

late than too soon. When she does, the greatest care should be taken to see that she works to the best advantage. "Fifteen minutes devoted to careful direction of the powers at the beginning of the second stage are more valuable than two hours of harsh exhortation after the patient has become fatigued" (Beck).

(Illustrated by Miss Sylvia Treadgold from pictures in De Lee and Greenhill's *Principles and Practice of Obstetrics* and the *American Journal of Obstetrics and Gynecology*. With acknowledgments to the authors and publishers.)

RHEUMATIC DISEASES AS DISEASES OF ADAPTATION

PROFESSOR HANS SELYE'S HEBERDEN ORATION

Professor Hans Selye, of Montreal, divided his Heberden Oration before the Heberden Society into two parts, delivering the first on June 2, and the second on the following morning. Both were delivered in the Old Library of B.M.A. House, which was packed to the doors. Dr. W. S. C. Copeman presided.

The subject chosen was "Rheumatic Diseases as Diseases of Adaptation." In the first part Professor Hans Selye gave an outline of the theoretical basis of treatment directed against the stress factors in disease, and illustrated the development of this concept by what he called a somatic sketch of the various physiological relations. Any disease or any exposure which might be within the limits of the physiologically normal would not only cause damage but would also stimulate defence. The same exposure to stress might produce manifold and varied results, the particular result being conditioned by hereditary or dietary or many other factors.

The clinical applicability of this concept had been made possible thanks to the enormous advances made by organic chemists, who had furnished the hormones which were essential to the working out of the hypothesis on the clinical plane. He mentioned in particular the work of Kendall and of C. H. Li. Considerable credit must also go to the clinicians who first described the clinical applicability of this type of therapy, especially to Philip Hench, who was his predecessor as Heberden orator two years ago.

Clinical Demonstrations

Professor Hans Selye then showed by means of comparative photographs the rapid clinical improvement and even cure brought about in certain cases by A.C.T.H. or cortisone. His first example was of rheumatoid arthritis of the elbow joint. Within four days of the administration of A.C.T.H. the relaxation of the joint was such as to permit the normal raising of the arm, which had only been very restricted before. The result seemed to be due to the great absorption of the granulation tissue which had accumulated around the joint. In another case of rheumatoid arthritis with swollen fingers there was marked regression within five days of the administration of A.C.T.H.

The next case demonstrated was one of lupus erythematosus. This patient came under treatment when she was almost moribund. She received A.C.T.H. at once. Before treatment she had the butterfly rash on the face, high fever, and extremely rapid sedimentation rate. A.C.T.H. was given in divided doses several times a day. Within a few weeks the skin of the face was completely normal, the fever had subsided, and the sedimentation rate was normal. Unfortunately it was to be observed that the facial expression had changed. Cushing's disease, with the typical "moon face," made its appearance. The patient had exchanged a fatal lupus erythematosus for Cushing's disease with its vascular hypertension, hirsutism, adiposity, and osteoporosis. But he was happy to add that, the A.C.T.H. administration having been stopped a few days subsequent to the picture revealing the Cushing's syndrome, the unusual manifestations disappeared completely and the lupus did not recur. The patient was now

a lovely-looking girl in perfect health. Recurrence of the disease must, of course, always be feared, sometimes almost immediately following withdrawal of treatment, sometimes a few weeks later, but this was an exceptional case.

Psoriasis was another disease of adaptation. It fitted in very well with what was known about changes in the collagen. He showed illustrations of a very bad case of psoriasis, one of the worst he had ever seen, and drew attention to the intense scaling. A few days after treatment—in this instance with cortisone, though A.C.T.H. acted in exactly the same way—the granuloma became acellular and starlike, and eventually there was completely healing. There were, however, several cases of psoriasis which were very resistant, and the reason for their resistance was still unknown.

Other Diseases of the Group

Gout was another disease of this general group. It did not belong to the collagen diseases in the strict sense of the word, but before A.C.T.H. had ever been conceived the attention of the medical profession was drawn to the consideration that gout might be a disease of adaptation. A gout attack might be produced by certain forms of stress—surgical shock, exposure, infections, etc.—and, based upon that, it was demonstrated early in 1948 in people who suffered from gout but were not having a gout attack at the time that gout could be precipitated by A.C.T.H. In these cases of predisposition not only could an attack of gout be precipitated by A.C.T.H., but, if smaller doses were given and given more gradually, the effect was to deplete the body of the uric acid store and so prevent an attack. An attack of gout could be precipitated or prevented, according to circumstances, by A.C.T.H. The orator showed photographs of a typical case of gout and of the same case only a few days later after the tophi had liquidated and the patient was much relieved.

A case of pancarditis treated with cortisone was next demonstrated. This was in a young boy who came to hospital with severe rheumatic pancarditis, so severe that it might be said that he was moribund. He was given cortisone in large doses in view of his condition, and here again there was clearance. Until a water-soluble cortisone was available—as he thought it would be within the next year—it was well to remember that A.C.T.H. was the more rapidly acting drug.

At this point the orator mentioned certain of the important laboratory findings in cortisone treatment—the temperature, the erythrocyte sedimentation rate, the ketosteroid excretion rate, and finally the eosinophils. In the case of pancarditis just mentioned the temperature before treatment was 103° F.; it suddenly dropped to normal within a couple of days, and remained low during the whole of the treatment. The ketosteroids rose rapidly with cortisone administration and then fell equally rapidly. Eosinophilia went back rapidly under the influence of cortisone, returning when treatment was discontinued. It had been proved that the characteristic blood changes were not due to any metabolic alteration, but to cortisone given by itself or liberated by A.C.T.H. There were very few, if any, changes with A.C.T.H. which did not also occur with cortisone.

Ophthalmic Conditions

He turned next to eye conditions. Many of the acute inflammations of the eye had been repeatedly referred to as of the rheumatic type. The rheumatic and allergic types were from a morphological point of view difficult to separate, and it was amazing how many entirely different conditions could be dramatically improved and in some cases brilliantly cured by A.C.T.H. or cortisone therapy. His first example was a case of conjunctivitis vernalis which, within 48 hours of the administration of the therapy, was almost normal, and a few days later completely normal. Another was a case of herpes zoster of the eye in a woman aged 64, which cleared up within four days of cortisone administration. Another was a case of acute choroiditis. This was first treated with a hormone derivative which had a cortisone-like action. The pharmaceutical industry in Canada had paid attention to a number of steroid derivatives of cortisone, but although he had tried all these so-called cortisone substitutes he had never been able quite to convince

himself that they had the efficacy of the original. The results with these substances were published by people who had never seen the action of cortisone itself. A number of substances would liberate A.C.T.H. endogenously, but the effects of cortisone itself were so dramatic that once they were observed they would be put in a different category from the others. At the same time it was not theoretically impossible for other steroids to act in man, even though not in animals, because in man the situation was so much more complex. He could only say that neither animal experiments nor clinical observation had given him personally any satisfactory and convincing proof that this had been actually accomplished up to now.

Of the other eye cases demonstrated one was of fulminating hypopyon. The colour photograph showed how cloudy was the anterior chamber. Two days later, after the administration of cortisone, the hyperaemia had receded, though it was not completely gone, the eye was transparent, and the whole of the keratinization was absorbed except for a thin film. Another case was one of specific choroiditis, which cleared up three days after cortisone treatment.

In connexion with the use of cortisone one big problem was that of complications and availability. When cortisone was available only in small amounts, preference should be given to those cases in which, if the disease were left alone, complications could occur. Some eye diseases, for example, might lead to blindness, but with cortisone marvellous results could be obtained—true cures and not mere remissions. Small quantities could be used, because cortisone acted locally and could be injected under the conjunctiva or used in the form of eye ointment. With 2 mg. of cortisone the eyesight might be saved, while 80 mg. might be used for rheumatoid arthritis and not do any good.

If time permitted he could show cases of the kind he had illustrated for hours and hours. He had recently reported the conditions under which improvement could be obtained under the influence of either cortisone or A.C.T.H. or both, but he thought the selection he had made was sufficient for his present purpose.

Disadvantages of the Therapy

It was necessary to mention the disadvantages of the therapy. He had already mentioned the production of Cushing manifestations. The possibility of producing severe renal complications was known. Other changes might be inhibited, but not renal changes, which might even be aggravated. On giving the hormones to animals, fulminating renal changes might be produced, with massive haemorrhage. In clinical cases so far this had occurred very rarely, but when it did occur it was serious. Another important point to remember was that brain manifestations were not at all inhibited by cortisone, and again might be aggravated. Patients under an overdose of cortisone showed excitement and marked euphoria, which might become psycho-pathological, and was often followed by depression. He had in mind two cases in which shock therapy was necessary because of schizophrenic manifestations. Such cases were extremely rare, but they had been mentioned. Another complication was osteoporosis. He had personally great hopes that it would be possible to overcome these complications and selectively produce one or other effect as desired. There were already indications experimentally that this could be done. What was wanted was selectively to eliminate all the changes save one.

He passed to a few criticisms which had been made. With regard to non-specific therapy, he reminded the audience that non-specific therapeutic agents, such as exposure to heat, and fever therapies of various kinds, had been long known for their beneficial effects in the rheumatic types of disease. People responded in different ways to the same stimulus, the particular way being determined by the metabolic habits of the individual, for there were metabolic habits as well as other habits which might, so to speak, be shaken out of their rut. He recalled Dr. Hench's Heberden oration of two years ago, in which he told how the reversibility of rheumatoid arthritis in pregnancy, jaundice, starvation, or after surgical operations gave him the idea for the application of this kind of therapy in clinical disease. The curative efforts of nature went on under condi-

tions of stress. All this had been reproduced in animals. It was his firm belief that all vital change following the use of these agents and of many others not mentioned which had been used by clinicians in non-specific therapy were due to stress factors and the liberation of A.C.T.H. endogenously.

The Philosophy of the Matter

Perhaps the most fundamental objection to the theory was that it seemed difficult to visualize how some pathogen could cause such a multiplicity of diseases in man. There was an opinion abroad that every disease must have its own separate cause. But in animals at least it had been proved that one agent could act differently, depending largely on the conditioning factors which sensitized or desensitized any one organ. This was a fundamental point in the philosophy of all this work. He asked his audience to place itself in the position of a group of physicians in the time before tuberculosis had been worked out. How surprised they would have been to be told that a multitude of manifestations, in the lungs, in the bone, in the skin, in the kidneys, in many organs and tissues, were due to the same pathogen. One could hardly find a more widely different group of diseases in internal medicine, and yet all caused by the same pathogen. It was not an unreasonable conjecture when it was suggested that a wide variety of so-called diseases of unknown origin were diseases of the adaptation syndrome.

Professor Hans Selye concluded by saying that in this oration he had been able to give only a brief outline of the whole concept. He had given only some of the theory and mentioned some of the facts. In medical research it was absolutely essential that the facts should be correct. The only purpose of a theory in medicine was to act as a line of guidance and lead to the elucidation of important new facts. He thought he could say safely that the facts which he had reported were correct. Whether the theories would be useful only their application to medicine would be able to prove.

A Brilliant Generalization

Sir Henry Cohen, president-designate of the Heberden Society, said that the Society had been privileged on many occasions to entertain distinguished orators, but he doubted whether there had been an orator who had surpassed Professor Hans Selye in the material he had brought forward, in the brilliance of his exposition, and in the keenness of his wit.

They had listened to a most fascinating laboratory story which had been applied to the wards. Not for a long time had there been a more striking demonstration of the importance of a fruitful hypothesis. We lived in a scientific world in which there was an almost overwhelming activity in relation to facts, and few people were sufficiently bold to attempt the wide generalization, the synthesis of those facts which meant so much for the philosophy of medicine. Professor Hans Selye had made that attempt and had done so with his eyes wide open. He knew that, sooner or later, some of the facts he had observed might be disputed, and some of the observations, clinical or other, might be found by other observers to be inadequate or to bear a different interpretation. It might well be that some of the theories which had been enunciated by Professor Hans Selye would have to undergo modification. That was the fate of all great generalizations.

This was another systematization of medicine. The history of medicine revealed a number of systematizations. About a century ago medicine was in the throes of a systematization in a way not unlike the present. It was then being urged that all diseases were the result either of stimulation or of repression. Patients were divided into sthenics and asthenics, with a sedative (opium) for the one and a stimulant (brandy) for the other. In either case the treatment was acceptable to the patient. Cortisone and the other preparations perhaps had not the same narcotic or exhilarating effect. But at all events here we had again this double conception. Perhaps one day they would have the rationalization of the manifold. But for this they must have a wide vision. They must have men of courage as well as men of learning and understanding, and men also who

were capable of expressing their views to lesser people who could not delve so deeply into the mysteries of nature.

The experience of listening to Professor Hans Selye had been one he would not have missed, and the rapt attention of the audience and the reception accorded to the oration showed how deeply this brilliant exposition of a most fascinating piece of research had been appreciated.

Dr. C. W. Buckley seconded the vote of thanks, and, in asking the president to bestow upon Professor Hans Selye the Heberden medal, mentioned that the last recipient of it was also from across the Atlantic—Dr. Hench. It should be a challenge to research workers in this country that this distinction had twice in succession gone overseas.

THE WORK OF W.H.O.

DIRECTOR-GENERAL'S ANNUAL REPORT

At the recent assembly of the World Health Organization in Geneva two large volumes¹ were placed before the delegates, one containing the report of the Organization's activities during 1949 and the other the proposed programme for 1951. The work to which it is committed and the further work proposed is spread over a very large field. It is in three major parts: central technical services, advisory services, and administrative services, the last being the executive and financial buttresses of the other two. The technical services range over epidemiological information, health statistics, biological standardization, and like activities, and the advisory services, which are carried out through the regional offices by joint action in the field with the respective governments, include the organization of public health services, campaigns against communicable disease, and the assistance of professional and technical education.

An obvious function for such a body as W.H.O. is the collection and distribution of epidemiological information on a world-wide basis. This is beyond the scope of any single national health administration. Indeed, the exchange of information of one kind or another is the first duty to be assigned to an international office, but this is not just a post office activity, as it might well be if all nations were on the same level of development and shared the same outlook in health matters. It calls for consideration of the medical position in each country, also local customs and traditions, and even certain sensibilities. W.H.O. has recently completed a *Pharmacopoeia Internationalis*, and part of the 1951 programme is the preparation of addenda to this work. Another field is the co-ordination of research, instanced by the recent establishment of a research office for tuberculosis in Copenhagen, which is charged with the collection and analysis of data concerning the international B.C.G. campaign and the investigation of B.C.G. vaccines and of the effectiveness of mass vaccination in prevention. Owing to the advantages to be derived from its standardization, B.C.G. vaccine tends to be very conspicuous in the work of W.H.O. Of other statistical studies two recent ones are of interest—the compilation of statistics of mortality according to causes of death in different sex and age groups in different European countries, and the collection of statistical material about cancer mortality in selected European countries over an extended period.

Communicable Diseases

Seven teams are working on malaria control in India, Pakistan, and adjoining countries. A striking instance of the help given to governments in promoting public health administration is afforded in Italy, where experts in malaria, tuberculosis, maternal and child health, environmental sanitation, and laboratory and other services have been provided. Regional offices for South-east Asia (at New Delhi) and for the Eastern Mediterranean (at Alexandria) were started last year. The other regional offices are for Europe, Africa, the Western

Pacific, and the Americas. From the office for Europe work is being done or is projected in almost every country of the continent, even including non-participating Bulgaria, which asked—and received—help in its projects for malaria and insect control and in the penicillin treatment of syphilis. To Bulgaria also two fellowships were awarded for the study of communicable disease. One of the most important projects in which W.H.O. participated last year was the organization of medical services in Syria, the Hashemite Kingdom of the Jordan, and Lebanon, to assist with the U.N. relief project for Palestine refugees. W.H.O. has fifteen expert committees, on all but one of which there is an expert from the United Kingdom eminent in his own field. Last year W.H.O. assembled forty conferences and study groups of various kinds, participated in 170 others, and published some 150 technical reports.

Attack on Tuberculosis

The programme for next year is contained in a heavy volume of 300 pages. In general it follows the plan already operating. One of the principal lines of attack will be upon tuberculosis. It is proposed to provide consultants or advisers in tuberculosis in each of the six regions and demonstration teams in five of them. The fellowship programme is being continued and developed. Its purpose is to select and train persons so that they may introduce new knowledge into their countries and be leaders in its application. The number of fellowships to be given in 1951 is 230, of which 85 will be in the European region. The scheme includes not only travelling fellowships, undergraduate and postgraduate, but scholarships in selected institutions. Nearly half a million dollars is to be provided for the assistance of educational colleges. It can be well understood that one of the most serious problems facing an organization of this kind is the lack of adequately trained people in many countries.

Perhaps the most imaginative report submitted to the assembly which closed on May 27 concerned the plans, conceived a year ago but now worked out in concrete form, for the help of under-developed countries, to enable them to build up their own public health services by making available to them the necessary medical knowledge and technical skill. The Director-General, Dr. Brock Chisholm, writes in his report: "The improvement of health—important as it is—is only one of the results which may be expected to come from W.H.O.'s contribution to the technical assistance programme. Since there is an unmistakably close relationship between health and production, intelligent investment in the health of the people is bound to increase considerably agricultural and industrial production in all countries. Increased productivity everywhere means the raising of living standards everywhere—a prerequisite for the establishment of lasting peace."

WEST LONDON MEDICO-CHIRURGICAL DINNER

The annual dinner of the West London Medico-Chirurgical Society was held at the Royal College of Surgeons on June 2. Mr. V. B. Green-Armytage, president of the Society, was in the chair. In proposing the toast of the Society Sir Cecil Wakeley, P.R.C.S., recalled the achievements of the West London Hospital, or the West of London Hospital as it was called originally, during the last 95 years. Several of his own teachers, including Sir David Ferrier and Sir Lenthal Cheatle, men of international repute, were originally on the staff of the West London. Two of the West London surgeons had become presidents of the Royal College. In one way the West London Hospital had had a "raw deal." It was asked to undertake postgraduate education, then undergraduate education, and now to give up undergraduate teaching and go back to postgraduate. But the staff there had done a great deal for the profession as a whole, as doctors all over the world would acknowledge.

Mr. Green-Armytage, in responding, said that the Society was formed for the mutual benefit of general practitioners and consultants with just over a hundred members. It reached 600

¹Official Records of the World Health Organization: No. 23, Proposed Programme and Budget Estimates for 1951; No. 24, Annual Report of Director-General, 1949, 1950, Geneva.