THERAPEUTIC TENDENCIES.*

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In an old book given to me by a patient, *Culpeper's Last Legacy*, the sixth edition, dated 1680, that famous seventeenth-century practitioner has set forth his "Choicest Secrets" for the benefit of posterity. For the most part it is an olla podrida of prescriptions for ailments of every kind culled from various authorities, many of an outrageous, disgusting or obviously superstitious nature, and some frankly ludicrous. One of Culpeper's remedies for epistaxis is to "put a piece of hot hog's turd as it comes from the hog up the nose!" Another, derived from Mizaldus, is to write *consummatus est* on the patient's forehead with his own blood. "If any be troubled with stomach worms," observes our good Nicholas, "let him hold a piece of a honey-comb in his mouth, and the worms will come out to the honey."

Still, Nicholas was no quack; no fool, either. Many of his suggestions are quite sound. He was, of course, a famous herbalist; he was also an anatomist, who made his own animal dissections, and had no scruples about giving Galen the lie direct when he found his descriptions inaccurate. In this last book, having previously dealt with simples on the same lines, he devoted several chapters to a synopsis of the compound remedies in general use in his day—and some of them are still far from obsolete—in which these are methodically tabulated according to their supposed general or local effects.

At no period has the practice of medicine been wholly empirical; and it certainly was not so in Culpeper's time. Among the great array of his remedies, genuine or supposititious, no choice could be made without guiding principles of some sort. We find these clearly indicated in Part III of his *Last Legacy*, entitled "Aphorisms." From this it appears that all medicines may be classified as heating, cooling, drying or moistening in effect; and that each of these qualities may be subdivided into four degrees. For example, a fluid which by outward application caused burns or blisters would be called heating in the fourth degree, and as such unfit for internal administration. Pathological conditions are similarly classified as hot, cold, dry or moist; and the general principle seems to have been that the kind and degree of pathological deviation, local or general, was a guide to the appropriate remedy. Thus, a condition of heat and dryness of the second degree would indicate a remedy cooling and moistening in the same degree. A moist remedy would be one which caused a flux of any kind—a purgative, diuretic or diaphoretic; a dry one would be a local or general astringent.

In addition to this primary classification, remedies are grouped in accordance with their topical affinities—what we should call their organotropisms. Part IV of the *Last Legacy* is devoted to aphorisms intended to guide the physician in the choice of drugs adapted to particular organs—for example, "cephalicks," "pectorals," "cordials" (that is, cardiac remedies), "renals," "hystericals" (that is, uterine agents), and so forth. Culpeper attached some importance to odour as a guide to remedies, particularly for those classified as "cephalicks," most of which are of a pleasant and aromatic or else of a decidedly nauseous odour. He thought that there was a special relation between the brain and the uterus, the joints and the stomach, so that all are similarly affected by the same drugs. He attached some importance to the doctrine of "signatures," that "yellow purges choler, black melancholy, white flegm," and so forth. He was also a professed astrologer, who was careful to gather his herbs under favourable aspects. But his mysticism is tempered by common sense, just as his inert or crude drugs are prescribed with suitable adjuvants or correctives. Such, then, in brief outline, were Culpeper's guiding lights. It will be interesting to compare with them those which underlie distinctively modern methods.

Of these, let us consider first the group of remedies comprised under the term vaccine therapy, a method rescued from empiricism by Pasteur's epoch-making discovery of

the rôle of the yeast plant in fermentation, and Davaine's identification of the anthrax bacillus. Like all great discoveries, this was but the bringing into clear light of a principle already adumbrated in the consciousness of mankind. The practice of inoculation for small-pox was begun in the early part of the eighteenth century, the famous Lady Mary Wortley Montagu having played a pioneer part in its popularization. When, in 1798, Edward Jenner, after twenty-five years' research, published his *Inquiry into the Causes and Effects of the Variolae Vaccinae*, the cruder form of prophylaxis was for some of his medical opponents a lucrative speciality. Jenner himself was led to investigate the subject by his frequent failure to inoculate with small-pox those of his country patients who had suffered from "cow-pox," and the discovery of a vague opinion among dairy folk that this was a preventive. It is the great principle of attenuation which is the foundation stone of vaccine therapy; and this stone was laid by Edward Jenner. I have searched Culpeper's book in vain for any evidence of awareness among seventeenth-century practitioners of the true nature of infection. In a section devoted to the Pestilence, he goes out of his way to combat the exaggerated terror of the disease, which in his day too often deprived sufferers of the services, not only of their neighbours, but even of a physician. He himself attributed the disease to a corrupted and unwholesome air caused by a malign conjunction of the superior planets. It is interesting, however, to find among Culpeper's prescriptions one recommending drachm doses of the desiccated and pulverized liver of a rabid dog as a remedy for the bite of such a dog. Also, there seems to be an anticipation of modern surgery in the strong recommendation of a linen cloth soaked in lime-water, prepared by pouring boiling water on quicklime in a clean new earthen vessel, as a dressing for wounds and ulcers. "This water," says Culpeper, "draws out the corruption of putrified sores. Mizaldus extols it to the skies."

The Jennerian method—that is to say, the introduction of pathogenic organisms in a living although attenuated state into the circulation—is not, of course, obsolete, but is, I think, in a fair way to become so. The awkward consequences that sometimes follow vaccination are, no doubt, in the majority of cases due to septic complications, but there must always be an element of uncertainty as to the behaviour of a living virus when introduced into a human organism. The modern tendency in vaccine therapy—a tendency accelerated, if not initiated, by the researches of Ehrlich and Almroth Wright—is to transform a biological and empirical into a chemical and truly rational method. These two distinguished men have approached the problem of the treatment of infective maladies the one from the chemical, the other from the biological point of view. Ehrlich's famous side-chain theory was an extension to the biological sphere of a hypothesis derived from the study of complex organic molecules, and was utilized by its inventor in an attempt to evolve an improved method of chemical treatment. Wright's opsonin theory was based on observation of the phenomena of infective and counter-infective processes, and is the basis of modern vaccine therapy. Yet the common aim of both investigations tends to a similar goal. In his recent investigations Wright has been drawn to inquire into the possibility of immunization *in vitro*, and deems it possible, "not only to test the efficiency of vaccines on normal blood *in vitro*, but also to determine upon the patient's blood *in vitro* what vaccine and what dose of that vaccine would give the desired effect." This clearly would be a close approximation to the ideal pharmacological method, especially in view of the fact that vaccines tend to conform to the chemical type of remedy, as isolated toxins of presumably definite and ascertainable composition. The term chemio-therapy calls to mind Ehrlich's epoch-making discovery of salvarsan (dioxydiamidoarsenobenzol dichlorhydrate), but the objective of his *therapia sterilisans* is, of course, achieved in a different way. With vaccines it is always an active immunity, due to exploitation of the latent phylactic resources of the patient, that is aimed at. Salvarsan is, by reason of its direct attack upon the spirochaete, comparable to an antibacterial serum, such, for example, as Yersin's bactericidal plague serum. This fact constitutes at once the strength and weakness of the method: on the one hand, the benefit is prompt and independent of the constitutional response of the patient; on the other hand, it is a merely quantitative effect, the

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number of spirochaetes rendered *hors de combat* is necessarily limited by the amount of "606" that can be brought to bear on them. The defensive process initiated or augmented by a vaccine bears no necessary proportion to the dose introduced; the effect is, it seems to me, qualitative rather than quantitative. On the other hand, as Wright himself admits, vaccine therapy is permissible only when the body is not already making its maximum immunizing response, and is also generally unsuccessful in presence of pyrexia and severe constitutional disturbances, unopened abscesses, and foul, discharging or sloughing wounds. It gives less favourable results in long-standing than recent infections. As between the direct attack of antibacterial or antitoxic serums upon the pathogenic organism or its toxins and the evocative action of vaccines the present therapeutic tendency is decidedly favourable to the latter method—that of active in preference to passive immunization.

It is an interesting, albeit somewhat speculative, question to ask how our views of drug therapy in general are being or are likely to be modified by the dominant conception of immunity. To some extent one can recognize a similar duality in the use of drugs to that involved in the distinction between vaccines and serums, active and passive immunity. "The whole ground of Physic," says Culpeper, "is comprehended in these two words, *Sympathy* and *Antipathy*; the one cures by strengthening the part of the body afflicted, the other by resisting the malady afflicting." Here, surely, are foreshadowed the two points of view which were later to split the profession into conflicting schools of thought. There is, however, nothing really incompatible in these two points of view; belief in the efficacy of Behring's serum does not preclude faith in that of anti-enteric vaccine. In a lecture delivered last year Sir Almroth Wright described experiments proving that "in response to inoculations of a staphylococcal vaccine the blood serum and lymph acquire bactericidal powers for both staphylococci and streptococci." In fact, it would seem that immunity is not, as has hitherto been thought, merely specific; inoculation may produce collateral as well as direct immunity. This conclusion suggests the questions whether something comparable to immunity be attainable by ordinary drugs, and whether the leaning towards vaccines rather than antitoxins—towards what Culpeper calls the method of "sympathy," of "strengthening the part afflicted"—be discernible in the wider field of modern medicine.

If, as can scarcely be questioned, the legitimate resources of drug therapy include the administration for curative purposes in medicinal doses of remedies capable of producing symptoms resembling those of the malady under treatment, it seems that the conditions of success must be approximately the same as those experimentally established in and for vaccine therapy. Such a method might appropriately be termed *synergic*, in distinction from the more widely applicable *corrective* medication, of which, say, the administration of a purge on general principles, of a dose of sulphonal or barbitone for insomnia, or of a combination of alkalis for acidosis, are examples. I have more than once observed symptoms suggestive of anaphylactic shock in endeavouring to push remedies like arsenic, and I am inclined to think that much better results might be obtained in drug treatment, and particularly with definitely organotropic remedies, by a modification of dosage and periodicity based on the assumption of the occurrence of a "negative phase" or period of diminished therapeutic susceptibility. It surely savours of crudity to jump straight to our maximum dose of such potent remedies as digitalis, nux vomica or strophanthus, and to give these for weeks together at intervals of three or four hours only, although when we push digitalis to clear up a dropsy we are after all using it correctively, not curatively.

Assuming that impaired nutrition is basic in most diseases, my suggestion is that a drug capable of acting as a physiological stimulus to a given organ will in smaller doses act as a *trophic* stimulus, and that such stimuli, if maintained long enough and never exceeded, will in some cases re-establish the normal nutrition and, consequently, the normal function. Further, that the maximum trophic effect will be produced by a dose just short of that productive of an appreciable physiological effect. This dose must not be regarded as a fixed quantity; as soon as tolerance of the original dose is established it should be

cautiously increased. As regards the spacing of doses no fixed rule can be laid down, but it should be long enough to preclude such heaping up of the trophic effect as would result in functional stimulation. Thus the medicine may be given night and morning, or, in some cases, once daily or less. The common observation that a remedy continued too long "loses its effect," the facts of drug and tobacco tolerance, and the enormous quantity of alcohol that some people can take with apparent impunity, all suggest that the principle of immunity has wider application than is yet commonly realized.

A closely related subject is that of toxic idiopathies, particularly those which manifest themselves in the form of coryza and bronchial asthma. Dr. John Freeman in a recent lecture showed that abnormal sensitivity to foreign proteins, such as grass pollens and animal emanations—for example, from the horse, cow, or, above all, the cat—can be detected by the production of conjunctival or cuti-reactions. In bronchial asthma, which he regards as the result of the endotoxin of the microbe causing the bronchitis, the skin reaction can be produced by using a solution of this microbe. Food idiosyncrasies can be tested for in the same way. Hypersensitiveness to foreign proteins is, he finds, commonly a family trait, but is apt to take diverse forms in its different members. I have myself often noted the occurrence of a liability to hay fever, asthma, or urticaria in members of the same family, and sometimes alternating in the same person. With regard to food idiosyncrasies, Dr. Freeman suggests that where mothers insist on faddy children finishing up their meals they are probably immunizing them against slight hypersensitiveness of this kind. In this, as in many other respects, modern mothers might with advantage revert to the sturdier methods of their Victorian forebears.

The department of modern medicine, comprised under the terms organotherapy, opotherapy, or endocrinology, may, I think, best be characterized as a realm of great expectations. We hope much of it, but, except in the treatment of such rare diseases as myxoedema, mongolism, or scleroderma, it is difficult to point to notable achievements. Although regarded as a distinctively modern method, its origin is deeply rooted in antiquity. "Dry a Bullock's, Sheep's, or Goat's bladder," writes Culpeper, "and beat it into powder, and give a drachm of it in water, vinegar, or any convenient liquor to such as cannot hold their water or use to piss abed and it will help them." In another section he affirms that the internal skin of a hen's gizzard "helpeth concoction"—that is, digestion—exceedingly; "nothing like it" if given after meals. Also he asserts that "the Brains of a Weazel dried and drunk in vinegar cures the Falling sickness." In a recent paper on the nervous system and the endocrine glands, Dr. Sybil Welsh suggests that below the level of the most simple type of nervous stimulus there is a set of systems of chemical control, aiding the co-ordination of the processes of nutrition, growth, and reproduction. In spite of the valuable work of Blair Bell and others, our knowledge of the mutual dependencies and reciprocal actions of the endocrine glands, and even of their individual effects, is still inadequate for confident generalization as to their therapeutic rôles. We are as yet mainly confined to the phase of empirical gleaning. The available secretions may be used in one of six ways: (1) diagnostically, to determine whether symptoms be due to excess or deficiency; (2) to compensate for a deficiency; (3) homo-stimulatively; (4) hetero-stimulatively—for example, in giving thyroid to promote ovarian secretion; (5) to inhibit excessive activity, as in the use of mammary extract to diminish ovarian activity; and (6) physiologically and occasionally, as in the use of adrenaline as a haemostatic or pituitrin to facilitate parturition. Of these six methods, by far the commonest and, so far, the most successful, are the second, of which thyroid feeding is a familiar example, and the last. It is in the exploitation of the homo- and hetero-stimulative and also of the inhibitory potentialities of endocrine remedies that the lack of adequate guidance is at present most evident. The treatment by pituitrin injections of uterine inertia, previously the commonest of indications for forceps delivery, is in my opinion the greatest advance made in obstetric practice for the past quarter of a century. I have been favourably impressed by the effects of parathyroid extract in cases of epilepsy. In one case of twenty-five years' standing the patient has been able to discontinue entirely the large doses of bromide she had been

taking for many years, and the seizures, although not entirely checked, are milder and followed by less mental disturbance. This drug is worth trying also in paralysis agitans, chorea, and the tremor of "shell-shock." Thymus gland extract is indicated in cases of rachitis and infantile marasmus, and is said to have cured some cases of carcinoma. Pineal gland is recommended for children of backward mentality, also for premature mental failure. Cases of genital infantilism in girls and young women are benefited by ovarian feeding, also some cases of hysteria and painful menstruation. Extracts of the corpora lutea are said to alleviate the psycho-neurosis of the natural or artificial menopause, and of pregnancy, and to diminish the risk of abortion. Mammary gland extract is indicated in those forms of menorrhagia, metrorrhagia and hysteria which are attributable to excessive activity of the ovaries, and will sometimes check the growth of uterine fibromyomata.

One frequently sees cases in which girls and women show considerable enlargement of the thyroid gland without any of the recognized symptoms of cretinism on the one hand or of Graves's disease on the other. Whatever the explanation, such patients are often benefited by the cautious administration of thyroid extract. Some years ago Maranon published the observation that in 87 per cent. of cases of hyperthyroidism slight friction of the skin of the neck, near or over the gland, readily produces an erythema, sometimes accompanied by swelling. If this test be reliable, hyperthyroidism is the exception in the numerous cases of thyroid enlargement I have seen recently. It may well be that perverted rather than merely excessive or decreased activity is the commonest concomitant of such enlargement.

To sum up, it may be said that, while the note of mastery which distinguishes modern surgery is still to seek in medicine, there are signs of a growing intimacy of touch and sureness of method. The prognosis is good.

VOLUNTARY HOSPITAL FINANCE.

INTERIM REPORT OF THE MINISTRY OF HEALTH COMMITTEE.

THE Committee appointed by the Minister of Health on January 25th, under the chairmanship of Viscount Cave, "to consider the present financial position of voluntary hospitals, and to make recommendations as to any action which should be taken to assist them," has made an interim report dated March 9th.

CONTRIBUTIONS BY APPROVED SOCIETIES.

The Committee states that the evidence already received has convinced it "that it is desirable, in the public interest, to maintain the voluntary system of hospital management, and also that—mainly owing to the large increase during and since the war of salaries and wages and the cost of provisions and materials—many of the hospitals are faced with a serious deficiency of income to meet necessary expenditure." The Committee intends in due course to make further recommendations, but its interim report is issued in order to deal with a pressing matter—namely, the propriety of the approved societies making contributions. The following is the text of the paragraphs dealing with this matter:

We understand that the quinquennial valuation of approved societies under the National Health Insurance Acts, which is now in hand, shows a considerable surplus over the amounts required for the purposes of the Acts. Excluding Ireland, the valuation of 4,926 societies and branches, containing 2,558,123 members (out of a total of approximately 10,000 societies and branches containing nearly 15,000,000 members), which had been completed on December 24th last, showed a total disposable surplus as at December 31st, 1918, of £2,171,576; and it is anticipated that when the valuation is completed the total disposable surplus of all the approved societies will not be less than £7,000,000. This result is attributed to a material extent to conditions arising out of the war, such as the reduction, owing to war conditions, of sickness, disablement, and maternity claims, and the release of reserves in respect of members killed on active service.

Under the provisions of the Acts the societies are empowered to submit to the Minister of Health for approval schemes for utilizing the disposable surplus in providing additional benefits during the next five years; and the list of additional benefits authorized by the Acts and

the Regulations made thereunder includes, besides such matters as increase of sickness, disablement, and maternity benefits, and the provision of dental treatment, the "payment of the whole or any part of the cost of the maintenance and treatment of members in a hospital or convalescent home."

We are strongly of opinion that, in the interests both of the hospitals and of the societies, the schemes to be approved should provide for the application of a substantial part of the disposable surplus in providing a contribution towards the cost of the maintenance of members in hospitals. It will not, we think, be denied that the work of the voluntary hospitals is of great value to the approved societies and their members. Of the patients treated at the hospitals a considerable portion, about 30 per cent. of the out-patients and a larger percentage of the in-patients, are insured persons, and the effect of hospital treatment is not only to relieve these patients from suffering, but also to reduce the periods during which they are a charge upon the insurance funds. The fact that while depleting the hospital funds the war has had the effect of greatly increasing the surplus available to the approved societies, seems to provide a special reason for the consideration by the societies of the claims of the hospitals. The power given to the societies by Section 21 of the 1911 Act to subscribe to hospitals has been little used, doubtless owing to the anxiety of those concerned in the management of societies that their resources shall be sufficient to meet all claims; but now that a surplus is in sight it seems probable that a different view will be taken.

The method which should be adopted in order to secure the above result requires some consideration. The contribution of an approved society might take the form either of a weekly payment towards the cost of the maintenance of any member of the society who might become an in-patient in a voluntary hospital, or of a quarterly or yearly subscription for the benefit of the hospital or hospitals concerned; but in the latter case some amendment of the regulations would appear to be required. In either case an arrangement might (if so desired) be made with the hospitals for relieving the members of the society from any obligation to make further payments in respect of their maintenance or treatment.

We have reason to believe that some of the largest approved societies would be glad to see these proposals generally accepted, and that the hospitals would welcome such a result.

We are aware that it is not the desire of the Ministry of Health to interfere unnecessarily with the schemes submitted by the different societies for the utilization of their surplus funds. But we are confident that if the proposals here made were brought to the notice of the members the general feeling would be in favour of providing this measure of assistance to the hospitals, and so of making some return for the great benefits which those institutions have so long and so generously conferred upon them.

We therefore recommend that the Ministry

- (1) should make any necessary amendment in the regulation;
- (2) should forthwith bring this matter to the notice of the societies concerned and advise them as to the amount of the contributions which might reasonably be made out of the available surplus; and
- (3) should not approve any scheme for the disposal of a surplus until the suggestion has received due consideration.

We should have preferred to include these recommendations in our general report, so that their relation to other parts of the report might be seen; but we understand that the matter is urgent, as some of the societies are now engaged in framing schemes under the Act.

The report is signed by all the members of the Committee—Viscount Cave, the Marquis of Linlithgow, Sir Clarendon Hyde, Sir W. B. Peat, Mr. Vernon Hartshorn, M.P., and Mr. R. C. Norman.

A SMALL epidemic of small-pox has recently occurred at Chicago, being apparently due to a case being mistaken for varicella. Up to December 116 cases had been notified.

The second International Congress of Eugenics will be held in New York from September 22nd to 28th. Further information can be obtained from the Secretary, Dr. C. Little, American Museum of Natural History, 77th Street, New York City.

THE mortality from tuberculosis in Austria has considerably increased during the last few years. Before the war it was on the decline, the number of deaths from this cause in Vienna among women being 2,635 in 1914. During the war this figure began to increase, and is now 5,018. The mortality is highest between 35 and 65.