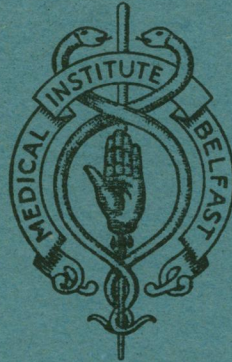


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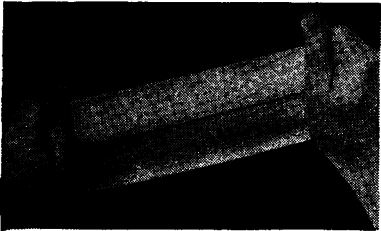
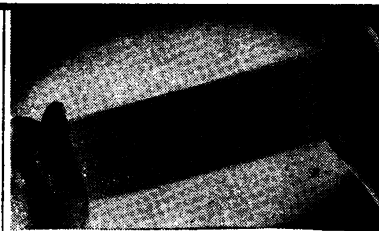
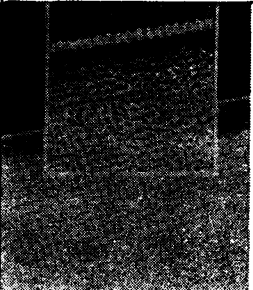
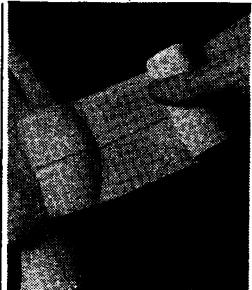
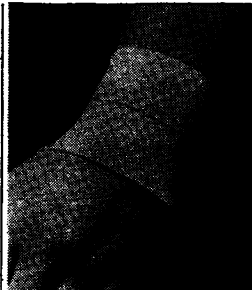
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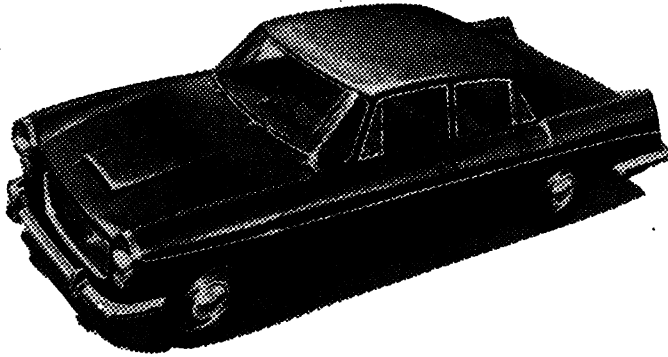
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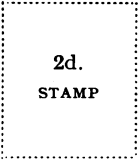
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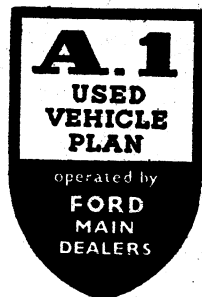
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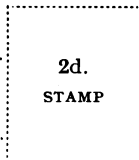
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THE OTHER SIDE OF MEDICINE

By FRANCIS A. MacLAUGHLIN, V.R.D., M.B., F.R.C.S., ENG.

PRESIDENTIAL ADDRESS

to Ulster Medical Society, 12th October, 1961

THIS address is an endeavour to deal with a vast, intriguing, and mainly abstract subject which has interested men, and particularly medical men, for thousands of years, which interests us just as much today, and which will concern those who follow us even more.

In the course of the progress of civilisation man has been creating sets of circumstances which produce hitherto unknown factors influencing our minds and bodies, many of them unforeseen and very real, and often harmful in their effects as producing immediate, or remote pathological effects. This fact demands that we must discover means to prevent these effects being harmful, and also to find means to cure them when they have actually harmed us.

While we have vanquished many diseases at an increasing speed, it would appear that we are discovering new ones to take their place at an even greater rate. So it seems that in the foreseeable future mankind will still have many diseases to afflict him, and ample opportunity to study their cure, if he has not by some slight mistake caused mass suicide, or slow genetic extinction, in the name of scientific progress. However, we hope that wisdom and good sense will make us stop short of this rather gloomy prognostication.

This address concerns us as individuals and our reactions upon one another, more particularly as doctors. It is that side of medicine which is not so much taught as acquired by precept, observation, and experience.

If we dip into the dicta and writings of the ancient fathers of medicine we find that these are just as true now as when they were first spoken, and written thousands of years ago, and I hope they will continue to be true into the far future—their statements usually had to do with their fellow-men and women, particularly those who suffered from some disability of mind or body, and much of what follows will be on the same theme.

It was Tennyson who wrote "Knowledge comes and wisdom lingers." One knows so well how much knowledge comes, but also unfortunately goes, and as one grows older one wonders just how much of all the knowledge we have acquired does stay with us. We can only hope that the effect of the absorption of so much knowledge results in the acquisition of wisdom. In the case of the doctor this should result in knowledge of disease, and wisdom in dealing with our fellows, who in this particular case are our patients.

The success of a doctor depends on several factors, and all who get the necessary knowledge in the course of their progress to a medical degree do not necessarily have the inherent wisdom, or acquired wisdom to match the knowledge, and so do not become successful as practising doctors; but I think the vast majority of those who feel the call to medicine have their share of that inherent wisdom, and are capable of acquiring more with experience.

The qualities for a physician are outlined by Osler, and perhaps I might quote passages from him—"In the first place, in the Physician or Surgeon, no quality takes rank with imperturbability." . . . "Imperturbability means coolness and presence of mind under all circumstances, calmness amid storm, clearness of judgment in moments of grave peril, immobility, impassiveness, or to use an old expressive word, 'phlegm.' It is a quality which is most appreciated by the laity though often misunderstood by them; and the physician who has the misfortune to be without it, who betrays indecision and worry, and who shows that he is flustered and flurried in ordinary emergencies loses rapidly the confidence of his patients." "In a true and perfect form, imperturbability is indissolubly associated with wide experience and an intimate knowledge of the varied aspects of disease."

I think this can be summed up as suggesting a well-educated individual, generally, as well as medically, with the confidence produced by knowledge, and with mental poise, combined with the wisdom of knowing the type of patient with whom he is dealing and how best to adjust his approach to that patient's particular needs, both physically and mentally. Sympathy without sentimentality is also a desirable ingredient to include. It all adds up to "Æquanimitas" such as has been possessed by many of our teachers, and is possessed by many of our colleagues.

Osler says: "One of the first essentials in securing a good-natured equanimity is not to expect too much of the people among whom you dwell." If this advice is followed then we will not adopt an air of superiority toward those with whom we work, and who may be less experienced and knowledgeable—and also it will enable us to live and think more on a level with those we treat, and try to help. This I think presupposes that we must try to adjust ourselves mentally to the level of the education and understanding of the patients with whom we are dealing, and to try and give our explanations and instructions in language and amount, readily understandable by the individual to whom we wish to convey them.

It is often a fault of youth in medicine to use technical words and expressions to describe methods of treatment to individuals who do not even understand the words in which the instructions are couched, and it is also a common fault when

describing the disease from which the patient suffers, and its course, to do so at too great length, and in too much detail. Because many of the patients show a very low level of mental absorbability of any facts to do with their bodies, and their maladies.

Frequently one takes it for granted that highly educated and cultured individuals have a high degree of knowledge of themselves, and it is with somewhat of a shock to discover that they are in fact profoundly ignorant of the structure and workings of their most precious possession; the same condition is found in those who have always been very healthy and have little contact with our profession—another characteristic of people like this is that they have relatively little sympathy with those who have suffered often, or long from illness, and are apt to regard them as inferior, and something to be disdained, rather than those to whom sympathy and consideration should be shown.

Particularly in hospital work it is advisable to give our patients some simple explanation or fact to which they can cling, rather than give a long and complicated explanation which they are unable to understand. The manner in which they can distort what has been told to them is often very surprising and disconcerting, as one often finds at a subsequent consultation, when the story is recounted back, it is unrecognisable.

This leads one to the fact that when our patients come to us they are often frightened—and here the causes of fear are often threefold. Firstly, when they visit a consultant they have probably not seen him before, and as this is one of life's milestones they are apt to let imagination run away, and to remember all the dreadful things they have been told by other patients who have gone to consultants, and who often exaggerate their experiences in a somewhat twisted attempt to magnify their own importance, in the reflected glory of the experience. Secondly, they have the usual human attitude towards the unknown and so feel frightened by something nameless, which they cannot put into words. Frequently patients from the country who live relatively isolated lives show this more than town-dwellers. Thirdly, and this may be present in those who are not worried by the first two causes—and indeed might well occur in you and me—the fear of what will be found, and what the future will hold.

When the patient goes to his general practitioner he probably knows the doctor as an individual and does not fear a visit to him, and also the experience is not so terrifying because it probably has happened before—but still the third factor remains—what will he be told? So it behoves us each time we see a patient to remember the three main causes of fear, and by our own efforts to do the best we can to remove them, and this is where wisdom rather than knowledge is so helpful.

Many doctors either have, or have developed an ease of manner when dealing with patients which makes it easy for themselves, and for their patients. Along with this is that indefinable characteristic of inspiring confidence in our patients, who will go to one man and say they would trust their lives to him, and to another and then say they would not let him touch them at any price.

This fact, of inspiring confidence, is one of the most valuable possessions of a doctor, and seems to be a compound of personality, ease of manner, confidence in himself, which usually comes from knowledge, and the reputation he has acquired in the eyes of his medical colleagues and former patients, along with his education generally, and last but far from least a sense of humour, and the fitness of things. Appearance, race, colour, and sartorial distinction have very little to do with this, as it seems the patient, when ill and anxious, has a perspicacity which sees beyond these things.

In relation to the amount that patients will absorb of what is told to them, a nervous patient does not take in much of what is said, and it is always wise to have a relative, to whom nothing is happening, in the room so that they may remember those facts, or some of them, that the patient may forget. Also frequently older patients are deaf, and more are mentally dull from their malady, and so unable to hear, or understand intelligently, what has been told to them.

In this connection a patient who is ill and anxious, by virtue of being placed in an unusual set of circumstances, may say, and do, things which normally he would not, and so a considerable modicum of tolerance and forbearance is demanded from the doctor, who can very easily let pass something which could not be disregarded in other circumstances.

It is always wise to remember that a great deal of the good we do to our patients depends on what we say; indeed, often it is more important than what we do.

Another interesting point is that often we can do a great deal of harm to our patients by what we do not say—in not giving some explanation of the condition from which they are suffering, and how we propose to deal with it—the over-anxious patient is inclined to think that either we do not know, or else that it is so terrible we are afraid to tell him. Can we afford to say we do not know? We can give a qualified “I do not know,” as is often the truth, and explain that we cannot give a definite opinion until we have carried out certain tests or until the patient has been seen by a specialist, or, if in the case of a consultant, by a specialist in another branch who has more knowledge, experience, and technical skill in the particular condition in question. An unqualified “I do not know” is dangerous, and one feels should only be given to someone who is intelligent and knowledgeable, and who is relatively well known to us, when they will respect us for being able to say it, and not misconstrue it for just plain incompetence and ignorance.

It often happens when one is not sure that we feel we would like to bring a colleague who may know more or have a different approach, or be more senior, and who will help to share the burden of difficult decisions, or actually assist in carrying out some difficult procedure. This approach, when made known to the patient or his friends, will often improve the mutual trust and confidence between doctor and patient. Patients are usually well aware that no doctor knows everything, and they soon bowl out the “know-all” and the “bluffer”—these are often those who have neither knowledge nor wisdom, and will eventually fall by the wayside.

It is always well to be completely honest with our patients, and if this is undesirable for any reason, say so much as may be true and refrain from saying any more. It is better to tell a half-truth than to tell a lie, and a half-truth is only permissible if it is to spare our patients' mental anguish, or a severe mental shock which could have serious consequences, but always make sure in these circumstances that the whole truth is given to a near, and preferably dear, relative, who will understand your motive.

Many doctors are born naturally courteous, others acquire courtesy later by experience, and it is always easy to be courteous to patients, particularly in hospital where, no matter how uncouth they may be, a courteous, sympathetic, and interested approach will tend to bring out the better side in the patients and so make the interview much more easy and pleasant—and also helpful to the patients, who will be put more at ease.

Sarcasm and cynicism should have no place in our dealings with patients, and indeed, if used, are boomerangs, as the patient who is already rather on edge is liable to hit back in the same manner, and so the doctor has spoiled what is really rather a delicately-poised relationship, and is unable to help his patient as adequately and efficiently as he otherwise might have done.

At times we encounter the abusive patient or relative, who perhaps, when we know all the facts, has some justification for indignation—it is well to listen to the story first and get at as much of the facts and truth of the matter as possible before judging, and very often the quiet and understanding response will quench the flames, whereas a quick or intolerant reply will only fan them, and indeed could produce a conflagration that might end in the courts.

If the doctor has been kindly and sympathetic and explained what is going on to the patient, and his anxious relatives, where things have not gone according to plan, or have gone badly, they will be more inclined to forgive; whereas if ignored or not treated courteously they will be more inclined to push the matter to any length in a spirit of revenge, and again the matter might well end in a charge of negligence, or incompetence against the doctor.

When receiving a patient, and during the time the patient is with you, always be sure to give your full attention and discourage any unnecessary interruptions, because the patient usually believes that he is the only one who matters, and you must behave as if you believed it also. Many consultants carry this so far that it is well-nigh impossible to get a word with them during their consulting hours, no matter how urgent it may be—but one usually finds that when an interruption does occur a few words of apology and explanation to the patient will set matters right.

In consulting practice it is often difficult to keep absolutely to time; an emergency may come in and require attention, and even a minor one requires time, and one seldom knows the exact nature of a case before it arrives. It may take only a few minutes to deal with, or may be a difficult problem requiring a considerable time for its solution. Here again a timely apology, accompanied by a broad explanation, will smooth any ruffled feathers.

It is always useful when discussing patients anywhere never to mention the name and the disease; one can be mentioned without giving a clue to the other, and this wise dictum is not only confined to other doctors, or to hospitals. It is wonderful the curiosity people have about other people's business, particularly their illness and defects, and wonderful to what lengths many will go to try and find out these facts, and often will try to use them against the sufferer. When asked by one of these busybodies about some mutual friend who happens to be one's patient, the problem can be passed over by being obviously obtuse, or perhaps irrelevantly flippant on some other subject. When one discovers some defect in a patient which is not obvious, or likely to be a handicap, or is a sequel of some cured condition, it is well to tell them not to mention it at all, and indeed if it is not brought out at intervals into the open, the possessor may forget about it, and permit others to do so.

There is always the temptation to patients to discuss their operation, and patients seem to feel some form of self-aggrandizement by so doing, and by perhaps adding just a little to it all—a kind of martyrdom complex.

This leads on to thinking of patients as falling into different types, and here at once we think of the two broad divisions of mental and physical types. All down the ages men have tried to divide people into various arbitrary divisions, and as mentioned early in this address most of it deals with the abstract, so are the divisions abstract in part, particularly the mental, but we are on more concrete ground where the physical divisions are concerned. The hard matter-of-fact statisticians and those who wish to measure everything scientifically have found the various classifications far from easy to make satisfactorily.

In the mental sphere the psychologists and psychiatrists have tried to correlate mental types with mental diseases and also mental diseases with physical types, with some measure of success, and in the physical sphere many well-known names from Hippocrates, down through the years to Sheldon in 1942, have tried to classify humanity into various physical types, and then to try and see if these physical types are predisposed to various groups of diseases and conditions.

Hippocrates divided men into two types—*habitus apoplecticus* and *habitus pthisticus*, and Sheldon, 1942, into three types—*endomorph*, *mesomorph*, and *ectomorph*. Gillilan, 1955, reiterated in more detail—*sympathotonia* and *vagotonia*, with which we have long been familiar, and added *amphotonia* as well. This is something which we all do, and years of experience have led us to various conclusions as to the different types of individuals who come to us as patients, and this experience helps us in our diagnosis, and also in having opinions as to how to deal with the different types, and adjusting our treatment to their special requirements.

The grouping of types according to their mental make-up is used by many as a guide in the approach to the patient; some are highly strung and some phlegmatic. A good example of this is how we are all impressed by the varying degrees of tolerance of pain, or often indeed the intolerance, and also in some cases the quick or slow reaction of various individuals to remedies directed

towards relief of their pain. The same thing we often see in the reactions of different types to anæsthetics, and particularly to premedication.

Many of the more sensitive patients are terrified at the thought of an operation under a local anæsthetic, others are terrified at the thought of having a general anæsthetic, and it is our duty, where we can, to try and allay the often un-reasoning fears of these patients by adequate verbal premedication beforehand, much of their fear being reactions to the unknown.

The examination of a patient is not only a matter of the simple inspection, palpation, percussion, and auscultation of the individual lying unclothed on the couch: it should begin as the patient walks into the room—and indeed often before that, as one may have received a letter from the patient which can provide various clues about him, or a telephone message—and then as soon as they enter all the senses should be used—vision, hearing, smell, and later touch. Such things as colour, gait, voice, accent, manner, and manners, along with the clothing and accessories, will give one clues as to type, temperament, intelligence, status, occupation, location of home, country of origin, race, etc., all of which are of great assistance in enabling the doctor to adjust himself and his treatment to the particular requirements of that patient—the patients' friends also unwittingly often provide clues as to the family environment, and may often be a help or a hindrance at the interview—as they may be to the patient elsewhere.

We do not often think of the sense of smell as a help at a consultation but if we pause to think, it is very intriguing to consider just how much we can learn about other people by its aid, and particularly about our patients, and their diseases—for example, perfume will tell quite a lot, either as an allure, a façade, a self-satisfaction, or a camouflage. Many diseases have a distinctive odour, such as acute rheumatism, acidosis, diphtheria, incontinence, atrophic rhinitis and many more, not excluding death itself.

A patient's hands will tell a great deal about their possessor, temperament, character, occupation, interests, and may show signs of certain diseases very clearly. Indeed, by looking at a person's hands a very good idea can often be obtained as to subjects of conversation which may interest them, and frequently an intelligent use of this fact may be the means of initiating an opening conversation at the beginning of a medical interview designed to put a nervous patient at ease, before starting the purely medical business of the consultation.

Another interesting clue to the patients' personality is to enquire into their hobbies and interests; some are gregarious in their recreations and others are solitary, and often those who have solitary hobbies are more sensitive and artistic, and appear to require more time alone to enable them to recover from the rush and tumble of every-day life. They are more sensitive to, and fatigued by, the impacts of our lives, and the reasons for their hobbies are often not understood, or are completely misunderstood even by those who think they know them well and who may be of a different and less understanding type.

Hence the greater understanding the doctor has of the mental and physical type of his patient the better is he able to advise according to the particular needs of the individual with whom he is dealing, and the closer will he get to his

patient in the mutual confidence so necessary for the successful treatment of mind and body.

Many doctors have an instinctive and finely adjusted sense which tells them how to deal with a complete stranger who comes as a patient, and may conduct some trivial or totally irrelevant conversation in order to give the nervous patient time to take in the surroundings of a consulting room, which in its turn may give them some idea of the manner of man they are meeting for the first time, as well as letting the patient have a mental look at the doctor before getting down to the real reason of the visit. This enables the patient to regain poise and equanimity.

The rooms in which we practise can be full of medical furniture and white enamel, and to many this is rather terrifying, or they can be more like a library or study and play down the medical side. This is particularly important where children are concerned, as they tend to be frightened of white coats, and medical equipment and instruments which are best kept at a minimum, or out of sight.

Very early in a consultation it is often possible to sense a fear and, as it proceeds, to get a more precise idea of what the fear really is, and it will often fall to the doctor to pin-point that fear by questioning, as the patient may not put it in words, or possibly will mention it when one is showing him, or more often her, out of the door. A patient at ease will give a more complete and accurate story than a flustered one, and the time spent in preparing them will often shorten the whole interview, and make it more satisfactory to both parties.

In the course of examination one should always give some short explanation of any procedure which could be unfamiliar to the patient, and not become irritated if he does not appear to be co-operating as intelligently as we might expect.

Most patients tend to ask: "Will it hurt, doctor?"—and to this it is wise to give a truthful answer, as far as possible, or they will not trust you the next time, and in this connection it is well to remember that what is a mere touch to one is acute pain to another. So the gentle hand always pays—and is something which, if not naturally present, should be carefully cultivated, as its use will get information not otherwise possible to acquire, owing to the resistance of the patient from fear of being hurt.

There are several items one should remember particularly in older people—never remove hope, always leave a loophole; be perhaps on the optimistic side, but never obviously unreasonably so. Do not be afraid to remark on some good point such as a strong heart, good hearing, a good colour, a fine head of hair, or good vision for their age, a very normal blood pressure, etc.; it is not suggested that all these points should be emphasised, but an occasional one does help the morale of the elderly, and often pointing out to them how many talents they still possess to counterbalance all the complaints they have brought to tell you gives moral uplift.

It always seems cruel to examine a patient and then tell them nothing at all, but that you will report it all to their doctor and he will in turn tell them what to do. This destroys a great deal of the value of a visit to a consultant; always

tell them something, but just enough that you do not embarrass their own doctor in any way when they return to see him.

The background, education, interests, and mental make-up are useful in deciding on the treatment. One who is artistic and sensitive is often upset disproportionately by what seems to be a small deviation from the normal—for example, a miniature painter with a very small refractive error, a singer with a comparatively slight deviation of the nasal septum—conditions which would not even be noticed by one of coarser fibre.

The relationship between intelligence, artistic capability, and allergy is one which is very real, and many cases of atypical migraine hitherto undiagnosed can be brought to light by starting with an assessment of the patient's personality, intelligence, interests, and hobbies, and when this has been done we are in a much better position to explain the condition to the patient, and suggest measures which may be helpful, and which may be more of the nature of advice as to the general hygiene and ordering of the patient's life than purely medical in nature.

When interviewing a patient try and create the atmosphere that one has all the time in the world. Do not hurry or fluster, but try and produce the impression that they are the only person in the world who is ill, and that the doctor is not interested in anything but their condition—a somewhat difficult thing to do when he knows that several others who are perhaps in much more urgent need of attention are waiting next door. Also when dealing with the discursive and circumstantial patients one so often meets it is always possible to bring them back from their beloved side avenues to the main road of the problem on hand by a well-timed question or remark.

You will possibly have noticed on a recent circular the quotation by Payn in 1884 that the "Busiest men have most leisure, idle folk have least," and as we look around our colleagues we see how true this is, as many of them who live busy lives have plenty of time to talk to all sorts of people, to share in administration, act on committees, and often have many hobbies and interests outside their work. This faculty is also shown in their professional lives by the characteristic of never seeming to be in a hurry, and yet never wasting time in idle or irrelevant conversation, and these are the ones who, while not spending long with any one patient, never create the impression of hurrying them in any way, and in being thoroughly interested.

Dealing with children as patients is partly a matter of temperament and partly acquired. Some of us have been fortunate in having younger relations early in life, some have children of their own, and some have had the good fortune of working in children's hospitals. All these give an ease of manner in dealing with children, and there are various factors which lead to success in this field. Children are extremely quick to size up adults, and seem to know, as dogs do, those who like them, and those who are not afraid of them, afraid in the sense of being ill at ease in their presence.

Always speak to a child as if you had known it all its life. Some children appreciate being spoken to first and being asked to take mummy into the consulting-room and get her a seat. It gives them something to do and also seems

to raise their sense of importance in their own eyes, and generates a feeling of responsibility. This does not always work with the rather timorous "apron-string," and somewhat spoiled small child, and then it is wise to let them come in relatively unnoticed and have time to look around, and form their own opinion of the doctor and his room—and this they will soon do. Usually the child who starts to cry straight off is one of these, or has been to a doctor before, and remembers an injection, or some other uncomfortable procedure—and then it is one's duty to try and erase this bad impression as far as possible for the next man, and frequently a considerable measure of success can be achieved.

When getting details of name, age, etc., about a child, start by asking the child, and let it go as far as possible before bringing the parent to the rescue. This enables the child to sum you up and feel that it is getting to know you, and at the same time enables you to assess the child's intelligence and reactions, for your own guidance in examining it. It is often difficult to get the parent to keep quiet, as many mothers will persist in answering questions which the child could answer quite as well, a "smothering" process, and often one has to ask the parent to stop, and it is well to explain later that this is the best way to let the child know the doctor, and vice versa. During this process one can study the child and parents, and how often one notices that the boys resemble mothers and the girls resemble fathers in appearance; and often this goes for nature as well, but not by any means always, and indeed one sees the whole process reversed. One supposes that only a small segment of the Mendelian law is seen in one family, as there are seldom enough children in any one human family to make it more obvious! Often the heredity of some condition can be traced back to one or other side of the family, like red hair, squints, etc., and help in diagnosis and lines of treatment.

So often the small child cannot help one much and the story of the parent and one's own observations, plus the child's reactions, give the necessary information, and in older children a great deal of information can come from what the child will say itself.

It is a very foolish thing to ask a child to give one anything, such as a toy it has brought. By all means ask the child to let you see it, and then admire it, as the toy brought is usually a very treasured possession, or newly acquired because the child is coming to see the doctor, as a sort of bribe. Small girls will very readily respond to admiration of some article of clothing or jewellery, and, as mothers usually put on the good clothes to go and see the doctor—and these are often new—admiration goes a long way to weld confidence. Small boys may be asked questions about trains, soldiers, playing games, etc.

When actually examining the child some silly joke about feeling for tickles, or such like, distracts its attention, and as children are always suspicious of instruments no attempt should be made to conceal them: the child's natural curiosity is at work and we should explain what they are and what they are for; this makes the unknown familiar in the child's mind and it will often co-operate as a sort of game. Some sideline can be introduced like showing them vessels

in their hand with a torch, if one has to examine in the dark, or perhaps doing it on mummy first, as this gives confidence.

If care is taken in this way the child will usually come back quite happily, and it is often a good idea to give some small reward, such as a sweet, at the end of the interview for having been good, and this is often the only thing remembered years after. It is foolish to give a bribe early on; let it always be a reward.

Some parents like to put the child out of the room when discussing its problem, and unless there is some very cogent reason, such as telling the doctor the child is adopted when it has not been told or of some congenital disease which it may have inherited, this is inadvisable because it may arouse suspicion of the parents or the doctor as to what the future may hold. It is far better to discuss the whole problem and mention any operation which may be desirable and explain the reason for it, and the benefit which the child will obtain from it. Most children will accept this, and if too young to comprehend what it is all about at least are not frightened.

When talking to a child never talk down to the child. Conduct the conversation on a "man-to-man" basis, of course in language which the child can understand; and in the case of older children try to inculcate a feeling of responsibility that it is something they will have to do for themselves in order to help themselves in the future, and that if they do not carry out what is asked they are going behind their own back, and not letting their parents down.

The occasional scrap of humour fitted to their comprehension, or the showing of some object which may interest them in the surgery or consulting-room, will help to make them feel that they are visiting a friend who happens to be a doctor.

For those of us who like children it is a joy to work with them and for those who do not like children, and who are ill at ease with them, it is hard to develop a manner with children which will deceive their quick instinct and perception. With those who are not happy in their company there will always be a curtain between them and the child which keeps them apart, and prevents the doctor doing all he might for the child. These people would be well to leave children's medicine and surgery severely alone.

Generally speaking, small boys are more difficult and large boys more resistant; small girls are less difficult and older ones more timid and fearful. Occasionally one is completely beaten by a small boy, but seldom by a small girl, and often if one ends the interview and brings them back they have got over the initial and rather unreasoning terror, and in the light of the first experience are more amenable on the second visit.

Very small children often resist examination very forcibly and at times it is necessary to have them held, preferably by a parent, and in this connection it is remarkable how much we can learn without the use of any instrument which seems to terrify them more than a human hand.

Small children respond well to voice, touch, and facial expression, and if they are not hurried will often submit happily enough to examination. If a child has

been frightened some effort should be made before their departure to try and remove the fear and leave a good impression for the next visit to oneself, or to another doctor.

During the war years it was very interesting to see the way in which many Servicemen responded to the civilian approach rather than the more disciplined service attitude. Of course the majority had been civilians before joining a service, but the regulars were very responsive to this approach, possibly being unaccustomed to it, and, as a rule, they did not take advantage of what to them may have seemed softness or weakness on the part of the medical officer, and this was good also in its effects on the doctor who would have to return to civilian practice in many cases when the war was over.

What has gone before is largely a summary gleaned from observation of methods dealing with patients by our teachers, colleagues, and pupils, and a great deal from experience of what has been found best down the years.

Each must find the method best suited to his own particular temperament and ideas, and as it is impossible to measure and delineate such things accurately, it all must remain decidedly abstract.

An appropriate ending might perhaps be from 1st Corinthians (ninth chapter, twenty-second verse) where St. Paul writes: "To the weak became I as weak, that I might gain the weak: I am made all things to all men, that I might by all means try to save some."

THE CONGENITAL HÆMOLYTIC ANÆMIAS

THE MENARY LECTURE

delivered 11th April, 1961

By E. W. HART, M.B.E., M.D., F.R.C.P., D.C.H.

Middlesex Hospital, London

I SHOULD like to express first of all my appreciation of the honour which has been paid to me by this invitation to deliver the Menary lecture.

I have chosen as the title of my lecture this afternoon the "Congenital Hæmolytic Anæmias." Let me be honest and admit that this is a thin disguise for a discussion of Cooley's Anæmia, a condition in which I have been interested for some years. This interest is not wholly academic. There are 45,000 Cypriots living in London and at times I suspect that they are all living within half a mile of my Infant Welfare Clinic at The Middlesex Hospital and are regular attenders. This interest in thalassæmia has therefore rather been thrust upon me.

It is approximately sixty years since the congenital hæmolytic anæmias were first described clinically, but it is only within recent years, however, that we have achieved some knowledge of the basic cell defects which are responsible for the clinical manifestations of these diseases.

This afternoon I should like to discuss three of these congenital or constitutional anæmias: hereditary spherocytosis or acholuric jaundice; sickle cell anæmia or drepanocytic anæmia; and that strangely complex condition which is variously called Cooley's anæmia, thalassæmia, or Mediterranean anæmia. My intention in discussing the first two conditions is to try and use the knowledge which has been acquired about their causation in an attempt to throw some light on the basic defect in thalassæmia.

The constitutional hæmolytic anæmias share many features in common but yet retain certain individual characteristics. There is a marked hereditary factor and often a strong racial tendency. The bone marrow shows marked hyperplasia, and produces defective red cells, often of characteristic type. The survival of the defective red cells is greatly reduced and the increased hæmolysis causes variable degrees of jaundice.

The investigation of these anæmias in the past has been based on the clinical features, and the morphological changes seen in the peripheral blood. Family studies have suggested strongly that the diseases were genetically determined but these studies have been difficult to interpret because of the infinite variations in clinical pattern and behaviour seen in the three anæmias. In recent years the recognition and exclusion of closely allied conditions have made these family studies much easier to interpret.

During the past ten years the discovery of the abnormal hæmoglobins has afforded a valuable method for the further investigation of the constitutional anæmias. The existence of foetal hæmoglobin has been known for almost one

hundred years and is sometimes called "resistant" hæmoglobin because of the difficulty with which it is denatured by strong alkali compared with adult hæmoglobin. In the normal newborn infant over 80 per cent. of the hæmoglobin is usually in the foetal form. After birth the A hæmoglobin gene suppresses the activity of the F gene and the percentage of F hæmoglobin falls to about 50 per cent. at the age of three months. After this time the foetal hæmoglobin disappears rapidly although small amounts persist for many months or even years. Opinions vary as to the level at which this foetal form may persist and figures of from 1-2 per cent. are variously quoted. Higher percentages have been found in patients suffering from hæmolytic anæmias, leukæmia, aplastic and pernicious anæmia. Foetal hæmoglobin is a naturally occurring form and is not an abnormal hæmoglobin although it is usually only found in the young baby.

The development of electrophoretic techniques has shown that many other hæmoglobins may occur in anæmias of special type. Solutions of hæmoglobin are prepared by the hæmolysis of red cells and the removal of the cell envelopes



FIG. 1.

The relative electrophoretic mobilities of hæmoglobin solutions in barbiturate buffer at pH 8.6.

and other proteins. A drop of solution of hæmoglobin is placed on a strip of filter paper kept moist with a buffer solution to control the pH. An electric current is passed along the paper and causes the hæmoglobin molecules to migrate towards the anode. Different hæmoglobins migrate at different speeds and may be separated and identified in this way. Figure 1 shows the different rates of migration of different hæmoglobins in veronal buffer at pH 8.6. The hæmoglobins are conventionally designated by the letters of the alphabet, A being the normal adult form and F the foetal, resistant form. Figure 2 shows strips which have been run to identify some of the abnormal hæmoglobins. A hæmoglobin has been subdivided into A_2 and A_3 components. A_3 moves further on the strip than A, but is probably only a chemical variant. A_2 is a slow moving component of this group and is probably closely related to F hæmoglobin. S hæmoglobin was first discovered by Pauling in patients suffering from sickle cell anæmia and C and D hæmoglobins were found very soon afterwards. Since that time the alphabet is rapidly being filled up with subsequent discoveries. Further separation of the hæmoglobins can be achieved by alteration in pH of the buffer solution or by the use of starch gel or resin column chromatography. Perhaps we could leave the significance of these hæmoglobins in clinical syndromes for later discussion.

I do not propose to deal with the clinical features of these anæmias at any length as I am sure that they are already well known to you.

HEREDITARY SPHEROCYTOSIS.

Hereditary spherocytosis or acholuric jaundice is a chronic familial anæmia often of slight degree with a variable enlargement of the spleen. There is a mild jaundice without bilirubin being present in the urine, and a great tendency to acute crises of hæmolytic with the rapid development of a marked anæmia.

The clinical picture is very often not manifest in early childhood but occasionally symptoms are present during the earliest days of life. I have seen hæmolytic crises as early as two months of age and splenectomy has been performed as early as the seventeenth day of life. The condition must be borne in mind in the differential diagnosis of neonatal jaundice, although it is not often discovered.

Between crises the general health is usually good with only a slight anæmia, icterus and splenomegaly. The crises often appear to be precipitated by inter-current infections and the child becomes feverish and ill; there is increased

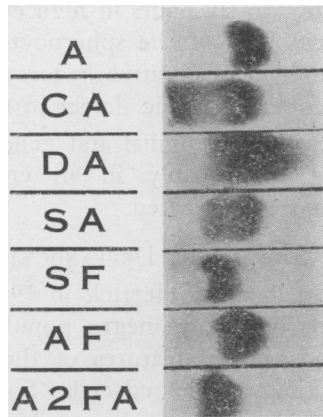


FIG. 2.

Electrophoretic strips showing migration of different hæmoglobins.

jaundice and enlargement of the spleen; and the hæmoglobin falls rapidly because of the increased hæmolytic. The degree of anæmias thus produced may be severe and require blood transfusion, but the average case requires no specific therapy and the stage of increased hæmolytic lasts only a week or two.

The hæmatological findings are those of a mild anæmia with a colour index near to unity but with the red cells showing microcytosis and spherocytosis. The white cell count is within normal limits. The peripheral blood between crises shows a constantly increased reticulocyte count and after a hæmolytic crisis this reticulocytosis may reach 50 per cent. or more, and macrocytes appear in the peripheral blood. The fragility of the erythrocytes in hypotonic saline is greatly increased and this is very characteristic of the disease, although the finding may be variable.

No abnormal hæmoglobin characteristic of the disease has yet been demonstrated although fœtal hæmoglobin is present in excess of normal levels.

Family studies suggest that the transmission of hereditary spherocytosis is by an incompletely or semi-dominant gene. Those who suffer from the disease are probably heterozygous and the true homozygous state is not detectable clinically.

The spherocytes seen in the peripheral blood are thought to be the characteristic cells of the disease and it is believed that they are the result of a defective enzyme system in the cell. It is known that about one-third of the energy output of the red cell is devoted to maintaining potassium in the cell and eliminating sodium. The spherocyte shows potassium depletion and an upset of normal glucose metabolism. There is a defect in the adenosine triphosphate enzyme system in those erythrocytes and therefore a breakdown of the normal glucose metabolism in the spherocyte. In conditions where there is a deficiency of glucose, or competition for glucose, the abnormal cell suffers in comparison with the normal cell, potassium depletion develops, and the cell "spheres" and is liable to destruction. Such conditions are found in the spleen where the red cells normally may be held for four to six hours in high concentration. The available glucose level is low and hæmolysis of the spherocytes occurs. For this reason splenectomy in acholuric jaundice is curative in terms of the clinical symptoms although it does nothing to alter the basic defect in the cells.

Acholuric jaundice is therefore a familial and genetically determined anæmia in which the basic defect is probably in an enzyme system within the erythrocytes, not all of whom are affected.

SICKLE CELL ANÆMIA OR DREPANOCYTIC ANÆMIA.

This anæmia was first described by Herrick in 1910 and the clinical reports have almost entirely been derived from negro populations. The anæmia shows the constitutional, racial and familial features of the congenital anæmias. The diagnostic feature is the sickling of the red cells. Some individuals suffer from the sickle trait and show the characteristic hæmatological features of the disease but suffer little from anæmia or from crises of hæmolysis. They are said to carry the trait or suffer from sicklæmia. The full-blown disease—sickle cell anæmia—is seen more commonly in children than in adults. Patients show progressive or severe anæmia, hæmolytic crises and marked splenomegaly with moderate jaundice. During the crises there is often joint, limb, or abdominal pain and fever. There is increased jaundice and splenomegaly and the anæmia may become profound. The pains are thought to be due to clumping of the abnormal cells in the vessels. Leg ulcers are not uncommon. The hæmatological findings between crises are those of definite anæmia, considerable variation in the size and shape of the red cells with some target forms and macrocytes, and a significant leucocytosis. There is considerable marrow hyperplasia. The typical sickle cell is not seen on examination of the ordinary blood smear but only in wet-drop preparations under conditions of cooling and anoxia, or if the hæmoglobin is reduced by sodium metabisulphite when the erythrocytes assume a sickle or holly leaf form. This characteristic is also present in individuals who carry the trait (Fig. 3, Pl. I). The fragility of the red cells is not characteristically altered. X-ray of the skeleton may show the changes of marrow hyperplasia.

The sickle trait is said to occur in 5-10 per cent. of North American negroes, but in Africa this proportion varies widely from tribe to tribe, the trait being present in 45 per cent. of some communities. In North American negroes about one in forty of the individuals carrying the trait shows the clinical picture of sickle cell anæmia. In 1949 Neel showed that the condition is genetically determined, the S gene being an allele of the A gene. The heterozygous carrier of the gene shows sicklæmia and it is only in the homozygous carrier that the full-blown picture of the sickle cell anæmia develops. In the same year Pauling demonstrated that the abnormal hæmoglobin S is the outward manifestation of this genetic abnormality. In the heterozygote S hæmoglobin is present to the extent of about 22-45 per cent. with the remainder of the hæmoglobin as A but in true sickle cell anæmia the patient who is homozygous for the gene shows 80-98 per cent. hæmoglobin S and the remainder 2-20 per cent. F hæmoglobin. The amount of S hæmoglobin varies from one individual to another, but remains constant for the individual.

The reduced form of S hæmoglobin is much less soluble than the oxygenated form and under conditions of anoxia the hæmoglobin goes into a filamentous gel form. It is this "gelling" which produces the sickle or holly leaf form of the cell and renders them liable to hæmolysis. The sickling occurs intravascularly under conditions where anoxia or stasis occurs and this is probably the cause of the crises of pain which occur in the disease. The hæmolytic crises are often aplastic crises where the marrow ceases to produce cells, normal or abnormal.

Thus sickle cell anæmia is a disease due to a genetically transmitted defect in hæmoglobin formation and the abnormal characteristics of the hæmoglobin in turn produce the clinical manifestations of the disease.

THALASSÆMIA.

Thalassæmia, in contrast to the two previous anæmias, is less easy to fit into a definite ætiological group.

Thalassæmia or Mediterranean anæmia was first described in 1921 by Cooley and the anæmia is often called by this name, despite Cooley's attempts to reject the title. At first it was thought that the disease was confined to individuals from the countries on the north shore of the Mediterranean. However, there have been many reports of the anæmia, or a closely allied anæmia, from India and other Eastern countries and from other parts of Europe, including the United Kingdom.

The congenital and familial aspects of the disease have been well established. Patients can be found who carry the trait and are said to suffer from thalassæmia minor. In contrast thalassæmia major is more commonly seen in young children than adults and they suffer from marked symptoms. Attempts have been made to establish other clinical subdivisions of the syndrome such as thalassæmia minima and thalassæmia intermedia, but these probably represent other genetic variants, and are conditions closely allied to thalassæmia but genetically different.

Thalassæmia minor shows a constant mild anæmia of the hypochromic type in which a lack of full hæmoglobinisation is compensated by high red cell counts,

although the typical hæmatological abnormalities are seen in the blood. Good general health may be enjoyed by these individuals.

Thalassæmia major is more usually seen in young children in whom a progressive anæmia develops with splenomegaly of quite marked degree. The anæmia and splenomegaly may develop in the early weeks of life and the earlier the symptoms appear the more rapid is the deterioration. We have seen the condition suspected at the age of three weeks and fully established by the sixth week of life. Hæmolytic crises are much less evident than in sickle cell anæmia although intercurrent infections seem to accelerate the rate of fall in the red cell count.

In established cases there is a muddy pallor of the complexion and the veins are abnormally visible. The liver and the spleen are considerably enlarged and are firm. These patients develop a characteristic facies which is described as Mongoloid and it has been said that they more closely resemble each other than they resemble their unaffected brothers and sisters (Figs. 4 and 5, Pl. II). The anæmia is progressive although the rate of progression varies widely from case to case, but few of the patients with severe symptoms live beyond the tenth year. In less severely affected patients the disease appears to slow its progression once the patients pass the age of ten. Death is usually from heart failure caused by the anæmia although intercurrent infections are also important. Hæmosiderosis is common and may partly be due to the repeated transfusions.

Hæmatological findings. The red cells show a marked hypochromia and the colour index is low, often 0.6. This feature is in marked distinction to the two other anæmias we have discussed. The red cells (Fig. 6, Pl. I) show marked variation in size and shape and large numbers of macrocytes are seen, large, thin, pancake-like cells poorly filled with hæmoglobin and distorted into the target or Mexican hat forms. There are large numbers of fragmented cells in the peripheral blood, and this, together with the high nucleated red cell count, shows the marked degree of red cell destruction which is occurring. The serum is usually definitely icteric. There serum iron is high (often 400 μ) and the iron binding capacity of the serum protein is low. The erythrocyte fragility in hypotonic saline is reduced and the fragility curve is on a wide base. This together with the hypochromic anæmia is characteristic.

There is marked extramedullary hæmatopoiesis and after some time the skeletal X-rays give evidence of this. The marrow spaces are wide and trabeculation is seen. In the skull there may be marked spiculation over the vertex (Fig. 7, Pl. III).

There is no treatment for the disease other than symptomatic. Although the disease is a hypochromic anæmia, iron therapy does nothing to slow the inevitable progression of the anæmia, or to lengthen the interval between the transfusions which become necessary to maintain life. The inherent defect in hæmoglobin synthesis prevents the use of the available iron. This patient is really living on transfused blood. The place of splenectomy in the disease has been the subject of controversy. In hereditary spherocytosis the cell destruction takes place largely in the spleen and splenectomy effects a clinical cure. In thalassæmia

the destruction of the abnormal red cells takes place elsewhere and may indeed take place in the marrow at the time of their formation. We had noticed the considerable variation in the size of the spleen before, during and after transfusion in some of the more severe cases requiring transfusion at intervals of a few weeks. This suggested that the spleen might be showing a secondary hypersplenism and negating the benefit of the transfusions. We have carried out splenectomy in four cases, but, as the slides show, without any convincing evidence that splenectomy has greatly lessened the frequency of need for transfusion (Fig. 8). There is, however, some evidence that splenectomy may be beneficial to some degree.

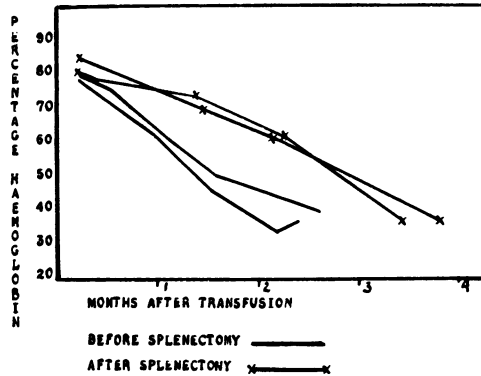


FIG. 8.

Showing response in thalassæmia to transfusion before and after splenectomy.

It is our impression that the treatment of any chronic focus of infection is of great benefit and in one case tonsillectomy seemed to confer a greater benefit than subsequently did removal of the spleen.

These patients require frequent transfusions and, especially in the younger children, this may create a great technical difficulty over veins. Intraperitoneal transfusion offers great advantages in this type of case. We have had an opportunity of seeing the peritoneal cavity of a child one week after an intraperitoneal transfusion of blood in an amount equal to one-third of the blood volume. At operation the peritoneum looked normal and all the blood had been absorbed. We have transfused blood intraperitoneally on ten occasions in one case, and on eighteen occasions in another patient. Absorption of the transfused blood continues satisfactorily in successive transfusions.

The prognosis in these cases without transfusion is very grave and if transfusion is required in the first two years of life the prognosis is virtually hopeless. In general, there appears to be an optimum hæmoglobin level at which these patients remain comfortable but above which the hæmoglobin level cannot long be retained. It is useless to transfuse above this level. Although it is believed that thalassæmia is genetically transmitted and that thalassæmia minor represents the heterozygote and thalassæmia major the homozygous carrier of the gene, the inheritance is not so clearly defined as in sickle cell anæmia. This slide shows

the familial nature of the anæmia (Fig. 9, Pl. IV). No characteristic abnormal hæmogoblin has been demonstrated although thalassæmia major patients have up to 80 per cent. of their hæmoglobin in the foetal, alkali resistant form. One of our cases of thalassæmia in a Persian boy aged 15 produced 79 per cent. F, 12 per cent. A₂ and only 9 per cent. of normal adult A hæmoglobin. Thalassæmia intermedia and minima do not fit well with this conception of transmission by a recessive gene, unless it is one with a very variable expression or unless there are several variants of the thalassæmia gene. The latter theory seems not improbable. In thalassæmia there is no special hæmoglobin which differentiates the condition from closely allied states. The presence of high percentages of hæmoglobin A₂ marks out some cases of thalassæmia from the rest.

Wide clinical variations are seen in the combination of the thalassæmia gene with other genes responsible for the production of abnormal hæmoglobins. Individuals who are heterozygous for hæmoglobin S or C, when simultaneously heterozygous for the thalassæmia gene, produce a clinical syndrome which is different from the picture seen with either of the genes separately or the homozygous state of either gene.

This combination of two genes, each inherited independently in the heterozygous state, sometimes produces much larger amounts of the abnormal hæmoglobin than in the heterozygote—so-called “interacting” thalassæmia. In thalassæmia-S anæmia the proportion of S hæmoglobin may be about 70 per cent. instead of the 30-40 per cent. usually seen in sicklæmia. This enhancement of the production of the abnormal hæmoglobin by the thalassæmia gene is not invariable and, together with the high level of A₂ in the homozygote, is a useful differentiation between “true” thalassæmia and closely similar conditions.

Another point of interest is the poor hæmoglobinisation which occurs even in the presence of high levels of serum iron.

The failure of real benefit from splenectomy suggests that the anæmia is due to a central defect and not to a peripheral destruction.

It has been suggested that in thalassæmia there is a marked destruction of red cells in the marrow at the time of formation as if the cells were too defective ever to reach the circulation. Alternatively, it has been suggested that the defect is a failure or inhibition of the A gene. The production of F or A₂ hæmoglobin is, therefore, a compensatory mechanism to hæmoglobinize the cells with a less efficient substitute. In thalassæmia-S syndromes the enhancement of production of S hæmoglobin suggests that this is easier to produce than F. Whichever of these reasons is the true one, it would appear that the basic defect in thalassæmia is genetically determined and that a defective cell is produced, the defect probably being in hæmoglobin synthesis without the production of a specific abnormal hæmoglobin.

These three anæmias, which show closely similar clinical syndromes, represent three distinct modes of production of red cells.

Much of what I have said remains speculative but I hope that it has not been too tedious for you to wander with me in the realms of speculation.

I wish to thank the Photographic Department of the Middlesex Hospital for the illustrations.

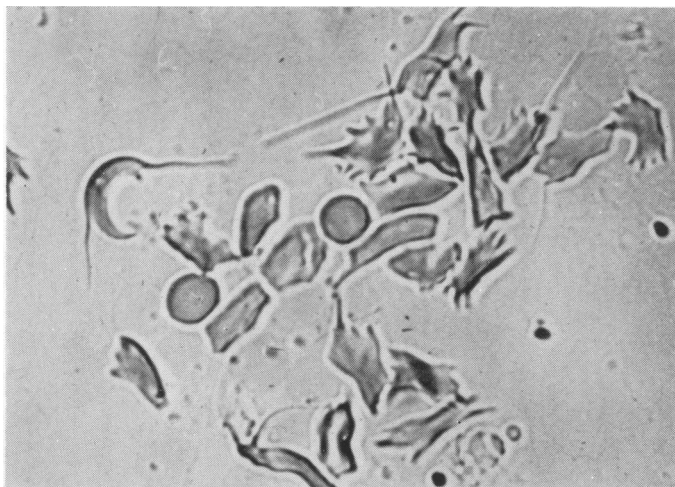


FIG. 3.
Blood film in sickle-cell anæmia.

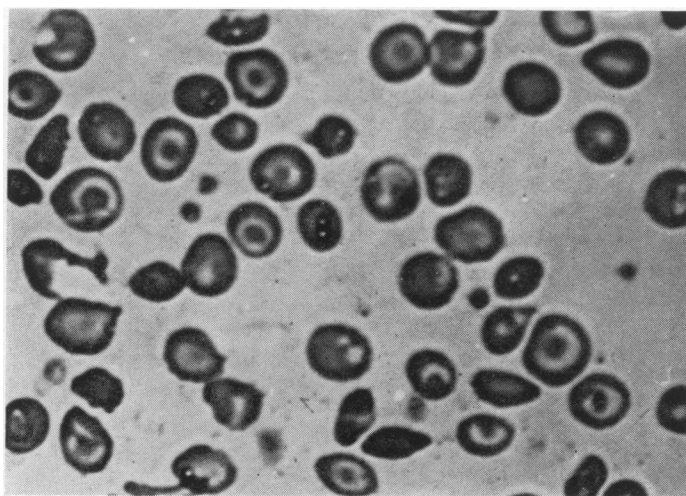


FIG. 6.
Blood film in thalassæmia showing target cells.

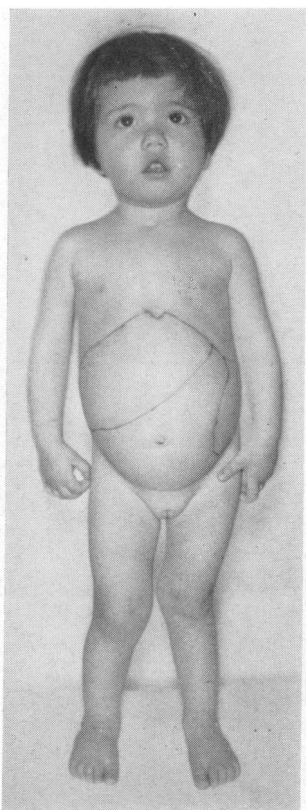


FIG. 4.
Facies and enlargement of spleen
and liver in thalassæmia.



FIG. 5.
Facies in thalassæmia.

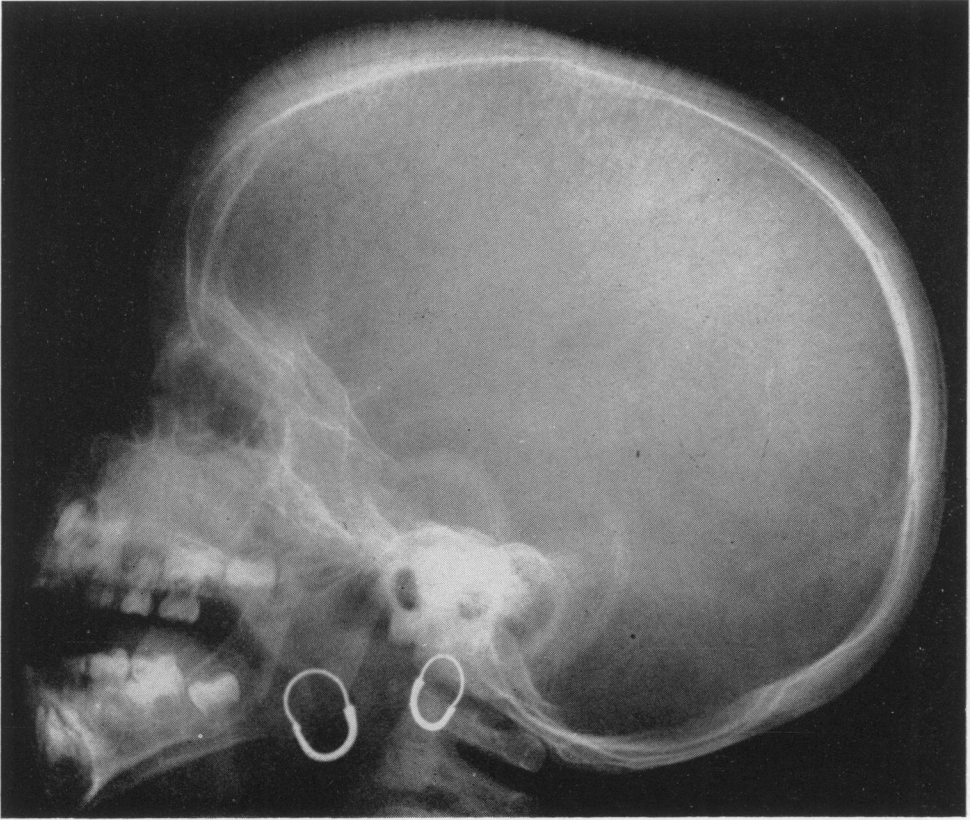


FIG. 7.
Skull in thalassæmia.

PLATE III

THE CONGENITAL HÆMOLYTIC ANÆMIAS

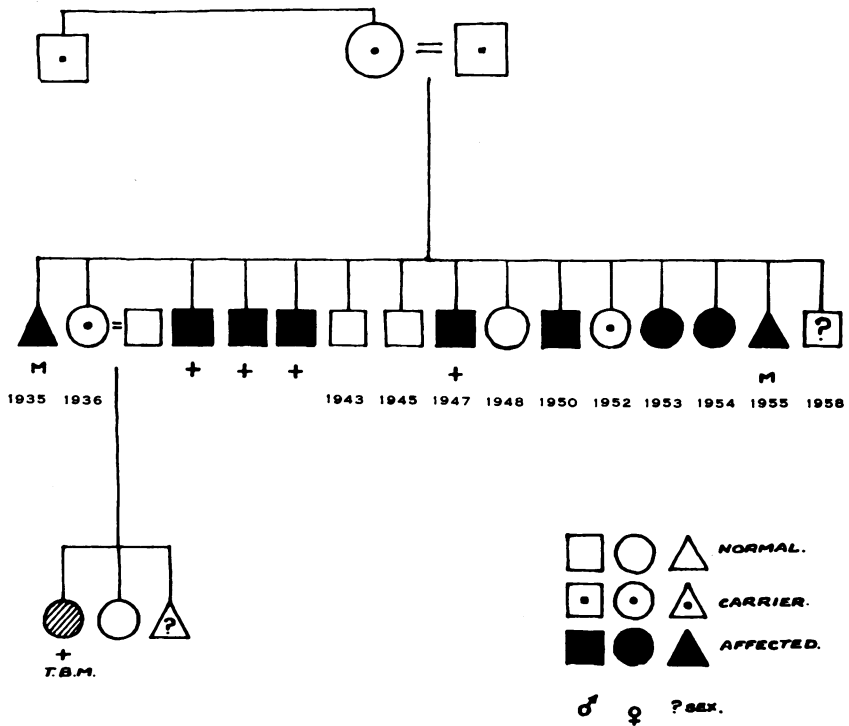


FIG. 9.
The familial inheritance of sickle-cell anæmia.

SCIENCE AND THE PROGRESS OF MEDICINE

By M. G. NELSON, M.D., F.R.C.P., F.R.C.P.(I), D.T.M. & H.

OPENING ADDRESS OF THE WINTER SESSION

Royal Victoria Hospital, 10th October, 1961

"A Physician is the Minister and Interpreter of Nature: . . . unless he obeys Nature, he cannot govern her."

—BAGLIVI.

MAN has, since prehistoric times, sought to explain the natural phenomena of the world in which he lived in terms which he found most easy to understand.

What we call the scientific discipline was evolved as a purposeful and basic method which made it possible to give unity and intelligibility to the facts of nature. This method utilises observation, measurement, reflection, and experiment. When first applied in the natural sciences, knowledge quickly followed, for the problems in these fields could be readily confined and the environmental factors controlled.

The situation in the biological sciences was less simple, but in none of the branches of this science was it as difficult as in medicine. Here human beings were involved who were incapable of complete isolation from both their external and internal environments and because of the claims of ethics precluded from experiment.

If we trace the application of the scientific discipline to medicine, we will see, nevertheless, how it has been responsible for much of the progress which has been made. We will also see how this has led medical men to seek to explain first the structure, then the function, and lastly the dynamics of the human body. At the same time, as the tools and technology of science improved, it became possible to study progressively smaller sub-units. First the body, then the organs, then the cells composing the organs, and lastly the intracellular components.

I wish to present the growth of medicine under the influence of science, to deal with ideas and principles rather than details of practice, and to take examples to illustrate the more recent advances from that branch of medicine with which I am most familiar—namely disorders of the blood.

A thousand years before the birth of Christ western medicine began in Greece. At that time the supremacy of Grecian culture was built on its serenity, its scholarship, and its spirit of freedom. Its medicine was originally a mystical cult derived from the rites of initiated sects and practised in the temples of Æsculapius. The physicians were priests who interpreted the dreams of patients admitted to the temples and supplemented these by clinical observations. Prayer and sacrifice were part of the ritual and the sacred snake was the emblem of healing.

Some two centuries later, in the time of our founder-father Hippocrates, medicine freed itself from religious domination and the dual rôle of priest-doctor, common in all primitive cultures, was broken. As a consequence, superstition and magic, as a cause of disease, were rejected. Hippocrates, for instance, said of epilepsy, long regarded as of supernatural origin, "It is not, in my opinion, any more divine or sacred than other diseases, but has a natural cause."

The writings on Greek medicine of this period are preserved in the *Corpus Hippocraticum*, a collection of works which include books on anatomy, on clinical medicine, and on ethics. A wit once said, regarding the poems of Homer, that they were not written by him but by another man of the same name. This might likewise apply to the Hippocratic writings, for during the period that the collection of works were written, there were seven physicians who bore the name of Hippocrates. It is generally agreed that the Father of Medicine was Hippocrates the Second.

For those about to embark on a study of medicine, Hippocrates had this to say, "He who wishes to acquire exact knowledge of the medical art, should possess a natural disposition for it, should attend a good school, should have a desire to work, and the time to dedicate to his studies."

Although Greek medicine has always been regarded as an empirical art, it recognised the necessity for a wide knowledge of the natural sciences, the need for keen observation, and a logical process of reasoning. It took as its aim the alleviation of suffering by the utilisation of the natural forces of the body. Thus under the influence of Hippocrates, medicine became a clinical science and no longer a mystical cult.

As the centuries passed, the purity of the Hippocratic code was debased by a dogmatic superstructure which was founded on the shifting sands of speculation rather than the solid rock of observation.

It was the scholars and artists of the Renaissance who restored observation into both art and science.

Modern medicine was born in the anatomical amphitheatre of the old University of Padua. It was here that Andreas Vesalius, the brilliant young Professor of Anatomy, carried out his public dissections and taught his students. In the year 1543, when he was 28 years of age, he published his great book—*De Humani Corporis Fabrica*. This book is an object lesson in scientific writing, not only for its correct observations and valid deductions, but also for the excellence of its illustrations. In this book Vesalius corrected many errors which existed in older text books of anatomy and flatly contradicted statements made by Galen. As a result, he was angrily attacked by all the leading medical scholars of his day who branded him a presumptuous upstart. Being of a sensitive nature, Vesalius was so upset he impulsively resigned his Chair of Anatomy, burned all his collected notes and left Padua for ever to become a court physician.

"*De Humani*" was the foundation of an accurate study of the structure of the human body—the first of the medical sciences. There are, no doubt, some in the audience who would consider that historical priority has been responsible for anatomy being given such importance in our undergraduate medical curriculum.

At the same University of Padua, Fabricius, successor to Vesalius, taught Harvey the basic scientific precepts which enabled him to make his momentous discovery—the circulation of the blood. The publication, in 1628 by Harvey, of his treatise “De Motu Cordis” was the beginning of a scientific study of normal bodily functions. The practice of medicine cannot, at that time, have been very scientific, for a contemporary and namesake of Harvey classified the physicians of his day into:

- Metal doctors—who cure all diseases with preparation of iron and copper.
- The medical ass-drivers—who put all their patients upon a diet of asses’ milk.
- The medical water-bailiffs—who drench their patients at the mineral springs.
- The butcher doctors—who always bleed their patients.
- The muck doctors, illustrious in their numbers—who expel diseases by purgation.

Nevertheless the seventeenth century was a period in English history during which mythology, astrology, witchcraft, and the acceptance of ancient writings were all coming under careful and critical scrutiny. The Reformation had introduced a challenging spirit which stimulated personal investigation and respect for the individual conscience.

Once anatomy and physiology had been established, knowledge was needed about the body in disease. This gap was bridged in the eighteenth century by another gifted member of the staff of the University of Padua—Giovanni Battista Morgagni. He performed an enormous number of post-mortems and kept careful case records. Shortly before his death the results of his studies appeared in a work entitled—“On the sites and causes of disease,” in which he established a correlation between the symptoms during life and the appearance of the body organs after death. This concept is still utilised to this day by every doctor who attempts to explain the symptoms of disease in terms of a lesion in the body organs.

Although we have become ever more accustomed to think in terms of organ pathology, we must widen our horizon to include pathological processes in body tissues. This idea was put forward by the great doctor Brissaud, it helps us to understand many widespread diseases with bizarre clinical manifestations, e.g., such diseases as affect the blood-forming organs can only be explained on the basis of a disorder, not of a single organ, but of a widespread body tissue.

This, then, was the beginning of the science of disease processes. It was at first morbid or pathological anatomy—a purely naked-eye descriptive discipline. As knowledge grew, it became evident that some new and unifying idea was needed. This came with the concept of the cell as the ultimate basis of life—as the biological unit of both structure and function. This advance was made possible by discoveries in other fields—in optics and in chemistry—by the introduction

of the compound microscope and the aniline dyes. Now fixed tissues could be stained and examined in detail under the microscope. Such studies revealed specific and identifiable inner structures within the cell.

The application of the cell theory to disease in man was largely the work of Virchow. In his studies of diseased tissues, he utilised the cell theory to explain what he found. He regarded disease, not as a disturbance of the bodily humours, as depicted by Galen, but as a malaise affecting the individual cells of the body organs. "To understand disease," he said, "we must study the organisation of these cell states, and the differing forms of harmony, anarchy, and revolution to which they are prone." This established the field of correlation, not only between the clinical symptoms and the affected organ, but between the disease and the microscopical changes in the cells.

This marked the beginning of the period of the intellectual supremacy of German scientific thought; a period which had as its aim the unravelling of the mystery of the smallest biological subunit using chemistry as its main tool, and microscopy as its probe. It laid the foundations of histology, histochemistry, and cellular pathology. It paved the way to the science of microbiology and to the discovery of the causes and control of infective disease.

The "cell states, where every cell is a citizen," pictured by Virchow, prompted others to study the individual body cells more closely. Among the cells which were so studied were those of the blood. This was a fluid invested with magical properties and around which highly speculative theories had been built. Now the opportunity presented itself to draw aside the veil and to penetrate the mystery.

The red cells had been seen by the discoverer of the microscope, the draper of Delft, Antony van Leewenhoek, a man with no preconceived ideas, but a keen observer. He described his findings in a communication to the Royal Society of London in 1674 as follows:

"I have diverse times endeavoured to see and to know what parts the blood consists of, and at length I have observed taking some blood out of my hand, that it consists of small round globules driven throught a crystalline humidity of water."

But the time was not ripe for men of science to accept microscopy as a technique of practical application in medicine, largely because physiological and biochemical knowledge was inadequate to allow the technique to be exploited.

The difficulties are best expressed in the words of a nineteenth-century worker, Hewson, who said:

"When we consider how many ingenious persons have been employed in examining the blood with the best microscopes, it will appear wonderful that the figure of these particles should have been mistaken. But our wonder will be lessened when we consider how many obvious things are overlooked until our attention is very particularly directed to them; and, besides the blood in the human subject is so full of these particles that it is with great difficulty we can see them separate unless we find out a method of diluting the blood. It is to such a discovery that I attribute my success in this

inquiry for, having examined the blood as it flows from the vessels of the human body, it appeared a confused mass. I spread it thin on a glass. . . . It then occurred to me to dilute it, not with water, for this I knew dissolved the particles, but with serum, in which they remained undissolved. With the serum I could dilute it to any degree, and therefore could view the particles distinct from each other. In these experiments I found that these particles of the blood were as flat as a guinea. I likewise observed that they had a dark spot in the middle which Father de la Torre took for a hole. But upon careful examination I found it was not a perforation, and therefore, that they were not annular.”

This was an important contribution to knowledge reported in lucid prose. The prose has a poetic ring—a personal quality—and is at the same time precise. Today somewhat stereotyped scientific publications are pouring from the presses of the great printing houses. Their lack of individuality in both method of presentation and style of writing results in a somewhat standardised product which is the hallmark of our age.

The recognition of the cells in normal blood and their relative proportions was the first step. Further progress had to await the application of staining techniques which were already in use in general pathology. The person who applied these methods to the study of the cells of the blood was Paul Ehrlich, regarded by many as the greatest scientific worker in medicine in the past century and by all as the Father of Hæmatology.

Whilst still an undergraduate, Ehrlich wrote a paper on the use of aniline dyes for staining and elaborated a chemical theory to explain why the different tissue elements were selectively stained. He then proceeded to stain and to describe the cells of the blood. This was the golden key which unlocked the door to progress in hæmatology. “Hæmatology at once threw off its colourless shackles and dazzled its devotees with dazzling colours.” Many were attracted to a study of disorders of the blood by the beauty of the stained preparations. It is interesting to record that Dr. J. Rankin, a former member of the staff of this hospital, worked in Ehrlich’s department, and helped to introduce his staining methods into our laboratory practice here.

Paul Ehrlich had introduced the era of descriptive hæmatology and out of the polemics and publications of this period there gradually emerged an idea of order—the first of the basic ideas central to science.

One of the cells described by Ehrlich was the megaloblast—a red cell precursor found in the blood and bone marrow of patients with pernicious anæmia. This cell was peculiar because it had an abnormal nuclear structure. Why it was abnormal was not understood, but in science “the study of things caused precedes the study of the causes of things.”

The discovery of the cause of this megaloblastic change marks the next step. It introduces the era of pathophysiology which attempts to explain the mechanism responsible for structural alterations. In the early part of this century, European hæmatologists were engrossed in blood cell structure. But in the New World

there was a different approach. The scientific method was being applied by clinical investigators.

Following the experimental demonstration of the beneficial effect of liver treatment on the hæmorrhagic anæmia of dogs, the effect of a diet of liver was tried empirically on pernicious anæmia patients with dramatic effect. In the following year, in the records of this hospital, it was reported that—"Dr. Houston had carried out a therapeutic trial of liver extract in the treatment of pernicious anæmia, an outcome of the work of Minot and Murphy of Boston, and reported on the revolution this treatment has produced in pernicious anæmia." This was but one of many contributions Sir Thomas Houston made to medicine. He was appointed as hæmatologist to the Royal in 1905, and this antedates by many years any similar hospital appointment anywhere in Great Britain. He was, during his long working life, the father-figure in hospital laboratory medicine and saw it develop from the obscurity of a back room to an important diagnostic service. His personality and achievements live on in the memory of those who knew him and his likeness is preserved for future generations in the fine portrait which hangs close to the laboratory in which he worked.

The discovery of liver treatment revitalised hæmatology. It placed the emphasis on disturbed function rather than disordered structure. It started a search for the active factor in liver which was curative in pernicious anæmia. Finally, research chemists discovered a red-coloured cobalt-containing substance which, in minute doses, was effective in pernicious anæmia patients. Vitamin B₁₂ had been isolated. Here was a substance which changed abnormal blood cells back to normal, which restored the distorted nucleus of the red cell precursors and cured the clinical manifestations. In this age of therapeutic miracles, we tend to accept such an event with little excitement. Yet this discovery was of profound significance. It demonstrated how a single chemical substance could restore both the structure and the function of pathological cells in the living body.

The chief function of Vitamin B₁₂ is to act as a cell nutrient to assist in the synthesis of protein. The blood is a fairly sensitive barometer of the deprivation of such necessary raw materials. This is due to the fact that the cells of the blood-forming tissues are in a constant state of active division. To maintain a steady cell population in the peripheral blood the bone marrow has to produce enough cells each day to replace normal losses from wear and tear. This means an output of nine thousand million cells every hour of the day and night. This phenomenal production effort cannot be maintained unless the essential components—the cell nutrients—are supplied. The main cause of deficiency is a long-continued interference with absorption from the intestinal tract. This is what occurs in pernicious anæmia. As a result, protein synthesis in cells is impaired. This affects particularly the formation of nuclear protein. As a result, the nuclear structure of red cell precursors is abnormal and this can be recognised under the microscope.

The red cell precursors in the bone marrow continue to divide, but do so in a frenzied and disorderly way. The output of distorted mature cells is insufficient to maintain the cell population of the peripheral blood. The mature cells

which are produced under these circumstances are functionally impaired. They are rapidly destroyed by the buffeting they sustain in the blood stream and survive only for a short time. The result is a severe form of anæmia—a form of anæmia which was called “pernicious” because it used to have a poor prognosis for the patient. But pernicious anæmia is no longer “pernicious” for it is entirely controllable by the constant administration of adequate amounts of Vitamin B₁₂.

Thus the recognition of an abnormal red cell precursor by Ehrlich, the demonstration of the cause of this change by the therapeutic effect of liver, the chemical isolation of the potent factor in liver have led us, step by step, to the basic biochemical defect responsible, not only for the structure change, but also for the functional disturbance affecting the cells in this disease.

The living cell has a body composed largely of protein with which are associated many enzymes. These enzymes promote the biochemical processes within the cell. But the cell is not just “a fermentation vat.” It is a “highly organised chemical factory with elaborate assembly lines,” which continuously convert raw materials into food and energy. These metabolic functions of the cell are programmed by the nucleus.

It has now become commonplace to seek some disturbance of intracellular metabolism as the cause of disease. In the elucidation of these problems the biochemists have brought their special skills to bear. Of the many metabolic processes which occur within a living cell, two are essential and basic. These are self-perpetuation and auto-regulation.

Self-perpetuation implies the ability of the cell to reduplicate itself to the last ultimate detail. The transmission of distinctive characteristics to daughter-cells during the process of cell division is a property of the genes.

One of the normal characteristics which is transmitted in this way is our blood group. This follows a rigid pattern of inheritance. Consequently knowledge of blood groups is of value to the geneticist in family studies and in the frequency association of certain diseases. As blood groups are relatively stable inherited traits, they are passed on from one generation to the next in the same proportion. As a consequence, blood group distributions can be used by the anthropologist in population surveys. Such a study carried out in Cyprus showed that the blood group pattern of the two main racial groups was similar, suggesting a common ethnic origin. Cypriot Greeks and Cypriot Turks, whatever their political affiliations, would appear to be brothers under the skin. Apart from these applications, knowledge about blood groups is of great practical importance in making blood transfusion possible and safe.

It has been shown that blood groups are highly complex and human red cells possess a large number of blood group systems. At first it was thought that blood group substances were found only on red cells. It was some time before it was realised that these antigens were to be found in cells widely distributed throughout the body. As a result we have come to recognise that the surface of all cells is a mosaic of chemical compounds intimately bound to the underlying protein. Their number and complexity suggests that each one of us has a cellular chemical composition which is as individual as our thumbprint.

Blood groups are normal characteristics and are transmitted by normal genes. But the genes can be altered either by spontaneous mutation or by physical, chemical or biological agents. Such defective genes will transmit the wrong kind of information. There is, for instance, a gene responsible for the shape of the red cell. Normal human red cells are biconcave discs but if the genetic determinant is abnormal the red cells may be oval or spheroid in shape.

The appearance of genetically induced spherocytic cells produces a well-recognised congenital and familial form of hæmolytic anæmia. A nineteenth-century worker said of the red cells in this disease, "The sphericity and the small size are the dominant characteristics. When these red cells pass through the splenic pulp they fall into obsolescence, being taken away from the active circulation."

Occasionally a somewhat similar but sporadic form of hæmolytic anæmia also occurs in adults. At first the cause of this type of acquired hæmolytic anæmia was thought to be some unknown intrinsic red cell defect. Experimental work showed that the defect was not in the red cell, but was in the plasma. An important link in the chain of evidence was forged when it was demonstrated that experimental hæmolytic anæmia could be produced in animals using an anti-serum prepared against their red cells. It was then postulated that a similar mechanism might be responsible for hæmolytic anæmia in man, but here the antibody must be self-produced. This introduced the idea of auto-immune diseases.

The possibility of autoimmunity has been strenuously opposed. Paul Ehrlich referred to it as the "Horror Autotoxicus," and said, "No living organism would be capable of producing—or would dare to produce, if you wish—an antibody against constituents of its own body, for this would be incompatible with life." It seems, on the face of it, a great biological mistake for the body to be capable of elaborating antibodies against its own cells. For normal body cells are considered to carry, among their antigenic material, a 'self marker' which enables the antibody-producing tissues to recognise its 'self.' However, it is now known that the 'marker' can be defaced either by chemical additions, by adherent virus particles or by the products of disease, so that it becomes 'non self.' It is then treated as foreign and stimulates an antibody response.

The whole theory of autoimmunisation has been extended to explain the mechanism for a number of diseases. Indeed, it may be found to be a basic biological process in the genesis of malignant disease.

While one essential function of a cell is a gene-dominated process of self-perpetuation, the second basic function is auto-regulation. By this we mean the ability of the individual cell to regulate its own complex biochemical processes by some built-in, self-monitoring system. This is so organised that the cell is capable of maintaining its functional stability even in the face of highly destructive forces.

In the investigation of disorders of intracellular metabolism, the biochemist has been greatly helped by the introduction of radioactive tracers which can be used as 'labels' to allow the process to be closely followed at every stage. But radioactive isotope tracers are not just research tools, they have become part of our

diagnostic armamentarium. In the field of isotope work a number of specialists from different disciplines are brought together. Clinicians, chemists, and physicists work as a team to attack the biological problem on a broad basis. In both medical research and medical practice this type of scientific teamwork forms the prevailing pattern.

In 1845 Virchow published a case report of a patient with what he called "white blood" as microscopical examination showed the blood to consist mainly of white corpuscles. He had, in fact, described a case of leukæmia. Although Virchow recognised leukæmia as a definite pathological entity, he himself admitted that this was not the first case to be observed. Many years previously Velpeau had reported a patient, a 63-year-old florist and seller of lemonade, . . . "who had abandoned himself to the abuse of spirituous liquor and of women, without, however, becoming syphilitic." This man had an enormously enlarged liver and spleen and blood which, because of the number of white cells, resembled gruel.

Leukæmia is a disease, like cancer, in which there is a purposeless and progressive proliferation of primitive blood cells which grow at the expense of other body cells and regardless of their needs. "The fundamental cause of leukæmia is to be sought in the larger mystery of the cause of cancer."

The treatment of leukæmia has been approached in a number of different ways. As the disease is associated with rapid cellular multiplication, it is possible, by using ionic radiation as X-rays or radioisotopes, to inhibit cell division. This method of attack has been successful, both in cancer and chronic leukæmia.

The disease called 'acute leukæmia' is greatly dreaded because of the rapid and often insidious generalisation of the leukæmia process. To treat this form of leukæmia with ionic radiation would require the widespread application of a heavy dose to the whole body. In the process of attempting to kill the malignant cells it is more than likely that normal body cells would also be damaged. The most susceptible body cells are the blood cell precursors in the bone marrow, which might be damaged beyond the point of spontaneous repair. It was suggested that it might be possible to treat patients with acute leukæmia by massive radiotherapy and then to transplant bone marrow from healthy donors. This would kill the malignant cells and provide blood-cell forming tissue. Preliminary experiments on leukæmic animals treated in this way supported this view. This method of treatment has been carried out on a number of patients. So far success has not been achieved either because the transplanted marrow has failed to survive or because the malignant cells begin to grow after a period of suppression. The failure of the transplanted marrow homograft to grow is explained by the fact that (apart from identical twins) the cells of two people are unlikely to be identical. The donor cells are regarded as 'foreign' in the body of the host and are rejected. The reactivation of the leukæmic process after its apparent disappearance would suggest that the potentiality for malignant change must reside in the most primitive precursor cells which are not affected by the radiation.

This is the chemotherapeutic age. It was ushered in by no less a person than Paul Ehrlich, who discovered a chemical compound which would cure syphilis.

This antisyphilitic organic arsenical prompted the testing of other antibacterial and antiparasitic substances. The chemists were not long in producing first the sulpha-drugs and then the antibiotics—an ever-increasing cloud of compounds varying in specificity and range of activity. The present chemotherapeutic era has been highly successful in controlling infective diseases. Its application to non-infective disorders is not so simple, for the cells being attacked are not dissimilar organisms but modified body cells. If chemotherapy is to be successful in the treatment of leukæmia, the antileukæmic agent must have a selective action on leukæmic cells. It has been shown that leukæmic cells differ in their metabolism from normal cells. This makes it possible to develop agents which act solely or mainly on the malignant cells and spare the normal body cells. These agents act by inhibiting the biosynthesis of certain essential cell nutrients. They have a close chemical resemblance to some known biological substance such as a vitamin, a hormone or a building stone of nuclear protein. They behave somewhat like a false key which, although it fits into a lock, cannot open it. So the antileukæmic drug 'may fit into some biological binding site and displace some natural substance without being capable of fulfilling its function.' This deprives the cell of an essential metabolite and the drugs are therefore called antimetabolites.

Chemotherapy of leukæmia is not always successful. In some forms of the disease the results achieved are most gratifying while in acute leukæmia temporary control is possible, but we cannot talk in terms of cure. Nonetheless, the introduction of antileukæmic agents has increased the eventual hope of cure.

In the search for the causes of disease, attention is being more and more directed towards the chemical components which form the structure of our body cells. Research workers have tackled the difficult problem of unravelling the mystery of the molecules of living cells.

The main protein constituent of the human red cell is the red-coloured compound hæmoglobin. The production of hæmoglobin is under genetic control and a faulty gene may transmit the wrong information for hæmoglobin synthesis. This may result in some or most of the hæmoglobin in the red cells being different from normal. This abnormal hæmoglobin may have deleterious effects on the survival of the red cell and lead to anæmia.

For instance, an abnormal hæmoglobin, called sickle-cell hæmoglobin, has a tendency to 'crystallise' when the oxygen tension is lowered. This distorts the red cell and makes it a sickled shape which impairs its survival. Furthermore, the sickled cells stick together, and cause vascular obstruction. This causes a form of hæmolytic anæmia which is common in the negro race.

Research workers set out to discover why hæmoglobin S differed from normal adult hæmoglobin. It was found that when normal hæmoglobin and hæmoglobin S were chemically tested, they were similar. However, when subjected to physical testing they differed. Further analysis of hæmoglobin S showed that the protein component was comprised of the correct number of aminoacids but the sequence of the units was different. They had different polypeptide chains. This did not affect the chemical composition but changed the physical response. Studies on other variant forms of hæmoglobin have shown specific changes in the polypeptide

chains of the protein part of the hæmoglobin molecule and that these abnormalities are genetically determined. This major break-through in biochemical genetics would not have been possible without the help of the sister sciences of physics and chemistry.

While the delineation of diseases which are due to genetic abnormalities is a first step, what is of fundamental importance is to discover how the gene transmits the information from one generation of cells to the next. Work carried out in the mid-twentieth century has shown that genes control the intracellular enzymes responsible for the metabolic processes. Furthermore, it is probable that there is one gene for each enzyme. Thus in the cell, each working enzyme has its own gene as a personal executive. This theory has been made much more specific by the studies on variant hæmoglobins for these have shown that the gene determines something more fundamental, namely the aminoacid composition and sequence in proteins. Thus the 'one-gene, one-enzyme' theory has had to be replaced by the more specific 'one-gene, one-protein' theory.

It was reasoned that the chemical structure of the gene could not be a complex of small molecules as otherwise its properties would depend on the average behaviour of its components. The gene must be a single large molecule. This would ensure stability and permanence. Gradually the chemical structure of the gene has been elucidated. The genetic substance is in the nucleus. The nucleus contains a protein called, for convenience, 'nucleic acid.' This nuclear protein consists largely of desoxyribonucleic acid. This D.N.A. is a long chain-like structure made up of thousands of sub-units which are linked together. These sub-units in their turn are composed of four different aminoacids which are arranged in varying combinations. The chemical coding of hereditary information is written in the sequence and order of the aminoacids in the D.N.A. chain.

The genes are the basic material responsible for both the chemical make-up and the functional integrity of our body cells. Scientists have perfected means of studying the gene carriers or chromosomes of the cell nucleus. They have correlated the number of chromosomes and their pattern with disease states. Already in this field of cytogenetics many exciting discoveries of clinical importance have recently been made.

What lies in the future is the more difficult problem of localisation of each gene on the nuclear chromosomes. When this has been done it should then be possible to isolate and analyse the genes and decode their chemical information. We will then be moving towards the ultimate in biological engineering which is to manufacture man-made genes with synthetic D.N.A. so as to provide the cell with its correct chemical code. This is, at the moment, still in the realms of science fiction, but may well become scientific fact.

In this presentation of the effect of science on medicine I have used a broad canvas, but I have not tried to paint a picture which is complete in every detail. I have, instead, attempted to obtain perspective on the subject by the presentation of an outline. The very fact that strong hæmatological highlights were used suggests some degree of conscious bias.

It can, nevertheless, be appreciated how knowledge in medicine has progressed from speculation to observation; from detailed description to clinical correlation; from appreciation of disturbed form to understanding of disordered function; from theories of causes to their proof by experiment or by clinical experience. These advances have followed the application of the scientific method which changed medicine from an empirical art into a biological science.

Modern men of science differ from medieval scientists and ancient philosophers, for it has become essential, in science, to separate off circumscribed areas of the universe for special consideration—for scientists to become chemists, physicists, astronomers, botanists, physicians, and so on. By doing this, the modern scientist tends to base his experience of the world “on an artificially separated fragment of experience.” The somewhat condensed version of the evolution of medicine which I have attempted is likewise far from complete. Its very orientation tends to present man as a colony of cells and knowledge of disease as being explicable on an understanding of disturbances of cell function. This is far from the truth. Nevertheless it is clearly apparent that a summation of knowledge of what is happening at the cellular level will eventually help us to understand more about the diseases which afflict man.

To study disease requires not only an investigation of the patient as a whole but also the disturbance of the cells of which he is composed. Consideration of one without the other is as illogical as trying to separate the theory of medicine from its practice.

Throughout the changing years medicine has been practised by men of wide culture and a strong sense of vocation; by skilled physicians whose limitations were those imposed by the available knowledge in their time. Chaucer, for instance, describes the Doctor in the Pardoners' Prologue as one who “was a very parfait practisour, the cause he knewe and of the cause the roote.” Even at the beginning of this century, knowledge about disease and its treatment was limited. Today the picture has changed. Knowledge has increased, highly complex instruments to assist in diagnosis and management are in daily use, therapeutic agents are more effective, and intricate biological techniques are being increasingly utilised. Science has permeated the very fabric of modern medical practice.

Medical men of every generation have been tempted to look back with pride on the progress which has been made in their time. The form of words used is strangely evocative. Listen to what Osler said in his day:

“Never has the outlook for the profession been brighter. Everywhere, the physician is better trained and better equipped than he was twenty-five years ago. Disease is understood more thoroughly, studied more carefully, and treated more skilfully. Diseases familiar to our fathers and grandfathers have disappeared and the public health measures have lessened the sorrows and brightened the lives of millions.”

Such pride in corporate knowledge is permissible to the older generation. Individual pride in personal knowledge is the privilege of youth. Then the

horizons of human understanding and human skills seem limitless. But pride like power corrupts. It can only be stayed by weight of years or the acquisition of humility. The practice of medicine will teach humility. There are occasions when the doctor is faced with a human situation where all the knowledge and all the acquired skills will prove inadequate. These apparent failures of medical science should serve as a spur for further research.

Medicine is a calling: a calling in which men practise a learned profession, acquire scientific knowledge and technical skills, and apply these in the public service for the benefit of the sick. At the same time there is in medicine a great tradition of duty—a duty of the doctor to his patient, to the medical profession, to the public whom he serves and to science as a whole. His patient is his first duty, and in this the physician is conditioned by a variety of cultural forces. These begin during the period of undergraduate instruction, for the medical faculty is not just an educational establishment—it is a cultural institution. Here, along with the formal education, there is inculcated the sense of being part of a learned profession with a strong vocational tradition. This attitude is reinforced once the student starts the clinical part of his course, for he will be then exposed to the influence and teaching of practising physicians and surgeons. These clinical teachers will, by their example and precept, portray the high humanistic values of medicine. This will serve to strengthen the ties between the young Æsculapian and his professional responsibilities.

The practice of medicine today requires a wide grasp of the fundamental processes which occur in disease. It demands the utilisation of all the technical advances which are now available. At the same time the patient, as a person, must not be forgotten. There has always been a fear which I think is quite unfounded, that in medicine the promotion of science will demote the patient. This was expressed over a hundred years ago by Trousseau, who said:

“Cellular pathology makes you forget the human being, makes you think only of cells, and you get lost in the abyss of the infinitely small.”

But this is not so. There is in medicine no real conflict between science and sympathy.

Although the emphasis is now on medicine as a biological science, art still remains. For the art of medicine is to utilise and apply biological science in order to relieve human suffering.

Medicine is today at the crossroads. It is like Janus, the guardian of the doorway, for it too looks both ways—behind at its glorious past—at a traditional humanistic art, and forward at our modern medicine which is largely a biological science. But neither the ancient art of medicine nor its modern science is enough unless transcended by love of humanity.

This was never better expressed than by Mahomet, who said: “He who has restored life to a man shall be accounted as if he had restored life to humanity.”

SOME OBSERVATIONS ON MIDWIFERY IN GENERAL PRACTICE

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THIS paper by a family doctor practising midwifery for the past fourteen years describes how the immeasurable social changes and scientific advances have altered the pre-1945 idea of the rôle of the general practitioner in obstetrics.

After war service and through the kindness of the visiting staff of the Royal Maternity Hospital, I became—with five other service doctors—a resident post-graduate student in hospital. We called ourselves the “broken down” doctors. The next six months were happy ones and we all learned a great deal through the kindly interest of the consultant staff of the Royal Maternity Hospital.

In 1946 Larne was a seaside town of 13,000 population, twenty miles from Belfast, and offered to the woman in labour three types of accommodation:—

- (1) Her home.
- (2) One of two small nursing homes.
- (3) The District Hospital.

The nursing homes and the District Hospital had even at this pre-Health Service stage become more popular during the war years and fewer women were being confined at home. It is often forgotten that the trend towards some form of institutional confinement had already started, at least in Larne, before July, 1948. The nursing homes were ordinary terrace houses staffed by one over-worked midwife and whatever domestic help she could get. The District Hospital at this time had a midwifery unit of six beds, available for the patients of general practitioners of the town. The accommodation was reasonably good but completely inadequate in the number of beds available.

Following the start of the Health Service, it was obvious that rapid changes were going to take place in the District Hospital, now named the Moyle Hospital. As one of the general practitioner members of the Hospital Management Committee, I was able to keep in touch with these developments and received much support from two consultant colleagues on the staff of the hospital, who had previously been general practitioners, in impressing upon the Committee the need for better and more suitable accommodation for the maternity patients of general practitioners. A ward formerly used for tuberculosis was transformed into a twenty-bed unit of six single unit rooms and fourteen general beds, all under the control of the local general practitioners. The capital expenditure for this project was £500 approximately. This low figure was achieved by utilizing the services of the maintenance staff of the hospital. The official estimate was

much more than this—£2,800 approximately. For the next six years much good work was done by the local doctors in this unit. We helped each other by giving anaesthetics as well as talking over any problems which presented. I think the standard of midwifery improved because our work, good or bad, could not be hidden and it was comforting to have the help and advice of a colleague when one felt worried.

At this time about 75 per cent. of my cases were confined in this unit and the provision of hospital maternity beds had altered considerably the proportion of home confinements. Whilst the facilities offered were a great improvement, there was still the problem of the patient requiring consultant help. All that could be done was to send her to the Royal Maternity Hospital or ask for the visit of a consultant from Belfast.

The next development was the appointment of a consultant obstetrician just after the completion of a new maternity ward. This was a Civil Defence dual-purpose building and its use as a maternity ward was certainly far from ideal, but more has been made out of the structure than could have been foreseen. There are in this unit twenty-two beds available for the patients of general practitioners.

The present arrangement provides the unusual experience of fifteen general practitioners working in harmony with each other and with their consultant. That this system works well is due, by and large, to three factors:—the generous co-operation coming from the consultant obstetrician, the keenness of the family doctor to do hospital midwifery and not lose touch with his patient and the desire of the patient to have, wherever possible, the services of her family doctor at her confinement.

There are certain difficulties but they are mainly due to the nature of the dual-purpose building. By this I mean that cases which have been handed over to the consultant lie cheek to jowl with those of the general practitioner patients. There is also the problem of treatment of ante-natal cases in the ward. To avoid confusion, all such cases admitted are placed under the care of the obstetrician. Provided labour progresses satisfactorily, the general practitioner conducts the labour and delivery, always bearing in mind the fact that this type of case is more likely to have complications in labour requiring help from the consultant.

As a result of this experience over the past three years, I think that the ideal accommodation in a provincial town of the size of Larne (now 16,000 population) where general practitioners attend their own cases, should consist of a small specialized section for the consultant and a larger separate wing or floor for the general practitioners. This system, or something like it, should enable the family doctor to maintain or improve his standard of work, knowing that the friendly help and advice of the consultant were readily available.

POST-GRADUATE TRAINING IN OBSTETRICS.

I think the majority of confinements will take place in hospital in future—indeed some long-term hospital planning has already anticipated this. This being so, and assuming that the family doctor will conduct more cases in hospital than

in the home, a period of resident post-graduate experience will be essential. There are two main reasons for this:—

1. The pre-registration year of the newly-qualified doctor is occupied fully by general medicine and surgery, by the end of which time his experience of practical midwifery is only a distant memory. In this age of an exacting and critical public, I cannot believe that the newly registered doctor is equipped adequately to accept the responsibility of full and satisfactory charge of a maternity case. In many cases I believe that they do not want to face the responsibility because they lack confidence in themselves.
2. The general practitioner should be conversant with hospital procedure if he is to play a useful and up-to-date part in the obstetric unit of the area in which he intends to spend his professional life.

The young doctor is conscious of the deficiency in his training and this fact is underlined by the increasing number of candidates for the Diploma in Obstetrics of the Royal College of Obstetricians and Gynæcologists.

It has been said that the achievement of this diploma creates the possibility of general practitioners attempting to do dangerous obstetrics. This is doubtful and the achievement of further knowledge and experience in the post-graduate period must always be of benefit. Such experience must be fitted in without unduly lengthening the period of pre-registration training or, alternatively, penalizing the young doctor anxious to enter general practice.

PARTNERSHIP IN GENERAL PRACTICE.

Until 1956 I was in single-handed practice but through the good relations of practitioner colleagues rarely performed the heroics so often necessary in the past. Before National Health Service days it was the custom to give anæsthetics for a friend and often without a fee. Today the same arrangement exists for home confinements (with a fee) but in the hospital anæsthetics are administered by one of the two anæsthetists on the hospital staff. This is a great comfort to the doctor and I hope not too great a nuisance to the anæsthetists whose skilled help is greatly appreciated.

In 1957 I was joined in partnership by Dr. Roy Mulligan. This arrangement has been most successful especially as regards obstetrics. My partner had the benefit of post-graduate experience in obstetrics in the Royal Maternity Hospital and obtained his Diploma and was therefore "midder-minded" when he joined me. Contrary to the usual custom in partnerships, we are both in attendance at our ante-natal clinic and see our maternity cases together on a set day at a special time clear of surgery house. This practice is by no means a waste of one man's time and has the advantage that the patient gets to know both equally well, and does not mind which is in attendance at the confinement. It ensures close co-operation and help to each other by exchanging opinions, and this method of joint action on maternity cases is strongly commended.

CO-OPERATION WITH THE LOCAL HEALTH AND WELFARE AUTHORITIES.

Close liaison with both Health and Welfare Authorities is essential in midwifery practice. That such liaison has not always existed cannot be denied nor can the

blame for failure be accurately defined. In Larne the general practitioners have enjoyed friendly relations with these authorities and they have allowed one of their local health visitors to attend our ante-natal clinic for approximately one hour each week. We have found this personal association most agreeable and helpful and much appreciated by the patients who have an opportunity of discussing, if necessary in another room, mothercraft problems. I believe the health visitors appreciate the contact they are making with practical ante-natal care—it is sad that they cannot be in attendance at the confinement.

HOME CONFINEMENTS.

The low rate of home confinements in our practice has already been mentioned. Whatever the arguments, the Ministerial recommendations, and even the inducement of increased financial benefit, the fact remains that home confinements have diminished and continue to do so, averaging only 12 per cent. over the past three years (Table 1).

No pressure is placed on patients to have a baby in hospital except to recommend the primipara, the dangerous multipara and the previously complicated case to book for hospital. Needless to say, should a case booked for confinement at home become complicated during the ante-natal period, e.g., pre-eclamptic toxæmia or abnormal presentation, every effort is made to arrange a hospital confinement.

I still enjoy doing a home confinement, especially when it is safely over. The traditional aura is still present except perhaps that the average surroundings are now cleaner and more spacious. It is a very different matter when things do not go well and one is faced with having to assist the delivery, arrest hæmorrhage or manually remove the placenta, not to mention resuscitation of the baby. It is under those circumstances that home confinements can become a horror to deal with, for which one is sadly ill-equipped. Knowing what should be done, usually quickly, and being reluctant to do it because of the lack of, say, suitable anæsthesia, is indeed a searching dilemma. Nevertheless, a temporary increase in the number of home confinements is a real possibility should hospital accommodation become restricted. In this event, extra care will be needed in the selection of these cases.

SHORT-TERM HOSPITALIZATION.

Twenty-four or forty-eight hours' stay in hospital following confinement has been advocated where scarcity of beds exist. It is an interesting idea but difficult to organize as it would need the closest co-operation between hospital, family doctor and local Health and Welfare Authorities. A very efficient home help would in most cases be needed for 8-12 hours daily. I am sure there are many general practitioners who would be keen to try this scheme, provided that they were in charge of the delivery.

THE RESULTS OF ONE'S WORK.

I have been able to obtain some figures of our last 350 or so cases (Table 1). This has been possible by keeping a record in simple column form of each

completed confinement. The time spent in this chore is two minutes per case. If you have an efficient system, the record keeping is really no trouble. Here are the headings:—

PREVIOUS REF. ANTE-NATAL HOURS IN
 NAME : AGE : GRAVID : PARA : COMPLICATIONS : RH. : NO. : COMPLICATIONS : D.C. : LABOUR

(continued)

LABOUR : FORCEPS : BREECH : L.U.S.C.S. : HOME : S.B. : SEX : WEIGHT : REMARKS
 COMPLICATIONS

I am most grateful to my partner for helping me with these records and also for checking them.

The figures are perhaps not of great statistical significance but they serve as an indication of the results of our work. It is so easy and convenient to forget one's errors and failures and to remember only the successes.

TABLE 1.

GENERAL.

Total cases	-	-	-	357	...	—
G.P. cases	-	-	-	342	...	—
Consultant cases	-	-	-	15	...	4.38 per cent.
Home confinements	-	-	-	44	...	12.8 "
Forceps delivery by ourselves	-	-	-	21	...	6.1 "
Forceps delivery by consultant	-	-	-	6	...	—
Forceps total	-	-	-	27	...	7.6 "

A few of the 342 cases have been seen and treated by our consultant, e.g., pre-eclamptic toxæmia, but they have come into the total 342 as the delivery was conducted by one of us. The forceps rate is low—not by design as [I believe] too much stress has been placed on a low forceps rate and much harm may result from leaving a patient too long in the second stage of labour.

I have compared the stillbirth and neo-natal death rates with those of County Antrim (Table 2).

Stillbirths are of importance in any practice, especially if any of them could have been avoided. I would therefore like to comment briefly on them.

Case 1—possibly closer ante-natal care to exclude any degree of pre-eclamptic toxæmia.

Cases 2 and 3 were both multiparæ—the first a diagnosed breech presentation which could not be turned in a well-attended ante-natal period. I did not anticipate trouble with this patient whom I had confined easily on a previous occasion. The delivery by breech of this 4 lb. 14 oz. premature baby was complicated by the presence of a $\frac{3}{4}$ -dilated os clamped tightly round the baby's head. Forcible extraction was necessary with the inevitable death of the baby.

TABLE 2.
STILLBIRTHS.

Total cases delivered	-	-	-	342
Total stillbirths	-	-	-	8
General Practitioners	-	-	-	7
Consultant	-	-	-	1
Co. Antrim (1959)	-	-	-	23.6
				per 1,000 registered births, i.e., 8.4 per 342 registered births.
GENERAL PRACTITIONER		CIRCUMSTANCES		CAUSE
Case 1	...	I.U.D.	...	Unknown
Case 2	...	Breech (4 lb. 14 oz.)	...	OS $\frac{3}{4}$ -dilated
Case 3	...	Breech (6 lb. 4 oz.)	...	OS $\frac{3}{4}$ -dilated. Poor A.N. care
Case 4	...	Accidental hæmorrhage	...	Unknown
Case 5	...	A.P.H. I.U.D.	...	Poor A.N. care
Case 6 (twins)	...	I.U.D. 37 weeks	...	Unknown
CONSULTANT (Deputy)				
Case 7	...	Prim. breech	...	—

Case 3 was also a breech at term, similarly complicated. She attended badly for ante-natal care and we failed to check this omission. The delivery of a 6 lb. 4 oz. baby by the breech was held up by a $\frac{3}{4}$ -dilated os around the head. Despite immediate chloroform anæsthesia, the os failed to relax. The baby died, due undoubtedly to forcible extraction necessary to deliver the head. This case occurred in the patient's home. The loss of these two babies was a blow to us, especially as one occurred soon after the other.

Case 4 was carefully attended in the ante-natal period. Accidental hæmorrhage was dramatically sudden and intra-uterine death was immediate.

Case 5—ante-partum hæmorrhage, pre-eclamptic toxæmia, intra-uterine death at thirty-two weeks. Previous history of three miscarriages, two intra-uterine deaths, two live births. Here I think more frequent ante-natal examination than the routine might have detected the pre-eclamptic toxæmia earlier. This still-birth therefore has a possible avoidable cause despite her previous bad history.

Case 6 (twins). Intra-uterine death, thirty-seven weeks. Was not rested at thirty-two weeks of pregnancy, otherwise the pregnancy was normal at routine examinations in the ante-natal period.

We now keep a list of ante-natal cases showing when they should attend for examination. Failure to attend is followed by a visit from the Health Visitor or, if necessary, a visit from one of us. This should help to obviate the case of early pre-eclamptic toxæmia or breech which might be turned and, if version is not possible, arrangements made for hospital delivery.

I think it is therefore fair self-criticism to say that the stillbirths in this series might have been fewer if better ante-natal care had been exercised in the case of 3, 5 and possibly 6, the twin pregnancy. At the same time I ask myself: "Do I really get enough practice with breech presentations?" I am sure I do not.

Table 3 shows the neo-natal mortality rates for the county and the series under review.

TABLE 3.
NEO-NATAL DEATHS.
(335 Live Births)

	Total cases of live births	-	-	335
	Total neo-natal deaths	-	-	3
	Co. Antrim (1959)	-	-	16.81
				per 1,000 live births, i.e., 5.63 per 335 live births.
NAME			CAUSE	
Case 1	-	-	-	Pre-eclamptic toxæmia. Intrauterine infection. Post-mortem inconclusive. Anoxia.
Case 2	-	-	-	Imperforate anus. Cerebral hæmorrhage.
Case 3	-	-	-	Atelectasis. Normal delivery. Foetal distress.

Again it is important to know if there are present any avoidable factors in these deaths. Case 1 had pre-eclamptic toxæmia complicated by intra-partum infection. I noted at the time of delivery that there was an offensive "fishy" odour present which became worse when the baby was born—post-mortem on the baby was inconclusive, the actual cause of death being attributed to an irreversible anoxia. There is little doubt that intra-partum infection followed the artificial rupture of membranes.

Case 2—normal delivery. Imperforate anus. The baby had repeated cyanotic attacks. Post-mortem revealed a cerebral hæmorrhage. A more rapid delivery by episiotomy might have helped here but at the time there was no apparent indication to interfere. The presence of an imperforate anus suggested the possibility of other abnormalities but none was detected at post-mortem.

Case 3 was a normal delivery with meconium staining near the completion of the second stage of labour. There did not appear to be any indication present to expedite delivery. So often meconium staining is present to be followed by the birth of a lusty baby, that I find it difficult to assess the danger of this sign in a normally progressing second stage. This case was obviously one which might have been helped by hastening the delivery by applying forceps.

The lessons from these cases are that one must not be lulled into a sense of false security by assuming that meconium staining usually does not mean much towards the end of the second stage; secondly, that a well-timed episiotomy

might lessen the possibility of a cerebral hæmorrhage in the baby; thirdly, that vaginal interference before labour is still fraught with the danger of infection.

To conclude, I hope I have been able to show that midwifery can still be an interesting part of general practice—indeed, I believe that it is one of the cornerstones of a rewarding life in general practice. It will be a tragedy if maternity work ceases to be part of the family doctor's daily task, as I believe is threatened. To avoid this and to meet the high standard of obstetrics now needed and indeed expected, I repeat what I have already said:—

- (a) Post-graduate experience is most helpful to the doctor in general practice.
- (b) General practitioner units in hospital should be carefully planned in all areas.
- (c) The local Consultant should encourage and help (as he does in Larne) the General Practitioners in their maternity work.
- (d) The results of one's work should be kept in some form of record, however simple. It is then possible at any time to examine these results and place oneself in the witness-box before the strictest judge of all—yourself.

I am particularly indebted to Mr. H. I. McClure, F.R.C.S., for his encouragement and help in the preparation of this paper for publication. I should also like to thank our consultant obstetrician, Mr. A. E. Stevenson, F.R.C.S., for his generous co-operation at all times.

REVIEW

A HANDBOOK FOR AMBULANCE ROOM ATTENDANTS. By C. E. Watson, M.A., M.B. (Pp. 120; figs. 20. 5s. 6d.) London: Baillière, Tindall and Cox, 1961.

This little book is written by a medical officer to The National Coal Board and addressed to factory or colliery ambulance men, who have already had some training in normal first-aid procedures.

The most useful chapters are those on abdominal pain and on the assessment and disposal of cases of illness.

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PÆDIATRICS AND THE GENERAL PRACTITIONER

*THE STEPHEN GARVIN MEMORIAL LECTURE
to the South Tyrone Clinical Society on 24th October, 1960*

† **By Professor F. M. B. ALLEN, M.D., F.R.C.P.**
Department of Child Health, Queen's University, Belfast

I REGARD myself as being greatly honoured and privileged to give this, the first Stephen Garvin Memorial Lecture. I met Stephen Garvin for the first time more than thirty years ago, and all his subsequent lifetime I enjoyed his personal friendship and that of his family. Apart from our medical association we had a common interest in another of his activities and he taught me a great deal.

He had an innate and abiding interest in the diseases and illnesses of children and he had acquired a profound knowledge of conditions which interfered with child health. I have no doubt that had he been born fifty years later he would have been a successful and distinguished consultant in pædiatrics.

I find that the first professional consultation I had with Stephen Garvin was thirty years ago. The child was suffering from tuberculous meningitis. This was always a depressing diagnosis to make and confirm, because it meant that in less than three weeks the child would be dead. In these days the disease is much less common and when the diagnosis is assured treatment is usually successful. I can recall when the medical ward was rarely without at least one patient with tuberculous meningitis—always fatal. Now examples are unusual and, when they do occur, one is not so pessimistic as one was thirty years ago. The reason for this dramatic change is due to the discovery of anti-tuberculous drugs, to better segregation of sufferers from active tuberculosis and to improved social conditions of housing and nutrition as well as increased education and wider knowledge among the general public.

The fact that tuberculous meningitis is now very rare, that tuberculosis is no longer the prime killing disease, and that effective treatment is available should not encourage us to be complacent. It is becoming generally recognised that the notifications of first infections has moved into the age group 35-50 years which was for long regarded as being relatively safe; and, of very great importance, that there is a massive reservoir of active tuberculosis, often of the fibroid type, among the elderly, now euphemistically referred to as the geriatric group.

It would seem therefore that instead of regarding the disease as conquered, we must keep our minds open and active to the change in the features and pattern of the disease so that we may do the best for our patients.

Along with the control of tuberculosis one of the outstanding events of recent years has been the reduction in the mortality from infectious diseases.

Measles and whooping cough took a heavy toll of infant lives in every epidemic. Bronchopneumonia, otitis media and the activation of a latent primary tuberculous

complex accounted for a high annual death roll. The sulphonamides and antibiotics have had an outstanding success in controlling the complications of these prevalent diseases. The annual deaths from measles have fallen from 420 to 0 in twenty-five years and from whooping cough from 70 to 8. Instead of being at the head of the table of causes of infant and childhood deaths, they have been replaced by accidents in the home and on the roads.

The control of diphtheria has been one of our great successes. The notifications in England and Wales in 1938 were 65,000, and 2,861 deaths occurred. As the result of widespread immunisation 4 deaths occurred in 1957. Comparable figures are available in Northern Ireland where there has been only one death in the last four years compared with 155 in 1935. Again, however, we must not be complacent because the proportion of children who are immunised is much too low. Public Health Authorities are justifiably worried because when less than 40 per cent. of the child population is immunised there is due cause for anxiety. There is no occasion for periodic panic immunisation schemes such as have occurred in Newtownabbey last year and in Derbyshire this summer. With an immunisation percentage of 75 there would be a reasonable guarantee that diphtheria would be kept under control. I am sufficiently pessimistic to believe that a recurrence of the disease in epidemic proportions will recur unless mothers can be persuaded that this disease is liable to reappear with all its deathly associations unless we all as doctors can achieve one of the first principles of our profession—to prevent disease. It must be realised that medical students of the modern generation are unfamiliar with the disease. They would fail to recognise the characteristic odour of the breath, and too often fail to consider the possibility of diphtheria in the differential diagnosis of a "sore throat."

Infections of the respiratory tract, particularly pneumonia and bronchopneumonia, have assumed a very different place in our duties. The former was a severe dramatic illness which lasted a few days. The latter was a serious condition often causing death, always distressing and full of anxiety and frequently associated with complications which lead to prolonged convalescence and permanent disability. The struggle of an infant contending with double bronchopneumonia, when respirations were 80 per minute and marked cyanosis and toxæmia were prominent, was a distressing sight. The use of sulphonamides and antibiotics have changed all this. Nowadays acute bronchiolitis and bronchopneumonia instead of creating an atmosphere of extreme anxiety are regarded with complacency (except in a few instances), and are treated successfully with modern drugs so that the whole illness is over in five days. Two years ago we admitted 143 infants under 2 years to the Royal Belfast Hospital for Sick Children in less than three months and of these all survived except three—deaths occurred in a mongol, a severe congenital heart, and in one infant who was moribund on admission.

We find that sulpha drugs are effective in the vast majority of these infants and children, thereby avoiding unpleasant injection of antibiotics and the creation of allergy. Penicillin and other antibiotics are reserved for the severely ill and for examples of laryngo-tracheobronchitis.

Acute infections of the upper respiratory tract arise when the child just goes to school. Tonsillitis and "head colds" become common, apart from the epidemics of measles, whooping cough, etc. Acute tonsillitis is usually due to a streptococcus and is often associated with the subsequent development of acute nephritis, rheumatic infection and Henoch-Schonlein purpura. Penicillin is indicated for the treatment of the acute illness, but it is now accepted that its use should be sufficiently prolonged not only to subdue the infection but to eradicate it. It is a good general rule that in acute tonsillitis it should be given in an adequate dose for at least five days to prevent the development of otitis media. Mastoid infection is now rare, but it is practically only found when the dose has been too low and the treatment has been terminated too soon. To avoid nephritis and Henoch-Schonlein purpura is probably not possible; but a prolonged recurring illness can be controlled by giving penicillin for 3-6 weeks. In rheumatic infection it is important to prevent second and subsequent infections and I advise continuing with the antibiotic for at least two years, and indeed until adolescence.

Before passing on to another topic may I emphasise, particularly in a rural community, the desirability of immunising children against tetanus. It is tragic to record that many patients die of the administration of anti-tetanic serum to prevent a disease which may not be impending. How much safer it would be to immunise the children against tetanus and thus avoid the risk of death as the result of giving serum which only creates a temporary passive immunity. The combined preventive inoculation of patients against whooping cough, diphtheria, and tetanus has much to commend it. If children were immunised against tetanus it would only be necessary to give a "booster" dose of toxoid if tetanus were a possibility without any risk of unpleasant or fatal results.

When Stephen Garvin and I were first associated in our professional activities vitamin deficiencies were declining. Scurvy was not uncommon, but rickets was common. The recognition that these were preventable diseases (and if preventable why not prevent them) was generally accepted. Doctors, infant welfare centres, and mothers gradually accepted this fact, and the result has been that, whereas vitamin D deficiency was a common experience in hospital out-patients it is now a rarity.

In the nutrition and care of the infant and the premature one can record progress. There is much more faith in the digestive competence of the infant so that the introduction of cereals earlier is common practice, even at the third month or before this. The mortality among prematures was probably 70 per cent. thirty-five years ago and now instead of losing 7 out of 10 more than 8 out of 10 are saved. This has been achieved by realising the special needs of the premature and the steps which are necessary to give it the best chance of survival. If the simple principles of providing warmth, preventing infection, maintaining nutrition, and having oxygen available are observed, many premature babies would be saved.

Rhesus incompatibility was unknown to us twenty-five years ago as an explanation of severe jaundice in the newborn. Now we can determine before the baby is born if the disease is impending and we can be prepared to undertake

an exchange transfusion, thereby preventing the loss of the baby or, if it survives, avoiding another victim of mental deficiency and neurological disorder.

Gastro-enteritis used to be a source of heavy infantile mortality. Family doctors, especially in urban communities, and out-patient departments were swamped with large numbers of infants with "D. & V." The annual epidemics seem to be under control as the result of better education in infant hygiene, the infant welfare services, and the use of modern chemo-therapeutic drugs. When one recalls the vast numbers of infants who died every year of "summer diarrhœa" and compares the situation now with twenty-eight deaths in 1958 one cannot be but grateful to the infant welfare services and the education of mothers and doctors for what has been achieved.

Another of the changes which has occurred is the advance in anæsthetics which has given the thoracic surgeon the opportunity to operate on diseases of the lungs and congenital malformations of the heart which were regarded as impossible fifteen years ago. Now children have one or more lobes of a lung removed for bronchiectasis, or a whole lung extirpated for a large cyst without undue risk. Malformations of the heart are remedied almost daily. Precision of diagnosis, modern anæsthesia, hypothermia and extra-corporeal heart-lung apparatus give the surgeon the opportunity to tie a patent ductus, resect a coarctation of the aorta or to repair a defect in the atrial or ventricular septum. As a consequence, many children destined to a short tenure of life, or prolonged invalidism, are restored to full activity. It is really astonishing to see these patients who have been handicapped in their physical exertions taking a new outlook on life and engaging in full activity within a very few days of their operation.

New diseases have been recognised in the later years. Hiatus hernia can be diagnosed for the first time from infancy to old age, hypercalcæmia may have been the result of over-enthusiastic use of vitamin D, or of individual idiosyncrasy to it. Biochemistry is opening a field of intense interest in mental deficiency. The inborn errors of metabolism of Garrod recognised six peculiar inherited abnormalities. Now they are multitudinous and include a vast number of abnormalities. Some of these are associated with mental deficiency of which phenylketonuria, galactosæmia, Hartnup disease, maple syrup disease, Wilson's disease, pyridoxine deficiency, argino-succinic aciduria and cystathioninuria are now recognised. I have no doubt that many other abnormalities associated with enzyme deficiencies will be discovered.

Thirty years ago rheumatic heart disease was fairly common. Children suffering from rheumatic infection or chorea were constant inmates of the medical ward and now are the subjects of cardiac failure, mitral valvotomy, etc., in an older generation. The victims of this insidious and destructive disease gradually became less numerous. Even before the introduction of sulphonamides and penicillin the reduced incidence was noted. These drugs, along with a general improvement of the healthy state of the nasopharynx gradually reduced the disease to vanishing point. Twenty years ago there were six or more children in the ward with active disease at a time and upwards of thirty in the convalescent hospital. Until recent weeks examples of active disease were rare and very few patients

were in the convalescent unit. But it is worth noting that the disease is becoming more common again and children with active disease are once more reaching hospital.

It is possible that the widespread use of penicillin and other anti-streptococcal drugs have brought the streptococcus to a state of near-surrender. There is a hope that by the continued use of penicillin for years a second infection would be prevented. It is difficult to assume that the streptococcus has become resistant to antibiotics, because it is notoriously vulnerable. Some other influence of which we are as yet unaware may be involved. But we are faced with the possibility that we are once more going to be faced with the recrudescence of rheumatic infection, possibly with a different type of onset.

What of the future? What will the speaker giving this address say in 1985? Of one thing, I am sure, that if he should look back upon the First Memorial Lecture of 1960 he would say—"How uninspiring! How lacking in knowledge and foresight!"

To meet that challenge in some small way I would suggest he will refer to the change in the precision of diagnosis by referring to the identification of specific viruses, by the recognition of minute changes in blood chemistry and improvements of radiological methods. In treatment there will be more specificity. Specific infections will demand the most appropriate chemical or antibiotic; disorders of blood chemistry will be remedied by removing the guilty fraction or substituting the missing enzyme. Congenital malformations will be better understood, and some of them prevented. Genetic influences will be elucidated and many diseases which are at present not understood will be explained and prevented.

Altogether the present generation of students of medicine have a wonderfully interesting future before them. And just as we can look back upon a generation of advance in knowledge and increase of medical interest so future generations of Garvins will, we hope, look back upon equally happy and stimulating experiences.

POST-OPERATIVE WOUND INFECTION DUE TO STAPHYLOCOCCUS PYOGENES

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It can be said with certainty that, in most general hospitals today, staphylococcal infection is the major bacteriological problem. The introduction of penicillin in 1941 proved so successful against this type of infection that many were lulled into a false sense of security. It has become increasingly apparent over the last ten years that the adaptability of the staphylococcus has been underestimated. The discovery of broad-spectrum antibiotics raised fresh hopes of conquering the staphylococcus, but today it is commonplace to find hospital epidemics of staphylococcal infection due to multiple drug-resistant strains.

Effective epidemiological investigation of cross-infection due to the *staphylococcus pyogenes* requires a system of typing within the species, in addition to test of coagulase production and antibiotic sensitivity. Since a routine service of bacteriophage typing was set up at The Laboratories, Belfast City Hospital, in the latter part of 1958, opportunity has been afforded to study some aspects of post-operative wound infection due to the pathogenic staphylococcus.

During 1959 two major outbreaks occurred in the surgical departments of hospitals in Northern Ireland which seem of special interest and are here reported. One of these was of a severe explosive nature, lasting one month, in which the infection was successfully eradicated; the second, though less severe, was of intractable form, and all attempts to terminate the epidemic failed.

BACTERIOLOGICAL METHODS.

Nose and wound swabs were plated directly on horse-blood nutrient agar and incubated at 37° C. for eighteen hours. Colonies of *staphylococcus aureus* were subjected to the tube coagulase test and positive strains were further examined for antibiotic sensitivity by the dried disc technique (Fairbrother and Martyn, 1951) and their phage type determined by the method of Anderson and Williams (1956).

The degree of bacterial contamination of the air in the wards and operating theatre was determined by the use of settling plates. Blood-agar plates were exposed for one hour during normal activity. After incubation, the number of colonies on each plate was counted and the results expressed as the number of infected particles falling per square foot per minute.

Blanket sweeps were carried out by stroking an exposed blood-agar plate over one-quarter of the total surface area of the blanket. The plates were incubated and the number of colonies counted per plate.

EPIDEMIC A.

The epidemic began in a surgical unit of a hospital, which consisted of an operating theatre and a male and a female ward, each containing twenty-four

beds. The wards were well ventilated and the beds were spaced approximately five feet apart.

Prior to the outbreak, wound sepsis had occurred on occasion, but was thought to be infrequent, though not recorded. However, in February, 1959, a steep rise in the post-operative sepsis rate was observed and bacteriological investigation was commenced.

Between 26th January, 1959, and 24th February, 1959, sixty-six clean, major or intermediate operations were carried out, sixteen of which subsequently developed wound infection, i.e., sepsis rate of 24 per cent. A feature of most cases was an early rise in temperature following operation and the development of pus deep in the wound. The day of onset of sepsis was determined by the presence of visible pus in the wound. Nose and wound swabs were taken from twelve of the sixteen cases of post-operative infection, details of which are shown in Table 1.

TABLE 1.
DETAILS OF SIXTEEN CASES OF POST-OPERATIVE WOUND INFECTION.

PATIENT	SEX	OPERATION	DAY OF ONSET		STAPH. AUREUS					
			OF SEPSIS	Wound	Nose					
*1	...	M	...	Resection of colon	...	10th	...	NE	...	NE
*2	...	F	...	Appendicectomy	...	10th	...	NE	...	NE
*3	...	F	...	Resection of colon	...	8th	...	NE	...	NE
*4	...	M	...	Gastrectomy	...	9th	...	NE	...	NE
5	...	F	...	Mastectomy	...	2nd	...	+	...	-
6	...	F	...	Lung Biopsy	...	2nd	...	+	...	+
7	...	F	...	Œsophageal repair	...	9th	...	+	...	+
8	...	F	...	Nephrolithotomy	...	7th	...	+	...	-
9	...	M	...	Femoral hernia	...	7th	...	+	...	+
10	...	M	...	Cholecystectomy	...	8th	...	+	...	-
11	...	M	...	Cholecystectomy	...	10th	...	+	...	+
12	...	M	...	Cystotomy	...	9th	...	+	...	-
13	...	M	...	Prostatectomy	...	5th	...	+	...	-
14	...	F	...	Mitral valvotomy	...	5th	...	+	...	-
15	...	F	...	Mitral valvotomy	...	4th	...	+	...	-
16	...	F	...	Exc. rectum	...	20th	...	+	...	-

N.E.=Not examined.

*=Fatal Infections.

Before bacteriological investigation had commenced, four patients known to have post-operative wound infections died, including patients 1 and 2 who burst their abdomens on the tenth day and failed to recover. Coagulase positive staphylococci were isolated at post mortem from the peritoneal exudate of one case, but the strain was unfortunately not kept for phage typing. Paralytic ileus developed on the eighth and ninth days in patients 3 and 4 respectively, and both

subsequently died. Patient 11 also had a burst abdomen on the tenth day, but survived. Following the operation of mitral valvotomy patients 14 and 15 developed empyemata on the fifth and fourth post-operative day respectively. Seven cases occurred in the male ward and nine in the female ward. Coagulase positive staphylococci were isolated from pus in the wounds of all twelve cases examined, and in four patients staphylococci were also isolated from the nose.

TABLE 2.

PHAGE PATTERNS AND ANTIBIOTIC SENSITIVITIES OF STAPHYLOCOCCI
CAUSING POST-OPERATIVE WOUND INFECTION.

PATIENT	PHAGE PATTERN	ANTIBIOTIC SENSITIVITY							
		Peni- cillin	Tetra- cycline	Strepto- mycin	Erythro- mycin	Chloram- phenicol			
5 ...	7/47/53/77+	...	R	...	R	...	S	...	S
6 ...	7/47/53/77+	...	R	...	R	...	S	...	S
7 ...	7/47/53/77+	...	R	...	R	...	S	...	S
8 ...	7/47/54/75+	...	R	...	R	...	S	...	S
9 ...	7/47/53/77+	...	R	...	R	...	S	...	S
10 ...	7/47/54/75+	...	R	...	R	...	S	...	S
11 ...	7/47/53/77+	...	R	...	R	...	S	...	S
12 ...	7/47/53/54/75/77	...	R	...	R	...	S	...	S
13 ...	7/47/54/75+	...	R	...	R	...	S	...	S
14 ...	7/47/53/77+	...	R	...	R	...	S	...	S
15 ...	7/47/53/54/75/77	...	R	...	R	...	S	...	S
16 ...	Not typable	...	R	...	R	...	S	...	S

+ = Additional minor reactions present.
R = Resistant and S = sensitive to the antibiotic.

In the interpretation of phage typing results the rule has been applied that two apparently similar strains are only regarded as different if one is lysed strongly by two phages that fail altogether to lyse the second (Anderson and Williams, 1956). In addition, weak lytic reactions not recorded in the table were taken into account. On this basis all the phage patterns recorded in Table 2 were considered to belong to the same epidemic type. The antibiotic sensitivity pattern was also consistent, all strains being resistant to penicillin, tetracycline and streptomycin, and sensitive to erythromycin and chloramphenicol. Four strains of staphylococci isolated from the nose of patients 6, 7, 9 and 11 proved to be of a different phage type and antibiotic spectrum to that of the epidemic strain.

In view of these findings, search was made to establish the source of the outbreak, and to institute measures to eradicate the infecting strain. Nasal swabs were taken from the entire staff of the surgical wards and theatre. This included surgeons, anaesthetists, nurses, domestics, orderlies and a physiotherapist, com-

prising thirty-seven members in all. Of these, nine (24 per cent.) were carrying the epidemic type of staphylococcus in the nose. The antibiotic spectrum was also identical to that of the epidemic strain. Eight further strains isolated were of differing phage types or not typable and all were tetracycline sensitive.

Of the theatre staff, only one surgeon and one nurse were carrying the epidemic strain. This particular surgeon had operated on only two patients (14 and 15) of the sixteen, who subsequently developed post-operative wound infection. On the other hand the theatre nurse carrying the epidemic strain had been associated with most of the operations. No member of the theatre staff had a septic skin lesion. The remaining seven individuals carrying the epidemic type were all nurses working in the wards.

Settling plates were exposed in both wards and in the theatre for one hour during normal activity. Coagulase positive staphylococci were isolated from all three plates, but only the ward strains were of the epidemic type.

The entire unit was closed down on 27th February, 1959. The wards and theatre were washed down and the unit partly repainted. All movable articles were disinfected by boiling or other means. Nasal carriers of the epidemic strain received 1 per cent. hibitane cream, applied to the nose, twice per day, for four weeks.

When the unit reopened on 5th March, 1959, nasal swabs were again taken from all staff. Only one nurse, who had not been in the unit during the epidemic, was carrying a strain similar in phage type to the epidemic strain. A course of nasal hibitane was given and repeat swabs proved negative.

No evidence of return of the epidemic strain was apparent over the following nine months and the post-operative sepsis rate remained less than 5 per cent.

EPIDEMIC B.

The epidemic took place in the surgical unit of a provincial hospital. The unit consisted of a theatre; three male wards containing six, seven and ten beds respectively; and three female wards with the same bed proportion, comprising forty-six beds altogether. The beds were spaced approximately three feet apart. There were twenty members in the surgical staff, including two surgeons, one anaesthetist, nurses, ward orderlies and domestics. In the wards the facilities for hand washing and dressings were generally poor. Cases, septic on admission, had of necessity to be put in wards where post-operative cases were being nursed. Post-operative wounds were routinely dressed in the wards on the fifth-sixth day.

In January, 1959, it was thought that the post-operative sepsis rate was higher than usual, but no accurate records were available for the preceding months. It was, therefore, decided to keep a wound book, recording the number of post-operative infections and to carry out routine bacteriological investigation of all infected wounds, the criterion of infection being the presence of visible pus in the wound.

Opportunity was afforded for studying the epidemic over a twelve-month period, during which time various measures were taken in an attempt to control the infection which, however, met with only limited success.

During the month of January, 1959, it was observed that of sixty-five clean operations (major or intermediate) performed, four (6.2 per cent.) subsequently developed wound infections due to coagulase positive staphylococci. Bacteriophage typing showed that three of these were type 77 and one type 52A. It was thought that type 77 might be a potential epidemic strain in view of its presence in three post-operative wounds occurring in the same unit. It was noted that the majority of wounds were clean at the first dressing on the fifth-sixth day, and sepsis, if it occurred, appeared on the ninth-twelfth post-operative day. Pus was usually visible in the wounds of these cases and was superficial in nature rather than forming deep abscesses.

TABLE 3.

TOTAL NUMBER OF OPERATIONS PERFORMED DURING 1959 AND
NUMBER DEVELOPING STAPHYLOCOCCAL WOUND INFECTION.

1959	NUMBER OF OPERATIONS	NUMBER FOLLOWED BY WOUND SEPSIS	EPIDEMIC TYPE	OTHER TYPES OR NOT TYPABLE
January	- 65	... 4 (6.2%)	... 3	... 1
February	- 36	... 6 (16.7%)	... 4	... 2
March	- 40	... 7 (17.5%)	... 4	... 3
April	- 85	... 1 (1.2%)	... 1	... 0
May	- 68	... 5 (7.4%)	... 3	... 2
June	- 79	... 4 (5.1%)	... 3	... 1
July	- 75	... 1 (1.3%)	... 1	... 0
August	- 90	... 2 (2.2%)	... 1	... 1
September	- 89	... 4 (4.5%)	... 3	... 1
October	- 113	... 7 (6.2%)	... 4	... 3
November	- 100	... 9 (9.0%)	... 6	... 3
December	- 53	... 9 (17.0%)	... 5	... 4
TOTAL	- 893	59	38	21

Table 3 sets out the post-operative staphylococcal sepsis rate during each month in 1959. In addition, the results of phage typing have been expressed as belonging to the epidemic type 77 or other types. The total number of infected wounds was slightly greater in the male wards, over the twelve-month period, but cases occurred in all six wards, the number from each being variable from month to month.

In March, the post-operative sepsis rate rose to 17.5 per cent. At this time the nasal carrier rate of pathogenic staphylococci among the twenty members of the surgical team was 25 per cent., three of the five strains being of the epidemic type. No nasal carriers were detected in the theatre staff. Settling

plates showed that there was considerable sedimentation of infected air-borne particles in the wards during dressings. The number of bacteria-carrying particles falling per square foot per minute varied between fifteen and fifty in the six surgical wards and was five in the theatre. No pathogenic staphylococci were detected in the latter, but in the wards the epidemic staphylococcus accounted for 0.75 to 3.25 particles settling per square foot per minute. Examination of dirty blankets from the wards by the technique described above yielded a mean growth of 1,000 colonies per plate, 1 per cent. of which were identified as coagulase positive staphylococci and the majority of these belonged to the phage type 77. After laundering, the mean growth was reduced to 2.5 saprophytic colonies per plate, indicating effective disinfection of the blankets.

In view of these findings, the unit was closed for complete disinfection and treatment of all nasal carriers among the surgical staff. Walls and floors were washed down with Roccal (4 oz. to 1 gallon) and all movable articles boiled as far as possible. Nasal carriers of coagulase positive staphylococci received neomycin and bacitracin ointment applied to the nose twice per day for two weeks. The unit reopened early in April and during this month the sepsis rate fell to one-seventh of that recorded for the month prior to disinfection. The epidemic strain, however, was still present and accounted for the one case of wound infection occurring during April. From May to November the sepsis rate fluctuated between 1.3 and 9.0 per cent., the epidemic strain still accounting for a large proportion of cases.

In December, re-examination of twenty-four members of the surgical staff showed a nasal carrier rate of pathogenic staphylococci of 37 per cent., two-thirds of which belonged to the epidemic type 77. No member of the theatre staff was carrying the epidemic strain. Settling plates and blanket sweeps again indicated a highly infected environment and as the staphylococcal sepsis rate had reached a peak of 17.0 per cent., the unit was again closed for disinfection and the treatment of nasal carriers. In addition, a room was provided for surgical dressings and there was a general revision of aseptic technique. Post-operative wounds were left untouched until the ninth-tenth day.

When the unit reopened in January, 1960, two nurses on ward duty were still carrying the epidemic type of staphylococcus in the nares and one case of wound infection, due to a type 77 strain, was recorded. The measures taken had apparently reduced the sepsis rate considerably, but had failed entirely to eradicate the epidemic strain.

Table 4 sets out in detail the phage patterns and antibiotic sensitivities of fifty-nine strains of staphylococci isolated from infected wounds over a twelve-month period. The epidemic type 77 and 75/77 accounted for 64.4 per cent. of all wound infections. The strains were consistently resistant to penicillin, tetracycline and streptomycin, and sensitive to erythromycin and chloramphenicol. Of the remainder, 11.9 per cent. of infections were due to other group III strains; 8.6 per cent. to group I; 1.7 per cent. to group II; and 13.6 per cent. of mixed groups or not typable.

TABLE 4.
PHAGE PATTERNS AND ANTIBIOTIC SENSITIVITIES OF ALL STRAINS
ISOLATED FROM POST-OPERATIVE WOUNDS DURING 1959.

PHAGE PATTERN	NO. OF STRAINS	PER CENT. OF TOTAL	ANTIBIOTIC SENSITIVITY				
			Peni- cillin	Tetra- cycline	Strepto- mycin	Erythro- mycin	Chloram- phenicol
<i>Group I</i>							
52A	... 3	... 5.1	... R	... S	... S	... S	
*52A/80	... 2	... 3.5	... R	... R	... S	... S	
<i>Group II</i>							
3c/55/71	... 1	... 1.7	... S	... S	... S	... S	
<i>Group III</i>							
6/47/53/54, etc.	... 5	... 8.5	... R	... R	... V	... S	
*53	... 1	... 1.7	... R	... R	... R	... S	
54	... 1	... 1.7	... R	... S	... S	... S	
75/77	... 16	... 64.4	... R	... R	... R	... S	
77	... 22		... R	... R	... R	... S	
<i>Mixed Groups</i>	... 4	... 6.8	... R	... V	... V	... S	
<i>Not Typable</i>	... 4	... 6.8	... R	... V	... V	... S	
TOTAL	... 59						

* = Typable by strong phage filtrates only.

R = Resistant and S = sensitive to the antibiotic.

V = variable result.

DISCUSSION.

Outbreaks of hospital staphylococcal infection usually fall into one of three broad patterns. In one type the outbreak is referable to a single carrier or septic lesion and the exclusion of such an individual terminates the epidemic. In the second type the epidemic strain is widespread in patients' wounds, in the noses of many of the staff, and in ward dust, etc. In this type of epidemic it is often necessary to close down the entire unit for complete disinfection (Blowers et al., 1955) in order to eradicate the infecting strain. In the third type of outbreak wounds and noses are colonized by a wide variety of phage types of staphylococci and no single epidemic strain can be identified. This type of epidemic is often due to lax surgical technique throughout the unit and can usually be controlled by improved standards.

In epidemic A the post-operative staphylococcal sepsis rate was 24 per cent. Most of these infections were thought to be theatre infections because of the early rise in temperature and the development of pus deep in the wound. Support

for this assumption was afforded by the fact that patients 14 and 15, who developed empyemata, due to the epidemic strain, were nursed in a ward outside the surgical unit concerned in the epidemic.

The nasal carrier rate of the epidemic strain amongst the surgical staff was 24 per cent. Only two of these, however, were members of the theatre team, one surgeon and one nurse. The surgeon was associated with only two cases which subsequently developed wound sepsis, whereas the nurse was present at most of the operations. It was thought that the theatre nurse may have been responsible initially for the outbreak, which subsequently became widespread throughout the wards with recovery of organisms from wounds, dust and the noses of many nurses.

The malignant nature of this outbreak is revealed by the fact that the mortality rate of sixteen wound infections was 25 per cent. Clinically these four cases were undoubtedly post-operative infections resulting in peritonitis and death. Unfortunately bacteriological studies were only carried out on one patient at post mortem, in which pathogenic staphylococci were isolated and this strain was not available for phage typing. Therefore, although definite proof was lacking that these patients were infected with the epidemic strain, it was thought highly probable.

The measures taken to control the epidemic included closure of the unit for one week for complete disinfection and the treatment of all nasal carriers with 1 per cent. hibitane cream. Following these measures, the sepsis rate fell dramatically to less than 5 per cent. and no epidemic strain was apparent during the following nine months.

In epidemic B it was established that 64.4 per cent. of post-operative wound infections, during 1959, were due to strains of staphylococci belonging to phage types 77 and 75/77. These two patterns were interpreted as belonging to the same epidemic type. The remaining 35.6 per cent. of septic wounds were attributable to a variety of phage types belonging to groups I, II, III, mixed and untypable.

It was observed that most post-operative wounds were clean at the time of the first dressing on the fifth-sixth day and sepsis only became apparent on the ninth-twelfth post-operative day. The wound infection was usually superficial and no case of deep abscess formation was recorded. These findings suggested that the majority of septic wounds were ward infections rather than theatre. Support for this view was afforded by the fact that the epidemic strain was widely disseminated throughout the wards, in the air, blankets and the noses of many nurses. No strains of staphylococci of the epidemic type were detected among theatre staff or from settling plates exposed during operations.

From these investigations, it was apparent that an epidemic strain was prevalent in the wards, but all infections were not due to this strain alone. It, therefore, seemed that two factors were involved in maintaining the outbreak, namely, the presence of an epidemic strain and poor aseptic technique throughout the unit.

The measures taken in March and December, to control the epidemic, were successful in eradicating practically all wound infection due to staphylococci

of phage types other than the epidemic type 77. Infection, due to type 77 strains, was considerably reduced after complete disinfection, but the measures taken were unsuccessful in eliminating the epidemic strain completely.

Analysis of these two epidemics highlights several important features of outbreaks of staphylococcal infection. The first and probably most important of these was the fact that considerable damage had already been done before phage typing was started, second, that an epidemic strain, thought to have originated from a single carrier in at least one of the epidemics, was responsible for most cases of severe infection, and, finally, the offending strains showed multiple drug resistance.

At present there is no way of recognising an epidemic strain which will certainly cause an outbreak of infection. It is true that certain phage types are more commonly associated with outbreaks of infection than others, but even the introduction of a known potentially epidemic strain into a unit does not always produce an outbreak. Furthermore, practically any phage type of staphylococcus seems capable of becoming epidemic at a particular time or place, and thus it appears that in either case local conditions must be favourable for a strain to flourish. In view of this, it seems doubtful if the investigation of nasal carriers among hospital staff is of any value in anticipating an outbreak of infection since some 35-50 per cent. of individuals normally carry a variety of phage types of staphylococci in the nose (Williams et al., 1960). It appears, therefore, that until a possible relationship between phage type and virulence has been elucidated the value of phage typing as an indicator of impending sources of sepsis is strictly limited. Moore (1960) has recently shown that strains of staphylococci, potentially dangerous from the epidemiological aspect, can often be identified by their ability to grow on an agar medium containing Hg Cl₂. If this work is confirmed it may prove a valuable adjunct to bacteriophage typing in epidemiological investigations.

A feature common to both epidemics was drug resistant epidemic strains which would appear to be a characteristic of most hospital outbreaks of staphylococcal infection recorded in recent years. If this trend continues, a stage may be reached when the more virulent hospital staphylococci outstrip the production of newer antibiotics and an era of complete antibiotic resistance is attained. An attempt has been made to bring about a reversal of antibiotic resistance in hospital staphylococcal infection by Barber et al. (1960). These workers, by strict limitation of the use of penicillin and the general employment of double chemotherapy, were successful in reducing the number of penicillin resistant infections from 70 per cent. to 36 per cent. This line of approach seems promising and hope for the future may depend on the application of a controlled antibiotic policy in all hospitals and constant vigilance in aseptic technique.

SUMMARY.

1. Two epidemics of post-operative staphylococcal infection are described. In epidemic A the sepsis rate was 24.0 per cent. and four patients died. Bacteriophage typing showed that all the infections were caused by one

epidemic type and the same strain was present in the anterior nares of 24.0 per cent. of the surgical staff. A theatre nurse was thought to be the originator of the outbreak, but this was not proved. Closing of the unit for one week for complete disinfection and treatment of nasal carriers was successful in terminating the epidemic.

2. Epidemic B was observed over a twelve-month period. Most of the wound infections were thought to have been acquired in the wards. Of fifty-nine post-operative infections occurring during 1959, 64.4 per cent. were due to an epidemic strain, while the remainder were caused by a variety of phage types. Examination of nasal swabs from the surgical staff, ward air and blanket sweeps showed that the epidemic strain was widely disseminated throughout the unit. Peaks of post-operative sepsis were recorded in March (17.5 per cent.) and December (17.0 per cent.), and on both occasions the unit was closed down, for disinfection and treatment of nasal carriers. A dramatic fall in the sepsis rate was observed on each occasion, but the measures taken failed entirely to eradicate the epidemic strain.
3. The difficulty of anticipating an outbreak of staphylococcal infection in hospital is discussed.

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DIETHYLPROPION IN THE TREATMENT OF OBESITY

A cross-over trial of a long-acting preparation

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DIETHYLPROPION ("Tenuate") has been shown to be useful in the treatment of refractory obesity (Seaton *et al.*, 1961). Appetite suppression with the standard preparation is reported to last about four hours (Spielman, 1959) and the drug must be taken at least three times daily. This paper reports the use of a long-acting preparation of the drug, which need be taken only once a day. It is marketed as "Tenuate Dospan" in which the active principle is incorporated with a hydrophilic colloid, which expands in the intestine and allows a continuous release of the drug. The advantage claimed, in addition to the virtual absence of undesirable central nervous stimulation (Wilson and Long, 1960; Nash, 1960), is that the sustained release tablet will provide hunger control for a full twelve hours.

Diethylpropion (α -diethylaminopropionophenone) is closely related structurally to amphetamine (B-aminopropylbenzene).

METHODS.

A double-blind cross-over technique was used. Patients with obesity who had been referred on this account to the general medical or metabolic departments of the Royal Victoria Hospital were considered for admission to the trial. Those with serious associated disease were excluded, and the remainder were asked if they wished to attend a special monthly clinic to help them lose weight. They were offered the attraction of a number of new drugs which might help in the treatment of their obesity.

They were fully examined at their first visit and a detailed family and dietary history elicited. They were weighed in normal indoor clothes, without shoes, by the same nurse on the same scales at each visit. (The scales are checked monthly for accuracy.) All patients were interviewed by the dietician attached to the Metabolic Clinic, and were given a standard 1100 calorie reduction diet containing 100 G. of carbohydrate, or told to continue their existing regime if they were already intended to consume less than 1100 calories on a recognised schedule. The discussion of methods of weight reduction was limited to encouragement to keep to the diet. The tablets were presented as an aid to weight loss, with no mention of their method of action, or possible side effects. The patients were not told that this was a double blind trial.

Those taking part in the trial were divided into two groups ("A" and "B") at their first visit, according to a sequence constructed from a table of random

numbers. Bottles, with detachable identification tags were available, containing four weeks' supply of either diethylpropion tablets (75 mg.), or an identically presented placebo. Each group commenced with one type of tablet, and after four weeks the distribution was reversed. Patients were instructed to take one tablet each morning before breakfast.

They were reviewed by one of us after four and eight weeks. No direct enquiries were made about the patients' subjective impressions of the drug or possible side effects. Only spontaneous complaints were noted. Neither the patients, the doctors, the dietitians nor the nursing staff knew which tablets contained the active preparation. A sealed envelope containing the manufacturer's key to the identification tags was opened when the trial was completed. It was then found that Group "A" had received the diethylpropion in the first month, and the placebo second; Group "B" had received the tablets in the opposite order.

TABLE 1.
STATISTICAL DATA CONCERNING THE TWO GROUPS.
Values are means, standard deviations and ranges.

	GROUP A 11 patients	GROUP B 11 patients	DIFFERENCE OF THE MEANS.		
			Standard deviation	t	Level of significance
Age (years) - -	40 ± 12.6 (17-59) ...	36 ± 16.3 (13-56) ...	14.35 ...	0.28 ...	0.8 > P > 0.7
Height (inches) -	63 ± 3.4 (59-68) ...	63 ± 3.0 (59-70) ...	1.45 ...	0.11 ...	P > 0.9
Initial weight (lb.) -	223 ± 32.8 (167-272) ...	206 ± 28.8 (160-239) ...	26.50 ...	0.65 ...	0.6 > P > 0.5
Standard weight (lb.)	144 ± 14.2 (121-165) ...	144 ± 19.5 (104-182) ...	7.30 ...	0.05 ...	P > 0.9
Per cent. overweight	54.8 ± 14.5 (23-72) ...	43.6 ± 22.2 (22-84) ...	8.36 ...	1.36 ...	0.2 > P > 0.1

THE PATIENTS.

Twenty-two patients completed the trial out of thirty-eight who were initially accepted.

A comparison of the two groups of patients "A" and "B" who completed the two months' treatment is shown in Table 1. The groups, having been selected at random, are comparable as regards age and height, and hence also standard weight, which is derived from these (Tables of the Life Extension Institute of New York). The mean percentage by which the patients in Group "A" exceed their standard weight is not significantly greater than that of Group "B" and neither are the slight differences in mean initial weight and height.

Nine in each group had a history of obesity exceeding ten years' duration: six in Group "A" and five in Group "B" had made a previous attempt at dieting. There was one male in each group, and seven of the women in each group were married. The mothers in Group "A" had a total of thirty children, and those in Group "B" twenty-two children. Only two patients out of the whole series spontaneously complained of hunger as a possible cause of their obesity.

There were six cases of maturity onset diabetes mellitus, already controlled by restriction of carbohydrate. Six patients had angina of effort but in only three was ischæmia apparent on the electrocardiogram, and none showed evidence of fluid retention. One patient had been treated for several years with thyroid extract for mild hypothyroidism (confirmed by radio-iodine studies) but was euthyroid prior to and during the trial. One showed clinical and biochemical features of mild adrenal virilism.

TABLE 2.
RESULTS OF CROSS-OVER TRIAL OF DIETHYLPROPION.

NUMBER OF PATIENTS	MEAN WEIGHT LOSS IN LB.		
	GROUP A 11	1st month diethylpropion 9.99	2nd month placebo 0.99
GROUP B 11	1st month placebo 2.54	2nd month diethylpropion 2.0	2 months combined 4.54

RESULTS.

These are recorded in Table 2. The best results were achieved in those who were treated first with diethylpropion, and these patients lost almost 10 lb. on average in this month. The mean loss in one month on diethylpropion for the whole series of twenty-two patients was almost 6 lb., which is significantly greater than the mean loss on the placebo, which was 1.75 lb. ($0.02 > P > 0.01$). As the drug was given under a "double blind" technique, this proves the effectiveness of the long-acting preparation of diethylpropion in the treatment of obesity. The "crossover" design allows assessment of the effect of the order of treatment. When diethylpropion was given first, the weight loss in the first month was significantly greater than the subsequent loss on the placebo ($P < 0.001$). When placebo was given first, the weight loss in the two periods was not significantly different ($0.7 > P > 0.6$). Thus, the drug was no more effective than the placebo when given in the second month.

The total weight loss in Group "A" after two months' treatment was not significantly different from that in Group "B" ($0.2 > P > 0.1$). The greatest individual weight loss during the two months was 40 lb., and one patient gained 9 lb. in spite of the treatment. There was no correlation between loss of weight and age, sex, height, initial weight or the amount by which the standard weight was exceeded. The patients placed little emphasis on the effects of the tablets on their appetite but eight volunteered that they felt less hungry while taking the diethylpropion. Two stated that appetite was reduced equally by the two agents; two others claimed that the placebo was more effective.

SIDE EFFECTS.

These were not enquired after directly, and only spontaneous statements by the patients of their own observations were noted. Only three of the total series made any reference to alteration in their sleeping habits. One stated that there was a very slight interference with sleep; the other two claimed increased somnolence, all during the period on diethylpropion. Four patients mentioned dryness of the mouth, accompanied by a salty taste but this was in no way troublesome. There were no complaints of restlessness or headache. There was no evidence of the development of schizophrenic symptoms or addiction to the tablets. None of the group, including those known to have mild coronary artery disease, experienced angina pectoris while on the trial. Treatment did not have to be stopped in any case.

DISCUSSION.

It is generally accepted that physiological weight loss can only be achieved following a negative calorie balance. Most patients who are already obese are unable to keep to a strict calorie limitation unaided. To encourage them to lose weight high fat or high protein diets, bulking agents and tranquilizers with or without psychotherapy have all been advocated, and shown to have some benefit. Appetite suppression, which was discovered as a side-effect of the amphetamine group of drugs, is a logical adjunct provided that the primary stimulant effect of these substances on the central nervous system is not troublesome. Previous reports and experience in the present trial have shown no evidence of such stimulation with diethylpropion.

During the course of treatment there was no evidence of the development of psychotic behaviour. The amphetamine-group of drugs are probably all equally liable to cause this if abused. Addiction and schizophrenia are well recognised following amphetamine (Connell, 1958; McConnell and McIlwaine, 1961) and a similar picture has been reported with phenmetrazine. There are, as yet, no reports of addiction or psychosis due to diethylpropion or any of the newer derivatives.

The mean weight loss in this series (5.99 lb.) is considerably greater than that reported by Seaton *et al.*, 1961 (2.58 lb.) after one month on diethylpropion. We consider our group more representative of obesity in general, as only about half would fall within their definition of "refractory" obesity (failure to respond to dietary instructions during the previous year). The results in the first month (9.99 lb.) are also superior to those reported by Briggs *et al.* (1961) in a more comparable group, taking phenmetrazine hydrochloride (6.5 lb.). Stevens (1961) reports a trial of a long-acting preparation of diethylpropion 60 mg. daily, which gave an average weight loss on the active tablet of 1.9 lb. in one month. He suggests that the dose should be slightly higher and the considerably better results in our own series confirm the effectiveness of 75 mg. daily. We would not advise further increase in dosage, as this may increase the liability to side effects.

Diethylpropion in long acting form was considerably less effective when given following a month on placebo. Jaffe (1961), in a trial in general practice, found

that weight loss during the first two months of a six-months period was greater than subsequently and this aspect is also well illustrated by the results of Seaton *et al.* (1961), where very little weight was lost after the first month. It would seem wisest to recommend the use of anorectic drugs of this type in intermittent courses of a few weeks' duration.

One aspect of the treatment of simple obesity is the extremely high incidence of defaulters (sixteen out of thirty-eight in the present series). This makes a large series difficult to accumulate, and is probably a further example of the general mental attitude of many who allow themselves to become overweight.

The price of one month's treatment with "Tenuate Dospan" is 11s. 2d.

SUMMARY.

A double-blind cross-over trial of diethylpropion (in a long-acting preparation) in the treatment of simple obesity in conjunction with a low calorie diet, is described.

The drug in this form is effective and without side effects.

Diethylpropion caused the greatest weight loss when it was given at the commencement of the trial. It was considerably less effective when administered after a month's treatment with a placebo. For this reason it is recommended that its clinical use should be restricted to short intermittent courses.

ACKNOWLEDGMENTS.

We acknowledge the helpful advice and criticism of Dr. D. A. D. Montgomery, M.B.E., Physician-in-Charge, Metabolic Unit, Royal Victoria Hospital, and of Professor E. A. Cheeseman, Medical Statistician to the Royal Victoria Hospital. We are very grateful to Sister M. Russell, Sister-in-Charge, Metabolic Extern, and Mrs. P. Steen and Miss M. Hurst, Dietitians attached to the Metabolic Clinic.

We thank Messrs. Merrell-National (Laboratories) Ltd., for supplies of Tenuate Dospan and the placebo tablets.

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CHRONIC ALCOHOLISM:

A Survey of the Incidence in Downe Hospital Area

By ALAN P. GRANT, M.D., F.R.C.P.I., M.R.C.P.(Lond.)

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MORE scientific interest in the incidence of chronic alcoholism is now being shown and a "Memorandum on Alcoholism" has recently been prepared by a Joint Committee of The British Medical Association and the Magistrates Association (1961). The need for more intensive research has been emphasized, especially into the nature and size of the problem.

Assessments of the incidence of chronic alcoholism in various countries have usually been based on the estimation formula devised by E. M. Jellinek and adopted by the World Health Organisation (W.H.O.) Expert Committee on Mental Health Alcoholism Sub-Committee 1951. This formula assumes that if the percentage contribution of alcoholism to cirrhosis of the liver is known, it is then possible to determine from reliable autopsy reports the total number of alcoholics with complications existing in a population in any given year. Recently there has been severe criticism of the accuracy of the original formula and modifications have been suggested by Seeley (1959) and Brenner (1959). Jellinek (1959) has admitted that the formula should no longer be retained and that field studies are necessary.

This publication reports a field study of the incidence of chronic alcoholism in a rural community in which we were intimately concerned. The sample analysed is small but it is suggested that further personal studies of this type from other areas in Northern Ireland would result in a more accurate estimate of the size of the problem.

MATERIAL.

The area studied was that served by the Downe Hospital, Downpatrick, to which, in 1958, we were acting as Consultant Physicians. We thus had close personal contact with all the practitioners using the hospital and a fairly intimate knowledge of the countryside and its population. The total population of all the practices in this zone in that year, obtained from the General Health Service Board for Northern Ireland, was 40,216. The area involved approximates to the two Urban Districts of Downpatrick where the County Mental Hospital is also sited and that of Newcastle, with the Rural District of Downpatrick. The predicted total population for these districts calculated from the 1951 Census for Northern Ireland (Registrar General, 1953), and making allowance for an intercensal increase, was 40,024, which agrees closely with the actual number obtained from the Board. It was possible, therefore, to use the 1951 Census figures with fair accuracy, and these have been applied in the calculations. In the county of Down the percentage of adults of over 19 years was 65, and males and females

made up 46.3 and 53.7 per cent. of the population respectively. The predicted population for the county in 1958 was 251,300 (personal communication, Registrar General).

METHODS.

Each General Practitioner was interviewed personally and given a form to complete in respect of each chronic alcoholic in his practice, giving details of age, sex, marital state, number of children, occupation, war service, age at onset of alcoholism, the usual intoxicants preferred and details of any previous mental hospital treatment.

Chronic alcoholism was defined as the habit of consuming intoxicants to such an extent as to lead to interference with the patient's work, disturbance of his domestic or social life, and/or damage to his mental and physical health.

Only three out of the seventeen practices serving the area could not be prevailed upon to co-operate. The remaining fourteen gave every assistance and represented in all 33,174 out of a total of 40,216 patients under the care of general practitioners in the area.

TABLE 1.
GENERAL RESULTS.

Alcoholics in Sample	-	-	-	-	-	-	46
Number in Sample	-	-	-	-	-	-	33,174
Total Population of Downe Hospital Area	-	-	-	-	-	-	40,216
Sample as percentage Total Population	-	-	-	-	-	-	82.5
Adults as percentage Total Population	-	-	-	-	-	-	65.7
Estimated Alcoholics in Downe Hospital Area	-	-	-	-	-	-	56
Rate per 100,000 Adults	-	-	-	-	-	-	214
Estimated Alcoholics in County Down	-	-	-	-	-	-	350
Total Alcoholic Admissions to County Mental Hospital in 1958	-	-	-	-	-	-	26
Alcoholic Admission Rate to Mental Hospitals per 100,000 adults	-	-	-	-	-	-	15.7

RESULTS.

The general results are shown in Table 1, where it may be seen that there were forty-six persons diagnosed as chronic alcoholics in the fourteen practices co-operating. From these figures and the number in the sample the rate per 100,000 adults was estimated at 214 in the Downe Hospital Area. Calculating on this basis, the incidence for Co. Down is estimated at 350 chronic alcoholic patients, of which twenty-six were admitted to the area Mental Hospital for treatment.

More detailed information about these patients is given in Table 2, where it may be seen that males predominated over females in a ratio of over 10/1 and married men over single, divorced or widowed men in a ratio of 2/1. Each man who had been married had on the average a family of four children. War

service was undertaken by only three affected males. The average age of the group was 53 years. In most patients, chronic alcoholism had arisen in early adult life; on average at 28 years of age. The majority of sufferers were farmers and shopkeepers, falling into Social Class II, a class which included four publicans. Whiskey was the usual drink preferred, although eleven persons in the lower social classes were stated as liable to drink any intoxicant.

TABLE 2.
PERSONAL DETAILS OF SAMPLE.

Sex	- - -	42 Males	4 Females				
Marital State	- - -	30 Married	10 Single	1 Divorced	5 Widowed		
Previous Treatment	-	20					
Age	- - -	53.04 years	SD 11.53				
Age at Onset	- - -	28.02 years	SD 9.3				
War Service	- - -	3					
Children	- - -	124					
Social Class	- - -	I 4	II 21	III 10	IV 2	V 9	
Usual Intoxicant	-	Spirits	-	-	-	-	32
	-	Wine	-	-	-	-	2
	-	Beer	-	-	-	-	1
	-	Anything including Methylated Spirit					11

DISCUSSION.

The World Health Organization Alcoholism Sub-Committee of the Expert Committee on Mental Health (1951) estimated the total alcoholism rate in England and Wales in 1948 to be 1,100 per 100,000 adults, but admitted that this was hardly better than a guess. These figures were based on the Jellinek estimation formula. The total alcoholism rate in the small area of Northern Ireland which we have investigated at 214 per 100,000 adults is obviously nowhere near this figure (1,100 per 100,000), and is much closer to the rate of 110 per 100,000 adults quoted in the large field study of Parr (1957). Parr received replies from 369 practitioners in the United Kingdom and his was the first attempt at assessment of a large field sample population in this country. He used the definition of chronic alcoholism of the World Health Organization Alcoholism Sub-Committee (1952): "Alcoholics are those excessive drinkers whose dependence upon alcohol has attained such a degree that it shows as a noticeable mental disturbance or an interference with their bodily and mental health, their inter-personal relationships and their smooth economic functioning, or who show the prodromal signs of such developments. They therefore require treatment." Our own definition and results are comparable. The figures obtained in our survey are, of course,

limited strictly to the small district concerned, but owing to personal contact are probably as accurate as this type of study can produce. As Glatt (1961) has pointed out, Parr's estimate may be low owing to a natural concealment of alcoholism from the doctor, but in a country area such as we have surveyed this is hardly possible. It must be admitted, of course, that any figures are greatly influenced by a practitioner's own attitude to the problem.

The sex ratio of over 10/1 in favour of males is very different from Parr's English figures of 2.2/1 in his series or even 3.1/1 in the 1952 Mental Hospital Survey. It is likely that different social habits between the two countries are responsible. In Irish country districts female drinking in public-houses is not as yet customary, and Parr's figure for rural districts gave a higher male preponderance at 5/1. This would suggest that female alcoholism was much more prevalent in cities and industrial environments where the social conscience is not so strong.

Mental hospital statistics do not give the true size of the problem. Out of our series of forty-six chronic alcoholics only twenty had ever had treatment in a mental institution, and for the whole county of Down in 1958 there were only twenty-six alcoholics admitted to the area mental hospital out of an estimated total for the county of 350. Figures for the previous year (1957) with twenty persons requiring mental hospital treatment were comparable, and of these there was a preponderance of males in the ratio of 9/1. Enquiries at that time suggested an alcoholism rate of 1.2 per practice of 2,000 persons (Grant, 1959).

Comparison of the marital status of alcoholics in the area with the census figures for the county did not suggest any significant influence nor was war service related. Money was to some extent important in that the sample showed most of those affected to be in the higher social classes. The relatively early age of onset of alcoholism in the group may be of significance indicating a strong predisposition. Unfortunately we have no data to suggest whether this is mainly due to heredity or environment.

Popham and Schmidt (1958) gave the following figures for consumption of alcohol and the percentage contribution of beer, wine and spirits to the total:

	BEER	WINE	SPIRITS	IMPERIAL GALLONS PER ADULT
United Kingdom, 1955 -	82	4	14	1.25
Ireland, 1954 -	73	4	23	0.95

These figures suggest that although the total alcohol consumption in Ireland is lower per person, yet more of it is taken in the form of spirits. This observation is supported by the alcoholic preference shown in this study. Comparable figures for occasional consumers of alcohol are not obtainable but these authors quote the New York Herald Tribune World Poll as stating that in Great Britain 73 per cent. of adults use alcohol but only 11 per cent. frequently. If this figure applies to Ireland, out of habitual users only 1 in 55 becomes a chronic alcoholic.

It is possible that our estimation rate of the incidence of chronic alcoholism may be higher than that of the United Kingdom because of the higher spirit consumption. Perhaps also there may be some racial lowering of resistance to

alcoholism as suggested by Williams (1947). Our results for the Downe area nevertheless are much below those suggested by the World Health Organization and it seems probable that by personal contact higher figures for the United Kingdom would be obtained than the 110 per 100,000 adults arrived at by Parr. Estimates for rural areas might be obtained by physicians in county hospitals with reasonable accuracy but figures from large towns would probably be artificially low because of the shifting nature of the population resulting in less personal relationship between some patients and their family doctors. This is especially the case with patients as unreliable as the chronic alcoholic. It would be of value, however, to check on Parr's figures by a series of local investigations either individually undertaken or under a central direction.

SUMMARY.

The alcoholism rate for the Downe Hospital Area in 1958 was 214 per 100,000 adults. This was the result of a direct field study. Fewer than half of such persons had ever had mental hospital treatment and whiskey was the drink of choice. The value of further small personal field studies in arriving at an accurate national estimate of the incidence of chronic alcoholism is advocated.

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We gratefully thank all the general practitioners in the Downpatrick area who helped us, and also Dr. R. Dougal for figures from the Mental Hospital.

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REVIEWS

NEUROMUSCULAR DISORDERS (THE MOTOR UNIT AND ITS DISORDERS).

By R. D. Adams, L. M. Eaton, G. M. Shy. Proceedings of the Association for Research in Nervous and Mental Disease. Vol. XXXVIII. (Pp. 791. 160s.) London: Baillière, Tindall & Cox, 1961.

THIS volume is a collection of papers given at a meeting of the Association for Research in Nervous and Mental Disease in December, 1958. Like its predecessors in the series of research publications sponsored by the Association, it is not merely the proceedings of a congress, but is a true symposium with predetermined subjects and contributors. The result is a volume of great significance to all interested in muscle and its disorders, particularly to clinicians.

There is no doubt that the clinical aspect of muscle disorders has been emphasised, but in its wide sense. This is all to the good when other symposia on muscle are primarily anatomical, physiological or pharmacological. The material has been arranged into parts dealing with the basic structure and function of muscle, experimental pathology, histopathology, revolving around the main section on clinical problems.

One's first reaction to the date of publication, over two years after the meeting, is to be apprehensive lest the book be no longer up to date. This fear is almost groundless. Advances in the knowledge of muscle in some of its aspects has indeed been rapid, but the material is widely scattered and its collection into one volume is useful. As a reference work, the volume, like its predecessors, is likely to be utilized for many years to come.

The contributors are mainly drawn from the United States, and most of the better known schools of medicine are represented. Knowledge in the basic sciences is excellently summarised as in the chapters on neuromuscular transmission by del Castillo and the ultrastructure of the muscle fibre by Hodge. New work is described in experimental pathology by both Denny Brown and Betty Banker. Although the histopathology of muscle disease is dealt with by Adams, much descriptive pathology is of necessity included in many of the clinical chapters. There is, therefore, much repetition, and some controversy, reflected to some extent in the verbatim discussions. Although the volume would be shorter with the discussions omitted, their inclusion is healthy if not economical. Among the outstanding clinical chapters Shy's paper on metabolic and endocrinological aspects, and Grob and John's contribution on disorders producing transient paralysis contain much that is new. A fresh approach to myasthenia is provided by Rowland and others who entitle their chapter "Myasthenic Syndromes."

"Congenital Neuromuscular Disorders" by Dodge will be surprisingly helpful to the neurologist in his clinic. Walton, one of the few English contributors, has attempted a classification of the myopathies, two pages long, as well as an assessment of the muscular dystrophies. But it is perhaps invidious to select these from other equally useful contributions. It is a pity that the meeting was held too soon for Coërs and Woolf's work on the pathology of the neuromuscular junction using vital stains to receive more than passing mentions.

The volume ends with several shorter articles outlining techniques of promise in the investigation of muscle disease, such as tissue culture, enzyme histochemistry, fluorescent antibody technique, and so on. With so much good material within its covers, and references to the same subjects scattered in many different chapters, a good index is essential. Unfortunately, the index provided is not adequate, and this is the one serious defect in the book. It bears evidence of compilation without any understanding or knowledge of the text. Publishers who insist on providing the index themselves are often to blame for this type of result.

Altogether, this book is a valuable addition to medical literature on a subject in which there is still a great deal of clinical and pathological confusion.

G. F. H.

MEDICINE AND THE NAVY. By Christopher Lloyd and Jack L. S. Coulter. Vol. III, 1714-1815. (Pp. xi + 401. Illustrated. 50s.) Edinburgh and London: E. & S. Livingstone, 1961.

This is the third volume of the truly magnificent work begun some three years ago by the late Surgeon-Commander Keevil, who after his retirement from the service was keeper of the library of the Royal College of Physicians. Of the present authors, Christopher Lloyd is assistant professor at the Royal Naval College, Greenwich, and Jack Coulter, surgeon captain in charge of the Royal Naval Medical School. The volume, which contains 370 pages of text and has a most extensive bibliography, is well illustrated and written in an easy pleasant style, unaffected by any trace of pedantry.

The period under review is, of course, probably the most important in British naval medical history because the prolonged wars which occurred during it required the deployment of so many men and ships on foreign and tropical stations and because it was at this time that considerably more men perished from disease than from the direct consequences of enemy action. Time and time again this point is brought out by the authors, together with the failure of the authorities to appreciate it. Thus, Dr. James Lind (whose name is only mentioned once in the standard 8 volume history of the Royal Navy, and then in the wrong connection and misspelled!) recommended that it was much better on tropical stations to keep the sick in hospital ships than in sick quarters ashore. We know now that this recommendation showed great prescience at a time when the rôle of the mosquito in leading to infection with malaria and yellow fever was not understood. But Lind's point is also a sound administrative foundation, which might well have been applied to the conduct of naval medical operations in the second great world war of this century: instead of setting up base hospitals with elaborate staffs and equipment at different points in the eastern theatre, as was originally done, it would have been better to have earlier concentrated on the provision of hospital ships, the mobile value of which especially was subsequently proved in the later phases of the war.

This is only one instance of the many interesting points that emerge from study of hospital administration, hygiene, and the disposal of medical personnel and equipment during the wars. But, probably the most interesting part of the book deals with the history of the naval surgeons, who began life in the humble capacity of surgeon's mate, the social status of whom at that time can be summed up by Smollett's description of the captain of a ship as being a person who was "too much of a gentleman to know a surgeon's mate by sight." Few branches of our profession have had so little recognition as these men and especially James Lind, Thomas Trotter, Robert Robertson, and Leonard Gillespie. Sir Gilbert Blane was in a different position, not having passed through the lower ranks and being given the eminent office of Physician to the Fleet under Rodney, and at another time a member of the Sick and Hurt Board, which he adorned. Leonard Gillespie has a special interest for us in Northern Ireland because he was born in Armagh, practised for a time in that city, left a memorable journal of his experiences, both afloat and ashore, which is preserved in the Public Records Office, and because he had the privilege of being shipmate with Admiral Lord Nelson in the months before the Battle of Trafalgar. No better account of everyday life on board the *Victory* has ever been given than that which he records in a letter to his sister. The book can be unhesitatingly recommended to all interested in the study of medical history and especially as this concerns the Royal Navy.

R. S. A.

OAKES' POCKET MEDICAL DICTIONARY. Compiled by Nancy Roper. Ninth Edition. (Pp. xii + 492. 8s. 6d.) Edinburgh and London: E. & S. Livingstone, 1961.

"Words are good servants but bad masters," wrote Samuel Butler. This small, simple dictionary is not meant for doctors, but many will find it useful to give to an inexperienced medical typist; with it she will understand what she is typing and she will spell the words correctly. The dictionary is meant for nurses and would be a useful book to slip into an already overloaded uniform pocket when doing "block."

O. L. W.

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It is in the field of general clinical pathology where, I think, there is room for criticism of the choice of recommended techniques. Some of the methods described are not the most satisfactory for the purpose.

In a small laboratory there would be considerable advantage in using tablet reagents rather than solutions for urine testing. These can be more readily stored, do not deteriorate as quickly as solutions and are simple and accurate in use.

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In the section on hæmatology the use of "Sequestrene" as a routine anticoagulant for blood samples is not mentioned and the Wintrobe method for sedimentation rates is recommended, although most laboratories nowadays have reverted to the use of the Westgren method.

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In the bacteriology section, the use of dark ground examination of a centrifuged deposit of citrated blood is recommended for the diagnosis of leptospirosis. This is a highly unsatisfactory method. The only useful method of diagnosis of leptospira are by isolation of the organism or by the leptospiral agglutination test. The use of the adhesion test as a serological diagnostic procedure is historical rather than practical.

In the section on hæmatology the use of "Sequestrene" as a routine anticoagulant for blood samples is not mentioned and the Wintrobe method for sedimentation rates is recommended, although most laboratories nowadays have reverted to the use of the Westgren method.

In the section of the book which deals with blood grouping, only ABO blood groups are mentioned. If this section is intended to assist in the problem of blood transfusion practice the omission of any reference to the Rhesus factor or to the less common blood group antigens is a serious omission.

Despite these criticisms, which I am sure will be corrected in future editions, this book will prove useful to doctors with limited laboratory experience working in small laboratories in the tropics. M. G. N.

A PHYSICIAN'S INTRODUCTION TO ELECTRONICS. By A. C. Morris, jun. (Pp. 50. 15s.) London: Pergamon Press, 1961.

ELECTRONIC engineers use a language and script of their own. This book provides a basis for their translation. In a very small compass it provides sufficient information for a non-expert to understand something of a circuit diagram. Part of the book consists of instructions for the building and operation of a circuit which illustrates the basic functions of many electronic components. It should prove a useful, cheap reference manual for the non-expert who uses electronic apparatus. G. M. B.

THE DAY HOSPITAL MOVEMENT IN GREAT BRITAIN. By James Farndale, B.Com., F.H.A., M.R.S.H., Barrister-at-Law. (Pp. 430. 84s.) Oxford: Pergamon Press, 1961.

Day hospitals have their traditional origins in Montreal and London in the year 1946. Since then, in the words of the author of this book, "They have grown up like mushrooms," so that at the time of his writing there were sixty-five such centres in the United Kingdom.

James Farndale has produced a work of reference on the subject and it is the more enjoyable for being read in this way. That it is pedantically detailed and somewhat repetitive is a criticism which is less valid if the book is read as a source of reference or even as a bedside book rather than from cover to cover.

Although a great deal of the book concerns psychiatric day hospitals and day centres, there is also some account of geriatric day hospitals and day centres, medical and industrial rehabilitation day centres, and day centres for handicapped persons run by welfare authorities. Day centres for the mentally sub-normal have been excluded, as they number some 350, and have a history dating back to 1914, but several day hospitals for the sub-normal are described.

The book is divided into two parts:—

Part one is a report on the special features and problems of day hospital administration, and includes chapters on costs, transport, drugs, and catering. The administrative aspects are stressed, and these sections will appeal only to those actively involved in either existing or projected day hospital schemes. However, the earlier chapters in part one do give a more general account and survey of the existing day hospitals and day centres, and these chapters should be of value to any person, whether administrator or clinician, who is interested in the possibilities of carrying treatment and after-care out of the in-patient hospital and into the community.

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The author is not a medical practitioner but a senior administrator at the Bethlem and Maudsley Hospital, seconded as an Honorary Research Fellow to the University of Manchester for a two-year period in 1958 and 1959 for the purpose of carrying out this survey. He has produced a work which is primarily an administrator's hand-book of day hospitals but which has in it something of interest to clinicians, especially those in the psychiatric and geriatric fields of medicine. The clinician interested in community care projects must of necessity concern himself with some of the administrative problems involved. A chapter devoted to "Transport and Ambulances" at first sight appears singularly lacking in interest, but if community care programmes are ever to be seriously considered for Northern Ireland as a whole rather than merely for Belfast and, perhaps, Londonderry, then such a subject is of the utmost practical importance.

The book is handsomely bound, is printed on high quality gloss paper, and contains numerous photographs. There is a useful bibliography and a good index. R. W. W.

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The text has been largely rewritten by a team of urologists, each an acknowledged expert on his particular subject. The result has been an up-to-date and comprehensive volume of modern urology that admirably reflects the great advances that have been made in this speciality since 1948.

There are five sections in the book. In Section 1 the embryology and the surgical anatomy of the genito-urinary apparatus are discussed, and there is a chapter on renal physiology.

In Section 2 the symptoms and signs of renal disease are described. In the chapter on cystoscopic investigation advice is given on the choice of a cystoscopy, and comments are made on the method of sterilization.

Section 3 deals with the physiology, diagnosis, and the treatment of renal disease. This is covered in a detailed manner, well illustrated, and with complete references.

In Section 4 such subjects as infertility, intersex, the rôle of the small intestine in genito-urinary surgery, and kidney homo-transplantation are discussed.

Section 5 is devoted entirely to operative surgery and anæsthesia. All the standard operations in modern urological practice are described.

This book must now be regarded as the standard work on urology in the English language. It should be in the library of every urological surgeon, as well as those general surgeons with an interest in urology. In addition it will be invaluable to the post-graduate studying for the fellowship examination.

J. M.C.I. M.

ONCOGENIC VIRUSES. By Ludwik Gross. (Pp. xi + 393; pls. 41. 80s.) Oxford, London, New York, Paris: Pergamon Press, 1961.

DURING the past ten years there has been a very rapid growth in tumour-virus experimental work, and consequently of the literature. Dr. Gross's excellent monograph has not only brought together a review of the known oncogenic viruses but also discusses the current status of the experimental approach to virus caused neoplasms. The book is not only attractively, clearly, and authoritatively written but is beautifully produced.

The first chapter presents a simple and straightforward introduction to the properties of viruses, the transplantation of tumours by cell graft and the transmission of tumours by filtrates. This introductory chapter provides all the necessary background information for the non-specialist who should not be deterred from reading this book because of its somewhat formidable sounding title. The subsequent chapters review all the important information on viruses causing tumours in animals, their transmission, epidemiology, and pathology. The viruses in this book have been "personalised," for not only are there numerous electron microscope photographs of the viruses and their tumours but also of twenty-seven of the men and women as well as of the mice associated with their discovery and study. Many readers will find the inclusion of photographs of contemporary virologists a most attractive feature.

The final chapter deals with the search for oncogenic viruses in humans and discusses the possible viral ætiology of cancer.

Each chapter of the book is followed by a very carefully compiled list of the most important bibliographical references which should prove of great use to the reader who is interested in a particular field.

This most readable book can be strongly recommended not only to virologists and pathologists but to all experimental biologists as well as to physicians and surgeons quite apart from its value as the most up-to-date reference book in this rapidly expanding field.

G. W. A. D.

TEXTBOOK OF MEDICAL TREATMENT. Edited by Sir Derrick Dunlop, Sir Stanley Davidson, and S. Alstead. Eighth Edition. (Pp. xix + 983. 60s.) Edinburgh and London: E. & S. Livingstone, 1961.

A REVIEWER once wrote that a new edition of a well-known textbook had grown in girth but not in stature. The new edition of this excellent and popular textbook has grown in stature but not in girth. It has been revised and some chapters radically altered. This is as it should be, for therapeutics change rapidly in this modern world.

I would like to see a short select bibliography at the end of each chapter so that students may be guided to some of the controversy and argument which it is impossible to deal with adequately in a textbook; but I have no hesitation in recommending this book for undergraduates. To graduates who used an earlier edition of this book in their student days and keep the old favourite to hand, I would say: "Get rid of the old and buy the new." This is good advice that will benefit all, including, I hope, the authors and the publishers.

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A SHORT HISTORY OF CLINICAL PATHOLOGY. By W. D. Foster, M.D.(Cantab.). (Pp. xi + 154; pls. 23. 27s. 6d.) Edinburgh and London: E. & S. Livingstone, 1961.

THIS book gives a brief and useful account of the historical development of clinical pathology. The author, like many others, has found himself in some difficulty in attempting to define the extent of what is called "clinical pathology." This branch of medicine is a child of many adoptions and embraces microscopy, pathological anatomy, clinical biochemistry, diagnostic microbiology, and hæmatology. It might indeed be better called "laboratory medicine," as it seeks to provide data obtained in the laboratory which will assist the clinician at the bedside in the diagnosis and management of his patients.

In this book the historical evolution of clinical pathology has been presented. To obtain clarity, the four major divisions of laboratory medicine are dealt with separately. There is also a chapter on the clinical laboratory facilities in hospitals in Great Britain. This shows how these have developed from relative obscurity of a back room to become a diagnostic hospital laboratory service. The chapter on the general organisation of clinical pathology today has been contributed by Dr. S. C. Dyke, a former President of the Association of Clinical Pathologists. Few can speak with greater authority than Dr. Dyke, for it was he who was most responsible for the development of the speciality of clinical pathology, and for the improvement in the professional status of the medical specialists who work in this field.

In considering the position of clinical pathology, Dr. Dyke very rightly points out that clinical pathology is not a separate and distinct discipline but an essential part of the 'corpus' of medicine. He also points out that any attempt to separate clinical pathology from the mainstream of medicine is likely to be harmful, not only to clinical pathology but to medicine as a whole.

This book is a valuable contribution to the field of the history of medicine. It fills a gap in the available literature. The style is pleasant and agreeable. The illustrations are appropriate and well reproduced. The author is to be congratulated on a book which, I am sure, will be read with interest by many and will grace the library shelves of every hospital laboratory.

M. G. N.

BACTERIOLOGY AND IMMUNITY FOR NURSES. By Ronald Hare, M.D. (Pp. viii + 193; pls. 12; figs. 30. 17s.) London: Longmans, 1961.

THIS first edition of a textbook for nurses is most comprehensive and provides a wealth of information which more than covers what the nurse needs to know.

There are twelve chapters, the first three of which deal with the structure and behaviour of micro-organisms, infection and immunity, and sources and modes of infection. Four chapters are devoted to methods for prevention of infection in the home, in the field, and in hospital. A feature is the description of methods for sterilisation in medical practice.

In the chapter on treatment of infection there is a useful table detailing the antibiotics and chemotherapeutic agents currently in use for the treatment of infections due to bacteria, fungi, and protozoa. The chapter on bacteriological methods used for the diagnosis of infections is particularly welcome, as many nurses (and doctors) appear not to have been taught the correct technique of taking, e.g., a throat swab, or that it should not be taken when the patient is having antibiotic treatment (especially oral antibiotics), after gargling or taking a hot drink.

The last six chapters describe in some detail the various pathogenic bacteria, spirochætes, fungi, viruses and rickettsiæ, indicating the bacteriological diagnosis, treatment, and prevention.

More space might have been given to details of high temperature, steam pressure sterilisers and their operation, in view of recent developments.

The plates are excellent and there are many useful figures, most of which are self-explanatory. The text is simple and lucidly expressed.

This is a book which should be of considerable value to the trained nurse and the nurse preparing for her Final State Examination; for the nurse in the Primary Training School it is much too advanced.

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A GUIDE TO CARDIOLOGY. By J. C. Leonard, M.D.(Lond.), M.R.C.P.(Lond.), and E. G. Galea, M.B.(Queensland), M.R.C.P.(Lond.), M.R.A.C.P. (Pp. xii + 267; figs. 72. 27s. 6s.) Edinburgh and London: E. & S. Livingstone, 1961.

This small book of 254 pages covers a wide field in the clinical aspects of clinical cardiology. It is intended for students and house physicians who wish to have a practical correlation of their theoretical knowledge of the subject. Most aspects of cardiac disease receive a mention and the presentation of the work is pleasing and interesting. Brief reference only to special techniques is included and there is an adequate supply of illustrations of common cardiac conditions. Minor criticisms only are justifiable, such as the persistence of the myth of unipolar interpretation of the electrocardiograph.

The book should be available to medical units dealing with cardiac cases. Those who follow its reasoning will be inspired to further reading of the speciality.

E. F.

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O. L. W.

OUTLINE OF ORTHOPÆDICS. By John Crawford Adams. Fourth Edition. (Pp. vii + 448; figs. 324. 35s.) Edinburgh and London: E. & S. Livingstone, 1961.

THIS book was first published in 1956 and this is the fourth edition. The third edition was published only in 1960. It says much for the keenness and interest of the author that he revises and keeps up to date this excellent book. The subjects of tuberculous spinal disease and bone tumours have been almost re-written and are now as up to date as they can be in a textbook.

The original plan of describing the clinical examination of each part remains the fundamental and important part of the book. The clear classifications and excellent lay-out are still retained and even improved.

It was a little disappointing to find no reference to Erb's palsy, and in a new edition one hoped that acute osteomyelitis might have been brought up to date, especially in relation to infants and the aged.

It is, without doubt, one of the best books from which to learn orthopædics and should be read by all students and candidates for higher examinations. R. I. W.

SYMPOSIUM ON ANTICOAGULANT THERAPY. Report of the Proceedings edited by Professor Sir G. W. Pickering. (Pp. xii + 284; illustrated. 21s.) London: Harvey & Blythe, 1961.

EVERYONE who is interested in cardiovascular disease should have access to this symposium on anticoagulant therapy held at the Royal Society of Medicine in November, 1960. All aspects of the subject are covered in eight sessions and there are over forty contributors, many of whom are of international status. Each section deals with a particular aspect of anticoagulant therapy and includes a discussion after presentation of a paper. Peripheral vascular disease, coronary artery disease, and cerebral vascular lesions are comprehensively surveyed. The reader will realise that current thoughts on anticoagulant treatment as yet remain indecisive about its application in different conditions. This book will also give the physician a balanced view of the complexity of the subject at the present time. E. F.

ESSENTIAL UROLOGY. By Dr. Fletcher H. Colby, M.D. Fourth Edition. (Pp. 603; figs. 284. 64s.) London: Baillière, Tindall & Cox, 1961.

THIS book exhibits the same features of previous editions. It is divided into three parts; the first deals with embryology, anatomy, and physiology of the genito-urinary organs; the second with the examination of the urological patient, and the third discusses the diseases of the genito-urinary organs.

This book is based on urological practice in the Department of Urology at the Massachusetts General Hospital. It is very readable and beautifully illustrated, and thoroughly up to date in this rapidly expanding subject both in its text and its references. It is an ideal book for the senior student and for the post-graduate who has an interest in urology.

It is highly recommended.

J. M^CI. M.

THE USE OF DRAWING IN THE STUDY OF ANATOMY AND PHYSIOLOGY.

By Charles R. Bannister, M.C.S.P. (Pp. 39; figs. 19. 17s. 6d.) Edinburgh and London: E. & S. Livingstone, 1961.

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