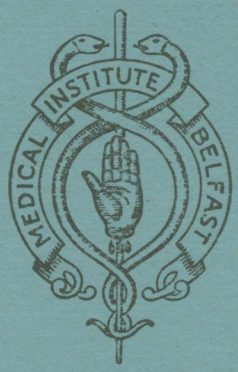
NOVEMBER, 1946

THE ULSTER MEDICAL JOURNAL



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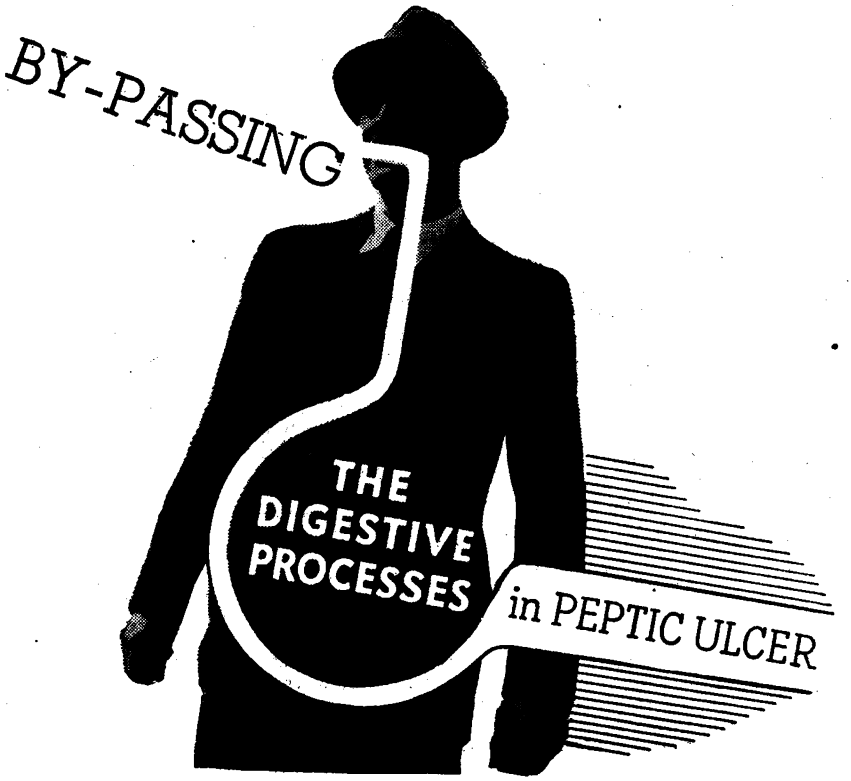

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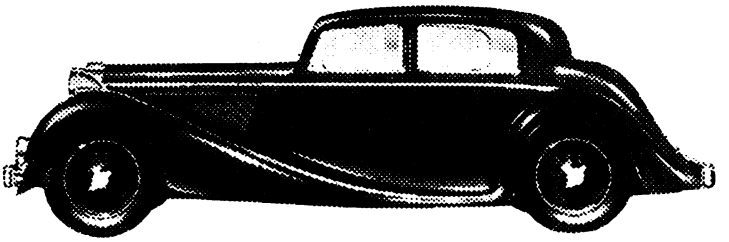

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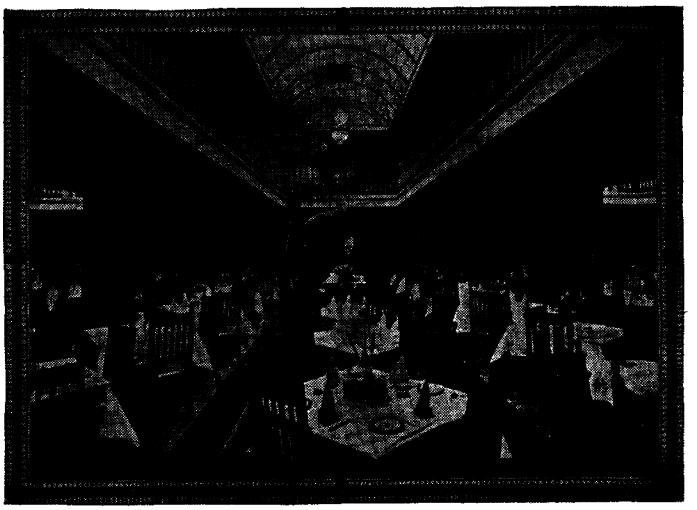

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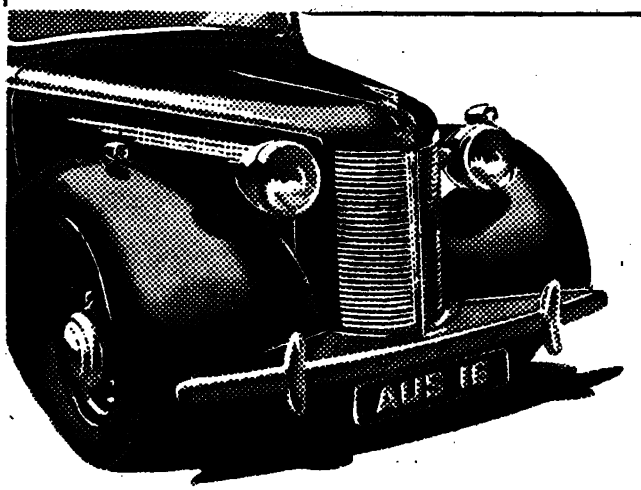

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Vol. XV 1st NOVEMBER, 1946 No. 2

The Use and Misuse of Tuberculin in the Treatment of Pulmonary Tuberculosis

By J. R. GILLESPIE, M.A, M.D., D.P.H.

Presidential Address, Ulster Medical Society, Session 1946-47

In 1890 Professor Koch, who had discovered the tubercle bacillus in 1882, announced that he had discovered a remedy for tuberculosis in tuberculin, made by growing virulent tubercle bacilli in a 5 per cent. glycerol broth medium for six to eight weeks at 38°C., the mature culture being sterilised in a water bath at 100°C., evaporated to one-tenth of its original volume, and filtered. The filtrate, which contains about 40 per cent. of glycerol, is known as tuberculin. It is labelled as T. (human) or P.T. (bovine), according as the bacilli used in its manufacture are of the human or bovine variety.

At first I got my tuberculin from the German firm who made tuberculin for Koch. But after war broke out in 1914 this was no longer obtainable, and I got it from Burroughs, Wellcome & Co., and could detect no difference between theirs and that made in Germany.

Not many of those present can remember, as I do, the excitement that was caused by Koch's announcement in 1890. At first the supply of tuberculin was limited, and anyone who wanted tuberculin treatment had to go to Germany for it. In 1891 wealthy patients from all over the British Isles, Belfast included, paid their doctors to accompany them to Germany. Some of these patients were so far through that they died on the outward journey, some in Germany, and some on the homeward journey. Koch had experimented on guinea-pigs, and found that these animals, when injected with a lethal dose of tubercle bacilli, lived much longer than otherwise if they got injections of tuberculin. But there had not been sufficient experience showing the proper dosage and intervals, and that tuberculin should not be given to febrile patients. Altogether, the doctors who went with patients to Germany in 1891 came back so disappointed with the results of tuberculin treatment, that

no one seems to have thought of using it in this country till 1910, when it was introduced by W. Camac Wilkinson.

Camac Wilkinson was a native of Sydney, Australia. After graduating with honours in Arts in Sydney University, he came to London to study medicine, and graduated M.B.Lond. in 1882, with first-class honours in medicine, gaining a scholarship and a gold medal. He proceeded M.D. two years later, and did post-graduate work at Strasbourg and Vienna. While on the Continent he became an ardent admirer of Koch. He was elected F.R.C.P.Eng. in 1902. He then returned to Sydney, and held hospital appointments and a lectureship in medicine and pathology, and gained experience in using tuberculin. In 1909 the Royal College of Physicians, London, awarded him the Weber-Parkes prize for the best essay on a subject connected with tuberculosis. The title of his essay was "Tuberculin in the Diagnosis and Treatment of Tuberculosis." This essay was published, with additions, in book form in 1912. Camac Wilkinson died in London last February, aged 88.

It was through one of his pupils that I became interested in tuberculin. This was Dr. Hilda Clarke, who opened a tuberculin dispensary in 1911, under the auspices of Portsmouth Borough Council. Dr. Hilda Clarke had become interested through her sister having recovered from pulmonary tuberculosis under tuberculin treatment given by Camac Wilkinson. In 1915 Dr. Hilda Clarke published a book entitled "Dispensary Treatment of Pulmonary Tuberculosis."

About thirteen years ago I was in Cardiff attending a medical meeting, and called on Professor Tytler, and tried to interest him in tuberculin treatment, but without success. He gave as his reason that he did not understand how tuberculin acted, whereas he could see the reason for collapse treatment. I told him I was getting as good results from tuberculin treatment as were got by collapse methods. But he was not interested. This reminds me of a story told of Rev. W. P. Nicholson when he was conducting a mission in Belfast about twenty years ago. To a man who said, "I can't believe anything I don't understand," Nicholson replied, "Do you understand how a red cow eats green grass and turns it into white milk?" And a Greater than Nicholson has said, "By their fruits ye shall know them." There are many things that we use every day that we do not fully understand. Men used light long before the wave theory was thought of by any of them.

There is, however, a very good working hypothesis of how tuberculin acts, the Wolff-Eisner theory. To lead up to this let us first consider certain phenomena which are easily verified. In the case of some persons who are suffering from tuberculosis, the subcutaneous injection of a minute quantity of tuberculin, say .0000001 c.c., or less even, is followed, after an incubation period varying from a few hours to two or three days, by some or all of the following reactions :—

1. *Local reaction*—Indicated by redness, swelling and pain round about the site of inoculation.
2. *General reaction*—Indicated by impairment of the patient's sense of well-being, loss of appetite and of weight, and increase of pulse-rate.
3. *Temperature reaction*—Indicated, when slight, by a diminution in the daily

range of the patient's temperature, commonly called "flattening of the temperature chart," or by a rise of temperature not exceeding 99°F. Any greater temperature reaction I call "febrile reaction."

4. *Focal reaction*—I.e., hyperæmia at the site of disease, with increase of discharge, if any. Hyperæmia is readily observed in cases where the lesion is in the skin. In pulmonary cases focal reactions, when sufficiently great, can be recognised by increase in the quantity of sputum.

If the reactions have not been too great, the indications of local and temperature reactions disappear in a day or two, and those of general and focal reactions may become reversed, the patient feeling better than before he got the injection, the appetite being improved, the weight increased, and the pulse-rate diminished.

In the case of other persons who are suffering from tuberculosis, however, the injection of so small a quantity of tuberculin may be followed by none of these reactions, in order to produce which, the dose may have to be multiplied hundreds or thousands or myriads of times; but the reactions *can* be produced by giving a sufficiently large dose.

Further, it is found that the condition of this latter class of persons in regard to tuberculin can be brought about artificially, in the case of the former class, by the administration of gradually increasing doses given at suitable intervals, the amount of tuberculin that can be tolerated being thus gradually increased. This gradually increasing tolerance of tuberculin can be produced by doses slightly less than would produce local or febrile reactions, as well as, or even better than, by doses producing the same.

Toxin Theory.

All the above phenomena, as to which observers are agreed, point to the action of a toxin; a toxin being a poisonous substance requiring an incubation period before it manifests itself, and bringing about, when introduced into the body of an animal in non-lethal doses, the production of a body that is an antidote to itself, called its anti-toxin. Whatever degree of tolerance of tuberculin is possessed by a person who has suffered from tuberculosis, may be attributed to the presence of anti-toxin in his tissues, produced as the result of previous inoculations of tuberculin, either administered artificially or admitted to the circulatory system from the patient's own lesion.

Modification of Toxin Theory Required.

But now another curious fact has to be considered, viz., that in the case of persons who have never suffered from tuberculosis, large quantities of tuberculin, say, .01 c.c., or more, can be injected subcutaneously without producing any apparent reaction. Now it is contrary to experience to find the presence of anti-toxin in the body, unless the anti-toxin has been either artificially bestowed or produced in response to the stimulus of the corresponding toxin.

Wolff-Eisner Theory.

It is therefore reasonable to conclude that tuberculin does not itself contain the toxin which produces the local, general, febrile, and focal reactions that may follow

its administration; but that there is, in the tissues of persons who have suffered from tuberculosis, some substance which, by reacting with something in the tuberculin, produces the toxin. Such substance, called by Wolff and Eisner tuberculolysin, we shall for convenience call lysin.

The fact that test doses of tuberculin have never, so far as I know, proved lethal, helps to confirm this theory. On one occasion I gave a patient a first test dose, T. .0002 c.c., which caused a sharp febrile reaction, the temperature going up to 102°F. A fortnight later the first treatment dose, P.T. .0000001 c.c., was given, and was followed by a reaction almost as great, the temperature rising to 101°F. T. is five to ten times as strong as P.T., so that the test dose was at least 10,000 times as strong as the one that produced almost as great reaction. If the toxin were ready-made in the tuberculin, one would expect that in a patient so sensitive that the smaller dose produced so much reaction, a dose 10,000 times as great would have killed him. But the fact that he was not even seriously injured is simply explained by the Wolff-Eisner theory, according to which the amount of lysin present sets a limit to the amount of toxin that can be produced from any dose of tuberculin, however great.

Further confirmation of the Wolff-Eisner theory may be derived from another consideration. It is well known that toxins are, as a class, thermolabile, i.e., they are easily altered by heat so as to lose their toxicity, a temperature of 60°C. being usually sufficient for the purpose. Now, in the preparation of tuberculin it is subjected to the heating effect of steam at a 100°C. for an hour, and yet toxic effects result from its administration, which confirms the view that the toxin is not ready-made at the time of the heating.

Factors to be Considered in the Administration of Tuberculin.

In administering tuberculin, then, we should take into account the following factors :—

1. The tuberculin, which can be measured. The essential ingredient, whatever it be, will be in proportion to the quantity of tuberculin used, so long as one variety of tuberculin is adhered to.
2. The lysin present in the patient's tissues.
3. The anti-toxin present in the patient's tissues.

The quantities of the last two can be estimated only indirectly, by comparison with the amount of tuberculin used, and observation of the effects produced.

The total toxin produced from a given dose of tuberculin will be the equivalent of the tuberculin or of the lysin, whichever be the less. Obviously it cannot be greater than either.

The free toxin produced will be the equivalent of the total toxin minus the anti-toxin, if this be a positive quantity. Otherwise there will be no free toxin.

Too Large Doses.

The maximum reactions will be obtained from the dose of tuberculin which is equivalent to the lysin present, the free toxin available for producing reactions

being in this case the equivalent of lysin minus anti-toxin. If the dose of tuberculin be in excess of the lysin, no greater reactions will be produced, and the excess of tuberculin is apparently eliminated in a few days. But in this case the operator has no control over events, as the effects produced do not depend on the only item that he can regulate, viz., the dose of tuberculin.

Hypersensitiveness.

We are now in a position to give a simple explanation of a condition of affairs which has been a puzzle to many workers. A certain dose of tuberculin having been given, and a febrile reaction produced, the same dose is repeated, and a greater febrile reaction follows. It may be repeated again and again with increasing reactions. This state of affairs has been attributed to hypersensitiveness on the part of the patient. But the proper inference is, not that there is anything abnormal on the part of the patient, but that the dose of tuberculin is in excess of the lysin, and that the latter has increased, as the result of each injection, faster than the anti-toxin.

If one persist, as some workers have done, in repeating the same dose, it may happen that the lysin will increase till it is greater than the equivalent of the dose of tuberculin, after which the total toxin produced by each dose will no longer increase, and the anti-toxin increasing with each dose, the free toxin will now grow less with each dose, till it is no longer able to produce reactions. But it is not a wise procedure, as the severe reactions which may result from it may be harmful. It is better to follow this rule :—

If a certain dose be followed by a febrile reaction, and its repetition by a greater reaction, reduce the dose.

Too Small Doses.

If the dose of tuberculin be less than the equivalent of the anti-toxin present, no free toxin will result, and, of course, no reactions, nor any stimulus toward healing of the lesion. But the patient will not be in statu quo ante. For a portion of his lysin and anti-toxin will have been used up, without the liberation of any free toxin to act as a stimulus toward producing more of these substances; thus rendering him liable to have reactions from smaller doses than before. This explains how it is that in Bardswell's words, "By the frequent repetition of a dose of moderate amount, intolerance, or hypersensitiveness, as the condition is usually termed, is actually encouraged."

Useful Doses.

We thus see that at any particular time in a patient's history there are certain rather narrow limits within which the dose of tuberculin, to be of benefit, must lie. It should exceed the equivalent of the patient's anti-toxin, otherwise there will be no useful stimulus from it; and it should not exceed it by much, lest the effects be injurious or beyond control.

From this we infer that the optimum dose at any time is one that falls but little short of producing some perceptible reaction. It is obvious that in order to be sure

that one is giving the right dose, one must occasionally give enough to produce reaction.

Fortunately, there are definite indications which usually give warning to a careful worker when he is in danger of overstepping the mark and causing febrile reaction. These have already been referred to, but it is well to emphasise them at this point. They are :—

(a) Local reaction.

(b) Elevation of temperature to a point not exceeding 99°F.

(c) Flattening of the temperature chart.

On the appearance of any of these indications, the ratio of increase of doses should be slightly diminished.

By observance of this rule one can almost entirely avoid the production of febrile reactions, at any rate, of severe ones.

Wrong Ways of Using Tuberculin.

It is clear from what has been said above that there is no rule of thumb scale of doses that can be applied all round. Success in giving tuberculin depends on continually adapting the ratio of increase of dose according to the effects produced.

Here are some wrong ways that have been used :—

1. *Auto-inoculation.*—Marcus Paterson used graduated exercise in the treatment of pulmonary tuberculosis, and attributed favourable results to tuberculin received by auto-inoculation.

I agree with Marcus Paterson that when a patient's temperature does not exceed normal, and pulse-rate not much above normal, it is good for him to be put on graduated exercise, increased by regular steps, with at least two days' interval between the steps. But I consider this a most uncertain way of giving tuberculin, and not to be compared with giving regular measured doses.

2. Sir Almroth Wright suggested that tuberculin should be given in small doses, with so long an interval that the effect of one dose might be expected to have passed off completely before the next dose was given, and that so the dose need not be increased.

Wright's method, which is said to have given good results in many varieties of non-pulmonary tuberculosis, has proved disappointing when tried in pulmonary cases, probably because : (1) it fails to control the temperature, and (2) owing to the disturbing effect of auto-inoculation, the optimum dose does not remain constant, but varies in a way that cannot be calculated.

Dr. Tom Houston (now Sir Thomas) tried Sir Almroth Wright's suggested method about thirty-five years ago at Forster Green Hospital, where he was then an honorary visiting physician. After about a year's trial, he observed no noteworthy difference between the patients who had been given tuberculin and those who had not. He then abandoned the use of tuberculin in pulmonary tuberculosis; and word went round the doctors in Belfast, "Houston has tried tuberculin treatment in pulmonary cases, and found it to be of no use." And the effect of this appears to have persisted to the present day, so that young graduates of our

University have the idea that there is no useful treatment for pulmonary tuberculosis but sanatorium treatment. This belief they convey to their patients, with the result that waiting-lists are swelled unnecessarily, and the waiting-time for beds is so great that the sanatoria do not get a fair chance.

3. Other physicians have tried to follow Koch's suggestion of giving injections at shorter intervals than Sir Almroth Wright suggested, and increasing the doses, but have failed to find the right way of increasing them. They very properly begin by making a series of dilutions : 1 in 10, 1 in 100, 1 in 1,000, 1 in 10,000, and 1 in 100,000.

Then beginning with the weakest preparation, some have given the following series of doses : 1/10th c.c., 2/10ths c.c., 3/10ths c.c., up to 9/10ths c.c., the next dose being 1 c.c., out of the same bottle, or 1/10th c.c. out of the next bottle. They then followed the same rule with the next bottle. These doses increase by 100 per cent., 50 per cent., 33⅓ per cent., 25 per cent., 20 per cent., 16⅔ per cent., 14 2/7 per cent., 12½ per cent., 11 1/9 per cent. Then, on moving up to the next bottle, the increase was suddenly made up to 100 per cent. Those who followed this method used to remark that violent reactions were apt to occur at the change from one bottle to the next higher; and, instead of realising that this was because they had suddenly changed the rate of increase from 11 1/9 per cent. to 100 per cent., they attributed these violent reactions to a supposed loss of strength in the more dilute preparation.

4. In 1932, being the jubilee of the discovery of the tubercle bacillus, it was arranged to have a discussion on "Tuberculin in Diagnosis and Treatment of Pulmonary Tuberculosis" in the Tuberculosis Section of the B.M.A. meeting in London that year. The discussion was in two parts, first on Diagnosis, and then on Treatment, the whole meeting lasting three hours. The opener in each part was allowed twenty minutes, the next speaker ten minutes, and those who followed fewer and fewer minutes. There were seventeen speakers in all, of whom I was the last with three minutes.

The opener on Treatment was Dr. R. A. Young, a very eminent physician on the staff of Brompton Hospital, but with no proper appreciation of how tuberculin should be given. He said that he gave the following series of doses to patients, which he supposed was as good as any :—1/500,000; 1/400,000; 1/300,000; 1/200,000; 1/100,000. He then said, "We can now increase more rapidly, and give 1/75,000; 1/50,000, etc." He concluded by saying that he considered tuberculin treatment worthy of further trial.

The speakers who followed, including Camac Wilkinson, read what they had prepared for reading in the time allotted to them. They had no time to refer to what had been said by those who had already spoken. When it came to my turn, instead of reading what I had prepared, I asked for a piece of chalk. The meeting was in a lecture room, the seats of the audience rising from front to rear. The wall facing the audience was mostly covered by blackboard. I wrote down Dr. Young's series of doses, and the percentage increase in going from each to the next,

as follows :—25 per cent., 33⅓ per cent., 50 per cent., 100 per cent. I then mentioned that Dr. Young said, "Now we can increase more rapidly," and increased by 33⅓ per cent. The people in the gallery laughed at this, but the people sitting with their backs to the blackboard, including Sir Robert Phillip, who presided, Dr. R. A. Young, and other distinguished persons, probably did not see what was written, or know what the others were laughing at.

I simply remarked that, having used tuberculin in that way, I was surprised that Dr. Young even thought it worthy of further trial.

My time was then up, Sir Robert Phillip rang his little bell, and declared the meeting at an end.

Some months later Dr. Young's paper was published unaltered in the *British Medical Journal,* and I wrote making the same criticism as I had made at the meeting. Dr. Young took this badly, and replied, saying that if he were going to be criticized in that way he wouldn't use tuberculin any more. It was, of course, better that he should not go on using, or misusing, it as he had been doing. But a better alternative would have been to try to discover the right way to use it.

This I shall now try to state clearly.

It has been shown above that the useful dose is not far above, nor far below, what would produce perceptible reaction. In cases where there is no doubt about the diagnosis I begin with P.T. .0000001 c.c. This rarely produces any febrile reaction. But in the rare cases in which it does, I go down a decimal point. I have never had to go lower than this.

Having given a dose which produces no reaction, I double the dose each time until some reaction occurs. This doubling of the dose avoids our remaining long at too small doses. When a dose has been reached that causes reaction, it is repeated till it causes no reaction, unless the repetition causes a greater reaction, in which case the dose is reduced. After this the dose is no longer to be doubled, but one has to find out by trial the highest rate of increase that can be maintained without producing reaction. The percentage increase of dose that suits best varies between wide limits, say from 10 per cent. to 70 per cent.

It not only differs for different patients, but even for the same patient at different parts of his course of treatment. Success in giving tuberculin treatment depends on continually adapting the rate of increase to the patient.

In order to maintain a ratio of increase that has been found beneficial in a certain case, the graduations on the barrel of the syringe are too coarse. I therefore have special pipettes, with rubber teats, made for me by R. B. Turner & Co., London. They are made of a special glass, so that they can be heated in the flame of a spirit lamp without breaking. Each pipette has a bulb blown on it, and is of such dimensions that the 1 c.c. mark is above the bulb, and the .1 c.c. mark a little below it. The stem below the latter is graduated into tenths and hundredths, so that small quantities can be measured with great accuracy. This pipette serves for making dilutions as well as for measuring doses.

Intervals between Doses.

I find the following scale of intervals satisfactory :—

Dose	Interval
P.T. .0000001 c.c. to P.T. .00001 c.c.	Three or four days (i.e., injections are given twice a week).
P.T. .00001 c.c. to P.T. .001 c.c.	One week.
P.T. .001 c.c., or T. .0001 c.c. to T. .001 c.c.	Two weeks.
T. .001 c.c. to T. .01 c.c.	Three weeks.
T. .01 c.c. to T. .1 c.c.	Four weeks.
T. .1 c.c. to T. .2 c.c.	Six weeks.
Above T. .2 c.c.	Eight weeks.

That the effect has not gone off at the end of these intervals is shown by the fact that the dose can still be increased at the end of them without producing reactions.

Advantages of Tuberculin Therapy.

There are two distinct advantages that may be gained by a series of properly regulated doses of tuberculin :—

1. *Control of the Patient's Temperature.*—It is well known that patients with pulmonary tuberculosis are liable to have their temperature raised by taking unaccustomed exercise. This is due to auto-inoculation, so that the rise of temperature is really a febrile tuberculin reaction. By a suitable series of tuberculin doses the amount of anti-toxin in the patient's system may be increased to such an extent that the amounts of tuberculin received by auto-inoculation become negligible. The patient may thus be freed from these, to him, capricious rises of temperature, often called "colds," associated with anorexia, wasting, night-sweats, and loss of strength.

Even in cases where the amount of lung impaired is very great and undergoes no diminution as a result of the treatment, or even gradually increases, it is worth while thus to keep the temperature under control when this can be done, as it sometimes can. It adds greatly to the comfort of the patient, enables him to enjoy his food, to take exercise without interruption, and so to train himself up till, in many cases, he is able to return to work.

I have some such patients who have been coming for their injections for many years, one of them for thirty-one years. They are now getting doses of over T. .2 c.c. One of them, whom I saw recently, got a dose of T. 1.1 c.c. They only come once in eight weeks, which does not interfere much with their work.

In some books 1 c.c. of undiluted tuberculin is termed the maximal or maximum dose. Such maximum is evidently fixed by the size of the syringe used, not by anything in the patient's constitution.

2. *Healing of the Lesion.*—It has been noted above that after a mild tuberculin reaction there may be improvement in the patient's sense of well-being, appetite,

CHART I.—SHEWING PERCENTAGE OF PATIENTS AT WORK

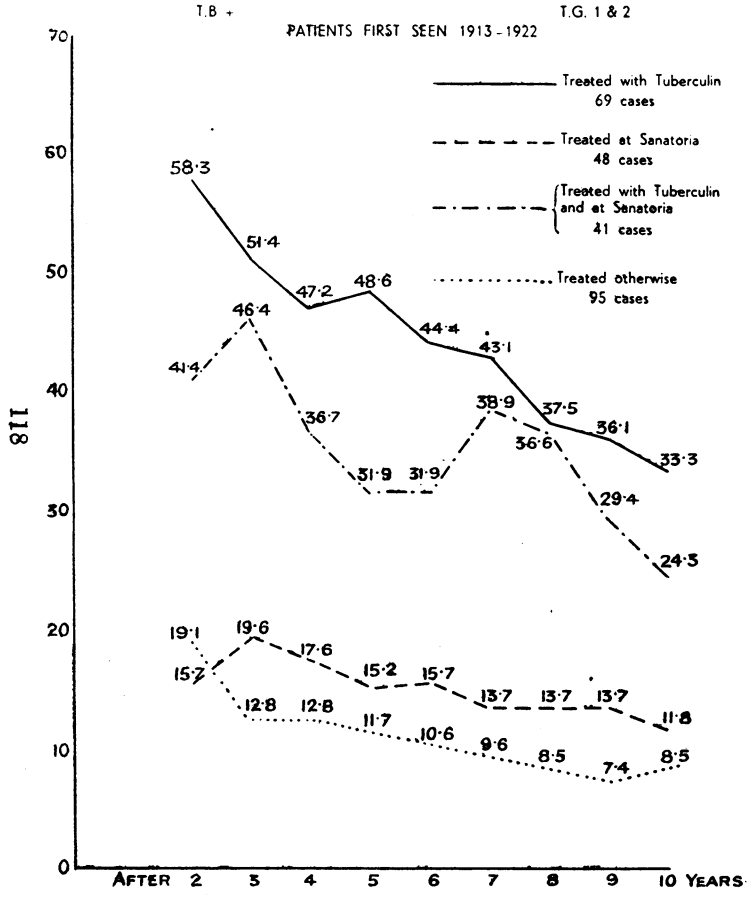
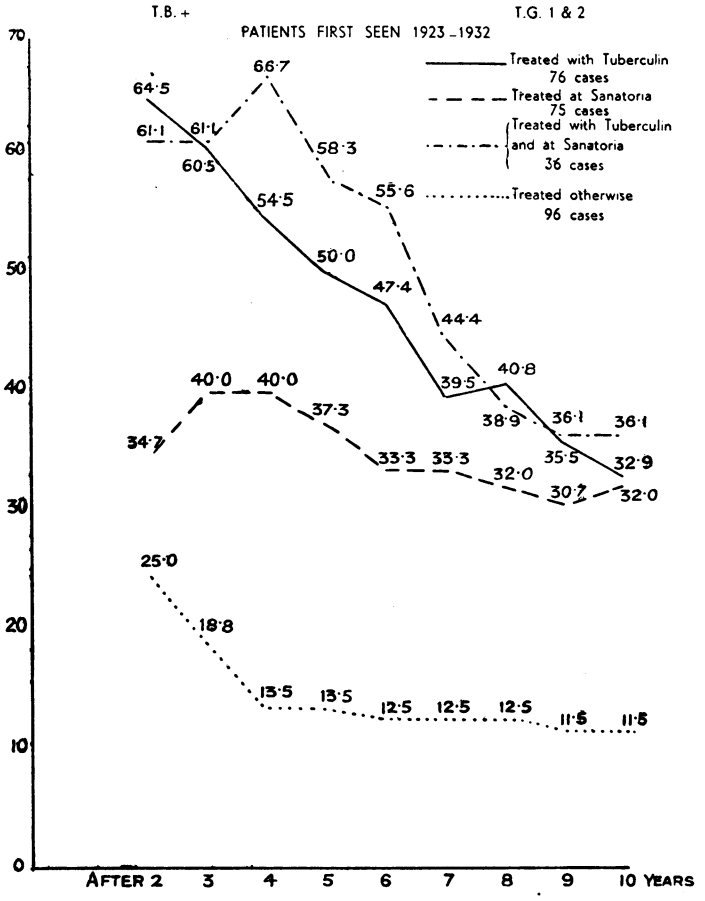


CHART III.—SHEWING PERCENTAGE OF PATIENTS AT WORK



weight, and pulse-rate. These desirable results can be produced as well, or better, by a dose a little less than would produce "reactions."

When the amount of impairment of lung is not great, one usually finds, after a series of suitable doses at suitable intervals for three months, that the "physical signs" are diminished, and the sputum is less in quantity and contains less yellow matter, and fewer tubercle bacilli when these have been present.

By continuing the course of treatment, one succeeds in some cases in abolishing all signs and symptoms of disease. After that, the treatment should be continued for at least three months to avoid danger of relapse.

Selection of Cases for Tuberculin Treatment.

Assuming that the diagnosis of pulmonary tuberculosis has been made, the clinical thermometer may be relied on to indicate the advisability, or otherwise, of tuberculin treatment.

The patient, or a friend who lives with him, is shown how to take and record the temperature. If the patient be not at work, he is instructed to record his temperature at 8 a.m., noon, 4 p.m., and 8 p.m.; if at work, to record it before breakfast, before dinner, and at 8 p.m. He is provided with a ruled card on which to keep this record; and at each visit to the dispensary the records on it are marked on the temperature chart which is kept at the dispensary. The charting of the temperature records is important, as it reveals alterations in the temperature curves which might not strike one on merely glancing at the card.

If it be found after a few days' observation, that none of the recorded temperatures exceeds normal, tuberculin treatment may be begun at once, no matter what the condition of the lungs may be, provided the patient is not in extremis. As has been mentioned above, even in cases where there has been extensive destruction of lung, and one has little or no hope of cure, the course of tuberculin may be of considerable benefit to the patient; and, if properly regulated, can do no harm.

If the temperature be found to exceed 98.4°F. at any time in the day, the patient is ordered to go to bed and stay there, resting as completely as possible, till the temperature has settled. When the temperature has settled, the patient is allowed to get up by successive steps. The longer the period of rest required to cause the temperature to settle, the slower must be the gradations by which the patient is brought back to activity. After the temperature has settled, tuberculin treatment may be begun as soon as convenient. If the patient be in a sanatorium, or on domiciliary treatment, it may be begun at once. But if he is to receive the injections at a dispensary, he must first reach the stage at which he can travel to the dispensary and back without putting up the temperature.

At whatever stage tuberculin therapy be begun, the graduated exercises are to be proceeded with all the same.

Results of Treatment.

Some good results have been obtained by me in the treatment with tuberculin of tubercular adenitis, peritonitis, nephritis, cystitis, and other non-pulmonary affections. But I am unable to make a comparison between them and others of a

CHART II.—SHEWING PERCENTAGE OF PATIENTS AT WORK

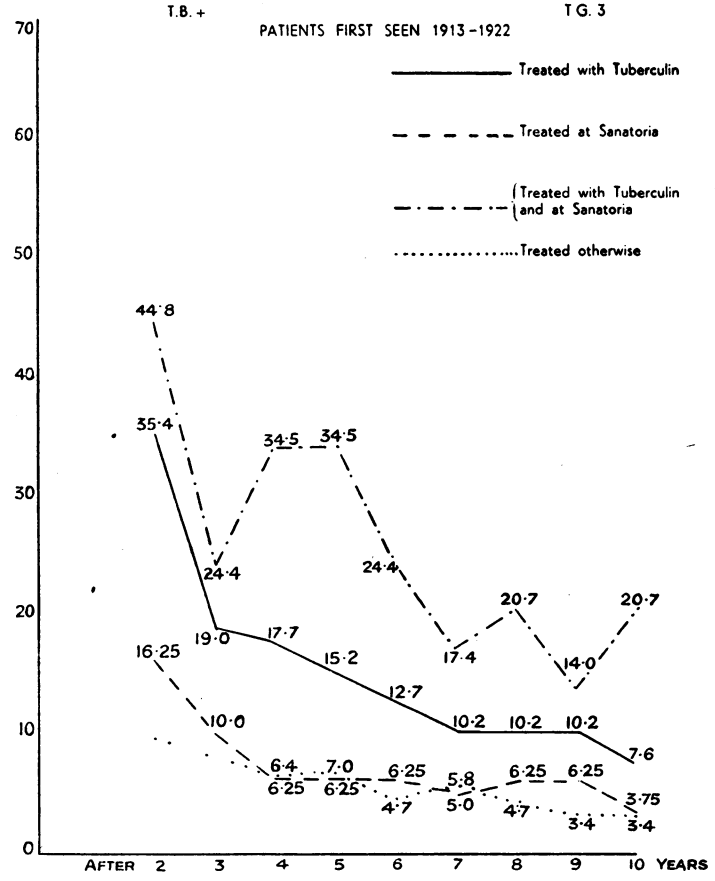
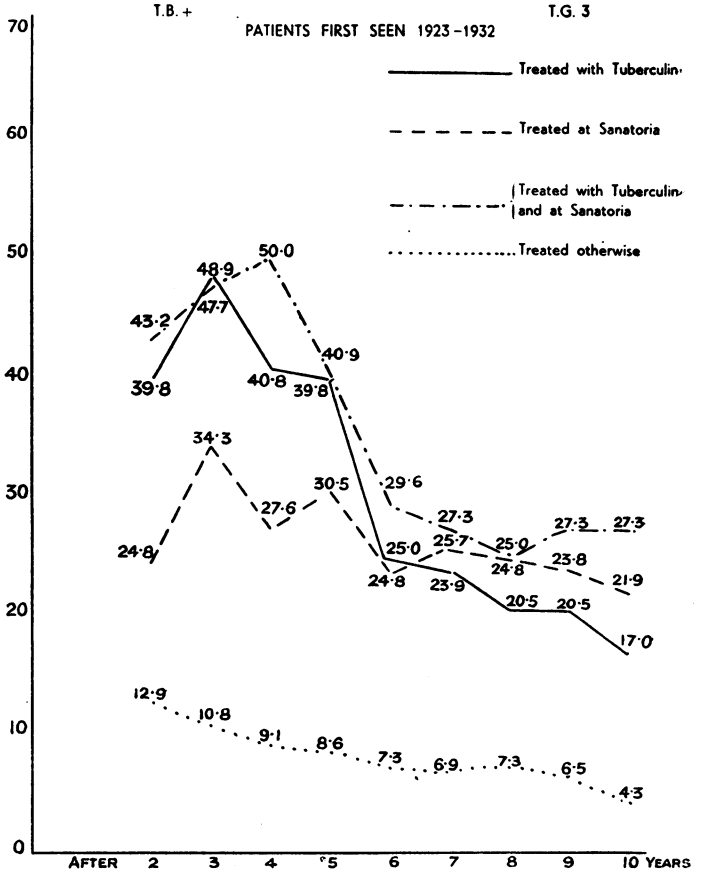


CHART IV.—SHEWING PERCENTAGE OF PATIENTS AT WORK



like nature treated without tuberculin. But in County Down there has been an opportunity to make such a comparison in regard to pulmonary cases. Every year, usually in the month of March, with the aid of my colleagues, I try to trace all the survivors among those whose names have been entered in our books as suffering from pulmonary tuberculosis; and we make a note as to whether each one is fit to work or not. We succeed in tracing almost all of them.

A comparison of the results of treatment by different methods needs to be made in a large number of cases that are reasonably comparable. Some patients have so little resisting power that no known method is able to check the disease. To say that a remedy is of no use because it fails, or is inapplicable, in such cases, would be absurd. In the comparison to which I am about to direct attention, no cases are included in which death took place within six months from the time when the patients were first seen by a tuberculosis medical officer. I have excluded also all cases in which tubercle bacilli were not found in the sputum. The prognosis in T.B. minus cases is very much better than in T.B. plus cases; and to mix them together in an investigation of this kind would cause confusion.

With the above exceptions, all the patients whose names were entered in our books as suffering from pulmonary tuberculosis from 1913 to 1922 inclusive are included in charts I and II, except a very few whom I have been unable to trace. In charts III and IV patients enrolled from 1923 to 1932 are similarly included. At the first examination each case was marked T.G. (Turban-Gerhardt) 1, 2, or 3, according to the extent of the disease in the lungs as revealed by physical examination. On this basis the cases have been divided into two groups, T.G. 1 and 2, and T.G. 3. This has been done because the prognosis is very much better in the former.

In County Down we have no county sanatorium. Those patients to whom sanatorium treatment was granted were sent in the first ten years to Forster Green Hospital or to the Royal National Hospital for Consumption, Newcastle, Co. Wicklow. Both of these stipulated that they were for early cases, or cases that had some prospect of recovering working power. Patients who did not show some sign of improvement were usually discharged before three months. In the comparison I have not classed as "Treated in Sanatorium" any patients who received less than three months' sanatorium treatment. Similarly, I have not classed as "Treated with Tuberculin" any who received less than three months' tuberculin treatment. Most of these were treated at dispensaries, but a few received tuberculin treatment at home from their own doctors, under the supervision of the tuberculosis medical officer.

In the second period of ten years very few patients were sent to Newcastle, Co. Wicklow, and the numbers sent to Forster Green Hospital increased. In this period both these sanatoria used sanocrysin and collapse therapy. Some patients were sent in this period to Rostrevor Sanatorium, but in charts III and IV these have not been included with the "Treated in Sanatorium," because Rostrevor Sanatorium was willing to keep patients whom we wished to isolate even when there was no

hope of their recovery; and therefore they had, as a whole, a worse class of cases than those treated at the other sanatoria or at dispensaries.

The group described as "Treated Otherwise" includes all who did not receive tuberculin treatment for three months, and did not receive three months' treatment in Forster Green Hospital or at Newcastle, Co. Wicklow. It includes some who received less than three months' treatment in one of these institutions, some who received less than three months' tuberculin treatment, and some who were treated in Rostrevor Sanatorium irrespective of the duration of this treatment.

In 1932 I read a paper before this Society, and showed charts I and II. The concluding paragraph of that paper was as follows :—

"None of these patients had artificial pneumothorax or sanocrysin, which have been introduced subsequently. When sufficient time has elapsed for these newer methods to produce their full effect, the sanatorium-treated cases should make a better showing. But they have a lot of leeway to make up before they equal the tuberculin-treated cases."

Comparing charts I and III, we see that this prediction has been fulfilled. The tuberculin curve is not very different in the two charts, while the sanatorium curve is more than twice as high in chart III as in chart I, and that for those who received both tuberculin and sanatorium treatment, about 50 per cent. higher.

The treated-otherwise curve is about 30 per cent. higher in chart III than in chart I. This may be due to a diminution in virulence of the tubercle bacilli, or an increase in the resisting power of the population, or to a greater willingness on the part of the patients on domiciliary treatment to obey instructions.

Comparison of charts II and IV also shows improvement in all the curves on chart IV, most pronounced in the case of the sanatorium-treated patients.

It is also noteworthy that the difference between the percentages at work of the tuberculin-treated and the sanatorium-treated patients is greatest in the early years, and is very much less when it comes to ten years. This is probably because our tuberculin-treated patients are encouraged to go on graduated exercise as soon as their temperatures are normal, and some have received the treatment and done well on it without giving up their work at all; whereas sanatorium-treated patients are often kept resting in bed for long periods, even when their temperatures are normal. This is a matter of great importance to the patient whose family is dependent on him.

It should also be noted that the highest curve of all is that for patients who received at least three months each of tuberculin and sanatorium treatment. These received the tuberculin treatment either before their admission to the sanatorium or after their discharge. I think it might be better still if they received the two simultaneously. I should like to have had the opportunity of putting this to the test.

The Development of Neuro-Surgery

By C. A. CALVERT, M.B., F.R.C.S.I.

Address at the Opening of the Winter Session 1946-47, Royal Victoria Hospital, Belfast

A LITTLE over 154 years ago a small dispensary, dedicated to the care of the sick poor, was opened in Smithfield. From this modest, but most worthy, beginning, our present noble heritage, the Royal Victoria Hospital, has been evolved by the zeal and self-sacrifice of an illustrious band of workers. Our meeting together here this morning marks the one hundred and nineteenth anniversary of the devotion of this institution to the teaching of medicine. It has long been customary at the opening ceremony of each winter session to extend a hearty welcome to the students of all years, but more especially to those who are about to walk the Hospital for the first time. On behalf of the medical staff, this I most cordially do, and I am persuaded that in the capacity in which I stand to-day I have the honour of addressing many who, in fullness of time, will look back on a life enriched by good service to their fellow-men, or, perhaps, even one who, by his genius, may introduce a new principle in the treatment of disease which will make humanity his debtor for all time.

We record with deep regret the death during the past year of two members of our consulting staff, Dr. Victor G. L. Fielden and Mr. Henry Hanna. Dr. Fielden, after many years of devoted service as senior anæsthetist to the Hospital, retired from the honorary visiting staff in 1932. At the time of his death he was our senior consultant. Generation after generation of medical students passing through the "Royal" were instructed by him. A man of sterling character, there dwelt beneath his rugged exterior a spirit of the very greatest kindliness.

Mr. Hanna was connected with our Hospital for a period of nearly forty years. As a specialist in diseases of the eye, ear, nose, and throat, he has bequeathed to us a memorial of the most eminent and devoted service. The high esteem in which he was held by his colleagues is indicated by his election to the presidency of the Irish Ophthalmological and the Ulster Medical Societies and also of his special section of the British Medical Association in 1937. He was chairman of the honorary visiting staff of the Royal Victoria Hospital at the time of his retirement. We honour and respect the memory of these two great men, and wish to extend to their families our deepest sympathy.

Let us linger for a few moments to pay tribute to the memory of three gallant young medical men, Humphrey Thomson, Robert Marshall, and Norman Purce, sons of members of our visiting staff, who, on the threshold of a life of the richest promise, made the supreme sacrifice in answer to the call of duty.

To-day it gives us great pleasure to welcome home and to the honorary medical staff, Lieutenant-Colonel Eric McMechan and Surgeon-Lieutenant Maurice Brown. We also extend a hearty welcome to two newly-appointed members of the honorary

medical staff, Mr. R. J. W. Withers and Dr. Reginald Hall. We are glad to have back with us again on the auxiliary staff Lieutenant-Colonel R. W. M. Strain, Squadron/Leader J. Nelson, Majors J. C. Davidson and D. F. C. Dawson. One of the most welcome features of the work at the Hospital during the past year has been the presence in our midst of so many post-graduate ex-service men as registrars and supernumerary house-surgeons in the various departments.

Lastly, and not least, we would like to extend a hearty welcome to Brigadier T. W. Davidson as our medical superintendent, and to Miss Elliott as matron of the Hospital, and to wish them both every success.

As my text for this morning I have chosen the development of neuro-surgery in the hope that something might be learnt, on the one hand, by reflection on the superstition and error which so long held science in bondage, and, on the other, from a consideration of the notable achievements of workers, not only in the domain of nervous disease, but also in that of the cognate departments of medicine, which have resulted in neuro-surgery being what it is to-day. The story is a long one, and is paralleled in the annals of any of the other branches of surgery, but if the examples which our study portrays of the unselfish devotion to duty of the pioneers of neuro-surgery should serve to stress the importance of a high professional code of conduction, I shall feel that such study as I have made of the subject has been well repaid.

Though the surgery of the nervous system is one of the youngest of the surgical specialities, there is considerable evidence to support the contention that operation on the skull was one of the earliest crafts resorted to by man in his attempt to deal with morbid states of the body. The researches of anthropologists have shown that trepanning was carried out by our ancestors beyond the dawn of history. That man had the temerity to make openings in the skull, and was able to do so successfully during the Late Stone Age, when he had nothing more serviceable to work with than a piece of flint, is well authenticated. What led the operator to undertake such an admittedly difficult and dangerous procedure, or the subject to submit to it, is a matter for conjecture, but there seems to be little doubt that the practice had its origin in a superstition which prevailed through all centuries of recorded time and is not without its adherents in our own day, namely, that of demoniac possession. The discoveries in regard to prehistoric trepanning date back to the year 1865, when a French general practitioner, Dr. Pruniere, exploring a dolmen, came across a human skull from which a large portion of bone had been cut away. At one point, the margin of the opening was curiously smoothed, and Pruniere came to the conclusion that the skull had been fashioned to make a drinking utensil—a practice not unknown amongst the savage peoples of to-day—a libation from such a vessel apparently enhancing the ecstacy of the victory already established over an erstwhile enemy. That Pruniere was wrong in his conjecture was proved by Professor Broca in 1877. He demonstrated that the smooth portion of the opening in the skull discovered by Pruniere, and the margins of many other "holed" neolithic skulls unearthed in France and other parts of Europe, showed indisputable evidence of a healed process, indicating that the artificial hole had been made during life. Tre-

panning was practised until quite recently by some of the few primitive peoples that still exist in the islands of Melanasia. These primitives carry out the operation for headaches, epilepsy, and some forms of insanity, employing fragments of volcanic glass, hard shell, or sharks' teeth for the purpose. Some of the tribes in New Ireland carry out the operation for depressed fractures sustained in combat: here, therefore, the procedure has a rational pathological basis, though amongst the New Irelanders trepanning is also sought by healthy individuals as a means of ensuring longevity.

Leaving the folk of the Stone Age and our present-day primitives, let us consider what research amongst the records left us by man down through the centuries has to tell concerning our subject. The oldest known scientific treatises are those of the ancient Egyptians, covering the period of from about 3500 to 1000 B.C. The story of this long expanse of time, during which Egyptian kingdoms waxed great only to fade again, is contained in the documents which have been recovered from their tombs. These portray their development from the earliest attempts at an organised community, with chipped flints and vessels of earthenware and stone, up to that of a highly sophisticated culture, with exquisite jewellery, graceful pottery, oil-cups and candles, razors, and what not. Our knowledge of Egyptian medicine is obtained from their papyri, or papers, of which the Edwin Smith papyrus, written in the sixteenth century before Christ, is chiefly surgical. In it forty-eight surgical cases are described, twenty-seven of which were head injuries. Deafness in fracture of the temporal bone is noted. In cases of closed fracture of the skull, decompression at the point of contusion is advised, but what instruments were used or how the operation was carried out is not known. Paralysis of the limbs and sphincters, in association with dislocation of the cervical spine, is regarded as being attended with a grave prognosis. In view of the present trend towards specialisation and the development of a State Medical Service, it is interesting to note that during the decadent period of Egyptian culture (about 1500 B.C.), medicine became very highly specialized; so that, as Herodotus tells us, "each physician applies himself to one disease only and not more."

To the ancient Greeks, who so greatly enriched mankind in nearly all branches of the arts and sciences, we owe the scientific approach to medicine. Hippocrates, the father of medicine, who lived and worked in the most illustrious period of Greek civilisation (about the fourth century B.C.), and the Hippocratic school, casting aside the elements of mysticism and vain speculation which had dominated the healing art from remote antiquity, introduced the careful and systematic clinical observation of the signs and symptoms of disease. Therapy was established on sound principles of inductive reasoning from experience gained at the bedside, and a practice of medicine based on the highest ethical standards was inculcated. Though the anatomy of the period was restricted to what could be observed on external examination of the body and pathology was very limited, yet it has been remarked that the Hippocratic descriptions of many diseases are so adequate that they might be transferred unaltered into any modern textbook. Hippocrates regarded all diseases as being due to a disturbance of the fluids or humours of the body. He

was contemptuous of the prevalent superstition that epilepsy was due to demoniac possession, regarding it rather as hereditary in nature and due to an affection of the brain itself, probably associated with an inundation of the gland with a condensed phlegm which could no longer be secreted. He based this hypothesis on the examination of goats which had died in convulsions, relating how, when the head was cut open, the brain was found to be humid, full of sweat, and having a bad smell. For him the brain was the seat of knowledge and of ability to discriminate between good and evil. He thought that excess of humidity of the brain was the cause of madness. Hippocrates wrote a book on head injuries which indicates a wide experience in this type of traumatic surgery. He emphasised the fact that no injuries of the head were to be regarded as trifling, since even a wound of the integuments might prove fatal. His classification of skull fractures is almost modern in complexion. The use of a trephine, quite up to date in appearance, is advised in certain cases. He emphasises the importance of cleanliness, good light, the proper positioning of the patient, and states that, as the trephine tends to become hot, it should be cooled from time to time, and that the greatest care must be taken to avoid injury to the dura. The subsequent wound-dressing employed was either a preparation of wine and honey or of tar—virtually an antiseptic application. He taught that primary healing of wounds should be aimed at and that suppuration was neither necessary nor indeed ideal, as was the doctrine not only of his predecessors, but remained the belief of those who followed him for close on two thousand years. According to the late Sir Charles Ballance, Hippocrates recommended the use of the trephine in cases of incipient blindness not due to disease of the eye. Thus, the father of medicine may have employed decompression for increased intra-cranial pressure, a procedure the value of which only came to be appreciated again some sixty years ago.

With the passing of Hippocrates, the glory of ancient Greece soon began to fade, though the establishment of the Museum at Alexandria in 331 B.C. kept the Hippocratic tradition alive for a time. Alexandrian medicine, however, soon developed into a school of empiricism, and before long therapy was once again a matter of exorcisims and charms and other forms of magic.

The western Roman Empire, which held sway over most of Europe from the second century B.C. to the sixth century A.D., had little interest in scientific medicine. Whilst the Romans prosecuted military science, the codification of laws, and the development of sanitation with assiduity, they depended largely on domestic herbals, votive offerings in the temples, and other superstitious observances in case of illness. Certain famous Greek physicians did indeed set up their consulting-rooms in Rome, but as the proud Romans despised and were suspicious of foreigners, it was some time before they attained a reputation for respectability. Eventually, by reason of their superior learning, their services came to be highly valued, and they were employed to look after the famous gladiators and gymnasts, though, unfortunately, the scientific outlook of the Hippocratic school was gradually replaced by a fondness for theorising, and medicine suffered accordingly. A few of the greater physicians of the earlier centuries of this period will be briefly alluded to because of the pro-

found influence exerted by their teaching on medical thought until well on in the Middle Ages. Celsus, whose name is well known to you in connection with the four cardinal signs of inflammation, wrote an important treatise 'concerning things medical' in A.D. 30. He indicates that under the Romans, operations were carried out for a wide variety of conditions, and that the surgeons of the period were equipped with many well-constructed instruments. Indeed, the standard of surgery which then prevailed was not attained to again until the time of Ambrose Paré in the sixteenth century.

Celsus deals with the problem of head injuries in considerable detail. He gives a good classification of skull fractures, and signifies his belief that these sometimes arise by contre coup. He urges careful enquiry regarding the immediate symptoms, such as unconsciousness, convulsions, loss of speech, etc., for if such have occurred, the outlook is serious. But if torpor develops with paralysis, the membrane of the brain is injured, and little hope need be entertained of recovery. When probing of a wound leaves uncertainty concerning the presence of fracture, he says a useful tip is to pour in some ink and scrape the bone, when a fissure will show as a black line. He mentions that bleeding from the membrane of the brain may occasionally occur in the absence of fracture, producing a clot with great pain and dimness of vision. In cases of compound fracture, he counsels an expectant attitude with local applications to allay irritation, such as wool soaked in vinegar. If, after a few days, there is no improvement, and fever sets in, with great pain and swelling on the glands in the neck, he advises opening the skull with a wimble, a sort of augur, and removing the fractured or depressed bone. In cases of epilepsy, he favours shaving the head and applying cupping-glasses, and in desperate cases resort to the use of the cautery.

Galen, who practised in Rome in the second century A.D., was the greatest Greek physician after Hippocrates. He was a man of outstanding talent, a great experimentalist, and a voluminous writer, but didactic and boastful and an incurable theorist. There was no problem for which he had not a ready answer. He was a monotheist, and emphasised the subservience of the body to the soul, so that his teaching met with the unqualified approval of the Christian Church. Indeed, in course of time, Galen's pronouncements came to be regarded as infallible, and his works remained a sort of Bible of Medicine until the time of Vesalius. Though he contributed greatly to the advancement of anatomy and physiology, his statements were by no means always correct, and his mania for speculation led him into many extravagant errors, which did much to delay the advance of medicine; for example, he subscribed to the pernicious doctrine that suppuration was an essential process in healing. After Galen, the quality of medicine and surgery quickly declined, and there was a steady deterioration in the ethical standards of the medical profession. Medicine in Byzantium, which had taken over after the barbarians had swept down into Italy, was largely given over to charms and spells, and salves and plasters to encourage laudable pus.

During the decline in Europe, which was destined to continue for well-nigh on a thousand years, medicine found sanctuary for a time in the great Moslem Empire.

In the seventh century, when Islam was rapidly extending its borders, its followers were hostile to all forms of science. Once the wars of conquest were over, however, the Arabs, who were able mathematicians and chemists, became interested in science, and their rulers greatly encouraged the introduction of learning from abroad. They commenced eagerly the translation of the Greek authors, including some of the Hippocratic collection, into Arabic. The Moslems, however, contributed little to medicine and still less to surgery, but to them is due the credit of preserving many of the works of the ancent Greeks and of transmitting them on to Europe at a later date.

During the Dark Ages European medicine was largely in the hands of the Church. The downfall of Rome had left the peoples of Europe in a state of chaos and at the mercy of wandering barbarians. An illuminating picture of the state of affairs at this time is given by Matthew Arnold in his well-known lines :—

> On that hard pagan world disgust
> And secret loathing fell,
> Deep weariness and sated lust
> Made human life a hell.

The Christian Church, with its mission of compassion for suffering, established monasteries dedicated by their founder, St. Benedict, "to prayer, study, and the healing of the brethren." Within their cloisters provision was made for the care of the sick. Little wonder that a distracted people, amongst the seething turmoil of the period, should seek the protection of the Church, particularly as the physicians of the time were utterly powerless in face of the devastating epidemics which swept the Continent at frequent intervals. Many of the monasteries came in time to have hospitals and physicians of their own, and in this way, possibly, originated the earliest hospitals in Europe. The Church, however, held certain views that were inimical to progress. Disease was attributed in many instances not to natural causes, but to divine retribution for sin, and was therefore naturally to be met by prayer and fasting rather than recourse to medicine.

The Church encouraged the monks to translate the Arabist versions of the works of the ancient Greeks into Latin. As already mentioned, the writings of Galen were especially esteemed by the Church, but, unfortunately, Galen had said that surgery was to be regarded merely as a branch of medicine, and this had been interpreted by the Arabs as meaning that surgery was an inferior type of work. This dangerous conception of the place of surgery was now carried forward into mediæval medicine. Physicians came to regard any method of treatment which involved the shedding of blood as beneath the dignity of anyone with the least pretence to culture. Surgery was therefore left, for the most part, in the hands of men not only devoid of culture, but without any regard for ethics, such as barbers, executioners, booth-keepers, sow-gelders, and charlatans of all sorts. Individuals of this type wandered about from village to village blood-letting, cutting for stone, operating for hernia, and combining these activities with sooth-saying and magic. Amongst these itinerant quacks were individuals who professed to be able to relieve insanity, idiocy, and other forms of mental disorder. A superficial incision was made in the scalp of the unfortunate victim, and stones, palmed in the hand of the operator,

were dexterously extracted from the wound at well-chosen intervals, and cast into a pail, conveniently placed, to the amazement and delectation of the onlookers, if with but little consolation for the sufferer. The great masters who taught at the few European universities, which had by this time sprung up, undoubtedly laboured on a loftier plane, but for the rank and file of the people the standard of medicine was very low and surgery often more dangerous than the disease. Many placed their faith in pilgrimages, incantations, and exorcisms, sorcery, and suchlike. A compilation of the great Salerno school, the first university in Europe, tells us that "blood-letting is the beginning of health. It strengthens the mind and memory, purges the bladder, dries out the brain, warms the spinal cord," and so forth, and, indeed, is as extravagant in its claims as some of the quack remedies of the present day. During the Middle Ages a few great masters of surgery did what they could to advance their art, but their teaching had little effect on their contemporaries. Theodoric, bishop of Cervia, wrote in 1266 :—"For it is not necessary, as all modern surgeons profess, that pus should be generated in wounds. No error can be greater than this. Such a practice is bound to hinder nature, to prolong the disease, and prevent coagulation and consolidation of the wound." But the correctness of his statement was not to be established for another six hundred years. Theodoric affirmed that an injury to one side of the head might produce paralysis of the contralateral side of the body. About thirty years later Lanfranc, working in Paris, and in effect the founder of French surgery, contributed further to the elucidation of the problem of head injuries by describing cerebral concussion for the first time, and pointing out that it was by no means necessary to resort to trephining in all cases of skull fracture, nor did the fragments of bone require to be removed unless they were pressing on and irritating the brain and its membranes. In the treatment of head injuries in the more advanced medical schools of the period, it was usual first to explore the wound gently with the finger, for, according to one author, there is no better method of recognising a fracture. If a fracture was found, the wound was enlarged by converting it into a cruciate incision with a razor. The resulting scalp-flaps were retracted with a blunt hook until the whole extent of the fracture was exposed. Loose bone-fragments having been removed, and bleeding controlled, the flaps were turned back into place, and the head bandaged with a linen cloth, previously soaked in white of egg. Roger of Salerno laid it down that any patient with a fractured skull must be regarded as in danger for a hundred days. A famous Italian surgeon of the thirteenth century, who endeavoured to put surgery on the same footing as medicine, makes a remark, possibly for the edification of his son—a medical student—which gives one an insight into the regard in which surgery was then held. He says : "A wise surgeon will refrain from stealing when he is actually in attendance upon a patient," and "that discretion should lead him not to employ reputedly bad characters as assistants."

The first step towards a recovery of the scientific spirit in medicine was in the domain of anatomy. Vesalius, in 1543, published his monumental treatise on human anatomy, "The Fabrica," which terminated for good and all the belief in the

infallibility of Galen which had pervaded medicine for thirteen centuries. Dissection of the human body was revived, and from henceforth the student of anatomy gained his knowledge at first hand. The spirit of investigation was once more abroad, and it was not long before the work begun by Vesalius had made itself felt in the realm of surgery. Ambrose Paré, the great French military surgeon of the sixteenth century, and one of the greatest surgeons of all time, introduced a rational attitude to the treatment of wounds, which, at the time, were being flooded with boiling oil, in the belief that they were invariably poisoned. He instituted in place of this savage custom, the principle of handling the tissues with the utmost gentleness and employing only such dressings as were non-irritating. He laboured incessantly to rid men's minds of the superstition that suppuration was a beneficent process, and to bring them to realise that healing was really effected by the tissues themselves. Advance in the science of physiology lagged somewhat behind that in anatomy, and it was not until 1628, for example, that William Harvey published his discovery of the circulation of the blood. By this time the microscope and thermometer, invented by Galileo, had become available. Medical science, already infused with a new spirit of research, began to make use of them, and soon scientific knowledge of the workings of the human body was replacing age-old theories, such as that of the four humours. Attempts were made to correlate the signs and symptoms of disease with the underlying pathology and to institute a rational therapy. Internal medicine was at last established on scientific grounds.

In 1760, Percival Pott published an important treatise on head injuries. In this there is an admirable account of extradural abscess following external violence to the head. He describes eleven cases treated by himself belonging to this group, in none of which was the skull fractured, and in six, indeed, the only visible evidence of local trauma was simple bruising of the scalp. It was in connection with these cases of extradural abscess that Pott described the puffy tumour with which his name is still associated. Of the eleven cases, three refused operation, and in a fourth interference was limited to the scalp; all of these patients died. In the remaining seven cases, trephine holes were made and the extradural abscess drained, and all except two recovered. Instead of the cruicate incision used from remotest antiquity, Pott exposed the skull by the unique method of cutting out a complete circle of scalp of whatever size seemed desirable. He divided skull fractures into those with and those without depression, and stated that use of the usual complex classification "is merely to load the memory without informing the understanding." He operated on all cases of depressed fracture, sacrificing the displaced fragments unless the injury was slight, when the bone was levered back into position. It was recognised by him that disturbance of consciousness might be due either to commotion of the brain or to compression by clot. He did not know, however, of any way of distinguishing between the two, though he states that impairment of consciousness developing immediately after an injury is more likely to be due to commotion of the brain, and, if delayed, to be the result of compression. He points out that the difficulties are further increased by the fact that there is no way of knowing when a clot is present, where it may be situated, and declares that

the whole problem of unconsciousness following head injuries is "involved in the most perplexing obscurity." Because of the impossibility of excluding the presence of a clot, he recommended the use of the trephine in all cases of fracture of the skull without depression, if the level of consciousness did not improve satisfactorily in spite of many and drastic bleedings, provided always that there was some evidence, in the form of a visible scalp lesion, to indicate where to make the perforation.

Again, the difficulties of localization were so unsurmountable that even in cases in which the presence of a clot seemed almost certain, he cautioned against the use of the trephine unless there was a local scalp injury to indicate where to operate. He recognises that this method of determining the site at which the skull opening is to be made is fallible and uncertain and that the clot may be far distant, but it is the only method available, and, unfortunately, the chances of the operation being serviceable are very few. Pott subdivided intra-cranial hæmorrhages into extradural, subdural, and intra-cerebral. He mentions the fact that he opened the dura for a clot situated beneath the membrane, but states that the procedure must be recognised as being attended with great hazard. The trephine which he employed was similar to the short-handled instrument that is occasionally used even at the present time.

Though Pott added considerably to our knowledge of head injuries, and men like himself and Chiselden did much to improve the craftsmanship and widen the scope of operations in general, no new principle was introduced into surgery from the time of Paré until the advent of John Hunter towards the close of the eighteenth century. Hunter founded the sciences of experimental and surgical pathology, and opened the way for the scientific application of surgery to the relief and cure of disease. He taught men that the true function of surgery was to seek out the cause of each malady, and to try and prevent it rather than to be content with measures directed towards the eradication of morbid processes already firmly established.

During the first half of the nineteenth century, surgical technique was developed to a state of perfection that could scarcely be excelled. It was inevitable, since no methods of relieving the excruciating pain of operation other than a dose of opium or a draught of whiskey was available, that speed and dexterity, combined with a precise knowledge of anatomy, were the hallmarks of the truly great surgeon. But the necessity for speedy surgery diminished the field of its application, and any inclination there might have been to employ a conservative procedure had often to be relinquished in favour of an operation of a sacrificial nature which could be more rapidly executed. But the restricted application of surgery was also determined by what the unfortunate patient was able to endure. The necessity for an anæsthetic was plain enough, and a solution of the problem was being eagerly sought. When Morton, in America, introduced ether in 1842, and Simpson of Edinburgh discovered chloroform in 1857, their names were at once on everyone's lips. The elimination of the agony until then inseparable from operative treatment was an advance the magnitude of which can hardly be computed. But it did not

widen the application of surgery as much as might have been expected. There was still the spectre of sepsis overshadowing all and stepping in almost as frequently to undo the best efforts of the operator. Even in the most up-to-date hospitals of the day, sloughing and gangrenous wounds were rife; secondary hæmorrhage an ever-present danger. It is said that Sir Astley Cooper, who, in 1820, removed a wen from the royal scalp of George the IV of England, was sick with anxiety, and could scarcely sleep for a couple of weeks, lest the wound should go septic and prove fatal. But good fortune attended his efforts, and he received a knighthood.

Apart from ovariectomy, the surgery of the body cavities was not attempted, it was so uniformly fatal. As far as the surgery of the nervous system was concerned, it was restricted to the treatment of scalp wounds and skull fractures. Knowledge of the physiology of the nervous system was very limited. That mental aberration, intellectual deterioration, or palsy might be the result of a space-occupying lesion within the skull was rarely thought of, except by some of the great physicians with an interest in neurology.

In 1867, just ten years after chloroform had become available, Lister introduced the principle of the antiseptic treatment of wounds which was to revolutionize the entire outlook of surgery. Within the next decade only hopeless surgical diehards continued to take unction to themselves because the flower in their buttonholes was undisturbed and their cuffs immaculate at the end of an amputation. Instead, surgeons everywhere were operating successfully for conditions that had hitherto been regarded as inoperable, such as lesions of the stomach and colon, gall-stones, renal tumours, and what-not. New techniques were established, and within a quarter of a century not many of the viscera could be regarded as sacrosanct from attack by the knife. Two regions of the body, however, remained, the surgery of which was slower in being developed than was the case elsewhere; partly on account of the difficulties of operative approach, but more so because the physiology and pathology of the contained viscera were not so well understood. I refer to the thorax and the central nervous system : my remarks will be restricted to the surgery of the latter.

At the time of Lister's introduction of the antiseptic principle, knowledge of diseases of the nervous system had already been considerably advanced by physicians and neurologists such as Robert Whytt, Richard Bright, William Stokes, and many others. Histologists and pathologists had made valuable contributions in regard to the normal structure of the nervous system and the changes wrought by disease. Experimental physiologists, amongst them Sir Charles Bell, Marshall Hall, Flourens, Majendie, Johannes Müller, to mention but a few, had established many facts of fundamental importance to an understanding of nervous function, but as yet only the fringe of this vast field could be said to have been explored. Von Helmholtz invented the ophthalmoscope in 1850, and already this instrument, so indispensable to all concerned in the study and treatment of diseases of the brain, was in use. In 1862, Broca discovered that the posterior end of the third left frontal convolution was the centre for articulate speech in right-handed individuals. He

was the first to trephine for a cerebral abscess, the situation of which had been diagnosed by his theory of cortical localization. Prior to the introduction of Lister's antiseptic principle, a brain tumour had never been removed successfully; indeed, the mere suggestion that such a project might some day prove feasible had been severely censured as bordering on a surgical impropriety. Apart from the centre for articulate speech, knowledge of the localization of cortical function was non-existent. Information concerning the function of the deeper parts of the brain was limited to a few salient facts, such as the presence of the vital centres in the medulla and the centres for co-ordination of movement and equilibration in the cerebellum. Accurate localization of a brain tumour, let alone its removal, would have been impossible at this period, when the pioneers in abdominal surgery had already made great advances and were doing magnificent work in reducing the sum total of human suffering and disability.

Neurologists such as Hughlings Jackson, David Ferrier, Gowers, and Charcot were busy in the latter half of the nineteenth century unravelling the syndromes of neurological disorders and building up, along with experimental physiologists, pathologists, and others, that great storehouse of knowledge on which the surgery of the nervous system was to be based. It was not long until tumours of the brain and spinal cord were being localized with a considerable degree of accuracy, but the surgeons of the day were not equipped to deal with them. Thus the pathology and life history of tumours of the nervous system were far from being fully understood. The circulation of the cerebro-spinal fluid had not yet been worked out, and the hydrostatic factors complicating space-occupying lesions within the skull had still to be learnt by bitter experience. The earliest attempts at removal of a brain tumour, even when correctly localized and benign in character, were almost invariably fatal. The first removal of a cerebral tumour was carried out in 1884 by Mr. Richman Godlee, who excised an encapsulated glioma about the size of a walnut from the post-central gyrus of a young farmer of 25 years. The position of the growth had been correctly localized by Dr. Hughes Bennett, who was present at the operation along with Hughlings Jackson and David Ferrier. A carbolic spray was kept going continuously throughout the procedure. The usual cruciate incision was made in the scalp and discs of bone were cut out with a trephine. The patient made good progress during the first three days after operation, but on the fourth the wound was swollen and there was a discharge with a decidedly putrefactive smell. A cerebral fungus had already developed by the fifth day. The patient died on the twenty-eighth day apparently as a result of a complicating infection. This might well have been the first successful removal of a brain tumour but for one unfortunate factor that was overlooked, namely, that at the time of operation the patient had several raw areas on the upper part of the back of his neck, resulting from the application of blisters to this region.

During the last two decades of the nineteenth century, knowledge of cerebral localization was immeasurably increased by the research of men like Ferrier and Sherrington in this country. One of the most brilliant workers in this field was Sir Victor Horsley, who may be said to have established the surgery of the central

nervous system on a scentific basis. Horsley standardized the methods of operative approach for brain and spinal cord tumours; thus the cruciate incision followed by a trephine opening was replaced by the semicircular scalp incision and osteoplastic bone flap now in use. He was one of the first to realise that vision could be preserved, headache relieved, and life prolonged by making a decompressive opening in the skull, and was the first to employ this procedure expressly for such tumours as were inaccessible or irremovable. Working in association with Sir William Gowers, he carried out the first successful removal of a spinal-cord tumour in 1887.

The pioneers in neuro-surgery had many technical problems to solve. Methods of handling the tissues which were perfectly satisfactory in other situations, such as sponging with gauze, ordinary modes of retraction, exploration with the fingers, and so forth, proved calamitous when applied to the delicate neural mechanisms. The use of small cotton patties and strips of gutta-percha and lintine to minimize the trauma produced by the lightest of malleable retractors had to be evolved. Ordinary methods of hæmostasis were found to be of little service. Loss of blood during a long-drawn-out struggle with a brain tumour averages about three to four times that of most major operations. Unless the greatest care be exercised, hæmorrhage may in itself determine a fatal issue, and special methods of hæmostasis had to be devised for every layer inwards from the scalp to the bed of the tumour. The methods in use to-day were only evolved very gradually and after much tribulation, and I will refer to some of them as we proceed. An early and most important advance was Horsley's solution of the problem of diploic bleeding by the use of wax.

As ordinary methods of exploration are inadmissible, accurate localization of a brain lesion is necessarily of capital importance. Unless the precise situation of a lesion is known, so that the surgeon may make the skull opening directly over it, removal either proves impossible or is attended with so much damage that the patient promptly succumbs or is left with such permanent incapacity that his survival may well be a tragedy. The neurologists and neuro-surgeons of fifty years ago had to rely solely on clinical methods of localization, and since even to-day the site of many brain tumours cannot be predicted by the most astute clinical judgment, it will be readily recognised that the position of the early neuro-surgeons was not a very enviable one.

Perhaps the most heart-breaking of all the problems of the pioneers in brain surgery was that of the raised intra-cranial pressure, which complicated so many of their cases and led to a devastating extrusion of cerebral tissue as soon as the dura was opened. Numerous expedients had to be resorted to before some sort of solution was forthcoming. The substitution of local for general anæsthesia by de Martel and others was found to diminish the hazard of operation to a certain extent. Some years were to elapse before Harvey Cushing found that an ominous situation might sometimes be transformed by the simple expedient of lumbar puncture. Still later, the insertion of a canula into the opposite ventricle, methods of dehydration, and intravenous administration of hypertonic solutions were pressed

into service. Related to the problem of increased pressure was that of leakage of cerebro-spinal fluid from the wound after operation, which frequently led to meningitis and death. To overcome this a special technique of wound closure had to be evolved, in addition to measures to control intra-cranial pressure post-operatively. Add to all this that many cerebral tumours are malignant or, if benign, so placed as to render access very difficult, and it can be readily understood why the successful removal of a brain tumour was not often attained in the early days of neuro-surgery.

One of the fields in which encouraging results were first secured was in the treatment of intra-cerebral abscess. Dr. Gowers and Mr. Baker recorded a successful case in 1886, and reports of a few similar results followed during the next few years. Knowledge of the subject was still very fragmentary, however, until Sir William McEwan published his classical work on the subject in 1893. Of twenty cases of intra-cerebral abscess on which he had operated, all except two recovered, giving an operative mortality of 10 per cent. McEwan's figures have not been surpassed or perhaps even equalled up to the present day. The precepts inculcated by him were soon being widely practised, and have resulted in the preservation of an untold number of useful lives.

In the opening year of the present century, a brilliant young surgeon named Harvey Cushing, who had just recently been appointed to the staff of the Johns Hopkins Hospital, Baltimore, decided to devote his life to the surgery of the nervous system. In preparation for his task he spent a year in Europe. After a brief visit to Horsley in London and a short stay in France, he went on to Berne, where he carried out investigations on intra-cranial pressure at the suggestion of Kocher. Finally, after a period in Italy, he spent four months with Sherrington in Liverpool. Returning to America in 1901, he gradually built up a school of neuro-surgery, first in Baltimore and subsequently in Boston, which came in time to make the United States the Mecca of neuro-surgery. Many of the famous neuro-surgeons of to-day were at one time or another pupils of Cushing's, such as Cairns and Dott in this country. Cushing's influence on neuro-surgical work was transcendental. There was a steady emenation of new ideas from his clinic : now some advance in operative technique, again the syndrome characteristic of a certain region, or it might be a classification of tumours belonging to a particular group facilitating their diagnosis and treatment. Two problems which perhaps not unnaturally engaged the attention of the pioneers in neuro-surgery at a very early stage were, the prevention of blindness due to pituitary enlargements and the relief of the inveterate pain of trigeminal neuralgia. The physiology of the tiny gland, once thought to be the habitation of the soul, and later allocated the more lowly office of producing the nasal secretions, was worked out by Cushing, and the enlargements to which it was subject were clearly defined. The endo-nasal operation devised by him for the relief of pressure on the optic nerves and chiasm remains the ideal one for certain types of pituitary growth even to the present day. Subsequently, an approach along the floor of the anterior fossa came into favour for the removal of tumours extending upwards through the diaphragma sellæ. X-ray therapy has proved invaluable in consolidating the visual improvement obtained by

operation, and it may indeed be the only form of treatment necessary when vision is not as yet seriously compromised.

Even before Lister's day, attempts had been made to relieve the almost unbearable pain of trigeminal neuralgia by dividing the main nerve trunks just outside the skull. Unfortunately, this difficult feat only resulted at best in temporary relief. Alcohol injection of the roots was not any more lasting in its effect. Attention was then directed to the gasserian ganglion, which was either injected with alcohol or completely rooted out. But these latter procedures, besides being dangerous and technically very difficult, had the drawback that vision in the corresponding eye was imperilled because of anæsthesia of the cornea. In 1901, Frazier, in America, introduced the less difficult operation of division of the sensory root of the fifth nerve behind the ganglion, at first completely, but later only in its outer two-thirds, so that corneal sensation was preserved and danger to vision eliminated. Frazier carried out this operation over one thousand times with a mortality rate of only a fraction of one per cent. Recently a Swedish surgeon has gone a step further, dividing the pain fibres, and the pain fibres only, as they lie within the brain stem.

At one time all tumours arising within the brain substance were considered so hopeless that they were just lumped together and classified as sarcomas—the most deadly of all tumours. Neuro-pathologists, however, demonstrated that these tumours arise from the supporting cells of the brain—the glia—and renamed them gliomata. Many types of glioma are now recognised, varying greatly in malignancy. Some are of such a fulminating nature that all forms of treatment are unavailing. Others melt away rapidly with complete relief of symptoms under the influence of X-rays, though, unfortunately, the respite is rarely for long. Still other gliomas, if completely excised, do not recur, and a lasting cure is provided. Thus the cerebellar astrocytomas of young people are amongst the most favourable of all intracranial new growths. The sorting out of the gliomas into different groups, the behaviour of which could be predicted from their cellular structure, was one of the finest achievements in neuro-surgery, and much of the credit belongs to the brilliant workers of the Cushing school. In the treatment of the gliomas, the help of the neuro-pathologist is indispensable. If the latter is supplied with a minute particle of the growth, he can tell the surgeon within a few minutes the type of glioma with which he has to deal. The surgeon is thus furnished with an invaluable guide on which to base his treatment. If the growth is a highly malignant one, for which operation would be quite futile, he will know to stay his hand. On the contrary, when the tumour is of a favourable nature, he will not permit himself to be easily turned aside from an effort to effect a complete removal. Though the number of cases in which operation is unprofitable is regrettably high, the outlook in regard to the gliomas in general is far from being as gloomy as was depicted a decade or two ago. Indeed, the results that can be achieved do not fall far short of those secured in cases of malignant disease in many other parts of the body.

One morning in 1895 the entire news-reading world was startled by the announcement that a ray with quite fantastic powers of penetration had just been discovered. Röntgen's name was at once a household word. Ill-informed speculation abounded,

and great alarm was felt in many quarters lest the new rays should get into the hands of unprincipled persons and be adapted to nefarious purposes; indeed, that the rays might mean an end to all decency and privacy. An enterprising London firm increased its turnover very handsomely by the sale of X-ray-proof underwear, and refined folk in New York made determined efforts to have legislation brought in prohibiting the "use of X-rays in opera glasses." In medical circles interest in the new discovery, though more prosaic, was equally great. In the domain of neuro-surgery films of the skull and spine furnished information of prime importance in cases of trauma, and evidence of diagnostic and localizing value was occasionally forthcoming in cases of brain and spinal-cord tumours. It was not, however, until 1918, when Dandy demonstrated that air could be used as a contrast medium to outline the ventricles, that the diagnostic value of X-rays came to be utilized to the full. Dandy thus provided a method whereby not only the situation but also the size of most brain tumours could be determined, and his contribution was epochal in importance. Another highly specialized form of radiological investigation, the possibilities of which have not yet been properly evaluated, is that of cerebral arteriography, in which an opaque medium is injected into the carotid and vertebral arteries, and X-ray shoots are made within the next few seconds. Departure from the normal configuration of the intra-cranial vessels affords a means of localizing such tumours as are clinically mute, and it is thought by those entitled to give an authorative opinion that cerebral arteriography may come to supply not only a topographical, but also a pathological diagnosis, when the vascular pattern of the various types of brain tumour have come to be sufficiently well known.

It would be wearisome to discuss all the important contributions to neuro-surgical technique that have been made since the beginning of the present century, and I shall restrict myself to a cursory reference to those of pre-eminent value. Mention might first be made of the simple device introduced by Cushing in 1911 for the control of the medium-sized vessels of the brain and meninges—the silver clip. The invention may not sound impressive, but it received the immediate blessing of neuro-surgeons everywhere. The vexatious and time-consuming manipulations necessary to control the fragile cerebral blood--vessels by ligature were superseded by an expedient precise, simple, less injurious. Another innovation of great value, evolved by Horsley and Cushing independently, was the so-called "muscle-stamp," for the control of oozing from the dura, the walls of the large venous sinuses, etc. A contribution of signal value was the introduction of the high-frequency current for the coagulation and cutting out of intra-cranial tumours by Cushing and Bovie in 1926. Diathermy served a dual purpose : it reduced the incidence of bleeding in intra-cranial work in general and paved the way for the extirpation of many tumours, the removal of which previously had had to be abandoned because of difficulties of access. It so happened that many of the tumours in which risks attending removal had been prohibitive were benign : the meningiomas, acoustic neuromas, cholesteatomas, and so forth comprising about 35 per cent. of intra-cranial growths. Thus the importance of endothermy to neuro-surgery can scarcely be exaggerated; it greatly increased the number of brain tumours in which hope of lasting cure might be entertained.

Two very recent additions to our operative resources which may well prove to rank in importance with those just mentioned, are substances prepared by the fractionation of human blood plasma, and named 'fibrin foam' and 'fibrin film' by their originators, Ingraham and Bailey of Boston. The foam is of immense value as a hæmostatic agent, whilst the film provides an excellent dural substitute which, as it does not develop adhesions to the underlying brain, may go a long way towards a solution of the problem of traumatic epilepsy.

In any history of neuro-surgery mention must be made of Professor Geoffrey Jefferson of Manchester, who was largely responsible for the inauguration of the British Society of Neuro-Surgeons in 1924, and who has remained one of the leading figures in neuro-surgery in this country since that date. He has been responsible for many important advances to which time, unfortunately, does not permit me to make reference. Amongst other distinguished pioneers in neuro-surgery in this country were Sir Charles Ballance, Wilfred Trotter, Sir Percy Sargent, Bathe Rawling, and Donald Armour, and also Mr. Adams McConnell of Dublin.

It is hardly necessary for me to allude to the way in which the gloom enshrouding the subject of pyogenic infections of the central nervous system was so largely dispelled by the introduction, first, of the sulphonamide drugs, and later, and more particularly, of penicillin. Many suppurative intra-cranial affections previously uniformly fatal clear up as if by magic, provided chemotherapy is instituted promptly and intelligently, e.g., pneumococcal meningitis, septic thrombosis of the cavernous sinus, diffuse subdural abscess. During the recent world war, the British mobile neuro-surgical teams, organised by Professor Sir Hugh Cairns, rendered magnificent service in the forward areas of the various battle-fronts. These teams carried their penicillin-sulphonamide powders with them, and carefully sprayed them on the walls of the complicated brain-tracks, which they had debrided at the earliest possible moment. Operations, the magnitude and complexity of which were not even envisaged in the 1914-18 war, were successfully carried out often in a matter of hours of the infliction of wounds so ghastly that, to the uninitiated, hope of survival seemed fantastic. A comparison of the results obtained in the treatment of penetrating wounds of the skull and brain in the recent war with those of twenty-five years ago gives some idea of the progress that has been made in the interval. In the 1914-18 war the death-rate from wounds in which the dura had been penetrated was between 55 and 60 per cent., though Professor Cushing, in his final series of cases, managed to reduce the mortality to what was then considered the astonishingly low figure of 28.8 per cent. In the recent war the death-rate from all forms of penetrating wounds of the brain was in the region of 9 to 10 per cent. (Even patients moribund on admission to hospital, who died within a few hours from overwhelming brain damage and not from infection, are included in the latter series.)

Neuro-surgeons have recently had the temerity to make an incursion into the territory of the psychiatrist, and have shown that certain most distressing and incapacitating forms of emotional disorder may be alleviated by operation. I refer to the procedure known as frontal leucotomy, which was devised by Moniz and

Lima for the treatment of anxiety and depressive states so profound as to render the sufferer incapable of any sort of useful employment. Though the range of application of the operation and a precise knowledge of the tracts in the frontal lobe to which section should be restricted still awaits accurate definition, many hundreds of leucotomies have already been performed, and the results indicate the undoubted merit of the procedure in carefully selected cases; patients who have had to be kept under institutional care for many years being enabled to resume useful and even responsible work with a contented and happy outlook on life.

This brief record of the contributions to neuro-surgery, unfortunately, fails to take note of the spirit which infused the daily lives of the great men who laid its foundations and built up its various departments. Amongst other attributes common to them all was honesty of purpose, a simple desire for the truth and nothing but the truth. It is given to but few in any age to make an outstanding discovery, but this spirit of the pioneers is within the reach of everyone. One might say of each of them, as Shakespeare said of Brutus, "His life was gentle, and the elements so mixed in him that nature might stand up and say to all the world, 'This was a man.' " In conclusion, I do not think I can do better than quote from the short address made by Sir Astley Cooper to the new members of the Royal College of Surgeons when he was president:—"And now, gentlemen, give me leave to tell you on what your success in life will depend. Firstly, upon a good and constantly increasing knowledge of your profession. Secondly, on an industrious discharge of its duties. Thirdly, upon the preservation of your moral character. Unless you possess the first, Knowledge, you ought not to succeed, and no honest man can wish you success. Without the second, Industry, no one will ever succeed; and unless you preserve your Moral Character, even if it were possible you could succeed, it would be impossible you could be happy."

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REVIEW

MODERN MANAGEMENT IN CLINICAL MEDICINE. By F. Kenneth Albrecht, M.D. Pp. 1,238. London: Bailliére, Tindall & Cox. 55s.

IN more senses than one, this book is a weighty contribution to our knowledge of American Medicine: it weighs five pounds. Published in London, this English edition is printed in America and is a beautiful example of the arts of printing and book production. Not everyone will like the arrangement of the pages in double columns, but it enables more matter to be presented in the space. The coloured plates are uniformly excellent and the diagrams almost invariably helpful. One feature which will strike the British reader is the bibliography at the end of each section, and one is afraid that it will make him wonder whether this book is a product of American "isolationism." There are, in all, 763 references to literature, of which 13 are to British medical literature. On this short list A. F. Hurst and P. Manson-Bahr score two each. T. Lewis and R. T. Grant share three, and there are references to the American publications of Robert Jones and "Watson-Jones"; the other British references are to less important sources. In the section on nervous and mental diseases there is a textual mention of the Gordon-Holmes (sic) rebound phenomenon, but no bibliographical references to any British neurologist. Alexander Fleming is credited with having discovered penicillin, but the reader is not referred to any British source among the fifty references which conclude the section on chemotherapy. (It is of minor importance that our author does not use the British titles of honour which these distinguished doctors have had conferred upon them.)

Although the book seems to depend on American sources, the British reader will find much that is familiar British teaching, much that is new and refreshing, and some statements which are a little surprising, as when he reads that in myxœdema "electro-cardiographic examination may reveal an inversion of T_1 . . . said to be almost pathognomonic of hypothyroidism." He will perhaps regret that Dr. Albrecht is either unfamiliar with, or has thought unworthy of inclusion, many recent advances in medicine, including, for example, the notable work of William Evans and his colleagues on the care and management of cardiac patients.

In spite of these criticisms, this is a most interesting and valuable book. Dr. Albrecht's opening words in his preface are that "this volume is intended for the doctor's office, not his library"; its admirable arrangement renders ready reference easy, but the numbered lists of symptoms, physical signs, and lines of treatment will commend themselves not only to the practising doctor, but also to those who are reading for examinations. His frequent use of tabular statements of comparison or contrast will remind old Queensmen of our own Professor Lindsay's teaching methods.

Perhaps the best section is that on diseases of the respiratory system, which is not surprising, as Dr. Albrecht is Consultant in Tuberculosis to the State of Kansas. Here a new type of pneumothorax apparatus (the Singer) is described; it appears to be an excellent one, and its sturdy construction renders it portable without anxiety. Two notable features of the book are the chapters on case-taking, which leaves nothing unsaid, and on the case of the ambulatory patient, with detailed instructions to those suffering from various diseases. There is also a helpful chapter, contributed by Dr. Seward E. Miller, on clinical laboratory medicine. R. M.

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Gynaecology in General Practice

By J. H. P. GIFF, M.D., D.P.H.

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IN choosing as my subject for this address "Gynæcology in General Practice," I want to reassure you.

First of all, I wish to assure the gynæcological specialist that I do not presume to offer them instruction in their work; and to my fellow-general practitioners I give the assurance that I do not wish to appear to presume to be their mentor.

The general practitioner has seldom the time for the systematic study of any speciality—he has to have a working knowledge of them all. I do think, however, that the modern trend amongst general practitioners is to fight shy of many conditions that do not appeal to them as being straightforward medical conditions. The reason for this may, no doubt, in large measure, be the lack of time I have already mentioned.

The woman with "backache"—and goodness knows backache seems to be a too common affliction of the female sex—may require too much time spent on investigation. The easy path is to pass the patient over to the man who specialises in investigating the causes of backache, and this eagerness on the part of the general practitioner to avoid responsibility in these matters has two adverse effects. It has produced a type of patient who is "specialist minded," and who is quite sure that only a specialist is competent to deal with her case. Moreover, it robs the doctor of an important and intimate contact with those who, despite all we males may think, are nevertheless, in most cases, the actual heads of the household and who do, in truth, direct the medical policy of the family.

A large number of the gynæcological complaints met with in the consulting-room, though extremely troublesome and often almost disabling to the patient, are capable of being quickly relieved by simple measures not difficult to apply.

This paper is based on the gynæcological complaints of 170 women met with in my own practice, and I endeavour to tell you of their complaints, the findings on examination, the treatment, and the end results. I have included only those cases which proved to be purely gynæcological, and in only a very few has operative treatment, when found necessary, been carried out by myself.

It is essential that the patient's history be carefully enquired into—none of her complaints is too insignificant to note. Each patient must be treated with individual technique. Modesty, prudery, fear, domestic complications may all tend to distort the history. A good deal of judgment may be required in assessing the value of the history. If she complains of pain, the nature of that pain requires careful investigation. Dull, aching pain suggests inflammation or congestion. Acute pain, if not dysmenorrhœa, may be due to abortion. Dragging pain, especially if relieved by rest, is a marked pointer to a label of "prolapse." Various pelvic conditions

are associated with pain in the sacrum, the lower abdomen, and the thighs, but in many cases pelvic pain is hysterical in origin—though a diagnosis of "hysteria" should be guarded. It is wonderful how often a large tumour may be found in a woman who appears to have no complaint. Menstrual history is most important and often the menstrual history may belie the physiological tumour found to be present. It is astounding how many women, because they are naturally shy of discussing such matters, will deny constipation and dyspareunia; and it is tragic how many delay their consultations until almost or altogether too late; quite sure, as the result of previous tête-à-tête with Mrs. Jones or Aunt Mary, that their complaint is "quite natural, my dear," or "only to be expected at your time of life, Mrs. X."

For obvious reasons, a history of previous health must be elicited. Consideration must be given to the patient's age, occupation, social stratum, and apparent intelligence. The woman who has to earn her own living or the hard-working farmer's wife is seldom obsessed with the awful possibilities of "the change of life" as is the neurotic, introspective, or indolent sister of a different situation in life. Assessment of vaginal loss may be difficult, because a woman who admits the use of half a dozen diapers per day may be bleeding freely, while the more fastidious patient might use many more with much less loss.

The equipment for dealing with gynæcological cases in the consulting-room need not be extensive: rubber gloves, a Sims duckbill, a fenestrated bi-valve, and a Ferguson speculum, a sponge-holder, a dressing forceps, an insufflator, and applicators practically complete the armamentarium. A small cautery machine is useful. With these combine gentleness and sensitivity of touch, and the equipment is complete. The patient should not be persuaded to be examined, but a refusal to give treatment or advice without examination is a persuasive as well as a wise attitude to adopt. In no case must a maid be examined at the request of an employer, without her own consent, and the results of such examination divulged to the employer without the patient's consent, in writing.

It is wise to give the patient the impression that, at the moment of examination, her case and hers alone involves your full attention. A friend of mine advises that for all gynæcological examinations an extra fee should be charged. Apart from the financial gain to the examiner, my friend suggests that this procedure impresses the patient with the special nature of the examination and substitutes business ideas for sexual ones.

The first step in examination should be inspection and manual examination of the abdomen, with percussion and auscultation if necessary. Then inspection of genitals, all abnormalities being noted. My own procedure is then to examine with a well-lighted speculum, and I prefer a bi-valve type, before proceeding to bi-manual examination.

In my series of cases the points I have emphasised are:—

HISTORY.

Age: married or single: pregnancies: frequency: scalding or pain: incontinence;

stress incontinence : leucorrhœa : backache : abdominal pain : menstrual history : dysmenorrhœa : metrorrhagia : uterine hæmorrhage : pruritus : constipation : feeling of pressure in vagina : dyspareunia : headache : dizziness.

Examination.

A general attempt to confirm the answers to above questions. Any abnormal appearance of vulva : evidence of pruritus : cystocele : rectocele : condition of vaginal mucosa : vaginal discharge and its nature : foreign bodies : condition of cervix-erosion, os opened or closed : polypi : position of uterus : contents of fornices : size of uterus : mobility of uterus.

In a paper of this kind brevity is imperative, but I would like to give, very briefly, my idea of the ordinary everyday findings and their indications from such examination as I have mentioned.

Abnormal appearance of vulva.—Hypertrophy of labia minora—suspect masturbation.

Oedema of vulva.—Cardio-renal disease : angio-neurotic œdema : intrapelvic pressure : toxæmia of pregnancy.

Varicose veins of vulva.—Any condition causing increase of intrapelvic pressure, such as tumour, whether pathological or physiological, or prolapse of the uterus.

Ulcers of vulva.—Thrush, diphtheria, or Lipschutt's disease, venereal disease or malignancy.

Swellings of vulva.—Bartholin cyst, with or without abscess formation, sebaceous cyst, or hæmatoma.

Warts of vulva suggest specific disease. A history or appearance of pruritis makes it imperative for one to seek such conditions as *intertrigo*—due to obesity, with excessive sweating or vaginal discharge, with lack of cleanliness; *eczema, lice, scabies, psoriasis,* and *ringworm,* and might I suggest that no case of pruritis should ever be dismissed without examination of urine for sugar. While pruritis may be a feature of any of the above conditions or a manifestation of the menopause, it is a common symptom in diabetes in the female.

In looking at the history of the series of cases under consideration, the two most common complaints are leucorrhœa and backache : 52 per cent. suffered from the former and 44 per cent. from the latter conditions.

I would like to discuss both of these conditions.

Leucorrhœa.

It is absurd, as well as useless, to attempt to cure vaginal discharge without making an endeavour to investigate the cause.

In my own case I make one exception to this, that is, in the case of the unmarried, and more especially the young, virgin.

In these cases I have found it useful to impress on the patient that there is a definite cause for all leucorrhœa and that leucorrhœa is an abnormal condition, but that for a beginning we will try simple measures. In such cases I always try a course of S.V.C. first.

If it is a success, the patient's confidence is definitely won. If it has not been a success the patient, impressed by our previous chat, is almost invariably interested enough to come back for further discussion, and is quite willing to submit to an E.U.A.

The origin of vaginal discharge may lie in vagina, cervix, uterus, or tubes, or from a fistula communicating with the pouch of Douglas or the rectum.

In my experience and in the series of cases under survey, the commonest causes of vaginal discharge are infection with trichomonas vaginalis or erosion of cervix or both.

The *trichomonas vaginalis* is a flagellate protozoa.

Short of microscopical exhibition, its presence may be diagnosed from the general appearance of the inflamed area. In fact, in the majority of cases, an absolutely correct diagnosis can be made from examination alone. In mild cases there may be only a persistent slight discharge. In severe cases the vaginal mucosa looks diffusely inflamed and, here and there, studded with pin-point red patches. The discharge is thin, often frothy, sometimes foul-smelling, and usually yellowish in colour. A common accompaniment is heat or itch in the vagina and irritation of the vulva. I have found that the condition is usually amenable to one or other of the following lines of treatment.

1. *S.V.C.*—Two tablets inserted three times daily for one week, then two tablets twice daily for one week, and then two tablets each night for a week. It is important to stress that the tablets be used during menstruation. An important adjunct to this is a daily douche of lactic acid—one drachm to a pint of blood-warm water.

2. *Picragol.*—One pessary inserted each night for twelve nights and daily attendance at the consulting-room for insufflation with picragol powder.

In the case of the virgo intacta, a failure of response to either of these treatments demands examination under anæsthesia.

The treatment of vaginal discharge in young children presents a big problem. It demands great patience. I have only seen one case due to gonorrhœa. I have also seen a case due to the introduction into the vagina, by the child herself, of a F.B. (cotton-wool it was in this case). Her persistence in continuing the practice decided me to call in the help of a psychiatrist. Most other cases of vulvo-vaginitis that I have seen in children could be accredited to debility or uncleanliness. These usually responded to gentle douching with boracic solution (one in fifty) coupled with general tonic treatment.

I have never seen a case of vaginal thrush in a child, but I have seen two in adults, and both of these are worthy of special mention. In the one case examination of the husband revealed that he was suffering from a similar infection of the penis. I treated both successfully with gentian violet painting, and left it to the parties themselves to decide who was the originator of the infection. Suffice it to say that both had negative Wasserman reactions.

The second case proved more difficult, and finally proved that my diagnosis of "thrush" was incorrect. The husband, in this case, was not suffering from the

condition. Both husband and wife showed negative W.R., and the woman's complaint kept recurring despite treatment with Mersagel and gentian violet.

The real worry to me in this case was, that each recurrence in the vagina was heralded by a similar condition in the mouth. I sought the help of a dermatologist and a gynæcologist, and the result of their deliberations was a diagnosis of "recurrent buccal and vaginal ulcers" or "Lipschutt's disease." This was a completely new condition to me. I have since learned that it is a rare condition caused by infection with bacillus crasus. We could find no suggestions as to treatment, so she was given a course of intra-muscular penicillin (250,000 units in all) and plugs soaked in penicillin cream were inserted into the vagina twice daily. In addition, she was given penicillin lozenges to suck. The condition responded well and was cleared up in a week. Up to the time of writing (two months later) there has been no recurrence.

One other case of leucorrhœa is worth mentioning. The patient was a woman of 40 years of age, a nullipara, though married for twenty years. She assured me that only once before in her life had she visited a doctor. She was then 18 years old, and the doctor had diagnosed some condition of the womb which had responded to manipulation by the doctor. What the treatment may have been I do not know, but I was able with difficulty to produce from her vagina a small watch-spring pessary, which was snugly fitting round the cervix. With a few days of douching her leucorrhœa completely disappeared. Could this F.B. also have been a cause of her sterility?

An *erosion of the cervix* is an area of cervix surrounding the os which has been denuded of epithelium. On appearance it is bright red, granular looking, and may have small projections on the surface. Sometimes it bleeds easily. To touch, it is soft and velvety.

There is great difficulty in differentiating an early epithelioma, but in my experience three findings help in deciding the diagnosis of malignancy:

1. The malignant lesion looks "fleshier."
2. It feels more granular and is more friable.
3. The edge is definitely raised and pronounced.

If the erosion is a small one, I have found that cautery followed by application of silver nitrate is sufficient to clear up the condition. This is especially so in the case of post-natal erosion. At the most, a couple of such treatments is all that is necessary, and the treatment can be conveniently carried out in the consulting-room with a small cautery machine. I have tried the method of applying silver nitrate, without cautery, but this is irksome to the patient, as it may require months of frequent attendance, and the result can never be guaranteed.

Larger erosions necessitate diathermy coagulation cautery in the operating theatre under anæsthesia. Such procedure has the advantage that it only necessitates absence from home of four or five days, and in the majority of cases the result is a source of great rejoicing to the patient, who for years has suffered discomfort under the opinion that "whites" is a female affliction, to be borne with the fortitude of the sex.

Backache.

Backache is a symptom of so many conditions. It requires such exhaustive investigation that the appearance in the consulting-room, during a busy surgery, of a patient suffering from backache is enough to tax one's vocabulary.

We are, however, at the minute concerned with gynæcological causes, and in the series of cases I present, backache was a feature in 75 cases out of 170—a mighty big proportion.

I think it probably correct to say, at any rate it seems to be my experience, that backache due to purely gynæcological cause is not accompanied by tenderness to touch, in the part of the back to which the pain is referred.

The backache is probably caused by pelvic congestion or by dragging on pelvic supports. It would seem to be rational then, that every case of backache should have a careful pelvic examination.

Cervical conditions responsible for vaginal discharge, e.g., erosion, gonorrhœa, or any inflammatory pelvic mass can cause congestion. The treatment of such cause will be the obvious course to adopt. Dragging on the uterine supports may be caused by displacement or prolapse of any degree or by pendulous abdomen.

It is scarcely likely that retroversion in a nulliparous woman, when the uterus is freely mobile, can be considered a cause of backache. On the other hand, if the uterus is not freely mobile, and especially if it is bulky or bound down by pelvic adhesion, it is almost certainly an aggravation if not a cause of the backache.

If the uterus is retroverted in a woman who has borne children, provided it is mobile, replacement and the insertion of a pessary for a few weeks may give great relief. Often the relief is maintained even after removal of the pessary.

If the abdomen is pendulous, a well-fitted supporting corset gives great relief. It is a further help if the patient is encouraged to put on and adjust the corset while lying flat on her back.

In any case of backache, especially those due to inflammatory causes, infra-red radiation of the lumbar region may be comforting.

And now, may I venture to submit to your attention a few of those very dry and boring things called statistics :—

I have placed them in groups according to age and parity. See Table A.

The largest number of women seen were in—

the age group 30—39 (37%)—of these, 71% were parous.
next the age group 20—29 (29%)—of these, 37% were parous.
next the age group 40—49 (21%)—of these, 80% were parous.
next the age group 50—59 (8%)—of these, 70% were parous.
then the age group 10—19 (3%)—of these, all were nulliparous.
and the age group 60 and over (1.8%)—of these, 66% were parous.

This means that the largest number of women seen lay within the child-bearing period. Of all these, 78 per cent. were housewives.

It is worth noting that these figures would imply that the women who are the most important members of the community are those who suffer the most ill-

health. And of these housewives, 77 per cent. were mothers having the added strain and responsibility of the upbringing of a family.

Of these 133 housewives, no less than 68 complained of backache. One can scarcely imagine any condition more crippling to a woman who, by reason of her calling, needs to be so active.

Taking the incidence of disease under the same age grouping. See Table B. A total of 71 suffered from erosion, i.e., 42%. Of these, 52 suffered from erosion alone, i.e., 30.6%, and 20% of those suffering from erosion were also the victims of prolapse. 94% of these women suffering from erosion were within the child-bearing age and 64.8% had borne children.

Of the thirteen women suffering from trichomonas infection, all were within the child-bearing age, but 8 were nulliparous. Of 29 cases of prolapse, 28 were parous; 17 had borne three or more children; of these, 20 were in the age group 30-49 years, and only 2 were between 20-29 years.

Twelve of the series of patients suffered from fibroids; eight of these were parous.

None was under 20 years of age, and ten were within the child-bearing age. In addition, there was one mother who had a fibroid and an ovarian cyst.

Four cases of Bartholin cyst came under attention. One could be attributed to gonorrhœal infection, the other three appeared to be attributable to injury.

The three cases of urethral caruncle included in the series were all over 60 years of age. It was only possible to establish a diagnosis of gonorrhœal infection, bacteriologically, in one case—an unmarried woman of 35 years of age. There were, however, two other cases of acute tubal infection, presumably gonorrhœal.

Both of these were married women. One was in the age group 20-29 and had four children, the other was between 30-39 years of age and had two children.

Epithelioma of cervix was demonstrated in one case—a woman of 57 years of age who had borne five children.

Malignant ovary was seen in one case—a virgin of 42 years of age. Ovarian cyst was the condition seen in four cases—one in each age group from 10 to 49 —and of these, two were nulliparous.

There was one other case of ovarian cyst where erosion of the cervix was an additional factor.

As regards displacements of the uterus, the two cases of anteflexion in the series were both nulliparæ, between 20-29 years of age. Retroflexion or retroversion or both was the finding in ten cases. Of these, six were of the group 30-39 years, and only one was nulliparous. Polypus was the cause of the complaint in two cases, both of whom were over 40 years of age and both had borne children.

Seven cases were seen whose troubles could definitely be attributed to neuroses and fears. Six were between 20-29 years of age, and it is interesting to note that four of these were nulliparous. Hormonal dysfunction, e.g., hyperthyroidism or immaturity, was the cause of the troubles of four of the series.

In only three cases was dyspareunia per se the condition complained of.

In three cases the condition requiring attention was abortion—either incomplete or missed.

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From all that I have said I would not wish to convey the impression that gynæcological diagnosis is always an easy matter. The diagnosis of any case may be impossible. A search of the literature simply leaves one convinced that here is a case so rare that it has never been met with by anyone else.

But so much can be treated and perhaps set right, by simple measures, that examination is always worth while and, as I have said before, so many of these simple measures are so easy to apply in the consulting-room. And should the general practitioner, following examination, feel that he is unable either to diagnose or treat the case himself, there is always the consultant colleague to refer to. Indeed, I feel certain that should the general practitioner feel that such a course is necessary, he loses no kudos. Instead, he probably cements his relationship with the patient, for not a few women like to be able to say, "Dr. X himself was completely baffled, and had to send me to a 'professor.' "

I need scarcely add that, in some cases, the reference to the specialist has also the saving grace that, should things eventually go wrong, the blame has been timely shifted to the "professorial" shoulders.

I heard someone say the other day, "Why is gynæcology such an uncertain science?"

I venture to assert that gynæcology, like all other departments of clinical study, is an uncertain science only to those who are inexperienced.

To those who have experience it is a fascinating branch of our work.

Experience can only be gained by practice, and practice can only be acquired by those interested enough to find out for themselves—and to record their findings.

TABLE A

The largest number of women seen, were in—

the age group 30—39 (37%)—of these, 71% were parous.
next the age group 20—29 (29%)—of these, 37% were parous.
next the age group 40—49 (21%)—of these, 80% were parous.
next the age group 50—59 (8%)—of these, 70% were parous.
then the age group 10—19 (3%)—of these, all were nulliparous.
and the age group 60 and over (1.8%)—of these, 66% were parous.

TABLE B

INCIDENCE OF DISEASE TAKEN UNDER SAME AGE GROUPING AS IN TABLE A.

Erosion.—A total of 71 (i.e., 42%).

Erosion alone: a total of 52 (i.e., 30.6%).

Erosion with prolapse: a total of 14 (i.e., 20% of these suffering from erosion were also the victims of prolapse). 94% of the women suffering from erosion were within the child-bearing age, and 64.8% had borne children.

Trichomonas.—13 cases: all within child-bearing age, but 8 were nulliparous.

Prolapse.—29 cases: 28 of these were parous, of whom 17 had borne three or more children; 20 in age group 30-49; 2 in age group 20-29.

Fibroids.—12 cases (none under 20 years of age) : 8 were parous; 10 were within the child-bearing period.

Fibroid with ovarian cyst.—1 case.

Bartholin cyst.—4 cases : gonorrhœal infection, 1 case; injury, 3 cases.

Urethral caruncle.—3 cases : all over 60 years of age.

Epithelioma of cervix.—1 case : the patient was 57 years of age and had borne five children.

Ovarian cyst.—5 cases : one in each age group from 10-49 (of these, 2 were nulliparous), and one where erosion of cervix also existed.

Uterine displacement.—Anteflexion : 2 cases, both nulliparæ, between 20 and 29 years of age. Retroflexion or retroversion : 10 cases, 6 in age group 30-39, and only one was nulliparous.

Polypus.—2 cases : both parous and both over 40 years of age.

Neuroses and fears.—7 cases : 6 of these in age group 20-29. 4 of them nulliparous.

Hormone dysfunction.—4 cases.

Dyspareunia.—3 cases.

Abortion.—3 cases.

REVIEWS

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The Problem of the Aged in Northern Ireland

By EILEEN M. HICKEY, M.D., F.R.C.P.I.

ANY person interested in geriatrics should be grateful to Dr. Duncan Lees for his outspoken Minority Report to the Nuffield Hospitals Survey in Northern Ireland. He states that "The conditions in which the aged are now forced to live are quite disgraceful for a civilized society. If a proper provision for T.B. is the most urgent measure on the grounds of public health, a better provision for the aged . . . is the most urgent on grounds of human decency."

The approach to the same problem in the recently published "Red Book," also concerned with Hospital Services but compiled by local observers, stands out in sharp contrast. In it the only references to this really urgent and most pathetic problem emanate from the woes of the mental hospitals. "These hospitals," it is said, "are becoming overcrowded by old people whose relatives either cannot or will not look after them at home." It would be interesting to know how many, if any, of the compilers of this little book have had to face this particular problem in their own homes! It is by no means a simple one. A further complaint is that, "since they are irrecoverable, they tend to distort the recovery rate and obscure the progress that has been made in the treatment of mental disease"; and, last but not least, they "give a false picture to the death rate." How perverse they seem to be!

What a contrast all this is to the spate of articles, pamphlets, schemes for special housing, Old People's Clubs, etc., that is now flooding England! Is the medical profession in Northern Ireland not prepared to present the case of the aged on its own merits and give it the very sympathetic consideration that it deserves?

There are two very cogent reasons why this problem should be tackled without delay. The principal reason is the existing state of affairs, of which most people here appear to be unaware but which is none the less deplorable. The second is the well-known fact that the ratio of aged to other groups in the community is going up steeply. Let us examine very briefly at least one aspect of this problem as it exists in our midst. It will come as a surprise to most people here to learn that there are at the moment more than two thousand old people in the Six Counties *living alone who are either wholly or partially unfit to look after themselves.* Each of these two thousand is therefore in immediate need of attention or help in some form other than mere monetary help. In addition to these two thousand, there are almost another thousand unfit or partially unfit in lodgings, so that one may say that there are approximately three thousand here and now in need of attention. No doubt, each one of these presents his or her own particular thorny problem, not to be solved by any mere coldblooded legislation. Each, no doubt, clings firmly to his or her own little corner, be it ever so cheerless, so dirty, so cold, yet who shall say comfortless, since it may posesss that comfort dearest to nearly every heart, of privacy and liberty? The lodger class is perhaps not quite so pitiable, as a kind landlady can mitigate some of the hardships.

Out of our population of one and a quarter millions in Northern Ireland there are approximately 95,000 old age pensioners. Of these, 14,500 are known to live alone in a single room or cottage or lodge in a stranger's house, having no near relative with whom they feel that they could make a home. This is a sad reflection on our civilization.

So much for present conditions, but what of the future? Turning for a moment to the Beveridge Report, we find that in Great Britain, men of 65 and over and women of 60 who in 1941 comprised 12 per cent. of the population, will in 1971 comprise 20.8 per cent. In 1945 there were 16 pensioners per 100 contributors; in 1975 there will be 31 pensioners for every 100 contributors. One out of every three contributors is therefore likely to have a pensioner to look after. Short of some unaccountable decrease in longevity, the increase in gross numbers from 5.6 millions to 9.6 millions is inevitable. If one assumes that the ratio is much the same for Northern Ireland, the number of pensioners will mount from 95,000 to about 165,000, and consequently the numbers of unfit old persons living alone will increase from 3,000 to over 5,000. Given a situation which is deteriorating so rapidly, it is clear that an attempt to grapple with it should not be delayed.

A brief survey of the existing institutions for coping with the problem will make it immediately obvious how inadequate the provisions are. Roughly speaking, there are five types of accommodation available, other than the workhouses and general hospitals.

	Approximate Number of Persons Accommodated
(1) Separate houses, i.e., Almshouses - -	50
(2) Common Lodging-Houses - - -	215
(3) Charitable Institutions - - -	284
(4) Hostels and Paying Homes - - -	100

These figures were obtained at a fairly recent survey.

It will readily be seen that the accommodation bears little relation to the size of the problem.

Another noticeable feature is that no step has yet been taken to cope with the saddest and most urgent problem, i.e., the provision of suitable hospital accommodation for those aged persons whose mental condition is such that institutional treatment is essential. That there are hundreds of such cases no one is likely to deny. Few adults have not had some experience of them and know the extraordinary difficulties that arise in their management.

There are naturally many arguments against herding old people together in large institutions; in fact, it should only be done as a last resort. The problem is a many-sided one and will need very many attempts at solution. More "Common Lodging Houses" are required: they appear to be very popular with a certain class. Hostels are needed, particularly those of the smaller type, e.g., twenty-five to thirty inmates with a 'homely atmosphere.' Houses, flatlets, cottages built specially to suit the requirements of the aged, should form part of every housing scheme.

Thought and care should be given not alone to the construction of houses, but even to furniture, beds, baths, stairs, lighting, etc., suited to old people. Colonies of small houses or cottages with communal dining facilities and a small hospital attached are most desirable. Clubs for old people in the cities and larger towns would be welcome. Old people's welfare committees should be established in every area. Adequate home-nursing facilities should be available under any comprehensive Government Health Service.

Most of all, perhaps, it is necessary to recognize that the problem in the main is not so much a financial one as a human one. There is probably no class so difficult to legislate for as the aged. Their peculiarities are more deeply ingrained than in any other section of the community. Some are naturally clean and tidy, others could never be made so; some are gregarious, others "wont neighbour." There will always be the lonely cottager who couldn't live away from the loveliness of his Mountains of Mourne or the sound of the waves, just as there will always be those to whom the hurdy-gurdy of the back streets is sweetest music. It will be difficult to find a solution to the whole problem, but with good will, sympathetic understanding, and wise planning much can be done. The medical profession have a share in the general responsibility, and might fittingly play a leading part.

REVIEW

INJURIES OF THE KNEE-JOINT. By I. S. Smillie, O.B.E., M.B., F.R.C.S.E., F.R.F.P.S. 1946. E. & S. Livingstone Ltd. 35s.

DURING the past five years Mr. Smillie has treated in hospital 2,235 cases of injury to the knee-joint, and, in addition, has had 2,700 consultations on cases of internal derangement. From this wealth of material he has produced a book in which every injury of cartilage, ligament, and bone is well described and beautifully illustrated by X-rays and diagrams. About one-third is devoted to the pathology, diagnosis, and treatment of injuries of the menisci. In these cases operation should be performed early, as continuous locking causes changes in the joint which may prevent complete recovery. The importance of rehabilitation of the quadriceps, and especially of the vastus medialis, is stressed.

Many original procedures are described. The author's method of repairing torn crucial ligaments by utilising the vascular peripheral portions of the meniscus is stated to give improved, if not complete, stability.

The text, clear, concise, and without padding, is a pleasure to read. It is a practical, well-thought-out work, which should be read by everyone interested in the treatment of injuries of the knee-joint.

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H. P. H.

Migraine

By F. A. MacLaughlin, M.B., F.R.C.S.(ENG.)

HEADACHE was mentioned early in history under the generic term of Cephalalgia.

Migraine has been known to medical science for nearly two thousand years, and in the first century of the Christian era Aretæus of Cappadocia mentioned heterocrania; the name hemicrania was introduced by Galen, and also mentioned by Celsus; Hippocrates did not attempt to differentiate it, however. Tissot, in 1784, described it in considerable detail in his Dictionary of Medicine.

The name hemicrania was modified to hemigrania, migranea, and megrim, and in the eighteenth century the name migraine came from the French school. The relationship of migraine with eczema, urticaria, asthma, hay-fever, and epilepsy was mentioned in the early part of the nineteenth century by the French Medical School also. So that it will be seen that migraine has joined that ignoble company of the "unsatisfactory diseases," and there it seems to be destined to remain, for the time being at any rate.

It has been stated by an American writer that approximately 7 per cent. of the population of U.S.A. suffers from migraine in some degree, and that 30 per cent. of the sufferers show signs of the disease before ten years of age.

INVESTIGATION.

A great deal of work has been done on the subject of migraine, if one is to judge by the large amount of literature on the subject; and it has been attacked from all angles: investigations into heredity, diet, allergic sensitisation, blood pressures, biochemistry, bacteriology, and the various focal causes, such as septic foci, ocular errors, diseases of various special systems, and, lastly, the E.E.G.

A great deal of information has thus been made available, and a great deal of help may be given to patients suffering from this disease.

DEFINITION.

One definition of migraine is given as "A paroxysmal disease (symptom complex) characterised by hemicrania, and symptomatic evidence of cortical involvement." Osler defined it as "A paroxysmal affection characterised by severe headache, usually unilateral, and often associated with disorders of vision." And these definitions cover it adequately, from a broad point of view.

TYPES.

Before passing to the disease itself, I think it is well to mention the types of people who seem to suffer from migraine, and here, after years of observation, one can give the average statement that they are usually the more sensitive and more emotional individuals of the community, and practically always those of superior intelligence; a glance at their hands will often give a clue to the personality, although in many cases the individual's occupation has modified the shape and texture of his hands; the usual type is a rather narrow hand with long fingers—the artistic hand. This, of course, is an average statement, and all types are seen.

The migraine sufferer is usually one who worries, and hence his mental make-up is such that his temperament lays him open to feel more acutely the vicissitudes of life, producing psychical changes predisposing to attacks; indeed, a vicious circle is formed.

Heredity.

And, of course, as these traits of personality are often handed on to the succeeding generations, we get a perpetuation of migraine in families, and also individuals tend to marry, in the main, those of similar mentality and outlook, with the result that the tendency is to increase the number of individuals predisposed to migraine, and, indeed, the same applies to the whole group of allergic diseases as well, and it will later be pointed out that there is a close clinical relationship between them and migraine.

Sex.

As regards the incidence of migraine according to sex, various observers have put the number at one woman to one man, varying up to four women to one man. My own impression, considering the numbers which I have seen, was about two to one, and this tends to fit in with the generally accepted fact that women are more sensitive in many ways than men, and perhaps more emotional as a rule, so more prone to migraine.

Age Onset.

The age of onset is interesting, as a number of children are seen with typical migraine, usually over 10 years of age, but few under, and in my own experience they have usually been of the quick, alert, restless, and rather fragile type, usually dark haired, and it is a point of interest that one seldom sees a fair-haired sufferer—but, of course, these compose a smaller proportion of the population. Timme has stated that adolescence is the average time of onset, and this fits in with one's own findings, between 10 to 20 being a safe average limit.

I think any manifestations before the age of 10 appear to be of the nature of cyclical vomiting or perhaps acidosis, because the child who gets acidosis is just the type who later may grow into the type of the typical migraine patient. This is a point on which perhaps those who see and treat many children could throw more light; I know that I have seldom had children referred to me before the age of 10 who could be definitely labelled migraine.

The number of attacks, and their severity, tends to become less as the patients grow older, and we seldom find old people who get attacks of a severity anything like those which they suffered when in early adult life; I know one man who still got occasional mild attacks at 70.

I have mentioned that the migraine patient is on the average of superior intelligence; this being so, one would expect to find a higher proportion of sufferers among university students and graduates, and a reference to statistics shows that this is evidently true. Balyeat (1939) mentions that in America the chief groups involved are students, teachers, doctors, nurses; and other statisticians have included clergymen and engineers as well. Balyeat states that about 8 per cent.

of all doctors and medical students suffer from migraine, whereas in labourers it is only about 4 per cent. From my own experience I would have thought 4 per cent. to be high, for I have no doubt that many of those present will agree that it is relatively seldom that one finds typical migraine in hospital practice, whereas in private it is fairly common, many cases being referred simply as headache, and only on careful taking of the history, both personal and family, can one definitely come to a diagnosis of migraine; many of these unfortunate people having done the rounds of a number of doctors before a definite diagnosis has been arrived at, and the condition explained, and put in its true light to them.

Occupations requiring much technical skill of a fine nature, and involving long continued concentration, also predispose to attacks, because the very nature of the occupation attracts the type of individual who is predisposed to migraine. It was interesting to observe among naval personnel how quite a number of men were referred with headache, which was so severe in times of stress as to interfere with their efficiency, and many of these men had attained to positions of relative eminence through their mental superiority, only to find that because of untimely attacks of migraine they were unable to maintain that eminence, and had, perforce, to change their specialist branch for some other which did not expose them to the same strain, and stress of mind.

Migraine and Allergy.

Balyeat, who believes that migraine is largely allergic in etiology, makes the interesting observations in regard to *allergic* patients, that *firstly,* their general health is considerably above average; and *secondly,* that a study of the mental activity of allergic children showed 75 per cent. to be either in the superior, very superior, or genius class. He concludes that these observations equally apply to migraine.

Interests.

For many years, when examining patients with headaches who have come for diagnosis and treatment, and also with typical migraine, I have enquired into their hobbies and recreations with decidedly interesting and helpful results. A very considerable proportion was musical, many capable of producing music, either vocal or instrumental, others who loved music and who listened to and appreciated it, without the gift of production having been developed. Some were artistic and able to draw or paint, or produce objects of an artistic kind—who were in effect creative —and again, many who could appreciate form and colour without being able to create. In this class one had some who were deeply interested in photography. Another group was given to horticulture, and spent much time laying out gardens and tending flowers and vegetables.

It was also striking how many of these people were interested in model-making and carpentry, usually of a fine type, such as cabinet-making; these were chiefly men, the women usually being interested in fine needlework. Then the groups interested in rhythm, those who were interested in poetry and the drama, were frequently met.

It appears to be relatively seldom that the out-and-out sportsman who plays

vigorous outdoor games, and spends much time out of doors in pursuit of his sport, suffers from migraine. I must make one exception to this and that is fishing, for a number of migraine sufferers are ardent followers of Izaac Walton. It will be seen from the above that the interests and hobbies of these patients are creative, and in many cases their pursuits are essentially solitary in nature.

One might perhaps hazard a guess at the reasons for this, namely, that this particular type requires, and seeks, more time for mental rest away from the rush and noise of society and work, in order to rearm his more sensitive make-up for the everyday work of life.

Heredity.

Many patients give a definite history of heredity, not necessarily of headache only, but often of one or several members of the group of allergic diseases. W. Timme (Oxford System Medicine) states 50 per cent. One is often struck by the number of times that the mother of the person under consideration has been the parent who has so suffered, rather than the father. This is borne out by W. Timme's statement that the mother transmits the disturbance in 75 per cent. of cases. Balyeat states that the inheritance cannot be sex-linked, and W. J. Allen, in Archives of International Medicine, who analysed four hundred cases, believes that it is transmitted as a dominant characteristic.

Time of Onset.

A further interesting series of facts which emerges from a study of this disease can often be elicited. Many women only get attacks at a menstrual period, and do not have any attacks when pregnant. Often one gets the history that the patient only gets attacks on a Sunday, or a Monday morning, and that they are liable to attacks if they remain in bed longer than usual, either at a week-end or when indisposed from some other cause. Others get attacks before undergoing some mental ordeal, such as an examination, a solo performance, a musical competition, reading a paper, a critical operation, etc., and others suffer when the ordeal is over, but, interestingly enough, few seem to get an attack during the ordeal.

Some attacks begin at night, and many people find a migraine present on awaking, or it may develop before arising, and again there are those who know on awaking that they will probably have an attack later in the day.

Length of Attack.

The length of attack varies greatly in different individuals, and also in the same individual. Some who are in the severe category may have attacks lasting up to a week, and get into a state of "status migrainous," becoming dehydrated and showing alkalosis from vomiting. One has met a number who get definite sugar hunger, characterised by a longing for something sweet to eat, and also persistent yawning without feeling sleepy or unduly tired; this is relieved by a meal, or even a solitary sweet will help.

Precipitating Causes.

Quite a variety of circumstances can give rise to attacks: firstly, *psychical,* such

as fear, apprehension, worry, annoyance, anger, and, indeed, any emotion is liable to produce an attack, including sexual excitement.

Physical: within the individual—we may find constipation, naso-pharyngeal infections, dental causes, sinus infections, gynæcological disorders, and various other physical conditions which may produce debilitating or toxic effects, and which may also affect the individual psychically as well as physically.

Physical: outside the individual's body—such as exposure to cold, bright light, explosions, irritating fumes to nose, excessive heat, etc. Changes in barometric pressure and humidity are important also. Diet is also quite a potent factor in some patients, and here migraine shows its fairly close alliance to allergy, an indiscretion being sure to produce an attack. Often a quorum of predisposing factors is necessary.

Prodromal Symptoms.

Frequently before the onset of an attack some people are definitely euphoric, feeling unusually well and happy, with a mind which is unduly active and acute; others feel depressed and dull, have no interest in work or play, and feel, and are, actually less efficient than normal; they may also be restless and irritable: this is said to occur before about 50 per cent. of attacks. Abnormal appetite is often complained of before the attack begins, accompanied by an unusual craving for certain foods.

Others, again, feel unduly sleepy and drowsy and have difficulty in concentrating on their work; they will tell you that they have had a marvellous night's sleep, but know this foretells an attack. Many have definite gastro-intestinal disturbance, such as diarrhœa, constipation, or undue flatulence, and an interesting fact which often emerges is, that both stools and flatus are definitely offensive on many occasions before an attack. These symptoms may occur in the same individual during successive attacks, or the changes may be rung from diarrhœa to constipation.

Attack—Auræ.

The actual attack is usually divided into the *aura* stage and the *attack* proper, which begins with the onset of pain, and later vomiting. The auræ are many and varied, and have been conveniently divided into groups by Balyeat:—

(a) Vertigo.—This is a dizziness of varying severity, from a mild sense of instability to very definite vertigo.

(b) Visual disturbances.—These are perhaps the best-known symptoms, being the most obtrusive and the most annoying.

The commonest are probably the zig-zag figures of the field of vision, and may be in one or both eyes, usually both, and tend to travel outwards and disappear; some patients get definite fortification figures instead, but they seem less common.

Another peculiar appearance seen is that of rippling waves of light, which may be coloured, and which seem to produce a shimmerng curtain between the observer and the object which he is fixing. Coloured spots and patches of different sizes and shapes, which may remain stationary or move about, or vary in shape and size, also occur. In this connection patients occasionally mention that they have had

dreams just before awaking with a migraine which included lights and explosions, and which would seem to suggest that the attack can begin during sleep; indeed, I have awakened with a full-blown migraine, and felt that the pain was the cause of my awakening, the aura presumably having occurred during sleep.

Some people always get one type of visual aura, while others get different types of aura in successive attacks. Central scotomata occur which are negative in type, a complete blank being present at the centre of vision, and the patient cannot read, or see accurately what he is doing; this gradually enlarges, and then seems to either get smaller, or just generally disperse; it occurs in both eyes as a rule.

Hemianopia is also a well-known phenomenon, but I have no personal experience of this, and there is some difference of opinion among the various authorities. Russell Brain states that it is a homonymous hemianopia, developing from the scotoma: it seems odd that I have come across very few of these in my own experience. Parsons mentions that the headache and the hemianopic field are on opposite sides. Wilfred Harris has mentioned that it suggests an epileptiform discharge spreading in the visual cortex, but Hubbell, quoted by Foster Moore, states that in fifteen hundred cases of migraine he was unable to find any association with epilepsy. Russell Brain and Foster Moore give confirmatory evidence for this also.

(c) Auditory symptoms occur—and may take the form of low buzzing tinnitus, or of definite dulness of hearing lasting a varying time.

(d) Olfactory phenomena are less common, but patients may complain of temporary changes in smell and taste, usually rather unpleasant in type.

(e) Sensory disturbances are common, such as paræsthesias and anæsthesias—these may occur in face or tongue and frequently in the arm, a glove anæsthesia being occasionally found, less commonly in the leg, and the sensation usually begins in fingers or toes and spreads upwards. Balyeat states that in Hemicrania the parasthesias occur on the side opposite to the headache; this I cannot confirm from personal experience, as one has noticed that the parasthesias occur in what may be termed severe attacks where the headache seems to overflow to, and to be present on the opposite side of the head as well. Sometimes tingling and undue sensitivity or itching of the skin occur.

(f) Motor disturbances seem to be rare, but, of course, temporary diplopia is well-known and is very alarming; it may be present for a few seconds to quite a long period, even days.

In this connection, perhaps, one might mention ophthalmoplegic migraine. There is some difference of opinion as regards the causation of this condition; many authorities, including Parsons, Russell Brain, and Carmichael, are of the opinion that it is doubtful if this condition exists as a functional disease, but that it is usually a manifestation of organic disease of the brain, one feature of the condition bearing this out being, that it is always on the one side, the headache sharing this character also. Another point of interest is, that attacks of migraine which begin later in life should be viewed with suspicion, for they are often the herald of some intra-cranial organic disease, or impending intra-cranial catastrophe.

Aphasia may perhaps be included under motor lesions, as the patient at one stage knows what he wishes to say, but just cannot articulate, and we may have agraphia as well. This merges into the next stage, where we have—

(g) Mental confusion—and here there is a very definite inability to think clearly, or even to call into consciousness the names of the most commonplace objects; this is very distressing, and renders the victim temporarily incapable of dealing with any of the ordinary activities of life; fortunately, however, with the march of symptoms, this is soon left behind.

(h) Vasomotor disturbances occur regularly, with pallor and chilliness and later flushing, throbbing, nasal congestion, and changes in the salivary secretion—being increased or diminished in different people.

Photophobia is frequently present in varying degree, and the patient usually craves darkness, warmth, silence, and solitude.

Attack Proper.

The attack proper usually begins with the onset of the headache, the pain starting as a hemicrania, which gradually increases in intensity, and is usually situated behind one eye or in the frontal region, of a boring and at times almost intolerable character, aggravated by any effort and also by ocular movements; coughing and stooping increase it markedly.

The pain often spreads across to the other side, and also more widely over the cranium generally. The usual rule is for the pain to follow the aura, but frequently the pain starts without the patient being aware of any aura. The severity varies greatly in different people and also in successive attacks in the same individual. Nausea and vomiting may occur before the headache starts, and, as a rule, if they are going to occur in the attack, will do so when the pain reaches its maximum intensity.

Vomiting is common in children, and, of course, this adds materially to the misery of the individual, as it increases the pain very materially during each bout of retching. Later in life the vomiting tends to become a less obtrusive feature, but nausea may persist with each attack instead. The vomiting does not produce any marked relief, and retching may continue for a considerable time, leaving the sufferer very weary, miserable, and exhausted. If it persists for long, a condition of alkalosis develops.

It has been stated that 80 per cent. of men and 90 per cent. of women have had vomiting at some time in the course of their migrainous attacks. The vomiting and pain gradually subside, and frequently the patient goes to sleep, awaking after a matter of hours feeling rested and free from symptoms. Many, however, are left with a definite post-migrainous condition, which is characterised by sleepiness, depression, exhaustion, and sometimes actual bodily soreness; this state is more common if the patient has not been able to go to sleep just after the attack.

Polyuria is a common post-migrainous symptom, large quantities of pale clear urine being passed at fairly frequent intervals. Between attacks, good health and a normal feeling of well-being are enjoyed by the large majority of sufferers.

Migraine has been divided into various types, quite unjustifiably I think, and this only tends to confuse, as one feels that they are really only different manifestations of the same condition, because the different types often occur in the same individual in different attacks and at different periods of life.

Pathology.

Migraine has no known pathology, being a functional disease, and no one appears to have died of migraine per se, so that no assistance of any value has been given by post-mortems.

Theories.

One has read with interest—but with relatively little benefit—much about the researches into the causation of the condition. The various laboratory examinations which have been carried out seem to give very inconclusive results, such as blood, urinary, metabolic, radiological, gastric, and allergic tests and examinations, although a considerable proportion shows allergic sensitivity : this is put somewhere about 90 per cent. by Balyeat, who did extensive allergic testing in a series of 350 cases, using both dermal and intra-dermal methods of testing, the latter apparently being the more sensitive test. It has been stated that the blood urea is raised during an attack, but apparently this is only definite if the patient has been vomiting for a considerable time, and he becomes dehydrated. Contraction of the retinal vessels on the affected side has been mentioned, but the majority of authors state that this is inconclusive, and during attacks on a number of occasions, I have asked my colleagues to look at my fundi, and they were unable to detect any difference in the calibre of the retinal vessels on the two sides.

The various theories put forward include :—

Reflex irritation from elsewhere in the body.—In this there is certainly a great deal of importance, as almost all the various systems can play a part in precipitating an attack: teeth, nose, eyes, ears, throat, gastro-intestinal tract, generative apparatus, acting as reflex irritants; perhaps the eyes being one of the most important in this group.

The fact that evidence of cortical irritation occurs has led to the promulgation of theories which presuppose interference with the cerebro-spinal circulation by changes in the choroid plexus. Moebius, in 1894, suggested adhesions between cortex and dura as a possible cause.

Intestinal stasis has been blamed, and certainly changes in bowel function do occur often before an attack comes on, as has been mentioned. Periodic swelling of the pituitary is another cause put forward by W. Timme (1926).

Toxic conditions are also blamed, and here again any part of the body which can act as a septic focus may be a factor in predetermining the frequency and severity of attacks, conditions such as apical dental abscess, or empyema of antrum, where the sepsis is closed, being very prone to aggravate the condition.

Endocrine dysfunction is another theory which is suggested, and here we have evidence that women who frequently have an attack at a period are free from

attacks during pregnancy, and after menopause also. Some hold that many sufferers show definite signs of endocrine dysfunction.

The vasomotor theory receives considerable support from observations of pallor, flushing, sweating, and the frequently observed sign or symptom of dilated superficial temporal vessels during the attack. Considerable experimental and pharmocological work has been done on this line of research.

Lastly, we have the allergic theory which presumes patches of œdema in the brain, produced by the circulation of substances in the blood, to which certain areas of the brain are allergically responsive, similar to the occurrence of urticaria elsewhere in the body. As has been truly said, where many theories as to causation exist, no one is completely satisfactory, and the same applies to treatment.

Migraine will hence be seen to be a functional disease to which an individual is predisposed by heredity, attacks being precipitated by many conditions and circumstances within and without the body of that individual.

Treatment.

The treatment of migraine has always been looked upon as unsatisfactory and the disease incurable, but I think this is an unduly pessimistic view, because a very great deal can be done towards cure, either complete or, at any rate, rendering the attacks less frequent and less severe. Many hours of misery can be spared by an intelligent and sympathetic approach to, and persistent prosecution of, the treatment.

Preventive.—As regards preventive treatment, probably the only method is eugenics, but as love is stated to be blind, and indeed often appears to be so, it is unlikely that at the present stage of our civilisation this method will be widely used.

Elimination of predisposing causes.—The elimination of predisposing causes is the first step in the treatment, and this covers a very wide range. Avoidance of undue and unnecessary physical and mental fatigue is important, but here it is the latter which is the more so, because the patient is often benefited by exercise in the open air, as it gives him a chance to forget the various anxieties and worries of life, and to keep himself physically fit. The migraine sufferer should so order his life, if possible, that excesses of emotion are avoided in work or play, and this is not always by any means easy, involving for some drastic changes in their habits of life, and also to see that there is sufficient rest of mind and body to suit their own special requirements.

Special senses.—Disturbance of special senses should be sought, and here, perhaps, the eyes are most important, as refractive error and muscular imbalance may play a large part, and it is an interesting fact that these patients are just the type from their artistic leanings (due to their better perception of small differences) where a small error may produce marked symptoms, and an accurate correction, a brilliant result—this was stressed by the late Colonel Elliott when writing on migraine.

Septic foci.—All the many and varied regions which may be acting as septic foci

should be searched, and if any definite cause is found, it should be eliminated where possible, teeth and sinuses being common offenders.

Surroundings.—Certain factors in the surroundings of the individual should receive attention, exposure to damp and cold, heat, bright light, and fumes of a character likely to produce respiratory irritation come into the picture.

Diet.—Diet is important, because many patients appear to be definitely allergic, and they will tell you that they cannot eat certain foods, as an attack follows promptly on what, for them, is a dietetic indiscretion. This is a difficult subject, for there is such a wide difference in individual sensitiveness, that each must be a law unto himself. Many writers have laid down diets for migraine, but one feels that no definite diet will cover all cases.

Constipation.—Constipation plays its part, and some will tell you that if on arising they have the warning signs of an impending attack, and succeed in emptying the bowel satisfactorily, the attack may be aborted, but this may apply also to those not predisposed to migraine, as is well known.

Gynæcological causes.—In women who get attacks at a menstrual period, some form of glandular therapy, such as ovarian extract, has been tried, but apparently with somewhat contradictory results.

Allergy.—Balyeat recommends that all patients who suffer from migraine should have the skin tests for allergy performed, and states that in his series 70 per cent. were skin-sensitive to one or more of the specific food factors and that those who did not so react should have food elimination tests, such as Rowe (Philadelphia) has devised. I have no doubt that where the individual can be proved sensitive to certain articles of food, removal of these from the diet will prove of great value.

A number of migraine patients also suffer from allergic rhinitis, and here the cause may be inhaled or ingested, and this is evidence for the allergic theory, unless the nasal allergy is a parallel affection in a predisposed individual. In the allergic patient desensitisation may be a useful line of treatment, and in a certain proportion of cases of migraine, may alleviate or even cure. A few people complain that excessive smoking is liable to precipitate an attack, and a certain proportion consider alcohol to be a factor in the production of an attack; others consider that alcohol tends to abort it, if taken early in the attack.

Surgery.—Surgery comes into the picture in the treatment of many of the reflex or toxic factors, such as sinuses, chronic appendix, deviated septum, teeth, and here impacted wisdoms can precipitate attacks, also gynæcological conditions may prove potent factors in keeping the tendency to frequent attacks operative.

Symptomatic.—The remedies recommended for treatment are legion, and almost as many drugs as we have in the Pharmacopeia have been suggested as cures, indicating the lack of efficacy of any one of them. In a relatively mild attack some of the sedatives, such as aspirin, luminal, triple powder, barbiturates, etc., are definitely helpful, but in the severe attack apparently most of these remedies are powerless to stem the march of the symptoms.

The patient is usually irritable, feels cold, and objects to noise and fuss, and these may be the reasons for the craving for solitude, quiet, warmth, and darkness, which

are so important; hence, probably the best treatment is bed with a hot jar, drawn blinds, and leave the patient alone, hoping that sleep will soon ensue; a warm bath is sometimes also beneficial.

Drugs.

In view of the fact that a stage of vaso-constriction appears to occur early in the attack, with chilliness, pallor, etc., vasadilators, such as nitroglycerin and amyl-nitrite, have been prescribed (Osler), but the results are variable. Following this stage comes one of vaso-dilatation with flushing, throbbing, nasal obstruction, sweating, etc., and here the use of vaso-constrictors has been suggested, but again with inconsistent results.

The presence of an oliguria early in an attack has been mentioned, followed by diuresis, and for this condition urea has been administered, with relief in some cases (J. A. Brown, *B.M.J.*, 1943). Carbachol has been tried with good result, as also has caffeine, probably because of their diuretic effects. In the early stages a drink of glucose helps a certain number, but with others tends to make them sick, later it may help the alkalosis, however. "Alkazane" has been found useful also in the early stages of the attack, but usually if taken late has no effect, before the severe stage is reached. In prolonged attacks Osler mentioned the use of bromides, probably to lower the patient's threshold and stop the persistent retching. In 1792 Parry observed that pressure on the carotid on the side of the headache produced relief, but on release of the vessel, the pain was increased, and so the theory of stretching of the temporal artery, in which probably the intra-cranial arteries share, has been put forward by Graham and Wolff (1938).

Experimental work confirmed this, and the injection of ergotamine tartarate .5 mg. intravenously or intramuscularly can produce rapid and complete relief, the former route, of course, being more rapid; the action of ergotamine tartarate is that of a vaso-constrictor, ergometrine has also been used, having a similar action. Recently, acetylcholine has been given in small doses, 1 mg. B.I.D., later reduced to a maintenance dose of 1 mg. once per day; the action of this drug is, of course, that of a vasodilator.

Post-Migraine.

In the post-migrainous stage the patient usually feels exhausted by the attack, if he has not gone to sleep, and as many are in a rather nervous and jumpy state, it is well to put them to bed with a warm drink and, if necessary, to induce sleep by some gentle narcotic. If suffering from nasal congestion, as some do, the use of a nasal astringent will give comfort, but this should not be irritating in character, and here benzedrine is best avoided on account of its stimulating tendency.

Between Attacks.

The treatment between attacks is largely the general hygiene of life, and here the avoidance of those factors which each patient rapidly learns to be precipitants is most important. And he well knows that, if through necessity or choice he transgresses, an attack is liable to follow. Overwork is one of the most potent of

these, and this brings in its train various other factors which tend to pile up, and force the victim to lower his tempo of life, or perhaps stop altogether, until he has had time to rehabilitate his overworked organism.

As regards drugs in the interim period, benefit has been derived from small doses of ergotamine tartarate (femergen), 1 mg. per day dissolved sublingually, the only danger being the remote one of ergotism. As before mentioned, a maintenance dose of acetylcholine has been used, and, I believe, with very satisfactory results, but of this I have no personal experience.

Phenobarbitone has been of assistance in limiting the frequency of attacks in certain cases, but it is well to avoid the use of habit-forming drugs for obvious reasons.

SUMMARY.

Hence it will be seen that while migraine is a very definite entity with a clear-cut symptomatology in its typical form, difficulty arises because its manifestations vary markedly in degree in successive attacks, and in different individuals.

The name migraine should not be loosely used for any form of headache, as so often appears to be the case.

The large number of drugs used in the treatment has been mentioned, but when one considers all that can be done in ways other than drugs, perhaps the treatment falls into better perspective, and the importance of drug treatment assumes smaller dimensions. It has been well said that many drugs owe their efficacy to the confidence with which they are offered, and the faith with which they are received.

I have not dealt with the differential diagnosis of migraine, but rather have endeavoured to outline the condition so that it may stand out more clearly from the other types of headache by virtue of its own characteristics.

I have presented this paper to you in the hope that with the accumulated knowledge and experience of the disease here present, some further facts may come to light from those whose knowledge of the treatment of this condition is wider than my own, and who, perhaps, see groups of people and types of cases which in the ordinary course do not pass my way.

REVIEW

FOOD AND NUTRITION. By E. W. H. Cruickshank. Edinburgh: E. & S. Livingstone Ltd. 16s.

To the busy practitioner or student who wishes to keep abreast of recent work on the problems of dietetics and nutrition, this book can be warmly recommended. In the brief space of 316 pages the author deals concisely with the constitution of different foodstuffs and their protein, fat, carbohydrate, and mineral salt content. The latest advances in our knowledge of vitamins is reviewed. Chapters on vegetarianism, the dehydration and preservation of foodstuffs, and dental caries lend much interest to a very readable and informative book. The concluding chapter is devoted to a discussion of the new Food and Agriculture World Organization. S. A.

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Chronic Bacillary Dysentery

By M. G. Nelson, M.D., M.R.C.P., M.R.C.P.I.

The investigation of chronic diarrhœa forms an important part of the examination of patients invalided from overseas commands, particularly from the tropics. This involves adequate laboratory examination for intestinal protozoa, flagellates, and dysentery organisms.

During the course of the laboratory investigations on seven hundred of such patients with a history of chronic diarrhœa, dysentery organisms were isolated from forty, and it is felt that the presentation of the laboratory findings in this small group may prove of some general interest and serve as a guide to other workers in this field.

This group of cases forms a fairly average sample of the types of case returning to this country with a previous history of repeated or relapsing amœbic and bacillary infection.

The history needs to be carefully retaken and previous diagnoses, unsupported by laboratory confirmation, not unduly stressed. Many cases with repeated attacks of diarrhœa are, in the tropics, diagnosed as amœbiasis, and treated on quite "a priori" grounds with courses of amœbicidal drugs. Therefore, previous *clinical* diagnoses of intestinal amœbiasis should be treated with some reserve.

Of the forty cases under review, only seventeen gave a clear-cut clinical history of acute bacillary dysentery; twelve were diagnosed as intestinal amœbiasis; three were unequivocal cases of sprue, and the remainder undiagnosed diarrhœa.

The previous treatment varied with the previous clinical diagnosis. Only nineteen had some form of sulpha-drug therapy, and the sulpha-drug was not always administered during the initial attack. This in some cases was due to the exigencies of war. For example, two of the cases were members of an air crew who were forced to bail out over enemy territory, where they developed bacillary dysentery, which remained untreated until they regained Allied lines.

Twenty of the cases had a full course of amœbicidal therapy.

Methods.

Stool Examinations.—Fresh normally passed stools were examined daily for three days for the presence of protozoa or flagellates. The stools were also cultured in parallel on eosin methylene blue agar and on the sodium desoxycholate citrate medium (Hyne's modification).

After carrying out biochemical tests on any intestinal pathogens isolated, they were then classified, using Oxford standards anti-sera. Final typing of Flexner strains was carried out, using specific absorbed monovalent sera.

Sigmoidoscopy.—The patients were prepared for sigmoidoscopy by having a rectal wash-out with saline at 20.00 hours. They took no further food or hot drinks until they presented themselves for examination the following morning. This simple preparation gave very satisfactory results. Any form of rectal wash-out prior to

examination is to be avoided, because the resultant hyperæmia tends to obscure many of the finer lesions as seen through the sigmoidoscope.

The "Coldlite" sigmoidoscope was employed with an X5 eyepiece, and the patients were examined in the knee-elbow position. The sigmoidoscopic findings in these cases can be briefly tabulated :—

Normal	12
Acute general inflammation	10
Hyperæmia with hæmorrhages	8
Pin-point craters	8
Stricture	1
Ulcer	1

Thus in eighteen of the cases the changes in the rectal mucosa were consistent with an active or healing bacillary dysentery infection. One case showed a deep ulcer, from the base of which E. histolytica could not be identified, but from which dysentery organisms were isolated. One case showed the presence of a stricture, which was caused during the acute bacillary dysenteric infection when the rectal mucosa sloughed, and was passed as a cast.

Pin-point craters were found on the rectal mucosa of eight of the cases. These lesions are regarded as pathognomonic of chronic amœbic dysentery (Cropper, 1945). However, Fairley and Boyd (1943) regard widespread pitting at the site of former ulcers as characteristic of the healing stage of bacillary dysentery. Of these eight cases showing crateriform lesions, there was a "history" of amœbiasis in five, but no trophozoites or cysts of E. hystolitica at the time of examination.

The diagnostic significance of such lesions at sigmoidoscopy is, therefore, of problematical value in distinguishing between amœbic and bacillary dysentery.

RESULTS :—

STOOL CULTURE AND SIGMOIDOSCOPY SWAB

	Stool− Sig. +	Stool+ Sig. +	Stool+ Sig. −	Positive Stool	Positive Sigmoidoscopy
Flexner	4	12	18	30	16
Sonne	0	0	0	1	Not performed
Shiga	0	2	0	2	2
Schmitz	0	0	3	3	0

CULTURAL RESULTS

	EMB.+ D.C. −	EMB.+ D.C. +	EMB.− D.C. +	Positive EMB.	Positive D.C.	TOTAL
Flexner	1	9	24	10	33	34
Sonne	0	1	0	1	1	1
Shiga	0	2	0	2	2	2
Schmitz	0	1	2	1	3	3

EMB. = Eosin methylene blue.

D.C. = Sodium desoxycholate medium (Hyne's modification).

BACTERIOLOGICAL CLASSIFICATION

Flexner 34; Sonne 1; Shiga 2; Schmitz 3; Total 40

Typing of Flexners.

The B. dysenteriæ Flexner strains isolated were typed, using specific absorbed monovalent sera, by slide agglutination, confirmed by tube agglutination in the water bath. The final types were found to be :—

B. dysenteriæ Flexner	I	15
Do.	II	8
Do.	III	4
Do.	IV	2
Do.	V	2
Do.	VI	3
		34

Discussion.

The cases represent a fair sample of the type of patient with chronic bowel infection invalided from overseas commands back to this country.

All had a history of long-continued or relapsing diarrhœa. The majority would satisfy the clinical criteria for the diagnosis of chronic bacillary dysentery, i.e., long-continued diarrhœa with exacerbation and the occasional passage of blood and mucus.

The cases could be arbitrarily divided into two groups, on the basis of the pathological changes found in the lower bowel on sigmoidoscopic examination.

1. Chronic bacillary dysentery.
   These show some pathological changes in the rectal mucosa, suggestive of chronic bacillary infection.
2. Chronic bacillary dysentery carriers.
   These showing a normal rectal mucosa.

The validity of such a division is problematical, but it is interesting that bacillary dysentery organisms were isolated from cases with a long history of diarrhœa, who showed no pathological changes in the rectum. The absence of demonstrable intestinal lesions in chronic dysentery carriers is in accordance with the views of the chronic carrier state in general, but contrary to that of Boyd and Fairley (1944), who consider that deep ulcers are always present in cases of chronic bacillary dysentery carriers. The absence of demonstrable ulcers in the lower bowel does not, however, exclude the possibility of the presence of such ulcers in some other part of the large bowel beyond the normal sigmoidoscopic range.

Only one case showed the presence of a deep ulcer in the rectum, which was thought to be of amœbic origin. Repeated examination of the stools failed to reveal any pathogenic protozoa or bacteria. A scraping taken during sigmoidoscopy from the base of the rectal ulcer showed no E. histolytica, but on culture, B. dysenteriæ Flexner VI (P. 88) was isolated. The ulcer healed satisfactorily after a course of sulphaguanidine.

In the investigation of cases of chronic diarrhœa, sigmoidoscopy is invaluable, for not only can the lower bowel be visualised and the nature and severity of the

pathological lesion determined, but specimens can also be taken directly from the wall of the gut or the bases of mucosal ulcers. Such specimens are sometimes culturally positive when frequent stool examinations are negative (four out of forty). Sigmoidoscopy swabs form, therefore, a useful diagnostic aid in the isolation of dysentery organisms in chronic cases and carriers, and combined with examination of specimens of stools, render the bacteriological diagnosis more certain.

In the isolation of dysentery organisms the selectivity of the desoxycholate medium (Hyne's modification) is well known. It must, however, be combined with a less selective medium, as occasional strains are completely inhibited on the selective medium, and only grow out on the less selective one.

Flexner dysentery organisms were isolated from thirty-four out of the forty cases. This is, in all probability, a reflection of the general incidence of Flexner dysentery rather than any predisposition by this organism to produce chronic bacillary dysentery or a chronic carrier state.

The further subdivision of the Flexner group is confused owing to the existence of three methods of classification. The English school have followed the work of Andrewes and Inman (1920), with a classification into five basic types:—V, W, X, Y, and Z, with intermediate variants, VZ and WX.

Boyd has added three other types: 103, P.118, and P.88 (Newcastle-Manchester-P.88 variant), and has shown that all the Flexners, except X and Y, possess a type specific antigen as well as a complex group antigenic component. Flexners X and Y are artificial products of the laboratory, and possess no type specific components of their own. As a result of this work, Boyd (1938) has suggseted a modified classification of the Flexner group, which depends on the possession of type specific antigenic components.

Andrewes and Inman			Boyd	
V	...	...	I	
W	...	...	II	
X	...	...	...	(degraded III)
Y	...	...	...	(degraded II)
Z	...	...	III	
103	...	...	IV	
P.118	...	...	V	
P.88	...	...	VI	

This work has been substantiated and amplified by Wheeler (1944) in America, who has suggested that it should be more widely adopted.

The majority of strains can be satisfactorily typed using Oxford standards anti-sera, but occasional strains, mainly of Flexner types I, II, and III, give equivocal results owing to group cross reaction.

The use of anti-sera, with the group component removed by absorption, offers a ready means of typing according to the specific antigenic component, and has been utilized in this investigation.

Occasional strains, however, occur with a normal type specific antigen, but abnormal group antigenic components. Wheeler has described a strain isolated in

America with the specific antigen of Flexner II and the group component of X, and I have isolated another aberrant strain from cases of bacillary dysentery in West Africa. Such strains prove difficult to type owing to group cross reactions. They can be shown to possess a specific antigenic component by reactions with absorbed homologous type specific sera, but sera prepared from such strains are not completely absorbed by the Flexner type, whose type specific antigen they possess, i.e., they have the specific component of one Flexner type associated with an aberrant group antigenic structure.

Complete antigenic analysis of aberrant strains would require the demonstration of the type specific and also the group antigenic components. Such a complete analysis is rarely necessary, except from an epidemiological point of view, but indicates the mounting complexity of the problem of the antigenic structure of the Flexner group.

Summary.

1. During the bacteriological examination of seven hundred cases of chronic diarrhœa and relapsing amœbic dysentery, organisms of the dysentery group were isolated from forty.
2. The value of the desoxycholate medium is again shown, together with the necessity for using a less selective medium in parallel if maximum isolation is to be obtained.
3. Sigmoidoscopy is an important diagnostic aid. Sigmoidoscopy swabs, although inferior to fæcal specimens, were culturally positive in four cases where repeated stool cultures proved negative.
4. The majority of the dysentery organisms isolated belonged to the Flexner group (thirty-four out of forty).
5. Some Flexner strains cannot be satisfactorily typed using Oxford standards sera.
6. Specific absorbed sera give clear-cut results, which allow of classification according to the major antigenic component.
7. Some Flexner strains exist with the specific antigen component associated with an aberrant group antigenic structure.

I wish to accord my thanks to the Royal Air Force Laboratory technicians for their willing assistance, interest, and co-operation.

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Some Clinical and Pathological Features of a Case of Tuberculous Meningitis

By YVONNE MACILWAINE, M.D., AND R. P. MAYBIN, M.B.

THIS case is considered to be of interest because of the pathological findings and of the problem of diagnosis presented by the signs and symptoms.

The patient was an unmarried woman aged 24. There was nothing relevant in the family history. Apart from pleurisy with effusion six months before admission, there was no history of any previous serious illness.

Early in December, 1945, intermittent 'numbness' of the right index finger was noticed. A week or two later this feeling began to appear in the right upper and lower limbs. It lasted about fifteen minutes at a time and recurred several times a day. In January, 1946, she noticed a tendency to trail the right foot, and found that the right hand was becoming clumsy and useless; for example, writing and buttoning clothes became very difficult.

Towards the end of January, in addition to the numbness in the arm and leg, there were attacks of pain in the right side of the face and head. She described this as being neuralgic in character. About the same time there was occasional vomiting. On 4th February she was admitted to hospital.

Following admission the condition improved; vomiting ceased and the temperature remained normal. Then suddenly on the 24th February there was a rise in temperature accompanied by headache, vomiting, photophobia and some neck rigidity. The cerebro-spinal fluid was found to be under increased pressure, but was otherwise normal. On 3rd March she was transferred to the Royal Victoria Hospital.

On examination there was no evidence of clouding of consciousness. On the contrary, she was exceptionally lucid and alert, and the impression was of a person well above average intelligence giving accurate responses to questions and sensory tests. There was no dysphasia.

The temperature was 99.8 and the pulse rate 110. There was slight neck rigidity and photophobia.

Examination of cranial nerve functions showed no impairment of the visual fields, and the discs and fundi were normal. The pupils were equal, central, and reacted to light and on accommodation. Lateral nystagmus was present, most marked on looking to the right. The functions of the remaining cranial nerves were normal. Tests for muscle-joint sense and for sensibility to vibration, touch, pain, and temperature showed no abnormality. There was no astereognosis.

The right upper limb showed some loss of tone associated with intention tremor, dysmetria, inability to carry out rapidly alternating movements, and slight weakness of grip in the right hand. The right lower limb showed slight generalised weakness, most marked in the dorsi-flexors of the foot, associated with a small degree of inco-ordination of movement. The left upper and lower limbs showed no motor abnormality. The tendon reflexes in the right upper and lower limbs were increased and the abdominal and plantar reflexes on the right side were indefinite. On the

left side all reflexes were normal. There was no history of any disturbance of the vesical or bowel sphincters.

The following investigations were carried out: X-ray of the skull and chest showed no abnormality. The white-cell count was 8,600 per c.mm. The blood sedimentation rate was 50 mm. in one hour (Westergren).

Lumbar puncture was performed on 5th March. The cerebro-spinal fluid pressure was 250 mm. water. There were 270 cells per c.mm., of which 70 per cent. were polymorphs. The protein was 210 mg. per cent. and the chlorides 680 mg. per cent. No organisms were found. (Cultures of the cerebro-spinal fluid for tubercle bacilli showed no growth at the end of six weeks.)

Summary of Clinical Findings.

The patient had had a pleural effusion six months before admission, and gave a history of sensory Jacksonian fits of three months' duration, suggesting a lesion in the left parietal region. There were two recent attacks of headache and vomiting, with slight neck rigidity and photophobia.

There were marked signs of cerebellar dysfunction all referred to the right side: hypotonia, impairment of rapidly alternating movements, intention tremor, dysmetria, and nystagmus. The sensory fits suggested a lesion in the left parietal region, and there was slight weakness of the right upper and lower limbs, with increased tendon reflexes and indefinite superficial reflexes on the right side. There were no objective sensory changes, no astereognosis, and no dysphasia. The cerebro-spinal fluid was under increased pressure (250 mm.) and contained 270 cells per c.mm. (70 per cent. polymorphs), 210 mg. protein, and 680 mg. chlorides per cent.

The possibility of tuberculous meningitis was considered, especially in view of the recent history of pleurisy and the unclouded mental state. The high cell content of the cerebro-spinal fluid with numerous polymorphs, together with focal signs, however, suggested the possibility of abscess. But localisation was obviously difficult. How could one reconcile the history of sensory fits which might be related to the left parietal cortex with the signs, on examination, which pointed to a right-sided cerebellar lesion? The complete absence of any difficulty related to stereognosis was striking, as was also, in a lesser degree, the absence of any dysphasia.

It was decided that it was impossible to exclude the possibility of abscess, and on 6th of March needling of the left parietal region and of the cerebellum was carried out, in both cases with negative results. Air ventriculography performed at the time of operation showed no abnormality.

Following operation, the patient's condition remained unchanged for several days. Consciousness continued bright. On 9th March the cerebro-spinal fluid contained 60 cells per c.mm. (equal numbers of lymphocytes and polymorphs), 149 mg. protein, and 610 mg. chlorides per 100 c.c. On that day (9th March) deterioration set in. Consciousness became clouded, gradually deepening to coma, and death took place on 15th March.

Post-Mortem Findings.

At post-mortem the brain was slightly swollen, with flattening of the convolutions. At the base of the brain there was a well-marked thick exudate. Over the vertex on the left side, just posterior to the Rolandic fissure, there was marked fibrous thickening of the meninges over an area about 1.5 cm. in the longest diameter. Towards the periphery of the fibrosed area a few yellowish-white nodules about 1 mm. in diameter were visible.

Direct examination of the exudate at the base of the brain showed the presence of tubercle bacilli.

On section of the brain after fixation, a yellowish-white nodule measuring just over 1 cm. in diameter was found lying deep in the post-central gyrus. Smaller areas were recognisable along the sulcus, and the infection appeared to spread towards the surface to reach the area of thickening in the meninges. There was slight dilatation of the ventricular system, and the ependymal lining was noted to be granular.

Histologically, the lesion was found to consist of an area of caseous necrosis involving both meninges and brain tissue. Towards the margin there was definite tubercle formation with aggregates of large mononuclears, lymphocytes, and giant cells.

The meninges showed much fibrous thickening, and even here tubercle formation and giant cells were common. The appearances were those of a slowly progressive lesion which had eventually ruptured into the sub-arachnoid space.

At the base of the brain the meningeal exudate was much more fulminant and acute. There was no tubercle formation. Polymorphs and large mononuclears were present, and there was marked exudation of fibrin and widespread caseation. The necrosis involved the blood-vessel walls; this had led to softening of the adjacent brain tissue. There was also slight extension of the infection along the perivascular space.

The wall of the lateral ventricle showed patchy loss of the lining cells, with swelling and œdema of the underlying tissue. There were also focal infiltrations of lymphocytes and large mononuclears. This ependymitis was believed to be the result of backwash of infected cerebro-spinal fluid into the ventricles.

Post-mortem examination of the rest of the body was not permitted. There was, however, no clinical evidence of miliary tuberculosis. The brain showed no other lesions on multiple section.

Relationship of Symptoms to Lesion.

The anatomical representation of the body on the sensory cortex of the post-central convolution is generally stated to follow that of the corresponding motor area. On this assumption, the order of spread of a sensory Jacksonian fit should be from the toes upwards over the leg to the hip, and thence to the shoulder, arm, fingers, and face. In the case under discussion one would have expected the paræsthesiæ which began in the fingers to spread simultaneously to the face and forearm. In fact, the extension was first to the forearm, arm, and lower limb, the

face only being involved several weeks later. Sittig,[2] in a clinical study of sensory Jacksonian fits, has described ten otherwise typical cases in which the spread of the attacks did not correspond to the accepted anatomical localisation. He refers to Head's assumption, "that there is a representation or 'schema' of the body on the brain; . . . this is not a fixed or pre-formed localisation, but rather a nervous structure which is especially often thrown into action, a pattern or a frequently employed functional mechanism." Sittig also refers to the researches of Leyton and Sherrington on anthropoids, in which they found that the same point of the electrically excitable cortex gives different reactions according to different sequences of stimulation, i.e., whether the stimulus is moved from above downwards, or inversely. He concludes that varying orders of spread of sensory Jacksonian fits are determined by the intensity of the stimulus: "If the excitation is slight, only a quite limited part of the body is affected, as the thumb and index finger; while if it is stronger, the excitation extends, and may follow a pre-formed functional pattern in the 'schema' or some other functional mechanism."

The disorders of tone and movement, which were most marked in the right upper limb, made it seem probable that there was a right-sided cerebellar lesion. Post-mortem examination of the brain showed that the only focal lesion was in the left parietal region, and these symptoms must have resulted from this lesion.

It is, of course, accepted that cortical lesions can cause disorders of movement and of tone. Head[2] states: "Any lesion which disturbs postural schemata will interfere with static tone. For, in order that a part of the body at rest may retain a normal posture, afferent postural impulses must exert a constant influence on the activity of the appropriate receptive centres of the cortex. These are the repository of spacial schemata. The physiological changes brought about by this stream of afferent impressions not only checks and controls voluntary movement, but ensures that the static tone of the part shall be adapted to maintain its position. Consciousness is in no way necessary for such co-ordination; in fact, the regulation of tonic innervation occurs entirely on the physiological level. Any lesion, which tends to destroy postural schemata, not only disorders voluntary movement, but under suitable conditions may diminish static tone."

In the case under discussion muscle-joint sense and the sensation of touch were not impaired, and the faculty of stereognosis was not in any way diminished. It is of interest here that these functions should have been left undamaged by a lesion which produced the degree of ataxia and hypotonia described, in addition to sensory Jacksonian fits of considerable extent.

Pathology.

Because of the frequent association of the two conditions, it was formerly believed that tuberculous meningitis was merely the meningeal manifestation of miliary dissemination. Rich was one of the first to point out that this was not so in the majority of cases. He considered that the lesion most commonly responsible for tuberculous meningitis is a focal plaque occurring either in the meninges or in the underlying brain. He believed that such foci originated as the result of a

bacteræmia occurring either during the primary infection or during a post-primary progressive infection. The resulting lesions (of which the one described in this case is an example) are in effect solitary tuberculomata in contact with the meninges, into which the organisms escape. If the number of organisms is small and the resistance good, the meningitis may remain localised, resulting merely in fibrosis and adhesion of the overlying meninges. An attempt at such a process was seen here. More often a generalised diffuse meningitis results, and perhaps due to some gravity effect, the exudate is most plentiful at the base of the brain.

The claim that it is these foci, and not miliary tuberculosis, which are responsible for the development of meningitis has been supported by both clinical and experimental work. Injection of large numbers of tubercle bacilli directly into the bloodstream of both normal and hypersensitive animals frequently results in miliary tuberculosis. Meningitis does not occur in these animals unless they develop a focal tuberculoma adjacent to the meninges. This is regarded as proof that meningitis does not develop from escape of bacilli directly into the meninges from the blood stream.

Clinically, miliary tuberculosis is much more common than tuberculous meningitis, and about 20 per cent. of the latter occur in cases without any miliary spread. Further, in many cases in which both conditions are found the histological age of the lesions differs; in fact, it has even been shown that in some cases the meningitis may be the origin of the miliary spread. Therefore, even when the two conditions co-exist, it should not be hastily assumed that their origin was simultaneous, or that the miliary lesions were the initiating factor in the meningitis.

Rich analysed eighty-two human cases of tuberculous meningitis, and found focal caseous lesions older than the meningitis in seventy-seven. Similar findings have subsequently been reported by other workers.

This case is regarded as being a classical example of the origin of meningitis from a focal tuberculous lesion in contact with the meninges. The appearances of the tuberculoma suggest that it had been present for several months. The situation in the left post-Rolandic area is such as to explain the focal nature of the original symptoms. The gradual extension of these symptoms would appear to be related to slow leakage of organisms over the adjacent cortex. When the lesion finally discharged into the sub-arachnoid space, there had been time for multiplication of organisms, and suitable conditions had been established for the development of a fulminating terminal meningitis.

We wish to thank Dr. R. S. Allison for criticism and advice, and Dr. Allison and Mr. G. R. B. Purce for permission to publish this case.

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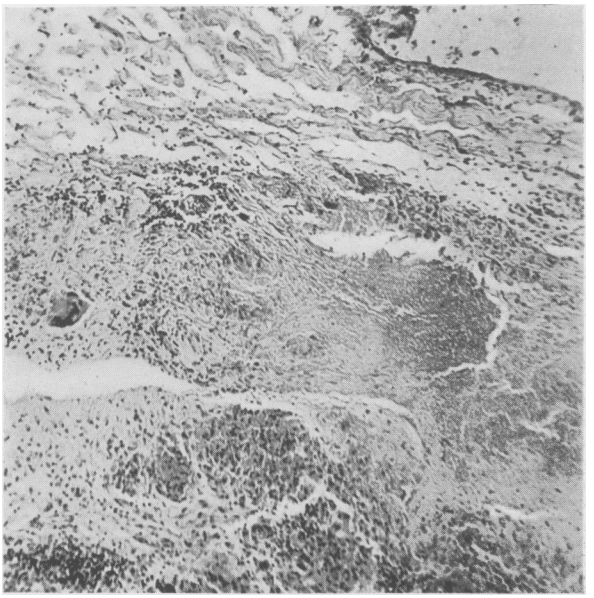

FIG. 1 (x 120)
The "Rich Focus" in the post-central sulcus, involving both brain and meninges. It consists of an area of caseation surrounded by small tuberculous follicles and fibrosed meninges.

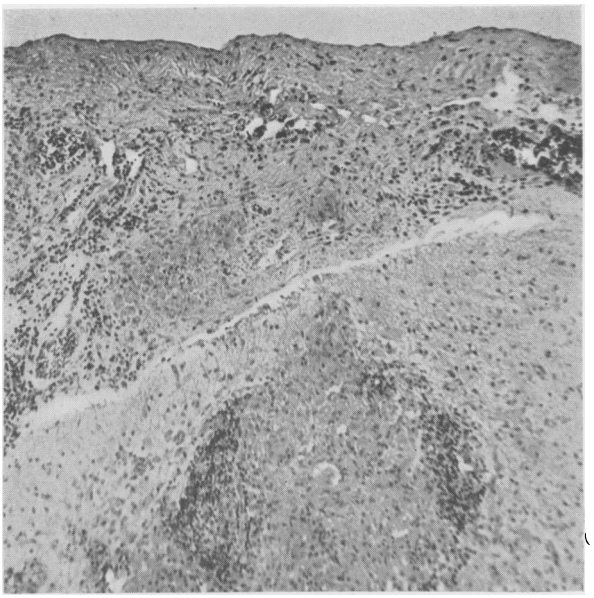

FIG. 2 (x 120)
To show the gross fibrosis of the meninges overlying the affected sulcus. The recent extension of the tuberculous process can be seen in the underlying cortex.

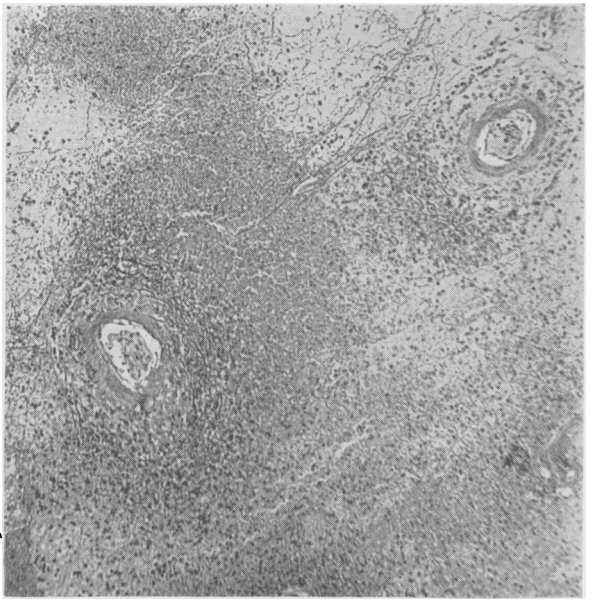

FIG. 3 (x 120)

Showing the fulminant type of reaction at the base of the brain. There is widespread caseation, involving vessel walls, and exudation of fibrin. Many polymorphs are present. Note the absence of tubercle formation.

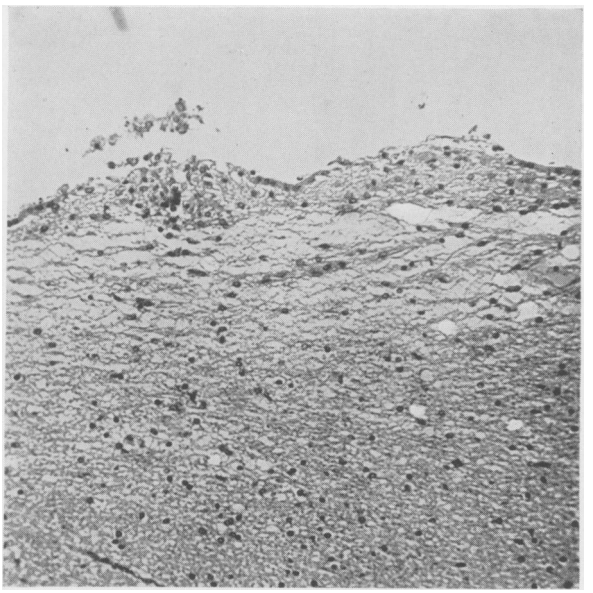

FIG. 4 (x 150)
Ventricular walls showing loss of ependymal cells, infiltration by mononuclear cells, and œdema of the deeper tissues.

Photographs by Mr. David Mehaffey, A.R.P.S.

Acute Encephalopathy and Arseno-Therapy of Syphilis

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ACUTE hæmorrhagic encephalitis or encephalopathy is, perhaps, one of the most dreaded of complications which can occur during arseno-therapy of syphilis. Before the introduction of intensive arseno-therapy by Chargin, Leifer, and Hyman (1935), the incidence of this condition was almost negligible; according to Harrison (1935), only eight cases were reported from 800,000 injections during the war of 1914-1918. Since the popularization of intensive arseno-therapy during World-War II, however, the incidence of encephalopathy has increased considerably. Its incidence varies considerably according to different workers: thus Young and Gordon (1944) report five fatalities from acute encephalopathy following about 10,000 injections at an East African Centre, the drug used being neoarsphenamine, 0.6 gramme twice weekly, in addition to two weekly injections of bismuth metal of 0.1 gramme each. Lydon (1944) reports that five out of fifty-three patients developed the condition during treatment by a short-term intensive course of mapharside; one of his patients died. Pillsbury et al. (1944) state that the reaction of encephalopathy did not occur frequently during intensive arseno-therapy by a modified twenty-day treatment. Lloyd Jones and Maitland (1945) report three cases out of a total of 241 (?) patients treated by a modified course of intensive arseno-therapy.

According to McDonagh (1920), the condition develops some forty-eight to seventy-two hours after the second or third injection. It is characterised by "mild to severe mental confusion, headaches, fever, convulsive seizures, in some cases coma. Spinal fluid sometimes shows marked increase in protein." (Pillsbury et al., quoting U.S.A. army circular letter No. 138 on Intensive Therapy for Early Syphilis.) The treatment most generally adopted is venesection, lumbar puncture, intravenous hypertonic glucose, and the administration of adrenaline or benzedrine, but the results of treatment have given varying results (McDonagh, 1920; Young and Gordon, 1944; Lydon, 1944). The use of thiosulphate intravenously has also been advocated (Sheppe, 1930).

Lydon (1944) brings out several points of interest and importance which do not appear to have been noted by other workers. In his series of cases he observed that the primary signs of encephalopathy occurred in the mental sphere either as a sudden explosive onset of acute apprehension and fear, or as a general slowing of cerebration. The resemblance of these mental changes to those of the two types of alcoholism led to a tentative suggestion that perhaps a similar pathological condition was present and that the condition might be avoided or improved upon the exhibition of vitamin B_1. Alcoholism is suggested as a predisposing factor. Upon this hypothesis vitamin B_1 was administered in the later cases of the series quoted with apparently marked beneficial effects.

The following case is of interest in the light of Lydon's observations and hypothesis :—

CASE HISTORY.

The patient was a male subject, aged 24 years, who was referred for examination on the 22nd September, 1944, for a possible syphilitic infection. He was undergoing treatment for co-existent scabies, and gave a history of exposure to infection in the previous March. He stated that in March, 1944, following exposure he had developed a urethral discharge which had been treated with sulphathiazole. He had had a penile swelling since the following May or June, and was using calomine lotion locally. He was sleeping poorly, due to the irritation caused by the scabies. He admitted to fairly heavy alcohol consumption up to three to four weeks previous to examination. On examination there was penile swelling, marginal ulceration, and induration of the prepuce, marked enlargement of the inginual glands, superficial ulceration of the right tonsil, with redness of both tonsillar regions. There was an indefinite secondary rash confined chiefly to the lower abdomen, though it was difficult to be certain about this on account of the superimposed scabies. He was suffering from considerable general malaise.

Due to the local treatment, the T. pallidum was not definitely demonstrated on the first examination, but was found on the patient's next reporting on the 25th September. Treatment was commenced on the same day, when 0.04 gramme mapharside in sodium thiosulphate solution was administered intravenously. On the 27th and 29th September and the 2nd October 0.06 gramme mapharside were given together with 0.1 gramme bismuth on each day. The patient lived in the country and returned home after each treatment. Several days after the fourth injection his doctor telephoned to say that the patient was confined to bed with "flu" and was unable to come for further treatment meantime; his doctor was not alarmed about his condition. On the 7th October a further message reported that the patient was still ill, but his doctor was still not unduly alarmed, but on the 9th October his condition was reported to be much worse and he was now delirious. There were personal difficulties about his admission to hospital which had delayed his earlier hospitalization, but it was obviously impossible to treat him by directions by telephone, and admission to hospital was urged and, as his condition had now become so much worse, consent was given, and he was admitted the same evening. A more coherent history of events was now obtained. He had gone to bed on account of a "cold" following his last injection; by the next day his temperature had risen to 103°F. He remained in bed, and his high temperature continued until the 6th October, when it fell to 99°F., and his condition improved somewhat, but on the 8th October he developed convulsive fits and became comatose in five to six hours' time. The coma lasted until the early hours of the following morning. He had been lethargic, and had taken very little food or liquids since his return home on the day of his last injection.

On admission to hospital, he was in a very excitable state and was shouting and struggling. He was quite unconscious of his surroundings and unable to recognise his mother. He appeared to be very apprehensive of all that was happening and

made violent efforts to get out of bed, being restrained with considerable difficulty, so much so that clinical examination was extremely difficult and unsatisfactory. There was a divergent strabismus of the left eye, marked neck rigidity, and a positive Kernig's sign. He was incontinent.

Further examination or interference were impossible for several hours, when a lumbar puncture was performed with some difficulty. The cerebro-spinal fluid was clear; about 20 c.c. was withdrawn and was reported on as follows: protein, 120 mg. per 100 c.c.; chlorides, 700 mg. per 100 c.c.; globulin plus; cells, 20 per c.mm.; lymphocytes.

Further treatment consisted of the intravenous administration of 50 c.c. 30 per cent. dextrose and 20 c.c. calcium gluconate.

10/10/44.—Nasal feed at 4 a.m.: two pints of glucose and sedatives given. Patient still very noisy and difficult to restrain in spite of sedatives. Fluids forced.

11/10/44.—Patient drowsy and quieter. When wakened for drinks, eyes and face quite expressionless.

12/10/44.—Patient somewhat brighter. Attempting to speak, but articulation difficult. Face still expressionless. Recognised mother.

13/10/44.—Patient more normal and able to take food and talk. He asked to be changed to another ward with other patients, as he said there was a tall dark man behind the curtain who kept looking at him during the night. (There was no curtain in the ward, of course.)

14/10/44.—Good night. Patient bright and talkative during the day and taking food normally.

His subsequent progress was uneventful. Lumbar puncture on the 21st October gave protein 40 mg. per 100 c.c.; globulin negative; chlorides 670 mg. per 100 c.c.; cells 10 per c.mm.; lymphocytes.

The question now arose as to his further treatment. Most authorities are agreed that further exhibition of arsenicals is absolutely contra-indicated following a crisis of the type described. Unfortunately, penicillin was not then available, and we were faced with the alternatives of either continuing treatment with bismuth or of risking a further cautious dose of an arsenical preparation. The position was, that here was a young man of 24 years of age who had had completely inadequate treatment for secondary syphilis and who was now faced with the alternatives of either inadequate treatment of a very serious condition, with all the dire possibilities consequent thereon, or the risk of further arseno-therapy. It was considered that, taking a long view of the possibilities of the case, a further cautious dose of mapharside should be tried.

His general condition was now much better than it had been at the beginning of treatment and he had shown no evidence of any further mental reactions, and on the 23rd October an injection of 0.02 gramme mapharside in high dilution and containing 0.45 gramme thiosulphate was given very slowly intravenously. About two hours after the injection the patient's face became flushed, his eyes became slightly injected, and he developed a headache which lasted until the following morning. The following day (24/10/44) it was decided to start injections of

vitamin B_1, and daily thereafter until his discharge from hospital on 16th November, 1944, he was given an intramuscular injection of 5 mg. of thiamin hydrochloride.

On 30/10/44 a further injection of 0.02 gramme mapharside was given with the same precautions as before, and the resultant reaction was very much less marked; the face became flushed, his eyes injected and his body warm about four hours after the injection, but the reaction was not only much less than before, but lasted for only about four to five hours. There was no headache. On 5/11/44 he was given 0.03 gramme of mapharside as before, and this time he had a slight feeling of warmth which lasted for a few minutes only, whilst following 0.04 gramme mapharside with the same precautions on the 13/11/44, there was no resultant reaction whatsoever.

Following his discharge from hospital, the patient had four further injections of 0.04 gramme mapharside without further untoward reaction, between 27/11/44 and 20/12/44. During the following twelve months he had two further courses of treatment, each consisting of ten weekly injections of 0.04 gramme mapharside and 0.1 gramme bismuth. During the first of these courses thiamin hydrochloride was given daily intramuscularly, and during subsequent treatment oral vitamin B therapy was administered. There was no further reaction of import during treatment, and his blood Wasserman and Dreyer reactions have remained negative for some considerable time. He is still under periodic observation.

Discussion.

It is difficult to draw definite conclusions from a single case of any given condition, but when that condition is, fortunately, a comparatively rare one, the accumulation of the reactions observed in individual cases becomes of considerable importance. The case described would appear to bear out at least some of the conclusions reached by Lydon (1944). Unfortunately, circumstances prevented personal observation of the symptoms during the onset of the condition, but from what was learned subsequently, the onset would appear to have been rather of the lethargic type as described by Lydon. The dosage of mapharside given in the early stages of treatment was not unusual, as most workers are agreed that the first three to four injections during arseno-therapy should be given over a period of some ten to fourteen days, and the treatment in this case was not out of harmony with recognised practice. The clinical findings and the result of lumbar puncture were very much those described in other cases of similar type. Lydon (1944) points out that Kernig's sign was not a feature of his cases, and suggests that the sign was probably one of nuchal rigidity in the one case which he noted: this may have been the case in the patient described here.

The chief point of interest in the case described is the response to treatment following encephalopathy. It was an admitted risk to recommence arseno-therapy, but the circumstances governing the subsequent treatment have already been discussed. In retrospect, perhaps an even smaller trial dose of the drug should have been administered. The subsequent reaction to the first injection of mapharside after his encephalopathy, and the rapidly decreasing reactions following the second and subsequent injections on the exhibition of vitamin B_1, would seem to bear out

Lydon's theory as to the importance of this vitamin in the prevention of arsenical encephalopathy.

The advent of penicillin for the treatment of syphilis brought with it high hopes that arsenical encephalopathy would be a thing of the past. It is now, however, becoming more generally realised that the best therapeutic results in the treatment of syphilis with penicillin are to be obtained, not with penicillin alone, but by combining penicillin with the older established methods of treatment. Some workers (e.g., Pillsbury, 1946) advocate a short intensive course of arseno-therapy with penicillin. The possibility of the occurrence of encephalopathy is thus still one of considerable importance, and the bearing of vitamin B_1 in its prevention or treatment is worthy of further investigation. The likelihood of alcoholism in the causation of the condition would also appear to be of considerable importance.

I am indebted to Surgeon-Commander Hugo Hall, R.N.V.R., Director, V.D. Clinic, Royal Victoria Hospital, Belfast, for his helpful criticism and advice on this short paper, and to Dr. F. Kane, Medical Superintendent, Purdysburn Fever Hospital, Belfast, for his co-operation and help during the early days of the patient's illness.

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REVIEW

THE PERIPHERAL CIRCULATION IN HEALTH AND DISEASE. By R. L. Richards. E. & S. Livingstone Ltd.

THE material for this book was collected while Dr. Richards was assistant physician at the M.R.C. Neuro-vascular Unit at Gogarburn, Edinburgh, under the direction of Professor J. R. Learmonth. It deals with the anatomy and physiology of the peripheral circulation, with occlusive vascular disease; Raynand's phenomenon; peripheral nerve injuries, and immersion foot. It is an excellent example of the clinical scientific method. A book for all specialists in peripheral vascular disease. A book for all interested in recent advances in clinical science. H. B.

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Beriberi: Etiological and Clinical Considerations

By J. F. PANTRIDGE, M.C., M.B.

FOR some time prior to the abrupt descent of the Rising Sun on 15th August, 1945, and for one month after that event, the writer had the opportunity of observing beriberi among British and Australian troops in various Japanese prison camps in Malaya, Siam, and Burma. Sporadic beriberi was always with us, and two outbreaks were seen.

ETIOLOGY.

Beriberi was recognised by the Chinese 3000 B.C. The etiology, however, remained obscure till 1870. In that year Eijkman, working in Java, noted an epidemic of paralysis among fowls fed on polished rice. He found that this polyneuritis gallinarum could be cured if an extract of rice polishings were added to the diet. That polyneuritis gallinarum corresponded to human beriberi was shown by Frazer and Stanton in 1910. These investigators produced beriberi in convicts by feeding them a diet consisting solely of overmilled rice. They also succeeded in curing the disease by adding rice polishings to the diet. Frazer and Stanton concluded that the pericarp aleurone layers and the embryo of grain which are removed in the production of polished rice contained an anti-beriberi substance.

The chemical composition of this substance was determined by Williams in 1935, and it was eventually synthesised by Williams and Spies in 1938. It was found to be a compound of pyrimidine and thiazole, to which Williams gave the name thiamin.

Beriberi was therefore defined as a disease resulting from a metabolic disturbance caused by deficiency of the ante-neuritic vitamin B_1, or thiamin. The minimal daily requirements of thiamin are in the region of 1 mg. or 333 I.U.

Recently, however, it has been recognised that factors in addition to thiamin deficiency are concerned in the production of beriberi. It has been observed that beriberi is an uncommon complication of simple starvation. The disease was rarely seen among the starving populations of Europe during the war. Beriberi complicating anorexia nervosa has only once been recorded.

The question of additional factors has been investigated by Cowgill in 1934 and by Williams and Spies in 1938. Cowgill as a result of his investigations came to the conclusion that the incidence of the disease was related to the ratio between the thiamin and the caloric value of the diet, rather than to the daily intake of thiamin. Williams and Spies attacked the problem by analysing typical Occidental and Oriental diets. They found that the differences in thiamin value was insufficient to explain the rarity of the occurrence of beriberi in association with the former diet and its frequency in association with the latter. They noted that the chief difference in the diets was the greater fat-content of the American diet. From this they concluded that fat had a B_1 sparing action. Analytically it was shown that the best index of the liability of a diet to produce beriberi was the relationship between the thiamin and the non-fat caloric value. This they express as the

T/N.F.C. ratio, where N.F.C. represents the daily calories derived from food other than fats, and T the daily thiamin content of the diet in micrograms. They noted that T/N.F.C. below .3 was indicative of a beriberi-producing diet.

These facts were substantiated by experience in Japanese prison camps.

The diet analysis shown of the period March-July, 1945, indicates that the daily thiamin intake was on an average little greater than one-third of the normal daily requirements. Yet on this diet rather less than 10 per cent. of the prisoners showed clinical evidence of beriberi.

The explanation is that the very low thiamin intake was associated with a low caloric intake, consequently the thiamin/fat calorie ratio did not fall much below the critical figure .3.

Within a few days of the capitulation of the Japanese on 15th August, 1945, the daily ration was increased by the addition of 4 oz. of rice and 2 oz. of protein. The thiamin content of the diet remained unaltered. Calculation shows that these additions to the diet cause the T/N.F.C. ratio to fall to a figure of .204. Beriberi was therefore to be expected, and an outbreak appeared toward the end of August. The short interval, fourteen days, as opposed to the ninety days dietetic imbalance commonly required to produce beriberi, is explicable on the grounds that prior to the change in diet the prisoners had lived on the beriberi threshold T/N.F.C. ratio just below .3.

Clinical Findings.

Sporadic Beriberi.

As a sporadic occurrence, beriberi affected some five to fifteen per cent. of the prisoners in Japanese prison camps. Three types of the disease are described and were seen—

(*a*) Neuritic.
(*b*) Oedematous.
(*c*) Cardiac.

Isolated involvement of the cardio-vascular or nervous system was infrequent. Oedema was, however, often the only manifestation.

Neuritic Beriberi.

The neuritic manifestations were similar to those of multiple neuritis of other origin. The degenerative lesions showed a predilection of the long nerves, so that wrist-drop and foot-drop were frequently seen. The anterior crural nerves were involved early, with usually weakness and wasting of the quadriceps extensor, leading to inability to rise from the squatting position. Inability to rise from the squatting position—a positive "squatting test"—was sometimes the first sign of beriberi. Occasionally the presenting symptom was hoarseness, due to involvement of the recurrent laryngeal nerve in the degenerative process.

The motor manifestations were usually preceded by the sensory symptoms of peripheral neuritis. There were complaints of numbness and tingling, particularly in the hands and feet and along the inner sides of the thighs.

Examination of sensory function showed a varying degree of impairment of superficial sensation. The areas most commonly affected were the distal parts of

the limbs and the inner sides of the thighs. The affected muscles were painful on deep pressure and the tendo Achilles usually insensitive.

The weak muscles—quadriceps, dorsiflexors of the feet, and extensors of the wrist—usually showed some degree of wasting. The tendon jerks were diminished or absent in the affected limbs.

Marked neuritic manifestations were almost invariably accompanied by cardio-vascular abnormalities. The commonest were (1) Persistent tachycardia; (2) Marked fall in blood pressure—systolic readings below 100 and diastolic readings below 60 were frequent; (3) Cardiac enlargement—usually slight in the absence of œdema.

Oedematous Beriberi.

A slight puffiness of the face and pitting œdema of the lower limbs below the knees were the most frequent manifestations of sporadic beriberi. Oedema of this degree was not usually accompanied by evidence of involvement of the cardio-vascular or nervous systems.

Massive œdema associated with cardiac failure—a common feature in one outbreak—was infrequent as a sporadic manifestation.

The following case showed a combination of the œdematous and neuritic types.

PTE. T., 7TH COAST REGT. R.A., admitted 23/8/45.

History.—For two years he has suffered from—

1. Periodic swelling of the face, and of the legs below the knees.
2. Numbness and tingling in the hands and feet.
3. Severe cramp-like pains in the muscles of the lower limbs.

Examination.—Marked wasting. Weight 9 st. 7 lb. Normal weight 13 st. 6 lb. No gross anæmia. There is pitting œdema of the lower limbs below the mid tibia. *Heart and lungs:* No clinical or radiological abnormality. *Abdomen:* Liver not enlarged. Spleen just palpable. *C.N.S.:* Positive findings—Impairment of all forms of superficial sensation in lower limbs below the knee-joints and along the medial aspect of the thighs. Marked tenderness in the muscles of the calves. Wasting of the quadriceps extensors. Squatting test positive. Slight weakness of the dorsiflexors of the ankles.

OUTBREAKS OF BERIBERI.

Two outbreaks of the disease were seen. Each presented unusual features.

Outbreak No. 1 was seen among those personnel of the ill-fated "F" Force who had survived the "death" march through Siam to the Burma border in 1943.

For many reasons, including the complete absence of paper, clinical records of this epidemic are not available. The striking feature was the high incidence of cardiac manifestations of the disease. Grave cardiac involvement appeared as—

(1) Acute cardiac beriberi.
(2) Congestive cardiac failure.
(3) Major conduction defects terminating in Stokes-Adams syndrome.

Acute Cardiac Beriberi:

Known by the Japanese as shôshin. Men apparently well or suffering from œdematous beriberi of moderate or mild degree would collapse at work with acute

pain in the chest. Death as a rule rapidly followed. When seen before death, they showed extreme dyspnœa, restlessness, cyanosis, and distention of the jugular veins. They complained of unbearable pain in the chest, radiating into the neck and arms. Clinical evidence of cardiac enlargement both to right and left was usually easily elicited. The heart-sounds were faint, distant, and tic tac in character. Intravenous administration of thiamin (when the drug was available) produced dramatic relief. In its absence, these men invariably died.

Congestive Cardiac Failure.

The features did not differ markedly from the congestive failures produced by the more common causes. Oedema partly of cardiac origin was as a rule generalised, involving limbs, trunk, and face. In the terminal stages these men were orthopnœic and cyanotic, with distended, pulsating jugular veins. The heart was always markedly enlarged, the sounds faint and tic tac in character. The first heart-sound heard over the displaced apex was frequently split. Signs of bilateral pleural effusion could be elicited. The liver was enlarged and the abdomen contained free fluid. Infection of the œdematous subcutaneous tissues, resulting in widespread cellulitis, often occurred preterminally.

Conduction Defects.

Evidence of defective conduction in association with beriberi is of interest, since this finding is contrary to that of the leadng authorities on the subject—Wenckebach (1928), Weiss (1940). We regarded splitting of the cardiac first sound as the earliest evidence of a conduction defect. Apart from this, cases were seen to progress through the stage of partial to complete heart-block and to terminate during their first or subsequent attack of typical Stokes-Adams syndrome.

It may be argued that since most of the men suffered from uncontrolled malaria and many were convalescent from cholera, in the production of the bundle damage some other factor was at work, such as the toxin of the malarial parasite or that of the cholera vibrio. These toxins may have been contributing factors.

Two observations, however, indicated that beriberi was the main factor:

(1) Gross conduction defects associated with Stokes-Adams syndrome did not occur in the absence of other signs of beriberi, either œdematous or neuritic.

(2) Thiamin, in the isolated case in which its effect was observed, rapidly brought about a return of normal conduction.

The case remembered is that of a R.A.M.C. staff-sergeant who while recovering from the congestive failure of beriberi developed bradycardia (P.R. 36) and Stokes-Adams attacks. He had some ten attacks in six days. 20 mg. of thiamin were then given intravenously, followed by 5 mg. daily for one week, after which the supply of the drug failed. Twenty-four hours after the initial dose the pulse-rate was normal; however, ten days after the drug was stopped, bradycardia and Stokes-Adams attacks reappeared. No attacks occurred while thiamin was given.

Outbreak No. 2.

This outbreak appeared toward the end of August, 1945, following an increase in the ration and upset of the thiamin non-fat calorie ratio of the diet. The mani-

festations were mainly œdematous. Some cases, however, showed a syndrome which, as far as can be ascertained from the literature available, has not previously received attention. The characteristics of this syndrome were :

(1) Acute generalised non-pitting œdema.

(2) Hypertension.

(3) Fairly rapid response of both œdema and hypertension to the parenteral administration of thiamin.

CASE REPORTS.

Case I—Pte. Z., 2/26 Bn. A.I.F. Admitted 23/8/45.

Previous Illnesses.—Amœbic dysentery, 1943; Malaria B.T., twenty attacks.

History of Complaint.—Since June, 1943, he has suffered from painful feet, cramps in the calves of the legs, and occasional swelling of the feet and ankles.

Four days prior to admission he has been passing less urine than usual. Three days before admission his face became swollen, and the day before admission he noticed that his "body became swollen all over." He had suffered from headaches and loss of appetite for ten days.

Examination.—Oedema involves the face, trunk, limbs, and genitals. Pitting can not be demonstrated. There is no cyanosis or distension of the jugular veins. *C.V.S.: Heart:* no clinical enlargement. Heart-sounds normal. B.P. 190/130. *Lungs:* N.A.D. *Abdomen:* Liver not enlarged. Spleen just palpable. *C.N.S.:* There is no muscle weakness or wasting and no sensory loss. The tendon jerks are present. Urine N.A.D.

Treatment.—Thiamin 50 mg. intravenously, followed by 50 mg. by intramuscular injection daily. Fluids restricted. No salt.

Response.—A rapid diuresis ensued. During the forty-eight hours following the commencement of treatment 418 oz. urine were passed. Oedema rapidly subsided. Five days after admission there remained only slight puffing of the face and ankles.

Blood Pressure.—Ten days after admission 140/90.

Case II—Pte. S., 2/30th Bn. A.I.F. Admitted 27/8/45.

Previous Illnesses.—Malaria B.T. at monthly intervals since 1942. No previous beriberi.

History.—During the past week he has been passing very little urine. Four days before admission, on waking he noticed his face swollen; swelling of the genitals then appeared, and gradually the swelling involved the trunk and limbs.

Examination.—Oedema involves the face, trunk, and limbs. There is no pitting. There is no dyspnœa, cyanosis, or distention of the jugular veins. *C.V.S.: Heart:* Not clinically enlarged. Heart sounds are hyperactive, but otherwise normal. B.P. 200/114. *Lungs:* N.A.D. *Abdomen:* Liver not enlarged. Spleen just palpable. *C.N.S.:* No sensory or motor abnormality. Tendon jerks present. *Urine:* N.A.D.

Treatment.—Thiamin 50 mg. I.V., followed by 50 mg. I.M. daily.
Fluid restriction. No salt.

Response.—A diuresis was established in four days. Seven days after commencement of treatment the œdema had gone. Fourteen days after admission the blood pressure had fallen to 160/100.

Case III—Pte. P., 2/20th Bn. A.I.F. Admitted 31/8/45.

This case showed, in addition to non-pitting œdema, hypertension syndrome, cardiac manifestations reminiscent of those seen in the first outbreak.

Previous Illnesses.—Malaria B.T. twenty attacks; Malaria M.T., two attacks; Bacilliary Dysentery, two attacks.

History.—He noticed swelling of the lower limbs four days prior to admission. This swelling gradually spread upwards, and soon the whole body became swollen. A severe continuous headache has been present since the appearance of this œdema.

On the evening prior to admission while lifting a bucket full of water he had a sudden severe pain in his chest and collapsed. Thiamin 50 mg., given intravenously by his unit medical officer, relieved the acute pain. He still complained of a feeling of tightness in his chest.

Examination.—A non-pitting œdema involves the face, thighs, limbs, and genitals. *Heart:* No clinical enlargement. Heart-sounds faint and tic-tac in character. Frequent extra systoles. B.P. 150/100. *Lungs and Abdomen:* N.A.D. *C.N.S.:* Impaired superficial sensation in the lower limbs below the knees. No other abnormality. *Urine:* N.A.D.

Treatment.—After an initial injection of 50 mg. of thiamin intravenously, 50 mg. were given daily by intramuscular injection. Oedema had completely gone by the fourth day after the commencement of treatment; tightness and discomfort in the chest disappeared. One week after admission his B.P. had fallen to 130/64. The heart-sounds were still tic-tac, but the extra systoles had gone.

Discussion.

Vitamin B_1, when absorbed, combines with pyrophosphoric acid to form thiamin pyrophosphate or co-carboxylase. Co-carboxylase is the enzyme essential for a vital stage in the oxidation of glucose by living cells. In its absence the breakdown of glucose is arrested at the pyruvic acid stage. Since nerve tissue depends almost entirely on the oxidation of glucose for its metabolism, the frequency of degenerative changes in the nervous system is explicable.

The involvement of the heart in the disease process is, however, less easily explicable. The finding at post-mortem is marked hypertrophy and dilatation of the right side of the heart.

Wenckebach assumes that the heart as a whole fails. The signs of right-sided failure and the marked dilatation of the right side of the heart found at post-mortem he explains on a purely mechanical basis: "In cases of increasing insufficiency of the whole heart, the right heart is doomed to suffer much more than the left side, even to suffer to the profit of the latter." The failure and hypertrophy

of the right heart he attributes to imbibition of fluid by the muscle-fibre. He offers no explanation as to why the hypertrophy of muscle-fibres produced by imbibition of fluid should be confined to the right side of the heart.

Whether or not the heart-muscle in beriberi imbibed fluid might be determined by comparing the weight of dried beriberi hearts with the weight of dried normal hearts. There is no record of this experiment having been performed in human beriberi. It has, however, been performed on pigeons. Newcomb (1930) found that the enlarged hearts of pigeons suffering from beriberi showed no abnormal water content.

That the disordered metabolism of beriberi might lead to the accumulation in the blood of metabolites having a toxic action on the myocardium must be considered. There is evidence pointing to such an accumulation. It is known that the blood pyruvic acid is high in beriberi, often reaching a figure of 2 mg./100 c.c. (normal .5 mg.) Lee and Platt (1938) have shown that in B_1 deficient states moderate exercise is followed by a marked rise in the blood pyruvate, whereas the normal subject must be exercised to exhaustion before any appreciable rise occurs. They further showed that the time required for the removal of the excess pyruvate is greater than normal.

Inawashiro and Hayasaka have noted a similar rise in the blood lactic acid and a delay in its removal.

Our experience showed that the cardiac manifestations of beriberi were related to muscular activity.

Thus, the first outbreak of the disease in which grave cardiac involvement was so frequent occurred among troops who had just completed a long and exhausting jungle march, and who at the time of development of the outbreak were working as slave labour on the Burma railway. Again, acute cardiac beriberi—shôshin—appeared while the individual was engaged in some strenuous muscular effort.

These findings would indicate that possibly pyruvic acid and lactic acid had a toxic action on the myocardium. Haynes and Weiss have failed to produce any toxic effect by injecting these acids into B_1 deficient animals. The toxic factor may, however, be a metabolite closely associated with pyruvic acid and lactic acid.

The occurrence of conduction defects must be regarded as unusual.

Aslsmeer found that even in the worst conditions of failure "the beriberi heart gave a perfectly normal electro-cardiograph without arrythmia, extra systoles, heterotopic rhythms, or disturbances of conduction in the bundle or in the conducting fibres of the ventricles."

Wenckebach stresses the contrast between the weakened muscle and an undisturbed or accelerated conduction. He uses this as an argument in favour of the theory of imbibition of fluid by the muscle-fibre, since it has been shown by Engelmann that the frog's heart immersed in water lost the power of contraction without disturbance of conductivity, and by De Boor that the human heart behaved in a similar manner.

Weiss reported the electro-cardiographic changes in two white men suffering from beriberi. In neither was there pathological prolongation of the P.R. interval.

Weiss et al. studied the electro-cardiographic changes in thiamin-deficient dogs. Changes were found in the T-waves and S.T. segments. Prolongation of the P.R. interval was not a feature.

Carter and Dury have, however, succeeded in producing heart-block in rice-fed pigeons. It would appear, therefore, that the effect of thiamin-deficiency on the animal heart required further investigation.

The nature of the œdema and the mechanism of its production in beriberi remain obscure. In most cases it occurred first in the dependent parts and pitted easily. On incision, the subcutaneous tissues serous fluid escaped. These features would indicate an extra cellular location in the tissues and a similarity to cardiac œdema. Many sporadic cases of beriberi, however, showed no cardio-vascular abnormality. The generalised distribution and absence of pitting of the œdema seen during the second outbreak suggested that it was at least partly intracellular. The association of this type of œdema with hypertension is of interest. Hypertension has not, as far as can be ascertained, been previously recorded in connection with beriberi. All authorities on the disease emphasise the lowering of the blood pressure which occurs, in particular the lowering of the diastolic pressure.

It is suggested that those showing the generalised non-pitting œdema hypertension syndrome produce as a result of their disturbance metabolism, a metabolite causing an increase in intracellular osmotic pressure, resulting in imbibition of fluid by the cell. An intracellular œdema affecting renal tissue might lead to renal ischæmia and hypertension.

Summary.

Sporadic cases and outbreaks of beriberi among prisoners of war are described.

Evidence is presented in favour of the operation of factors in addition to thiamin-deficiency in the production of the disease.

An unusual beriberi syndrome is described.

The occurrence of heart-block in association with beriberi is recorded.

DIET ANALYSIS

March—July, 1945.

Prison of War Camp, Changi, Singapore.

March	C.	P.	F.	Cal.	N.F.C.	T.	T/N.F.C.
H. -	306	36	56	1,800		370	.26
L. -	260	38	50	1,560		335	.3
April							
H. -	350	45	67	2,100	1,418	450	.31
M -	250	41	61	1,700	1,210	390	.33
L. -	210	40	61	1,500	970	382	.4
May							
H. -	350	44	65	2,244	1,595	480	.31
M. -	280	41	58	1,876	1,280	420	.32
L. -	238	39	58	1,690	1,100	403	.4

JUNE														
H.	-	312	...	46	...	63	...	2,041	...	1,442	...	386	...	.27
M.	-	255	...	43	...	57	...	1,731	...	1,206	...	315	...	.26
L.	-	213	...	41	...	57	...	1,559	...	1,016	...	327	...	.32
JULY														
H.	-	318	...	34	...	57	...	1,973	...	1,444	...	410	...	.28
M.	-	245	...	30	...	51	...	1,602	...	1,129	...	328	...	.29
L.	-	205	...	27	...	51	...	1,425	...	956	...	303	...	.32

C.—Carbohydrate.
P.—Protein.
F.—Fat.
Cal.—Calorie value.
N.F.C.—Non-fat calorie.
T.—Thiamin in micrograms.
T/N.F.C.—Thiamin/non-fat calorie.

SCALES OF RATIONS.
H.—High.
M.—Medium.
L.—Low.

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REVIEW

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A brief historical review is given of the advances made in the knowledge of the fœtal circulation since Galen, in the second century A.D., described the foramen ovale. This is followed by an account of the conclusions reached from observations made on fœtal lambs with the aid of cine-radiographic apparatus. The text is well illustrated by X-ray photographs, obtained after the injection of radio-opaque substances into the blood stream.

As the author states, much research remains to be done along these lines, and further publications will be awaited with interest. This pamphlet will well repay the attention of senior students of biology and is moderately priced.

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The practical instructions for the individual tests are given concisely and clearly with due regard to safety precautions, economy of material, and the limitations imposed by large classes. Special stress is laid on the importance of control tests. The book starts with a valuable chapter on scientific method, and goes on to deal very briefly with fundamental points such as experimental error, accuracy of results, and statistical method. This is followed by a section on general rules for laboratory work, including safety precautions and methods of cleaning and calibrating apparatus. In connection with the last point, it is stated that Ostwald pipettes, calibrated for delivery, are used like ordinary type pipettes. The author has not made it clear that most Ostwald delivery pipettes are calibrated to be used by blowing out the last drop and not, as with ordinary pipettes, by merely draining. Neglect of this point could lead to quite a substantial error with a small pipette.

A possible criticism of this book is that it contains far more experiments than can be done in the time available for chemistry in the medical curriculum, and while the author may feel that the ideal curriculum should make room for the whole of the work described, it seems unlikely that the time devoted to chemistry can be increased, especially as new subjects, such as normal psychology, are creeping into the pre-clinical period. The author admits that, at present, a selection must be made from the experiments described, but one feels that a more balanced course might result if the author himself made this selection in writing his book. Moreover, the unfortunate medical students would not then be faced with still another textbook containing far more than they are expected to know or even to read. Students often complain of this, and have even been known to cut out the "important" parts of their larger textbooks in order to make a scrapbook of more reasonable size for revision. The purely chemical part might be somewhat shortened, and the sections dealing with topics such as the reactions of proteins and the spectroscopy of blood pigments might be drastically curtailed, since they are dealt with later in the bio-chemistry classes. Apart from this criticism of length, the book is excellent. It is well arranged, with a good index and numerous cross references, and, for a first edition, miraculously free from misprints. All teachers of elementary chemistry would find it well worth while to read this book, and medical graduates wishing to refresh their knowledge of the fundamentals of modern chemistry and the scientific basis of some of the tests they use, would do well to read through many of the chapters.

D. C. H.

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more emphasises the many cases of functional nervous disorders presenting symptoms of a physical kind and the importance of such a book as this helps in their diagnosis. The book can be recommended to both student and practitioner with confidence. H. H. S.

AIDS TO DERMATOLOGY. By R. M. B. MacKenna, M.A., M.D., B.Ch. (Camb.), F.R.C.P.(Lond.). Third Edition. Pp. viii + 309, with 7 figs. Bailliére, Tindall & Cox. 6s.

FOR the first time since the original publication of this book in 1929, dermatology is dealt with alone; and a book dealing with venereal diseases will soon be published as a separate volume.

This book, published in January, 1946, has been fully revised up to that date. The dermatitis-eczema complex is well set out and should prove helpful to the student in obtaining a clear conception of this common skin reaction. The newer treatments for the coccal and parasitic infections are included.

If criticism of this excellent book were to be offered, it would be that for the student and general practitioner it is much too comprehensive. Many very rare diseases are mentioned—some admittedly in small print—but in view of the minor part which is unfortunately allocated to dermatology in most final examinations, it might safely be reduced to include only the really common skin diseases.

Of necessity, too, presumably on account of the price of the book, only seven figures are included; but it is a pity that such a pictorial subject as dermatology should have to be dealt with in book form without the aid of illustrations. R. H.

SURGERY OF THE HAND. By R. M. Handfield-Jones, M.C., M.S., F.R.C.S. Pp. 164. 20s.

To all those in the profession who treat infections and injuries of the hand, this book will provide a valuable addition to their library. Based as it is on the well-known treatise of Kanavel, anatomy receives its due recognition. In dealing with infections, it is stated that the presence of pus and its exact anatomical location must be known before accurate treatment can be carried out. Stress is laid upon general anæsthesia and an air-compression tourniquet to give a bloodless operation field. Indications for penicillin therapy are outlined. The author's twelve principles in dealing with infections of the hand are indeed classical. One can only say that if they were followed in every case, then dysfunction and disability of the hand and fingers would be a very much rarer phenomenon than it is at present.

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