indeed gone with the wind. In neurosurgery it is the same story, but it is the same story everywhere. It is a pleasure to record the indebtedness of surgeons to the anaesthetist whose understanding and expert partnership have won him a new respect and importance. It is right and proper that much of what has happened should have been of British origin, because for at least two generations we have led the world in this vital matter.

No record of the time would be complete without mention of urology, dominated in its middle period by Thomson-Walker, that master of endoscopy like his follower Macalpine. The surgery of the prostate alone would call for a long chapter, with biochemistry again to the fore in the case of carcinoma, the development of the cold-punch technique, and Hey's championing of prostatectomy for retention—all most important advances. Similarly, no more than a bare mention can be made of plastic surgery, a subject in which Britain has for long been in the world leadership under the guidance of Sir Harold Gillies and his coadjutors, T. P. Kilner and Sir Archibald McIndoe. In surgical pathology the work of Sampson Handley on breast carcinoma and the melanomas clarified the distinction between embolism and the process he named lymphatic permeation. This was an addition to knowledge of lasting value; comparable to it were the researches of Jamieson and Dobson on the visceral lymphatics. Nor should Sir Lenthal Cheate's microscopy of chronic interstitial mastitis and Paget's disease be overlooked.

Conclusion

Looking back over the foregoing there have been a hundred omissions of men who deserve our gratitude and thanks, whose quiet and unassuming work has fortified and held the lines of communications of the more glamorous few. For although we cannot do without the adventurers it is the solid body who do the work, who accept the good and quietly discard the valueless. These men whose worth is often realized only by their near colleagues do invaluable services to mankind. But there are other names who clamour for more description of their work; Wilfred Trotter, who was the greatest intellect of them all, but will not fit into any scheme, has hidden himself somewhere. Perhaps his advocacy of the treatment of malignant disease in a rational way and not as a purely anatomical exercise in formal excisions would have most interested a Paget or a Hutchinson or a Billroth.

Nor has Victor Horsley's part as an experimenter and innovator been given sufficient place. Nor, again, is A. E. Barker here to whom we owed the development of local analgesia in this country, a debt indeed. And so, too, Butlin and Makins, Ernest Miles and Lockhart Mummery are not in the list, though they should have been, as should A. H. Tubby, the author of the most comprehensive work on orthopaedics in English. And what of Sir Thomas Dunhill, to whom we owed the modern operation of thyroidectomy and improvements in the management of thyrotoxicosis—and of Joll and Morley, who contributed so largely to this subject? And of Keynes's work on thymus and thyroid? Also omitted is the surgery of the sympathetic nervous system in which Stopford and Telford, Gask and Paterson Ross and James Learmonth pioneered; and not least in the surgery of malignant disease, in the developmental period of radiotherapeutics, the names of Sir Ernest Rock Carling and Sir Stanford Cade deserve gratitude not only for their technical skill but for their common sense in matters that call for the utmost in balanced judgment, a commodity that single-minded enthusiasts often lack.

It would not be out of place in this *Journal* for a surgeon to lay some stress on the part that the general practitioner has played in passing on to his patients the new benefits that surgery could afford them. It is often to him as much as to the surgeon that a patient's thanks should be given for his cure. But the practitioner himself had to learn, and we should not forget the great student teachers, Russell Howard at the London, Reginald Vick at Bart's, Mitchiner at St. Thomas's, Julian Taylor at U.C.H., and a score of others in London and the provinces who would as soon be remembered for this work as for their other contributions to surgery.

So brief a précis of all that has happened, of all the knowledge that has accrued by the labours of all those who have devoted their lives to the various branches of surgery, is almost derisory in its baldness. A life-time of active work and rich result has sometimes had to be recorded by a name, and by no means all of these could be cast into the framework of a sentence. But readers know to whom the palms should be awarded and they will pay in reflection their own silent homage to those to whom it should be made. But this brief chronicle is already in danger of stretching itself too far; a line must willy-nilly be drawn across the page.

FIFTY YEARS OF MIDWIFERY

BY

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No span of fifty years has seen such great advances in midwifery as the first half of the present century. The principal milestones are the birth and growth of the idea of antenatal care, the discovery of vital fresh knowledge about the aetiology of puerperal infection, the discovery of the sulphonamides and penicillin, the notable improvement in the methods and results of caesarean section, and the increased facilities for and better understanding of blood transfusion. The conquest of "puerperal fever," for centuries the scourge of childbirth, would alone justify my opening claim, for it has transformed the maternal mortality tables of the Registrars-General. From this and other causes the maternal mortality has been falling more rapidly than the general mortality, and it looks as if in a few years the death rate of pregnant women—admittedly a selected class—would be less than that of non-pregnant women in the same age group. But while this achievement has been the greatest and the most spectacular, the growth of the idea of antenatal care has been the most pervasive influence, and has worked the most widespread changes in the obstetrical outlook.

The Idea of Antenatal Care

At the beginning of this century any special care deliberately devoted to the object of preserving the health of the expectant mother, of treating any unhealthy conditions during pregnancy, and of foreseeing and, if possible, forestalling dangers likely to arise in her labour, so as to bring her and her baby safely through, was virtually unknown. In that admirable standard textbook of the period, W. S. Playfair's *Science and Practice of Midwifery* (1898), there are several chapters on disease in pregnancy, but two paragraphs, mainly concerned with the control

of constipation and the value of proper corsetry, are all that can be said to deal with the maintenance of normal health in pregnancy. There is no mention of antenatal examinations as such; no reference to the diagnosis of presentation and position by abdominal palpation either before or during labour; no suggestion of the pre-partum assessment of pelvic capacity in primigravidae, or even of routine testing of the urine for albumin and sugar.

As a result of this attitude of the medical mind the public mind showed a complete apathy on the subject and an ignorance of the "facts of life" (other than those immediately connected with impregnation) which was genteelly cloaked under the false modesty of convention. The young married woman when pregnant passed into "an interesting condition" not to be revealed even to the family doctor until a few weeks before his attendance was likely to be required, unless, indeed, gross symptoms such as vomiting, bleeding, or dropsy necessitated it.

Two sentences from Playfair exemplify what has just been said. "It is often sufficiently easy to recognize a pelvic presentation by abdominal examination *if we have occasion to make one*" (my italics). And again: "It rarely happens that deformities of the pelvis, except of the gravest kind, are suspected before labour has actually commenced, and therefore we are not often called upon to give an opinion as to the condition of the pelvis before delivery."

But the beginning of the century saw the dawn of the idea of preventive medicine, and when the new light fell upon obstetrics it ushered in the era of antenatal supervision. It was in Edinburgh that the new idea first germinated. Dr. Haig Ferguson at that time supervised the health of the inmates of a pre-maternity rescue home close to the old Royal Maternity Hospital. So impressed did he become with the normality of these girls' pregnancies and with the fine condition of their babies that he persuaded the hospital managers to offer similar supervision by means of an out-patient clinic to the married women proposing to come to the hospital for their delivery. To protect these respectable women from embarrassment, entrance to the clinic was arranged from an unfrequented side street, and I well remember the great consideration that had to be given to their modesty in putting up an unobtrusive and discreetly worded direction-board.

One of Haig Ferguson's colleagues on the hospital staff was J. W. Ballantyne, whose absorbing interest in foetal pathology had led him to wonder if anything could be done to prevent foetal abnormalities by treatment of the mother during pregnancy. He was persuaded to take over the management of this antenatal clinic—the first in this country—and in 1901 a bed in the hospital was endowed for the study of diseases of pregnancy—the forerunner of the antenatal wards of every modern maternity hospital. After some time Ballantyne recognized that the immediate value of antenatal care was much more in the interests of the mother than of the foetus, and, having grasped this truth, he very soon made himself the great apostle of the new gospel.

Teachers of midwifery hardly needed to be converted, so that the ultimate spread of the new doctrine was ensured, but it was greatly expedited by the shock to the national conscience caused by the deplorable revelations of national physique in the reports of the Ministry of National Service during and after the first world war. With unusual perspicacity it was recognized that the best place to start any reform was at the beginning, and that healthy babies required to have healthy mothers. Legislation permitting local authorities to establish antenatal clinics followed, and

under the pressure of public opinion those of almost all the larger centres of population did so. As a result the organized practice of antenatal care may be said to have "got going" from the early 'twenties, and it is after that period that the national figures may be scrutinized for its effects. Nowadays there is a statutory obligation upon every practitioner undertaking maternity work that he will give at least the prescribed minimum of antenatal supervision to his patients, and it is estimated that in Britain about eight out of every ten expectant mothers do receive this measure of antenatal care, perfunctory though some of it would still appear to be.

In passing it is worthy of note that the same period, the early 'twenties, saw a nation-wide campaign started by the public health authorities against rickets, with the important incidental result that the frequency of contracted pelvis has been very greatly diminished amongst the young women who in these last ten years have become mothers.

A New Outlook

The results of antenatal care form an impressionist picture that must not be looked at from too near. To try to estimate the position by scrutiny of direct and detailed results is to get a wholly inadequate and disappointing impression. But if we stand well back and make a broad retrospective survey we realize that the great achievement of the teaching and practice of antenatal care has been to transform the whole outlook upon midwifery. It has made the medical profession "maternity-minded" to a degree hitherto unprecedented, with results that have pervaded every branch of clinical practice as well as the study of the basic medical sciences. One consequence of this in its turn has been that the lay mind has also developed a new and wholesome interest in maternity questions. The young married women of to-day respond with eagerness and intelligence to antenatal and mothercraft teaching. They demand a higher standard of obstetrical attention, and this has combined with the housing famine following two long wars to produce a very marked change-over in popular custom from domiciliary to hospital delivery, the potential results of which are far-reaching.

Regarded from this point of view, the influence of the idea of antenatal care has far exceeded the expectations of those who first cherished it. But while we consider this the most helpful viewpoint, let us not entirely disregard the details.

One line along which midwifery has been enormously improved by the antenatal idea is in the practice of the physical examination of the pregnant woman from both the medical and the obstetrical points of view. Abdominal palpation of the presentation and position of the child in the later weeks of pregnancy, investigation of the capacity of the pelvis—leading directly to the great modern contribution of the radiologist to accurate pelvimetry—the routine examination of the heart and lungs, the routine estimation of the arterial pressure, and the regular examination of the urine—all these are innovations of this century.

The almost religious attention that is now paid to the diet of the pregnant woman is an outcome of antenatal care which has been intensively fostered by the many years of compulsory national austerity. The results have been amazingly good, and dietetics is now our main hope in the prevention of abortions and premature births, and in the maintenance of healthy pregnancy generally.

Yet another far-reaching outcome of the antenatal idea is the increasingly great consideration now being given to

the life of the foetus in the choice and development of methods of delivery. Gone are the bad old days when dangers, unforeseen, had to be treated when and where they arose, and when consequently the obstetrician was often faced with a conflict between the interest of the mother and that of the child. As the preference had almost invariably to be given to the mother, the results to the child were often distressing, and it is gratifying to think that such a conflict rarely arises in good modern obstetrics. Examples of this modern trend are to be seen in the practice of external version in breech presentations recognized during pregnancy as well as in the general technique of breech deliveries; in the trial of labour with caesarean section in reserve in cases of moderate disproportion; and in the resort to the same operation in central placenta praevia.

How all this antenatal work shows up in the national statistics of maternal and infant mortality is a question to be approached with trepidation; so many possible factors are involved which are not obvious. The big facts are that in the years under consideration the maternal mortality rate has fallen to less than one-quarter of what it was and the infant mortality rate to about one-third. The maternal mortality figures showed no significant change until 1935, when a downward trend manifested itself, becoming precipitously steep in 1941. Analysis of the figures under the individual causes of death shows that puerperal and post-abortion sepsis, which used to be far and away the greatest factor, has now dropped to about one-sixteenth of what it was in the early 'thirties, and the rate for "toxaemias" (formerly the second greatest factor) to about one-quarter. Leaving sepsis out of account for the moment, this means that there has been a great diminution in the number of deaths due to hyperemesis gravidarum, pre-eclampsia, and eclampsia. Since there has been no great new development in the recent treatment of these diseases to which this rather sudden improvement could be attributed, it seems reasonable to give some of the credit to the progressive influence of antenatal care, although we ought not to overlook the possible but as yet unassessed effect of the increased vitamin B content of our "lower extraction" flour—one of the few and well-disguised blessings of the war. This distribution of the credit seems to be borne out by our own clinical experience that for ten years before the war severe hyperemesis was steadily diminishing, and that during the war it suddenly became practically an extinct disease, and has remained so. With regard to eclampsia, the improved figures strongly underline the value and importance of routine antenatal examinations; for the subjective symptoms of pre-eclampsia, so long as it is mild and comparatively amenable to treatment, are negligible, and only routine examinations will reveal them.

The Decline and Fall of Puerperal Sepsis

The dramatic drop in the maternal death rate from puerperal infection, which at the beginning of the century was as potent a lethal factor as all the other diseases and accidents of pregnancy and labour put together, has been mentioned. There seems no valid reason to doubt that we owe the "fall" of this dread scourge of womankind to the discovery of the sulphonamides and penicillin, but it was preceded by a "decline" for which obstetricians can take some credit. A quarter of a century's work in close association with bacteriologists had elucidated in great measure the aetiology of the disease. The principal organism was known to be the streptococcus, although on occasion a host of others could be found as well in infected

lochia. It was generally accepted that much the commonest explanation of its presence was that it had been introduced into the birth canal from without—on imperfectly cleansed or contaminated hands, instruments, or dressings. The occasional presence of streptococci in the vagina prior to labour, although in a devitalized form owing to their inimical environment, was accepted as a conceivable but very rare explanation. Most of the responsibility therefore seemed to rest fairly and squarely on the attendants—doctors and midwives.

The next step was the classification of the various types or groups of streptococci by Lancefield and Hare, and the recognition that fatal cases were most often due to streptococci of Group A, less frequently of Group B. All this led to a tightening up of the aseptic and antiseptic technique of obstetric practice, but only a minor and disappointing degree of improvement ensued. The possibility of air-borne infection was therefore questioned, and when Smith, of Aberdeen, was able in no fewer than twelve cases to identify the streptococcus present in the lochia of women suffering from puerperal infection as precisely the same as that found in the nose or throat of one of their attendants (doctor, nurse, or student) the clue—"droplet" or "spray" infection—was in our hands. The wearing of sterilized masks over the mouth and nose became an important and integral part of our preventive technique, and we began to feel that we had at least gained some considerably increased control over infection.

Then almost before the full results of our preventive efforts could be assessed came Domagk's discovery of "prontosil," the clinical trials of which by Colebrook, under the aegis of the M.R.C., were extraordinarily successful. The sulphonamide era in therapeutics had begun, and its history is familiar. The conquest of puerperal fever had also begun, and the national statistics in due course began to show it. But the story was not yet ended. Whilst we were yet congratulating ourselves on the sulphonamides came the still stranger story of Fleming and Florey's discovery of penicillin, and the rout of this fell disease was soon complete. The position now is that a healthy woman, who has been kept fit throughout her pregnancy by intelligent antenatal supervision and delivered in decent circumstances with proper care and adequate precautions against infection, need have no fear of puerperal sepsis. And if, owing to some breach in technique, infection does occur, our powers of coping with it are immeasurably greater than they were fifty years ago.

The Haemorrhages

The figures of the Registrars-General reveal that in the last few years there has been a striking diminution in the number of fatalities from placenta praevia and a less noticeable improvement in regard to accidental haemorrhage. These facts may be taken to reflect recent changes in treatment, which may be summed up as (1) the transference of all cases of ante-partum haemorrhage to hospital where possible, and if possible without previous vaginal examination; (2) the avoidance of vaginal packing except where circumstances make it imperative as a temporary measure; (3) expectant treatment in hospital in suitable cases; (4) caesarean section in certain well-defined types of case; and (5) the replacement of lost blood by blood transfusion. Fifty years ago the maternal mortality rate in ante-partum haemorrhage ran at about 12% and the foetal rate at rather more than 50%. A general reduction in the maternal figures to about 6% with no corresponding improvement in the outlook for the child was reached in many hospitals a few years ago. But Macafee showed in

1945 what could be done by concentrating the management of these cases under one person or a team working on a regular plan, by treating 174 cases of placenta praevia with a maternal death rate of 0.57% and a foetal death rate of 19%. For various reasons the foetal death rate in such cases will always be much higher than the maternal.

Post-partum haemorrhage, however, shows little sign yet of becoming a less menacing component of the maternal death rate, and this despite greatly increased facilities for blood transfusion. We have to remember that that remedy is itself not free from grave risk. But the wider adoption of the "flying-squad" system—whereby a selected team of doctors and nurses with obstetric skill and experience and familiar with the technique of blood transfusion can be sent at very short notice from a central maternity hospital to the patient's home, complete with all necessary equipment either to treat her there or more commonly to give her emergency treatment and then remove her to hospital by ambulance—would seem to be the best method of tackling this danger. We may reasonably hope to see better statistics on this point in a few years.

Operative Obstetrics

The most notable advance in this field has been in the methods and results of caesarean section. Apart from the increased safety given by the new chemotherapy and blood transfusion, the main source of this improvement has been the almost universal adoption of the lower-segment operation in place of the old upper-segment or "classical" operation. This bids fair to counteract the disconcerting frequency of rupture of the uterus in a subsequent pregnancy or labour which was the sequel of the wide employment of the older operation. In passing, it is interesting to recall that this method of incising the uterus was first suggested by Robert Wallace Johnson as long ago as 1769. We are not always as modern as we think.

The increasing recourse to caesarean section has meant a corresponding diminution in the use of the forceps in one field in particular in which the obstetricians of 1900 would have accorded that instrument the highest honours. I refer to contracted pelvis, or, more correctly, to cephalopelvic disproportion. The detection of pelvic contraction during pregnancy by antenatal examination, the more accurate assessment of the situation by radiography, and the adoption of the method of "trial labour" in appropriate cases, with caesarean section in reserve for cases in which the trial fails—all these have narrowed the scope of the forceps in this complication to a very small field. The "high" forceps operation has no place in modern obstetrics. "Axis traction" is now, therefore, of academic and historical interest rather than of living practical value. *Sic transit gloria.*

The Relief of Pain

It is just over a century since Sir James Young Simpson made history, as much by doing something previously undreamed of even by the most humane—namely, administering an anaesthetic (ether) for the relief of pain in childbirth—as by subsequently discovering that chloroform was a better drug for the same purpose. For fifty years and more doctors and their patients were content—and with very good reason, for chloroform, used as Simpson taught that it should be used, is still a first-rate anaesthetic towards the close of the second stage of labour. But the early years of this century saw the beginning of gropings after an analgesic suitable for use throughout the greater part of a labour, and "twilight sleep" with morphine and scopolamine was the first result. This was found to be not wholly safe for the infant, and in the last thirty years

a great variety of sedative drugs, which seemed to pour out of the manufacturing chemists' laboratories in endless succession, have been tried with varying degrees of satisfaction. One of the last of these—pethidine—seems to have come to stay.

Public demand for some method of analgesia which could be safely administered by the midwife working without medical supervision led to the wide employment of nitrous oxide gas and air, but the necessary apparatus is too heavy for easy transport. "Trilene," which is free from that drawback, is now displacing it.

The importance of the control of the emotions and their bearing on the suffering experienced in labour has also been the subject of considerable study, and more is likely to be heard of this method of approach in the future.

Local analgesia by infiltration is widely and most beneficially practised during the period of distension of the pelvic floor and for immediate perineal repairs. Spinal analgesia is used by some in caesarean sections, and low spinal or caudal analgesia during vaginal delivery. Continuous caudal anaesthesia is more used in America than in this country.

Diabetes

Fifty years ago the diabetic woman rarely became pregnant, because the disease profoundly depressed ovarian function, and when she did so the prospect was gloomy in the extreme. One or even two out of every three such cases ended fatally, usually in coma, and the prospect of obtaining a living child was never more than about 50%. The discovery of insulin in 1921 completely transformed the scene. The number of diabetic women becoming pregnant is now quite considerable, and the maternal mortality in good hospital practice under the combined care of a physician and an obstetrician has been reduced to almost vanishing-point. For the child also the prospects are improved, although not to anything like the same extent. The undue size of these infants is a well-recognized factor of risk, but we do not yet know the reason for the intra-uterine deaths which often supervene in the last week or two of pregnancy.

Diagnostic Methods

The gaining of our new knowledge of the physiology of the female reproductive system has been one of the most dramatic happenings in the period under review, but for the most part it belongs to the sphere of gynaecology. It did, however, give obstetricians new biological methods of diagnosing early pregnancy with almost complete accuracy. The original Aschheim-Zondek test with mice was followed by the more rapid Friedman test in rabbits, and now the *Xenopus* toad holds the field. It is a more economical animal in that it gives its oracular answer by shedding its eggs and does not need to be killed and have its ovaries inspected.

Apart from pregnancy tests the use of the sex hormones in obstetrics has become limited by a process of trial and failure to the condition of missed abortion, in which very large doses of oestrogen seem to be helpful. Much was hoped, and even claimed, from the use of progesterone in the treatment of threatened abortion and more particularly in the prevention of "habitual" abortion, but extended trial has not fulfilled our hopes.

The diagnostic uses of radiography in obstetrics are so numerous that an x-ray plant is now an integral part of the equipment of any modern maternity hospital. In earliness of diagnosis radiography cannot, of course, compete with the hormonal tests, but in the second half of pregnancy it helps us in the diagnosis of foetal death, of

foetal structural abnormalities, of presentation and position, of plural pregnancy, of placenta praevia, hydramnios, and the like, as well as giving us methods of accurate assessment of the mother's pelvic capacity.

In this brief survey of the progress of midwifery I have had to avoid some attractive digressions into gynaecology, haematology (Rh factor), cardiology, foetal pathology (rubella in early pregnancy), and paediatrics. I have omitted any reference to the training of the medical student in midwifery, because it is too wide a topic, and to the training and control of midwives, because that falls under "Legislation." But there is one last achievement which must be mentioned, since it is not merely a milestone but a monument to the progress of obstetrics and gynaecology.

The Royal College of Obstetricians and Gynaecologists

In 1928 the British College of Obstetricians and Gynaecologists was founded, with William Blair Bell as its first president and William Fletcher Shaw as its first secretary. Broadly and briefly speaking, the establishment of the College was the natural and evolutionary outcome of the maturity of obstetrics and gynaecology as a conjoined branch of medicine. It signaled the blossoming of the branch, and we are now beginning to see the beneficial fruiting. The phenomenal success of the College in its first twenty-one years has been the best proof of how much it was needed in the interests of the two subjects not only in Britain but throughout the whole British Commonwealth. It has been singularly helped by royal favour, not only in the grant of a royal title and charter but in the active and generous personal interest of Her Majesty the Queen, who is an Honorary Fellow as well as Patron. Better proof of the "maternity-mindedness" of this generation could not be offered.

FIFTY YEARS OF MEDICAL RESEARCH AND PRACTICE

BY

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"The art of progress is to preserve order amid change, and to preserve change amid order."—
A. N. WHITEHEAD in *Process and Reality*.

"The last fifty years!" The phrase slips glibly off the tongue. Yet no era in the world's history has been so crowded with events of greater import for man or medicine. The twentieth century opened with Victoria still on the throne, and four monarchs were to succeed her. The conflict still raged in South Africa, and two wars were to follow and embroil the whole world. Each war was to overshadow its predecessor in ferocity, cruelty, tragedy, and destruction, until in the last it seemed that civilization itself might perish. Yet "out of evil came forth good," and medicine was enriched through the envies, bitterness, and follies of mankind. The third Marquess of Salisbury was Prime Minister; to-day his grandson is a notable figure in the House of Lords. The first underground electrical railway—the Central—opened in London in 1900; the first motor-bus and aeroplane, the first cinema and radio programme, and a host of other amenities and amusements without which it is to-day almost impossible for the vast majority of mankind to contemplate an acceptable life were still

unknown. And legislation was to change, for good or evil, the social structure in every country in the world.

It is in this background and perspective that we must view the advances in medical knowledge and practice in the same period, for the history of medicine reflects the philosophy of its time. The dramatic discoveries in the basic sciences during this period gave to medicine its most potent instruments of research and tended to place the focus of medical advance in the laboratory rather than at the bedside, but the older methods which had their roots in the nineteenth century and even earlier were still to yield a rich harvest. For advance in knowledge is essentially evolutionary, not episodic; and no advance in clinical research leaves uninfluenced for long the practice of medicine.

Methods of Clinical Research

The methods by which clinical research and practice have progressed defy clear-cut enunciation. Few discoveries reach maturity without all known methods being employed, but in most can be discerned the motivating and predominant role of one of four methods. First, the recognition of clinical syndromes or recurring patterns of disease, commonly called "entities" or "diseases," and their investigation by all available techniques—pathological, biochemical, radiological, epidemiological, statistical, etc. When new techniques are developed they can be applied to earlier established syndromes and new knowledge gained. For example, the development of bacteriological techniques and their application led to the aetiology of many infectious diseases being revealed.

Secondly, experimental laboratory research has pointed the way to the interpretation of known clinical syndromes; from this, for example, we learnt to associate diabetes mellitus with the pancreas and diabetes insipidus with the hypothalamus.

Thirdly, there is the chance observation; the story of penicillin illustrates vividly the fact that though good fortune may attend discovery it comes only to the mind prepared for it.

And fourthly, there are the major discoveries in the cognate sciences—physics, chemistry, biology, psychology, and sociology—applied to the investigation of health and disease in the hope that these may yield some of their secrets.

It is of interest to trace in a few of the major advances in medicine in the last half-century the part played by these various methods, and the importance of perspicacious planning, a clear objective, concentrated effort, and team-work to clinical research.

Endocrinology

In few fields can the influence of these principles be better exemplified than in those of endocrinology and nutrition. Graves's disease, Addison's disease, myxoedema, and acromegaly had been described and their morbid anatomy was known before the century opened; and experimental excision of the adrenals had been shown to produce a fatal syndrome analogous to Addison's disease, and pancreatectomy a fatal glycosuria. But the science of endocrinology as we know it to-day is virtually a product of this century and begins with the discovery by Bayliss and Starling in 1902 of secretin, the first of the "hormones," or chemical messengers, which exerted a humoral as contrasted with a nervous control in the body. It was soon recognized by clinical observation and its correlation with pathological findings, by observing the effects of excision of glands both in the experimental animal and, in