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RES MEDICA

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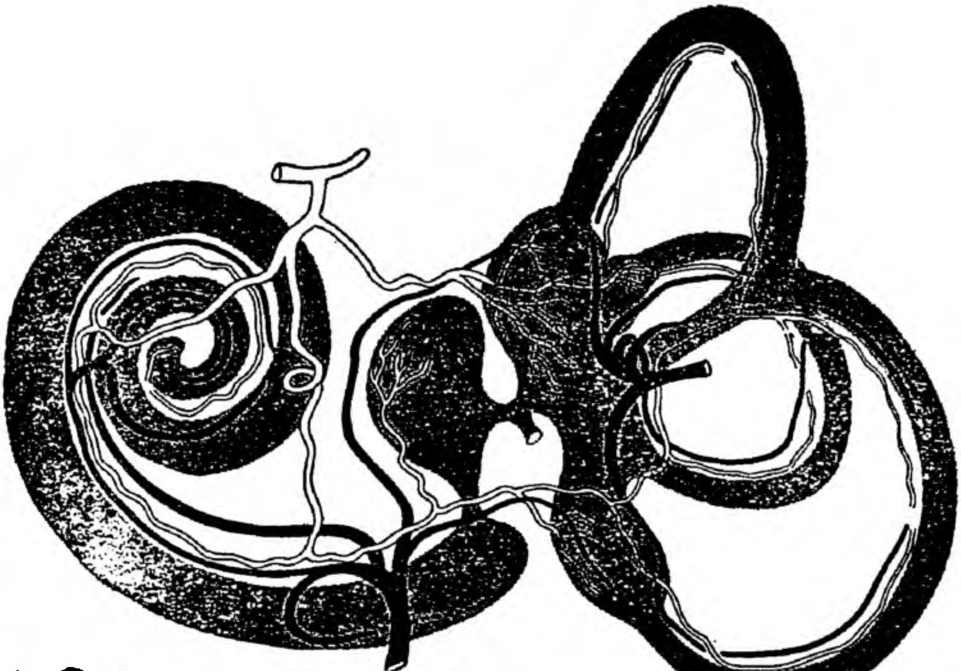

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CONTENTS OF NEXT ISSUE

January 1959

RES MEDICA

THE JOURNAL OF THE ROYAL MEDICAL SOCIETY

Editor: DAVID J. CLARK

Editorial Committee: WILLIAM L. FORD, HENRY C. DRYSDALE
E. A. W. SLATER

Editorial

It seems to the student of medicine that arguments about the method by which his education can be accomplished with most effect, will never cease. Thus he is perpetually hearing, from this source or from that, that one system is better and another worse, one more and another less suited to turn a doctor loose upon an unsuspecting and at times positively unfortunate public. The system of teaching students in small tutorial groups has many advantages, and the existence of an intimate student-teacher relationship will always rank high amongst them. This system of education which is practised in a number of English universities is in marked contrast to the Scottish university system which consists of a formal lecture course, accompanied by clinical instruction in scarcely less formal cliniques. The lecture course tends to be authoritative and up to date since it is usually shared out amongst a number of lecturers, each dealing with that aspect of the whole subject in which he is specially interested. Further, in contrast to the Tutorial system the course can be carefully planned in advance, and each aspect treated in due perspective since the student cannot divert his teacher's attention from the main stream of thought. None the less it must be admitted that there are many students who find the process of expressing their own views before an intelligent audience, or equally of criticising the expressed views of their fellows, an instructive and a stimulating exercise. It is of course true that when in clinique, the student is often allowed, sometimes even encouraged, to discuss his teacher's views in a critical fashion, but, unfortunately, time is limited and the cliniques manifestly overcrowded. Here is a deficiency in our education for which the Royal Medical Society attempts to compensate, and it is our claim that we provide facilities for the student to become a more able speaker and a more critical thinker.

A sense of duty need not be the excuse for a student to join the Society, because an evening at the Royal Medical is spent in good and friendly company and needs no further recommendation than its own excellence. It combines the teaching potential of a group study session with the pleasure of good fellowship and entertainment.

Gilbert Blane, a President of the Royal Medical Society in 1784, said of the Society's founders, on the occasion of the purchase of the new hall: "Here they learned to reason and think for themselves; here they combated prejudice and error, however sanctified by antiquity and authority, and it was here that they learned to love and esteem each other and to cement the bonds of true friendship, a friendship severe and durable inasmuch as it was founded on a virtuous and liberal intercourse."

Res Medica has now entered its second year, and although its achievements so far are not to be depreciated, it is now encountering new problems along the road to establishment and maturity. The members of the first Editorial Committee shouldered their responsibilities with a pioneering zeal and *Res Medica* will indeed be fortunate if its future committees are of the same calibre.

The aim now must be to establish a tradition for the Journal which will be as durable and as honourable as that of the parent Society. Advance in this direction depends on the members keeping in mind that the sole purpose of the Journal is to be of service to the interests of the Society. *Res Medica* will become more and more effective in doing this if, after the novelty has worn off, the members continue to show an interest in its progress.

SYLLABUS FOR THE 222ND SESSION

AFTER 31ST OCTOBER

1958			
Thur.	Nov.	6	PRESIDENT'S ANNUAL DINNER. Royal College of Surgeons, 7.15 for 7.30 p.m. Guest of Honour: T. McW. MILLAR, Esq., F.C.R.S.E.
Fri.	„	7	Dissertation: A. L. CROMBIE, Esq. "Rockets, Men, and Medicine."
Fri.	„	14	Dissertation: C. M. MAILER, Esq. "Ulcerative Colitis."
Thur.	„	20	Debate with the Glasgow University Medico-Chirurgical Society, in Glasgow. "That We Regret that the Student of To-day is the Doctor of To-morrow."
Fri.	„	21	To be arranged.
Fri.	„	28	ADDRESS: Professor MICHAEL SWANN, M.A., Ph.D. "Growth: Normal and Abnormal."
Fri.	Dec.	5	Dissertation: J. H. TURNER, Esq. "Pulmonary Signs and Symptoms."
Fri.	„	12	TALK: Dc C. R. S. JACKSON, M.A., M.D., D.O.M.S., F.R.S.E. "An Oculist Looks at Endocrine Exophthalmos."
1959			
Fri.	Jan.	9	Dissertation: F. A. BODDY, Esq. "The Changing Face of Medical Practice."
Fri.	„	16	Dissertation: J. McKENDRICK, Esq. "The Treatment of Cancer."
Fri.	„	23	ADDRESS: Professor M. F. WOODRUFF, C.B.E., M.D., M.S., F.R.C.S., F.R.A.C.S. "The Biological Basis of Individuality."
Fri.	„	30	Dissertation: G. T. MILLAR, Esq. "Abdominal Pain."
Fri.	Feb.	6	TALK: F. J. GILLINGHAM, Esq., M.B.E., F.R.C.S., F.R.C.S.E. "Whither Neurosurgery."
Fri.	„	13	Dissertation: F. COCKBURN, Esq. "Endocrine Disorders in Childhood."
Fri.	„	20	ADDRESS: Professor W. I. C. MORRS, F.R.C.S., F.R.C.O.G. "John and William Hunter and Their Cronies."
Fri.	„	27	Dissertation: D. J. CLARK, Esq. "Rheumatic Fever."
Fri.	Mar.	6	President's Valedictory Address.
Wed.	„	11	Annual Extraordinary General Meeting.

Private Business at 7 p.m.

Public Business at 8 p.m. unless otherwise stated.

Clinical Meetings, Film Meetings, and Industrial Visits will be arranged during the Session. Due notice of these will be given.

The date for the Society's ANNUAL BALL will be announced later.

CANCER RESEARCH: ITS HISTORY AND PROSPECTS

By PROFESSOR ALEXANDER HADDOW
M.D., D.Sc., F.R.S., Director of the Chester Beattie Research Institute, Royal Cancer Hospital, London.

Inaugural Address of the 222nd Session, read before the Society on 10th October, 1958.

Of all the invitations one has ever been privileged to receive, I wish you to know that the arrival of your own was a special honour, and a special delight to accept—giving me, among other things, the opportunity to re-visit the house of our ancient Society, and to recall at close hand many happy occasions within these walls some thirty years ago. It was the time of the great Sir Alfred Ewing as Vice-Chancellor, and, in the Medical School, of Sir John Fraser and Sir David Wilkie of glorious memory, whose portraits adorn your walls. We generated then, as doubtless you generate now, abiding affection for Edinburgh and its University, and not only affection but I confess it, sentiment, for our Royal Medical Society. Reading the leading article in the second number of *Res Medica*, I have been greatly struck by its closing sentences: "At a time when religions, cultures and individuals are menaced by nuclear weapons and foreign ideologies, living traditions assume an importance never envisaged by their inaugurators. Let us then foster unity and friendship and be worthy heirs of our heritage." This is the ever-renewing and ever more significant function of the Royal Medical Society, and I esteem the great honour of inaugurating your two hundred and twenty-second Session. I mention these things to show how it is and why, that I received your invitation with such pleasure and gratitude.

I have taken as my subject the history and the prospects of cancer research. It could be regarded as a morbid one, but I hope to show that this is not necessarily so; on the contrary, that the history of the field is romantic and inspiring, that its present state is active and exciting, and that its future—although by far the greater part remains to do—is full of hope and promise.

Cancer research can be regarded from two aspects—the purely medical, as a great endeavour directed to the solution of a human problem; and scientifically, from the unique character of the disease, as an integral part of modern biology. It is unique since its basis lies in a permanent accession in the growth of cells. Its history has largely been coterminous with that of the microscope, permitting the development of the cell theory, which has been described as one of the greatest conceptions of the human mind, and which, although it had many precursors, was finally established as recently as the early part of the nineteenth century.

It is often said that the cancer cell has acquired the power of unlimited growth. This is strictly not so, since most normal cells are equally capable of unlimited growth in appropriate conditions. More and more certainly, cancer appears rather as due to the release or unmasking of that growth potential which cells all along possess, although exquisitely restrained. The mechanics of cell division appear devised to effect an equal distribution. Yet soon in development is superposed the mysterious feature of differentiation, while the rate of growth declines. Even in the adult, however, cell division continues, either temporarily as in the healing of wounds, or continuously as in the tissues of the bone marrow, intestine and skin. The main feature here is a matchless orderliness and precision. In the words of Dr Isaac Watts in one of his hymns, "Strange that a harp of a thousand strings, should keep in tune so long." Sooner or later, however, a single cell may become transformed to a cancer cell, with altered growth properties which are now and henceforth no longer subservient to the needs of the body, but independent and frequently autonomous. The liability to this change appears inherent in all cells capable of growth. It is not surprising, therefore, that we should find evidence of it throughout the whole of the plant and animal kingdom, not only in historic but also in pre-historic times.

So far we have spoken of the nature of cancer. What of its cause or causes? Modern cancer research largely dates from the time of Rudolf Virchow, whose *Die Cellularpathologie* was published almost exactly one hundred years ago. Remembered for his dictum *omnis cellula e cellula*, he applied the cell theory to pathology, and inaugurated several decades of investigation of the microscopical structure of cancer in man and animals, carried out first in the great schools of Germany and then the world over. Although historically necessary and important, this was not, however, sufficient. Towards the close of the century a need became ever clearer, namely, for the use of the experimental method. In this country, the new outlook led in 1902 to the establishment of the Imperial Cancer Research Fund, and in 1909 to that of the Research Institute of the Cancer Hospital in London. The first director of the former institution was E. F. Bashford, who with great genius and foresight, and with the support of a small but brilliant staff, was able within a brief ten years to lay the main foundations of the whole subject, and to forecast its likely development and requirements for many further years ahead. All this helped to prompt, or was accompanied by, similar developments in the United States, in Europe, and in Japan.

Although purely medical methods alone were to prove insufficient, it should be noted that the first and vital clues arose from observations made in the field of occupational and industrial medicine. Towards the end of the eighteenth century, Sir Percivall Pott had described the special liability of chimney sweeps to cancer of the scrotum, and had traced the cause to contamination of the skin with soot. With the industrial revolution came many more examples, mainly due to occupational exposure to mineral oil and tar. A notable case was the so-called "paraffin cancer" in the Scottish shalefield, described by the celebrated Joseph Bell, of whose association with the Royal Medical Society we are justly proud. Experimental proof that mineral oil, coal tar and pitch do in fact induce skin cancer had, however, to be long deferred, indeed until 1915, when Yamagiwa first produced cancer artificially through chemical means, by applying coal tar to the skin of the rabbit ear. Coal tar being a complex mixture of a great host of chemical individuals, the search then began for the responsible agent or carcinogen. In the early 'twenties, Bloch in Zurich adduced evidence that the agent might be a complex hydrocarbon, that is, a compound containing hydrogen and carbon only—and virtual proof of this was later obtained by my own predecessor, Sir Ernest Kennaway, at the Cancer Hospital. Through his work and that of his school, the picture gradually emerged of carcinogenic substances built through the conjugation of benzene rings.

Early in these investigations, it was repeatedly noted that cancer-producing tars exhibited the property of fluorescence in ultraviolet light, that is, to absorb invisible light of short wave-length, and to emit visible light of longer wave-length. In 1927, W. V. Mayneord, again at the Cancer Hospital, took the matter decisively forward when he indicated that the fluorescence spectra of such tars showed qualities which appeared to be characteristic. This spectrum of cancer-producing tar proved to be, in Kennaway's words, "the single thread that led all through this labyrinth," and it soon enabled him, and his colleagues, to track down the carcinogenic agent. Since it was already suspected to be a complex hydrocarbon, the next step was to examine the spectra of those polycyclic hydrocarbons already known in pure form, and constituted from the fusion of various numbers of benzene rings. Very shortly, Hieger was able to make the key discovery that *1:2-benzanthracene*, (comprising four such rings), also possessed the characteristic spectrum. By a curious accident, Clar in 1929 had just described the synthesis of the related hydrocarbon containing five fused rings, (*1:2:5:6-dibenzanthracene*), and in the same year Kennaway and Hieger proved this substance to be carcinogenic in mice—the first pure chemical individual to be recognised as possessing this property. The fluorescent spectrum was also used to great purpose in the isolation of the naturally-occurring carcinogenic agent from pitch. This proved to be another pentacyclic aromatic hydrocarbon, namely *3:4-benzpyrene*, which Cook and Hewett were soon (in 1933) to prove by synthesis. In the same year, Cook and Haslewood produced *methylcholanthrene* from a bile-acid, so raising the whole question—still undecided—whether traces of highly potent carcinogens can be formed *in vivo* from perturbations of the normal metabolism of steroids. A chief result of all this work was eventually to provide an amazingly satisfying and complete picture of the relationship existing, within this series, between chemical constitution and biological action.

In the intervening years, many older chemical classes had been uncovered, in no way related to the cyclic hydrocarbons, but equally endowed with carcinogenic qualities—various aromatic amines, especially those involved in the causation of cancer of the bladder; a host of azo dyestuffs with the special propensity to evoke tumours of the liver; a series of aminostilbenes with very diversified carcinogenic properties; and many others. To these we must add a great range of purely physical agents, including ultraviolet radiation itself, X-rays, radium and thorium, and a host of radio-isotopes arising from the atomic energy programme, especially radiophosphorous, radioiodine and radiostrontium. Of late we have also recognised the carginogenicity of many macromolecules and plastics, and the special function in carcinogenesis which may be played by the metals, as also the role of many biological agents, e.g. those viruses responsible for the induction and propagation of certain tumours in animals (although not so far in man)—topics any one of which could easily exhaust a whole lecture in itself.

In none of these cases have we precise knowledge of the mode of action, or of the site at which it is excited within the cell. Only in the past few years have there come certain hints, through the discovery of carcinogenicity in yet another chemical class, namely the nitrogen mustards—substances developed in the Second War for the purpose of chemical warfare, and nitrogen analogues of that sulphur mustard or "mustard gas" which had been used in the War of 1914-18. The nitrogen mustards have the advantage of relative chemical simplicity, with features which are suggestive, or even indicative, of possible modes of action. The action upon dividing cells is highly direct, leading to cytological abnormalities indistinguishable from many which can equally be produced by ionising radiation. On this account they are not unreasonably described as radiomimetic, and it is certainly remarkable that just as X-radiation is employed in the treatment of cancer, so also can some of the mustards, in the palliation of certain forms at least. Contrariwise, just as X-rays can be cancer-producing, so also can the mustards. In many cases the tumours so produced bear signs—as a kind of imprint—that the action has involved the nuclei and chromosomes. A certain extent of chemical reactivity is required, suggesting again that the biological end-result may depend upon reaction with some cellular component so far undefined. The main features of the nitrogen mustards is their possession of two or more haloalkyl side-chains. Within the series this indeed appears to be a requirement for biological activity, and led to the proposal that activity might in fact depend upon chemical cross-linkage, as for example between the contiguous linear macromolecules of the chromosomes themselves. Although this hypothesis is now known to be unduly simple, it proved tremendously fruitful in development, leading for example to the application of much knowledge already available in the field of cross-linking agents in textile technology, and hence to the rapid discovery of other series with similar biological effects—epoxides, polyethylene imines and dimesyl compounds—now classed under the general heading of biological alkylating agents.

The exact nature of the biological receptor is still not known. It is very probably genetical in function, as reaction within the nucleus and upon the chromosomes might infer. However, such reaction would certainly introduce widespread repercussions in the cytoplasm, and direct action by certain carcinogens upon the organelles of the cytoplasm is by no means excluded. Notwithstanding, a prominent candidate for the seat of action of the carcinogenic alkylating agents is without doubt—and for many reasons although none is as yet decisive—the deoxyribonucleic acid of the chromosome structure, as the chemical basis of cell genetics and heredity. A great impetus has been given to these studies by the proposals for nucleic acid structure put forward by Crick and Watson—of the bonding of pyrimidine and purine base pairs to yield essentially superposable structures, and of the complementary disposition of these as bridges in a double helix of phosphate-sugar chains; and we already have some precise chemical information as to the action upon such a structure both of ionising radiations and of the ions yielded by alkylating agents. But further advance must largely depend upon our deeper knowledge of chromosome structure. While waiting, we can gain much through the use of what is still the most favourable material—namely the giant chromosomes of the salivary gland of the fruit fly *Drosophila*—in studies of the chemical basis of biological mutation generally, of which carcinogenesis may be a special case. Acting upon such material, the alkylating agents frequently produce changes of the nature of deletion, and this, with other considerations, has led to the view that cancer causation could be due to combination of the agent with nucleic acid, so leading to defects in its synthesis or structure. This process would interrupt the essential precision of the nucleic acid, and prevent the formation of certain protein molecules (and especially perhaps growth-regulatory enzyme-proteins vital to the control of normal cell division), for which we know the integrity of the nucleic acid structure is necessary and responsible. In the case of the carcinogenic hydrocarbons and azo-dyestuffs, there is also evidence that the same deletion of key proteins can be brought about by combination of the carcinogen with protein molecules themselves, directly.

We therefore approach the view that carcinogenesis is a process of biological mutation by loss, and that there is no true acquisition of a new growth property on the part of the cancer cell, but rather the unmasking of the growth potential which its normal precursor had all along possessed. The general conception has still to be tested, and could clearly have the widest implications. There is an increasing number of diseases recognised as due to enzyme deficiency, and some of them can be controlled by restoring the defect through a kind of substitutive chemotherapy. It well may be, in the future, that cancer too will fall in this class, and become amenable to control through a re-imposition, from without, of that growth regulation which the cancer cell itself has lost forever. At any rate it can fairly be said we are at least approaching certain correlations, between the reactive properties of given carcinogens, the places at which and the methods by which they combine in the cell, and the permanent alterations in growth behaviour, which come about as the result. Although so much remains to do, the story is great and growing. When one day it comes finally to be told, it will be seen to have meaning far beyond the sphere of medicine alone, and to be in part a model of what can be achieved by the human mind through the interaction of biology, chemistry and physics.

I end as I began, with thanks to the Society and all its members for this kindly privilege. I also wish to record special indebtedness to my colleague Mr K. G. Moreman, and to the officers of the Society for indispensable assistance. May the Society enjoy strength and prosperity not only in the present new Session, but in all those which lie ahead, in a future which we are confident will continue that unfolding of the art, science, and achievements of Medicine, towards which the Society itself, in its long history, has made no mean contribution.

Floreat Res Medica!

THE SOCIETY'S LIBRARY

Based on a Dissertation read before the Royal Medical Society on Friday, 28th February 1958.

By J. J. C. CORMACK

Amongst all the inventions, attainments and discoveries which have marked Man's strange progression from Darwinian prehistory to this modern, hectic but stimulating civilisation, the realisation of his ability to communicate his thoughts and ideas in permanent form must rank extremely high. Few will deny that the discovery of writing, the manufacture of paper and the invention of the printing press are among the greatest landmarks in human history. Certainly in Medicine we can consider books to be amongst the most useful and basic of the tools of our trade—for here we can draw upon the wisdom and learning of preceding ages and it is here that we have contact with the minds of those generations of our predecessors who have risen and passed away. We in this Society rightly value the traditions of our past and I make no apology in presenting briefly some facts and some thoughts on that greatest of our links with the past—and not only with the past but with the future as well—our Library. I should like to tell you something of its history and of its present state; I should like to whet your appetite for exploration by exhibiting a few of its treasures and I should like to evaluate the place of the Library in the Society's life, and its prospects for the future.

It is not surprising that a Society such as ours should have wished to acquire a representative collection of medical books. That it began to form its Library early is shown by the fact that sixteen years after the Society's formal foundation, in 1753, a library was being accumulated in the room set aside for the use of the Society in the old Royal Infirmary; books being purchased with funds which had previously paid for tavern accommodation. This room soon became inadequate; the Library being "not in such a situation as could be desired either with regard to conveniency or preservation." In 1755 the foundation stone of the new Hall was laid by the venerable Dr Cullen. This Hall, which is well known to us from Shepherd's engraving, stood in the south west corner of Surgeons Square—the site of which is now the courtyard of the Physics Department in Drummond Street. In 1778 the Society petitioned the King for a Royal Charter, and among their reasons for so doing they instanced "That the Society, by contributions of the Members have gradually made a collection of Medical Books, which is daily increasing . . . " This Charter was granted on 14th December 1778 and now stands in the Society's Hall.

In November 1852 the Society moved to its present premises. The old Medical Hall stood on ground which was needed for extension by the Managers of the Royal Infirmary, and after prolonged negotiations the Society sold the old Hall to the Infirmary for £1700 and moved to 7 Melbourne Place, which it was hoped would provide "full accommodation for the Library, now amounting to 14,000 volumes, selected with a care unexampled in any other institution."

Throughout the ensuing years the problems of sorting, listing and cataloguing the Society's books presented constant worries to each successive Library Committee. Our earliest extant copy of a catalogue is one published in 1812, and the one which is most up to date, and by which this Library is known elsewhere, was published in 1895. Continually efforts were being made to carry on with cataloguing and indexing the Society's volumes, but the struggle was an uphill one and repeated agonised appeals to members for help in this work seemed to be of little avail.

A great step forward was taken in 1937 when the room opposite the Bramwell Room was renovated and set aside for our oldest and most valued books (including the Dissertations) as a memorial to J. R. Young. A further most shrewd and progressive step was taken in 1956, under the Librarianship of J. G. Birkbeck, when some 1000 works of non-medical interest, having been vetted beforehand, were alienated and sold for a gratifyingly large sum of which a proportion was invested for the use of the Library Committee and the remainder used for some much-needed redecorating.

The present time sees the start of a new venture; with the generous financial assistance of the Carnegie Trust we have been able to obtain expert help in the much-needed work of re-cataloguing the Library. The devoted skill of Miss Wingate has already accomplished a large part of this mammoth task. With this work in hand, and with the newly established appointment of an Honorary Librarian to act as "guide, philosopher and friend" to successive Librarians, thus ensuring a measure of continuity, the Library would seem to be taking on a new lease of life.

What does this, our present Library, comprise? Approximately speaking some 11,700 volumes, falling roughly into the following seven categories:

1. Dissertations—215.
2. Record books.
3. Old and rare books (16th, 17th and 18th Centuries)—704.
4. 19th and early 20th Century monographs and text books—3538.
5. Out-of-date editions of current textbooks—325.
6. Current textbooks—183.
7. Journals—3545.

Amidst all these there are books of unique interest to the Society because of their connection, either by authorship or presentation, with our own members, past and present.

Space does not permit me even to review the cream of this collection—it must suffice for me to say that the whole sweep of medical history, and more, the history of our own Society, is mirrored here—from the early fathers Hippocrates, Aristotle, Galen, Celsus and Avicenna, through Vesalius, Eustachius, Harvey, Willis, Cullen and Boerhaave, the Monros and the Hunters, Simpson, Syme and Lister, down to the most modern authors. To illustrate but two of our treasures we have here a page from the works of Ambroise Paré—a truly fascinating volume from the pen of the father of modern surgery and a giant among men; and this rare link with the discovery of digitalis—Withering's "Account of the Foxglove" with its inscription to the Society.

We should be proud to possess these volumes, but at the same time we must be aware of the problems which face us in our responsibility for caring for these treasures and also ensuring that the Library gives the best possible service to members.

It will probably be clear from what I have already said that the major interest of this Society's Library is a historical one. For many years now it has been the case that the Society has been unable to keep a stock of current textbooks which can be lent out to members. This type of service is provided by our subscription to Messrs Ferriers Lending Library, and with the increasing speed with which new textbooks or new editions of old textbooks are being published, I do not think that the Society will ever again be in a position to organise any large-scale lending library facilities of its own. It may well be that if the Society increases its membership we should augment our already overburdened subscription to Ferriers.

This lending service is supplemented by the current textbooks available in the Consultation Press. It is imperative that this section of our Library should be kept as up to date as possible, and indeed that it should be enlarged as soon as financial circumstances permit. Ideally it should contain an entire collection of the standard textbooks and books of reference currently in use at this School. This ideal has not been fulfilled, but it should certainly be our aim. We should also aim to have the older books which we possess in proper order, and in such a state that members will be able to find any particular volume with ease. Members should also be able to browse through some of the books which have been written and read by their predecessors without running the risk of covering themselves with the dust of ages or having precious tomes disintegrate in their hands.

Obviously the major work of re-cataloguing is the first step towards restoring the Library to its rightful usefulness. Work has already started. How is it to proceed? First of all the volumes in each room must be classified, as far as the limitations of the shelving will allow, into subjects—this is the work which is proceeding just now in the North Library—then the major task of completing the card-index author catalogue and the subject-index will begin.

When this preliminary work is completed the Library Committee and the Society will be faced with important decisions concerning the alienation of books. We have quite a number of duplicate volumes on the Library's shelves which should almost certainly be sold. There are also in many cases numerous editions of popular textbooks—in these instances it might be best to keep copies of the earliest and latest editions and discard the remainder. On these issues it may be relatively easy to decide, but more difficult problems of alienation present themselves. Many of our books are written in a language no longer understood by the majority of medical students—namely Latin. We have also some works in Greek and a considerable number in French and German. How many of these are worth keeping? Obviously it will be for the Society to decide at a later date; personally I feel that many of the medical classics of the 16th and 17th centuries should be most carefully preserved and cherished, and if possible that they should be supplemented by English translations where such are available. Even if their content is not fully understood they illustrate the steps which have been taken from earliest times along the road of medical progress.

However, it is more doubtful whether many of our 18th and 19th century German and French works are really of much value to the Society either for instruction or for interest. Some, though not all of them, may well be taking up space on the shelves when they could serve better purpose by being sold and providing money for much-needed improvements. We also possess odd incomplete sets of Journals of doubtful value and their alienation too will require to be considered. But I must emphasise that it would be the utmost folly to consider such pruning of our collection before all the books are listed and indexed, and when the time comes we shall certainly need to obtain the most expert advice. Too often in the past zeal and enthusiasm have outrun discretion, and sound schemes have been defeated by precipitate action.

After we have decided what we wish to discard and what to retain, in the light of the value of the main bulk of the Library to the Society as an historical collection which mirrors both the history of medicine and the history of the Society, the next step will be to decide on the proper lay-out of the Library.

Once a decision is made on this, books will have to be shifted to conform. This may mean large scale upheavals, but it will be worth doing if the job is to be properly completed. This finished, permanent shelf marks

Title page of Withering's *Account of the Foxglove* which he donated to the Royal Medical Society.

Page from the Collected Works of Ambroise Paré showing restitution of dislocated shoulder.

can be allocated to books and the catalogue then completed. As far as possible the books in the North Library and Museum would be in logical categories, but the provision of shelf marks would certainly mean that by using the catalogue any particular book could be rapidly traced. At this juncture the Society should be in possession of a complete card-index author catalogue and subject index of all its books. A decision will then have to be made on the publication of a revised catalogue to replace the 1896 edition. Owing to high costs of printing it might be advisable to restrain our ambition in this direction, but even a cyclestyled copy of an up-to-date author catalogue would be of value for the information of other libraries and interested bodies and for our own prestige, as well as its obvious use to members.

Once we have a catalogue it will be imperative that successive Librarians keep it up to date. As our rate of expansion is now not high (nor is it desirable that it should be) this task will probably not be very onerous, but it will be most important. With the appointment of an Honorary Librarian the problem of continuity should be at least partially solved.

However, even with our Library pruned, re-sorted and re-catalogued, we will still have further problems to face. The three most important of these are those of preservation, protection and access. A vast number of our older volumes are in a very bad state of repair—some of the more important were re-bound in 1937, but many are still in a heart-breaking condition. The cost of binding is astronomical and it is unlikely that we will ever be able to afford to undertake a complete programme of this sort, but as a palliative measure we might be well advised to repair some of the less damaged volumes ourselves with adhesive tape. This is a practical step which falls short of perfection, but which might indeed save some of our volumes from a much worse state. The addresses in the metal box in the Young Room should also be bound, or at least placed in folders.

Allied to the problem of preservation is that of protection. Though untroubled by moth and rust we do have to contend with the awful ravages of dust, and I suspect that thieves break in. Even to-day books "walk" from our shelves and, though they may yet turn up, I am inclined to wonder where are our copies of Jenner, of Akenside's *De Dysenteria* inscribed "for Dr. Cullen from Dr. Hunter," or de Quincey's *Opium Eater* or Dover's *Ancient Physician*. These are treasures which are at present lost, and though they may have only strayed I fear it is more likely that they have been stolen. Most of our cases must perforce be locked, and with regard to the havoc already wrought by dust it is most desirable that they should be glass- or perspex-fronted. We have baulked at this latter problem before, but I feel that the time is now ripe for further investigation as to the cost of such a measure and we should give very serious consideration to ways and means. The locking of cases in turn raises the problem of access. Ideally any member should be at liberty to browse around the shelves. However, as past experience has shown this to be scarcely practicable, we must devise some scheme whereby books could be consulted at specified times or whereby keys could be "signed out" for limited periods. This again is not an easy problem, but it should not be beyond our ingenuity to solve it satisfactorily.

Finally, how is the Library to expand? We have already seen that rapid expansion is not possible on our limited budget, and it is probably not even desirable. We certainly should continue to build up our collection of Journals, and we should, perhaps, do more about filing pamphlets and reports, but we do constantly need new books of general medical interest and replacements for textbooks. The trickle of such books bought by the

Society is at the moment pitifully small. Some of our old members and friends (such as Dr Douglas Guthrie) from time to time present us with books, but I should like humbly to suggest that present members when they are about to relinquish active membership of the Society might like to present a book to the Library as a mark of their gratitude to the Society as a whole for the benefits they have obtained here—and if such presentation be made after consultation with the Library Committee as to present needs it would be of all the more value to the Society.

In attempting to give you some idea of the history and scope of our Library, and some of the problems which will face us in the future, I hope I have been able to show what a magnificent, but challenging heritage we have fallen heir to. In this Library we have our contacts with our own past and with the accumulated wisdom of centuries. The responsibilities for preserving and maintaining what is good and useful in this unique collection, while at the same time providing for intelligent expansion and progress, are grave, but we owe it to our predecessors and to our successors in this place to grasp the opportunity which now presents itself of consolidating and improving this most precious of our tangible assets—The Society's Library.

BIOLOGICAL RESERVES

By Sir JAMES LEARMONTH

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"Life," wrote McNair Wilson, "interested John Hunter to the exclusion of everything else, and he studied life as he had begun to see it—namely, as the supreme resistance to the blind forces which surrounded it and impinged upon it . . . Life, on this showing, was self protective." This "supreme resistance" of life leads in health to longevity, in disease or after injury to survival; and therefore it is of peculiar interest to surgeons. It appears to depend on an urge for continuing life common to all tissues, and easily demonstrated for certain cells in the laboratory by examining the resistance offered by renal and hepatic cells to a sequence of injuries produced by chemicals (for example uranium nitrate and carbon tetrachloride). Tissues differ from one to another in the tenacity with which they cling to life, some giving up before others. This may be of importance in the practice of the future, as the population of this and other countries ages. According to the Government Actuary's projection, provided the general mortality rate continues to decline and the fertility rate remains about the same, between 1951 and 1979 the total population of this country may rise by 7% to 52,250,000; the pensionable population may rise by 43% to 9,500,000, while the number of children may fall by about 4% to 10,500,000. Doctors (and incidentally hospital planners) will have to deal with and provide for more aged and ageing tissues and for fewer children; they will also be able to determine whether the tissues of children of the present generation, who are growing to be larger and who are maturing earlier than the children of 25 or 50 years ago, will in fact retain their "desire for life" to ages sufficient to project them into the pensionable groups (males over 65, females over 60), a possibility at present unresolved.

At all levels of animal life, the desire for life expresses itself in the possession of three forms of biological reserve—*self-defence*, *self-repair*, and *self-adjustment*. As I intend to deal particularly with *self-adjustment*, I shall deal with *self-defence* and *self-repair* only briefly.

Self-defence

There are, of course, two contributory factors to self-defence: the general response, which is an immunological one, and the local response, which can also be examined by histological methods. Both these aspects can be investigated in the laboratory, for the general pattern of response in laboratory animals resembles that in man. What does vary is the efficacy of defence against the various forms of noxious stimulus; physical, chemical and bacterial. The possibility of differences in efficacy is present not only between laboratory animals and man (though they are not uniformly present), but also between the various species of laboratory animals. And more importantly, there may be such differences between human races. Thus the resistance of the peritoneal cavity of the African to pyogenic organisms is greater than that of the European or the Asian. This is obviously the kind of difference which will become of increasing importance as world distances are reduced by better and faster means of communication. It is already of great importance in prognosis for those who practise in multiracial societies.

Self-Repair

The capacity to repair injured tissues and to regenerate lost tissues appears early in animal life; it is found in those animals whose constituent cells increase in number after they first become individual. The capacity may be the expression of a physiological process necessary to replace the wear and tear of use in such epiblastic structures as skin and hair, and such mesoblastic structures as the cells of the liver and the pancreas, and those of the blood. The capacity may be extended to the replacement of tissues lost or interrupted, which is called healing. In lower animals, for example in the lizard, a complex structure such as a tail may be replaced not only in bulk but also in anatomical structure. Higher animals do not possess this useful capacity. In man the most complex repair is the restoration of the epithelial lining of the gut, which includes the restoration of glands appropriate to the segment of gut involved. Repair in the covering epithelium, the skin, includes the nails but not hair or glands. It is curious that the only other epiblastic structure which has the capacity for self-repair is peripheral nerve, because (to take a motor nerve as an example) it is merely the intermediate link in the function of movement, and neither the initiator of movements (the brain) nor their effector (the muscles) has the capacity to regenerate. In some mesoblastic structures in lower vertebrates (the liver of the dog for example) regeneration in bulk quickly occurs after removal of large parts of the organ. The removal must of course leave behind enough parenchyma to sustain life, but it is curious that the organ should at once set about rebuilding parenchyma far in excess of physiological needs.

The capacity to regenerate complex tissues decreases as the evolutionary scale is ascended; and finally includes—because of its survival value—only the replacement of commonly injured tissues. All other losses are replaced by connective tissue during the process of healing. I doubt the desirability of attempting to modify so fundamental a process, especially since departures from normal timing in the process of self-repair often lead to instability of the repair.

All these varieties of self-repair—physiological, replacement in form and replacement in bulk—can be studied in the laboratory, for in higher animals including man the primary structures—bone, muscle, and nerve tissue—are the same. It is of interest to recall the possibilities of repair indicated by Sir James Paget in his famous Lectures on Surgical Pathology (3rd edition, 1870).

1. In tissues formed entirely by nutrient repetition—blood, epithelia.
2. In tissues of lowest organization, or lowest chemical character—connective tissue, bone.
3. The tissues inserted into other tissues, connecting them with other structures—nerve fibres, blood vessels.

This classification might well be used today.

Self-Adjustment

The capacity for self-adjustment is most important for survival in the animal kingdom, and particularly so in man. It comprises two different kinds of adjustment. In the one, the patient "makes do" with what he has after some disease or injury has deprived him of completeness in some physiological function. An example of this type of adjustment are the trick movements possible after paralysis of certain peripheral nerves, as when in paralysis of the radial nerve extension of the wrist is partly carried out by strongly flexing the fingers and so tightening the extensor tendons.

In the other type of adjustment structures and viscera have to undertake to function under conditions imposed by the surgeon, for example after the transplantation of muscles from the preaxial to the postaxial aspect of the forearm to relieve radial palsy, or after anastomosis of the jejunum to the stomach in the operation of gastroenterostomy. In many of the operations of surgery the success and even the safety of the procedures depend on the capacity of the human body for self-adjustment. Wonderfully efficacious as this capacity usually is, it may often be improved, and its final attainment of maximum competence hastened, by the judicious use of all the social, mental and physical auxiliaries which are collectively called rehabilitation.

1. The simplest form of self-adjustment is seen after the destruction or removal of one of paired organs such as the kidney. The remaining organ, although containing ample parenchyma for physiological needs, usually enlarges a little, as if to provide a little biological reserve. Adjustment to the loss of single organs is not possible. Sometimes the loss is fatal if not artificially compensated (pancreas); sometimes it gives rise to profound changes in function of the most complex description (pituitary).

2. Sometimes adjustment is possible in virtue of the excess of parenchyma in an organ or tissue, over what is the minimum physiological requirement. The body adjusts itself at once to the loss of five or six hundred cubic centimetres of blood, as donors who give blood for transfusion well know. Such structures as the liver and the thyroid are constructed on such generous lines as almost to give the impression that they are prepared to lose portions from disease or from injury; it is difficult to associate this with any evolutionary process. On the other hand it seems a little odd that although other structures should have plenty of spare parenchyma, so important a structure as the pituitary gland should have little or none, which leaves it very vulnerable to disease.

3. Instead of using excess of parenchyma for making adjustments, the body may utilise the fact that there is overlapping of function between organs. Thus after removal of one cerebral hemisphere, not all cerebral control is lost over the contralateral side of the body; which helps to compensate for the lack of self-repair in the central nervous system. The stomach may be completely removed by the operation of total gastrectomy, after which the intestinal juices are capable of completing the digestion of food. Compensations such as these are not possible when there is no overlapping of function, as in the case of the pituitary or the pancreas, which are the only sources of their secretions.

4. One of the most important self-adjustments made by the body is to some extent a normal physiological process: the maintenance of the constant composition of the body fluids—the *milieu intérieur* of Claude Bernard. This composition is altered by a great variety of causes, ranging from the metabolic disturbances which follow injuries (including operations) to the complex alterations seen when the alimentary tract is obstructed. The rapidity and completeness with which the body can make these adjustments is much reduced by other factors to deal with which no completely satisfactory bodily mechanisms seem to have been evolved; extreme fatigue, extreme malnutrition, the presence of "stress," and in cases of trauma the presence of gross infection.

5. A vast number of adjustments can be made which are related to the conduits of the human body. The simplest division of these is into channels to which there is an alternative, and channels which are single.

   Alternative channels can be subdivided again. There are those which are provided by nature, and which are already in existence, such as the anastomosing arteries, veins, and lymphatics which may form a collateral circulation when the main vessels are blocked by injury or disease. There are "relief" alternative channels the result of disease, as when an infected distended gall-bladder ruptures into the neighbouring duodenum; the anastomoses formed by these *internal fistulae* are seldom completely satisfactory from an engineering point of view, because of awkward and abnormal differences of pressure in the hollow structures so joined, and the lack of accurate union of their respective epithelial linings. Finally, there are those made by the surgeon, to which the body must accustom itself—such as gastro-enterostomy, or the deviation of the flow of urine into the bowel. Arrangements such as the latter may be only "one-way" affairs, for while urine-to-colon is an adjustable arrangement, faeces-to-urinary bladder is not.

   When there is no alternative to a given conduit, the problems posed to the body differ. When the passage is a mere tube without muscular walls, such as the Aqueduct of Sylvius, then the body is powerless. When the conduit has muscular walls, the body uses for the necessary adjustment the capacity of plain muscle to hypertrophy, to ensure that an obstruction in the conduit will be at least temporarily overcome. This useful property of plain muscle was first noted by John Hunter; the possibility of hypertrophy is also present in cardiac muscle (to overcome vascular resistance) and in striated muscle (to increase capacity for work).

   Tubes such as each ureter and the alimentary canal are not provided with alternative routes. But when they are totally obstructed the technical problems they present are different. The ureter is straight and has not excess length, so that the upper and lower ends cannot be brought together after a piece of it has been removed. On the other hand the alimentary tract is mobile, and excessively long, and the surgeon can make abnormal junctions between its proximal and distal parts, to which the body has been proved by trial to be capable of self-adjustment.

These three biological reserves—the capacity for self-defence, the capacity for self-repair and the capacity for self-adjustment are essential for the continuance of the human race. When the surgeon intervenes, it must be to provide a solution which has not been elaborated by the body itself in the process of evolution. And he must always be careful rather to aid the efforts of the body itself than to attempt to substitute his own.

THE CAUSATION AND SPREAD OF EPIDEMIC INFLUENZA

By WILLIAM IAN SHEDDEN
B.Sc. (Hons.)

This article is based on Mr Shedden's entry for the Lewis Cameron Prize which he shared with Mr Tom Kennedy, another memuer oı the Royal Medical Society.

Prior to 1933, aetiological studies of human influenza yielded little precise information. In 1938 Shope showed that swine influenza, the analagous disease of pigs, was caused by a bacterium (Haemophilus influenzae suis) and a virus, in symbiosis. Two years later, Smith et al reproduced the signs of influenza in ferrets by the intra nasal injection of bacteria free garglings from cases of human epidemic influenza. The suspected virus actiology was thus confirmed. This classic WS strain of the virus, and all subsequently isolated, serologically related strains were collectively designated the "influenza A" group of viruses. At least two other major serological groups have since been identified and these have been designated "B" and "C" respectively. Epidemiological studies have indicated that epidemic influenza, in its widespread form, is caused by viruses of the A group.

A *mobilis in mobile* relationship exists between the influenza A virus on the one hand and the human host population on the other. Always in nature the tendency is towards a balanced inter-relationship between living species. Disturbances in the balance between virus and host, due to gross changes in either, or less marked in both, may result in epidemics. The extent and severity of the outbreak is proportional to the degree of imbalance.

The effect of changes in the nature of the parasite is to increase the number of susceptible potential hosts without any necessary accompanying immological or physical change in the latter. A mass of information has been accumulated which confirms that the influenza A virus is capable of much variation. Hirst (1952) absorbed rabbit immune sera with several heterologous strains of influenza A virus and was able to show that in the period 1933 to 1952, seven specific antigenic types established temporary prevalence. Burnet has since demonstrated that finer antigenic differences may be detected almost annually, and that the process of antigenic change is therefore more continuous than Hirst suggests. This heritable variation would appear to be the result of discontinuous mutation, essentially similar to gene mutations in higher forms. Soon after a new antigenic type arises, it becomes the dominant form responsible for epidemics all over the world. The mass transformation is the end result of selective survival and overgrowth of one mutant type. In Hirst's series referred to above each mutation involved the appearance of a new antigenic component, which was added to the old antigenic pattern. In other words the immunity resulting from infection by an epidemic strain of influenza A virus, will be effective against all previously occuring epidemic strains, though not against further mutational changes, provided no back mutation occurs. Between 1933 and 1952 there had been no reversal to an earlier antigenic pattern. Evidence has, however, been produced which would suggest that in 1957 a back mutation may have occurred. Mulder, in the Netherlands, showed that persons alive in 1890 possessed type specific antibodies against the A/Asian/57 strain, whereas the rest of the community did not. There may therefore be a reasonable premise for considering a long term cycle of antigenic variation of influenza A.

Mutation to a form of greater transmissability would also appear to be of importance in the initiation and spread of an influenza epidemic As yet this change is little understood, and little direct work has been done on the subject. The "O" phase of the virus is said to be more readily transmissable than the "D" phase. The significance of this fact is not clear.

The clinical manifestations of epidemic influenza are dependent on more factors than spread of infection. The nature of the observed variation in virulence of the influenza A virus has not been explained. Perry et al (1954) have postulated the existence of "virulent genes" which undergo spontaneous mutation to a state of increased or diminished virulence. This adaptation is probably a step-ladder like process with many inheritable intermediate grades. The results of animal experiments suggest that the more widespread an epidemic becomes, the more likely it is to assume lethal characteristics. This work is still largely of academic importance.

In summary, virus mutation facilitates the commencement of an epidemic by the production of novel antigenic types, against which immunity is decreased, minimal or absent, depending on the extent of the change. Variation in transmissability may be important in facilitating spread. Variation in virulence probably accounts for observed differences in severity of clinical symptoms and death rate.

The changes which take place in the nature of the influenza virus are well known, though inadequately understood. Too little attention has been paid to the changing nature of the host population. These changes are twofold—immunological and physiological.

Specific antiviral antibodies are important in protecting the host against influenza. Francis (1941) has found evidence that in immune persons, antibody is present in the secretions of the respiratory tract. Local tissue immunity would also seem to be significant, but is difficult to evaluate. These mechanisms are the result of previous encounter with the virus. Potential hosts are characterised by a low level of specific antibodies. Such hosts may arise by one of three mechanisms—birth, entry from a community in which influenza is unknown, or lastly, waning of previous immunity. Neutralising antiviral antibodies have been shown to undergo cyclical changes. High and low antibody levels have been correlated with reduced and increased susceptibility to infection. Studies have shown that levels are highest after an epidemic. Moreover anti-influenzal antibody is type specific. Hence the slight protection afforded by a lowered antibody is further reduced due to the small degree of cross-immunity against a mutant epidemic strain.

The most important physiological factor concerned in epidemic influenza would appear to be the age structure of the population. This may be a direct physiological effect *per se* or it may act through the mediation of the immune response. In infancy the defence is poor. Infection occurs readily and there is little inflammatory response. Mortality is high. On the other hand the 6-12 year old group shows high resistance. In the 1918 pandemic the number of deaths in this age group was negligible. In young adult life there is apparently an increased susceptibility to epidemic infection. This was seen in the 1918-1919 pandemic. However, this susceptibility may be more apparent than real, since, in the active period of life, exposure to infection is more frequent.

After middle age, the resistance to infection becomes poor. This group shows a high morbidity and mortality in influenza epidemics. Experiments performed by Burnet and Beveridge suggest that the physiological resistance of the mature host is associated with the presence of increased quantities of pharmalogically active substances, producing inflammatory change. Epidemic influenza therefore will spread more rapidly, and produce the highest mortality amongst the very old and the very young. Exceptions to this general rule have been tentatively explained in terms of increased exposure to infection.

In addition to the well-established effects of immunological status and age, certain non-specific factors seem to be involved in determining whether influenzal infection will take place. For instance, climatic factors may have an influence on the respiratory mucosa, predisposing to infection. This may be brought about directly *via* the blood supply, or indirectly by a complex hormonal mechanism.

Having considered the factors predisposing the individual host to infection let us turn our attention to the spread of the influenza virus throughout the community. Epidemic influenza is a disease of civilisation. At the dawn of man's life on this planet the social unit was a small group consisting, at most, of a few families. There was little intercourse between the different groups. Under such conditions the evolution of the influenza virus as a specific human parasite would be difficult. Before an epidemic can occur it is necessary that the host should live under social conditions which admit of large community aggregates. In this way the epidemic spread of a pathogen can occur. Modern civilisation has provided the large communities, and its forms of rapid transport can convey an infected person from one community to another in a few hours. In doing so the seeds of disease are spread far and wide. The epidemic will persist until an ecological climax state is established, with the restoration of equilibrium between host and parasite.

By analogy with other disease conditions three sources of infection are possible. These are the patient showing the disease, sub-clinical cases, and healthy carriers. The overt case of influenza remains infective for about five days and is probably of paramount importance in the spread of the disease.

Hirst (1947) has suggested that some cases are more significant than others in this respect. He showed that it was usually necessary to incubate eggs with undiluted, filtered garglings from cases of influenza before lethal infection of the egg was produced. Occasionally, however, relatively enormous quantities of virus were present so that 0·1 ml. of gargling contained 10^6 lethal egg doses. Infection therefore may be spread by a few highly infective individuals, rather than by the members of a group to an equal extent.

Burnet et al (1940) made observations on laboratory staff, and patients, of a mental hospital. The number in each group developing clinical influenza was compared with the number showing serological evidence of infection. This experiment served to demonstrate that a symptomatic infection with influenza A virus can occur. Hosts suffering from sub-clinical infection may well be of importance in the spread of the disease. The insidious nature of the danger may perhaps make them of greater importance than those with clinical infection.

It has never yet been ascertained whether or not the human host can act as a healthy carrier of influenza. Such a conception would be useful since it would offer a convenient explanation for the survival of the virus between epidemics. Burnet has suggested that the influenza virus might exist in pathologically altered cells around some chronic lesion in the respiratory tract. Thence it might be liberated in response to some non-specific infection or environmental stimulus. No proof of this hypothesis yet exists.

Though little or no work has been done on the subject, it is logical to assume that the influenza virus is spread from source to potential host via the air. The seasonal incidence of influenza suggests this, as does the rapidity of spread of an epidemic. It is assumed that the virus, once liberated from the damaged respiratory tract epithelium, passes upwards into the pharynx and is expelled via the saliva. Thence it reaches a new host in some ill-understood fashion.

In 1945 Duguid showed that most of the droplets of saliva expelled by speaking, coughing or sneezing originate in the front of the mouth, few if any coming from the nose or throat. The fate of these droplets depends on their size. The larger droplets fall to the ground in one or two seconds. The smaller ones (under 0·1 mm. in diameter) evaporate immediately leaving solid droplet nuclei. An average number of 10^6 droplet nuclei may be produced by one sneeze. Though workers have been unable to isolate micro-organisms from droplet nuclei, their possible importance in the spread of epidemic influenza is very real. When larger droplets fall to the ground they evaporate and subsequent dust-raising activities may give rise to dust-borne contamination of the air.

It is possible that transmission of the influenza virus from donor to recipient may take place by primary (droplet nuclei) or secondary (dust borne) air contamination. Spread by fomites or direct spraying, though possible, are less likely. This fascinating subject awaits full investigation before the relative importance of the various possible methods of infection can be ascertained.

As yet there are vast gaps in our knowledge of epidemic influenza. This is reflected in the fact that, so far, epidemic outbreaks have been impossible to control. It may be, however, as Stuart-Harris has said, that the present era is the first phase in our efforts towards that end. It is only through a better understanding of the biological variation of the influenza virus and its means of spread, that the goal of prevention of epidemic infection may be reached.

SOME ASPECTS OF POLIOMYELITIS

Based on a Dissertation read before the Royal Medical Society on Friday, 14th February 1958.

By ALLAN MILNE
M.B., Ch.B.

This article is an attempt to present a few of the interesting facets of poliomyelitis. It certainly does not include all the important aspects; these can be found in any standard text-book.

There is evidence that poliomyelitis occurred in very early times; indeed, Osler in his Textbook of Medicine in the 1890's believes the first recorded case to be in the Bible—2 Samuel, ch. 4, verse 4—"And Jonathan, Saul's son, had a son that was lame on his feet. He was five years old when the tidings came of Saul and Jonathan out of Jezreel, and his nurse took him up and fled: and it came to pass, as she made haste to flee, that he fell, and became lame. And his name was Mephibosheth." It was common belief that this paralysis followed a minor accident, and that it was cause and effect; this belief persisted until well into the nineteenth century. Thus Mephibosheth fell and became lame at the age of five. Was he the first recorded case of poliomyelitis? Osler believes so.

The first description of poliomyelitis as a distinct clinical entity was in 1789, by Michael Underwood in "A Treatise on the Diseases of Children." The first epidemic was reported by Sir Charles Bell from St. Helena in 1836. In the first half of the nineteenth century, clinical cases of poliomyelitis were rare, and largely confined to infants, whilst epidemics were conspicuous by their absence. In the second half of the nineteenth century, epidemics began to appear, as in Stockholm in 1887 and 1895. These were studied by Médin, and his name is contained in one of the synonyms of poliomyelitis—Heine-Médin's disease—Heine being an orthopaedic surgeon in Germany in 1840. Médin, on an epidemiological basis, showed the probability of poliomyelitis being an infectious disease, but it was Landsteiner who, in 1908, proved its infective nature conclusively by transmitting the disease to monkeys. In the past forty years, vast amounts of research have led to considerable increase in our knowledge of poliomyelitis.

The actual virus is minute, 15-20 millimicrons in diameter, and is thus one of the smallest viruses known. It can be grown by tissue culture from human specimens. Immunological typing resulted in a total of 600 distinct serological types, but fortunately, they fall into three major immunological groups:

Type 1 or Brunhilde
Type 2 or Lansing
Type 3 or Leon

Types 1 and 3 are responsible for most epidemics, Type 2 but rarely.

The virus is world-wide; poliomyelitis as a disease is world-wide too. In an outbreak of poliomyelitis, a large proportion of the population is infected with the virus, but only a few develop poliomyelitis as a clinical disease. This concept of high proportion of infection with very small proportion of clinical disease is fundamental.

The virus can be recovered during epidemics from a large proportion of "contacts"—especially from their faeces and nasopharyngeal secretions.

Spread of infection is probably by carrier contamination of food, and by food contamination by flies.

The incidence of infection is best studied from serum antibody levels. The following facts stand out:

1. Newly born infants have some degree of immunity transmitted across the placenta.
2. Approximately 150 latent cases of poliomyelitis—though some authorities quote 1000—occur for every case of paralytic poliomyelitis.
3. In countries with poor standards of hygiene, infection occurs early in life, in a great proportion of the population, but the incidence of clinical poliomyelitis is low; i.e. the higher the standards of hygiene and civilisation, the higher the incidence of poliomyelitis. The explanation of this is that in less hygienic areas, early infection results in a good, lasting, immunity.
4. The relationship with age: (*a*) incidence of infection increases with age; (*b*) incidence of paralysis increases with age; (*c*) the mortality rises with the age at the time of the infection.

The virus is presented to the person to be infected, either in food, or in "droplets." Spread in the body *via* the axons of peripheral nerves is not now believed to be the avenue of invasion. The present day opinion is that the virus enters the alimentary tract, passing from there to the blood stream; this phase of viraemia occurs prior to the clinical signs of poliomyelitis. Neutralising antibodies develop rapidly and become maximal at at the time of the "major" illness. This must bring the viraemia to a close, and also explains why the virus is so infrequently isolated after the paralysis has set in. The virus is regularly found in the central nervous system soon after the onset of symptoms, and there must take place in the central nervous system, the gravest battle between host and virus, a few hours or days after the viraemia has ended. The outcome of this battle determines the degree of paralysis.

Typically the illness is biphasic, the phases by custom termed the "minor" and "major" illnesses.

The minor illness is a slight catarrhal upset, occurring in about 40% of paralytic cases a few days before the major illness. It is often only recognised in retrospect. The minor phase is believed to coincide with the invasion of the blood stream by the virus. The variety of clinical pictures of the minor illness is tremendous, and no uniform diagnostic syndrome is recognised.

There is often an interval of a few days between the major and minor illnesses in which the patient feels well.

The major illness is usually easily recognised. It is abrupt in onset. The major illness may not lead to paralysis, and the term non-paralytic major poliomyelitis avoids ambiguity. Neither the severity of the symptoms at the beginning of the major illness, nor the changes in the cerebro-spinal fluid, make it possible to say which case will develop paralysis.

The physical examination should be planned to give the maximum information with the minimum disturbance and fatigue to the patient. The patient should be observed carefully, noting the level of consciousness, the presence or absence of a squint, the respiratory rate, etc. The mental state is important: poliomyelitis patients are usually fully conscious, and adult patients may become hysterical with the onset of respiratory difficulty. By looking at the airway, listening to the breath sounds, and observing the irregular and embarrassed efforts to breathe through a pool of mucus, respiratory distress may be discovered.

Respiratory failure may be recognised, provided the larynx is not affected, by getting the patient to count rapidly, observing how far he can count in one breath; 20 or more is normal, but with paralysis and respiratory failure it may be less than 10.

There are certain factors which affect the vulnerability of the motor nerve cells. The first of these is physical activity, and this must be considered from two angles, before the onset, and after the onset of the major illness. Exercise before the onset of the major illness does not have any clear-cut association with the degree of damage to the anterior horn cells. Exercise after the onset of the major illness, however, is extremely dangerous. The type of physical activity is closely related to the site of paralysis; e.g. running—lower limbs: piano playing—fingers and hands. The second factor is tonsillectomy; it was found in 1947 that many cases of bulbar poliomyelitis occurred 7-30 days after the patient's tonsils and adenoids had been removed. The virus was probably present at the time of the operation. The third factor is that of inoculations. It was shown in 1950 that poliomyelitis following within one month of a prophylactic inoculation is liable to take the form of a paralysis of the limb injected. Alum in the diphtheria inoculations was especially incriminated; probably any intra-muscular injection has a similar effect. The conclusion reached is that such factors may affect the segmental blood supply to the cord, interfering with the blood brain barrier, with the preferential settling of the virus in those segments.

Treatment of the minor illness is symptomatic. It is most improbable that the label "polio" can be attached at this stage, and all that is required is for the patient to be protected from undue fatigue.

Treatment of the major illness can give rise to many problems. Physical activity is dangerous, and psychological rest must be ensured at the earliest possible moment. Should the patient be kept at home or sent to hospital? There is no doubt that a journey to hospital may be frightening and exhausting just at the time when rest is essential. Under epidemic conditions the indiscriminate transfer of all suspected cases of poliomyelitis to hospital is probably undesirable, seriously overburdening the hospital staff. The decision to move the patient to hospital should be based on the patient's interests alone; the other members of the family have probably already been exposed to the virus, so that from that aspect, transfer is of no added value.

Isolation is generally practised, although the effectiveness of it in this disease has never been proved.

In considering the care of a patient with poliomyelitis, it should be appreciated that 80% of patients with acute poliomyelitis survive the acute phase however they are treated; their lives are never in danger. Unfortunately, however, an expert degree of supervision is required to recognise early the cases needing special measures. The prevention of dangerous complications should be the aim of every unit admitting patients suffering from poliomyelitis, while the other aspects of treatment such as care of limb muscles is of secondary importance in the acute phase.

In clear-cut cases, "lumbar puncture" gains very little, but if there is the slightest doubt in the diagnosis, it is an essential.

Nursing care plays a tremendous part in the management of a case of poliomyelitis. The confidence and reassurance of an efficient nurse can go a long way to acquire the relaxation, both physical and mental, so valuable to the patient.

Passive movements of the limbs, with the muscles and joints being put through their full range, are the keystone in the management of the paralysed parts. This is to obviate the tendency of paralysed muscles to shorten.

After the full extent of the paralysis becomes evident, the value of bed rest is slight. Muscle recovery takes place for at least six months, and this recovery is believed to be a hypertrophy and increased efficiency of the non-affected muscle fibres.

All the time, the patient must be led along, perhaps at times driven, by the physiotherapist, the doctor, the orthopaedic surgeon, and by his family and friends, all of whom have their part to play. The psychological make-up of the patient needs as much attention as the physical state.

Education of the patient is very important, for with the defect in "brawn," "brain" becomes of even greater importance; the prolonged treatment of hopeless muscles should be avoided, if it is going to interfere with much more important matters concerning the patient's future.

Much is now known about poliomyelitis, but there is still a great deal to be learned before we can feel we know all about it. It will always be one of the most fascinating conditions a doctor can meet.

Book Review

CLINICAL CHEMISTRY IN PRACTICAL MEDICINE

By C. P. Stewart and D. M. Dunlop. Fifth edition, 1958. E. & S. Livingstone Ltd., 27s 6d.

To the casual observer, this new edition would seem to differ from its predecessors only in a somewhat more logical order, an additional 22 pages and an increase in price. Closer examination reveals, however, that a far more extensive revision has been undertaken, and that as many sections, notably the gastric and renal tests, have been reduced, the amount of new material included is greater than the additional pages might suggest. Large increases are to be found in those sections devoted to water and electrolyte balance, to the steroid hormones, and to the metabolic abnormalities, while the accounts of such subjects as electrophoretic fractionation, the histamine stimulation of gastric function and the intravenous glucose tolerance curves are much expanded.

In the methods appendix there have also been extensive changes, much of the more recondite material having been replaced by more modern and more simple alternatives. Of especial interest is the appearance of the Clinitest, Ictotest and other similar proprietary methods now fully established, and the inclusion of paper chromatography for the identification of specific sugars.

This is a book of which one's seniors speak well, and to one about to embark upon his clinical work there can be little doubt that this new edition is a most desirable pre-requisite.

OPERA OCCULTA

COLLECTED FROM THE SOCIETY'S ARCHIVES BY HENRY C. DRYSDALE

On the Linear Transmission of Disease (J. R. SCOTT)

This simple people [Chayma Indians] have an insuperable dislike to cohabit with any deformed woman. This is indeed common to most savage tribes in a state of Nature, which is a state of great equality. Unless a woman be well formed she is neglected and dies barren. In Europe and wherever artificial manners prevail, ugly and even deformed women marry. The cupid of commercial countries is not the cupid of Pastoral poets.

* * *

. . . He speaks too of a gentleman begetting a daughter with eyes and hair differently coloured from any of his children, his wife, or himself, and imagining this arose from his thinking (sub coitu) on a little brunette he had taken a fancy to. It might or might not be from this cause, but I have no idea that hanging the bridal bed with a pall, would tend in the least to produce a Negro child. The sight of a Negro footman might be added without danger; but their contact would be more effectual in changing the colour of a first born. Physiognomy is no doubt varied by causes operational on the mind at or about the time of conception or it may be on the senses, and it is between the Physiognomy of man in its varieties and the variety of colour in domesticated animals that the analogy seems chiefly to exist.

On Typhus (R. F. Osborne)

It is recommended by some to bleed from a large orifice in the erect posture or as near it as circumstances will allow "ad diliquium animi." I must confess that if bleeding is to be performed I rank myself among this class—for of all things I think half measures the most abominable. There may be cases that require them but they are comparatively few. . . . I conceive that bleeding performed in this way is one of the most powerful remedies that can be employed in the case of fever. It may be said really to induce a state of the system totally incompatible for the tissue with febrile action, and the quantity of blood lost is so trivial that it rather serves to ease the system of the burthen of its suppressed secretions than to induce that state of alleged debility which the antivenesectors cry out so much about.

* * *

Blisters—though objected to by a few, seem to meet with the approbation of the generality of Practitioners. It is not easy to say how they alleviate the symptoms for which they are employed. It is said by some to be by derivation, by others, by the fluid which they cause to be secreted, or by both of these ways—and it has even been attributed to the absorption of the cantharides, etc.

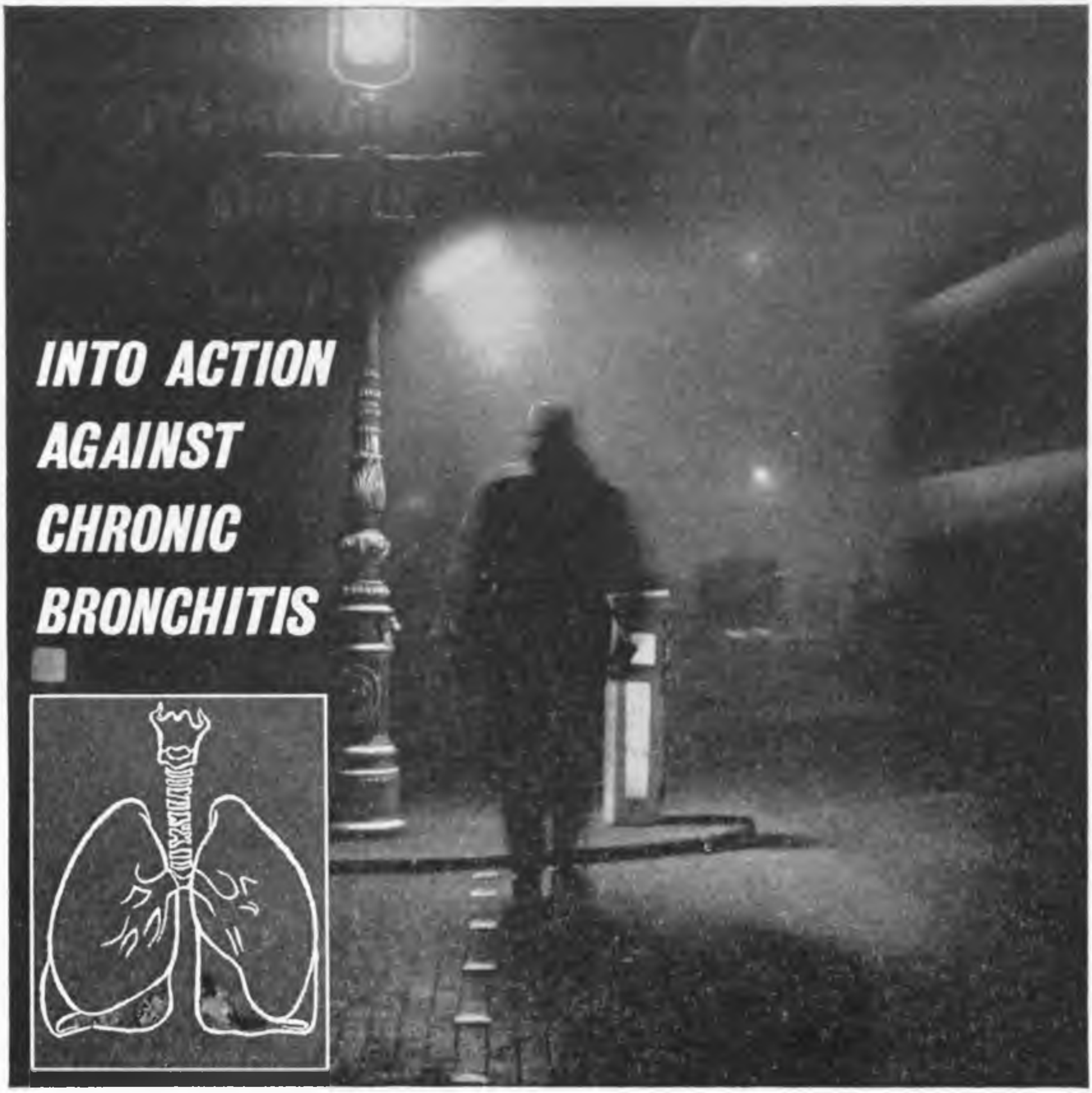
It is certain, however, I believe, that they so relieve in general the violent headache and other symptoms for which they are used. They are sometimes in desperate cases applied as general stimulants to rouse the vital principles—but scarcely ever with success. I understand they have been recommended to be placed along the spinal cord to allay the inflammation which is supposed generally to affect its membranes in cases of Typhus.

On Paralysis (J. Cochrane)

Rubefacients, the most particular of which are sulphuric acid and nitric acids interblended with unctuous substances, ammonia, the essential oil of Turpentine, oil of Amber, mustard and Cantharides; seem to be more beneficial when frequently repeated and a moderate stimulus kept up, than when by their long continuance they inflame the part.

On Exercise (A. G. Moller)

Speaking of the hypertrophy of muscle with great use . . .
When in uncovering the sad relics of humanity in the hospitals and dissecting rooms of Paris how well and how beautifully marked do we trace in the French subject those well developed muscles the voluntary motion of



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* * *

Exercise should also be moderate as to its general quantity, and this on account of the mind as well as the body. Moderate exercise invigorates and improves the mind and fits it for its proper offices. Too much devotion to it, indeed to all bodily pleasure, weakens or debases both; and though Socrates disdained not to learn dancing to preserve his health, though the wise and learned queen of Palmyra delighted in the exercise of the chase, though the divine Plato from a "broad-shouldered wrestler" became a philosopher, it will perhaps generally be found that those entirely devoted to such pursuits are men of brutal disposition and incapable of purely mental excitements and enjoyments.

* * *

Exercises should be attended to as it influences the passions of the mind. Hence those exercises should be used which moderately excite the better passions, and those avoided which call forth the worse. For this cause we must disapprove of such exercises as Boxing, Fencing, and others which, however they may be attended with some advantages, are too likely to call forth the violent passions of anger, hatred and revenge. These passions are calculated to produce very bad effects on the bodily health as well as on the moral and intellectual systems. Topical injuries also and even sudden death are very likely to occur during these exercises, either by accident or in consequence of the excitation of those passions.

Enteritis (G. B. WADDELL)

When the ulceration takes place in a rapid manner the intestines are sometimes perforated with holes so that their contents escape into the cavity of the abdomen. . . . Dr Baillie remarks that he has seen a communication established in this manner between the Vagina and Rectum in the Female, and between the Bladder and Rectum of the Male, moreover he has observed that connections formed between the Kidney and Intestines, where this morbid state existed. This is a wise provision of nature, by which the purulent matter, that would otherwise have been evacuated into the general cavity of the abdomen, is conveyed off by a ready channel and thus the supervention of peritoneal inflammation which would shortly have destroyed life is prevented.

The Enteric Fever of the West Indies (W. GRAHAM, M.D.)

It may not be irrelevant to add very briefly to the necessity of keeping up the cuticular discharge which is so essentially conducive to a state of health in tropical climates, and in proportions as the pores are open is evinced the superiority of the system to resist the effects of augmented temperature; during violent exercise, or while pursuing a journey, it will be necessary to recruit the exhausted frame by frequent libations of a beverage more renovating and more potent than water. The safety of the practice is proved by the universal adoption of it by the inhabitants of the West Indies, who never experience any of the dreadful effects, which a late author so ingeniously ascribed to indulgence in the Sangaree bowl.

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A man may be wealthy but what is the use?
  If the same man's not healthy his life's just abuse!
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It is pleasant to taste, it is pleasant to smell
  But a Guinness is more – it's a tonic as well.

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