discharge rate, very closely followed by patients of the manic type. At the other extreme must be placed juvenile and depressed cases. The latter only remit well enough to be discharged with about one-third the frequency of expansive cases, while "stuporose," "simple dementing," and "tabo-paretic" types, which each give very much the same discharge percentage, only do so one-half as frequently as expansive cases. On combining the percentages of discharged and improved patients, one finds that the total is over 50 per cent. in the expansive and manic types, compared with 22 per cent. only in depressed cases. The latter type also gives the highest mortality percentage—nearly three times that of the manic, which of all types seems to have the greatest resistance to both the *Spironema pallidum* and the rigour of the treatment.

REMARKS ON TREATMENT

As is to be expected, there is a definite tendency for early treatment—that is, two to five months after the first manifestation of general paralysis—to give better results, since not only is the discharge rate higher in the earlier months, but the unimproved cases tend to increase proportionately as time elapses, such a tendency being even more marked in the mortality percentages.

It is still a subject for conjecture when dealing with a disease of which the general public is so fully aware and in which, in the large majority of cases, the primary lesion is so easily observable, how infrequently one is able to obtain any history of its occurrence or treatment. It is almost as remarkable that patients who are able to give such a history remit well enough to be discharged twice as often as the others. One doubts whether this is entirely due to the primary treatment, for there is less than a 5 per cent. difference in the results obtained from cases treated with the organic arsenicals alone, or mercury and iodides only. What I have previously termed the incubation period of neurosyphilis—the length of time elapsing from the primary infection up to the development of the first symptoms of general paralysis—averaged in this collection of cases ten to fourteen years, with extremes of two and forty-three years, and, apart from a slightly greater tendency in patients who develop the disease early—that is, from two to six years after the chancre—to remain unimproved, there was no relationship between incubation period and result. Similarly, the quantitative pathological findings in the serum and cerebro-spinal fluids show no relationship to the result. Two points are worthy of comment here. The first is the increased frequency with which one is encountering patients who have a negative serum Wassermann reaction and positive spinal fluid findings, so much so that one is almost inclined to suggest that lumbar puncture should be routine in all new cases admitted to a mental hospital. The second is the ability of both the macro- and the micro-Meinicke reactions to pick out partially treated cases of neurosyphilis when the Wassermann reaction gives a negative result.

Among the factors making for success in the treatment of general paralysis is a short course of trypanamide before the induction of the pyrexia. This tends to lessen the activity of the cortical spirochaetosis, and allows the patient to rehabilitate his or her general condition and partially eliminate the causes of the toxic disturbances so commonly found in these cases on admission, thus better fitting them to withstand the exhaustion of the fever. The evidence of such improvement is to be found in the increased weight, diminution in the severity of the tremors, and improvement in muscular co-ordination.

Malaria is still our most successful pyretic agent, for, excepting sulfosin and allied sulphur preparations, the introduction of which is of too recent a date for a correct

assessment of their value to be made, the other agents are uncertain in their ability to produce any reaction in the organism or, having become effective, are uncontrollable in their course. From a review of this group of cases it appears that one should aim at the production of ten or more pyrexial peaks of 103° or over, while there is some evidence to support the belief that up to an optimum the longer the fever the greater the immunity response. Unfortunately, malaria *per se* has a recognizable mortality rate, but this, as is recommended by the Ministry of Health workers, Horton Mental Hospital, can be controlled to a large extent by the daily enumeration of the number of parasites and the temporary cessation of the fever with small doses of quinine whenever the count gives a higher number than 25 per field.

Again, if the malaria is followed up with novarsenobenzene or sulfarsenol, one may expect a result better by over 10 per cent. than if the treatment consists of malaria alone, while further factors in the continued remission of discharged patients are periodic clinical and serological re-examinations, accompanied by further treatment with trypanamide whenever mental or neurological abnormalities present themselves or if the spinal fluid findings show tardiness in reverting to the normal.

SUMMARY

To recapitulate briefly: pregnancy doubles the chances of remission; patients below the age of 40 years make the most economically satisfactory remission, although this should not prevent every patient whose physical state will stand it from receiving treatment quite irrespective of age. In this country expansive and manic paretics give the best prognosis, while depressed and juvenile cases do not respond very satisfactorily to treatment. The ability to remember the primary infection and its treatment is of prognostic value, although neither the length of time elapsing before the onset of neurosyphilis nor the pathological findings are of any value in this respect. Treatment must be thorough, and should be supported by a subsidiary course of organic arsenic after the fever.

TREATMENT OF TRUE RHEUMATOID ARTHRITIS BY BLOOD TRANS- FUSION AND INSULIN*

BY

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The treatment of true rheumatoid arthritis by orthodox methods yields, on the whole, disappointing results, even when the condition is in an early stage. In this respect it is unlike the other types of arthritis in which the results of proper treatment appear to be in direct relation to the period of the disease at which such treatment is commenced. The treatment here described has been evolved during the last three years, and is an attempt to improve the condition of these patients physiologically by increasing their blood resistance and body weight, since it is assumed that these two factors are the key to the rapid downhill course which is usually observed in these cases.

DEFINITION AND ETIOLOGY

The term "rheumatoid arthritis" is generally used too loosely. For the purposes of this paper I refer only to the condition which occurs almost exclusively among

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young women in the child-bearing period, and which is characterized by lassitude, pallor, loss of weight, and often dyspepsia. The condition commences insidiously, but often runs its course in one or two years, leaving the patient a cripple, the residual ankylosis generally being of a bony nature. The initial lesion appears generally to be a symmetrical, bilateral wasting of the small muscles of the hands, followed shortly by a peri-articular swelling of the mid-phalangeal joints, generally, it seems, of the middle or ring fingers. The metacarpo-phalangeal joints rapidly suffer in similar fashion, as do the wrists, elbows, and feet, if the condition is neglected. As Ray¹ points out, one of the chief characteristics of the established condition is the wasting and atrophy of the skin, muscle, and bone. The skin has a glossy white appearance, and is very transparent. Certain muscle groups tend to waste selectively, particularly extensor groups, and this produces the deformities typical of the condition; the x rays show a marked decalcification of the bones, with little other change; the blood nearly always shows a secondary anaemia, while an enlargement of the main lymphatic glands is not unusual.

With regard to the etiology of the condition, very little can be stated with certainty. A toxic focus is generally assumed, but can be located comparatively rarely, while, if such a focus be found, the results of its removal are apt to prove disappointing.

The sex incidence, the age period (which is prior to dental sepsis in most cases), the menstrual disturbances, the symmetry of the lesions, and the intermissions which often occur in its course, are somewhat suggestive of an endocrine disturbance, while the undoubted psychic element which is often present at the onset points in the same direction.

Recently it has been suggested that this condition may have to be classed, in the future, among the "deficiency" diseases.

THEORY OF TREATMENT

If the theory be held that a toxic focus is responsible for the manifestations of rheumatoid arthritis, but at the same time no such focus can be found for removal, the physiological method of dealing with such a case is to increase the antitoxic power of the blood. This is the rationale of vaccine treatment, but this treatment has proved insufficient by itself to deal adequately with these cases, in the experience of most people. The indication would therefore appear to be for an immuno-transfusion, in which the donor is immunized with a specific vaccine prior to giving his blood. This method has been used with some success by Willcox and Dyson in one (unpublished) instance, but in the majority of cases this method would appear to be too cumbersome, in view of the uncertainty with regard to the specific nature of most organisms which might be cultured from the patient, and the necessity for a regular donor. In the present series of cases ordinary large transfusions were employed.

It has been pointed out by Wyatt² that one of the most important factors in preparing the soil for rheumatoid arthritis is "under-weight," and it has been stated that the disease never occurs in those whose body weight is up to the average. Since this was considered to be probable, a method was sought whereby these patients could be made to regain their "expected" weight—a very difficult matter in most cases.

It was found that no dietetic measures appeared to have any effect upon the body weight of these patients, who were, on an average, about one stone under the weight which would be expected for their age and height.

Pemberton³ reported that the sugar tolerance of the rheumatoid arthritic is generally impaired, and although this was in the present instance not found to be an

invariable rule, the majority of cases did show a definitely delayed blood glucose curve, without glycosuria.

As a result of these findings it was thought that insulin might be of value in these patients in order to increase the combustion and storage of carbohydrates, and to induce a mild degree of hypoglycaemia before meals, which would lead to an increased appetite, and therefore, it was hoped, to an increase in body weight. These patients generally have very poor appetites, and it is customary to cut down their carbohydrates very considerably. It was found that the use of insulin was, in a majority of cases, instrumental in increasing the body weight, as had been hoped, and that the patients stated that they felt better in every way.

It will be well to consider in turn (a) transfusion, (b) insulin, and (c) the combined treatment, since this was the evolutionary sequence followed clinically.

TRANSFUSION

In sixteen cases which have been reported,⁴ ordinary blood transfusions were employed with satisfactory, although never dramatic, results. The patients were taken into hospital and a thorough search made for a toxic focus. In no case among these patients was this found. They were then given a blood transfusion of 500 c.cm., after which intensive physical treatment was given to the affected limbs and muscles on the same day, since the antitoxic power of the patient's blood, if it had been raised by the addition of normal blood, might be expected to be at its maximum at this time. This was repeated every day, and it was found that more treatment could be tolerated than prior to the transfusion. The whole transfusion procedure was then repeated on the eighth day. The citrate method was employed in all these cases, although it is possible that the defibrinated blood method might be more effective, on theoretical grounds. These patients very seldom complained of any reaction, except for a slight headache for a few hours. In two or three cases pain was complained of in the affected joints, lasting a few minutes only, after which the joints remained considerably less painful than previously. This improvement in the pain and in the general condition of the patients (including the appearance of the skin) has been so far maintained for nearly three years in two instances, and for lesser periods in the case of those patients treated subsequently. It was claimed, therefore, that this method of treatment was able to show an advance on other methods in so far as it appeared to arrest the acute course of the disease, and to improve the clinical condition generally. It supplements the more usual methods of treatment, and should in no particular supersede them.

INSULIN

The method adopted is similar to that advocated by Hunt⁵ (for cases of viscerotoposis), but much higher doses are used. The patient receives initially two injections daily of 5 units of insulin a quarter of an hour prior to luncheon and dinner. The next day 10 units are given in the same way; while on the third day, if no reaction has been experienced, a dose of 30 units is given and continued daily for about three weeks. The patient is not put on a special diet, but is given, as far as possible, what she likes, and is asked to consume, in addition, 1 lb. of glucose in the twenty-four hours. This is best taken as a drink with water or soda-water. It is wise to restrict drinking until after meals. Some of the glucose should be taken last thing at night to prevent any delayed hypoglycaemia occurring during sleep, and a bar of chocolate may, in addition, be eaten after each meal. The course ordinarily lasts for three weeks,

although it may be continued in the out-patient department with one injection daily (according to F. Howitt) for several months, with advantage. Three examples will suffice to demonstrate the type of improvement in the body weight which may be expected in an average case during the initial period of treatment.

Weight Table

Case	Age	Weight on Admission			Date	Weight on Discharge			Date	Increase in Weight		No. of Days of Treatment
		st.	lb.	oz.		st.	lb.	oz.		lb.	oz.	
L. W.	28	6	12	4	20/5/31	7	2	5	24/6/31	4	1	35
B. L.	24	6	4	0	19/4/31	6	7	0	8/5/31	3	0	28
F. O'R.	54	6	13	1	4/8/31	7	4	3	28/8/31	5	2	24

COMBINED TREATMENT

The best method of dealing with a case of rheumatoid arthritis which fails to respond to ordinary measures appears, as the result of trial in a limited number of hospital cases, to be by a combination of the two preceding methods. No harm will result, and in most cases considerable benefit may be expected. The complete procedure will therefore be as follows.

SUMMARY OF COMBINED TREATMENT SUGGESTED

1. Search for toxic focus; appropriate treatment if found (not forgetting bowel as a "focus").
2. If this produces no improvement, estimate (a) the blood sedimentation rate, to see whether a hidden focus of infection is probable, (b) the sugar tolerance curve, in view of future treatment with insulin.

3. Place the patient in bed, and carry out the transfusion treatment as described above; two injections at an interval of eight days with intensive physical treatment after each. With nervous patients it is often best to refer to the procedure as a blood "injection," rather than as a "transfusion."

4. Get the patient up on the ninth day. It is important to do this (if she is fit enough) before the psychological effect of the procedure has worn off, particularly with a patient who is almost resigned to being bed-ridden, as is so often the case. The patient must be keen to help, and her co-operation and interest must be sought if the best results are to be obtained.

5. Put the patient on the insulin regime, as described above, and make her weigh herself every day and chart her weight as a curve to stimulate her interest in the method. Most patients will gain about 1 lb. in the first week, and after that about 1 to 2 lb. per week in favourable cases. If the patient has been losing weight prior to the institution of this method, a "latent period" of seven to ten days must be expected before any gain in weight is made. The patient must be cautioned against the expectation of any "miraculous" result, but should be told to expect and report gradual improvement in her general and local condition and weight, the effect on the general health and mental outlook generally being the initial signs of permanent improvement.

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THE RATIONAL DOSAGE OF DIPHTHERIA ANTITOXIN

BY

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Since the introduction of diphtheria antitoxin, many attempts have been made to standardize the dosage of serum, adequate and not excessive, for the different stages and varying degrees of severity of the disease. At one extreme Park¹ suggests that doses of 10,000 to 20,000 units are sufficient for the most severe cases, while Bie² maintains that the rational dosage for a severe malignant case should be at least 160,000 to 220,000 units, and, where possible, 20,000 of this should be administered by the intravenous route. In the treatment of cases in which the condition is local and not associated with appreciable toxæmia it is held³ that antitoxin is of no value, yet although this is probably true, a failure to inject any definite case of diphtheria, even though mild, would lead to difficulties should the infection progress to a more severe stage.

Another point in dispute is that of re-injection of the case after a preliminary injection on diagnosis. Park states: "The injection of a single dose only, of sufficient quantity, is required, and multiple doses, although not harmful, are useless." Friedemann⁴ holds that the repetition of large doses is an important factor in the cure of severe cases. It must be almost impossible to judge in advance the requisite dose in all cases, and re-injection must therefore be necessary in some cases at least. The route of administration has been the subject of a good deal of controversy in the past, but since Rolleston⁵ pointed out that intramuscular injection is not only more

efficacious, but also safer than subcutaneous injection, the latter method has become obsolete. Intravenous injection has recently been used, but this method is attended by many dangers in a severely ill and somewhat frightened child, and, unless used immediately, is not so satisfactory as an earlier intramuscular injection. An attempt will be made to show that intravenous injection is not called for.

The following table will indicate the diversity of opinion on the subject of necessary dosage.

	Mild	Moderately Severe	Malignant	Laryngeal
Park...	I.M. 3,000 to 4,000	I.M. or I.V. 5,000 to 10,000	I.V. 10,000 to 20,000	—
Thompson...	6,000	—	40,000	18,000
Banks and McCracken	I.M. 14,500	I.V. 19,000	I.V. 71,000	I.V. 22,000
Bie ...	I.M. 16,000 to 20,000	I.M. 19,000	I.M. 31,000	I.M. 29,000
		I.M. 64,000 to 80,000	I.V. 20,000	—
			I.M. 140,000 to 200,000	

I.M. = Intramuscular injection. I.V. = Intravenous injection.

Banks and McCracken, as well as Bie, re-inject after a short period, and, in malignant cases, repeat the injection once or twice according to the needs of the more severe cases. Parks injects all the antitoxin in the primary dose.

In a recent investigation, Bie came to the following conclusions:

1. Diphtheria antitoxin has no effect in reducing the temperature in cases of diphtheria.
2. The membranous condition in the throat frequently spreads after the first injection of antitoxin.
3. Antitoxin hastens the separation of the membrane, but this effect is not marked.