with deep sutures. A suitable bandage is all that is necessary in the way of treatment.

Mental symptoms of a mild type have been present in several of my patients. One old man used to weep like a child without any apparent reason. My nurses say that a prostate patient is always a little "queer," and many of them are very difficult to deal with. I have not met with an acute outbreak requiring restraint.

Notwithstanding the low mortality in this series of cases I cannot say that I look lightly upon the operation of prostatectomy. Many are the pitfalls before the patient can be pronounced free from danger, and the medical attendant must give the closest attention to the after-treatment if he is to bring the case to a successful issue.

The patient, from his point of view, usually indicates to his medical attendant when his sufferings have reached the limit of endurance, and it is for the surgeon to determine whether the case is suitable for operation or not. In the future, I believe, cases will be subjected to operation earlier, before permanent damage is done to the urinary organs, with a corresponding diminution in the mortality.

SOME PROBLEMS CONNECTED WITH RHEUMATOID ARTHRITIS.

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THOUGH we are now able to distinguish rheumatoid arthritis from other forms of arthritis, and definite criteria have been established upon which to base a reasonably sound diagnosis, little corresponding advance has been made with reference to the pathogeny of the disease, and in consequence our methods of treatment are still almost entirely empirical. Attempts have been made towards a rational form of treatment—first, by the administration of intestinal antiseptics, on the assumption that the disease is a result of intestinal toxæmia; and secondly, by vaccine-therapy, on the assumption that the disease is a general infection. Neither of these assumptions is proved, and our present somewhat blindly directed methods of treatment are anything but uniformly successful in cutting short the disease, and it only too frequently happens that the victims of this relentless disorder get steadily worse. The swollen and tender joints become progressively more ugly, the wasted and distorted limbs more burdensome and useless. The false hopes engendered by remission are promptly quenched by the inevitable relapse. In no case, however slight, can we look upon the disease as otherwise than serious, and it is incumbent on all who see much of the disorder to consider carefully the bearings of such knowledge as we now possess relative to the intrinsic nature of the disease, and to see in what direction further investigations might profitably be undertaken to establish an accurate and complete pathological basis.

Rheumatoid arthritis may be defined as a disease, characterized by the occurrence of more or less symmetrical, spindle shaped, inflammatory swellings of the peri-articular structures, affecting first the smaller joints of the hands and feet, and accompanied by wasting, cramps, and contractures of muscles. The more severe cases are marked by moderate fever, anaemia, and occasional swelling of lymphatic glands and spleen, and most cases show more or less well marked sensory abnormalities and vasomotor changes. The disease tends to last for many years, with occasional intermissions of varying duration. Nearly every joint in the body may be ultimately affected, and the later stages may be complicated by osteophytic outgrowths resembling the condition found in osteoarthritis. The intensity of the disease varies within wide limits, and the clinical picture may be correspondingly diverse. The fact that various local foci of infection may be associated with the disorder has given rise to the suggestion that the cases presenting the above-mentioned characteristics do not constitute one disease. The tendency in some quarters is to limit the term "rheumatoid arthritis" to the more acute type occurring in young women, more particularly after childbirth, the less severe and less typical cases being considered in a different category under

the term "infective arthritis." The proof that the associated infective foci are the direct cause of the disorder is insufficient, and clinically one is able to trace a complete series of cases, from the severe type mentioned above to those in which the characteristic joint lesions, themselves slight, constitute almost the only evidence of the disease. It would appear more correct in the present state of our knowledge to confine the term "infective arthritis" to those conditions such as pneumonic, tuberculous, pyogenic, and gonococcal infections, in which there is indubitable proof of the microbic origin of the joint lesions. The term "rheumatoid arthritis" indicates by common consent a certain combination of clinical phenomena, and, as regards doubtful etiological factors, is entirely non-committal. On the other hand, the term "infective arthritis," as applied to conditions conforming more or less closely to the rheumatoid type, implies knowledge which we can hardly claim and conveys no indication of clinical features.

The more closely we become acquainted with this condition, the more patent does it become that we are dealing, not with a localized condition of arthritis, but with a general disorder by which the whole system is profoundly affected. The anaemia, wasting, glandular enlargements, vasomotor symptoms, cramps, and trophic disorders, all point the same way, though in the slighter cases these symptoms are less prominent and apt to be overlooked.

Apart from the joint lesions, one of the most noticeable and constant phenomena in true rheumatoid arthritis is a remarkable condition of vasomotor instability of the extremities.

No one who is frequently brought into contact with the disease can fail to notice the constancy of these associated vasomotor changes, from which patients suffer great discomfort and considerable pain. A condition in which the extremities look blue, congested, and puffy, giving rise to a tense, swollen sensation, alternates with a form of spasmodic ischaemia, in which the fingers are cold, pallid, waxy, and numb. The intensity of these vascular changes varies within considerable limits, but may be so great as to suggest the presence of Raynaud's disease. In illustration of this I may be allowed to quote the case of a well-known member of our own profession with typical rheumatoid lesions of both hands, who at the commencement of his illness, before joint lesions became manifest, diagnosed his own condition as Raynaud's disease.

The vasomotor abnormalities may exist in greater or lesser degree for long periods before other symptoms of rheumatoid arthritis supervene. Patients will frequently state that they have been subject to "bad circulation" or "dead fingers" for many years before the onset of joint lesions. One middle-aged patient stated that for something like thirty years there had been such a severe tendency for the fingers to become "numbed and dead" that ordinary housework was almost impossible, and it is not uncommon for patients to give a history of five or more years during which they have noticed similar symptoms.

A study of the histories of a considerable number of cases suggests that the tendency to marked vasomotor instability is an index of some personal idiosyncrasy predisposing to the disease, rather than a direct result of the exciting cause.

Associated with the vasomotor changes are the muscular cramps, which are very characteristic of the disease, and occur with great frequency. They do not necessarily occur in the muscles directly connected with the affected joints, and may occur entirely in the legs when the hands and arms are the site of the more severe articular lesions. In such a case I have known walking to be entirely prevented owing to the pain occasioned by violent cramps in the calves directly the patient attempted to get about. The coexistence, in both rheumatoid arthritis and Raynaud's disease, of spasmodic ischaemia of the extremities and cramp of the limbs, suggests that the latter is due in both conditions to spasms of the arteries supplying the muscles, with resultant accumulation of metabolic end products.

The early incidence of rheumatoid arthritis on the nervous system is indicated by the marked increase of reflexes, early wasting, and definite sensory disorders, which together go to make up a large part of the clinical

picture presented by the disease. The late Dr. W. M. Ord was the earliest to suggest that the disease was primarily a nervous disorder, and though the exact significance of the nervous symptoms has not been determined, further researches in this direction may possibly throw light on the essential nature of the disease.

The well-marked increase of deep reflexes is a notable feature in the early stages of the disease, and Dr. R. J. Llewellyn, who has made a careful study of the superficial reflexes, states that these also may be definitely increased. Muscular wasting may ensue with considerable rapidity, and even precede any marked lesions of the joints. In addition to the general wasting associated with the disease, the extensor muscles of the affected joints seem to be specially picked out. As the shoulder-joint is frequently affected next in order to the joints of the hands and wrist, it not uncommonly happens that the early wasting of the deltoids, together with the smaller muscles of the hands, is somewhat suggestive of the early stages of progressive muscular atrophy.

Sensory changes, as numbness, formication, and sensations of pins and needles, are constant and early phenomena. The exact distribution of sensory changes and of the pain associated with the disease is a matter of considerable interest. Llewellyn finds the sensory changes to correspond with segmental areas, and points to certain abnormalities of superficial and deep reflexes as bearing out the suggestion. I must admit that I have been unable to demonstrate in my own cases any clearly defined segmental distribution. On the whole, the distribution of sensory changes has seemed to me to follow that of peripheral nerve branches rather than of spinal segments, but in this connexion we must remember the possibility, suggested by Dr. James MacKenzie, that intrinsic lesions of the joints may themselves give rise to referred pains of segmental distribution.

The whole subject of the motor and sensory phenomena associated with rheumatoid arthritis is one of much interest, and affords a large field for further investigation. Unfortunately the few recorded *post-mortem* examinations throw little if any light on the question, and as, in the nature of things, we are likely to get little help from this source in eliciting the character of the earlier stages of the disease, accurate clinical observation becomes doubly necessary.

The above mentioned nervous and vasomotor phenomena, together with the anaemia, debility, and symmetrical joint lesions, point to the conclusion that rheumatoid arthritis is essentially a widespread systematic intoxication, and the question remains whether it is a toxæmia from without due to bacterial invasion, or a disorder from within due to qualitative or quantitative changes disturbing the balance of the various internal secretions.

From the time when Drs. Bannatyne and Wohlmann first demonstrated organisms in the synovial fluid till the present, numerous investigations have been carried out, both in this country and abroad, with a view to the isolation of a specific organism, either from the joints or blood. Many observers have failed to demonstrate organisms at all, while in the cases where they have been found there is no uniformity of results. Instances of improvement following a course of vaccine-therapy have been recorded, but their number is not sufficiently great to enable us to say whether the administration of vaccine, generally speaking, is likely to prove more efficacious than other methods of treatment. Though there is a good deal of clinical evidence, and a certain amount of experimental evidence to support it, the hypothesis of the bacterial origin of the disease must still be considered *sub judice*.

Efforts have been made to correlate the disorder with the presence of different local foci of infection, and pyorrhoea alveolaris, rhinitis, otorrhoea, sinusitis, endometritis, and inflammatory conditions of the gastro-intestinal tract have been severally considered responsible for the condition. Here, again, the evidence is inconclusive. The very multiplicity of the affections named, and the variety of organisms responsible for them, suggest that whatever influence they may have as predisposing factors, we must look elsewhere for the determining cause. Further, such conditions as pyorrhoea, uterine discharges, and septic conditions generally are so extremely common that if they were direct causes of

rheumatoid arthritis we should expect the latter to be far more frequent than it is.

In a large proportion of cases of rheumatoid arthritis there is no demonstrable site of infection. In these the supporters of the chronic infective theory are forced to postulate some cryptic source of infection in the gastro-intestinal tract, and we cannot dismiss the possibility that chronic intestinal toxæmia may stand in a more direct relationship to the disease. Patients frequently complain of chronic dyspeptic symptoms as an antecedent to the joint troubles. Strangeways states that 39 per cent. give a history of antecedent gastric disorders, but unfortunately the cases from which the statistics are derived included forms of arthritis other than rheumatoid. In my own cases symptoms of gastric ulcer, latent or otherwise, have occurred sufficiently often to be very suggestive of some association between the two diseases, but the number of cases has not been great enough to render statistics on the point of any value. The removal of decayed teeth and treatment of pyorrhoea alveolaris are frequently followed by striking improvement in rheumatoid symptoms, but this is probably to be explained by the marked improvement in general health and vitality which results from the removal of digestive disorders. Intestinal antiseptics certainly have an influence for good in the disease, and, as far as my experience goes, small repeated doses of grey powder seem to have done more good in the treatment of the more acute types than any other remedy, though salol, β -naphthol, and other antiseptic drugs no doubt possess similar properties in varying degrees.

Thus the theory of gastro-intestinal toxæmia is sufficiently plausible, and borne out to a certain extent by therapeutic tests, but further investigations are required as to any bacterial or chemical features of the gastro-intestinal tract, peculiar to the disease, before we can unreservedly accept it.

Whatever views we may hold as to the infective origin of rheumatoid arthritis, there can be no doubt but that the personal element is an important factor in the genesis of the disease. The fact that about 80 per cent. of the cases occur in women, nearly all between puberty and the menopause, is in itself suggestive. Again, many of the sufferers come of a distinctly arthritic stock. Garrod quotes over 40 per cent. as having a family history of gout or "rheumatism," and it is no uncommon thing to find two or more members of a family suffering from the disease. I have notes of one case in which no less than seven members of one family, in two generations, suffered from the same, or at least a similar, disease at the same time—namely, father, mother, three sisters, and two female first cousins.

Consider, again, the age and sex relationship of rheumatoid arthritis to gout. Whereas nearly 90 per cent. of cases of rheumatoid arthritis occurring in women fall between the age of 15 and 45, arthritic gout in the female sex is extremely uncommon between these ages. Thus it would appear that there is some powerful agency at work in women during the reproductive age which is as conducive to rheumatoid arthritis as it is antagonistic to gout.

On the other hand, the vast majority of cases of Graves's disease correspond in sex and age limits to those of rheumatoid arthritis, and the general relationship of the two diseases suggests the existence of some important factor common to both. Numerous cases have been recorded by McAlister, Llewellyn, Sprigg, and others in which definite Graves's disease and rheumatoid arthritis have existed simultaneously in the same patient, and symptoms of hyperthyroidism, in the form of tremor, soft rapid pulse, moist skin, and tendency to pigmentation, are amongst the most constant features in the more severe cases of rheumatoid arthritis.

Whether the profound constitutional changes found in both diseases are due to microbial infection is at present uncertain, but this question does not affect the conviction to which we are by circumstances forced, that in both rheumatoid arthritis and Graves's disease there exists a strong personal predisposing factor, which is enormously enhanced in the female sex, especially during the period of reproductive activity. In both diseases there appears to be some deep-seated metabolic error, involving important changes in internal secretions, and the personal factor predisposing to either may consist in a congenital or

acquired instability of the normal relationships which govern secretory activities.

However this may be, there is a strong family resemblance between Raynaud's disease, rheumatoid arthritis, and exophthalmic goitre. Whether there is any etiological or pathogenic factor common to those diseases remains to be seen. At the present time the pathology of all three is equally secure, and the nature of any relationship between them is entirely conjectural.

Whatever its relationship to other diseases, rheumatoid arthritis presents in itself many points of interest and many features of obscurity. I have attempted to indicate briefly certain problems in connexion with it which require to be elucidated before we can claim to have a sound knowledge of its pathology. On the clinical side a wide field of investigation is afforded in the systematic and careful consideration of family history and individual peculiarities in so far as they indicate a personal factor predisposing to the disease, together with precise investigations as to the nature and significance of the so-called accessory symptoms as they affect the nervous and vascular systems respectively. On the pathological side we require to know what relationship, if any, exists between the various foci of infection which frequently precede the disease and the subsequent phenomena, and more especially the importance of gastric and intestinal toxæmia as an etiological factor. It is possible that expert bacteriological examination of the flora of the gastro-intestinal tract in a series of cases might throw considerable light on this aspect of the question, and such investigations are urgently required.

Systematic chemical and bacteriological examination of the urine, to determine not only the presence or absence of disease of the urinary tract, but more particularly the standard of renal efficiency and the presence of any peculiar features of excretory activity, are also required to throw further light on any metabolic peculiarities incidental to the disease.

THE OCCURRENCE OF ACUTE PNEUMONIA DURING TREATMENT WITH ARSENIC.*

BY

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In a few cases I have observed the sudden occurrence of pneumonia in children whilst they were undergoing arsenical therapy on account of lymphadenoma or some other disease, and it has appeared to me that the association was no chance one, but that the pneumonia was in some way dependent on the taking of arsenic, as is arsenical herpes zoster. Two of the patients likewise had attacks of arsenical herpes zoster. The rapid recovery from the lung disease was another striking feature.

CASE I.

Sophie T., aged 15, under my care at the German Hospital in 1902 for lymphadenoma, was a thin anaemic girl. The lymphatic glands on the right side of the neck and the spleen were greatly enlarged. Enlarged cervical glands had been present as early as 1898. In June, 1902, whilst under arsenical treatment, she had a short acute attack of pneumonia at the base of the left lung, accompanied by very little fever. It may be noted that about a year previously (1901) whilst taking arsenic she had had a mild attack of herpes zoster (doubtless arsenical herpes zoster) on the left side of the chest, though in regard to her general condition the arsenic seemed to have done her good. The herpes zoster apparently caused her no pain or inconvenience.

She died in December, 1902, and the necropsy showed the presence of considerable (partly miliary) tuberculosis in addition to old lymphadenoma. The spleen was enlarged to about five times the normal size and contained whitish masses. Microscopically the spleen, and the liver also, were found to contain minute tubercles. A hard, fibrous mass situated at the back of the upper part of the abdomen and displacing the stomach and liver forwards, had microscopically the appearance of chronic hard lymphadenoma.

CASE II.

A boy, Roger S., aged 8 years, suffered from typical Hodgkin's disease (lymphadenoma), which involved the cervical lymphatic glands and the spleen. In 1902 he was under the care of my colleague Dr. Karl Fürth, who has kindly allowed me to refer to the case. The disease, which was supposed to have com-

menced about three years earlier, was apparently diminishing under arsenical treatment, when in December, 1902, he developed signs of pneumonia (dullness and bronchial breathing at the base of the left lung) accompanied by only slight fever. The arsenic was discontinued. The boy had likewise typical herpes zoster on the right side of the chest and a generalized eruption of minute vesicles on the trunk, possibly due to arsenic. This was followed by a good deal of desquamation, especially on the palms of the hands (? arsenical).

The boy seemed fairly well when he left the hospital in January, 1903. But he did not live long.

CASE III.

A boy, Freddy J., aged 7½ years, was admitted under my care in June, 1905, for chorea minor. The case had a special interest of its own, inasmuch as the patient was left-handed and the right half of his head was distinctly bigger than the left half. The choreic trouble, which was specially marked in the left upper extremity, was temporarily associated with loss of speech ("choreic aphasia"). Auscultation of the heart showed a slight mitral systolic murmur, when he left the hospital in September, 1905.

In the following year he was readmitted for slight chorea, and whilst under arsenical treatment, on March 6th, 1906, he developed pneumonia of the lower part of the left lung (impairment of resonance and crepitation) with considerable fever. There was no fever after March 13th, but crepitation could be heard over the affected lung for some days more. The pneumonia seemed to be of a mild type. There was very little cough and no pain.

CASE IV.

A little girl, Anna G., aged 4 years, when being treated, during 1910, with liquor arsenicalis for a lichen-like affection, developed acute pneumonia (with dullness and bronchial breathing) at the base of both lungs. There was considerable fever, but the pneumonic signs cleared up very well. There was for a time in this case a diffuse cutaneous erythema, which may have been of arsenical origin, and was followed by slight general desquamation and brownish pigmentation.

CASE V.

A girl, Theresa E., aged 14 years, who was undergoing radium treatment and was taking arsenic and iron for an acute and malignant type of Hodgkin's disease (lymphadenoma). A lymphatic glandular swelling had been first noticed on the left side of the neck in January, 1912, and, after operative removal of this in May, 1912, a fresh glandular tumour had rapidly formed on the same side of the neck. Radium treatment was tried in August, and was followed by great diminution of the swelling in the neck, but soon afterwards a striking enlargement of the spleen, and probably of intra-abdominal lymphatic glands also, occurred. She was losing ground in spite of treatment by arsenic and iron and the radium therapy, when, on December 5th, 1912, I saw her with Dr. Smulian for acute lobar pneumonia of the lower part of the left lung (dullness, bronchial breathing, and some crepitation) with moderate fever. The respirations were 46 a minute, and the pulse 120. The pneumonia had apparently commenced with general convulsions three days previously, and it seemed (considering the patient's bad general condition) to have come as a "terminal" infection. However, on the next day the patient was already recovering from the pneumonia, and in a few days she was able to leave her room and go out for drives. The lymphadenomatous disease nevertheless rapidly progressed, and she soon died.

In the foregoing cases the patients were all young, and the recovery from the pneumonia was excellent, even when the general condition, as in the last case, was extremely bad. There was little in the way of distressing cough or pain. It seems to me that arsenic may possibly predispose some persons to an attack of (? pneumococcal) pneumonia, just as it is acknowledged to predispose some individuals to an attack of herpes zoster, which is perhaps, like pneumonia, a disease of infectious (microbic) origin. On the other hand, my cases are too few in number to draw any certain conclusions from, and I do not know that any similar cases have been described in the literature on the effects of arsenic, or in that on pneumonia. It must not, however, be forgotten that it is only comparatively recently that herpes zoster has been acknowledged to be in some cases a consequence of the ingestion of arsenic, as a medicine or otherwise—as, for instance, as a contamination of beer in the English epidemic of arsenical poisoning in 1900.

I think it highly probable that cases of pneumonia similar to those which I have recorded will soon be observed by others amongst children and young persons undergoing arsenical treatment. If other cases should be found to confirm my suggestions, I would be tempted to think that the arsenic, whilst predisposing towards pneumonia, must also exert a favourable effect on the reaction of the body towards the disease—that is to say, that when pneumococcal pneumonia occurs in patients who are being treated with arsenic the pneumococcal infection is quickly

* A paper read at the Medical Section of the Royal Society of Medicine on January 28th.