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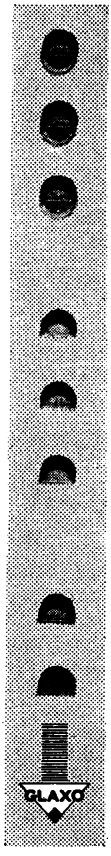

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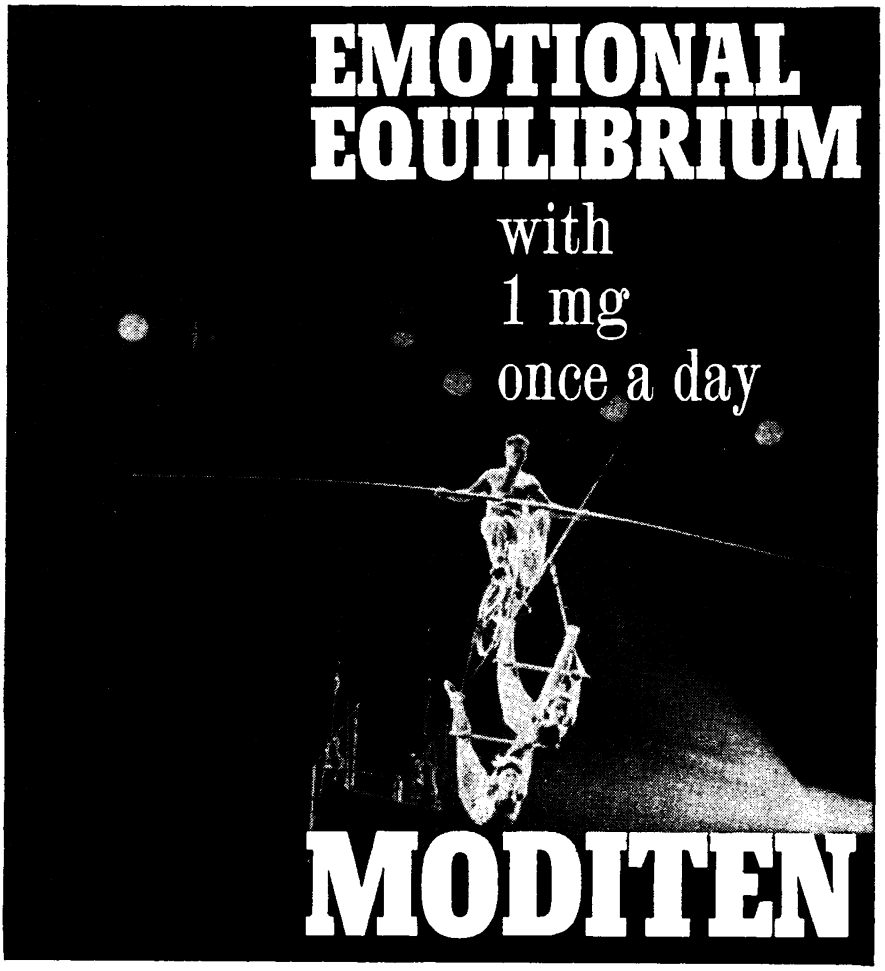

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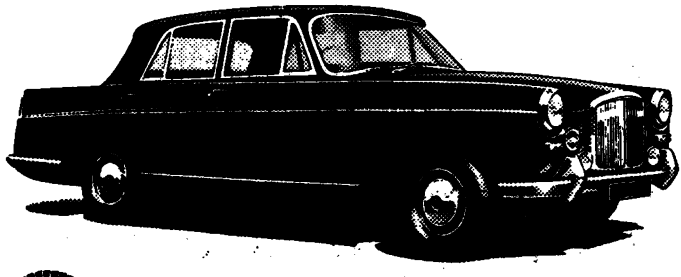

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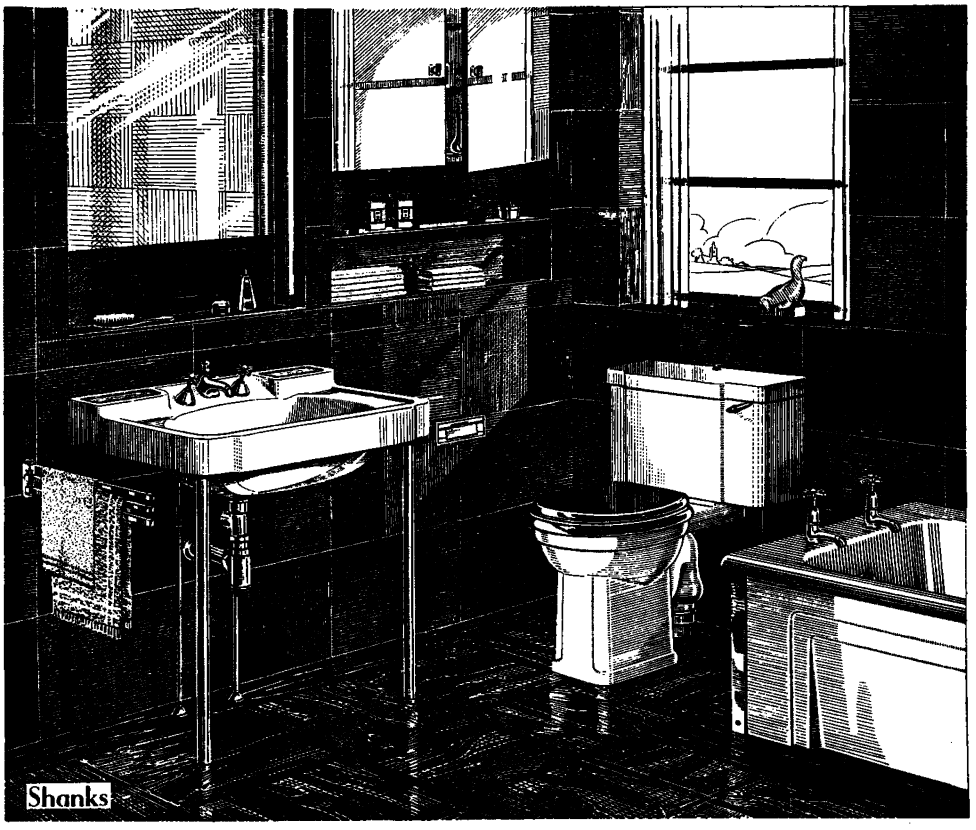

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VOL. XXX

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1961

CONTENTS

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No. 2 : December, 1961

CONTENTS

Fellows and Members of the Ulster Medical Society receive the Journal Free. Subscriptions to non-members, fifteen shillings annually.

THE ULSTER MEDICAL JOURNAL

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THE
ULSTER MEDICAL JOURNAL

PUBLISHED ON BEHALF OF THE ULSTER MEDICAL SOCIETY

Vol. XXX 1st JUNE, 1961 No. 1

SURGICAL TREATMENT OF DEAFNESS

By TERENCE CAWTHORNE, F.R.C.S.
King's College Hospital, London

THE ROBERT CAMPBELL MEMORIAL ORATION
9th March, 1961

ROBERT CAMPBELL, in honour of whose memory this lecture is held, was one of the great pioneers of aseptic surgery. He was the first surgeon to use rubber gloves in the British Isles, and he was responsible for many advances in our craft. He had a particular interest in the surgery of repair, and his appointment at the Children's Hospital gave him many opportunities to restore by means of reparative surgery young people to an active, happy, and full life. His labours ended all too soon in 1920 at the early age of 55, but had he been spared, I am sure that he would have rejoiced at the remarkable advances which have been made in recent years in the surgical management of disorders which in his time were regarded as incurable. Deafness was one of these.

Tonight I have been honoured with the task of telling you something of the really remarkable advances which have been made in recent years in the restoration, by means of delicate surgical operations, of the sense of hearing which had been dulled by otosclerosis or by the ravages of middle ear suppuration. I must tell you at once that we cannot as yet offer surgical help to those whose deafness is due to a defective nerve or end organ of hearing; but when deafness is the result of impaired transmission of sound across the middle ear, it is often possible by refashioning the sound conducting system to enable sounds of normal or near normal intensity to be conducted to a responsive nerve of hearing inside the internal ear.

Robert Campbell would have been one of the first to encourage the application of simple surgical principles to the ear, which has resulted in so much benefit to so many. At the same time it has raised the art of aural surgery from the messy business of letting out pus and removing infected bone to the more elegant level of aseptic surgery in a clean field.

Emboldened by the protective cover of antibiotics and with his vision enhanced by brilliant illumination and by the magnification afforded by the dissecting microscope, the aural surgeon of today can now embark on delicate operations with much less trepidation than his brave predecessors whose hardy essays into the functional surgery of the ear command our admiration, even though they were rarely rewarded by success.

Before we consider the operations which are now being done to relieve conductive deafness, I would like to tell you something about the sense of hearing and of the effects of deafness. It is through the sense of hearing that man, and indeed other members of the animal kingdom which breathe the air, communicate with one another. Airborne sounds from other living creatures are picked up and appreciated and vocalisation develops. Through vocalisation animals are able to communicate emotions, but man has been able to organise his vocalisation into speech, and this enables him to communicate ideas as well as emotions. It is through the sense of hearing that language and speech have developed, and these have enabled man to reach his supreme position in the kingdom of living things. Without hearing there would be no speech, as we know in the case of children who are born deaf and who in consequence are dumb. The sense of hearing may be described as the social sense, and after all man is a social animal who likes to talk and who is occasionally prepared to listen. If he becomes deaf he feels left out of things, and indeed is only too often left out of things. Consequently, the deaf are lonely people who tend to become indrawn and even withdrawn. The more thoughtful among them fear that they may be a nuisance to those around them, and often this is so. The deaf yearn for the sympathy they are so often denied; for the person with normal hearing finds it difficult to give to those afflicted with deafness the same sympathetic consideration he does to those more obviously handicapped, such as the crippled and the blind. The whole trouble is that the deaf look normal and give the impression of being stupid, so they often forfeit the sympathy and consideration to which they feel their handicap entitles them. The deafened housewife may feel she is being a burden to her family, and she may often be a greater burden than she realises. This is emphasised when the family sits round the television set because the deafened member of the family has to have it on too loudly for the comfort of the rest. Again, a hard of hearing man may find that he is passed over for promotion, or he may even be demoted to a position unworthy of his abilities but appropriate to his sensory defect.

To be able to restore the housewife to full participation in family life and a man to a position appropriate to his talents, though it may not be so dramatic as saving life, does give immense satisfaction to the patient and, I may add, to the surgeon.

Now before I tell you something about the operations for deafness, it will be helpful to consider for a moment the way in which sound waves reach the organ of hearing from the outside world. Airborne sound waves pass down the external ear canal to reach the ear drum which they set into vibration. This movement is transmitted through the ossicular chain which connects the ear drum with the oval window in the bony labyrinth leading to the inner ear. The fluid perilymph

contained in the inner ear responds to the to and fro movement transmitted to it through the oval window, and a fluid wave is set up which travels in the direction of the other window in the bony labyrinth, the round window. This fluid wave moves the elastic basilar membrane upon which is seated the organ of Corti, the end organ of hearing, and this stimulates its hair cells and hearing results.

Anything which interferes with the conduction of the sound wave through the labyrinthine windows will result in conductive deafness which is the deafness that can often be helped by surgery. The two conditions which can be helped are otosclerosis, where bony deposits impede the movement of the stapes footplate in the oval window, and the effects of middle ear suppuration, which, by perforation of the ear drum or interruption of the ossicular chain by necrosis, will interfere with the normal sound conducting mechanism.

The earliest recorded operation for deafness was that of Sir Astley Cooper who on several occasions incised the tympanic membrane, though this was never successful. About a century before this an operation to relieve deafness was proposed by the English surgeon, Cheselden, in rather curious circumstances. Cheselden was Surgeon to King George II, and one of the Queen's ladies, the Countess of Suffolk, suffered from deafness. She was a great favourite of the King, and Cheselden suggested to her that she might be interested in an operation for deafness which he had thought of but which he had not as yet attempted. Cheselden proposed that he should try the operation on a condemned criminal who in turn for submitting to this procedure would be pardoned. The Countess of Suffolk persuaded the King to agree to this and Cheselden, armed with the pardon, went to Newgate and selected a young man who had been condemned to die. The condemned man was delivered up to Cheselden, but unfortunately it became known that the young man was Cheselden's nephew, and it was rightly assumed that this was a ruse to save his young relative. Cheselden was in disgrace at Court and the King had to continue to shout into the Countess's ear what prudence must have indicated he should have whispered.

We now go forward to almost a century ago when Toynbee, the English otologist, noted that in some of the temporal bones which he had collected from subjects who had been profoundly deaf the stapes were firmly fixed in the oval window in the labyrinth, though almost half a century elapsed before Adam Politzer of Vienna gave the name 'otosclerosis' to this bony fixation.

We now know that otosclerosis is the commonest cause of deafness in active adult life, and it is this deafness due to otosclerosis which responds most readily to surgical treatment.

But you may well ask what is otosclerosis and why is it so common; so perhaps at this stage I may be allowed to tell you my views about otosclerosis, and to do this we must consider for a moment the bony capsule of the labyrinth which has been singled out as the only part of the bony skeleton which has the power of attracting to its surface patchy deposits of otosclerotic bone.

The bony capsule of the labyrinth, together with the ossicles, is the only part of the bony skeleton which is fully developed at birth. Like much of the rest of the bony skeleton, the labyrinth develops from cartilage. There are six centres

of ossification in the primary otic cartilage which coalesce to form the bony labyrinth. Just in front of the oval window of the labyrinth where two of these centres join together there is a constant fissure, the fissula ante fenestram, which, if large enough, may be filled with cartilage. When otosclerotic bone occurs, it is found in this situation in at least 90 per cent. of cases, which may be regarded as the site of election for deposits of otosclerotic bone. Guild has estimated that patches of otosclerotic bone can be found on the labyrinth in some 5 per cent. of the population, though it is only in about a tenth of these that the otosclerotic bone spreads across the oval window to seal in the stapes and cause deafness. Now deafness due to otosclerosis often first appears in adolescence, and in women who have children the deafness may start or grow worse during the last weeks of pregnancy. It is interesting to recall that both during adolescence and during the last weeks of pregnancy there is great activity in bone growth which takes place where cartilage joins bone. It seems likely that the stimulus responsible for changing cartilage into bone is a bone growth promoting substance which at these times is released into the circulation, and it is precisely at these times that patches of otosclerotic bone are being deposited on the bony labyrinth, usually in the fissula ante fenestram where there is a collection of immature cartilage. This cartilaginous rest in the bony capsule of the labyrinth is very constant in position but varies in size from person to person. It seems as though the larger the rest the more likely is it to attract a bony deposit, and it is not unreasonable I feel to postulate a familial tendency towards large rests which would account for the fact that in at least half the cases of otosclerosis there is a history of a similar kind of deafness in the family. Another point in favour of bone growth promoting substances being attracted to the labyrinth is that otosclerotic deafness is sometimes initiated or made worse by accidents involving the bony skeleton, and in one particular disorder, fragilitus ossium, bony deposits on the labyrinth causing deafness are quite common.

Thus it seems that the bony capsule of the labyrinth has the power of attracting deposits of bone to its surface during periods of active bone growth, and that if these deposits encroach upon the windows which allow sound vibrations to enter the labyrinth then conductive deafness will ensue. Clearly it is neither possible nor desirable to prevent normal bone growth, and so it is hardly surprising that the incidence of otosclerotic deafness is not less than $\frac{1}{2}$ per cent. of the population.

The operations to re-establish the sound conducting mechanism which had been so bravely tried during the last quarter of the nineteenth century were by general consent abandoned by the turn of the century, but the subject was re-opened by Jenkins at the International Congress of Medicine and Surgery in London in 1913 when he described how he had made an opening into the lateral semicircular canal in cases of otosclerosis. In the discussion which followed his paper, Barany of Hungary also gave his experiences of this procedure which he had carried out several times. At the outbreak of World War I, Barany, who had received the Nobel Prize for his work on vestibular physiology, was called to serve in the Austrian Army and was captured by the Russians. The Red Cross

asked for his release and the Russians agreed that he should be released to a neutral country, if in return one of their nationals who was interned in Hungary should also be released. This was agreed to and Barany was sent to Sweden and the Russian national, who happened to be Nijinsky the leading dancer of the Russian Ballet, was released to America.

In Sweden Barany captured the interest of Gunnar Holmgren, who had played a major part in getting him released, and Holmgren took up the work and carried it on until one of his pupils, the Frenchman Sourdille, went a step further and laid the foundations which enabled the American, Lempert, to perfect the fenestration operation. In this operation the original idea of Jenkins was perfected so that in otosclerosis the sealed up oval window was by-passed and sound waves were allowed to enter the labyrinth by an opening in the lateral semicircular canal so as to mobilise the contained fluids, and thus allow the airborne sound waves to activate the organ of Corti in the cochlea. Such a delicate operation as this was made possible by aseptic surgery, by the use of antibiotics and, because of the small size of the operative field, by adequate illumination and by the magnification afforded by special glasses and by the operating microscope. This fenestration operation opened up a new field for the aural surgeon who could now devote his energies to restoring hearing to those, so often in the first flush of life, whose careers were threatened by deafness. No longer had the aural surgeon to dread the interview with the young man or woman overcome by deafness due to otosclerosis. Instead of condemning them to a life-time of deafness, he could offer them the expectation of restored hearing. But, of course, there were the drawbacks, slight enough in comparison with their deafness, that they would be left with a mastoid cavity which might discharge and which would require attention from time to time.

This led to the reintroduction by Rosen of New York of the direct approach to the fixed stapes by remobilisation of the stapes in the oval window. This was one of the operations which had been abandoned in the last years of the nineteenth century. For some years it gave quite good results, but the reason why it had been abandoned earlier became apparent as so many of those in whom it had been initially successful became deaf again as the stapes refixed itself in the oval window.

Then in 1956 John Shea of Memphis, Tennessee, conceived the idea of removing the whole stapes, covering the oval window with a mobile membrane made from a vein graft and connecting this with the rest of the ossicular chain by a tiny polythene strut.

Others, including myself, had previously tried out the effect of removing the stapes (Cornelli, Cawthorne), but we had not at the time been able to devise a satisfactory way of reconstructing the ossicular chain.

Thus the principle established by Shea in 1956 of removing the whole of the stapes footplate and replacing this by a mobile membrane has proved to be the most effective and lasting way of restoring hearing to those deafened by otosclerosis.

The operation is delicate and tricky but the functional results are very rewarding, and in skilled hands it can offer a 90 per cent. chance of restoration of hearing. It is a slight operation from the patient's point of view which leaves him or her with a normal auditory apparatus. The risk of damaging the delicate auditory apparatus is ever present, though small, and the chance of the hearing in the operated ear being made worse is less than 3 per cent.

It has been my good fortune to be brought up in this exciting era of aural surgery, for Jenkins, who started the, what I might term, Renaissance of Aural Surgery, was my chief, and the others, Holmgren, Sourdille, Lempert, Rosen, and Shea, have been my friends. Alas! I must use the past tense, for Gunnar Holmgren died in 1955. I am glad to have this opportunity of bringing their great work to your notice.

In quite another field of aural surgery it has been possible to repair the ravages of sepsis on the sound conducting mechanism of the ear by means of tympanoplastic operations to restore the sound conducting mechanism, and for this we are indebted to the work of Zollner of Freiburg and Wullstein of Ziegen. They have shown that when the essential parts of the sound conducting mechanism of the middle ear, the drum and the ossicular chain, have been disorganised by suppuration, plastic operations combined with the eradication of sepsis have often been able to seal off the auditory mechanism and restore hearing.

The end of this part of the story has not yet been reached, but the principle has been established that in any case of conductive deafness there is always the hope that by surgical means sound can be conducted to a normal organ of hearing, so that the patient can hear again and be restored to a normal and active life.

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THE SURGEON AND THE CHEMOTHERAPY PROGRAMME IN MALIGNANT DISEASE

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SIR THOMAS AND LADY EDITH DIXON LECTURE
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ONCE pain, hæmorrhage, and infection were brought under reasonable control, and as our knowledge of normal and abnormal function became more secure, the magnitude of an operation could be extended nearly indefinitely. Many operations came to be looked upon as subtotal eviscerations. Surgeons often believed that the end results of the surgery for many malignant tumours would be greatly improved merely by extending the limits of resection. Unfortunately, we have come to know that once malignant disease has spread beyond the organ of its origin, it is all too often extraordinarily difficult to eradicate. While the end results of surgery for cancer of the major viscera have without doubt improved during the last twenty-five years, they have not improved sufficiently to still the search for better methods of therapy.

We must admit that the time to cure cancer, except in occasional instance, is when it is strictly a local disease. Early diagnosis and early adequate operation, or adequate radiation for a limited group of the malignancies, are the only means at our disposal for significantly increasing the number of five- and ten-year survivals free from the disease. Even then we cannot be sure of cure. Unfortunately, surgeons must now admit that further extension of surgical or radiation therapy gives little hope of greatly improving the presently accepted end results.

Dr. Michael Shimkin, in his paper before the Fourth National Cancer Conference, said, "Our opponent is tough and elusive. Our victories are uncomfortably small and our progress is painfully slow. But there have been indubitable victories, and there is continued progress. Our steps forward empower us to maintain our optimism.

"One manifestation of our progress is that our concepts regarding cancer have not remained static. A whole series of changed and changing ideas and approaches has occurred during the past few years, many since the last National Cancer Conference in Detroit in 1956.

"This, of course, is not surprising. All of medicine shares in the technological revolution of our times. Discoveries and opportunities are upon us at a rate that exceeds available resources of men, space, and time to exploit them. Cancer research certainly is not an exception."

There are too many generalizations concerning cancer. All too frequently it is spoken of as if it were a single disease. The intimation is that the life history of cancer in a major viscus is always the same. Actually we know that it is often not the same disease even in the same organ. In some instances the lesion spreads so slowly that one wonders whether it is truly a malignant lesion, and in other instances a cancer which histologically looks quite similar spreads as rapidly as a prairie fire.

Thoughtful internists, surgeons, and radiologists realize more than ever before the present inadequacies of therapy. The majority of these individuals admit freely that once malignant disease has spread beyond the organ of its origin it is nearly impossible to eradicate. It must be freely admitted that cancer confronts the surgeon with many of his most difficult and exasperating problems. Three and five years survivals for such common carcinomas as those of the stomach and the breast taken as a whole do not exceed 10 and 30 per cent. respectively, where there has been no selection of cases.

An obvious way to improve these data is to establish the diagnosis earlier in an attempt to forestall the spread of the disease beyond the range of the scalpel. Extensive education of physicians and laity has been undertaken. Diagnostic methods are being improved. Pathologic examinations of cells exfoliated from the surfaces of the lung and uterus offer promise for the diagnosis of early not easily accessible cancers, and may be widely applicable to cancers of hollow organs, although as yet they have not been proven to be as useful as we had initially hoped they would be. Cancer cells can be found in the blood stream of patients with cancer of certain of the major viscera, and this finding is so frequent that one wonders why any patient can ever survive once the disease has been initiated.

Due to the insidious nature of the disease, its failure to produce symptoms in its incipient stages, and its often extremely rapid spread to distant locations, it is evident that under the best practical conditions of diagnosis and technical liberty, surgery, as we know it now, can anticipate a level of efficiency well below a desirable standard. We shall have to find more potent adjuncts of therapy before cancer is better controlled. We must have a keener insight into the character of cancerous tissues, their failure to conform with normal cellular organization, and their energetic metabolic needs.

Extirpation of tissue alone, or in conjunction with radiotherapy is perhaps, at present, the best available regimen. Their possibilities are perhaps not yet exhausted, but we must begin to look for other means of therapy as the limitations of these older methods have been reached. The surgeon rightly in my own country has been aligning himself with other investigators into the nature of neoplastic tissue. There can be no phase of this subject for which the surgeon does not have a pertinent concern. Surgeons must know what is being done in research in malignant disease and must vigorously assist in the clinical application of the research findings.

Antibiotic and chemotherapeutic agents have assisted greatly in the surgical care of suppurative infections. The surgical treatment of certain patients with

tuberculosis by lobectomy and pneumonectomy, discarded years ago as being unsurmountably perilous, has been revised, not because of streptomycin, but because of the wider knowledge of the physiologic basis of thoracic surgery and the increased knowledge of the disease itself. Due to the poorly understood, but unequivocal inhibitory influence of the spleen on the cellular elements of the blood, splenectomy is a dramatic therapy for certain anæmias, leukopenias, and thrombocytopenias, and the syndrome of depression of all three elements, hypersplenism, or primary splenic panhematocytopenia.

In many of our university institutions and in certain of our distinguished cancer institutes, and no doubt in similar institutions in your own country, individuals are concerned with basic research in order that new knowledge may assist in unravelling the problems associated with the causes and nature of malignant disease. In many of these institutions, and especially in many of our great hospitals, other individuals, primarily clinicians who have had varying amounts of training in good clinical research, are playing significant rôles in the chemotherapy of late malignant disease with the hope that through the use of a variety of chemotherapeutic agents which are being made available, we may find better methods for the complete therapy of malignant tumours.

I am sure that there exists areas in which our concepts of cancer are not changing as rapidly as the facts warrant. There are many areas where the application of research findings has lagged. The clinician must play his full part in this work. Who else knows the life history of clinical cancer so well?

A number of young surgeons are participating actively in the use of chemotherapeutic agents which are being administered to patients at the time of operation for cancer of the lung, cancer of the stomach, cancer of the colon, cancer of the prostate, and cancer of the ovary. This is being done with the hope that certain of these agents will improve the end results which are now being obtained by surgery, or by surgery and X-ray alone. Already data are available to show that in the case of mammary cancer this can be done.

I have had it said to me that the adjuvant chemotherapy programme, as well as certain aspects of the chemotherapy programme in general, is an irrational approach to the major problems of malignant disease. Individuals who support this point of view believe that we must first have a fuller understanding of the precise basic nature of cancer. The history of medical progress does not support their point of view. I am afraid that these individuals may not be fully conversant with previous contributions to medicine which over many, many years have come to significantly effect a variety of disorders which have plagued mankind.

Lister knew very little about bacteriology when he developed the aseptic theory for the control of infection at operation. While Banting and Best made insulin available in 1921, scientists have been working in the intervening years in order that we might have a clearer concept of the manner in which insulin acts. The sulphonamides became available in the mid-thirties, and ten years later we were not sure of the biological processes by which these agents acted. Penicillin became available in 1943, and within the next ten years an increasing number of antibiotics became available for clinical therapy, at a time when it

was not clear what biological reactions were concerned in the control of the organisms causing infection.

I must agree with Paul Weiss when he said, "Real science is earthy; just one of many branches of the human enterprise; one to be cultivated, but not a cult. Science must make more men its devotees, but none its priests."

Finally it is said by many internists in my country that surgeons ought not to be playing a significant rôle in the chemotherapy of malignant tumours. I have on more than one occasion counselled my medical colleagues to read Harvey Cushing's address on "Realignments of the Greater Medicine and Surgery," which address was given at the Third International Congress on Medicine and Surgery in London in June, 1913. It was then that he said, "The young surgeon of the future will be an internist first and a surgeon later."

The surgeons of this country and of mine really control at one time or another the majority of patients with solid malignant tumours. Many of these individuals are experienced investigators and a worthwhile number of them have made significant contributions to our basic knowledge of a variety of disordered states. This is a field in which basic scientists, internists, and surgeons must work together, each functioning in that particular area in which he has a major interest. Are we doing everything possible to advance research findings from the basic science laboratory to the clinic? Unless we all realize our responsibilities, we may well be in the position of retarding progress. We must be awake to the many exciting findings being uncovered in your country and mine which have a close relationship to the cancer problem.

In an article on the "Chemotherapy of Solid Tumours," by Dr. Robert Glenn Ravdin and William L. Elkins the following statement is found, "The situation at present in the chemotherapy of solid tumours is perhaps comparable to that in surgery at the turn of the century or in radiotherapy some three decades ago: a number of different techniques compete for attention, most of which are unstandardized, inadequately evaluated, heavily influenced by vogue and attended by considerable morbidity, not to say hazard. At the same time, a few outstandingly brilliant accomplishments indicate that labours along these lines are not fruitless. In order to lay a groundwork for a more specific discussion, some generalities can be first dealt with."

It cannot be denied that the chemotherapy of malignant tumours is a specialized endeavour. Many of the agents are toxic and require considerable experience in their administration. They do not act uniformly even on similar tumours. There are available, however, a group of agents of varying chemical design which do affect a variety of malignant tumours. These and related agents deserve careful scrutiny through clinical trial. Such studies must be carried out in fairly large-scaled programmes. We are even at this time not yet completely sure as to the optimal dosage of certain of these agents, the rate of their administration, and the method of their administration.

Some of these drugs are not toxic when given in minimal dosage, but it is equally true that they are not cancerocidal unless they are administered to the point of toxicity. As Ravdin and Elkins have pointed out, "The differential

between the susceptibility of tumours and that of normal tissues is relatively small (for the agents we now have); a tumour will probably not be affected by a dose of drug which is not injurious to the more sensitive of the normal tissues: Tumour cells share the common biochemical mechanisms of normal cells; extensive investigation at the biochemical level has turned up only quantitative differences, and many of these are not pronounced. Exploitation of these differences has not reached a stage that may in any sense be described as refined. Indeed, the most effective drugs seem in essence to affect cells in rough proportion to their growth rate, and therefore, in somewhat varying degree, to be particularly noxious to hematopoietic tissue and the gastrointestinal mucosa. However, the concept of reaching a desired goal by subjecting a patient to an injurious procedure is not foreign to the surgeon. It should be noted parenthetically that although chemotherapeutic agents may interfere with host resistance in certain experimental situations in animals bearing transplanted tumours, there is no convincing evidence that these findings may be extrapolated to spontaneous tumours in the human. This is by no means a closed question."

The idea that the progress of malignant diseases might be controlled in part or in whole by chemotherapy is surely not a new one. Androgens and estrogens have been demonstrated to retard the spread of certain malignant tumours of the breast and to cause regression in areas of metastasis once this has taken place. Other agents have been found to be useful in certain of the leukemias. It is an unfortunate circumstance that while many of these agents have been found to be extraordinarily useful in certain tumours of a malignant nature found in experimental animals that they have not been found to be useful when used in similar tumours in man. The agents that we are using are classified as alkylating agents, antimetabolites, antibiotics, and a miscellaneous group of agents such as the hormones.

The alkylating agents, which are frequently called the mustards, have been used in a wide variety of malignant tumours. The exact mechanism by which they function is not as yet definitely determined. These nitrogen mustards, as they are very commonly called, act by making the nucleic acids as their targets. Thio-TEPA, TEM, Myleran, and Cytoxan or Endoxan belong to this general group. Some of these can be given orally which is at times a decided advantage. Cytoxan rarely produces thrombocytopenia even in dosage levels which cause serious reduction in the lymphocytes. This provides a safety feature which we believe permits greater dosage than can be obtained with other alkylating agents. In our hands they have been most effective against the lymphomas, reticulum cell sarcoma, ovarian and mammary carcinoma. While we have had some dramatic results with the use of certain of these agents, the dramatic improvement shown following therapy has been all too short. Perhaps readjustments of the methods of dosage of administration of the drug might change this, but we must look for more potent agents in this series.

The antimetabolites constitute a group of diverse character which have the common characteristic "of accurately counterfeiting some normal cellular constituent."

In the area of antibiotic therapy for tumours the most widely used agent has been actinomycin D. It is a very effective agent for the embryonal carcinomas of the kidney, the Wilms' tumour. It is also effective in certain tumours of the testis and in rhabdomyosarcomas and certain other undifferentiated sarcomas, especially those in children.

We must attempt by every conceivable method to improve the activity of these agents against the malignant tumours, and at the same time to reduce the toxicity, a task that now seems nearly hopeless. A large group of chemists in and out of government, and in and out of our chemical industries and our universities, are attempting to develop such additional agents for clinical trial following careful pharmacological study and screening of the agents in experimental systems. Certain individuals are suggesting combined therapy, and in the choriocarcinomas of the testis, methotrexate, chlorambucil, and actinomycin D used together have certainly proved to be superior to either one of these agents used alone. Some investigators are rigorously attempting to find less toxic agents which will potentiate the more effective toxic agents.

There is increasing evidence that radiation and chemotherapy will provide end results which are better than those when either therapy is used alone. This area is now being very carefully investigated.

Warren Cole suggested that greater salvage might be achieved by the concurrent administration of effective chemotherapeutic agents at the time of and immediately subsequent to major surgical procedures. There is now evidence available to show that in carcinoma of the breast this is true, and it is highly probable that as more effective agents become available for other tumours, this attack may be broadened.

I am sure that this audience is familiar with the method developed in Dr. Creech's department at Tulane University in New Orleans and by other surgical groups in which high concentrations of an effective agent are introduced into an isolated circulation of a limited area. Thus, high concentrations of drugs can be obtained without producing general toxicity. Whether this method will prove of permanent usefulness remains yet to be determined but certain areas of the body can be perfused in what is essentially a closed vascular system.

I would hope that certain of the younger members of this audience will become sufficiently interested in this important area of effort to spend a portion of their time carefully studying the effect of a variety of agents now available and those which will soon be available in careful clinical investigation. Beware of pitfalls in this field! Subjective improvement is not a very reliable criterion. There are many pitfalls in this area which the clinical investigator must come to know. Decrease in the volume of a measurable tumour mass is the most important criterion of effect. It is an unfortunate circumstance that so often one cannot get bona fide measurements. In some instances biochemical properties of the tumour prove to provide valuable criteria of effectiveness, but the most important criterion is the extension of a useful life.

The organized Co-operative Clinical Studies now being carried on in my country have yielded solid quantitative data in a much shorter time than any

single institution could possibly have achieved. It has stimulated the interest and co-operation of many internists and surgeons in the care and chemotherapy of advanced malignant disease. It has gained the confidence and active collaboration of the pharmaceutical industry. The programme has assisted in the training of hundreds of scientists and clinicians, not only in cancer research but in closely related fields. It has organized a national standard reporting system of end results in malignant disease, and such reports are now being made on more than 50,000 new cancer cases a year. It has developed biometric units in a number of our medical schools and other research institutions to provide statistical consultation not only for cancer chemotherapy, but for other research. It has made available the first truly unselected, complete data on a national basis of operative complications and mortality from gastric, pulmonary, and colorectal resections, and it has set the pattern for other research areas where extensive interinstitutional efforts are needed.

The bulk of the chemicals examined during the past two years have come from the antibiotics programmes of industry and consist of crude beers. No rational approach is possible in the selection of anti-cancer antibiotics. Great skill and experience, however, will account for the greater success of some laboratories. This programme of necessity must be largely empirical.

The rapid progress in the study of hormone analogues could not have been achieved by individual or unco-ordinated effort.

A similar study of the vast number of plant natural products is being undertaken.

The three tumour mouse screen is being subjected to careful analysis. This method, as well as all other screening methods, can be evaluated only when a sufficient number of candidate compounds show true effectiveness against tumours in man.

The vast majority of scientists interested in cancer chemotherapy are prepared to drop any method of screening presently employed when a more specific method is discovered. Until then it is essential to continue along the lines presently followed.

Preclinical pharmacology must be expanded to meet the needs of the clinician. It is understandable that pharmacologists are not anxious to undertake huge programmes of preclinical pharmacology without assurance that the compound is of real interest to clinicians. It is also clear that the clinician can evaluate the anti-cancer properties of a compound more quickly and accurately if he has precise information concerning time-dose relationships, excretion, metabolism, and distribution in the tumour and in the body.

The co-operative clinical studies carried out with the aid of the Center through its clinical panel have been responsible for achievements which could not have been brought about by any other organizational pattern or sponsorship to my knowledge. The large number of institutions and doctors who have voluntarily agreed to study the response to anti-cancer agents are organised to work together in small groups on the basis of protocols representative of specific experimental

designs adopted as representative of the best methods of evaluation of chemotherapeutic agents.

Extensive modifications may arise from the critical evaluations presently under way. The greatest importance of the clinical co-operative trials lies in the fact that a large-scale attempt has been effectively carried out for actual clinical investigation based upon predetermined criteria. Data emanating from such studies permit analysis which otherwise could not be possible. The goals of individual studies in this co-operative plan were selected as much to achieve familiarity with this kind of clinical investigation as for the purpose of clinical investigation itself. It must be remembered that this kind of work is not as exciting as research of an individual scientist. It calls for obedience to rules, democratically achieved and agreed to. A by-product of such clinical interest is the great improvement in the care of patients with advanced cancer, and the conveyance of hope to the patient with such a serious problem because of the increased tempo of research activity concerning his or her problem. An important by-product, too, is the collection of information concerning the life history and biologic behaviour of the various forms of cancer. These by-products alone are worth the effort of the entire clinical programme so far.

Time does not permit me to describe the many exciting areas of research that are being prosecuted. In 1956, at the Third National Cancer Conference, Wendell Stanley suggested that for research purposes at least we might assume that all human cancer was viral in origin. The evidence is becoming stronger that Wendell Stanley may well be correct, and if he is, the justification of chemotherapy will indeed be on a firmer basis.

While the gains have been substantial, we have not yet achieved the goal which we have set before us to achieve. I need not tell this audience that this large field, which takes such a heavy toll each year in your country, and in mine, and in many other countries in the world, will be solved. When it is we will understand that understanding science is a way of thinking and that science's task is to serve man.

1960 ANNUAL REPORT

VIRUS REFERENCE LABORATORY*

Department of Microbiology, the Queen's University of Belfast

During 1960 the following have contributed to the work of the virus reference laboratory: J. H. Connolly, M.D.; J. R. L. Forsyth, M.B.; D. H. Simpson, M.B.; M. Haire, M.B.; J. K. Clarke, B.Sc.; D. S. Dane, M.B., and G. W. A. Dick, M.D.; J. Evans, J. Cummings, and J. J. McAlister, F.I.M.L.T.

THE Virus Reference Laboratory has now been in operation for four years and it seems a suitable time to consider what types of investigation have proved to be most valuable, so that in the future the work of the laboratory will not be dissipated in unrewarding investigations, but can be channelled in the directions where it will be most useful to the community.

It must be appreciated that a virus reference laboratory is *not* the virological equivalent of a routine diagnostic bacteriology laboratory. The reason for this is that at the present time, with the exception of poliomyelitis and a few other virus infections, the available diagnostic techniques cannot provide a laboratory diagnosis with the same speed as can be provided for many bacterial infections. Thus, frequently a virological diagnosis can only be made when it is too late to influence the course of treatment. There is only one group of viruses (Lymphogranuloma venereum and Trachoma) which are known to produce chronic infections, and with other chronic infections it is most unlikely that the virus reference laboratory can be of any help. The often time-consuming investigation of an isolated illness of supposed viral ætiology has seldom been rewarding to the clinician or the virologist. The function of a virus reference laboratory is to undertake special investigations rather than routine diagnostic work, and in our experience it has been the special investigations that have given the most useful results.

The types of investigation which have in the past been valuable and on which we consider the Virus Reference Laboratory should devote most effort are as follows:—

(a) The diagnosis of all cases of poliomyelitis, encephalitis, and aseptic meningitis.

(b) The surveillance of poliomyelitis vaccination, the evaluation of the safety and effectiveness of other viral vaccines, such as influenza vaccine, and the provision of information necessary for planning and assessing measures for the prevention and control of virus diseases.

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*This laboratory is supported by a grant from the Northern Ireland Hospitals Authority.

(c) To provide early warning or rapid confirmation of possible outbreaks or importations of virus infection, e.g., in such enterprises as the World Health Organization influenza spotting scheme and in the diagnosis of suspected cases of smallpox.

(d) To assist in special studies, e.g., the Medical Research Council chronic bronchitis trial and other special investigations, such as viral myocarditis, in collaboration with clinicians.

Poliomyelitis.

Laboratory Diagnosis of Notified Cases.

During 1960 there were fifteen notifications of poliomyelitis cases in Northern Ireland, of whom eleven were paralysed. One of the paralysed patients died. Revised diagnoses of scurvy, staphylococcal meningitis, tonsillitis or Coxsackie B_5 aseptic meningitis were made in the four notified non-paralytic infections. The viruses isolated from these notified cases are shown below.

Viruses recovered from Patients notified as Suffering from Poliomyelitis.

Notified	Number of Cases	Number Immunized	Viruses Isolated: Polio Type I	Polio Type II	Polio Type III	Coxsackie B_5	Untyped Entero-Viruses	Total Viruses Isolated
Paralysed	11*	0	4	–	6	–	1	11
Not Paralysed	4	2	–	–	–	1	–	1

*Includes one death.

It will be seen that there was one paralysed individual (a baby of 6 months) from whom an unidentified enterovirus was isolated.

The four type I paralytic infections occurred in the first quarter of the year, and with one exception came from the Belfast area. The type III infections were all from the Newry area except for a 34-year-old adult who was infected and became paralysed in Eire. The ages of the paralysed individuals from whom polioviruses were isolated were as follows:

Years	0–1	1	2	3	4	5	34
Number	1	4	1	0	2	1	1

In addition to these virologically confirmed cases there was serological evidence suggesting that a type II virus may have been responsible for wasting of the right calf and buttocks of a 4-year-old boy who had an undiagnosed illness in November, 1959.

Asymptomatic infections.

Two type I viruses and one type III virus were isolated from contacts of paralytic cases, and two type I viruses from asymptomatic infections.

Vaccine surveillance.

As in previous years efforts were made to follow up all diagnosed cases and to obtain information on their poliomyelitis vaccination status and their history of recent injections, etc. *None of the individuals paralysed during 1960 had received any immunization against poliomyelitis.* In none of them was there any history of other inoculations which might have suggested provocation paralysis.

The ages of the paralysed patients, all of whom, except the adult from Eire, were 5 years old or under stresses the risk of paralytic polio in pre-schoolchildren in Northern Ireland and the importance of paying particular attention to the immunization of this age group.

Epidemiology of type III outbreak in Newry area.

Since 1958 no type III poliovirus has been isolated in Northern Ireland. On 23rd July, 1960, a boy aged 4 years travelled from Coventry to Newry. He was ill during the journey and the following day he was paralysed. He was admitted to hospital on 25th July with paralysis of all limbs and was shown to be infected with type III poliovirus. As so commonly happens when there is a hospitalized child in a family, his sister, aged 3 years, stayed with friends in another part of Newry while the mother was visiting the hospital. The sister, although showing no signs of illness, was also excreting type III virus and a second paralytic case due to type III virus occurred in an 18-months-old baby living in the street where the sister had stayed. The brother of this baby was in the habit of visiting an aunt at Bessbrook, and on 21st September a child of $4\frac{1}{2}$ years living there became paralysed with type III virus. The siblings of the Bessbrook child played with a family in Camlough, one of whom, a child of 18 months, became paralysed on 18th October; again type III virus was isolated. A fifth case in a $2\frac{1}{2}$-year-old child due to type III virus occurred at Cladybeg, eight miles from Camlough, on 17th December.

It is clear that the type III virus was imported from England and spread slowly in the area, resulting in the paralysis of four other children. It is reasonable to assume that if the sister of the first paralysed child had been quarantined to house and garden, four paralytic cases would have been prevented.

Outbreak control in 1961.

There seems little doubt that within the next few years epidemics of poliomyelitis will cease in countries where there are *high* rates of immunization with poliovirus vaccines. It may well be that in vaccinated communities polioviruses will virtually disappear as had occurred with *C. diphtheria* in well-immunized populations. However, it also seems likely that, as with diphtheria, cases will continue to occur from time to time as a result of "importations" of virus from elsewhere. There is increasing evidence in favour of the "narrow stream" spread of epidemic poliomyelitis where the source of infection of the paralytic cases can be traced to direct contact with other paralytic cases or their immediate contacts. It seems reasonable, therefore, that attempts should now be made to

see whether the spread of poliovirus can be restricted by using measures similar to those adopted for the control of diphtheria and smallpox.

In consultation with Medical Officers of Health and the Ministry of Health it has been decided to institute immediately the following measures on the clinical diagnosis of a case of paralytic poliomyelitis.

(1) Immediate quarantine of the patient.

(2) House and garden quarantine of siblings and close familial child contacts.

(3) Immunization of contacts who have not been immunized, or who are inadequately immunized, with high potency inactive virus vaccine.

(4) The distribution of a pamphlet explaining about the spread and prevention of poliomyelitis and the importance of minor illnesses, etc. (Appendix I).

(5) Immunization and boosting where necessary of children in the periphery of the area where the case has occurred with the vaccines in routine use.

The effectiveness of these measures on the control of spread of the virus will be studied by the laboratory. Whether or not they can be successful will depend on (a) the physician *immediately* informing the Medical Officer of Health when a case is diagnosed clinically and (b) on the rapidity with which the outbreak prevention methods are brought into operation.

Survey of poliovirus antibody in Co. Down children.

In order to provide information on whether a fourth dose of inactivated poliovirus vaccine was necessary and also to obtain an index of the immune status of the child population for future comparative studies, an immunological survey was made in Co. Down in the summer of 1960. The results of the survey in the under-16-year-old population of whom 95 per cent. had received three doses of vaccine may be summarized as follows:

(a) Ninety-nine per cent. of the children had antibody to type II virus and 94 per cent. to type III virus.

(b) Immunity to type I virus which causes most paralysis was less satisfactory in the 1 to 5 year age group, for only 72 per cent. of these children had antibody to this virus compared with 98 per cent. of older children.

(c) In the 1 to 5 year age group it was found that 94 per cent. of children tested within a year after receiving the third dose of vaccine had antibody to type I virus, but only 64 per cent. of children of this age group tested more than one year after the third dose had antibody.

It may be concluded from these studies that a fourth dose of vaccine is desirable for the younger children in Northern Ireland about one year after the third dose in order to boost their immunity to type I virus. The results of this study will be published in detail elsewhere (Dane and Dick, in press).

Aseptic meningitis.

In forty-eight patients with aseptic meningitis, mumps virus was the causative agent in four and the following enteroviruses were isolated from the others:

Coxsackie B_5		Other Enteroviruses		Total
28	...	16	...	44

The mumps virus infections were diagnosed serologically, and in one of these infections Coxsackie B_5 virus was also present. The commonest cause of aseptic meningitis during 1960 was Coxsackie B_5 virus. This is in contrast to 1959 when there was no evidence of any marked prevalence of any particular enterovirus, and to 1958 and 1957 when mumps and type I poliovirus were respectively the most important causes of aseptic meningitis. It is noteworthy that not a single case of aseptic meningitis during 1960 was due to poliovirus.

Coxsackie Infections.

Coxsackie B_5 virus.

During 1960 there were many infections with Coxsackie B_5 virus in the United Kingdom. In Northern Ireland Coxsackie B_5 virus was isolated from many asymptomatic patients and was found to be associated with the following illnesses:

Aseptic meningitis	28
Bornholm disease	16
"Flu"-like illness	9
Respiratory infection	3

While there is little doubt about this virus being the cause of Bornholm disease and aseptic meningitis during 1960, it is less certain that it was responsible for the "flu"-like illnesses and other respiratory infections, for it is possible that in some of these illnesses Coxsackie B_5 was merely a fellow-traveller.

The best evidence for the implication of an enterovirus as the cause of a particular illness is usually found in outbreaks of disease such as occurred in a boys' school during 1960. During June and July fifty-one boys in a preparatory boarding school became ill. Unfortunately we did not hear of this outbreak until towards the end of the epidemic when nineteen boys were found to be excreting Coxsackie B_5 virus in their fæces.

The symptoms and signs of illness in these nineteen boys were:

Signs and Symptoms	No.
Pyrexia and malaise	19
Headache	18
Pharyngitis	13
Nausea	10
Chest pain	9
Vomiting	8
Abdominal pain	6
Backache	3
Neck stiffness	3
Dizziness	2

Six had relapses after apparent recovery, with recrudescence of symptoms and signs. One boy had electrocardiographic evidence of myocarditis for nine weeks (Connolly, 1961) and another boy was admitted to hospital with a diagnosis of meningitis. Convalescence after these Coxsackie B_5 infections was characterized by marked lassitude, but in all cases recovery was complete.

Coxsackie B_5 virus was isolated from three contacts of ill patients, from one patient with appendicitis and from forty-nine fæcal samples collected from 888 children admitted to the Royal Belfast Hospital for Sick Children, and from one healthy baby. A review of the case histories of the children from whom this virus was isolated provided the following diagnoses:

Respiratory illness - - - -	28
Meningitis - - - - -	3
Vomiting and abdominal pain - - -	4
Miscellaneous - - - - -	14

In many cases the clinical conditions for which they were admitted could have been caused by this virus.

Coxsackie B_1 virus.

In two patients with cardiac symptoms there was serological evidence of infection with Coxsackie B_1 virus. One of these was a man of 53 years who had clinical and electrocardiographic evidence of pericarditis; his electrocardiograph remained abnormal for at least three months after infection. The other patient was a woman of 37 years who had Bornholm disease which symptomatically resembled coronary occlusion. Her electrocardiograph was normal.

Other Enterovirus Investigations.

Investigation in Babies.

A preliminary investigation of the enteroviral flora of the infant gut was made in babies born at the Royal Maternity Hospital. An attempt was made to obtain a weekly fæcal specimen from these babies during the first year of life and to test the specimens for enteroviruses. Of thirteen babies born between April, 1959, and January, 1960, from whom *regular* weekly fæcal samples were obtained, ten were found to be excreting virus at one time or another. Forty-three viruses were isolated, including a type I poliovirus and a Coxsackie B_5 virus. There was no evidence of a seasonal incidence of virus infection nor was infection related to any particular period in the first year of life in this small sample. Three of the babies were excreting virus within 9, 15, and 23 days of birth respectively.

Samples from children admitted to the Royal Belfast Hospital for Sick Children.

In an attempt to obtain some index of the polioviruses circulating in the community, fæcal specimens were collected from 888 children admitted to the Royal Belfast Hospital for Sick Children. Only one type I poliovirus was isolated from an asymptomatic carrier. Although the sampling of this population was not as complete as had been hoped for when the study commenced, the single

positive specimen did not indicate a wide dissemination of poliovirus. In contrast to the single isolate of poliovirus a total of 139 other enteroviruses were isolated.

Respiratory Viruses.

Influenza.

As part of the World Health Organization influenza-spotting scheme, the laboratory continued attempts to detect the presence of influenza virus in the community. This scheme depends entirely on the collaboration of general practitioners. Although the coverage during 1960 was less satisfactory than in previous years, there was little evidence of influenza virus in the community during 1960. In March and April serological evidence of infection with influenza A virus was obtained in two patients, one of whom had a staphylococcal pneumonia and the other "pleurisy." In May a strain of Asian virus was isolated from an adult male with influenza. During the autumn and early winter there was no evidence of influenza virus in the community preceding the explosive outbreak at the beginning of 1961.

Medical Research Council chronic bronchitis trial.

In collaboration with Dr. Eileen O. Bartley and the Department of Therapeutics specimens collected from patients under study in the Medical Research Council chronic bronchitis trial are being examined for viruses.

Respiratory viruses in children.

An investigation of the viral ætiology of 117 respiratory infections in children was made in collaboration with Professor F. M. B. Allen. Although this study provided experience with techniques required for the study of some of the more recently isolated respiratory viruses, it has been unrewarding to the clinicians and virologists. No adeno- or *para-influenza* viruses were isolated from these children, but serological evidence of recent adenovirus infection was found in three children with pneumonia and in three other children with pneumonia there was evidence of recent infection with para-influenza 3 virus. A number of enteroviruses (four Coxsackie group B virus and two Echo viruses) were isolated from children with respiratory illnesses. While certain of the enteroviruses have been associated with respiratory illnesses, in the absence of an epidemic of respiratory infection associated with one or other type of enterovirus their ætiological importance remains uncertain.

The association of para-influenza viruses and adenoviruses with pneumonia in children requires further investigation, and most information will be obtained from virological investigation of outbreaks or a series of cases, rather than of isolated respiratory illnesses.

Special Investigations.

Rickettsioses and multiple sclerosis.

LeGac, Giroud, and Dumas (1960) have claimed that cases of multiple sclerosis have an epidemiological pattern and histological lesions similar to that of rickettsial infections. Although there is no evidence of Q fever (Murray, Dane, and Dick, 1958) or other rickettsial infections in Northern Ireland and no evidence of any similarity of the histological lesions of rickettsioses and fatal multiple sclerosis

cases in Northern Ireland (Professor J. H. Biggart, personal communication), the Virus Reference Laboratory was requested to carry out some tests for Q fever antibody in the sera of patients with a clinical diagnosis of multiple sclerosis.

Sera from thirty patients with multiple sclerosis were tested for complement fixing antibody to the Nine mile strain of *Rickettsia burnetii*. Of these sera twenty-seven were negative at a dilution of 1 : 4 and the remaining three were anticomplementary. There is thus no evidence of an association of *R. burnetii* infection and multiple sclerosis in Northern Ireland.

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POLIOMYELITIS

ADVICE TO PARENTS

THIS NOTICE IS SENT TO YOU BECAUSE A CASE OF POLIOMYELITIS HAS OCCURRED IN YOUR NEIGHBOURHOOD.

Poliomyelitis is an infectious disease that spreads from person to person, and it may be spread by people who are not themselves ill. It is most unlikely that you or any of your family will become ill, but you can do several things to make this even less likely and to assist in measures to prevent the disease spreading.

These are the rules we would like you to follow:

1. Make quite sure that you and your family have been properly immunized against poliomyelitis. If in doubt ask your doctor or health visitor about this. Arrangements are now being made to immunize all those who need it.

2. Wash your hands after going to the lavatory and see that your children do this too. Also wash your hands before preparing food.

3. Avoid kissing small children outside your own family and do not let your children visit or play with other children who are unwell themselves or have a brother or sister who is ill.

4. Avoid crowds and do not travel unnecessarily with children.

5. If anyone in your household is off-colour or ill make sure they stay at home and go to bed and that you inform your doctor immediately. Do not allow visitors, particularly other children.

Don't forget about immunization, but remember that it is a few days before it can give any protection and therefore it needs to be done as soon as possible.

Don't be alarmed. Very few of the people who get infected with the poliomyelitis virus become ill, and of the few who do become ill many recover completely. You have been sent this notice because if you and everyone else follow the rules outlined above we can prevent some cases of poliomyelitis.

PRIMITIVE MEDICINE

By **R. J. KERNOHAN, M.D., F.R.C.P.I., M.R.C.P.**

ANNUAL ADDRESS, SESSION 1960
North-East Ulster Division, British Medical Association

It was Sir Winston Churchill who remarked in 1944, when addressing the Royal College of Physicians, that "the longer you can look back, the further you can look forward." Probably in no field is this more true than in the biological sciences. An understanding of their evolution in a historical sense at once provides a perspective and a background to knowledge which illuminates the path to further effort.

In the days of early civilization, and even today among primitive peoples, the conceptions of medicine, magic, and religion are closely connected, and the separation of one from the other is difficult or impossible. Medicine has not always been an autonomous institution as it is today in modern society. Among primitive peoples it is difficult to draw a definite line between medicine and religion.

If the beliefs of mankind in general concerning the causation of disease are examined, it is found that the causes may be grouped in three main classes:—

(1) Human agency, in which it is believed that disease is directly due to the action of some human being;
(2) The action of some spiritual or supernatural being;
(3) What we ordinarily call natural causes.

Among civilized people there are indications of the presence of all three kinds of belief, and this was certainly so in the not very remote past. We now only think of human agency in cases of poison and injury. The second category still exists in the "hand of God" of our statutes. In modern medicine, the attitude towards disease is regulated by the concept in its production by natural causes. Disease is thus regarded as the result of a change in the environment quite independent of human or superhuman agency.

If, on the other hand, the culture of savage people is examined, it is found that their beliefs concerning the causation of disease fall, by and large, into one or other of the first two categories. The best known form of mediæval magic was one in which spiritual agents play an important rôle. The magic of peoples of rude culture differs widely from this in that disease is ascribed to human agency even when the real cause would seem to be obvious. In this category three main classes can be distinguished:—

(1) Those in which some substance is projected into the body of the victim;
(2) Those in which something is abstracted from the body;

(3) Those in which the sorcerer acts on some part of the body of a person or on some object which has been connected with the body of a person, in the belief that thereby he can act on the person as a whole.

In cases of illness caused by the introduction of substances projected into the body the aim of treatment is to extract the object from the body. In parts of New Guinea there are men and women who are believed to have the power of removing objects, usually by sucking some part of the body. After the performance of this action a stone or other object is shown to the patient, and this often leads to a cure by suggestion.

To whom the honour of having first invented medicines is unknown. Osiris and Isis, Bacchus, Apollo, father of the famous physician Æsculapius, and Chiron the Centaur are among the many mythological personages who have been accredited with the invention of physic. It is certain that the art of compounding medicines is extraordinarily ancient. There is a papyrus in the British Museum containing medical prescriptions which was written about 1200 B.C.; and the famous Ebers papyrus, which is devoted to medical matters, is reckoned to date from about the year 1550 B.C. It is interesting to note that in the prescriptions given in the latter papyrus, as seems to be the case throughout the history of medicine, the principle that the efficacy of a medicine is in proportion to its nastiness appears to have been the main idea. Many old medicines contained ingredients of the most disgusting nature imaginable. A mediæval remedy known as oil of puppies, made by cutting up two newly-born puppies, and boiling them with one pound of live earth worms may be cited as an example of the remedies used in the days when all sorts of excreta were prescribed as medicines. When Cardinal Richelieu was on his death-bed a female charlatan prescribed for him a mixture of horse dung in white wine.

At first sight the methods that have been used to treat disease appear to be numerous and dissimilar but they are simply variations of three basic measures. First, faith healing; second, hygienic therapy; and third, drug cures. In faith healing an attempt is made to remove morbid states by means of influences exerted upon the mind. The early and mediæval Christians were practising faith healing when they exorcised the devils that to them seemed to cause disease, and in so doing they followed a principle which has been developed among primitive peoples. The same principle persists today as Christian Science and as psycho-analysis. Leucotomy is perhaps the modern method of exorcising devils. The second means of treatment, hygienic therapy, is founded on the recognition of the fact that the body tends to cure itself and that people recover from disease. This treatment includes rest, sunlight, bathing, fresh air, and diet. The third means of treatment, the use of drugs, is a relic of poison lore.

In various stages of civilization, at various times, each of these three methods of treating disease has had periods of ascendancy. In the lowest grades of civilization faith healing predominates, while in the highest grades of civilization hygienic therapy predominates, but is assisted by the use of drugs. Faith healing is the characteristic medicine of primitive and superstitious people, and until

five hundred years before Christ it was the principal method of treating disease. At that time hygienic therapy began among the Greeks, and, somewhat later, drug cures were gradually combined with it. When the Christian religion came in, the influence of its mysticism slowly forced out these measures and treatment returned once more to faith healing. For thirteen centuries faith healing maintained its ascendancy. A form of drug treatment persisted, however, and at the time of the Renaissance its use increased extensively. Religious forms of faith healing were slowly discarded. The drugs, which were used, were for the most part useless and some were actually harmful. As knowledge gradually accumulated, hygienic therapy slowly returned and drugs were relegated to a subordinate position.

Primitive man sees in disease the working of supernatural forces. For him disease is caused by a demon; or is induced by human enemies through the power of sorcery; or is caused by the evil influence of a spirit which may be that of a dead man, or an animal, or even of a plant. It was the business of the medicine-man to drive away the demon, outwith the sorcery of the enemy, and placate the dead. To accomplish these ends he distracted the patient's attention from his sufferings; he inspired him with a confidence in his recovery; and finally left him with a token to remind him of the efficiency of the cure. To fix the patient's attention the medicine-man dressed fantastically. Sometimes he clothed himself in animal skin until he resembled a huge bear standing on its hind legs. He shouted and danced and waved a rattle. After he had completed his personal treatment he provided the patient with an amulet to be worn on his person to ward off the demons. Amulets can be of any material—mineral, crystal or precious stone.

Faith healing that is practised today among civilized peoples differs only in form from the faith healing of primitive people. The howling medicine-man of former times and the quiet Christian Science healer of today use the same principles, viz., to gain the patient's confidence, and inspire him with faith in his recovery. It must be frankly recognised that some diseases can be cured in this manner, and the symptoms of others may be relieved temporarily. Faith healing has many names. Its opponents call it superstition; its advocates call it psychic healing, the laying-on of hands, psycho-analysis or Christian Science.

Faith healing is not to be dismissed lightly. It has its dangers, but it also makes its cures. The dangers come when it is tried with fanatical persistence for those diseases which it does not benefit, and which, if not treated positively, result in disablement or death. It is in hysteria, which is characterized by bodily dysfunction due to mental conflict, that faith healing can be dramatic. "Hysteros" in Greek means uterus, and the Greeks in naming hysteria conceived of the uterus as the centre of the disease. They thus anticipated Freud's views on sex repression and its neuroses by twenty-five hundred years. The classical examples of hysteria are afforded by the female saints who were subject to so-called demoniacal obsession.

The faith healer believes that all disease is mental and he carries his belief to fanatical extremes. The belief in faith cures rests upon testimony, and there is no form of reasoning more fallacious, i.e., the argument post hoc ergo propter hoc.

One of the most successful charlatans of faith healing was Cagliostro, who lived in the time of Louis XVI. He used alchemy and mysticism as trappings for his cures. He sold beds that provided painless childbirth, chairs that cured rheumatism, and he supplied an elixir of life. The outstanding faith healer of the nineteeth century was Quimby, of Maine, U.S.A. Quimby began faith healing with the use of hypnotism which was then called animal magnetism. This had been extensively exploited by Mesmer in the eighteenth century. For a time it was believed that persons under the influence of hypnotism could be made to commit crimes, even murder. The story of Trilby, the servant girl with a croaking voice, and the hypnotist Svengali, who made of her an operatic prima donna, illustrates this belief. We now know, of course, that persons during the hypnotic state can do nothing which is contrary to their natural characteristics. Quimby taught that there is no evil in the world. Evil exists only in the mind and illness results from evil thoughts. When the evil thoughts are expelled from the mind, disease disappears.

This metaphysical conception of disease led to the founding of Christian Science by Mrs. Eddy. As a child she was neurotic, and at the age of twenty-two she married a stone mason who died six months later and before the birth of her only child. After ten years of widowhood she married an itinerant dentist who deserted her after eight years, and from him she subsequently obtained a divorce. She developed delusions of persecution, and felt that malicious animal magnetism, emanating from her enemies, was producing many ills and had caused the death of her third husband. She even instigated a suit to enjoin her enemies from exerting this influence, and to have them punished for doing so. Malicious animal magnetism is merely another name for witchcraft. It is, in fact, the exact opposite of faith healing. When Mrs. Eddy assigned hysterical ailments to malicious animal magnetism, and asked the courts to punish alleged persecutors she was attempting to revive witchcraft and the punishment of witches. Along with this black magic she introduced white magic. Her treatment of disease was based upon the ancient metaphysical conception that as matter is known only through the senses, it has no existence except in mind. Matter is merely an illusion. Mind is all and matter nought. Mind is not sick and matter cannot be. The cure of disease is effected by making the disease appear to be an illusion.

There is a close connection between drug cures and faith healing. Drug cures and faith healing have produced similar results because both are evaluated by the same fallacious test. Sick men touched holy relics and they afterward got well; therefore they assumed that they were cured by the relics. Similarly, sick men took drugs and afterward got well; therefore they assumed that they were cured by the drugs. As a result of this type of reasoning almost every conceivable substance that could be taken internally has been used in the treatment of disease.

Curative properties have been attributed to nearly every substance when it was new, or difficult to obtain, and which can be forced into the human system. The potato, when first introduced into Europe, was not used as a food, but as a medicine. Gold dissolved in acid, "potable gold," was once a sovereign remedy for nearly every ailment. Powdered mummy was a prominent ingredient of mediæval prescriptions. Most of the mummy used was adulterated. Unicorn's horn was another highly valued remedy of mediæval times. The horn, supposedly derived from the mythical unicorn, was in reality nothing but ivory. The cost of unicorn's horn confined its use to the nobility.

Greek medical practice, as established by Hippocrates five hundred years before Christ, did not include an extensive use of drugs. At the great University of Alexandria, however, a more extensive use of drugs was grafted upon Greek medical learning. After the fall of Corinth, Greek physicians migrated to Rome. The combined influence of Greek, Alexandrian, and Roman medicine brought in an extensive use of drugs. Dioscordes, who was a surgeon in the army of Nero, travelled from country to country with the army. He collected information concerning the remedies in use in each country and he compiled a list of drugs, the first extensive materia medica. The substances listed in Dioscordes' book were worked into a system by Galen, who was born in Pergamon in Asia Minor in A.D. 131. This system of Galen was the medical religion of the Christian era up to the seventeenth century. It has left its mark on medicine even to this day and vegetable preparations are still called galenicals. Galen insisted on having a theory for every phenomenon. His superficial theories displaced the less showy and more laborious methods of Hippocrates, which were based upon direct observations and logical interpretation. Galen developed an elaborate theory of disease and its treatment based on the prevalent metaphysical conceptions of the nature of the body.

The mixtures of herbs which were recommended by Galen were largely inert, but they did not do the patient much harm. Conditions changed when such poisonous drugs as mercury and antimony were introduced. The use of these powerful drugs was due largely to Paracelsus, one of the most striking figures in the history of medicine. He not only founded a system of therapy, but dabbled extensively in mysticism. He was born in 1493 in Switzerland. It was the century of the great reformers—Luther in religion, Vesalius in anatomy, Paré in surgery, and Paracelsus in therapy. At the age of 32 he was appointed Professor of Medicine at Basle. His first official act was to burn the works of Galen. This was a most courageous act, and he was reviled by medical men of the times. The medical teachings of Paracelsus are overlaid by a nonsensical mass of astrology, mysticism, and alchemy. He held the doctrine of so-called "signatures." This theory is founded on the astrological conception that the stars impress the "signature" of disease upon drugs, and that the medicinal value of plants and minerals is indicated by their external form. Thus the root of the orchid, because it is shaped like a testicle, should be used in curing diseases of that organ; and mandrake whose roots resemble the human form is used as a cure for sterility; and since the black spot in the flower euphrasia—eyebright—

resembles the pupil of the eye, it is used for diseases of the eye, and nutmeg, which vaguely resembles the brain, is used for diseases of the brain. Allied to this doctrine is the belief that the lungs of foxes are good for bronchial trouble, or that the heart of a lion will endow one with courage.

Paracelsus was the first to contest the authority of Galen. He ridiculed the absurd mixture of herbs that Galen advocated. He had a profound interest in chemistry—then called alchemy—and he maintained that the preparation of new and better drugs was the chief business of chemistry. He introduced the use of mercury, and not only supplied a cure of syphilis but he was the first physician to describe the stages of the disease and its transmission to children. Patients with syphilis were dosed with mercury internally and rubbed with it externally until the saliva flowed from their mouths, their teeth were loosened, and their health permanently impaired by mercury poisoning.

The evolution of medicine from the primitive beliefs of our ancestors has followed tortuous paths. The history of medicine is at once the history of human wisdom and the history of human folly. Primitive people attributed disease to the malignant operation of evil spirits and other supernatural causes. Disease is now regarded as a natural phenomenon which is subject to natural laws, and to be treated as any other department of nature.

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REPORT ON THE MYCOLOGICAL DIAGNOSTIC LABORATORY THE QUEEN'S UNIVERSITY OF BELFAST, 1960

By D. W. R. MACKENZIE, B.Sc., Ph.D.,
L. CORKIN, and HILARY BELL

THIS is the second annual report of the Mycological Diagnostic Service and covers the work done during 1960. After September, 1960, the laboratory was incorporated into the Queen's University Department of Microbiology without any change in the scope or function of the diagnostic service. The laboratory continued to offer to general practitioners, hospital laboratories, and clinics a routine service for the isolation and identification of fungi associated with humans.

During 1960 mycological examinations were made on 1,376 specimens from 897 patients, received from 26 hospitals or clinics, or from practices in Northern Ireland. Almost 98 per cent. of the specimens received came from dermatological clinics or practices, those originating from general practice accounting for only 2.2 per cent. of the total number received. Pathogenic fungi were cultured on 350 occasions from 237 patients, but an additional 50 specimens showed the presence of fungi by microscopy alone.

RINGWORM.

As in 1959, ringworm fungi were the most common group, accounting for 271 (77.5 per cent.) of the 350 pathogenic fungi obtained in culture. Details are shown in Table 1.

TABLE 1.

SPECIES OF RINGWORM FUNGI ISOLATED 1959-1960.

SPECIES	NUMBER ISOLATED	
	1959	1960
Trichophyton verrucosum	40	52
Trichophyton sulfureum	48	37
Microsporum canis	42	27
Trichophyton mentagrophytes	11	19
Trichophyton interdigitale	10	10
Trichophyton rubrum	19	16
Epidermophyton floccosum	12	13
Trichophyton persicolor	–	1
Others	3	–
TOTAL	185	175

T. sulfureum was again the most common organism isolated from scalp infections of children, and probably remains its most common cause in Northern Ireland (Beare, 1958). Specimens were received from more girls than boys, in the ratio of 2.33 : 1. Unlike 1959, the high number of infections amongst girls was not dependent on the discovery of an outbreak at a girls' school.

A marked reduction in the number of isolates of *M. canis* is evident, and in the first six months of 1960 only six new patients with this infection were confirmed. No material from adult infections was received.

Inflammatory ringworm of the body of three children caused by *T. mentagrophytes* was found to have originated from pet white mice.

T. persicolor, a rare species, was isolated on one occasion from a lesion on the lip of a 47-year-old woman, this apparently being the first isolation in Northern Ireland.

Cattle ringworm (*T. verrucosum*) was the most common fungus, ringworm or otherwise, isolated in the laboratory usually from lesions on the hands, forearms, body, and scalp of individuals living in rural communities. Seven cases of tinea barbæ were confirmed.

Other Pathogenic Fungi.

Candida albicans was isolated from 41 patients as follows: nails (9 occasions), foot, i.e. interdigital clefts (8), perineum (6), tongue (6), genitalia (4), fæces (2), sputum (1), pharynx (1), and scalp (1). Several other pathogenic yeasts were isolated, including *C. tropicalis* (3), *C. parapsilosis* (2), and *Geotrichum candidum* (1).

Malassezia furfur, the cause of pityriasis versicolor, was recorded on eight occasions. Fungi associated primarily with middle ear infections included *Aspergillus fumigatus*, *A. flavus*, *A. niger* and *A. versicolor*. *Scopulariopsis brevicaulis*, a species of apparently low pathogenicity, was isolated on two occasions, from a finger lesion and a superficial infection of the eyelid.

Keratinomyces ajelloi, an organism related to ringworm fungi and capable of experimental infection in humans was isolated from household dust at the home of a child with a *T. sulfureum* scalp infection. Several subsequent isolates of this fungus were made, again constituting a new record for Northern Ireland.

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AMPHETAMINE SUBSTANCES AND MENTAL ILLNESS IN NORTHERN IRELAND

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THE use of amphetamine and its analogues as stimulants and as slimming aids is well known. It is not so widely appreciated that they can produce both acute psychiatric disturbances and addiction. Young and Scoville (1938) were the first to describe a paranoid illness in three patients who were taking amphetamine for narcolepsy. Subsequently other reports confirmed the association of this psychosis with amphetamine, but only six cases were recorded in Great Britain prior to 1956. Connell (1958), in a prospective study, recorded forty-two cases in a three-year period showing the problem to be more common than had been appreciated. He found it impossible to separate the condition from paranoid schizophrenia unless there was evidence of ingestion of the drug and differentiated the two groups by testing the patient's urine for amphetamine end products.

In other cultures amphetamine abuse is a serious problem. For instance, in 1954 the Pharmacist Association of Japan estimated that one and a half millions of their population of eighty-three millions abused the drug. In one survey of fifty-two male amphetamine addicts, auditory hallucinations and paranoid delusions featured in most cases (Hara et al., 1954). Sakurai surveyed 110 addicts, finding 90 per cent. with symptoms resembling schizophrenia. While most cases recovered in thirty days, some needed at least fifty days for their symptoms to disappear. The whole Japanese problem was the subject of a memorandum presented by Masaki to the World Health Organization in 1956.

In Northern Ireland within twenty-eight months twenty-seven patients (about 2 per cent. of total referrals in the same period) have been seen at this department in whom amphetamine compounds or phenmetrazine have played an important part in their illnesses. There were nineteen females and eight males with ages ranging from 20 to 56 years. They separated easily into three groups. One group presented with symptoms clinically indistinguishable from paranoid schizophrenia, a second contained those who were habituated or addicted, and the remainder had miscellaneous symptoms, probably attributable to amphetamine, as withdrawal of the drug resulted in their disappearance.

I. SCHIZOPHRENIC-LIKE GROUP.

The ages of these five patients—four females and one male—ranged from 22 to 46 years. The onset of illness was acute in four, but one woman had been ill for ten years.

All were tense, evasive, and suspicious. Two were over-active, talked excessively and at times their conversation was incoherent. Disorders of thought, including

thought-blocking and illogicality, occurred. Objectively mood was shallow, but subjectively there were complaints of depression. Ideas of reference were described in that newspapers, television, and radio were felt to be making specific and personal comments. The prominent feature of all was the presence of paranoid delusions. The two married women alleged that their husbands were trying to poison them and were being unfaithful. The male patient felt the police were accusing him of a serious crime and other misdemeanours. Another felt that ugly rumours were circulating about her past. Somehow everything would be altered and made acceptable if she slashed her wrist and lost some blood. Various hallucinations, both auditory and visual, were described. The auditory form was frequently of God's voice and some complained of hearing bells. In the visual sphere one patient remarked that she had seen the Virgin Mary, who winked at her. Another was plagued by the staring eyes of an old man.

These patients were at all times correctly orientated, though distractible, with poor powers of attention and concentration.

Initially only one patient admitted taking drugs and laboratory evidence was necessary to decide that these substances were involved in the illnesses of the others. Even when this was presented, three persisted in their denial.

During the early part of his stay in hospital, one patient developed a pyrexia. Investigation showed the only abnormality to be a high excretion of amine in the urine and amphetamine may have been responsible for this rise in temperature which settled with conservative measures.

II. The Group of Patients dependent on these Drugs.

There were eighteen patients—twelve females and six males—in this group, and their ages ranged from 20 to 56 years. This number could be divided into two sub-groups. Firstly, the so-called "symptomatic addicts" (Meerloo, 1952), that is people who at different times would be dependent on various drugs. There were six patients in this sub-group. As well as amphetamine, five had been dependent on alcohol at times, five had taken barbiturates, and one pethidine. The other sub-group of twelve patients took these drugs alone. Ten had started in an attempt to increase energy and drive, and two to slim. Any benefit experienced was short-lived and when seen all were agitated and depressed in spite of having increased the dose. Routine tasks were impossible for them without amphetamine, and for some it was necessary to enable them to get out of bed.

III. The Group with Miscellaneous Symptoms attributable to Amphetamine.

Side effects of amphetamine were prominent as presenting symptoms in four patients. Two were referred with anxiety, tension, and restlessness. Dysmenorrhœa was being treated in one, depression in the other. With immediate withdrawal, the additional symptoms regressed rapidly. As psychological efficiency is reputed to be enhanced by these preparations, it was prescribed for a businessman who had subjective complaints of memory loss and poor concentration. The result

was to make him tense and anxious, increasing his memory difficulty and seriously decreasing his efficiency at work. There was a dramatic overall improvement following amphetamine withdrawal. In the fourth instance, the patient was given amphetamine for apathy and tiredness, the result of domestic difficulty. Severe headache and copious vomiting began suddenly and were relieved as quickly by discontinuing amphetamine. The original symptoms of these four patients did not respond to the medication and became rapidly submerged by side effects.

Discussion.

The evidence presented suggests strongly that misuse of amphetamine occurs in this community. About 2 per cent. of referrals have, as their main complaints, symptoms caused by amphetamine. This figure is probably an underestimate as the presenting symptoms are not specific and it has not been possible as yet to introduce the test for urinary amine as a routine. Again, these patients are often reluctant to admit their dependence. The experience with this group was that they denied taking these substances, sometimes even when confronted with laboratory evidence. This was in contrast to the patients from a different cultural background who usually admitted taking the drugs (Connell, 1958). Consequently considerable importance is placed on the laboratory tests. Even when misuse was admitted, evidence from other sources showed that the amount stated was usually a very conservative estimate, a situation also found with alcoholics. Probably this substance should be looked for routinely in the urine of all psychiatric patients. It is much more commonly found than either a positive Wasserman reaction or a raised blood bromide.

It has been stated that recovery from the schizophreniform illness should take place in one week once the drug is withdrawn (Connell, 1958), and if longer is taken the diagnosis should be revised. On the other hand, Sakurai concluded that some patients may need over fifty days to recover. Our experience would possibly reconcile these statements. The longer period may be necessary because, in fact, the patient continues to take a reduced dose, evading the strictest supervision. As Sakurai had no laboratory tests available at that time, it was impossible to confirm abstinence, which is necessary for prompt recovery.

In a number of published cases a raised temperature has been associated with amphetamine consumption and death in hyperpyrexia has occurred. (Gericke (1945), Mitchell and Denton (1950), Pretorius (1953), Bernheim and Cox (1960), Jordan and Hampson (1960).) The pyrexia shown by one of these patients could be explained on this basis. In view of the secretiveness shown by patients dependent on these products, this cause should be considered in the differential diagnosis of pyrexia of unknown origin.

It is apparent that a real problem exists in this community, the extent of which remains to be determined. These substances have few and very limited therapeutic indications, and their widespread use greatly exceeds any possible need. The risks to mental and physical health should be taken into account in every instance where their use is considered either alone or in the various proprietary preparations in which they are combined with other drugs. Martindale (1958) mentions

twenty-eight such preparations, and further combinations are still being introduced. In spite of the stringent regulations applicable to Schedule 4 drugs, it has not been possible to prevent misuse of these compounds but it is hoped that a greater awareness of the problem may help to rectify the situation.

Summary.

The misuse of amphetamine causes illness. Some forms of presentation are mentioned and discussed. The diagnosis may be overlooked as the symptomatology is not specific and reliance is placed on laboratory tests.

We wish to thank Professor J. G. Gibson for his advice and encouragement in the preparation of this paper and his permission to publish these findings.

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REVIEW

SURGERY IS DESTINED TO THE PRACTICE OF MEDICINE. By Sir Reginald Watson-Jones. (Pp. 81; figs. 77. 21s.) Edinburgh and London: E. & S. Livingstone, 1961.

This monograph, which was the Hunterian Oration given by Sir Reginald Watson-Jones to the Royal College of Surgeons of England in 1959, traces the life of John Hunter and his contribution to surgery. As the title suggests, Sir Reginald has taken his stand, along with Hunter, that the last part of surgery, namely operating, is a reflection on the healing art. In orthopædic surgery the author indicates what many have discovered, that the art of surgery is ending surgery. The decline of cutting operations in surgical treatment is enlarged upon, and the triumphs of medicine in what were once surgical fields are enumerated. Even in the treatment of injuries, surgery is ending surgery, not so much by the surgeon giving up cutting, but by the fact that he should only cut once at the proper time and with proper preparation and consideration.

Sir Reginald stresses that the days are over for multiple surgical adventures in orthopædic surgery. The pattern of orthopædic medicine replacing orthopædic surgery has depended on advances in many fields and the basic sciences. Sir Reginald stresses that orthopædic surgeons of mature thought have for so long recognised that not more than a small percentage of their patients need operative treatment, that it may be in other fields of surgery that this principle is accepted less readily.

The monograph ends by stressing that in fact surgery is medicine.

This monograph is a most stimulating one and should be read by all interested in the advances of medicine, and by all who are concerned in relegating surgery to its proper place in the therapeutics of orthopædic illness. R. J. W. W.

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MEGALOBLASTS IN THE PERIPHERAL BLOOD

By N. J. AINLEY, M.D., M.R.C.P.I., and M. E. WHITE, A.I.M.L.T.
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THE finding of megaloblasts in the peripheral blood is often regarded as an uncommon event, confined to patients with severe anæmia. Methods of concentrating the megaloblasts by making preparations from the "buffy coat" of the hæmatocrit have been described (Goodall, 1957, Whitby and Britton, 1957). This paper records our experience of examining the peripheral blood for megaloblasts.

METHOD.

It has been our custom for a number of years to examine carefully the routine blood film from patients with anæmia where there is macrocytosis or a dimorphic picture, or if the neutrophils show a shift to the right. In many of these, megaloblasts were found in the tail or along the edges of the film. If no megaloblasts are found, "buffy coat" preparations are made as described by Goodall (1957) and if these are negative the bone marrow is examined.

The routine blood film is made either from an ear prick, or from venous blood within two hours of collection, using Sequestrene (EDTA) as anticoagulant. Red cell counts and absolute values are not done routinely.

RESULTS.

During the calendar years 1957, 1958, and 1959 there were 247 cases of megaloblastic anæmia diagnosed in this laboratory.

Method of Diagnosis.

Routine blood film -	- 104 (42 per cent.)
"Buffy coat" preparation -	- 35 (14 per cent.)
Bone marrow examination	- 108 (44 per cent.)

DISCUSSION.

The table shows that over half of the cases were diagnosed by examination of the peripheral blood alone and in the majority of these megaloblasts were found in the routine blood film. The response to specific treatment and subsequent course of these patients indicated that the diagnosis was correct. The degree of anæmia was not always severe; many patients had hæmoglobin levels over 7g. at the time of diagnosis.

We feel that the procedures described reduce the amount of technical work by eliminating red cell counts and absolute values, and spare the patient the discomfort of marrow examination.

SUMMARY.

Megaloblasts were present in the peripheral blood in 139 out of 247 cases of megaloblastic anæmia. In 104 of these, megaloblasts were seen in the routine blood film. They were present in "buffy coat" preparations from the other 35 cases.

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SALVAGE HIP PROCEDURES IN THE AGED

By **JOHN H. LOWRY, F.R.C.S.**
(Orthopædic Registrar, Royal Victoria Hospital, Belfast)

and NORMAN W. McLEOD, F.R.C.S.
(Orthopædic Registrar, Musgrave Park Hospital, Belfast)

PAPER READ AT THE MEETING OF THE IRISH ORTHOPÆDIC CLUB in Belfast in November, 1960

THIS paper describes the use of the prosthetic head in the treatment of recent fractures of the neck of the femur, in patients in whom Smith Peterson pins had failed, and degenerative hip disease in the aged.

It is of interest that the first metal prosthetic head used in Britain was designed and inserted by Mr. N. S. Martin at Musgrave Park Hospital, Belfast, in 1948. Hey Groves, on one occasion in 1922, used an ivory prosthesis.

METHOD.

The prosthesis we have used over the past four years is the Austin Moore (1957) head. The patient is placed in the lateral position, lying on the good side. The area to be incised is infiltrated with saline containing 1/400,000 adrenaline. The incision is similar to that described by Kocher, running from the posterior superior iliac spine to the greater trochanter and then down the lateral border of the femur. The gleuteus maximus is split in the direction of its fibres, the sciatic nerve identified and retracted medially and the posterior rotator muscles divided with diathermy at their attachment to the greater trochanter. The capsule of the hip is opened by a cruciate incision and the hip dislocated posteriorly by internally rotating the leg. In the case of fractures, the head is easily removed with a bone lever. The neck of the femur is trimmed as far distally as half an inch medial to the trochanteric line, a notch being cut close to the attachment of the lesser glutei. A prosthesis of suitable size is then inserted, the hip reduced and the wound closed in layers.

Post-operatively, the leg should be maintained in a position of external rotation with a hip spica bandage. One of our cases of dislocation may have been due to neglect of this. If the leg is kept in external rotation, the tendency for posterior dislocation of the hip is removed.

RESULTS.

Patients may be divided into three groups before operation, and the results expressed in three grades.

Pre-operative Groups.

1. A patient who was able to get about without any difficulty and without assistance.
2. A patient who, with assistance, could get about the house and, possibly, walk for short distances outside, with or without pain.
3. A patient who was either chair- or bed-ridden.

Post-operative Grades.

1. Good—a patient who is free from pain and can, with the assistance of a stick, walk from one to two miles.
2. Fair—a patient who, with a little assistance, can get about the house and is free from pain but is unable to go outside.
3. Poor—a patient who, with or without pain, is chair- or bed-ridden.

TABLE 1.

FRESH FRACTURES.

	PRE-OPERATIVE GROUP	COMPLICATIONS	AVERAGE FOLLOW-UP	MORTALITY	RESULT
No. of cases 29	(1) 23	Sepsis	18 months	13.7%—4 cases	Good 18
	(2) 6	removal			Fair 4
Average age 74		of head - 1 case		*Causes of death*	Poor 0
Youngest 60				Broncho-pneumonia 2 cases	
Oldest 83				Cerebral thrombosis 1 case	3 cases too
				Coronary thrombosis 1 case	early for
					grading

FAILED PINS.

No. of cases 15	(1)* 11	Dislocation	16 months	6.6%—1 case	Good 8
	(2) 4	of hip - 2 cases			Fair 5
Average age 72		Post-operative			Poor 1
Youngest 60		shock - 1 case			
Oldest 87		Sepsis			
		removal			
		of deep			
		sutures - 1 case			

OSTEO-ARTHRITIS IN THE AGED.

No. of cases 10	(2) 10	Pulmonary	16 months	10%—1 case	Good 8
		embolism - 1 case			Fair 1
				Cause of death	
				Cerebral embolism	

*Pre-operative grading means pre-pinning.

It will be noted that, in the grading of these cases post-operatively, no mention has been made of hip movements. These have been considered as only of academic interest in the age group involved, the main objectives being degree of mobilisation of the patient and absence of pain.

Discussion.

1. *Fresh Fractures.*

The results of this are shown in Table 1. The indications used for this treatment were: —

(a) Cases where a stable anatomical reduction was impossible due to comminution of the posterior part of the femoral neck.

(b) When the age of the patient and general condition required rapid mobilisation after operation.

(c) Fractures thought to be pathological (one case in this series was a secondary deposit from a renal carcinoma and one case a secondary breast carcinoma).

The results in this group have been very good. The only adverse criticism was the mortality. We feel, however, that as this occurred in elderly people, it could be considered to be due more to their senility than to the operative trauma.

In a consecutive series of 64 cases treated in the Belfast City Hospital by Smith Peterson pinning, the mortality was 9 per cent. and, in a series of 150 cases at the Royal Victoria Hospital, Belfast, the mortality was 3.4 per cent. We feel, however, that the latter figure was exceptional and would be difficult to repeat.

In addition, the results of pinning of fractures of the neck of the femur are not as satisfactory as most of the literature would suggest and many successful pins, at a later date, require a salvage operation.

We must stress, however, that we would not contemplate this form of treatment on a patient whose expectation of life exceeded ten years.

2. *Failed Pins.*

As a salvage procedure, the Austin Moore head has been very satisfactory. The operation is simple, the result saisfactory, and immobilisation afterwards negligible. We, however, would not suggest this form of salvage for the younger patient who would require a McMurray's osteotomy.

3. *Osteo-arthritis in the Aged.*

In this group the results have also been very satisfactory. The indications for operation have been patients who would not be able to stand plaster immobilisation following either an osteotomy or an arthrodesis of the hip.

Once again no difficulties are encountered in the post-operative period. The operation gives a pain-free result and the patients have been very satisfied with it. The hip, in this case, is very much more stable than following a pseudo-arthrosis.

Summary.

The results of 54 cases of femoral head replacement with the Austin Moore head have been summarised along with our indications for the operation. We feel that these results justify a further trial. Of course, this operation is not the answer to all hip problems.

Acknowledgments.

We would like to thank Mr. N. S. Martin, Consultant Orthopædic Surgeon at Musgrave Park Hospital, Belfast, for his considerable help in the preparation of this paper and for allowing us to use his cases. Also our thanks go to the other surgeons in this group for the use of their cases.

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REVIEWS

LAENNEC: HIS LIFE AND TIMES. By Roger Kervran, M.D., translated by D. C. Abrahams-Curiel. (Pp. x + 213. 21s.) Oxford: Pergamon Press, 1960.

This is a detailed and authoritative, but very readable, biography, and it has already been widely acclaimed in France. Laennec's family background, his life and tribulations in Quimper and Nantes during the troubled days of the French revolution and the "vendée" wars and in Paris during the Napoleonic period are described. In his early years in Paris he was busy with pathological studies in the midst of a large hospital and private practice and he made many friends and enemies. The account of the development of the stethoscope, which was his crowning and best-known achievement, is well centred against a background of fierce medical controversy, personal rivalry, and official neglect. At all times Laennec drew inspiration from the coast and countryside of Brittany and from its language and culture. There he returned sick and exhausted to return again to the stormy struggle in Paris which was to end at last in fame and recognition. There he returned finally to die at the age of 45 from chronic tuberculosis which throughout most of his active life had been his most deadly enemy.

It is surprising that no complete biography of this man already existed. Many scattered French studies are listed, but readers, both French and British, will welcome this account of one who made an abiding contribution to medicine. J. E. M.

MARY ANN GOES TO HOSPITAL. By Mary Cockett. (Pp. 63. 7s. 6d.) London: Methuen, 1961.

This little book has been lent to several children, and even those conditioned by "Emergency Ward 10" have found it of absorbing interest and have discussed it freely. It would seem admirable in its attempt to explain what happens in hospital so that much of the fear of the unknown is removed.

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THE CARCINOID SYNDROME

By **JACK STRAHAN, M.B., B.Ch., D.R.C.O.G.**
Musgrave Park Hospital, Belfast

THE first description of a carcinoid tumour was as early as 1888 (Lubarsch). Later attention was drawn to the possibility that the cells of these tumours (known as argentaffinomas) act as secretors of some "endocrine" substance. "Enteramine" or "serotonin" (5 hydroxytryptamine or 5 H.T.) was later isolated from carcinoid tumours and recently its degradation product—5 hydroxy-indole-acetic acid or 5 H.I.A.A.—has been isolated from the urine in cases of carcinoid tumours.

Carcinoid tumours have been reported in any part of the alimentary tract from the cardia to the ano-rectal junction, the gall bladder, the lungs and in ovarian and testicular teratoids (Thorson). These tumours when associated with the clinical syndrome of vasomotor, gastro-intestinal, cardiopulmonary and nutritional disturbances have been reported chiefly in cases where there were marked hepatic secondary deposits. Carcinoid tumours commonly found in the appendix do not usually metastasize nor give rise to the clinical syndrome. The clinical syndrome has been described in cases of bronchial carcinoid without hepatic metastases (Jackson and Konzelmann, 1937).

At least three cases of carcinoid tumour associated with the clinical syndrome have been reported in Ulster (Fraser, 1955; Bridges et al., 1957; Nelson, 1957). A fourth case was seen in December, 1960.

CASE REPORT.

This was a man aged 67 years with a history of diarrhœa for eighteen months. He showed general wasting, dependant œdema and had a lump palpable in the right iliac fossa with an enlarged irregular liver. A provisional diagnosis of carcinoma of the cæcum was made prior to laparotomy. At operation the tumour with lymphatic and liver metastases was confirmed and an ileo-transverse colostomy and liver biopsy were carried out. Histologically, the liver biopsy showed argentaffin carcinoma and this diagnosis was confirmed by finding a raised level of 5 H.I.A.A. in the urine—740 mgms./24 hrs. (normal < 10 mgms./24 hrs.). Several other features of the carcinoid syndrome were found in this patient.

1. *Vasomotor disturbances* which were episodic (flushing and Raynaud's phenomenon) and permanent (dusky cyanosis and telangiectasis).
2. *Gastro-intestinal disturbances* of anorexia and chronic diarrhœa.
3. *Cardiopulmonary disturbances* of mild asthmatic attacks and congestive cardiac failure.
4. *Nutritional disturbances* resulting in marked weight loss.
5. *Mental disturbances* of confusion and euphoria.

The patient's general condition gradually deteriorated and he died four weeks following operation. Post-mortem examination confirmed the findings noted at laparotomy but there was no apparent involvement of the endocardium or valves of the right side of the heart.

Some features are worthy of note in the four cases already reported in Ulster.

All occurred in the 60-70 age group.

All showed vasomotor, cardiopulmonary, gastro-intestinal and nutritional disturbances of variable degree. It is to be noted that the first presenting symptom was diarrhœa in three of the cases, and œdema in dependant areas in the fourth.

Where a lump was felt in the abdomen in three of the cases the pre-operative diagnosis was carcinoma of the cæcum. In these cases it was the pathologist who suggested the correct diagnosis.

In all cases the primary-lesion was a small submucosal polyp—less than 2 cms. in diameter (multiple in two cases) with extensive extramural lymph gland and hepatic involvement.

Right heart endocardial or valvular lesions were noted in three of the cases.

In the later stages of this disease confusional states were present in three of the cases, accompanied by euphoria in two of these.

ACKNOWLEDGMENTS.

I should like to thank Mr. J. McI. Megaw, who was in charge of this patient, for his permission to publish the case report and others who offered much help and suggestions.

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REVIEW

PRINCIPLES OF GENERAL NEUROPHYSIOLOGY RELATING TO ANÆSTHESIA AND SURGERY. By Barry D. Wyke. (Pp. ix + 136; figs. 26. 21s.) London: Butterworths, 1960.

THIS little book is essentially a reprint of Dr. Wyke's chapter on the same subject in Volume 1 of General Anæsthesia (Editors: F. T. Evans and T. C. Gray). It deals with cellular neurophysiology, interneuronal communications including the effect of anæsthetics on the electroencephalogram and the cerebral circulation and metabolism. While the emphasis is primarily on anæsthesia, it contains a vast amount of information for other readers. This volume places this knowledge at the disposal of physiologists and others who may not desire to purchase the large book from which it is reprinted. J. W. D.

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REVIEW

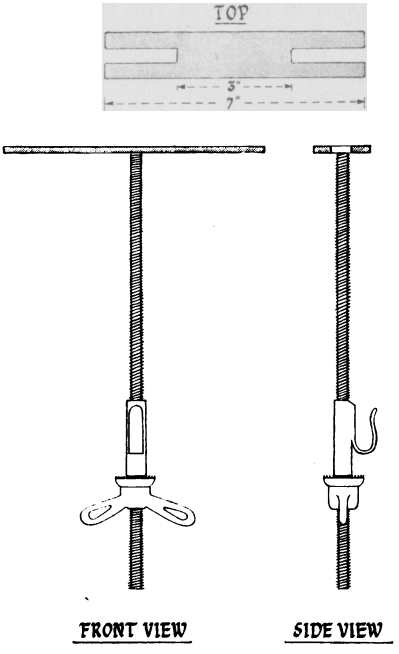
PRINCIPLES OF GENERAL NEUROPHYSIOLOGY RELATING TO ANÆSTHESIA AND SURGERY. By Barry D. Wyke. (Pp. ix + 136; figs. 26. 21s.) London: Butterworths, 1960.

THIS little book is essentially a reprint of Dr. Wyke's chapter on the same subject in Volume 1 of General Anæsthesia (Editors: F. T. Evans and T. C. Gray). It deals with cellular neurophysiology, interneuronal communications including the effect of anæsthetics on the electroencephalogram and the cerebral circulation and metabolism. While the emphasis is primarily on anæsthesia, it contains a vast amount of information for other readers. This volume places this knowledge at the disposal of physiologists and others who may not desire to purchase the large book from which it is reprinted. J. W. D.

SCREW ADJUSTMENT FOR FIXED TRACTION WITH THOMAS SPLINT

By **NORMAN W. McLEOD, M.B., F.R.C.S.**
Musgrave Park Hospital, Belfast

FRACTURE of the shaft of the femur, admitted to the traumatic wards of the Royal Victoria Hospital, Belfast, under the care of Mr. R. J. W. Withers and Mr. R. I. Wilson, are usually treated by closed reduction and fixed traction in a Thomas splint. As the Thomas splint acts as an exoskeleton the traction from the leg must, therefore, be fastened to the splint. The right degree of tension must be used to prevent overlapping of the ends and shortening of the limb, yet not produce distraction with the risk of either slow or non-union.



The conventional method of tying the tapes from the skin traction to the end of the splint and then tightening with a "Spanish windlass" is rather crude and not very effective, particularly if, as is common, the Thomas splint is only 4″-6″ longer than the limb. We, therefore, decided to try to improve traction control and the screw traction apparatus was made.

DESCRIPTION.

The apparatus consists of a 7″ x 1¼″ x 3-16″ spreader bar with slots ½″ x 2″ cut from either end. An 11″ x 5-16″ threaded steel bar is riveted in the middle but placed ⅜″ above dead centre. A ½″ x 2″ steel tube with ½″ x 1-16″ steel clip is then slipped over the threaded bar and finally a standard wing-nut.

METHOD OF USE.

The slots in the spreader are slipped over the side bars at the lower end of the Thomas splint and the clip in the steel tube over the V in the transverse bar. The tapes from the skin traction are then passed into the slots in the spreader bar and tied. As the central portion between the slots is 3″ in width pressure on the heel is avoided. The exact degree of tension required is easily obtained by tightening the wing-nut.

RESULTS.

This apparatus has now been in use for six months and has proved itself to be extremely accurate and effective in both fractures of the shaft of femur,

treated in routine manner with skin traction, and also in cases of supracondylar fractures, when traction has been applied by a Steinmann pin through the tibial tuberosity and Pearson's knee flexion irons applied to the Thomas splint. In the latter case, a loop of cord has been passed from the stirrup to the screw traction apparatus. We have found no tendency for the screw to loosen spontaneously.

Conclusion.

This apparatus is simple, cheap, and effective, and enables the exact tension of traction required to be maintained until union of the fracture has occurred.

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SCIENTIFIC ASPECTS OF NEUROLOGY. Edited by Hugh Garland, T.D., M.D., F.R.C.P. (Pp. xi + 264. illustrated. 50s.) Edinburgh and London: E. & S. Livingstone, 1961.

This book comprises a series of lectures given in the Leeds Medical School by various neurologists, mostly British. The book is compiled, as the editor says, to show how neurologists are thinking in the mid-twentieth century.

Most aspects of neurology have been included—anatomy, physiology, pharmacology, psychology, in addition to the clinical aspects.

Clinical chapters include the up-to-date thinking on vascular accidents, such as "Basilar Insufficiency," "Treatment of Posterior Communicating Aneurysms," and "The Radiology of Strokes." "Facilitation or Arrest of Epileptic Seizures" is an interesting chapter, and "The Pathology and Pathogenesis of Multiple Sclerosis" is a stimulating contribution. Physiological contributions include "Sleep" and "Calcarine Cortex and Cerebral Organization." There is a fascinating chapter by Dr. Denis Harriman on "The Diagnostic Value of Motor-Point Muscle Biopsy." The method described shows the care and patience required, both in the taking of the specimens and in the interpretation. The coloured illustrations are excellent.

The book is an excellent production, and Dr. Garland is to be congratulated on his choice of lecturers.

The book can be recommended to both neurologists and general physicians. H. H. S.

ESSENTIALS OF MEDICINE FOR DENTAL STUDENTS. By A. C. Kennedy, M.D., M.R.C.P.E., F.R.F.P.S. (Pp. vii + 272; figs. 38; pls. 27. 25s.) Edinburgh and London: E. & S. Livingstone, 1960.

This volume is aimed to present to dental students and practitioners the basic principles of medicine, with special emphasis on those disorders that relate particularly to their practice. It is clearly desirable that the dentist should be able to recognise an epileptic fit from a simple "faint"; that he should be familiar with the clinical appearance of patients in respiratory or cardiac failure and that he be familiar with the modern anticoagulant treatment for myocardial infarction. These subjects, together with the other important medical aspects of dentistry, are well displayed in this book. The text is clear and the English concise. There are tables and diagrams summarising and illustrating important subjects, and the photographic presentations of various clinical features of disease are good. R. W.

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THOSE of us who have enjoyed the privilege of hearing Dr. Strain lecture on the Belfast Charitable Society, or have seen the thesis on this subject which he presented for the Ph.D. degree of the Queen's University, have looked forward to reading this book; and we are not disappointed. He has presented us with a truly remarkable achievement. It was in 1946 that he accepted an invitation to become Physician to the Society, and it is not surprising that he became more and more interested, not only in the old people who had found in "the Charitable" a quiet refuge so near the very centre of the busy city, but also in the lovely old house itself, and the Society which created and maintains it. The more deeply he delved into the past the more he found the roots entwined with, or even to be the actual roots of, many other beneficent institutions: the General Hospital and Dispensary, the linen and cotton trades, the civic water supply—it was indeed "a widening circle of philanthropy." The Society anticipated Beveridge's desire to serve from "the cradle to the grave," for did it not provide the new burying ground?

Books on local history are prone to fall into two categories: the purely factual and statistical, which can be dreadfully dull, and the anecdotal, where the writer records odd and whimsical stories he has found. Dr. Strain has given us the facts, but has done so in such a fashion that one reads on, fascinated by the tale which he unfolds. Nor does he, like the sundial, count only the sunny hours. He tells us candidly and without bitterness the sorry story of the unending struggle to gain funds; how "the Poores Money" was embezzled; of the miserable and cheese-paring measures thought sufficient for the relief of abject misery; of the "severe flogging" of a boy who sought to escape from the "House," with its cramping restrictions, into the free world, with its hazards and dangers; of the acrid bickering between the Donegall family and the Society.

The Society earned a precarious income for many years by supplying the citizens of Belfast with water, and Dr. Strain has devoted four chapters (61 pages) to tracing the varied courses of these waters. This has not been done so precisely before, and it is now on record for all time. The pond in our Vice-Chancellor's garden was once a reservoir, and gave a good deal of trouble in maintenance. History repeats itself: it is again in the hands of experts.

Throughout the book the author retains our interest, not only in the subject matter, but in the manner of its presentation. He has a gift of writing as if he were speaking. One reason for this very pleasing style may be that he has lectured on this subject more than once; indeed has lived with it for the past ten years. His final chapter, and not the least interesting, is entitled "Clifton House to-day." He has modestly omitted all reference to his own splendid contribution to the welfare of its inmates, although in his Preface he has written "I would be very proud to think that after so many years my work might be recalled like that of one of the surgeons to the House in 1777: 'Mr. White attended and dressed the wounds of those in the Infirmary with care and humanity.'"

William Strain may rest assured that this will indeed be so, and that for this cause, as well as for his book, he has earned the gratitude, not only of those who are natives of Belfast, but of all those whom fate has brought to know and love our city and its people.

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The causes of amblyopia are briefly discussed and the objects and methods of treatment are outlined. The book is mainly composed of exercises, or games, devised to help the amblyope, and it is as suitable for use in the home as in the clinic. These include proof reading where deliberate errors have been made in extracts from 'Alice in Wonderland,' and various arrangements of numbers, designs, drawings, tracings, and photographs, all of which require attention to details and improve hand-eye co-ordination. There are also a series of simple exercises for amblyopes with eccentric fixation.

The theoretical considerations of the subject are brief, lucid, and up to date.

Uniocular amblyopia in strabismus has long been recognised and treated, but there is still not universal agreement as to which is cause and effect.

Jean Sedan emphasises that in amblyopia there is not only a defect of visual acuity, but also a defect of visual discrimination. This can be shown by measuring the difference between the visual acuity obtained with individual test types and that obtained with a line of letters on the test chart. Similarly, the acuity may vary when the test types are presented in different positions and planes.

The inhibition of amblyopia is treated by occlusion of the fixing eye and progressive exercises such as reading and tracing, using the amblyopic eye. The importance of continuing these measures to maintain the improvement is stressed.

Eccentric fixation, or extra muscular fixation, is a disturbance of spatial localisation which occurs in some cases of strabismus and does not respond to occlusion of the non-squinting eye. Such occlusion is more likely to reinforce the eccentric fixation. Occlusion of the amblyopic eye, however, breaks down the function of the false macula, and with the aid of ingenious instruments such as the euthyscope and the co-ordinator, which stimulate the true macula, normal macular fixation may be obtained.

The restoration of full or useful vision in an amblyopic eye fully rewards the time and patience expended, and this book should prove most useful in sustaining the efforts of all concerned with the treatment of squint and amblyopia. V. A. F. M.

DENTISTRY FOR THE PRE-SCHOOL CHILD. By G. N. Davies, D.D.S.(N.Z.), and Richard M. King, B.D.S.(N.Z.), M.S.(Univ. Mich.). (Pp. vii + 268; figs. 51. 32s. 6d.) Edinburgh and London: E. & S. Livingstone, 1960.

THIS book, which deals with the dental problems of the very young, is very welcome, as this important age group has, to date, been given but scant attention in the textbooks.

It contains sound practical advice on the proper approach and management of small children in the dental surgery. Diet and nutrition are given just prominence and measures for the control and prevention of dental caries are set out clearly in a logical sequence. Also included here is a very worthwhile critical analysis of the values of the so-called therapeutic dentifrices.

In some other sections their touch is perhaps not quite so sure. For instance, in their chapter dealing with the anomalies affecting the deciduous dentition they describe the anomalies but fail to comment upon the possible significance of these in so far as the permanent successors are concerned. Likewise, when discussing traumatic injuries, a note on the possible effects on the permanent teeth would have been valuable. Nevertheless, despite the above omissions, the practitioner interested in the treatment of children, and the student, should find much additional material of value in this readable volume which one enjoyed very much. D. J. S.

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AIDS TO FORENSIC MEDICINE AND TOXICOLOGY. By Sir W. Bentley Purchase, C.B.E., M.C., M.B., M.A., M.R.C.S., L.R.C.P. Thirteenth Edition. (Pp. 299. 12s. 6d.) London: Baillière, Tindall & Cox, 1960.

THIS book conforms with others in the Aids series. Its restriction to 250 pages has, inevitably, posed the problem of what to include and what to omit and the author has aimed to "provide a knowledge of forensic medicine sufficient to enable the student, the houseman, and the average doctor to appreciate the impact of the law and social custom on medical practice." Part I, comprising 100 pages, deals with the law relating to medicine and dentistry, and reflects Sir Bentley Purchase's legal training and his long experience as a coroner. It is well written and adequately fulfils its purpose. For some reason, sexual offences and abortion are also discussed here, in separate chapters. Infanticide is disposed of in one paragraph.

The next 60 pages deal with identification and aspects of forensic pathology. This section suffers the most from the necessity to restrict the text and although the general descriptions of the causes of asphyxia, types of wounds and effects of heat and electricity are adequate, pathological detail is missing. There are a few inaccuracies. For instance, the author favours asphyxia rather than biochemical changes as the cause of death in fresh-water drowning which he fails to distinguish from drowing in salt water, and he ascribes the colour change of traumatic asphyxia to bruising.

Part III is devoted to toxicology. In the preface the author states that the subject is so big that it has been possible only to touch upon it. Nevertheless within the compass of 90 pages he mentions the law relating to poisons and dangerous drugs, drug addiction, the treatment of poisoning and the effects of over sixty different substances. The result is too sketchy. It would have been better to expand the description of the duties of doctors and dentists under the Poisons and Dangerous Drugs Acts and to deal with fewer substances at greater length.

Considering the restrictions imposed on the author the aim of the book has been fulfilled. But whilst the reader will no doubt appreciate the impact of the law on medical practice the book is inadequate for students preparing for examination in forensic medicine and it is insufficient as a handy reference book for the doctor's bag or bookshelf. T. M.

HANDBOOK OF BACTERIOLOGY. By Mackie and McCartney. Edited by Robert Cruikshank, M.D., F.R.C.P., D.P.H., F.R.S.E. Tenth Edition. (Pp. xi + 980; figs. 45. 40s.) Edinburgh and London: E. & S. Livingstone, 1960.

THE many bacteriologists who have come to regard a copy of "Mackie and McCartney" as one of their most essential pieces of laboratory equipment will be grateful to Professor Cruikshank and his colleagues at Edinburgh for this new edition. The most notable change from the previous edition is the inclusion of a much larger section on viruses. This section is admirable as far as it goes, but laboratories actually engaged in the diagnosis of virus diseases will find the need for a more specialized book giving further details of tissue culture techniques, the preparation of viral antigens and the various diagnostic tests in current use. The general chapters on microbial biology, infection, and immunity have been expanded and to a large extent rewritten, and that part of the book dealing with systematic bacteriology has been fully revised and brought up to date.

The editor states in his preface that he hopes the handbook in its present form will be even more widely used by medical students and others than it has been in the past. However, it seems unlikely that the wealth of technical detail will appeal to medical students who might reasonably prefer a smaller textbook containing not much more than they were expected to know. The new edition of the handbook therefore remains essentially a laboratory manual for the bacteriologist. The virologist will probably find too little information, and most medical students and practitioners will find too much. D. S. D.

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Part III is devoted to toxicology. In the preface the author states that the subject is so big that it has been possible only to touch upon it. Nevertheless within the compass of 90 pages he mentions the law relating to poisons and dangerous drugs, drug addiction, the treatment of poisoning and the effects of over sixty different substances. The result is too sketchy. It would have been better to expand the description of the duties of doctors and dentists under the Poisons and Dangerous Drugs Acts and to deal with fewer substances at greater length.

Considering the restrictions imposed on the author the aim of the book has been fulfilled. But whilst the reader will no doubt appreciate the impact of the law on medical practice the book is inadequate for students preparing for examination in forensic medicine and it is insufficient as a handy reference book for the doctor's bag or bookshelf. T. M.

HANDBOOK OF BACTERIOLOGY. By Mackie and McCartney. Edited by Robert Cruikshank, M.D., F.R.C.P., D.P.H., F.R.S.E. Tenth Edition. (Pp. xi + 980; figs. 45. 40s.) Edinburgh and London: E. & S. Livingstone, 1960.

THE many bacteriologists who have come to regard a copy of "Mackie and McCartney" as one of their most essential pieces of laboratory equipment will be grateful to Professor Cruikshank and his colleagues at Edinburgh for this new edition. The most notable change from the previous edition is the inclusion of a much larger section on viruses. This section is admirable as far as it goes, but laboratories actually engaged in the diagnosis of virus diseases will find the need for a more specialized book giving further details of tissue culture techniques, the preparation of viral antigens and the various diagnostic tests in current use. The general chapters on microbial biology, infection, and immunity have been expanded and to a large extent rewritten, and that part of the book dealing with systematic bacteriology has been fully revised and brought up to date.

The editor states in his preface that he hopes the handbook in its present form will be even more widely used by medical students and others than it has been in the past. However, it seems unlikely that the wealth of technical detail will appeal to medical students who might reasonably prefer a smaller textbook containing not much more than they were expected to know. The new edition of the handbook therefore remains essentially a laboratory manual for the bacteriologist. The virologist will probably find too little information, and most medical students and practitioners will find too much. D. S. D.

CONGENITAL DEFORMITIES. By Gavin C. Gordon, M.B., F.R.C.S. (Pp. vii + 128; figs. 113. 37s. 6d.) Edinburgh and London: E. & S. Livingstone, 1960.

BONE and joint tuberculosis in children has almost disappeared, and perhaps we may now expect a similar fall in the incidence of paralytic poliomyelitis. The relative importance of congenital deformities must therefore inevitably rise, and it may even be that, with a falling neonatal mortality, there will be a rise also in the absolute incidence of major congenital defects. Consequently any new book which by its title promises to advance our knowledge of the ætiology and therefore the treatment of congenital deformities must attract the attention of all orthopædic surgeons; and for this same reason I have found Mr. Gordon's monograph a great disappointment—and an even greater puzzle. It is basically the exposition of a very personal theory centred round a detailed and careful study of congenital dislocation of the hip, and leading on by connecting links of thought which are by no means clear to a discussion of the mechanics of McMurray's osteotomy, the treatment of acute osteomyelitis, the causation of Perthes' disease and slipped upper femoral epiphysis, and the ætiology of cerebral palsy. The book has a dream-like, will-o'-the-wisp quality which leads the reader on through a maze of fact and fancy, always with the promise of a clear conclusion and a practical application, and then—having got him deep into the wood—suddenly disappears. I cannot say that I enjoyed reading it. G. W. B.

A LABORATORY HANDBOOK OF BLOOD TRANSFUSION TECHNIQUES. By A. Derek Farr, F.I.M.L.T., A.I.S.T. (Pp. xi + 135; figs. 34. 17s. 6d.) London: Heinemann Medical Books, 1961.

THIS book covers the non-serological aspects of transfusion work dealing with the preparation of crystalloid solutions and the processing of blood and its products for transfusion. It is intended to cover a gap in the literature on general transfusion work which is not adequately dealt with by existing works on blood group serology and requires the reader to have a sound knowledge of this subject. It is difficult to find a place for this book. It is felt that the absence of a section on serology greatly decreases its value to the student technologist to whom it is otherwise mainly directly. Again, although it may be of more interest to specialists in transfusion work, it can hardly be regarded as a comprehensive manual on this subject. J. R.

CANCER OF THE RECTUM. Edited by Cuthbert E. Dukes, O.B.E., M.D., M.Sc., F.R.C.S. (Pp. 303; figs. 82. 50s.) Edinburgh and London: E. & S. Livingstone, 1960.

THIS book is devoted to the ætiology, diagnosis, pathology, treatment, and results of cancer of the rectum. It is written by the experts on the subject. One must mention the names of Gabriel, Abel, Naunton Morgan, Lloyd Davies, Goligher, as well as Dukes, to show that the subject has been dealt with in a most comprehensive manner.

Dukes gives interesting reflections on the causation and control of rectal cancer as well as a very complete monograph on the pathology. The clinical diagnosis and the various operations are described in detail. The difficult problem of the malignant polyp is debated and a scheme is given for dealing with it, based both on published views and on experience at St. Mark's Hospital. The minor rôle of radiotherapy in the treatment of certain cases is also discussed. It is important to remember that we have progressed from the era when X-ray treatment had no effect to the phase where it has some effect.

The production is on high quality paper and the print and illustrations are excellent. In a book such as this with so many contributors, there is bound to be some overlap and also some minor differences of opinion. To the reader, however, this is not a drawback—rather it tends to be stimulating.

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ONE of the interesting features of medical education is the continuing theme that runs through successive generations. If one reads the writings of the Ancient Physician, some five hundred years before Hippocrates, the theme is still the same as that of today. The prayer of Ebu-e-Maymoun in the twelfth century in Teheran contains the philosophy which we hope to instil into our students today. "O Lord, grant me an opportunity to improve and extend my training since there is no limit to knowledge. Help me to correct and supplement my educational defects as the scope of science and its horizon widen day by day. Give me the courage to realize my daily mistakes so that tomorrow I shall be able to see and understand in a better light what I could not comprehend in the dim light of yesterday. Bless me with a spirit of devotion and self-sacrifice, so that I can trust and heal Thy suffering servants and prevent and preserve health to the best of my ability and knowledge."

In this volume to which speakers from not only the relatively well-endowed countries but also those from countries in which the medical problems are still immense and the proportions of trained medical men to the population at risk is still small there is a curious unanimity of opinion. Indeed there is no international problem in which a similar common purpose exists.

All medical men realise that medicine is a life-long study. The advances in the last twenty-five years have brought this home to even the least enterprising. The issue is really how the medical school can best contribute to the continuing education of the medical graduates. The problem is not simply that of further scientific education. In a sense medical educators face a dilemma: "how to educate men who are scientific in outlook and yet sensitive to many aspects of human life not amenable to laboratory analysis." This may seem impossible, but the continuing theme from the Ancient Physician through the ages seems to suggest that though no clear-cut solution is available a pragmatic solution for each generation will be found.

The faculty, as a whole, must engage in the most radical kind of study of its own rôle. "This is to ponder on the mission of the medical school in its university setting and in the larger community. One must work out and state clearly the educational objectives and to be fully meaningful this must be done afresh by each generation in each medical faculty." This states the problem very succinctly. The important thing is that medical teachers should have constantly under review the medical curriculum. What emanates from their discussions is probably of less importance.

Once upon a time I invited the Department of Education to advise upon the structure of the medical curriculum. It found itself inadequate. So I should think we shall go on as heretofore, seeing our problems, facing our dilemmas, and hoping that the medical graduate will continue to meet the needs of the community in which he lives to the best of his ability.

This is an interesting collection of papers reflecting the problem of medical post-graduate education in many countries. Here and there one occasionally senses that it is the teacher, not the system, that creates success, and that fundamentally those who impart an appreciation of method and of logic have a more lasting influence than those who contribute merely a knowledge of facts. J. H. B.

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It is not fully realised at present the damage that is possible with an imbalance of amino acids in the diet, especially to the liver cell. N. A. J. C.

CHOLERA. ITS PATHOLOGY AND PATHOGENESIS. By S. N. De, M.B., D.T.M. (Calcutta), Ph.D.(Lond.). (Pp. xi + 141; figs. 50. 25s.) Edinburgh: Oliver & Boyd, 1961.

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The book is fully documented and written in clear, precise English, and is a credit to Indian scholarship and medicine. J. E. M.

INTRODUCTION TO DENTAL ANATOMY. By J. H. Scott, D.Sc., M.D., L.D.S., and N. B. B. Symons, M.Sc., B.D.S. Third Edition. (Pp. xi + 388; figs. 239. 45s.) Edinburgh and London: E. & S. Livingstone, 1960.

THE appearance of a third edition within three years of the second issue proves the continuing popularity of what has become the standard textbook for this subject. The whole book has been revised and the repeated alteration of a single word or phrase shows the care with which this revision has been done. Much new material has been added, there now being 388 pages against the 344 of the second edition, and the presentation has been improved: long paragraphs have been broken down into shorter paragraphs, making reading easier, and the book itself has been divided into five major sections—the form and arrangement of the teeth, the development and growth of the face, teeth, and jaws, the development and histology of the dental and paradontal tissues, the functional anatomy of the oral cavity, and comparative dental anatomy. The order of treatment of some of the subject matter has been varied with advantage. New work is discussed and the bibliography has been brought up to date; there are many references to original articles published in 1960. Some of the figures have been enlarged or replaced by better ones and in others, especially those showing the macroscopic anatomy of the teeth, the shading has been varied to make the pictures clearer.

Throughout the emphasis has been on the functional unity of the masticatory apparatus.

The book can be strongly recommended. P. J. S.

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PRACTICAL NOTES ON NURSING PROCEDURES. By Jessie D. Britten, S.R.N. (Pp. viii + 199; figs. 135. 15s.) Edinburgh and London: E. & S. Livingstone, 1960.

On reading through a book—any book—on nursing 'procedures' I am reminded of the man who said that he 'did not like to read a dictionary as he always lost the thread of the story in the wealth of detail.' To say this is no disparagement of Miss Britten's book, the third edition of which is no worse, and in many respects very much better than others of its kind.

The material is presented, as in previous editions, with clarity and precision, there is no waste of words, the diagrams are neat and well labelled, trays and trolleys are uncluttered and student nurses and others who use it should find no difficulty in identifying items. For these reasons it should continue to find favour with students and trained staff alike. True, most hospital staffs have their own 'native' plan of 'procedure,' evolved either from years of experience or by taking from various sources what they consider to be best, but some may still prefer to use a textbook.

Most useful and necessary information concerning hospital is to be found in chapter 1, but I regret to see that the patient is still placed last on the nurse's list of 'Loyalties.' In the past nurses were told that their first duty was to their patients. Was it too simple? Will some writer of textbooks please tell the student nurses that they, too, have a right to expect loyalty from all those to whom they are expected to give it.

Nurses may continue to raise their eyebrows at the perpetuation in modern books on nursing of what appear to them to be out-moded forms of treatment, for example, blistering, leeching, and cupping (the latter is still, I understand, widely practised in different regions of the world). Even Leiter's coils are illustrated and may yet stage a 'come-back.' Nurses will not seek in vain for information on such up-to-date matters as radioactive substances, radium therapy, Geiger counters, and electric thermometers, in addition to such everyday items as fluid balance, preparations for laboratory tests, and infant bathing and feeding.

I like this book, even though I personally have never acquired a palate for this 'dehydrated' form of nursing; that is 'procedures' divorced from the 'art.' I dislike the word 'procedure' in relation to nursing, because it creates a tendency to make the tray or trolley the focal point of the nurse's attention. Nevertheless, the book should prove useful both to the habitual seeker after knowledge and to the last-minute 'swotter.'

One criticism which I would make is of the widespread use of receivers for sterile as well as for soiled articles. With the extension of a central sterilising service, however, the risk of possible confusion should be eliminated.

I hope that nurses will buy, or even borrow this book from the classroom library. There may be a few points upon Miss Britten and other tutors may agree to differ, but that fact should present no difficulty to the right kind of people. G. C.

FROM GIRLHOOD TO WOMANHOOD. By Albert Sharman, M.D., D.Sc., F.R.C.O.G. (Pp. vii + 67; figs. 4. 6s.) Edinburgh and London: E. & S. Livingstone Ltd., 1960.

This short book, written for the non-medical reader by a well-known gynæcologist, is primarily designed to enlighten the teenage girl. The author gives a clear and concise account of the various physiological changes which occur in the female during adolescence. The information given will also be found invaluable by a mother anxious to prepare her daughter for the onset and hygiene of menstruation.

The latter part of the book, however, contains details of pregnancy, ante-natal care, labour, and infertility, in the opinion of the reviewer more suitable reading for the young married woman. Perhaps the author should have published two volumes.

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CELL AND TISSUE CULTURE. By Dr. John Paul. Second Edition. (Pp. 324; figs. 129. 32s. 6d.) Edinburgh and London: E. & S. Livingstone, 1960.

It can be said without any hesitation that the culture of cells and tissues will be the basic techniques of future biological research. Because micro-organisms require a relatively simple chemical environment, and viruses parasitize living cells, the microbiologist has been able to study these forms of life far more readily than the biologist has been able to investigate the more complex cells of plants and animals. The gap has now been closed. Zoologists, if they wish to, can culture insect or other animal cells and study their growth and metabolism; botanists can make plant cells multiply and differentiate under tissue culture conditions; biochemists can unravel the pathways of biosynthesis in animal cells and break down the chemical processes of cell division into sequential events. In the medical field, the culture of cells is both advancing knowledge of virus multiplication, and the understanding of chromosome abnormalities in human disease. Organ culture, in which the characteristic morphology of an organ is preserved, is ideal for studying the rôle of hormones and vitamins in the control of tissue development; the most recent research in this field shows how one cell population can influence the morphogenetic development of another cell population.

The second edition of "Cell and Tissue Culture," by Dr. John Paul, is, in this reviewer's opinion, the most up-to-date and comprehensive guide to current tissue culture and organ culture techniques. The first part of this book, one-third of the whole text, is a concise survey of our existing knowledge of cell structure, cell metabolism, and of the chemical environments in which cells from animals and plants can grow. Although this section covers a lot of ground, it deals critically with the material available, and presents to the reader the conflicting results of experiments in recent years. One does not always agree with Dr. Paul's interpretation, but he undoubtedly provides the stimulus for future investigations with culture techniques.

The major part of the book deals with the practical details of technique. For many years the uncertainties and complications of tissue culture work have discouraged investigators from applying it to medical and biological research. The situation is completely changed by the introduction of antibiotics and the development of media which are chemically-defined. It is true that the latter are complicated if one is not a chemist by training, but once everything, from the distilled water to the set of chemical substances, has been decided and tried, there is no difficulty in culturing cells from human, animal, or plant sources. Where difficulties arise it is frequently found that the source is small traces of oil in pipes, in the autoclave and in glassware, or inadequately prepared glass surfaces.

Dr. Paul's book is the product of much experience in dealing with these technicalities, and it describes the facts admirably. It is unfortunate that the newcomer to the field has still to decide, or get advice from someone, on which particular media to use. The hard fact is that it is too early for anyone to simplify matters by stating that one chemical formula is adequate for a particular type of cell growth or maintenance.

Although the second edition of this book appears only one year after the original text, it is substantially enlarged and most of the additional material concerns the practical technical details of cell and organ culture. Diagrams have been increased and improved, and there are excellent photographs of healthy cell cultures, which should encourage anyone not to be content with second best in his or her results. Dr. Paul's attempt in the last section to describe special applications, such as histological staining or biochemical analysis in culture work, is not wholly successful. This reviewer finds in it methods which he has tried and discarded for one reason or another. However, it is always possible to acquire the cytological or biochemical techniques from other sources, or from one's colleagues. The valuable aspect of the text is that it presents lucidly and in great detail the practical information which should lead to a wider use of tissue culture in many fields of investigation. I. L.

AIDS TO THEATRE TECHNIQUE. By Marjorie Houghton, M.B.E., S.R.N., S.C.M., D.N., and Jean Hudd, S.R.N. Third Edition. (Pp. 234; plates 52. 8s. 6d.) London: Baillière, Tindall & Cox, 1961.

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The section dealing with nurses' duties in the theatre has been clearly written, and perhaps the most important comment is that the nurse's efficiency depends on her ability to anticipate the surgeon's next step in a particular operation. The importance of this cannot be over-emphasized.

The steps to be taken in a case of cardiac arrest are fully and clearly enumerated and should be carefully studied by every nurse.

The chapter on traumatic surgery is also worthy of serious study and some help will be found in the chapter on plaster of paris technique, although one felt that this chapter could have been a little longer.

Altogether, this should prove a very useful edition in the "Aids Series." D. M. B.

THE CLOSED TREATMENT OF COMMON FRACTURES. By John Charnley, B.Sc., M.B., F.R.C.S. (Pp. xi + 272. figs. 215. 50s.) Edinburgh and London: E. & S. Livingstone, 1961.

THE author is too modest when he simply claims that the book is written for the resident casualty surgeon. The book should prove a great stimulus to the mature orthopædic surgeon, especially if "fixed in his thinking"—there is much in the book to force him to re-examine his pet ideas, and maybe even to alter them in the light of Mr. Charnley's persuasive presentation.

The nature of fracture repair is extremely well described and the differences between union in cancellous and cortical fractures excellently presented.

That part dealing with the mechanics of reduction and conservative treatment of fractures demonstrates that, in so far as mechanical principles can be applied to the intricate biological process of fracture healing, Mr. Charnley's ideas are well in advance of those underlying common practice in many casualty departments.

In Chapter XV, on fractures of the tibial shafts, the author attempts to explain some of the baffling problems of delayed union and non-union, and puts forward a rational basis for prophylactic bone grafting in certain anatomical types.

Throughout the book the conservative approach in treatment is stressed and the dangers of the depression of osteogenic activity in the fragments of fractures by the operative exposure of long bones is emphasised.

This is an excellent book which will be read, and I hope reread several times, by all surgeons who have to treat injured limbs, with interest to themselves and profit to their patients. R. J. W. W.

AIDS TO PSYCHIATRY. By W. S. Dawson and E. W. Anderson. Eighth Edition. (Pp. viii + 310. 12s. 6d.) London: Baillière, Tindall and Cox, 1960.

THIS book, set in small type, is addressed to a wide audience, extending from occupational therapists to embryo psychiatrists. It claims to give a concise account of current practical psychiatry, and within its limitations achieves this aim. In the reviewer's opinion its value would be greatly enhanced if the range of disciplines that are contributing to the further development of psychiatry were given more emphasis. J. G. G.

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