between the past and the present. The history of the medical library is part of the history of our civilisation. Medical collections have dated back to thousands of years before Christ. The birthplace of our western civilisation, the Mesopotamian valley, was also the birthplace of libraries. Some of the earliest medical records were found in this area.

There are about 30,000 clay fragments dating from the Sumerian civilisation, about 3000 B.C., which are currently kept in the British Museum. Several hundreds of these tablets deal with medical matters. The tablets had been broken when the

Chaldeans sacked the Assyrian city of Nineveh in 625 B.C. burning the great Royal Library with the rest of the city. The books could not be burnt because they were written on clay tablets. The Royal Library was largely the creation of the Babylonians who had conquered the Sumerians about 2600 B.C. In this library material was well organised and placed in jars in rows upon shelves. Each jar had a tag and all were catalogued. The code of Hammurabi, the Babylonian King, laid down rules and regulations for the conduct of surgery. Medicine was practiced by the priesthood who were answerable to the gods. But surgeons were laymen and received fees which depended on the social standing of the patient. However, if the operation was not a success the surgeon was liable to penalties which might even amount to losing both hands. Among the chief contributions to civilisation of the Sumerian, Babylonian and Assyrian peoples was the Cuneiform script and the development of an economical, readily available and nearly permanent writing material.

There were close trading relations between Mesopotamia and Egypt and it is probably safe to assume that there were cultural exchanges including the exchange of medical knowledge. It is logical to suppose that the Egyptians imported the art of writing from the Sumerians. The Egyptians however wrote with pen and ink on reed-paper, a perishable material, so that very little of their extensive medical literature has survived. Some temples in Egypt were centres of healing and almost certainly contained collections of medical books. In the Temple of Thoth one of the priests was called "Keeper of the Sacred Books" and his female assistant, "Lady of Letters, Mistress of the House of Books." Librarians in the medical library in Heliopolis were given such titles as "Scribe of the Double House of Life" and "Learned men of the Magic Library." In the Hall of Rolls in Heliopolis long lists of diseases and their cures were found. Specialisation in Egypt was highly developed. There was a keeper of the Pharoah's right eye and also a keeper of his left eye. From hieroglyphics on a tomb we know that around 2500 B.C. a certain doctor Iry was keeper of the Pharoah's rectum. They were really the equivalent of honorary surgeons to the Royal household. The papyri discovered by Ebers and Emith, date from 1500 B.C. and were almost exclusively medical in context. The former is a list of remedies with appropriate spells and incantations and the latter is a surgical treatise on the treatment of wounds and other injuries. In the libraries individual scrolls were encased in leather or cloth covers and stored in jars.

The Greeks were prolific writers on medical matters. Hippocrates collected a private library. Aristotle also had a private collection which was reputed to contain every known work. The Greeks employed the classification system of pinakes. These were tablets which contained the names of authors arranged chronologically in divisions of their type of literature. Medicine was one of these pinake divisions. Near Epidauros there was a famous centre of healing which developed into a medical school and library and flourished from 500 B.C. to 100 A.D. Other medical schools developed at Cos, Cnidos, Rhodes, Cyrene and Alexandria, and each with its medical library. According to one tradition the library at Cnidos was burned at the order of Hippocrates because its students refused to follow his teachings.

The most famous Greek library of all, indeed the most famous of all antiquity was not in Greece but in Egypt. The Alexandrian library flourished for at least 200 years and was a great centre of Hellenic culture. About 47 B.C. the city of Alexandria was completely destroyed along with its great library. Rome followed Alexandria as the medical centre but Romans were not greatly concerned with medical literature. During the early centuries of the Christian Era Greek doctors flocked to Rome, the most illustrious was Galen who continued the Hippocratic method. The contribution of Rome to medicine was negligible compared to Greece except in matters of public health.

During the early centuries A.D. there was a decline in learning although the Byzantine Empire preserved something of Greek culture. Also one of the greatest services to medicine rendered by the Christian church before the Renaissance was the preservation and transcription of classical Greek medical manuscripts. The great monastic medical library at Monti Cassino was founded about 550 A.D. and monastic medicine was spread by the Benedictine Monks who also helped to keep alive classical learning for several centuries. The Monastry at Monti Cassino, you will remember, was regrettably destroyed by Field Marshal Alexander's army during the Italian Campaign, but I understand that it has been almost completely rebuilt.

The rise of Arabian civilisation between the 10th and 12th century formed another link between classical Greek learning and the renaissance of Western Europe. Medical centres were developed throughout Islam. Medical schools and great libraries were founded at Cordova in Spain and Bukhara in Persia. Avicenna was born near Bukhara in 980 and became a court physician at the age of 18. His principle medical work, the Canon of Medicine, was used at many European medical schools and as late as 1650 at Montpellier. It also seems quite possible that the inspiration for the early universities in Italy, France and England came from established centres of learning in Moslem Spain.

At the time that Arabian medicine flourished, there was established at Salerno in Southern Italy the first organised medical school in Christian Europe and later other schools were established at Montpellier and Paris, and later still at Bologna and Padua. Studying medicine consisted of memorising and copying the works of Hippocrates and Galen. With the invention of printing there was a great spread of knowledge and important medical texts were printed in the vernacular. From the 15th to the 19th century medical societies developed extensively and doctors began to meet in groups to exchange ideas and perform experiments. They also shared expenses for the creation of libraries.

The Royal College of Physicians was founded in 1518 by charter granted by Henry VIII. It established the first medical library of any consequence in Britain. However it was destroyed with the rest of the college in 1666 by the Great Fire of London. Dr. Christopher Merrett, Keeper of the Library and Museum, together with the Beadle, did what they could to save its contents. They removed some of the treasures to places of safety, the charters, the four volumes of Annals, the

insignia of the President, a case of surgical instruments, the memorial inscription to Harvey, the portraits of Harvey and Foxe and about 140 volumes from the library. The new college at Warwick Lane was opened in 1679. Lord Dorchester presented his library of some 3,000 volumes to the college; it was reputed to be the finest collection of physic, mathematics and law in private ownership in Europe and valued at £4,000. A special library was built at Warwick Lane to house it and this was finished in 1688.

In 1708 the President of the college, Dr. Edward Browne (son of Sir Thomas Browne, author of Religio Medici) set up a committee to find ways to make the library more useful. One member of this committee was a Dr. Hans Sloane. The committee recommended that in addition to the library Keeper there should be an under-library Keeper, who should understand Latin and Greek and, if possible, modern languages, that he should keep the library clean with the help of an assistant paid 10 shillings a quarter, that he should take out and put back all the books used, and that he should make a complete catalogue. He was also to insure that there were no candles or tobacco smoking in the library.

Hans Sloane, who later became president of the college, was born in Killyleagh, Co. Down in 1660, the seventh son of Alexander and Sarah Sloane. Alexander was the trusted steward of Lord Clanbrassil, Second Viscount Clandeboye, and was also receiver of taxes for the County of Down. His wife Sarah was the daughter of the Rev. Hicks, prebendary of Winchester and Curate to Archbishop Laud. She had come to Ireland with Ann Carey who married James Hamilton the second Viscount Clandeboye. Only three of the Sloane sons survived, James, William and Hans and all were successful in their careers. James became a barrister in London and a Member of Parliament, and William a Belfast Merchant who is reputed to have left £100,000; no mean sum when the pound in your pocket was a golden sovereign. It is possible that the Sloanes were distant relatives of the Hamiltons whose influence must have helped the brothers, especially Hans. The Hamiltons were recovering from a heavy fine as they had supported the Royalist cause in Ireland during the Cromwellian wars; however with the restoration of the Monarchy they were again in favour at Court.

Hans from an early age was very interested in natural history, and living on the shores of Strangford Lough gave him ample opportunity to study wild life, flora and fauna. One of his earliest contributions to the Royal Society was a description of the local people gathering dulse and seaweed and how the Irish used it as a cure for scurvy. For three years from the age of 16 to 19 he was ill and confined to his room. He had been spitting up blood.Thus as a young man he acquired quiet and sober habits, and all his long life he eschewed wine and strong drink and ate sparingly. On recovery from his illness he went to London to study medicine and lodged with a Nicholas Staphorst, a chemist, chemical operator to the Society of Apothecaries. In fact he soon acquired many talented friends among them John Ray the botanist and Robert Boyle the chemist. When he was 23 he went to Paris to complete his studies. He attended lectures at the Hôspital de la Charité in Botany, Chemistry and Anatomy. From 6 a.m. to 8 a.m. he attended the Royal

Garden of Plants (under Professor Tournefort) and later a Monsieur Duporty expounded on the medicinal virtues of the various plants from 8 a.m. to 10 a.m. In the afternoon he had lectures in anatomy and chemistry. He was also expected to attend the wards of la Charité so that he must have had a very busy time. He found in Tournefort, professor of botany, a kindred spirit and he was encouraged by him to continue his studies at Montpellier with its library of priceless manuscripts. On the way south he was also advised by Dr. Hotton, professor of Botany at Leyden, that he could take his degree of Doctor of Physic at the University of Orange. Orange is an ancient town in the South of France and its university was subject to William, Prince of Orange, afterwards William III of England. Its graduates were recruited from Hugenot families who were debarred from taking degrees at Paris and Montpellier. It seems to have been merely an examining body, a shadow university with a shadow medical school. An old document states that it conferred degrees in all faculties upon "vagabond, ribald, unprofitable and ignorant scholars who had been refused degrees elsewhere." Sloane was admitted to his degree M.D. Aurantii in 1683 "with great applause."

Later he continued his studies at Montpellier and spent time collecting botanical specimens and slowly journeyed home to London where he reported to Boyle and Ray all that had happened to him in France. Boyle was immediately able to help him start in practice, as his friend Thomas Sydenham was stricken with gout and the stone and required an assistant. When Sloane attended upon the Hippocrates of British Medicine he presented his credentials which stated that Sloane was a "ripe scholar, a good botanist and a skilful anatomist." The great pragmatic physician was not at all impressed and said "All this is mighty fine, but it won't do. Anatomy, botany—nonsense! Sir, I know an old woman in Covent Garden who understands botany better. As for anatomy, my butcher can dissect a joint full and well. No young man, all this is stuff. You must go to the bedside; it is there alone you can learn disease." (Quite a mouthful, but famous quotations tend to become encrusted with age). Sydenham is also reputed to have said, when asked what textbook of Medicine he advised. "Read Don Quixote, a very good book, I read it myself."

However Sydenham developed a great liking for Sloane. He took him into his house and recommended him to his patients, and wholeheartedly promoted his interests. This close contact with so great a clinician was very important to Sloane at this formative time in his career. Sydenham taught him to note with utmost exactitude the signs and symptoms seen in each patient just as he was accustomed to describe his botanical specimens. It was by this process that Sydenham had already separated measles and scarlet fever.

When the Duke of Albermarle was appointed governor of the island of Jamaica he asked his doctor to look for someone who would accompany him and look after him and his family. Sloane was recommended and sailed in 1678 the year he was made a Fellow of the Royal College of Physicians. Although he lost his patient, he wrote the Natural History of Jamaica and purchased large quantities of Peruvian Bark, an investment which was to yield him a handsome profit. His book deals with his journeys, the habits of the natives, medical cases he treated and a full description

with copper plates as large as life of 800 plants he collected there. The death of the Duke cut short his stay to 20 months and on his return the Duchess appointed him her domestic physician and introduced him to fashionable practice. It was about this time he had the good sense to marry a wealthy widow which allowed him to increase his collections, his chief hobby.

Samuel Pepys was president of the Royal Society in 1685 when Sloane was elected a fellow at the age of 25. Pepys later became a patient of Sloane. At that time there was a galaxy of talent in the Society; Newton, Boyle, Wren, Sydenham and Ray the botanist, among others. All were, or were to become, Sloane's friends and intimates. When Sloane returned to England from the West Indies he found the Royal Society in the doldrums and his first step in resuscitating it was to revive the publications of the Philosophical Transactions which had been interrupted since 1687. The transactions were to be a useful means of publishing his many papers on natural history and medicine. Volume 17 for the year 1693 is the first of the resumed publications and in this number Sloane had a paper entitled "A description of the Jamaica Pepper tree and of the tree that bears the Cortex Winteranus." The heading of this paper indicates that he was then secretary to the Society and later he became vice-president and in 1727, on Newton's death, he was elected president to become the only man ever to have been president of both the Royal Society and Royal College of Physicians. To have been elected to succeed Sir Isaac Newton was of course a very great honour. Newton's was a difficult place to fill and, failing a peer, Sloane was the obvious choice. Others were more eminent scientists but there was no one who combined in such a degree, the scientific interest, overseas contacts and zeal for the affairs of the Society. When President he put the Society on its feet financially and served it faithfully until he was forced to retire from the presidency after 14 years, at the age of 82, because the power in his legs was failing him. Sloane cannot be considered however to rank among the great names of botanical science, an accomplished amateur and great collector rather than an original worker. Nor did he contribute to any great degree to medical science. He was a fashionable physician, a competent and cautious doctor, but he was a moving spirit in bringing the subject of innoculation against smallpox to the notice of the public. He was also largely responsible for revising the London pharmacopeica ridding it of many of its more gruesome prescriptions; yet we read that he advised 50 live millipedes in a glass of water twice daily. He is recorded in the history of the College of carrying out an experiment in the College garden. A professional viper-catcher was demonstrating the efficacy of olive oil for a viper's bite. Unfortunately the viper bit the catcher who nearly died and no one was impressed.

To house his ever growing collection of books, curiosities, precious stones and botanical specimens Sloane had bought the manor house in Chelsea and it was here when 88 years old he was visited by the Prince and Princess of Wales. The manor house was about 100 feet square with a central courtyard. Three front rooms had tables down the middle which were spread with cases containing all sorts of precious stones in their natural states—emeralds, amethyst, topaz, garnets, sapphires, rubies and diamonds; when the royal visitors had viewed one room and entered another

the scene was changed for when they returned the same tables were covered for a second course with all sorts of jewels polished and set. For the third course the tables were spread with gold and silver ore, ornaments from all over the world, ancient coins and medals. The gallery was filled with corals, butterflies, painted shells and brilliant birds. Other rooms were filled with books, volumes of dried plants and valuable manuscripts. Below stairs were more rooms filled with curious remains of Egypt, Greece, Etruria, Rome, Britain and the Indies, and many animals preserved in their skins. Fifty volumes of folio scarce sufficed to contain the catalogue of this museum consisting of 200,000 articles. Altogether his library contained 50,000 printed volumes and 2,000 manuscripts.

Sloane, now Sir Hans, reckoned that his museum had cost him £50,000 and that it was worth £80,000. The collection was too valuable to be given away without wronging his family so he bequeathed it to his country. His executors were instructed to offer it to his most excellent Majesty George II for the sum of £20,000. He died in January, 1753 aged 92. In the same year an Act of Parliament was passed, entitled "An Act for the Purchase of the Museum or Collection of Sir Hans Sloane, Baronet." £100,000 was raised by lottery to buy the museum and the mansion of the Duke of Montague. The New British Museum was opened for study and inspection in 1759, a splendid memorial to a son of County Down.

The British Museum Library at present contains millions of books, manuscripts and periodicals. Being a copyright library, by law, a copy of every single published document in the United Kingdom must be deposited there. In theory any medical student could find there all the textbooks he needs, but in practice he would not be allowed to occupy the space, as there are many other libraries already available to him. There are other copyright libraries at Oxford, Cambridge and Trinity College, Dublin. In 1973 the British Library was created. This was formed by the amalgamation of the British Museum Library, the National Lending Library, and the National Reference Library for Science and Invention, the National Central Library and the British National Bibliography.

The former National Reference Library for Science and Invention is particularly rich in technology. Anyone wishing to search the scientific literature in detail would be well advised to go there. Much of the material is in open access which means that readers may go to the shelves. Closed access means that the library staff bring the material to the readers. It is important that certain material must be in closed access because if it gets out of order, books may be lost. In the National Library in Madrid, a Leonardo da Vinci manuscript was lost for 300 years because it had been misplaced. Most National Libraries in the world are in closed access because of the risk of theft; scholars seem to be completely amoral in this respect.

The National Lending Library for Science and Technology, now called the British Library Lending Division has been a most important factor in the development of medical libraries in this country. All journals in the Index Medicus are held by the library. Only libraries can become members and the individual librarian assumes responsibility for all loans. It is now possible to get virtually any recent literature by return of post at a low cost.

The library of the Royal College of Physicians is now largely historical and bibliographical. The Wellcome Historical Library was founded by Sir Henry Wellcome. He started to build up his library in 1895 and it was opened to the public in 1949. It is the largest medico-historical library in the British Isles. Both libraries have magnificent collections of rare books.

Many small libraries grew from reading clubs and small medical societies. The Royal Society of Medicine was formed in 1907 by the joining together of 18 medical societies; chief among them being the Royal Medico-Chirurgical Society. The library of the British Medical Association was founded in 1887 and was based on the collection of Sir Charles Hasting. Our medical library was moved from Queen's to the Royal Victoria Hospital site in 1954. For many years spasmodic donations of books had been made by the Ulster Medical Society which was formed in 1862 by the amalgamation of the Belfast Clinical and Pathological Society and Belfast Medical Society. The Belfast Medical Society was founded in 1806 and had by 1826 already established a lending library for its members. The complete collection of the Ulster Medical Society's sixteenth, seventeenth and eighteenth century works on medicine was presented to Queen's in 1915. More recently since the Society moved from the Whitla Institute in College Square North the University Medical Library has housed the Society's Library.

Another collection acquired by our medical library was the fine collection of the late Dr. Samuel Simms. This was bought in 1964 with a grant from the Wellcome Trust.

Already our medical library is too small and it is intended to move it to larger premises on the site, possibly the Mullhouse block. I hope that when this happens the Marshall and Thomson rooms will be reconstituted in the new building. Robert Marshall Junior qualified with me and with many in this room in 1940 and was killed on active service in Burmah in 1945. He was the only son of the late Dr. Robert Marshall one time senior physician to this hospital. Humphrey Thomson was killed in 1942 tending the wounded before the fall of Singapore. He too was a friend of many in this room. He was the only child of the late Sir William Thomson, who was our very popular Professor of Medicine from 1923 to 1949.

In 1964 the Management Committee of the Royal Victoria Hospital appointed Dr. R. S. Allison, its first Honorary Archivist, a position he has held with great distinction and to date he has published a number of books on historical medical topics including "The Seeds of Time" a history of this hospital from 1850 to 1903.

The Captains and the Kings may have departed and all our pomp of yesterday is one with Nineveh and Tyre, but you have inherited at least one asset—the English language, which is now the international language of science and a medical passport to the world.

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PRESCRIBING IN NORTHERN IRELAND

Methods of Analysis

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from

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THE prescription scripts written by general practitioners in Northern Ireland are sent every month by pharmacists to the Pricing Bureau in Belfast so that pharmacists may be paid for the drugs and dressings they supply to patients. Since the beginning of the National Health Service these prescriptions have been scrutinised by the health authorities to determine the overall cost of the pharmaceutical services and monitor the cost of each doctor's prescribing.

Since 1963, as a consequence of the thalidomide disaster, the details of all prescriptions, recorded at first on Hollerith cards but since 1966 on a computer printout, have been made available to the Department of Therapeutics and Pharmacology of Queen's University on a confidential basis to aid in the detection of serious adverse reactions to drugs and allow analysis of the use of drugs in the community. The work carried out by the University Department has been entirely concerned with the medical aspects of prescribing.

Initial studies by Professor Wade and Helen Hood (Wade and Hood, 1972a and b) were of considerable interest. They showed that over the years individual doctors are consistent in their prescribing habits both as to the drugs they prescribe and the amount of prescribing they do. There are, however, very great differences between doctors and strangely these differences are often found to have a geographical pattern. For instance, practitioners in Newry prescribe more oral antidiabetic drugs for their diabetic patients than do practitioners in Londonderry (Wade, Hadden and Hood, 1973), and practitioners around Ballymena prescribe more antihypertensive drugs than doctors around Enniskillen.

Since 1971, it has been possible with the help of the World Health Organisation to extend these studies of drug use to Norway and Sweden. It has been found that the levels of prescribing of certain groups of drugs are different in Northern Ireland from Norway and different again from Sweden. As yet it has not been possible to relate the prescribing of drugs in any of these countries to the incidence of disease or to the therapeutic benefits that patients derive, but it is a real possibility that further investigations may help to determine which patterns of prescribing and which drugs are of most value in the community (Bergman, Elmes, Halse, Halvorsen, Hood, Lunde, Sjöqvist, Wade and Westerholm, 1975).

The patterns of prescribing change with time, because old doctors retire and are replaced by new ones and because new drugs are introduced which replace or partly replace old ones. The Department of Therapeutics now has complete records of

prescribing in Northern Ireland since 1966, when the computer was first used in the Pricing Bureau. It is proposed to describe and discuss the changes in prescribing that have occurred over the first eight years of this survey in a series of short papers.

The method of measurement of prescribing

In order to give the prescribing figures meaning, and to allow comparison with other countries, the amounts of each drug prescribed is related to the population size. To compare the prescribing of different drugs used for the same purpose, such as the various diuretics or antibiotics, the amount is expressed in "agreed daily doses" rather than in grams or milligrams because the dosage within a group of similar drugs can differ widely. Occasionally, if a proprietary medicine contains a mixture of two or more drugs, the agreed daily dose is expressed as one or more tablets of the preparation. A list of "agreed daily doses" drawn up in collaboration with colleagues in Norway and Sweden is given in the table and a full list is available in Drug Dose Statistics published by the Norwegian Drug Monopoly (Norsk

Table

Agreed daily doses for some commonly used preparations

APPROVED NAME	COMMON PROPRIETARY NAMES	AGREED DAILY DOSE
Cardiac glycosides		
Digoxin	Lanoxin	0.25 mg
Digitoxin		0.1 mg
Tranquillisers and hypnotics		
Chlordiazepoxide	Librium	30 mg
Diazepam	Valium	10 mg
Nitrazepam	Mogadon	5 mg
Methaqualone and diphenhydramine	Mandrax	1 tablet
Antidiabetic drugs		
Insulin		40 units
Chlorpropamide	Diabinese	0.375 G
Tolbutamide	Rastinon	1.5 G
Metformin	Glucophage	2 G
Phenformin	Dibotin	0.1 G
Antibiotics		
Ampicillin	Penbritin	2.0 G
Phenoxymethylpenicillin	Penicillin V	1.5 m.IU
Hypotensives		
Debrisoquine	Declinax	30 mg
Guanethidine	Ismelin	30 mg
Methyldopa	Aldomet	1 G
Reserpine	Serpasil	0.5 G
Methoserpidine	Decaserpyl	20 mg
Diuretics		
Furosemide (=Frusemide)	Lasix	40 mg
Chlorthalidone	Hygroton	50 mg
Polythiazide	Nephril	1 mg

Medisinaldepot 1975). Thus the "agreed daily dose" of digoxin for a normal adult for the purpose of these studies is 0.25 mgm. per day and for digitoxin is 0.1 mg. per day. Of these two only digoxin is used in significant quantity in Northern Ireland. In the second quarter of 1974, 10.22 daily doses of digoxin were prescribed per day per 1,000 patients on doctors' lists. This indicates that doctors prescribed on average 2.55 mgm. of digoxin (10.22 doses of 0.25 mgm.) for every 1,000 patients in their practice. It also means that if doctors are prescribing on the average 0.25 mg. of digoxin a day for patients that need the drug, there are 10.22 patients in every thousand of the population receiving digoxin. When comparing the use of drugs in different practices, areas or countries, if the use of cardiac glycosides is found to be more than the average (10.22 daily doses per 1,000 patients per day), it suggests either that there are more than the usual number of patients in that practice or area with heart failure, that the criteria by which doctors recognise heart failure are different, or that patients are receiving unusually large doses of cardiac glycosides. In this last instance, it might be expected that in that practice or area, digitalis intoxication might be a more frequent cause of admission to hospital than in other areas.

One of the defects of this system is that prescribing of drugs by doctors may not truely represent the consumption of drugs. Drugs supplied by pharmacists may not be taken as instructed, may be left on the bathroom shelf for years deteriorating all the time, or may be used, often inappropriately, by other members of the family. The extent to which drugs are consumed as prescribed is known as the 'compliance'. Studies in Northern Ireland, Norway and Birmingham are being started to measure the compliance of patients to the wishes of doctors about drug taking, and these studies should be of considerable help in estimating the true consumption of drugs in the community.

The authors would like to thank the staffs of the Northern Ireland General Health Services Board, now the Central Services Agency, and the Computer Branch of the Research and Intelligence Branch of the Department of Health and Social Services, Northern Ireland, for their willing co-operation and help over many years, which has made it possible for these studies, the first of their kind ever made by a Health Service, to be carried out. We are also grateful for permission to publish the results of the studies which have been undertaken in such a way as to maintain complete confidentiality concerning the prescribing of individual doctors.

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CLOMIPHENE AND NEURAL TUBE DEFECTS

by

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THE aetiology of anencephaly and/or spina bifida (neural tube defects) is still obscure. Most investigators are now agreed on a multifactorial causation with an important genetic factor and a substantial environmental component. The genetic factor is probably polygenic, but the mechanism by which it acts remains unknown. Recently, drugs that stimulate ovulation, particularly clomiphene, have been implicated in the aetiology of neural tube defects (Dyson & Kohler, 1973; Sandler, 1973; Barrett & Hakim, 1973; Field & Kerr, 1974). Although six infants with anencephaly and/or spina bifida have been born to mothers receiving clomiphene, it is impossible on present evidence to conclude whether the malformation rate for neural tube defects is greater than would have been expected. This report describes four patients on clomiphene who produced a total of five infants each with a neural tube defect.

Case Reports

Patient 1. This patient was aged 20 years when first seen on November 29, 1971, because of secondary amenorrhoea. Since her menarche at age 19 years, she had had only one menstrual period (February, 1971). Clinical examination was normal except for hirsutes on the thighs and upper arms and poor breast development. The uterus was small, mobile, and anteverted. Skull X-rays, adrenal steroid excretion and thyroid function tests were normal.

Treatment by clomiphene, 50 mgms. daily for five days was commenced on March 27, 1973. A pregnancy test was positive on May 14, 1973. At examination on May 21, 1973 and on June 8, 1973 the size of the uterus corresponded to six weeks and eight weeks gestation respectively. From July 1973, the size of the uterus was always in excess of the period of amenorrhoea. On October 12, 1973, the size of the uterus corresponded to 32 weeks, whereas the interval since ovulation was 26 weeks. An ultrasonic scan confirmed gross polyhydramnios and the absence of a fetal skull. A transabdominal amniocentesis was carried out; the amniotic fluid alpha-fetoprotein level was 43.0 μg/ml. At 26 weeks gestation the mean amniotic fluid alpha-fetoprotein level is 3.15 μg/ml; and the 95th percentile 5.82 μg/ml (Nevin, Thompson & Nesbitt, 1974). A straight X-ray confirmed the presence of an anencephalic fetus. Five days later, following induction, the patient delivered a stillborn female fetus weighing 1134 g with anencephaly and a meningomyelocele.
Patient 2: This patient, aged 23 years was first seen in February 1972. She had a normal menarche, aged 11 years, with menstrual periods lasting 21 to 35 days. For six months after her marriage in April, 1969, she had been taking an oral contra-

ceptive. After stopping the pill, there was a three-month period of amenorrhoea. For the next two and a half years, she had been trying unsuccessfully to conceive. Clinical and pelvic examination was normal. The uterus was anteverted and of normal size. There was no histoligical evidence of cyclic activity in the endometrium. Tubal insufflation was normal. In addition, vaginal cytology on five occasions from September 13, 1972 to October 11, 1972, showed no evidence of oestrogenic fluctuation throughout the cycle or any indication that ovulation had occurred.

The following courses of clomiphene, each lasting five days, were started in 1973: —

March, 23	50 mg daily
May, 9	100 mg daily
June, 6	200 mg daily

The temperature chart indicated that ovulation had occurred on July 20, 1973, but a subsequent pregnancy test on August 1, 1973 was negative. She had a normal menstrual period on October 14, 1973. Further courses of clomiphene, each lasting five days was given on: —

March, 1974	400 mg daily
April, 1974	400 mg daily
June, 1974	400 mg daily

She had a normal menstrual period on June 14, 1974. She had had only two and a half days treatment of the last course of clomiphene. On July 31, 1974, the size of the uterus corresponded to 6 to 8 weeks gestation. A pregnancy test on August 1, 1974, was positive.

At 24 weeks gestation on December 18, 1974, she was admitted to hospital because of an intrauterine death. Following syntocinon induction, on December 19, 1974, she was delivered of a macerated male fetus, weighing 590 g with iniencephaly.
Patient 3: This patient who was born May 31, 1951, was married on February 6, 1970. Her first pregnancy on March 26, 1972 was a stillborn anencephalic female. There had been no history of clomiphene treatment during this pregnancy. In 1972 her second pregnancy ended in a spontaneous abortion at 10 weeks gestation. This pregnancy was followed by secondary amenorrhoea. The following courses of clomiphene, each lasting five days were given in 1973: —

March, 1973	50 mg daily
April, 1973	50 mg daily
May, 1973	50 mg daily

The temperature chart indicated that ovulation had occurred on May 23, 1973. The pregnancy progressed normally. On March 14, 1974, she delivered a female with microcephaly and an encephalocele. The infant died 30 minutes after birth.
Patient 4: This patient, aged 22 years, was first seen in 1968 because of irregular menses. Her menarche was at the age of 17 years. Examination did not reveal any

abnormality. The uterus was small and anteverted with a uterine cavity length of 2 inches. Histologically, the endometrium showed only proliferative phase.

She was married in 1970 and two years later was again seen because of irregular menses. In the last 8 months she had had only two menstrual periods. Skull X-ray, thyroid function tests and steroid analysis were normal. Clomiphene therapy, 50 mg daily for five days, was started on July 31, 1972, and this was increased to 100 mg daily for five days on August 3, 1972. The temperature chart suggested that ovulation had occurred on August 20, 1972. Pregnancy tests on September 11 and 18, 1972, were positive, but two subsequent tests (September 19 and 20) were negative. She began to stain vaginally on September 16 and, as this failed to subside, a dilatation and curettage was undertaken on September 22, 1972. Histologically, the endometrium showed decidual reaction.

A third course of clomiphene, 100 mg daily for 5 days was given on November 7, 1972. No further treatment was given until September, 1973, when she had a fourth course of clomiphene—100 mg daily for five days. The temperature chart suggested that ovulation had taken place on October 1, 1973. On November 5, 1973, the pregnancy test was positive. Spontaneous labour took place on June 23, 1974, and she delivered a female infant with microcephaly, frontal encephalocele, and a meningomyelocele. This baby died 3 hours later.

A fifth course of clomiphene—100 mg daily for 5 days was given on May 6, 1975. Slight vaginal bleeding occurred on June 28 and July 4, 1975. On July 11, 1975, the size of the uterus corresponded to 11 weeks gestation. On July 14, 1975, she had an episode of crampy low back pain, and two days later, fresh vaginal bleeding. The pregnancy terminated on July 19, 1975 in a spontaneous abortion; the fetus had anencephaly.

Discussion

The use of ovulation stimulation agents such as clomiphene in the management of infertility has become widespread. Until recently, the only problems encountered in the use of clomiphene has been the high incidence of multiple pregnancy, and a high rate of early abortion (Whitelaw, et al, 1970; Murray, et al, 1971; Hack, et al 1972). Within the past few years, it has been suggested that clomiphene may have a teratogenic action (Table). In 1973, Dyson and Kohler, described two patients who produced infants with anencephaly and spina bifida following treatment with clomiphene. Since this initial report, several similar observations have been reported (Sandler, 1973; Barrett & Hakim, 1973; Field & Kerr, 1974). To date there have been six patients on clomiphene who had infants with a neural tube defect (Table). The present paper describes four women receiving clomiphene who produced five infants with a neural tube defect; two had anencephaly and/or spina bifida; of the remaining three cases one had iniencephaly; another microcephaly and an encephalocele, and the fifth microcephaly, frontal encephalocele and meningomyelocoele. Interestingly, although clomiphene has been used extensively in the United States, there are no published reports suggesting a casual association of neural tube defects and clomiphene.

TABLE

Neural-tube Defects following Ovulation Stimulation by Clomiphene

Author	*Case*	*Previous Obstetric History*	*Sex*	*Birth Weight (g)*	*Description of Abnormality*
Dyson & Kohler (1973)	1	Primigravida	F	1030	Cervical spina bifida, anencephaly, kyphoscolosis of thoracic spine and mild bilateral hydronephrosis
	2	One spontaneous abortion	M	NR	Anencephaly
Sandler (1973)	1	Primigravida	M	936	Anencephaly and severe spina bifida
Barrett & Hakim (1973)	1	Four previous pregnancies; first a female anencephalic infant; and the other 3 normal female infants	M	NR	Anencephaly
Field & Kerr (1974)	1	One normal male while on clomiphene therapy	M	NR	Lumbar meningomyelocele
	2	Primigravida	F	—	Anencephaly
Present Authors (1975)	1	Primigravida	F	1134	Anencephaly and meningomyelocele
	2	Primigravida	M	590	Iniencephaly
	3	Two pregnancies; first a stillborn anencephalic infant; and the other a spontaneous abortion	F	1432	Microcephaly and encephalocele
	4	One spontaneous abortion while on clomiphene	F	NR	Microcephaly, frontal encephalocele and a meningomyelocele
			NR	NR	Anencephaly

NR=not recorded

However, several large series of women receiving ovulation stimulation agents for a variety of causes of infertility have been reported but without any indication of an increased incidence of neural tube defects or indeed any congenital abnormality among their offspring. Goldfarb, et al (1968) found no increase in the incidence of congenital abnormalities in the offspring of women on clomiphene. In 166 infants and 17 abortuses in their study, only two congenital abnormalities, both haemangiomas, were noted. In the series reported by Whitelaw, et al (1970) of 88 pregnancies which resulted in 67 livebirths, there was no mention of congenital abnormalities. However, of the 104 infants born to 86 women on clomiphene reported by Hack, et al (1972), six had congenital abnormalities. One infant had a double aorta, hypoplasia of the right arch and a preductile coarctation of left arch with a patent ductus arteriosus; another infant had absence of second and fifth

digits; two additional infants had congenital dislocation of the hip; and another two had pyloric stenosis. None of the 104 infants had neural tube defects. Although they concluded that the "incidence of congenital malformations did not differ significantly from that found in the general population", six of 104 infants with a congenital abnormality should not be dismissed lightly.

An alternate explanation for the association of anencephaly and clomiphene is that couples who have infants with neural tube defects are subfertile and, therefore, likely to receive ovulation stimulation agents (Dyson & Kohler, 1973; James, 1973, 1974). Several epidemiological surveys of anencephaly have shown a longer fallow interval or conception wait before the anencephalic birth than in controlled groups (Smithells, et al, 1964; James, 1974). James (1974) using the data of the British Perinatal Mortality Survey (1963) and taking only patients with no previous obstetric history showed the following: of 134 cases of anencephaly, in 74 cases the marriage to confinement interval exceeded the median of the distribution of the control group. He concluded that although this finding was not statistically significant, it did suggest that primiparous mothers of anencephalic infants have a longer marriage to conception interval. As there is an association between dizygotic twinning (due to double ovulation) and anencephaly, Elwood (1974) has suggested that perhaps clomiphene acts via a mechanism which increases the risk of both.

Couples who produce infants with anencephaly may be subfertile, not because they are less able to conceive, but because they have a high spontaneous abortion rate (Record & McKeown, 1950; Coffey & Jessop, 1958; James, 1974). Thus, among their pregnancies there is a higher proportion of recognised and unrecognised spontaneous abortion.

There is undoubtedly a need for more information on the relationship between fertility and neural tube defects. A prospective survey of women receiving clomiphene is being carried out and a complete ascertainment of families with an infant with a neural tube defect born 1971–1974 inclusive, has been undertaken to determine some of the parameters of fertility. However, it is also important not to ignore the possible teratogenic effect of clomiphene.

Summary

This paper describes four patients who had five infants with neural tube defects while receiving clomiphene for infertility. Of the five infants two had anencephaly and/or spina bifida; one had iniencephaly; another, microcephaly and an encephalocele; and the fifth, microcephaly, a frontal encephalocele and a meningomyelocele. The possible teratogenic effect of clomiphene is discussed but it is also suggested that anencephalic-prone-couples are subfertile and thus anencephalic births would be associated, but not casually, with the administration of drugs designed to alleviate infertility.

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GLUCAGON: ITS SIGNIFICANCE IN HEALTH AND DISEASE

by

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HISTORICAL

IN the early 1920's when crude extracts of pancreas were used as the source of insulin for animal experiments, it was noted that a transient rise in blood sugar often occurred before the expected insulin hypoglycaemia. The effect was at first wrongly attributed to adrenaline but soon the presence of a hitherto unknown hyperglycaemic agent was suspected.

Glucagon, the fraction responsible for the hyperglycaemia, was isolated by Collens and Murlin in 1929. However, it was not until the 1950's, following the introduction of new electrophoretic and chromatographic techniques that glucagon was obtained in sufficiently pure form to allow chemical characterization (Staub, Sinn and Behrens, 1953). Porcine glucagon was shown to be a single chain polypeptide of 29 amino acids with molecular weight 3485 (Bromer, Sinn and Behrens, 1957). Subsequently immunofluorescent techniques revealed that the alpha cells of the pancreatic islets were its source (Baum, Simons, Unger and Madison, 1962).

The glucagon molecule shows a striking similarity to the secretin molecule chemically and shares some biological properties with it. Secretin is composed of 27 amino acids. Starting from the N-terminus 14 positions are occupied by the same amino acids. Under certain conditions both hormones can stimulate lipolysis and insulin secretion.

PHYSIOLOGY

Following secretion from the pancreas glucagon is either degraded by proteolytic enzymes in the plasma (Eisentraut, Whissen and Unger, 1968) or metabolised and cleared by the liver (Buchanan et al, 1968) and kidneys (Lefebvre, Luyckx and Nizet, 1974). Degraded hormone has no biological activity. At present little is known about the physiological factors controlling rate of breakdown and clearance of the hormone.

Regulation of glucagon secretion by changes in plasma glucose appears to be as sensitive as regulation of insulin secretion by this means. Hypoglycaemia induced by insulin (Ohneda et al, 1969; Gerich et al, 1974c), by a sulphonylurea (Buchanan et al, 1969) or by starvation (Aguilar-Parada et al, 1969) is associated with a rise in glucagon levels while hyperglycaemia causes a fall in the level (Unger et al, 1970). More recently glucagon has been shown to have a role in the maintenance of blood sugar during overnight fasting (Alford et al, 1974; Gerich et al, 1975). In the liver

glucagon stimulates glycogenolysis and gluconeogenesis while inhibiting glycogen synthesis; these changes being associated with a rise in hepatocyte cyclic 3^1, 5^1-adenosine monophosphate (cAMP) level.

Aminoacids stimulate both insulin and glucagon secretion, the rise in glucagon serves to limit the fall in glucose that would occur if insulin alone was secreted after a mainly protein meal (Unger et al, 1969). The aminogenic glucagon response is abolished by hyperglycaemia (Müller et al, 1970) but where there has been prolonged dietary carbohydrate restriction there is a brisk aminogenic glucagon response from an already elevated basal glucagon level (Müller et al, 1971a).

Glucagon can cause lipolysis in rat (Hagen 1961) and avian (Langslow & Hales, 1970) adipose tissue and triglyceride breakdown in perfused rat liver (Penhos et al, 1966). However, it has been difficult to show a lipolytic effect of glucagon at physiological levels in man. Supraphysiological levels have lipolytic and ketogenic effects in the human (Liljenquist et al, 1974). Free fatty acid (FFA) levels and glucagon levels have an inverse relationship in humans (Gerich et al, 1974a) and dogs (Luyckx and Lefebvre, 1969). However, in man should hyperglycaemia coexist with very low FFA levels the effect of glucose on glucagon secretion will predominate (Gerich et al, 1974). Absorption of a fat meal leading to a rise in plasma triglyceride (TG) level causes no change in plasma glucagon level in humans but is associated with a rise in dogs. In dogs, infused TG causes no glucagon rise and it has been postulated that an enteric signal such as pancreozymin may be responsible for the hyperglucagonaemia following a fat meal (Böttger et al, 1973). At pharmacological levels glucagon will lower plasma TG levels (Eaton, 1973) but this effect has not yet been shown at physiological levels of the hormone.

Glucagon at physiological concentrations stimulates insulin release (Ketterer et al, 1967). The insulinogenic and hyper glycaemic properties of glucagon are independent, the former probably being important for insulin-dependent glucose metabolism in peripheral tissues during times of starvation or low carbohydrate intake.

Insulin exerts a strong influence over glucagon secretion. High glucagon levels found in experimental insulin deficiency in dogs are promptly lowered by insulin administration (Müller et al, 1971b). Similarly when insulin-deficient isolated pancreatic islets were incubated in high glucose media glucagon secretion was suppressed only after addition of insulin (Buchanan and Mawhinney, 1973).

Although glucagon at pharmacological levels can cause catecholamine release (Sarcione et al, 1963; Sheps and Maher, 1968) this seems not to occur at physiological levels (Broadus et al, 1970). Glucagon secretion rises abruptly under acute stress (Bloom, 1973) and during adrenaline infusion (Gerich, Karam and Forsham, 1973). It is now clear that the autonomic nervous system, especially the parasympathetic is important in mediating the glucagon response to hypoglycaemia (Bloom, Edwards and Vaughan, 1974) and in man following truncal vagotomy this response is very poor (Bloom, Vaughan, Russell, 1974).

Energy consumption rises abruptly with exercise and it is not surprising that levels of glucagon, a fuel mobilizer, rise too. This response can be blocked by propranolol pretreatment (Luyckx and Lefebvre, 1974) and is probably dependent on the sympathetic nervous system.

Food (or its absorption products) and the autonomic nervous system seem to have major roles in the control of glucagon secretion. Secretion can be modified by substances which change the intracellular cAMP level (Marco et al, 1973) or destroy the microtubular apparatus of the alpha cell (Leclercq-Meyer et al, 1974; Edwards, 1973). Potassium imbalance modifies secretion (Kuzuya et al, 1974; Santeusanio et al, 1973). Whereas it has been clearly shown that low calcium levels cause decreased insulin secretion either under experimental conditions (Grodsky and Bennett, 1966) or in man (Laron and Rosenberg, 1970), the role of calcium in glucagon secretion remains controversial (Leclercq-Meyer et al, 1973; Gerich et al, 1974b).

Somatostatin is a tetradecapeptide isolated from the hypothalamus. Recently it has been found in the D cells of pancreatic islets. Somatostatin (growth hormone release inhibiting factor) inhibits the release of both insulin and glucagon.

Other actions of glucagon possibly only of pharmacological importance are augmented urinary excretion of sodium, potassium, calcium, phosphate and magnesium (Birge and Avioli, 1969), positive inotropism on the myocardium (Parmley et al, 1968), inhibition of gastric motility (Necheles et al, 1966) and stimulation of growth hormone release (Mitchell et al, 1969).

Measurement of glucagon

Attempts at precise measurement of circulating levels of pancreatic glucagon have met with many technical problems. Circulating levels are low and radioimmunoassay has been the method of choice. One of the important basic needs for a sensitive and precise radioimmunoassay is an antibody with high specificity for the hormone (or antigen) being measured. Experienced workers have found that most antibodies raised to purified glucagon of pancreatic origin will cross-react with a number of polypeptides from the gastrointestinal tract. These peptides are as yet poorly characterized and their relationships to pancreatic glucagon remain obscure. A few antibodies have been found which show little cross-reactivity with these gut peptides.

Measurements of plasma 'glucagon' levels with such antibodies have been used to define the physiological circulating levels of glucagon. Such an antibody was first discovered in 1968 (Eisentraut et al, 1968); since then a great deal of work has been done to define glucagon's role in health and disease. In the resting, non-stressed state in normal individuals the peripheral venous level falls in the range 40–200 pg/ml; the portal venous level is several times greater.

Clinical syndromes in which glucagon is, or may be, important

(*a*) *Glucagonoma syndrome*

The most convincing evidence that elevated glucagon levels, in the presence of normal insulin secretion, can cause the diabetic syndrome comes from a single case report. Lightman and Bloom (1974) have reported the return of completely normal glucose tolerance in a previously insulin-dependent diabetic following the removal of a glucagonoma.

Glucagonomas are tumours of the pancreatic alpha cells found in patients who have often presented at dermatology clinics with a striking necrolytic, migratory erythematous rash, usually affecting the lower trunk and groin areas. In addition to the rash there is stomatitis, carbohydrate intolerance (usually mild), anaemia and a history of weight loss (Mallinson et al, 1974). Hypoaminoacidaemia is often present as well as the high plasma glucose and the diagnostic high plasma glucagon levels. The high plasma glucagon levels are of aetiological importance in the development of the diabetic state.

(*b*) *Idiopathic diabetes mellitus*

Glucagonomas are rare and the role played by glucagon in the aetiology of idiopathic diabetes mellitus is not as fully understood. In the complex biochemical situation occurring in diabetes it may be difficult to decide which abnormalities are primary and possibly of aetiological importance and which occur as a consequence of the diabetic state. It is generally agreed that pathophysiological changes which occur early in the course of a genetic disease are more closely related to the primary disorder than are those which occur later. Since genetic factors are important in the development of diabetes, assessment of persons supposed to be at high risk of developing the disease has always been an area of active investigation. For example, it has been shown that otherwise healthy monozygotic twin sibs of diabetic patients may have decreased and delayed insulin responses to glucose infusion (Cerasi and Luft, 1967). Day and Tattersall (1975) doing a similar study, found that the mean glucagon levels in the unaffected twins tended to be higher than in other healthy control subjects. This would support the concept that in idopathic diabetes mellitus there may be an inherited abnormality of glucagon secretion or metabolism as well as a primary abnormality of insulin secretion.

In established idiopathic diabetes several abnormalities of glucagon secretion have been reported. There is relative or absolute basal hyper-glucagonaemia (Unger et al, 1970; Müller et al, 1970; Buchanan and McCarroll, 1972; Wise et al, 1973a). Ingested or infused glucose has been reported to cause no suppression or even paradoxical rise in glucagon levels (Müller et al, 1970; Buchanan and McCarroll, 1972).

Although in experimental insulin deficiency the alpha cell unresponsiveness to hyperglycaemia is promptly reversed by administration of insulin (see above) in the human diabetic this unresponsiveness is not fully corrected even by massive doses of insulin (Unger et al, 1972) suggesting that there is some other (perhaps primary) abnormality of the alpha cell in this condition.

Whereas in normal individuals there is a striking rise in glucagon level in response to hypoglycaemia, this response was absent in a group of insulin-dependent diabetics where hypoglycaemia was produced by insulin (Gerich et al, 1973a). This finding again suggests an intrinsic alpha cell abnormality in diabetes. Aminogenic glucagon secretion is exaggerated in diabetics despite hyperglycaemia which in non-diabetics abolishes the aminogenic stimulus (Unger et al, 1970; Müller et al, 1970; Wise et al, 1973a).

For some time it has been known that very high levels of glucagon may occur in diabetic ketoacidosis (Assan et al, 1969; Unger et al, 1970). Recently Gerich and coworkers (1975) have shown that glucagon had aetiological importance in the development of the ketoacidotic state. When they withheld insulin from a group of insulin-dependent diabetics there was a prompt rise in plasma glucagon, glucose and ketone levels. In the same diabetics if glucagon secretion was blocked (by infusion of somatostatin) at the same time as insulin was withheld then plasma glucose rose slowly and ketone levels rose very little over the time period studied (18 hours).

In idiopathic diabetes there is, therefore, some evidence of primary alpha cell abnormalities. In established cases relative or absolute hyperglucagonaemia contributes to the hyper glycaemia and glucagon probably plays a key role in development of diabetic ketoacidosis.

Do glucagon levels change with diabetic management and control? In a large group of mild maturity-onset diabetics treated by dietary methods only, there was very little change in glucagon levels after six months' treatment which resulted in significant improvement both in the glucose tolerance and insulin secretion on glucose challenge. (Care was taken to ensure a similar carbohydrate intake for one week before the initial GTT and the test carried out at six months), (Trimble, 1975).

It has been mentioned above that high glucagon levels associated with ketoacidosis do tend to drop with insulin treatment, however, there is no evidence that the alpha cell responsiveness to glucose is ever fully restored. Unger and coworkers (Unger et al, 1970) found that the glucagon response to arginine was exaggerated and unrelated to duration of diabetes, body weight, or type of diabetic treatment (the diabetic group included juvenile and maturity-onset types and treatment was either by insulin, sulphonylureas or diet alone).

There are contradictory reports in the literature about the effect of sulphonylureas on glucagon secretion. Suppression (Samols et al, 1969), non-suppression (Pek et al, 1972) and stimulation (Harrison and Samols, 1975) have been recorded. It would appear that sulphonylureas may lower glucagon levels if they are already raised by the stimulus of hypoglycaemia. However, it cannot be inferred from the above publications that this is a primary effect on the alpha cell; it may be secondary to the effect of the sulphonylurea-induced insulin secretion on the alpha cell.

(c) *Renal and hepatic disease*

The kidneys and liver are the important sites of glucagon breakdown and clearance. There is a high incidence of carbohydrate intolerance in renal and liver failure.

Hyperglucagonaemia has been reported in uraemia (Assan, 1972; Bilbrey et al, 1974). Since the hyperglucagonaemia of renal failure may occur early on and in the absence of glucose intolerance (Trimble, McEvoy and Buchanan, unpublished data) it may be of aetiological importance in the development of diabetes in this situation.

High levels of glucagon have also been found in cirrhosis (Marco et al, 1973). However, if liver glycogen stores are poor it is less likely that glucagon plays any role in the development of hyperglycaemia in this situation.

(d) *Other endocrine disorders*

High glucagon levels occur in Cushing's syndrome (Wise et al, 1973b) and myxoedema but not thyrotoxicosis (Seino et al, 1974). In acromegaly the levels have been reported on as being slightly elevated (Lawrence, 1972) but this could not be confirmed by others (Trimble, 1975).

Adrenaline increases glucagon and decreases insulin secretion, both of these changes probably contribute to the glucose intolerance seen in situations associated with raised catecholamine levels.

The stress reaction may be implicated in the hyperglucagonaemia seen in cases of trauma (Meguid et al, 1972), burns (Wilmore et al, 1974), severe infections (Rocha et al, 1973) and coronary thrombosis (Willerson et al, 1973).

(e) *Obesity*

Stimulated glucagon output has been reported as decreased (Wise et al, 1973a) or increased (Gossain et al, 1974; Gerich, Langlois, Noacco, 1973) in obesity. At present it is doubtful whether glucagon is important in the carbohydrate intolerance associated with obesity.

(f) *Primary endogenous hypertriglyceridaemia*

In many patients with primary endogenous hypertriglyceridaemia the glucagon levels are high. Eaton and Schades (1973) have postulated that there is resistance to the triglyceride lowering action of glucagon in this situation.

(g) *Disease involving exocrine pancreas*

In chronic pancreatitis the glucagon and insulin response to arginine infusion falls into two patterns. In one group of individuals there may be a concomitant decrease in glucagon and insulin secretion while the other group which includes those with severe insulinopenia show relative hyperglucagonaemia (Kalk et al, 1974). In cystic fibrosis Stahl and coworkers (1974) found that there was a tendency for stimulated glucagon output to be decreased by about the same amount as was insulin secretion. However, others have found high, 'normal', and low aminogenic glucagon secretion in patients with cystic fibrosis (Redmond, Buchanan and Trimble; in preparation). High levels of glucagon in this series were found in those with most severe pulmonary involvement. Late in the disease extensive pancreatic fibrosis could theoretically limit both insulin and glucagon secretion, earlier on other factors such as stress and bacterial infections may be important.

In acute pancreatitis mild elevations of glucagon have been reported but in the more severe cases glucagon levels have been reported as low (Day et al, 1972).

Summary

Although it has been known for a long time that glucagon has many powerful biological activities in the in vitro situation the importance of glucagon has always been overshadowed by that of insulin because of difficulty in proving that its actions are significant at physiological circulating levels in the intact human. The development of (relatively) specific assay systems for its measurement has led to many advances in our understanding of the hormone. If any other single item can be picked as having made an outstanding contribution to our knowledge of the physiological importance of the hormone it has been the experimental use of the hormone somatostatin. Glucagon and insulin often act as a bihormonal unit, there being few situations in which changes in the level of one is not accompanied by changes in the level of the other. Consequently, biological effects noted have been due to the sum of glucagon and insulin activities. By the use of somatostatin the endogenous secretion of both can be blocked and the biological effects of infused glucagon can be observed. Unfortunately, somatostatin has side effects which will probably preclude its further use in humans. However, there is unequivocal evidence that glucagon is a hormone with significant physiological activity and that it is also of importance in many common clinical syndromes.

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(The above represent key references quoted in this paper. The complete references may be obtained from the author, c/o The Metabolic Unit, Royal Victoria Hospital, Belfast BT12 6BA).

PSYCHIATRY AT A MISSION HOSPITAL IN SOUTH AFRICA

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THIS paper reviews the psychiatric presentations seen during a two month elective pupilship at a 220-bed mission hospital in a rural area of South Africa. The hospital served the medical and surgical needs of the local Bantu population of approximately 330,000, and had a staff of four full-time and five part-time doctors. An average of 300 patients were seen daily in the outpatient and casualty departments, about 50 of whom required admission. Psychiatric cases accounted for a significant proportion of the work load.

Problems in the Psychiatric Field

Because of the heavy work load and the shortage of doctors, clinical assessments had to be brief and investigations were limited by the lack of facilities. The language problems and the limited education of the patients made history taking difficult and there were frequently no relatives able to give an independent account of the

Table

Range of disorders encountered

		Number seen
Acute Organic Mental Illness	– Toxic Confusional States – alcoholic	17
	pyrexial	9
	hypoglycaemia	1
	– Puerperal Psychosis	3
	– Head Injury	2
Chronic Organic Mental Illness	– Korsakov's Psychosis	4
	– Dementias – senile	2
	pre-senile (Pick's Disease)	1
	pellagra	6
	– Paranoid Epileptic Psychosis	5
Schizophreniform Psychoses	– Schizophrenia	29
	– Paranoid Reactions	8
Affective Psychoses	– Manic/Hypomanic Illness	2
Other Psychoses	– Acute Reactive Psychotic Episodes	6
Psychoneuroses	– Anxiety States	75
	– 'Brain Fag Syndrome'	10
	– Behaviour Disorders	4
	– Depressive Reactions	6
Mental Subnormality	–	6

patient. But, despite these problems, a reasonable consensus diagnosis could usually be arrived at between staff members.

Psychiatric patients requiring admission were referred from the outpatient and casualty departments, and were admitted to the general medical wards under the care of a general physician as there was no separate psychiatric ward. Grossly disturbed patients were usually transferred to a psychiatric hospital about fifty miles away. The hospital was visited only once a fortnight by a psychiatrist; the day-to-day care of the patients was carried out by doctors who were not specialists in any field. Indeed, in the outpatient and casualty departments, much of the work was carried out without direct supervision by students.

The wide range of mental disorders encountered in the two months are shown in the table.

Presentation of Psychiatric Disorders in this Population

Anxiety states were common, making up about 40 per cent of all the cases seen, and typically presented with physical symptoms such as headache and abdominal pain. There were more males than females in this group, unlike European practice, and young people in educational settings such as trainee teachers and student nurses, were over-representative amongst the neurotic patients.

A number of the neurotic patients fitted the category of the 'brain-fag syndrome' described by Prince in 1960 in Nigeria. This condition affects young males in educational settings and is typically associated with disturbances of concentration and sensory functions, particularly visual. It is thought to be related to the imposition of European learning techniques upon the African personality.

Schizophrenia tended to present in a dramatic way with florid symptomatology; this may well be inherent in the Bantu make-up or may reflect selection in that the quieter patients whether affectively or schizophrenically ill may well stay in their village and only the grossly disturbed patients get to the hospital.

Paranoid reactions were fairly common in this sample and were typically associated with ideas instilled into the patients by witch-doctors. The witch-doctor habitually projected the explanation of evil, illness and misfortune on to spirits, relatives of the patient and so forth and hence these people developed persecutory ideas which occasionally led to their committing murder.

A number of cases of pellagra are included in this study since they initially presented with psychiatric symptoms. The condition, which is due to nicotinic acid deficiency, is fairly common in the Bantu people due to their poor diet and is classically associated with the three Ds, dermatitis, dementia and diarrhoea. The psychiatric manifestations included irritability and forgetfullness in the early stages and a late organic psychosis with memory impairment, confusion and disorientation. Treatment with nicotinic acid usually produced a dramatic improvement within 24 hours.

A significant number of psychiatric emergencies presented and were mostly acutely disturbed behavioural problems, frequently with an organic element, and the acute confusional states. Unfortunately physical restraint was used to some extent to control these patients but we found that this was unnecessary if chlorpromazine in adequate doses was given coupled with good nursing.

Summary

Psychiatric disorders proved to comprise a significant proportion of the work load of a busy rural hospital and their study and management proved both interesting and worthwhile.

There is no doubt that cultural differences played a part in the different presentations of the disorders seen, but nevertheless, the basic nature of the underlying conditions were similar to those seen in Northern Ireland. Many people have the idea that neurosis is a condition of the affluent Westerner, however it seems just as common in the African Bantu if you care to look for it.

I am indebted to the Mental Health Research Fund for a travelling scholarship in psychiatry which enabled me to do this overseas elective pupilship.

My thanks are also due to Dr. W. O. McCormick, Senior Lecturer in Mental Health at The Queen's University of Belfast, for all his help and encouragement in the writing of this article.

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PSORIATIC CLEARANCE DURING HAEMODIALYSIS

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PSORIASIS is an ancient and puzzling disorder of the skin with a very variable natural history. Nevertheless, complete clearance is extremely rare and therefore perhaps worthy of recording.

Case Report

The patient, a forty-three year old male, had psoriasis since the age of twelve years. His brother and a niece have psoriasis, and his brother also has psoriatic arthropathy. No previous family history of the condition is known. The usual local treatment over the years produced little relief.

He came under the care of one of us (J.McE.) at the Nephrology Clinic some years ago because of chronic renal failure on a basis of chronic pyelonephritis. This was managed conservatively with the usual fluid and dietary restrictions, but the condition progressed and eventually became terminal in August, 1973. At that stage he was admitted with a view to assessment for the chronic dialysis/transplant programme.

He was seen at that time for assessment of his psoriasis (by A.M.T.K.). At this stage he was noted to have extensive psoriasis involving trunk, limbs, palms of hands, nails, and scalp. It was feared that the constructions of an arterio-venous fistula to facilitate repeated dialysis might prove impractical because of the Koebner phenomenon. An effort was made to control the psoriasis by the local application of dilute steroid preparations resulting only in a complicating furunculosis which responded to appropriate treatment. Nevertheless, an arteriovenous fistula was constructed without complication and haemodialysis was commenced in September, 1973, twice weekly on Tuesdays and Fridays. Contrary to expectation psoriasis did not develop in the fistula scar, nor at puncture sites, but rather his psoriasis began to clear after the third dialysis. By the conclusion of the fourth treatment it was completely gone. Bi-weekly dialysis was continued for twelve months until September, 1974, during which time no drugs were given. In September, 1974 a successful renal transplant was carried out and followed up with the usual maintenance immunosuppressive therapy of prednisolone 20 mgs. daily and azothroprine 200 mgs. daily. In August, 1975 he remains clear from psoriatic lesions.

Discussion

Ingram (1964) regards psoriasis as an essentially epidermal disorder. He felt however, that the subject merited the attention of those working as physiologists and pathologists because a better understanding of the disease might well uncover some new pathological mechanism which could throw light on generalised disease of obscure aetiology. In his opinion the mechanism of a disorder so common, yet so unusual, could not concern the skin alone. Shuster (1971) reviewing the research on the subject over the previous decade finds that all the recent work takes us back again and again to the skin alone. He concludes that psoriasis remains a disease of the skin itself, but he makes the point that this conclusion in no way excludes a humoral component, though it does imply that any such component will only be significant in relation to the skin.

The normal sequence of events whereby a basal cell becomes keratinized takes twenty-five days. In psoriasis a similar process is accomplished in about four days (Van Scott et al 1964; Weinstein and Van Scott 1965). Shuster feels that psoriasis is a disease of faulty epidermopoiesis possibly due to impaired autocontrol mechanisms. A stimulator control has been suggested by some (Bullough 1967), an inhibitory control is suggested by others (Hell 1970), but the exact cause of psoriasis remains obscure.

Haemodialysis in this patient appears to have had a beneficial effect in the clearance of his chronic psoriasis. This may have been purely coincidental. If the disease is due to faulty epidermopoiesis caused by either a circulating humoral stimulatory or inhibitory substance, one could speculate that haemodialysis had removed this as yet unidentified psoriatic factor. One would have to postulate that this factor is not capable of clearance by normal kidneys but is cleared perhaps by adhesion to the dialysing membrane. In this case one would have expected the psoriasis to recur following transplantation unless immunosuppressive therapy is now the controlling factor. Had the donor been an identical twin immunosuppressive agents would not have been required to prevent rejection (and possibly suppress the psoriatic process), in which case the outcome would have been of even greater interest.

We feel that it is worth reporting this single case

(a) because it may suggest some line of approach to those interested in research into psoriasis, and

(b) because it seems to us that a few episodes of haemodialysis might be worth trying in the more disabling forms of the disease.

Summary

A male patient with chronic psoriasis since the age of twelve years commenced haemodialysis for chronic renal failure in August, 1973. His psoriasis began to clear after the third dialysis and remained clear throughout the entire year of twice weekly dialysis, and subsequently following successful renal transplantation.

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SERUM CREATINE PHOSPHOKINASE IN THE DETECTION OF CARRIERS OF DUCHENNE'S MUSCULAR DYSTROPHY IN NORTHERN IRELAND

by

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IT has been known for many years that since Duchenne muscular dystrophy is inherited as an X-linked recessive trait only boys will manifest the disease and girls in affected families will have a 50 per cent chance of being genetic carriers of the condition. Although Duchenne dystrophy is a relatively uncommon condition with possibly about 70 patients in Northern Ireland, the number of potential carriers is much greater, since sisters, maternal aunts, and female cousins of the patient all fall into this category. From incidence and prevalence figures (Nevin, 1975) it can be calculated that, as a conservative estimate, there are about 500 potential carriers in Northern Ireland, and the real figure may be much greater.

A considerable amount of effort has been put into the development of methods of detecting carriers. All of the methods used are based on the "Lyon hypothesis" (Lyon, 1961) that carriers suffer from a sub-clinical form of the disease. This hypothesis has been criticised recently, but nevertheless it has formed a useful basis for the investigation of the carrier state. Occasionally, clinical signs and symptoms of the disease have been found in carriers and these findings include pseudo-hypertrophy and weakness (Chung, Morton, Peters, 1960; Emery, 1963). If then, the carrier has a sub-clinical form of the disease, it follows that the methods which have been used for carrier detection have been mainly those which are used in diagnosing the fully expressed disease. Muscle morphology has been used at light and electron microscopic levels, and abnormalities have been reported (Pearson, Fowler and Wright, 1963; Gardner-Medwin, Pennington and Walton, 1971; Craig, Allen and McCormick, in preparation). Electromyography has also been used with some reported success (Gardner-Medwin, 1968). Several more exotic methods such as muscle cell culture and muscle protein turnover rate have been used but these methods have not been widely adopted largely due to the technical problems involved.

It was with the development of diagnostic serum enzymology from 1950 onwards that advances in carrier detection were made. The first positive results came in 1960 when Chung *et al* using aldolase and transaminase reported increased levels of these enzymes in the serum of 15 per cent of mothers of boys with Duchenne muscular dystrophy. Schapiro *et al*, also in 1960 reported increased levels of aldolase and creatine phosphokinase (CPK) in 30 per cent of known carriers. Following progressive technical improvements in the method of serum CPK analysis, detection rates steadily increased until detection rates of up to 75 per cent of known carriers were possible (Walton and Gardner-Medwin 1969).

In the present paper we would like to present our results for carrier detection in Northern Ireland during the last few years, dealing exclusively with the results from CPK analysis. Light microscopy, electron microscopy and electromyography are also used, but because of the ease of obtaining the material (clotted blood) it has been possible to investigate more carriers using CPK analysis than by the other techniques.

Materials and Methods

In our survey of serum CPK in carriers we have up to the present analysed specimens from 125 potential carriers who were divided into three categories according to the classification of Walton and Gardner-Medwin (1969): —

Definite Carriers: Mothers of an affected son who have also an affected brother, maternal uncle, sister's son or other male relative in the female line of inheritance.

Probable Carriers: Mothers of two or more affected sons, who have no other affected relatives.

Possible Carriers: Mothers of isolated cases and sisters and other female relatives of affected males.

Five millilitres of clotted blood samples were taken from the subjects and serum CPK was estimated, usually within two hours, using the Boehringer Test Combination 15790 (Boehringer, Mannheim, G.M.B.H.).

Results

In using CPK analysis to maximum advantage it is important that a well defined normal range is determined and that one is aware of the many possible factors which can interfere with serum CPK levels. Our normal range for females was established using blood samples from 163 blood donors. The mean value was found to be 16.3 mU/ml with a normal range of 1.7–37.5 mU/ml.

Table I

	No. of cases	*No. of cases with elevated CPK*	*Per cent of cases with elevated CPK*
DEFINITE CARRIERS	12	11	91.7
PROBABLE CARRIERS	8	6	75.0
POSSIBLE CARRIERS	105	31	29.5

The percentage of individuals with elevated CPK in each of the categories of carrier is presented in Table I. From this it can be seen that elevated CPK was found in all but one of the definite carriers. The one exception in this category was

found to have normal levels of CPK on three separate occasions. In the group of probable carriers 75 per cent of individuals had increased levels of CPK. Elevated levels were found in about 30 per cent of potential carriers, this being a very heterogeneous group consisting of aunts, cousins and sisters of dystrophy patients and mother's of isolated cases.

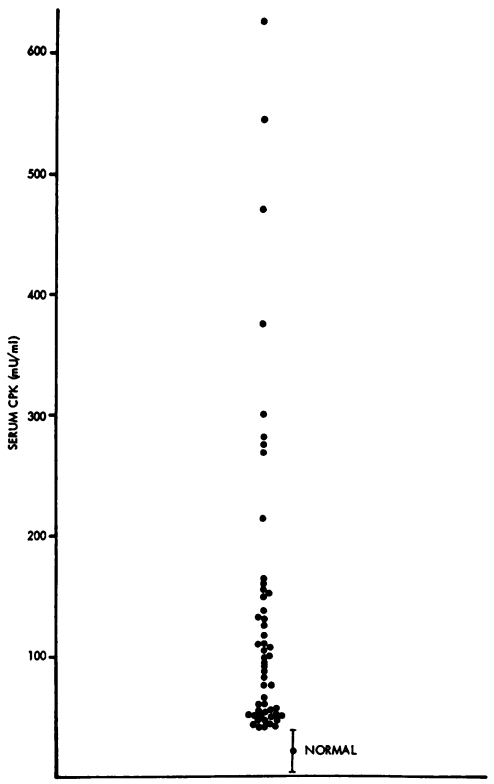

FIG. 1. *Values for serum CPK in potential carriers with elevated levels. The normal range is represented by the vertical bar.*

The scatter of CPK values in potential carriers with elevated levels is illustrated in the figure. There is a wide range with values up to 15 times normal with a marked cluster of results just above the upper limit of normal.

DISCUSSION

A consideration of the effectiveness of any method of carrier detection must clearly be limited to the definite carriers since they are the only ones with known genetic status. In the present investigation 11 of the 12 definite carriers had elevated CPK indicating that CPK analysis is a very efficient indicator of the carrier state. However, it is significant that one individual in this group had normal levels on three occasions, raising the possibility that some carriers may be inherently undetectable by the CPK method. This confirms the advisability of using more than one

method of carrier detection as it is suspected that normal CPK is not necessarily accompanied by normal results in other carrier detection tests. Although CPK estimation is in general the most sensitive test we have found two possible carriers with normal CPK levels but marked abnormalities in muscle histology (Craig, Allen and McCormick, 1975).

Since the "possible carrier" group is a heterogeneous one it is impossible to estimate the number of carriers which it contains. It is obviously the group in which carrier detection tests are very important since these subjects, at the time of testing, have one or no dystrophic children and are of unknown genetic status. Our results in the other categories suggest that most of the actual carriers within this group will be detected by CPK analysis, but we again stress the desirability of using as many criteria of carrier status as possible e.g. muscle histopathology, electron microscopy, electromyography.

Although some carriers have grossly elevated levels of CPK there are many in whom the increase is much less marked. For an accurate assessment of those results it is necessary to have a precisely defined upper limit of normal, and subjects who have values in the "borderline" range (just above or just below the limit) should be tested on a number of occasions. Although multiple testing is most important in this "borderline" group it should be done routinely in all subjects if possible since occasional high values are found in normal individuals as a result of factors such as unaccustomed muscular exercise and sub-clinical disease states (Griffiths, 1966; Graig and Smith, 1965). In particular, it should be noted that electromyography and surgical procedures cause increased levels of CPK (Maeyens and Pitner, 1968; Phornphutkul *et al*, (1974). For this reason it is essential that on hospital admission CPK estimation is performed before electromyography or muscle biopsy.

Summary

Serum CPK estimation is a simple investigative procedure requiring only small samples of blood and the present survey indicates that it produces a detection rate of about 90 per cent for carriers of Duchenne muscular dystrophy. The importance of a well defined normal range, multiple CPK analyses and an awareness of the possibility of false positive results is stressed. In addition it is desirable when possible to use other methods for carrier detection such as muscle histopathology and electromyography.

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ACTIVE CHRONIC HEPATITIS: Part I

by

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INTRODUCTION

IN 1950 Waldenström first drew attention to the occurrence of a form of chronic liver disease in young people, predominantly adolescent girls, in whom there was moderate jaundice, enlargement of the liver and spleen, acne, amenorrhoea and hyperglobulinaemia. The occurrence of fever, arthralgia and Cushingoid features was noted (Kunkel et al 1951, Bearn et al 1956), the LE cell phenomenon was reported (Joske and King 1955) and the condition was called lupoid hepatitis (Mackay et al 1956). Over the years it has been given many other names including liver disease in young women (Bearn et al 1956) with hypergammaglobulinaemia (Jones and Castleman 1962), active juvenile cirrhosis (Read et al 1963), plasma cell hepatitis (Page et al 1964), autoclastic lupoid hepatitis (Naish 1960) and autoimmune hepatitis (Mackay et al 1965), each emphasising particular pathological or clinical features. In recent years the term active chronic hepatitis has gained general acceptance because it embodies two of the essential pathological and clinical features of the disorder, namely its chronic and therefore usually progressive nature and the activity of the process typically manifested by the recurring episodes of hepatitis which punctuate its course. Lately Sherlock (1975), with a view to further refining the nomenclature of chronic hepatitis, has proposed that the classical type be called active chronic "lupoid" (HBAg negative) hepatitis.

Although the main pathological process occurs in the liver the striking immunological disturbance and the wide spectrum of symptoms indicate that it is a systemic disease. Discussion continues on the role of altered immune responses in the pathogenesis of active chronic hepatitis, and the absence of a marker for the virus of hepatitis A has been a great obstacle to progress. It seems probable that liver cell damage caused by a variety of agents including drugs (Reynolds et al 1971, Hoyumpa and Connell 1973, Russell et al 1973) may, in susceptible individuals, initiate self-perpetuating hepatitis. The growing belief that genetic factors may predetermine the susceptibility of the host has been strengthened by the discovery of a high prevalence of antibodies and of abnormal levels of immunoglobulins in relatives of patients with active chronic hepatitis, and also by a significant associated incidence of diseases which are normally regarded as having an immunological basis (Galbraith et al 1974). The high frequency of histocompatibility antigens HL-A 1 and HL-A 8 in patients with HBAg negative active chronic hepatitis is in sharp contrast with the normal frequency of HL-A 1 and the

total absence of HL-A 8 in patients with HBAg positive active chronic hepatitis (Galbraith et al 1974). The experimental production of a chronic aggressive hepatitis-like lesion in rabbits by prolonged immunisation with human liver-specific lipoprotein, and the confirmaton of the presence of hypersensitivity to human liver-specific lipoprotein in patients with active chronic hepatitis, have underlined the probable role of disturbances of cellular immunity in the pathogenesis of active chronic hepatitis. It seems likely that the non-organ-specific auto-antibodies (anti-nuclear antibody, smooth muscle antibody and mitochondrial antibody) merely reflect an abnormal immune system, perhaps genetically determined, and stimulated to auto-antibody production by viral or drug-induced hepatic damage (Smith et al 1975).

Definition

Active chronic hepatitis is an inflammatory disease of the liver which has a variable and usually unremitting course characterised by the clinical, laboratory and histological changes of both active and chronic hepatitis. While a presumptive diagnosis can often be made from the clinical and laboratory data, a definitive diagnosis requires histological examination of the liver, for only in this way may it be possible to differentiate active chronic hepatitis from prolonged virus hepatitis, chronic persistent hepatitis, primary biliary cirrhosis and certain other disorders.

Patients

The 40 patients who form the basis of this investigation were seen personally at the Royal Victoria Hospital during the 15-year period 1961–1975 and include all those in whom a firm diagnosis of HBAg negative active chronic hepatitis was made. Many of them continue to attend the Liver Clinic regularly and have been followed up for between four months and 13 years, the mean follow-up being five and a half years.

In general the diagnosis was based on the history and clinical findings, the biochemical, haematological and serological data and the information provided by histological examination of the liver. Those patients in whom liver biopsy was initially omitted, contraindicated or refused (4) or was technically unsuccessful (2) were accepted on the strength of the other evidence available.

A diagnosis of active chronic hepatitis is entertained when there is clinical or biochemical evidence of inflammatory liver disease for a period of at least six months. It must be distinguished from prolonged virus hepatitis and chronic persistent hepatitis both of which are likely to heal completely without treatment. Active chronic hepatitis associated with HBAg and that due to the administration of drugs such as oxyphenisatin, methyldopa, isonicotinic acid and, rarely, chlorpromazine. Wilson's Disease and alpha$_1$ antitrypsin deficiency also have to be kept in mind.

Pathology

Liver histology was available in 35 patients, in 27 following percutaneous needle liver biopsy and in a further 7 following wedge biopsy obtained at laparotomy. The only histological material available in one case was obtained at autopsy more than four years after the onset of the illness.

In 29 cases the appearances were those of active chronic hepatitis in various stages of activity and progression (De Groote et al 1968, Scheuer 1968). In 13 there was perilobular liver cell degeneration and necrosis with collapse of the reticulin framework particularly in the neighbourhood of the portal triads and resulting in disruption of the limiting plates. Piecemeal necrosis was noted and the severity of the parenchymal lesion varied considerably from lobule to lobule. A striking inflammatory cell infiltrate, consisting mainly of lymphocytes with plasma cells and some polymorphs and eosinophils, was usually concentrated in and around the enlarged portal tracts. In some cases lymphoid follicles were present and the inflammatory cells extended into the lobules to a varying degree. Fine fibrous septa were seen to radiate from the portal tracts and to divide up the liver lobules into clumps of cells from which early regenerative nodules might be expected to arise and in 11 cases irregular parenchymal regeneration, intralobular septa formation and portal tract fibrosis indicated the development of early cirrhosis.

In five cases the initial appearances of acute, mainly perilobular, hepatitis were seen to give way in subsequent biopsies to those of early active cirrhosis or late relatively inactive cirrhosis with little continuing liver cell necrosis or inflammatory cell infiltration.

There were two patients in whom the initial biopsy was performed either too early, and merely showed the changes of acute hepatitis, or too late when post-necrotic cirrhosis had already developed. In three patients diagnoses of chronic persistent hepatitis, primary biliary cirrhosis, and ? hepatitis ? cholangitis were suggested but these patients were also accepted on the basis of the other information available. Two patients in whom liver biopsy showed chronic aggressive hepatitis and early cirrhosis with persistent activity respectively, but with clinical features of advanced cirrhosis with portal hypertension, were excluded from the series. Others with clinical and biochemical features in keeping with active chronic hepatitis but with the histological changes of well developed cirrhosis were also omitted.

The possible effects of sampling error, progression from one type of liver disorder to another and changes brought about by moderate dosage immunosuppressive therapy were observed in two patients. In the first, the initial biopsy showed the changes of chronic persistent hepatitis whereas 33 months later, in the absence of treatment, a further biopsy showed active chronic hepatitis with early cirrhosis. In the second patient, the appearances in the initial biopsy were those of active chronic hepatitis but after 14 months corticotrophin therapy the second biopsy showed chronic persistent hepatitis.

The patchy distribution of the pathological changes in the liver, the small amount of tissue available for examination and the performance of the biopsy too early or too late in the course of the illness may greatly detract from the value of the information which such an examination would be expected to provide. Sherlock (1975) stresses that serial liver biopsies may be necessary to make a diagnosis of active chronic hepatitis. Cirrhosis is said to develop early in the course of the disease and to be already present in one-third of cases when the diagnosis is first made. Within two years of the onset some degree of cirrhosis is almost inevitable. Recurring episodes of necrosis with further stromal collapse and fibrosis lead to increasingly severe macronodular cirrhosis often with shrinkage of the liver.

Clinical Features

Age and Sex

The age at onset ranged from 9 to 74 years and in 28 patients (70 per cent) symptoms commenced between the ages of 30 and 59. This contrasts sharply with the experience of others (Mistilis and Blackburn 1970, Sherlock 1975) who reported that half of their patients were in the age groups 10–30 and 10–20 respectively. On the other hand Soloway et al (1972) found the onset to occur after the age of 40 in approximately 60 per cent of cases.

It is possible that the differences between these series in the age of onset of active chronic hepatitis are due in part to differences in the populations from which the cases are drawn. In view of the fact that in Belfast there are two busy teaching hospitals devoted to the care of sick children and a large infectious diseases hospital to which cases of virus hepatitis in children and adults are admitted, it would not be surprising if a series of patients seen only at the Royal Victoria Hospital contained a relatively small proportion of those in the first two decades of life. As anticipated there was a considerable female preponderance—28 out of 40 (70 per cent).

Previous History

In six patients there was a previous history of jaundice highly suggestive of hepatitis A. The illness occurred between the ages of 5 and 9 in three patients and at 20, 29 and 42 in the other three. The intervals between these episodes of jaundice and the onset of active chronic hepatitis were 53, 26, 37, 26, 26 and 17 years respectively.

Family History

A history of jaundice, probably due mainly to hepatitis A, was obtained in near-relatives of seven patients. Thyroid disease occurred in the immediate families of 10 patients and there were at least six cases of thyrotoxicosis. Diabetes was reported in five families and where this was insulin-dependant, the patient also had insulin-dependant diabetes which long preceded the onset of the liver disorder. Major allergy, anaemia and rheumatic fever were each noted in three families but there were no instances of ulcerative colitis, rheumatoid arthritis or systemic lupus erythematosus.

Onset of the Disease

In 26 patients (65 per cent) the illness began abruptly and was indistinguishable from acute virus hepatitis. In at least two cases, a boy aged 9 and a girl of 15, the illness occurred when other children in the same class at school had hepatitis A. Symptoms such as anorexia, nausea, vomiting, fatigue, malaise, fever, polyarthralgia, right upper abdominal discomfort and the passage of dark urine usually developed over a period of one to two weeks by which time jaundice was apparent.

In the majority of cases of acute onset symptoms died down after a few weeks. Jaundice faded, hepatic tenderness and enlargement diminished and the various laboratory tests showed improvement. In a small minority of such patients (4) all symptoms and clinical signs of the disorder disappeared completely without any treatment but there was persistent elevation of serum transaminase and gammaglobulin levels. After an interval of a few weeks or months (and in one instance 5 years) these patients suffered a hepatitic relapse with recurrence of symptoms closely resembling those at the onset of the illness. In a good many more patients (10) recovery began but was incomplete. Appetite and energy were not fully restored, jaundice faded but did not disappear and some liver enlargement remained. After a few weeks or months there was further deterioration of appetite and energy, nausea returned, jaundice deepened and hepatic tenderness reappeared. Some patients experienced several such remissions and relapses in the space of 6–9 months. In yet others (11) the expected recovery failed to occur and the symptoms of onset persisted in varying degree. Disinclination for food coupled with sickness and occasionally troublesome diarrhoea led to considerable weight loss and debility. In some the disorder followed a fluctuating course with variation in the severity of the symptoms and clinical findings from month to month. After recovery from the hepatitic illness one patient developed painful swelling of many of the limb joints. In another an erythematous rash considered to be typical of lupus erythematosus appeared across the bridge of the nose and there was painful swelling of a number of the finger joints. LE cells were present in both patients. Although jaundice was absent, the liver was enlarged and firm and serum transaminase and gammaglobulin levels were considerably elevated.

In 14 patients (35 per cent) the onset of the illness was insidious and symptoms developed over a period of 3 to 14 months. They included polyarthralgia and sometimes swelling of the affected joints, unaccustomed tiredness, an indifferent appetite, occasional mild nausea, considerable loss of weight, a degree of malaise, unexplained fever, an unhealthy colour and the eventual appearance of overt jaundice. One patient however, a girl of 13, has not been noted to be jaundiced at any time since the onset of the illness. In the four patients in whom polyarthralgia was the first symptom, the joints usually affected were the fingers, wrists, knees, ankles and feet and they were often tender and sometimes slightly swollen. A diagnosis of early rheumatoid arthritis was made in two of them and appropriate treatment was commenced. Three to 14 months after the onset of polyarthralgia, symptoms of hepatitis developed acutely in two patients and insidiously in the other two patients.

Established Disease

As the months passed and the disease progressed, the syndromes of onset made way for the gradually emerging clinical picture of active chronic hepatitis. Many of the early symptoms remained but others were added and examination disclosed a number of striking new physical signs.

Tables I and II show the principal clinical features in the 40 patients at the time of diagnosis. Those symptoms occurring most frequently during the course of the illness were fatigue, rapidly dissipated energy, an indifferent appetite, intermittent

TABLE I

Symptoms in 40 patients with untreated active chronic hepatitis

	Number	*Percentage*
Fatigue	31	78
Anorexia	30	75
Nausea with or without vomiting	26	65
Weight loss	22	55
Fever	18	45
Itching	14	35
Abdominal discomfort	11	28
Polyarthralgia	10	25
Amenorrhoea	7	64*
Epistaxis	5	13
Diarrhoea	5	13

* There were 11 premenopausal female patients

nausea and in over half the patients weight loss ranging from 4 to 40 lb (1.8–18 k) with an average of 15 lb (6.8 k). Almost half the patients were feverish and in 10 out of 18 this exceeded 100°F (37.8 C).

In 9 of the 11 patients with abdominal discomfort the illness had commenced as acute hepatitis and the incidence of hepatic enlargement and tenderness was above average. Enlargement of the liver was usually present from the onset and when the disease became established, firm smooth hepatomegaly was the rule with tenderness in about one-third of cases. In 12 (30 per cent) there was considerable hepatic enlargement, the lower edge of the right lobe being felt 3–4 finger-breadths (fb) (6–8 cm) below the right costal margin in full inspiration.

Enlargement of the spleen was felt in 16 patients (40 per cent) at the time of diagnosis and in 6 the lower pole could be felt 2–4 fb (4–8 cm) below the left costal margin in full inspiration. In only four of the patients with splenomegaly was there any suspicion of cirrhosis and none of them had very large spleens. In 11 LE cells were detected and in six they were found regularly and at times in considerable numbers.

TABLE II

Clinical findings in 40 patients with untreated active chronic hepatitis

	Number	*Percentage*
Jaundice	37	93
Hepatomegaly	33	83
Hepatic tenderness	14	35
Splenomegaly	16	40
Oedema, ascites and encephalopathy	1	2.5
Vascular spiders	19	48
Dilated facial venules	12	30
Palmar erythema	9	23
Acne	3	7.5
Polyarthritis	5	13
SLE rash	3	7.5
Pleurisy and pericarditis with effusion	1	2.5
Bilateral pneumonitis and pleurisy with effusion	1	2.5
Thyroid enlargement	4	10

Jaundice was present in all but three patients at the time of diagnosis. It was mild in 19 and deep in 11. Itching occurred in one-third of the patients and correlated surprisingly poorly with the intensity of jaundice, being present in only 6 of the 11 most deeply icteric patients. There was no better correlation between itching and high serum alkaline phosphatase levels, only 6 of the 13 patients with serum alkaline phosphatase levels above 30 King Armstrong units complaining of itching.

Vascular spiders were present in almost half the patients but only five patients (13 per cent) had more than five spiders. However the presence of vascular spiders and dilated facial venules proved useful in raising the index of suspicion of active chronic hepatitis in patients with nondescript symptoms and few other physical signs.

Only one patient developed oedema, ascites and mild hepatic encephalopathy early in the course of the illness before treatment was commenced. He made a slow but eventually excellent recovery and remains well 11 years later, never having had any recurrence of liver cell failure or hepatic encephalopathy. Transient encephalopathy occurred in one other very deeply jaundiced patient as treatment with prednisolone was being introduced. There was no accompanying oedema or ascites and she also made a rapid recovery. Years later she developed macronodular cirrhosis with portal hypertension and variceal bleeding but when last seen 11 years after the onset of the illness had no fluid retention and was mentally clear.

Systemic Manifestations and Associated Conditions

"Active chronic hepatitis of lupoid type is not a condition confined to the liver" (Sherlock 1975). It is a systemic disease in which almost half the sufferers have associated conditions which are apparently unrelated to the liver. Among these are polyarthralgia, polyarthritis, a variety of skin lesions including those of lupus erythematosus, pericarditis, myocarditis, pleurisy, transient pulmonary infiltrations, fibrosing alveolitis, glomerulonephritis, renal tubular acidosis, the sicca syndrome, ulcerative colitis and a number of endocrine disorders such as amenorrhoea, Cushing's syndrome, diabetes and various thyroid abnormalities including Hashimoto's thyroiditis. These extra-hepatic syndromes may precede, coincide with or more frequently follow the onset of clinical liver disease but in general the clinical picture is dominated by the features of the hepatic lesion.

Amenorrhoea was often present from the beginning of the illness and became established in 7 of the 11 premenopausal patients but other endocrine disorders such as obesity, facial mooning, striae livida and hirsutism, traditionally associated with active chronic hepatitis, did not occur and acne was observed in only three patients prior to the commencement of corticosteroid or corticotrophin therapy. This may be partly due to the small number in this series of girls and young women in whom such symptoms are said to occur most commonly.

Three patients, each with a direct family history, had insulin-dependant diabetes which long preceded the onset of active chronic hepatitis. Of the five patients with a thyroid disorder two had non-toxic goitre, one had thyrotoxicosis, another had thyrotoxicosis treated with radioactive iodine years prior to the onset of active chronic hepatitis and the fifth patient was found at autopsy to have lymphocytic thyroiditis.

Polyarthralgia with or without swelling and tenderness of the affected joints was an important symptom in ten patients (25 per cent) and tended to occur at the onset or early in the course of the established disease. The joints most frequently affected were the metacarpo-pharyngeal and proximal interphalangeal joints of the fingers, the wrists, elbows, ankles and knees. There was no evidence of erosive arthritis nor were there any of the extraarticular manifestations of rheumatoid disease. The Rose Waaler D.A.T. was positive in two patients and then only intermittently and in low titre. In nine of the ten patients however the LE cell phenomenon was positive and repeatedly so in six patients.

Skin rashes accepted as lupus erythematosus by dermatologists occurred in three patients. In two patients typical butterfly rashes were seen on the face and there were two instances of widely distributed lesions on the limbs.

Pericarditis and bilateral pleurisy with effusion occurred two or three months after the onset of acute hepatitis in one patient in whom LE cells were repeatedly demonstrated. A complete clinical recovery occurred over a period of six months without treatment but the electrocardiogram did not return to normal for almost one year and the serum transaminase and gammaglobulin levels remained elevated. In another patient pneumonitis and bilateral pleurisy with effusion occurred four

months after the onset of the illness which was characterised by polyarthritis. LE cells were also demonstrated repeatedly in this patient whose condition did not begin to improve until prednisolone was given in high dosage. During life this patient did not exhibit any signs of renal or thyroid disease but was found at autopsy to have electron microscopic appearances diagnostic of the renal lesion of lupus erythematosus and the histological changes of lymphocytic thyroiditis suggestive of Hashimoto's disease.

Diarrhoea was a prominent symptom from the onset of the illness in five patients, only disappearing in three patients when corticosteroid or corticotrophin therapy was commenced and continuing in the other two. The changes of ulcerative colitis have not been demonstrated in any of these patients though this condition has been reported to occur in up to 11 per cent of cases of active chronic hepatitis (Mistilis 1969). Instances of the sicca syndrome, renal tubular acidosis and interstitial pulmonary fibrosis were not observed in this series.

Course of the Disease

From time to time the tempo of the illness quickened with the occurrence of episodes of active hepatitis or polyarthritis. While these were most frequent early in the course of the disease, patients remained liable to such reactivation many years after the onset. Of the 40 patients in this series, 30 suffered a total of more than 56 relapses while not receiving treatment, and 47 of these episodes seemed to be purely hepatic in type. Six relapses, all occurring in the same patient, were characterised by painful and swollen joints, a butterfly rash on the face and splenomegaly, but with no clinical or biochemical evidence of reactivation of the liver lesion save in one episode. In another patient the relapse consisted solely of polyarthritis and there was no evidence of accompanying liver involvement. In the remaining two relapses, patients had painful swollen joints and also symptoms and signs of active hepatitis.

In some of the relapses, symptoms came on quickly while in others they developed insidiously over a period of several weeks. They often closely resembled those which originally ushered in the illness. They varied in severity from little more than tiredness, malaise and an indifferent appetite with moderate elevation of serum transaminase and gammaglobulin levels to grave illness with deep jaundice, peripheral oedema, ascites and hepatic encephalopathy. Three of the relapses were symptomless and were discovered only as a result of routine biochemical screening. Some occurred spontaneously while others were precipitated by intercurrent infection especially influenza and other virus infections. Similar relapses have been seen in patients receiving corticosteroid or corticotrophin therapy and have often followed injudicious reduction of dosage or premature withdrawal of treatment.

Minor relapses sometimes resolved spontaneously but the initiation of effective treatment usually brought about a quick remission so that even those with evidence of serious liver-cell failure made a remarkable recovery over a period of a few weeks or months.

Often between such episodes appetite and energy returned, jaundice vanished and hepatic tenderness and enlargement disappeared. In some, evidence of a persisting hepatic disorder was to be found only by repeating the relevant biochemical tests though it is well recognised that the histological abnormalities remain. The disease is said ultimately to become inactive in about 40 per cent of cases by which time established cirrhosis is present. At the other extreme however the course of the disease is progressively downhill and as cirrhosis advances the liver shrinks, portal hypertension develops and the spleen enlarges. Episodes of variceal bleeding occur and there is increasingly severe liver cell failure and hepatic encephalopathy.

Active chronic hepatitis is a disease in which there is considerable morbidity. During the early stages, this is due to the fluctuating course with episodes of active hepatitis and to persisting debility, but during the later stages it results mainly from the complications of cirrhosis. The mortality rate is also high particularly in the early stages when activity of the process is greatest and the prognosis is said to be somewhat better in patients who survive the first two or three years. Death is usually due to liver cell failure, sometimes precipitated by gastro-intestinal haemorrhage but septicaemia, associated ulcerative colitis or the complications of prolonged corticosteroid or corticotrophin therapy may also contribute.

Haematological, Boichemical and Serological Features

The serum haematological and biochemical findings are shown in Table III. For each investigation the immediate pre-treatment result or the mean of several results for each patient was used to calculate the median and range for the whole group.

Table III

Haematological and biochemical findings in patients with untreated active chronic hepatitis

	Number	*Median*	*Range*
ESR (mm/1 hour Westergren)	38	39	4 – 125
RCC (10^6 per microlitre)	22	4.2	2.7 – 5.0
WCC (per microlitre)	36	5,300	2,800 – 11,300
Serum bilirubin (mg/decilitre)	40	4.4	0.6 – 28
Serum alkaline phosphatase (King Armstrong units)	40	27	10 – 150
SGOT (Karmen units)	39	350	90 – 3,000
SGPT (Karmen units)	39	320	60 – 1,720
Serum pseudocholinesterase (Michel units)	34	36	5 – 119
Prothrombin concentration (%)	24	45	17.5 – 93
Serum albumin (g/decilitre)	36	3.5	2.3 – 4.6
Serum γ-globulin (g/decilitre)	36	2.7	1.1 – 6.0
Serum IgG (mg/decilitre)	20	2,000	1,000 – >3,000
Serum IgM (mg/decilitre)	20	270	86 – >400

The ESR varied widely, values of more than 100 mm being recorded in 6 patients and less than 20 in 9 patients. A platelet count of less than 150,000/ml was obtained in almost one-third of patients, the total white cell count was less than 4,000/ml in almost one-quarter of patients and mild anaemia was not uncommon.

Serum bilirubin was less than 1 mg in 3 patients, 1–5 mg in 19 patients, 5–10 mg in 7 patients and more than 10 mg in 11 patients with figures exceeding 20 mg in 4 patients. Serum alkaline phosphatase was usually increased above 15 King Armstrong units and levels of over 30 King Armstrong units were recorded in 13 patients. Serum transaminases were increased to at least twice the upper limit of normal in every case and often reached levels occurring in acute virus hepatitis, being more than 1,000 Karmen units in 12 patients (30 per cent).

Impairment of liver cell synthesizing function was reflected in depressed serum pseudo-cholinesterase, prothrombin and albumin concentrations. Pseudo-cholinesterase was reduced below 53 Michel units in 28 patients (82 per cent) and below 20 Michel units in three patients. Hypoprothrombinaemia was frequent and the prothrombin concentration was less than 30 per cent (Quick one-stage method) in five patients (20 per cent). Serum albumin levels of less than 3 g/dl were recorded in eight patients (22 per cent), but marked hypoalbuminaemia was unusual until the later stages of the disease.

Serum gammaglobulin levels were higher than 1.5 g/dl in 30 patients (83 per cent) and over 3 g/dl in 15 (42 per cent). The serum Ig G and Ig M levels were increased above the upper limit of normal in 60 per cent and 80 per cent of patients respectively.

Serum $alpha_1$ antitrypsin phenotyping was performed in 20 patients and proved to be Pi M (Pi MM or Pi M–) in all (Glasgow et al 1976). In Northern Ireland this is the commonest $alpha_1$ antitrypsin phenotype, accounting for more than 80 per cent of individuals in the normal adult population.

In active chronic hepatitis a wide range of antibodies reacting with various tissues may be present in the serum (Doniach et al 1966, Smith et al 1975). Persistently high titres of smooth muscle antibody may be found in two out of three cases and this is an important aid in diagnosis though the antibody is also found in up to half of patients with primary biliary cirrhosis and transiently and in low titre in acute virus hepatitis. Mitochondrial antibody, which has a special relationship to primary biliary cirrhosis where it is found in 90 to 95 per cent of cases, may also be detected in about one-quarter of patients with active chronic hepatitis. Antinuclear factor in a titre of more than 1/20 has been reported in 50 to 60 per cent of cases of active chronic hepatitis, while the incidence of the LE cell phenomenon varies between 15 per cent (Sherlock 1975) and 34 per cent (Soloway et al 1972) and is said to depend upon the diligence of the search and the phase of the disease. The results of the various serological tests are shown in Table IV. The presence of LE cells in 50 per cent of patients, often repeatedly and in large numbers, is noteworthy.

TABLE IV

LE cells and serological reactions in patients with active chronic hepatitis

	Number tested	*Number positive*
LE cells	40	20 (50%)
Antinuclear factor	39	21 (54%)
Smooth muscle antibody	38	27 (71%)
Mitochondrial antibody	37	18 (49%)
Rheumatoid factor – Latex	17	7 (41%)
– DAT	17	2 (12%)
HB_sAg	38	0

DIFFERENTIAL DIAGNOSIS

Active chronic hepatitis may be distinguished from a prolonged attack of virus hepatitis and from chronic persistent hepatitis by the presence of various clinical stigmata of chronic liver disease, low serum levels of prothrombin and pseudocholinesterase, hypergammaglobulinaemia, the presence of smooth muscle antibody and the distinctive histological changes in the liver biopsy. Occasionally patients with Gilbert's syndrome are suspected of having active chronic hepatitis because of intermittent or persistent jaundice, fatigue, an indifferent appetite and vague upper abdominal discomfort. However the absence of abnormal physical signs other than mild jaundice, and the completely normal liver tests apart from hyperbilirubinaemia of unconjugated type, obviate the need for liver biopsy.

There are a small number of patients with active chronic hepatitis whose symptoms and signs closely resemble those of primary biliary cirrhosis. They tend to be middle-aged women who complain of troublesome itching and often have persistent mild jaundice. There is disproportionate elevation of serum alkaline phosphatase levels and mitochondrial antibodies are usually present in high titre. This "overlap group" follows a cholestatic course and the response to corticosteroid or corticotrophin therapy is unpredictable and often unsatisfactory. The longterm outlook is appreciably worse in these patients.

Active chronic hepatitis may have to be distinguished from benign recurrent cholestasis, pericholangitis associated with ulcerative colitis, the various hepatic granulomas especially sarcoidosis, alcoholic liver disease, fully developed macronodular cirrhosis, sclerosing cholangitis and primary hepatoma.

DISCUSSION

The fundamental cause of active chronic hepatitis is still unknown. It may be due to chronic infection with one of the hepatitis viruses and/or to a disorder of immunity. There is a good deal of indirect evidence in support of both of these

possibilities. It is probable that the disease is not due to a single cause but is a continuing hepatic and systemic response to liver cell injury initially of varied aetiology in genetically predisposed individuals. In the majority of cases, however, it is likely that the initial liver damage is caused by virus infection and in the early stages of the disease the clinical picture may be indistinguishable from acute hepatitis. This was so in 65 per cent of cases in the present series and in some the illness commenced during local epidemics of hepatitis A infection.

This high incidence of illness of acute onset appears to be connected with the unusually frequent occurrence of a positive LE cell test (50 per cent). Rather more than half of these patients had splenomegaly while the median gammaglobulin level (2.9 gms.) was higher than in those with a negative LE cell test. This was also the experience of Soloway et al (1972) who concluded that a positive LE cell test was associated with disease of greater acuteness and severity and with a poorer prognosis in the absence of effective treatment. However they were unable to identify any clinical, biochemical, immunochemical or pathological features that characterised lupoid hepatitis as a separate entity from LE-negative patients. Nevertheless the discovery by Davis and Read (1975) in 42 per cent of their patients with active chronic hepatitis of levels of antibody to double-stranded (native) DNA, usually only found in systemic lupus erythematosus, again raises the question of the relationship between these two conditions. They suggest that these antibodies, previously shown to have a high degree of specificity for systemic lupus erythematosus, may play a specific role in the immunopathogenesis of active chronic hepatitis.

The occurrence in patients with LE-cell-positive active chronic hepatitis of relapses with features indistinguishable from those seen in systemic lupus erythematosus is of considerable interest. Thus during the long hot summer of 1975 a 54-year-old woman taking 7.5 mg of prednisolone daily developed an acute erythematous and oedematous rash across the bridge of the nose, on the cheeks, round the eyes and on the backs of the hands and flitting polyarthralgia with slight swelling and tenderness of some of the limb joints. There was no clinical or biochemical evidence of reactivation of the hepatic lesion and the condition subsided uneventfully with appropriate treatment.

In the knowledge that some cases of non-alcoholic cirrhosis of later life have their beginnings in clinically silent active chronic hepatitis and that with immunosuppressive treatment it is often possible to retard the activity and progress of this disorder, the physician is increasingly conscious of the need to make a firm diagnosis as early as possible. In addition to careful clinical, biochemical and haematological investigation this involves needle liver biopsy. With the widespread use of biochemical screening procedures examples are coming to light of apparently healthy persons with abnormal liver tests of the type seen in active chronic hepatitis (Plotz 1975). Whether or not early treatment of the asymptomatic person with chronic aggressive hepatitis favourably influences possible longterm progression to symptomatic cirrhosis and death has yet to be determined. In the great majority of symptomatic cases of active chronic hepatitis spontaneous remissions tend to be of limited degree and duration. Even in those patients with few

or no remaining symptoms or signs and only minimal changes in liver function tests the histological appearances may still indicate considerably activity of the underlying process. It is therefore probable that other similar cases may pass unrecognised until advanced cirrhosis has developed. By that time the histological appearances of activity may have lessened and if the patient presents with variceal bleeding, ascites or encephalopathy the diagnosis likely to be made is one of cryptogenic cirrhosis.

In this series as in most others, the great majority of patients with active chronic hepatitis were mildly jaundiced at the time of diagnosis. Those who are not may present with unexplained debility, mysterious weight loss, pyrexia of unknown origin, painless hepatosplenomegaly, amenorrhoea, anaemia or polyarthralgia. The diagnosis should always be considered in cases of prolonged hepato-cellular jaundice, especially in women, when a careful history for possible medications is negative and there is a personal or family history of diseases having an immunological basis.

Summary

Data from 40 consecutive patients seen at the Royal Victoria Hospital fulfilling the diagnostic criteria of active chronic hepatitis have been analysed in order to gain insight into the many variations that occur in the clinical syndrome. In general the clinical and laboratory findings correspond to those recorded in other series though there were significant differences. The peak age of onset may have been influenced as much by the availability of large specialised hospitals for the care of sick children and for the treatment of infectious diseases as by any real variation in the age incidence. The onset was acute in two-thirds of the patients and insidious in the remaining one-third which is the reverse of experience elsewhere. The LE cell phenomenon was positive in 50 per cent of patients and it is notable that in three-quarters of these the onset of the illness was abrupt and indistinguishable from acute virus hepatitis. There was a close correlation between the incidence of anti-nuclear factor and a positive LE cell phenomenon while smooth muscle antibodies and mitochondrial antibodies were present in 71 per cent and 49 per cent respectively. Considered in conjunction with the personal and family history of thyroid disease, insulin-dependant diabetes, major allergy and rheumatic fever, and in the light of evidence now becoming available through HL-A histocompatibility studies, there are grounds for believing that genetic influences predetermine susceptibility to active chronic hepatitis. The relationship between this condition and systemic lupus erythematosus requires further investigation.

Acknowledgments

We are greatly indebted to Mr. G. W. Johnston, FRCS, for his never failing clinical co-operation and skill in performing many of the liver biopsies and to Dr. J. D. Biggart for invaluable assistance with histological interpretation. We wish to thank our many colleagues in the Royal Victoria Hospital and in hospitals throughout Northern Ireland for their kindness in referring patients under their care. Our thanks are also due to Mrs. Ann Sullivan and Miss May Weller for secretarial assistance. This paper is dedicated to the sisters and nurses of Wards 7 and 8 who have so kindly and expertly cared for these patients over the years.

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BOOK REVIEWS

THE ACUTE CORONARY ATTACK. By J. F. Pantridge, M.C., M.D., F.R.C.P., F.A.C.C.; A. A. Adgey, M.D., M.R.C.P.; J. S. Geddes, B.Sc., M.D., F.R.C.P.; S. W. Webb, B.Sc., M.D., M.R.C.P. (Pp. 141. Illustrated. £6.00). London: Pitman Medical Publishing Co. Ltd. 1975.

WHEN Professor Pantridge in 1966 emulated the idea of Napoleon's surgeon, Larrey, and took intensive care to the patient, he not only initiated a service which altered the high rate of mortality of patients suffering from the acute coronary attack, but also uncovered a whole new region of cardiac patho-physiology.

It was known that two-thirds of premature deaths occurred within one hour of the onset of symptoms, so that the majority of patiens died ouside hospital. For those lucky enough to reach hospital alive intensive care units were already developed or being developed. In Belfast in 1965 hospital admission was in a large proportion of patients delayed for more than twelve hours and the median delay was more than eight hours. In other cities it was at least equally bad and often worse.

By 1969, three years after the introduction of the mobile cardiac resuscitation service, 27.5 per cent of affected patients came under intensive care within one hour, and the median delay for admission had been reduced to one hour forty minutes.

The introduction of the patient to early medical care engendered new problems—a higher incidence of vagal bradycardia and of ventricular fibrillation than in those patients who had formerly been admitted to the coronary care units. Fortunately, methods of cardiac resuscitation were being developed. In 1960 Koventhoven had shown the possibility of external cardiac massage, whilst the value of direct current or capacitor discharge had been demonstrated in the correction of ventricular fibrillation. Vagal bradycardia could be abolished by atropine and other dysrhythmias and autonomic disturbances rectified. Nor in this wealth of physical and pharmacological therapeusis was the patient forgotten. Anxiety and pain could be greatly modified by heroin and other drugs.

In a series of seven chapters this monograph clearly sets out the problems of the patient with an acute coronary attack. Early diagnosis and therapy are shown not only to reduce mortality, but in many cases to limit the size of the area of infarction and to decrease the incidence of cardiac shock and of pump failure. Numerous methods are shown to be available for improving the chances for survival of ischaemic myocardium and hence increase the possibility of the re-establishment of sufficient cardiac function to allow the patient's return to a normal way of life. Indeed, these observations constitute the most pungent reasons for the development of early rational treatment.

Obviously early cardiac treatment is not always available. Potential patients must be alerted as to the danger: early treatment must be made available: general pracitioners must be trained and must have in their possession for immediate use defibrillators and the small quantum of the necessary drugs. Differing areas demand different solutions, but the necessary equipment is not excessive. To this end Professor Pantridge and his team have given their minds to the development of a smaller, less expensive, more transportable, but equally effective defibrillator, reducing weight from 55 lbs to 7 lbs, and there is hope that it can be still further miniaturised. Indeed, it may become possible for every general practitioner—and indeed paramedical personnel—each to have his own.

Considering that cardiovascular disease is the most frequent cause of death, that our knowledge of methods of prevention of coronary attacks is still so tenuous, these summated efforts of the Belfast group have an immense role to play. There is a role for everyone—the public themselves who will eventually be the patients—the general practitioner who must be furbished with the necessary impedimenta—paramedical personnel who must be trained—administrators

who must be taught to facilitate, and cardiologists who must continue to ask the right questions of the problems involved and strive to seek the answers to them.

Professor Pantridge and his team are to be congratulated on their initiative, on their vision in seeing what the essential problems are and on their pertinacity in pressuring their aims. Their thesis is well argued.

J.H.B.

A MANUAL OF ADVERSE DRUG INTERACTIONS. By J. P. Griffin and P. F. D'Arcy. (Pp. XII + 347, figures 13. £7.00). Bristol: Wright. 1973.

THIS excellent little book meets the need for all prescribing doctors for up-to-date guidance on how to prevent adverse reactions when they prescribe more than one drug to a patient. It contains a 48-page text which explains the mechanisms of drug interactions with extreme clarity using examples which are within the experience of most prescribing doctors. This text is divided into chapters on reactions which occur before the patient receives the drug (in the drip bottle, etc.) in the gut and intestinal wall, in the blood at the receptor site and so on. It is well illustrated and has a good selection of references for those who wish to follow up any particular aspect of the problem.

The bulk of the book consists of an alphabetical list of drug groupings "Anticoagulants", "Antihypertensives", "General Anaesthetic Agents", etc., with an index which includes both the official and the proprietary names of all the drugs. Unlike most of the tables that are available for this purpose, this one is arranged so that you can discover both what interactions may develop if you add a new drug to a long-term medication, but also those likely on the simultaneous initiation of treatment with two or more drugs. The other advance is that there is excellent advice on how to avoid serious adverse reactions by care with dosage and monitoring of blood levels, etc. In previous tables of this sort it was implied that combinations of drugs reported to have caused adverse reactions should be avoided altogether. This table tells you how to use the combination, get the benefit of both drugs and at the same time avoid an adverse reaction.

This is a field of rapid advances in knowledge. One must congratulate the authors in getting their book into print so quickly that it is reasonably up-to-date. One does not envy them the task of keeping up-to-date because this requires a new edition every 2-3 years.

I wish every prescribing doctor would read the first 48 pages of this book and would refer to the table whenever he embarks on multiple prescribing.

P.C.E.

HEMATOLOGY PHYSIOLOGIC, PATHOPHYSIOLOGIC, AND CLINICAL PRINCIPLES. By J. W. Linman. (Pp. XIII + 1055; illustrated. £21). New York: MacMillan Publishing Co. Inc. 1975.

THIS is a further addition to the large and expanding range of general textbooks in haematology. Although a new addition, it is based on "The Principles of Haematology" by the same author, which was first published in 1966 and from which part of the material is obtained.

The claim on the dust cover is that "This clinically oriented reference volume presents up-to-date information on the diagnosis and treatment of all types of haematologic disorders, both primary and secondary. Its goal is to provide descriptions of disease based on modern physiologic and pathophysiologic concepts".

The presentation follows the traditional pattern and the chapters indicate the extent of the subject coverage. The only quarrel which British readers might have is with some of the trans-Atlantic nomenclature. We had hoped that the 'rubriblast' and its progeny had been decently buried, and that the synonym of 'agnogenic myeloid metaplasia' had at long last been supplanted.

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The book is heavy and the cost considerable (£21). However, it is very well bound, well printed in the modern style of double columns and on good art paper. It has attractive chapter headings, artistically arranged tables and is exceedingly well paginated. The text is eminently readable, the style is clear, and the information authoritative and up-to-date. The book is liberally illustrated throughout with well chosen tables and figures. Most of the illustrations are in black and white, which is just as well. While colour plate No. 1 is acceptable if somewhat pastel in shade as is usual with Wright stained smears, the only other colour plate, No. 11 would have been better not included. The E.M. photographs are of very high quality and the black and white photographs of peripheral blood and bone marrow smears are all good, but this does not apply to many of the histology illustrations, some of which fall short of the general standard (e.g. 16/27).

The book achieves its declared aim, and, based on pathophysiologic principles provides a useful understanding of the fundamental basis of haematological disorders, helps in promoting diagnosis and rationalising therapy. This textbook should find a place as a working manual in many a hospital ward and departmental library where it will become much used by both clinicians and trainee haematologists. The specialist haematologist will also find it very useful reading, for although each disorder has a short histological introduction, there is no lengthy discussion of the gradual development of knowledge of each condition, and without being comprehensive, most of the references included are up-to-date.

It is unusual in this day and age for such a comprehensive textbook to be produced by a single author, i.e. apart from the chapter on monoclonal gammopathies which was contributed by Dr. Kyle and Dr. Bayrd. However, the advantages gained are those of continuity in style and absence of overlap. This textbook represents an enormous amount of work, time, energy and devotion on the part of the author, and deserves success in a highly competitive field.

M.G.N.

GYNAECOLOGICAL MALIGNANCY: CLINICAL AND EXPERIMENTAL STUDIES. Edited by M. G. Brush and R. W. Taylor. (Pp. XIV + 274; Figures 74. £7.00). London: Bailliere Tindell. 1975.

THIS does not claim to be a comprehensive treatise or even a complete review of gynaecological malignancies. It is a series of papers arising out of a conference examining different aspects of carcinoma of the cervix, ovary and endometrium. Emphasis is on epidemiology and aetiology and on therapy. There is discussion of herpes virus infection in cervical cancer and of cystic hyperplasia and endocrine influences in endometrial cancer. A valuable chapter by P. Rhodes gives a forthright exposition of his personal views on carcinoma of the cervix, and one by V. Lewis discusses discusses diagnosis and management of metastatic cancer in pelvic lymph glands. A chapter on epidemiology of ovarian cancer to many will show little but the lamentable lack of agreement on terminology. An interesting progress report by A. W. Harcus and K. D. MacRae on the Ovarian Cancer Clinical Survey with therapy by combination of Depostat and cytotoxic agents is presented.

There is no apparent cross-fertilisation between the papers and no discussion is recorded. While some of the papers are of considerable interest, others such as those on organ cultures of the cervix and endometrium and identification of particles in ovarian tissue are less relevant.

There is much of interest in this volume, but it presents only a few facets of the problem and lacks balance and is uneven in quality.

J.E.M.

The book is heavy and the cost considerable (£21). However, it is very well bound, well printed in the modern style of double columns and on good art paper. It has attractive chapter headings, artistically arranged tables and is exceedingly well paginated. The text is eminently readable, the style is clear, and the information authoritative and up-to-date. The book is liberally illustrated throughout with well chosen tables and figures. Most of the illustrations are in black and white, which is just as well. While colour plate No. 1 is acceptable if somewhat pastel in shade as is usual with Wright stained smears, the only other colour plate, No. 11 would have been better not included. The E.M. photographs are of very high quality and the black and white photographs of peripheral blood and bone marrow smears are all good, but this does not apply to many of the histology illustrations, some of which fall short of the general standard (e.g. 16/27).

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It is unusual in this day and age for such a comprehensive textbook to be produced by a single author, i.e. apart from the chapter on monoclonal gammopathies which was contributed by Dr. Kyle and Dr. Bayrd. However, the advantages gained are those of continuity in style and absence of overlap. This textbook represents an enormous amount of work, time, energy and devotion on the part of the author, and deserves success in a highly competitive field.

M.G.N.

GYNAECOLOGICAL MALIGNANCY: CLINICAL AND EXPERIMENTAL STUDIES. Edited by M. G. Brush and R. W. Taylor. (Pp. XIV + 274; Figures 74. £7.00). London: Bailliere Tindell. 1975.

THIS does not claim to be a comprehensive treatise or even a complete review of gynaecological malignancies. It is a series of papers arising out of a conference examining different aspects of carcinoma of the cervix, ovary and endometrium. Emphasis is on epidemiology and aetiology and on therapy. There is discussion of herpes virus infection in cervical cancer and of cystic hyperplasia and endocrine influences in endometrial cancer. A valuable chapter by P. Rhodes gives a forthright exposition of his personal views on carcinoma of the cervix, and one by V. Lewis discusses discusses diagnosis and management of metastatic cancer in pelvic lymph glands. A chapter on epidemiology of ovarian cancer to many will show little but the lamentable lack of agreement on terminology. An interesting progress report by A. W. Harcus and K. D. MacRae on the Ovarian Cancer Clinical Survey with therapy by combination of Depostat and cytotoxic agents is presented.

There is no apparent cross-fertilisation between the papers and no discussion is recorded. While some of the papers are of considerable interest, others such as those on organ cultures of the cervix and endometrium and identification of particles in ovarian tissue are less relevant.

There is much of interest in this volume, but it presents only a few facets of the problem and lacks balance and is uneven in quality.

J.E.M.

HEART DISEASE. By Earl N. Silber and the late Louis N. Katz. (Pp. X + 1430. Illustrated. £24.00). London: Bailliere Tindall. 1975.

THIS is a heavy book in more ways than one, weighing 8 lb and running to 1430 pages, but it is not a dull book.

In the preface the authors refer to the huge advances in knowledge in the basic and physiological sciences related to cardiology, and to the new understanding of clinical heart disease which they have brought. Then, with the practising cardiologist in mind, they have divided the book into sections dealing with the physiology of the circulation, the pathophysiology of heart disease, the clinico-physiological approach to diagnosis and the manifestations of heart disease. These chapters are well written and extremely valuable. The authors wisely recognise that not all cardiologists have access to the most modern diagnostic facilities. For example in the section on the diagnosis of angina pectoris, in addition to numerous recent references to the value of the graded treadmill exercise test now employed in most progressive cardiac units, some references are given to the largely obsolete step tests.

The chapters on the specific disorders of the heart are less outstanding. It is sometimes irritating to have to refer backwards or forwards for further information on patho-physiology or treatment. It is little compensation that most chapters are compact enough to be read at a sitting since few will use the book in this way. It is essentially a reference book and a source of other references. The number of these is vast, eg 448 relating to diseases of the pericardium. The chapters on treatment vary in quality from extremely poor (hypertensive diseases) through indifferent (ischaemic heart disease) to excellent (surgery of the cardiac patient).

When this book appeared last year the world literature on heart disease had doubled since the late Charles Friedbergs' book was published nine years earlier. It is not twice as good but I know of no better.

M.E.S.

PRELUDE TO HARMONY ON A COMMUNITY THEME: Health Care insurance policies in the Six and Britain. By Josef Van Langendonck. English text edited and introduced by Gordon Forsyth. (Pp. XII + 303. £8.00). London: Oxford University Press for Nuffield Provincial Hospitals Trust. 1975.

THIS major study of health care insurance in the six founding nations of the European Economic Community was originally presented by Doctor Van Langendonck for his doctoral thesis. This book is an updated version of his thesis and emanates from the Institute of European Health Services Research of the University of Leuven, Belgium. The Institute was set up in 1972 as a multidepartmental consortium and has already made significant contributions to health service research in Europe.

This book, produced in conjunction with The Nuffield Provincial Hospitals Trust is proclaimed as the most comprehensive work yet in English on the subject of health care insurance policies in the six founding nations of the EEC. It is introduced by Gordon Forsyth, reader in social administration at the University of Manchester: Mr. Forsyth gives a lucid and concise history of the British National Health Service. He compares and contrasts the present British system of direct government responsibility for health with the continental system of compulsory membership of self managed insurance schemes. It was of interest to be reminded that it was the Dawson Report of 1920 which recommended the integration of curative and preventive medicine with health centres. His account of the profession's relationship with the independent review body on doctor's pay and the tiny role of private beds within the NHS make interesting reading in the light of recent political developments. Some of his assertions, however, are open to question. He states for instance that 'pragmatism determined the characteristics of the NHS far more than political ideology and it was the waste and inefficiency of compulsory insurance which led to the abandonment of the insurance principle'. The prospect of the migration of doctors within the EEC is examined and Mr. Forsyth sus-

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In the main body of the book Dr. Van Langendonck gives a very thorough description of the various insurance schemes employed in the founding six nations of the EEC. As he admits himself, though, the method that he has chosen for this description is somewhat repetitive viz. he first sets out common features and then reviews differences between the six nations. He goes on to analyse the evolution of the main elements of the different national systems, pointing out diverting and converging trends. He believes that economic integration in Europe cannot exist without social integration. He states that national social legislations could best be integrated by harmonisation (changing and converging national laws) rather than by co-ordination (fitting existing national laws together). He gives a historical sketch which is to the most part thorough but I was disappointed with his lack of coverage on two momentous events i.e. the inception of health insurance in 1883 by Bismarck and the setting up of the EEC in 1957. Some very interesting points emerge; in France a doctor has a choice of 8000 drug preparations from which to prescribe, whereas in Italy he has about 17,000 ! In France there are fifteen different insurance schemes operating and a few special schemes for good measure. It is consoling to learn that continental doctors are every bit as resistant to change as British doctors and probably more so.

In the final section of the book the proposals for harmonisation are put forward. One of the main proposals is for an extension of health care insurance to cover the total population. At present a small percentage of the population is without cover. Another is for the adoption of the Dutch system of compulsory insurance. He makes some comment on our health service. He feels that our system is entirely in keeping with his ideals of harmonisation. He did suggest that suppliers of medical care in the NHS should be made responsible for the good use of money. Mr. Forsyth also broached the question of effectiveness and efficiency in the NHS. Both writers seem to be somewhat complacent about the NHS. Surely our system has things to learn from the continental systems. Certainly in terms of adequate pay for doctors but primarily in the field of health care. One only has to compare infant mortality rates here with some continental countries to realise that there is just as much room for improvement in the NHS as there is in some aspects of the continental systems.

A.E.

AN ATLAS OF CLINICAL NEUROLOGY. By J. D. Spillane. Second Edition. (Pp. VIII + 438; figures 592. £9.00). London: Oxford University Press. 1975.

DR. SPILLANE when he wrote the first edition was concerned that his book would be "too old fashioned" to be popular; he has been reassured by its great success and appeal for medical students and their teachers. A clinical neurologist of the first rank and a medical author of distinction he obviously enjoys bedside teaching and this book allows students to benefit from his skill in this respect. The book is built around the remarkable photographs but the text is just as interesting and full of valuable clinical observations. It is not written as a textbook of neurology but as a beside teaching book for undergraduate and postgraduate students. The introduction is most enjoyable and the best potted history of neurology I have read. The price has not deterred 10,000 buyers of the first edition and considering there are 600 photographs this fine production is well worth £9.

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TOXICOLOGY—THE BASIC SCIENCE OF POISONS. Edited Louis J. Casarett and John Doull. (Pp. 768; figures 15. £14.50). London: Bailliere Tindall. 1975.

THIS is a weighty and heavily documented textbook which should prove of great value to experimental toxicologists. It is arranged in four sections, each section consisting of a number of chapters reviewing the literature on a single aspect of toxicology. There are 35 contributors. The first section of 150 pages is concerned with general principles of toxicology, the absorption, metabolism and excretion of toxins, and the way in which these influence the dose response relationship. This rather detailed treatment is probably not appropriate for medical readers who would be better served by consulting medical textbooks of pharmacology and biochemistry. However, it should be valuable to non-medical toxicologists. In the next two sections occupying 400 pages, the current experimental toxicological field is reviewed in two ways. First by going through the systems of the body (central nervous system, liver, kidney, etc.) and second by going through all the groups of toxins (teratogens, carcinogens, pesticides, metals, etc.). Consequently, there is an almost complete duplication of information in these two sections. This is made worse by a duplication of coverage between say the section on carcinogens which deals with metals and the section on metals which deals with carcinogenesis. This duplication of coverage, coupled with the emphasis on information derived from animal experiments and neglect of clinical information, reduces the value of the book to medical readers.

The final section is concerned with the organisation and work load of units concerned with such specialist fields as "clinical toxicology", "forensic toxicology", "veterinary toxicology" and so on and again contains little of value to the medical reader.

Out of this mass of carefully documented information, I gleaned two often repeated messages:—

1. that in almost all the fields the animal data shows such species variation that it is difficult to apply to man.

2. that there is an urgent need to collect accurate quantitative information in humans. Several writers refer to the conflicting advice about treatment in the medical literature. But without proper documentation of initial tissue or blood levels, etc., claims for successful treatment are valueless.

P.C.E.

VIRAL DISEASES: A SYMPOSIUM. Edited by A. T. Proudfoot. (Pp. 134. £2.40). Edinburgh: Royal College of Physicians. 1975.

ALL the contributors to the symposium which is reported in the book are recognised authorities on the subject with which they deal. Hence the accounts are reliable, up-to-date, useful and sometimes entertaining. The articles vary in length and content, those on rubella and bronchitis being of most direct clinical interest, that on influenza covering most aspects of the disease and that on measles and multiple sclerosis most terse and properly non-committal. The epidemiologists score heavily in presenting the human situation; many senior medical students will wish that their teaching was as good as this. Thus the bag is mixed and the editor has provided no foreword to indicate the purpose of the symposium. Present-day understanding of some common virus diseases would be a suitable sub-title.

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COMMUNITY HEALTH PREVENTIVE MEDICINE AND SOCIAL SERVICES. (Concise Medical Textbook). By J. B. Meredith Davies. Third Edition. (Pp. 510; figures 17. £3.75). London: Bailliere and Tindall. 1975.

THIS is the third edition of a book originally published under the title "Preventive Medicine, Community Health and Social Services" (1966). It is hard to see what has been gained by re-shuffling the words in this rather lengthy title. The publishers say that the book is written for medical students, doctors, social workers and all members of the primary health care team. This edition has been extensively revised following the recent widespread reorganisation of the health services.

The book has always been popular with medical students, because of its compactness, low cost, and its attempt to deal with the full range of social medicine in a succinct and authoritative manner.

The major drawback for local readers is the complete lack of information on Northern Ireland Services. Under the title "Reorganised Health Services in the U.K." separate details are given for England, for Scotland and for Wales. Nevertheless, due to its scope, the book will be found useful for reference.

R.B.

GENERAL PRACTICE FOR STUDENTS OF MEDICINE. By R. Harvard Davis. (Pp. 111. Illustrated. £2.20). London, New York, San Francisco: Academic Press. 1975.

THIS monograph is a useful contribution to the growing body of literature which attempts to define the content of the specialty of primary care. The writer describes specific roles which characterise the primary care physician. These are best illustrated in general practice or family medicine. The book is written to appeal to undergraduate and postgraduate students. Unfortunately Harvard Davis does not attempt to define the teaching boundaries between them. He re-defines known concepts of the true nature of illness and disease. In the setting of general practice, ill health may often be interpreted in terms of disturbed function, the result of an upset equilibrium between the patient and his own environment. The author outlines succinctly the principles behind the delivery of primary care and its characteristics. In particular he considers the skills of early diagnosis and decision making, the doctor patient relationship, comprehensive patient assessment and the integration of curative and preventive clinical procedures. Clinical techniques of pre-symptomatic diagnosis and follow-up are discussed. The sections on finance and the history of the health services in the United Kingdom take on particular relevance at this time. The future of primary care is discussed and career possibilities are not neglected. The short chapter on research is useful. Finally variations of primary care systems seen in other countries are outlined. At £2.20 this is an interesting book especially for undergraduates. It is a pity, however, that such an experienced teacher of general practice did not enlarge more on the clinical content and include a chapter on the methodology of teaching general practice to students. His lucid definition of the specific roles of the primary care physician has training implications for the 'graduate clinical training' phase advocated by the Merrison Report (1975).

REFERENCE

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THE first edition of Principles of Pathobiology appeared in 1971 and the success of the book can be judged by the rapid appearance of the second edition.

The concept of Pathobiology as a new science integrating cell biology and classical pathology is possibly a false one in that classical pathology has since the nineteenth century attempted to explain disease in cellular terms. Nevertheless the student faced with the problem of explaining abnormal structure and function in subcellular terms will welcome a book devoted to that purpose. The range of pathological reactions discussed is wide, eg there are detailed chapters on inflammation, immunology, neoplasia and the chapter on cellular reaction to injury has been extensively revised and is now more relevant to human disease. This book can be recommended to medical undergraduates or to biology students and would be useful reading for post-graduates preparing for any of the fellowship examinations.

I.V.A.

REVIEW OF GROSS ANATOMY. By B. Pansky and E. L. House. Third Edition. (Pp. 508. 257 Illustrations. £6.50). London: Balliere, Tindall. 1975.

PREVIOUS editions of this American work have been appreciated by preclinical students and others, and this new edition can be recommended. The concepts in which Gross Anatomy deals are for the most part expressed more economically by illustrations rather than by verbal constructions. A textbook, unless it sets out to be a mere key to an atlas, is to be judged on its illustrations as much as on its verbal text. By this criterion, the authors have apportioned their effort successfully, claiming to have written the text around the pictures rather than vice-versa. Most double-page openings have on the right a set of small diagrams, and on the left accompanying text, in lecture-note form, with emphasis of key words and abundant use of tabular presentation. Surface anatomy and normal radiological appearances are included. There are some notes on clinical applications. The internal anatomy of the central nervous system is excluded (apart from the ventricular system).

The book is well produced. A clear type-face and liberal spacing make for legibility. Dr. Pansky's line diagrams, over a thousand of them, are the best one has seen of their kind. In this edition, some have had colour added, with consequent increase in clarity. One would wish to see such use of colour made much wider, and would sacrifice a section of seven overcrowded coloured plates, entitled an atlas of regional anatomy, added to this edition from another of Dr. Pansky's publications.

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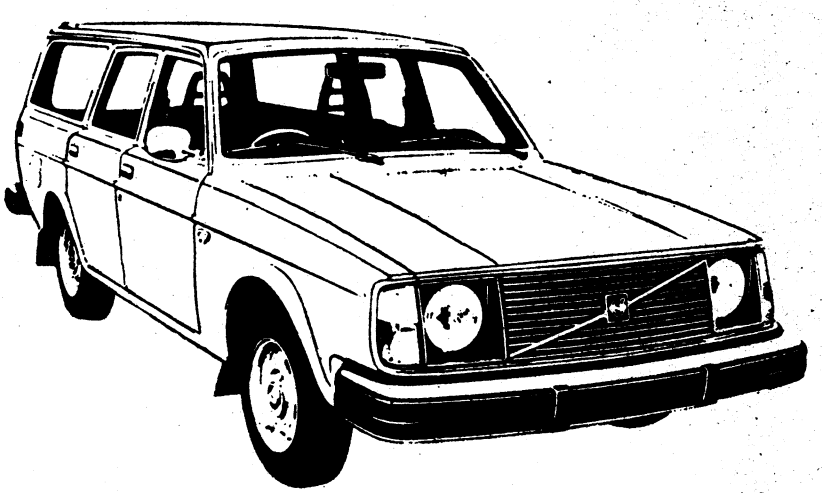
J.W.C.

VOLVO



A Volvo never had looks like this before.

The new Volvo 245 is getting admiring glances from all sides. And no wonder. It's better looking than Volvo estates have ever been before.

It's got a new 2.1 litre engine with sporty things like an overhead camshaft and an aluminium head. Yet it is just as flexible. Even more reliable. And, remarkably, runs happily on two-star petrol.*

It's got the kind of seating that wouldn't disgrace your lounge and is gentle on the spine.

With its new front suspension and steering, you'll find it very sure-footed.

With 67 cu. ft. of space in the back, it's big enough to hold an entire team's kit, and some of the team too.

It's defence against accidents, with dual braking systems and 50 mph crumple-zones, is remarkable.

And at £4180 (delivered Belfast) you're paying for years of reliable, trouble-free motoring.

Come in now, and see why everyone's looking at the new Volvo 245.

The new Volvo 245.

*All 1976 models run on low octane petrol.

The Stanley Motor Works Limited

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