and that of ulceration or fissures about the mouth of the infected infant.

In conclusion I have to apologise for the disjointed and fragmentary character of these lectures. In reality they deal with only a very limited portion of the subject of infantile syphilis. Important questions, such as diseases of the nervous system, vaccinal syphilis, prognosis, treatment, and many others, I have preferred to altogether omit rather than to attempt to treat in a perfunctory manner. In fact, my selection has been manifestly based on controversial grounds rather than any other.

RHEUMATOID ARTHRITIS: ITS CLINICAL HISTORY, ETIOLOGY, AND PATHOLOGY.

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With a Report on its Bacteriology

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UNTIL quite a few years ago rheumatism, like gout, was almost universally regarded as a disease of "chemical" origin. Lactic acid, as a product of disturbed metabolism, played the part of uric acid in gout, and the possibility of a pathogenic micro-organism scarcely entered into the range of serious discussion. Even three years ago, when first we started on our search for the *materies morbi* of rheumatoid arthritis, the idea of an organism as a causative factor in any one of the group of "rheumatic" diseases seemed somewhat wild and improbable; but since then several suggestive papers, notably that of Newsholme,[1] have thrown fresh light on the subject, and have at least accustomed one to the idea that acute rheumatism may probably prove to be an acute specific disease caused by a definite pathogenic microbe. It was the close analogy of rheumatoid arthritis to tuberculosis that first suggested to our minds the possibility of a micro-organism as the cause of the disease; and, once started on that idea, the clinical symptoms, so difficult to account for on the usual nervous and other theories of causation, readily fell into their place in a natural and explicable sequence until long before we had actually found the organism we were quite convinced of its presence.

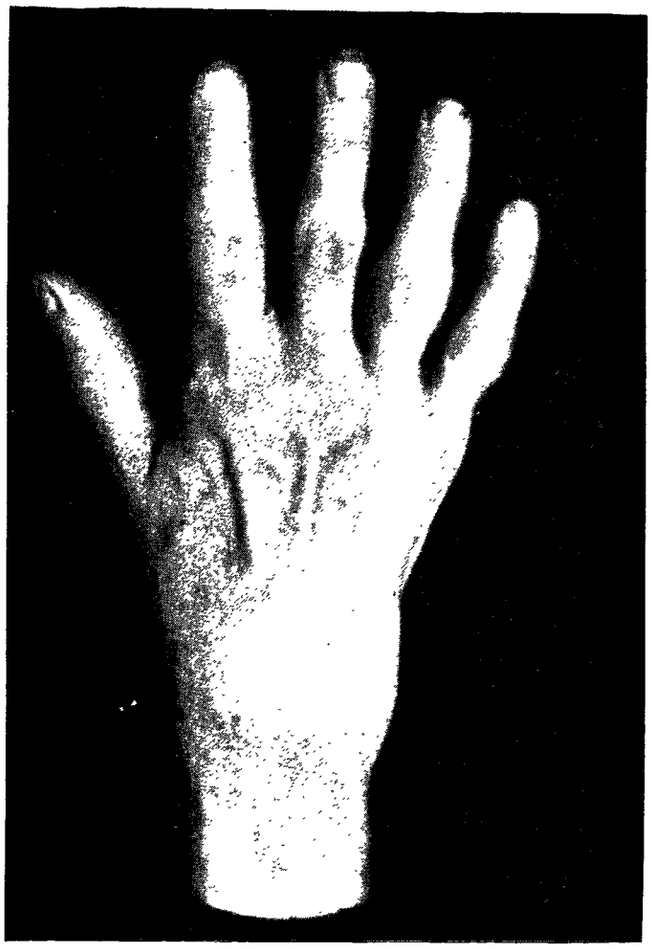
But at the very outset we were met by great difficulties in obtaining pathological material. Clinical material we had in abundance, but the opportunity of examining post mortem the joints of a patient suffering from rheumatoid arthritis was an event of such extreme rarity that we were forced to be content with the examination of synovial fluid obtained during life. And here, again, of course, came the difficulty that the number of cases of synovial distension honestly likely to be benefited by tapping was extremely limited, forming a very minute proportion of the hundreds of cases passing through our hands; in consequence there was great delay and we had often to wait months for fresh material. The cases from which our synovial fluid was, as a rule, obtained were those of rheumatoid arthritis in which there was great distension of a joint, generally the knee, occasionally the wrist or fingers, which did not yield to blistering and other medical means. In such a case, the skin over the joint having been made aseptic and a simple form of aspirator carefully sterilised, the needle was plunged into the joint and the fluid withdrawn. Often, although the joint seemed distended with fluid, none could be obtained in the aspirator bottle, but in such cases there would generally be found a drop of fluid or a plug of synovial membrane in the point of the needle which would be sufficient for our purpose. With a sterilised platinum wire various culture tubes were then inoculated on the spot, several coverslip preparations made of the fluid or membrane, and the fluid in the bottle retained for further examination in the laboratory. The limb was placed on a splint for a few days, the needle-wound being dressed with cyanide gauze, and slight pressure kept up with a bandage. The aspiration generally relieved the pain, but often the fluid would return requiring a second and sometimes even a third tapping. In no case was any injurious effect apparent on the joint. In the microscopic preparations so obtained we found in 24 cases out of 25 rheumatoid joints examined: (*a*) a micro-organism; (*b*) always the same organism, so far at least as size, appearance, staining properties, and behaviour in culture media were concerned; and (*c*) the organisms were present in considerable, sometimes in enormous, numbers. To Dr. Blaxall of the British Institute of Preventive Medicine, to whom we are very greatly indebted, we leave the task of describing, with fuller detail and with more practised hand, the appearance, the properties, and the life-history, so far as is at present known, of the microbe as found by him in the specimens of synovial fluid which we have sent him.

Before going on to discuss the etiology of rheumatoid arthritis let us make it perfectly clear of what disease it is that we are speaking. Probably in no department of medicine is there more hopeless confusion of nomenclature than in the group of so-called "rheumatic" diseases. An acute disease with its rapid onset, its definite course, and its tangible and immediate results can hardly fail to impress the observer; it is seized upon, studied, named, and classified. With a chronic disease, on the other hand, the wearisome chain of indefinite symptoms ends by wearing out alike the time, the patience, and the interest of the observer; and hence it is that under the heading of chronic rheumatism or of osteo-arthritis there are probably massed almost as many diseases as formerly there were under "fever" or "paralysis." Provisionally, then, we divide the rheumatic and allied groups as follows: (1) acute rheumatism, (2) chronic rheumatism, (3) gout, (4) rheumatoid arthritis, and (5) osteo-arthritis.

And here let us pause for a moment to point out what we mean by chronic rheumatism and by osteo-arthritis. To the heading of chronic rheumatism we would relegate those cases of stiffened, painful, and often distorted joints left as a sequel of acute or subacute rheumatism, the distortion in this case being apparently due to alterations in ligaments, tendons, and muscles, rather than to bony or cartilaginous changes, these latter, if present, being only secondary and due to superimposed osteo-arthritis. Absolutely indistinguishable clinically is the great group of cases in which there is no history obtainable of acute rheumatism, but which are yet known familiarly to everyone as chronic rheumatism. Whether these cases are really identical with the last is uncertain, but in the present state of our knowledge we must be content to allow them to remain in the same category.

It is when we come to osteo-arthritis that we begin to tread on uncertain ground. In the official nomenclature rheumatoid arthritis and osteo-arthritis are used as interchangeable terms for the same disease, but of late, with the further differentiation of the clinical features, there has been a growing tendency to retain the term rheumatoid arthritis for the specific disease we are about to describe and to keep osteo-arthritis for the more common mechanical condition characterised by lipping of bone, osteophytic growth, and erosion. As it seems a pity to attempt to add fresh words to our nomenclature we have retained the term rheumatoid arthritis for use in this narrower sense. By osteo-arthritis, then, we mean a local joint condition in which we find erosion of cartilage, thickening, eburnation, and lipping of bone, with or without fluid effusion. These changes may arise in a joint injured by accident, by occupation, or by the mere wear and tear of life; in such cases the affection may be a mon-arthritis, or, if multiple, asymmetrical, and picking out the joints in a definite manner and according to well-known physical laws, as shown long ago by Arbuthnot Lane, a summary of whose views will be found in a recent number of the *Clinical Journal*; or they may appear to be merely secondary changes ensuing in a joint already damaged by rheumatism, by gout, or by rheumatoid arthritis. In the latter case the joints involved may be multiple and the disease may appear to exhibit a quasi-symmetry. The condition appears to be purely local, and, except in so far as pain and inactivity hamper the functions, the rest of the

[1] THE LANCET, March 9th and 16th, 1895.



Showing characteristic spindle-shaped swelling of Phalangeal joints, swelling of wrist and muscular atrophy.

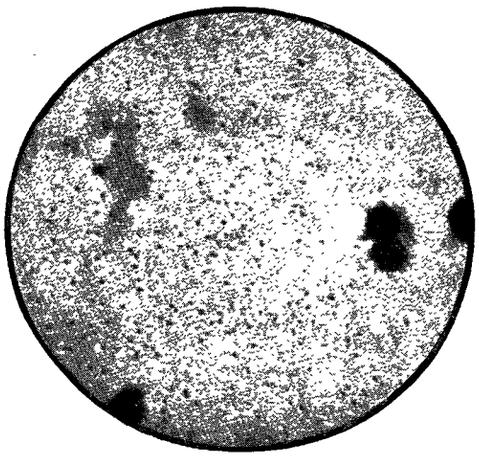


Fig. I.

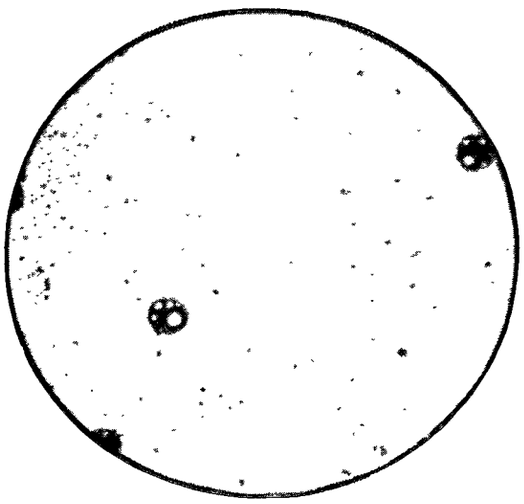


Fig. II.

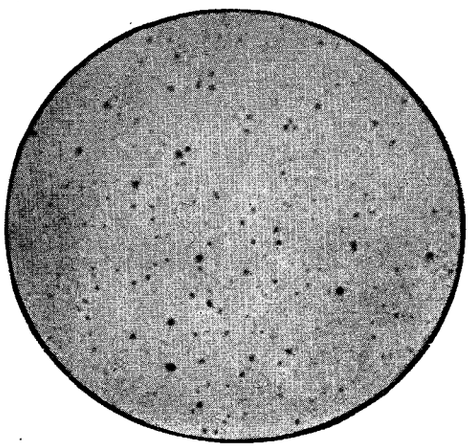


Fig. III.

TO ILLUSTRATE AN ARTICLE ON ***RHEUMATOID ARTHRITIS*** *BY*

DR. GILBERT A. BANNATYNE, DR. ARTHUR S. WOHLMANN, AND DR. FRANK R. BLAXALL

organism would seem to be absolutely unaffected by the disease.

Turning now to rheumatoid arthritis, we find a very different state of affairs. It is a "constitutional" rather than a local disease; the whole organism is affected; the joint condition is by far the most important *symptom*, but it is only a symptom, and not the whole disease. In contradistinction to osteo-arthritis, rheumatoid arthritis is a disease of women rather than of men (of 100 consecutive cases taken at random 85 were females and 15 were males); of comparative youth rather than of age (the average age of the above series of cases at the commencement of the disease was twenty-eight, the eldest sixty and the youngest four). There would, however, appear, as pointed out by Fortescue Fox and others, to be two periods of greatest frequency of onset: one—and this embraces the larger number of cases—of early adult life, say from eighteen to twenty-five; the other the period of the climacteric. With respect to the family history we are unable to make any very definite statements. Hugh Lane[2] maintained that the disease is caused by the amalgamation of the hereditary taints of gout and tubercle. From our own experience we are unable either to confirm or refute this statement. In the case of a child who died from rheumatoid arthritis we were fortunate enough to secure a family history through four generations on the mother's side and two on the father's. In this case, of eight brothers and sisters, one died in infancy and six were very "delicate"; the mother suffered severely from rheumatism, while her three sisters had acute rheumatism and heart disease; the grandmother had "rheumatism," while the great-grandmother died from phthisis. On the other side, the father was normal; the grandfather had "rheumatism." Anyone, however, who has gone into the subject of family history in hospital patients will admit the extreme unreliability of the statements obtained. Rheumatoid arthritis is predisposed to by any debilitating cause, more especially by anything particularly weakening the resisting power of the joints. Of all predisposing causes acute rheumatism seems to be the most potent (of the above series of 100 cases 38 gave a history of previous acute rheumatism). But here two obvious fallacies have to be taken into account. The onset of the disease if at all acute, as is not unfrequently the case, may be mistaken for a mild attack of acute rheumatism; while, on the other hand, in the rheumatic fever of childhood the joint symptoms are often so little pronounced that the nature of the disease is entirely unsuspected. In a very large proportion of the cases we find a history of menstrual disturbance, amenorrhœa, dysmenorrhœa, or too frequent menstruation; in a still larger proportion the menstrual trouble comes on after the rheumatoid disease has well developed.

Amongst other debilitating causes should be mentioned the chlorosis of puberty, rapid child-bearing, prolonged lactation, worry, over-work, ill-feeding, and such diseases as typhoid fever. As a rule, the first manifestation of the disease is the gradual onset of a painful spindle-shaped swelling of the proximal interphalangeal joints of the ring- and middle-fingers; sometimes the pain precedes the swelling, sometimes the swelling precedes the pain. Usually both hands are affected within a few months of each other. Occasionally the disease commences in the wrists; rarely in other joints—e.g., the knee. Spreading fairly symmetrically from joint to joint the disease involves, in definite order of frequency, the wrists, the rest of the fingers, the articulations of the cervical vertebræ and of the jaw, the knees, elbows, ankles, tarsal-joints, and shoulders. The other joints usually escape, though the hips occasionally suffer, and we have seen the toes spindle-shaped like the fingers, though this is rare. The thumbs and great toes generally escape.

Clinically the joints may be affected in one of two ways. There may be a deceptive appearance of bony nodular enlargement; this is most noticeable about the finger-joints and is usually due to tense distension of small synovial pouches connected with the joint cavity; firm pressure with the finger will show the true nature of these swellings, while unexpected confirmation of this opinion has recently been furnished by the application of the Roentgen rays, but more often there is a soft, doughy-looking swelling blurring the outlines of the articulation. In such a case there appears to be little or no fluid in the joint, but the synovial membrane is greatly thickened and swollen, while the ligaments and fasciæ about the articulation are softened and infiltrated. Bony grating is not obtained in such a joint; it is only later, when secondary osteo-arthritic changes have taken place, that the harsh grating of erosion is obtained. The skin over an affected joint generally feels distinctly hot to the touch, and if the process is at all acute there may be a distinct blush closely resembling that of acute rheumatism. The pain is usually severe, fluctuating considerably, and in some cases apparently largely influenced by changes of weather. The body temperature is generally raised about a degree at night, falling to normal in the morning. In children, in whom the disease is always more acute, the temperature may rise to 101° F. or even more every evening. Another peculiarity of the disease in children, to which Dr. G. F. Still first drew our attention, is the frequency with which the lymphatic glands are enlarged. We have noticed this, too, in acute cases in adults. As the joint trouble becomes pronounced other symptoms appear and advance with it *pari passu;* occasionally they may even *precede* any manifestation of articular disturbance (Dr. Spender).[3] Anæmia is generally noticeable early in the case and may become profound: it appears to be due rather to deficiency of hæmoglobin than to destruction of corpuscles. Muscular atrophy is a very marked symptom and one always present. Although as a rule there is a general atrophy of fat and muscle distributed over the whole body and contributing to that cachectic facies so universal in this disease, yet there is a distinct selective agency at work. Some muscles suffer more than others, notably the extensor muscles of the forearms, the abductor indicis, the interossei, and the muscles forming the thenar eminence. Muscles, if affected at all, suffer throughout their entire length, and the atrophy is not limited to the portion near or distal to a joint. The reaction of degeneration is not usually marked. In addition to the muscular atrophies there are various other evidences of trophic and vaso-motorial disturbance. Sudden flushing of the skin of the whole body with copious outburst of sweating is common, while a very profuse cold perspiration of the palms of the hands and fingers is present in almost every case, and may be so copious as literally to drip off. The extremities are usually cold and clammy, and a peculiar livid mottling of the hands, especially over affected joints, is common. The fingers have a great tendency to "go dead," and in five cases we have seen this condition so marked as to merit the title of Raynaud's Disease, there being actual gangrene under the nails. In none of these cases was there any hæmoglobinuria. It was Dr. Spender who first drew attention to the pigmentary changes of the skin in this disease. The changes may consist of minute black freckles, most common on the backs of the forearm, of dark washes of colour under the eyes or across the forehead, or of a general darkening of the complexion. The same writer, too, draws attention to the changes in the cardiac rhythm and lays great stress on the tachycardia often present. We would wish to point out in addition that it is by no means rare to find an apical systolic bruit (? hæmic) in cases of rheumatoid arthritis in which no history can be obtained of a previous attack of acute rheumatism, while it is quite common to find a booming alteration of the first sound. Pericarditis is occasionally found, but how far it is of a rheumatic and how far of a rheumatoid origin is at present uncertain. Ecchymoses in the skin are quite common. Peripheral neuritis may be present, but there is never any marked disturbance of the sensory nerves. The reflexes, as a rule, are normal.

To sum up, then, the points of special significance in the diagnosis of the disease are: (1) the sex and age of the patient; (2) the soft spindle enlargement of the finger-joints and the swelling of the wrists; together these form the most constant symptom, and in nine cases out of ten the disease can be easily and certainly diagnosed from the hands alone; the accompanying illustration shows excellently the typical deformities, together with the atrophy of the interossei; (3) the cold sweating palms; (4) the affection of the jaws and neck; (5) the cachexia and wasting; and of less importance (6) pigment changes and (7) tachycardia. It is hardly within the scope of this paper to enter into the subject of treatment. At best it is but unsatisfactory. Treatment based on the assumption that the disease is a "rheumatic gout," with consequent deprivation of meat and stimulants, may soon bring the patient to an almost moribund condition. The resisting powers of the tissues must be strengthened to the utmost; rich, nourishing

[2] The Rheumatic Diseases (so-called).

[3] Brit. Med. Jour., 1893.

food, alcohol if necessary, cod-liver oil, iron, arsenic, may all prove useful, but, above all, fresh air and sunshine. The wasting and stiffness may be relieved by massage, the stiffness and the pain, which is usually very severe, by hot baths and mild counter-irritants. The prognosis as regards life is fairly good; as regards complete recovery extremely bad. The disease steadily progresses through years of suffering until, the soft structures of the joints being destroyed, either fibrous ankylosis occurs or ordinary osteo-arthritic changes take place, and the disease, having exhausted its pabulum, wears itself out and becomes quiescent. Just as in fibroid phthisis the fibrous tissue is a protective effort of nature to limit the growth of the bacillus, so in the fibrous and osteo-sclerotic ankylosis of joints in rheumatoid arthritis we have a similar defensive action; in neither case, apparently, do the microbes survive in the new-formed tissues.

Turning, then, to the pathology of the disease, as we understand it, we have a disease due to the presence of micro-organisms found in the joint fluids and tissues, and which must until disproved be regarded as specific. How these micro-organisms gain access to the blood is not at present definitely known, but they probably do so through some chronic catarrh of the gastro-intestinal or genito-urinary systems, and such catarrhs are not far to seek. In not a few cases it has been traced, with almost absolute certainty, to the tonsils. Having gained a footing in the circulation the micro-organisms pass freely to all the organs of the body, thus explaining the symmetry of the disorder and why one joint after another should be involved. They now proceed to select a suitable nidus for their growth, and, like all other pathogenic bacteria, they exercise a selective action in their choice which never varies. What governs this selective action is not known; but it appears curious that out of all the sites to which they gain access they should, so far as we at present know, only choose the joints for their habitat. We may note that joint tissues seem specially liable to bacterial infection, *vide* such diseases as pyæmia and gonorrhœa. It is possible that the endocardium and pericardium are also liable to their attacks, as otherwise it is difficult to account for the symptoms referable to those tissues. This point has not been fully elucidated, and, so far, we have no proof one way or another. Probably, also, the micro-organisms grow and propagate in the lesions through which they gain access to the blood, giving rise to those local catarrhs so common during the course of the disease. Owing to the want of post-mortem material these points must be left for future consideration. In the joints we found proof that the micro-organisms grow and propagate, doing so, not only in the synovial membrane, ligaments, &c., but also in the bone marrow and cartilaginous structures. Their presence gives rise to acute inflammatory changes leading to ulceration, erosion, and destruction of the hard as well as of the soft joint tissues. Our specimens are so few that this is only a provisional statement. This process varies in intensity and, usually as the disease progresses a coincident but varying amount of reparative change is seen, which ends in general hardening and thickening of both bones and ligaments. The presence of micro-organisms can be demonstrated in the joint fluid by staining and also in the tissues on section. The joint and heart symptoms are those only which would appear to be due to the direct action of the micro-organisms, and may therefore be regarded as primary or essential, whilst those which are due to their indirect action, through their products, may be regarded as secondary or symptomatic. These latter may vary in every case, not only in intensity, but in nature, yet they would all appear to have a common origin in toxic action.

During their life cycle these, like all other bacteria, give rise to poisonous products, which, being absorbed, pass to the body generally, and, what is of more importance, to the nervous system locally. Here, again, we see either a peculiar selective action on the part of the products acting on or else a peculiar susceptibility of the parts acted on. In this as in other bacterial diseases, we have no definite proof that it is not the micro-organisms themselves which cause the changes in the nerve system, but all argument, analogy, and proof is against it, and, therefore, we may assume that such is the case. As evidences we have the experiments of MM. Vidal and Bezançon,[4] which show that several micro-organisms have the power of producing central nerve degeneration, and although they have been isolated from the blood, yet they have not been found in the central nerve tissues. They therefore appear to act by the elaboration of a soluble poison. Such would appear to be the case in rheumatoid disease. With regard to the toxic action of bacterial poisons on the nervous system, it is of importance to note that nutritional as well as actual organic change may result. Although these nutritional changes are more common in the peripheral nerves, yet toxic agents exhibit such a remarkable selective action, and as we do not as yet know what are the influences which determine such susceptibility it would not be surprising to find similar changes in the central nerve system. From every side evidence is gathering that what may at first be only a depression of the function of a certain centre or group of centres may end, if the irritation be severe, whether it be applied locally in the shape of a toxine or reflexly, in becoming an organic degeneration, not only of that centre or group of centres, but also of the nerve path or paths descending from them. Erb,[5] speaking of progressive muscular dystrophy, says there is a possibility that the disease, starting in a functional disturbance, might in the long run become associated with a coarse lesion of the spinal centres. He says there are many things about such a condition which agree well with this supposition. From this we may conclude that bacterial poisons act on either the peripheral or central nerve systems, producing in one case an organic lesion and in another only a functional depression. Now let us look at the rheumatoid symptoms due to such a condition of the nerve system. The principal and most difficult to explain is undoubtedly the muscular atrophy which occurs not only early in the disease, but is one of the most constant symptoms. The atrophy extends to the whole of a muscle and not only to that part which is in contact with the joint or distal to it, and it follows so closely on the first appearance of the joint troubles as to preclude the possibility of an extension of the inflammation from the joint to the nerves or muscles. Apart from true rheumatoid atrophy we have atrophy occurring as a consequence of a neuritis distinctly secondary in character and only seen in the later stages. Such a condition has been described by Sabourin,[6] Valtat,[7] Strümpell,[8] Duplay and Cazin,[9] and is of less interest than the true rheumatoidal atrophy, and can be easily distinguished from it as it presents all the characters of ordinary muscular atrophy in the reaction of degeneration and alteration in the muscle structure, &c. This is absent in the true form in which the extensors are principally affected, but not exclusively so. The selective character of the atrophy is sufficient proof that the changes cannot be set down to mere disease. How, then, do we account for it? We think it is due to an abnormal condition of the multipolar nerve cells of the anterior cornua.[10] It is reasonable to suppose that, given a soluble poison circulating in the blood, some areas in the central nerve system should be affected, and these all the more especially as they are in all probability predisposed to it by reflex irritation from the joints. That such an irritation does occur has been stated by many observers and has been even said to be sufficient to cause the atrophy itself (Paget, Vulpian,[11] Charcot,[12] and others). It has been argued that, assuming a derangement of the motor cells of the cord determined by the morbid impulses from the joint nerves, the influences from the motor cells will in all probability determine the alterations in the muscle nutrition. In the light of the discovery of the micro-organisms and of recent observations with regard to the action of toxines on the nerve system we may disregard this reflex irritation, except in so far as only to regard it as a predisposing cause. On turning again to the cells themselves we find, according to Ferrier,[13] that the cell-body, with its nucleus

[4] Annales de l'Institut Pasteur, February, 1895.

[5] Progressive Muscular Dystrophy.

[6] Thèse de Paris, 1873.

[7] Archives Générales, 1877.

[8] Münchener Medicinische Wochenschrift, 1888.

[9] Archives Générales, January, 1891.

[10] The path of motor innervation is composed of two portions: (*a*) the pyramidal cell with its dendritic processes and centrifugal or axis cylinder process, coursing along the pyramidal tract; and (*b*) the spinal multipolar cell with its processes and axis cylinder process, ending in the muscle fibre. It has been shown by Golgi's (Schäfer: Brain, vol. xvi., p. 147) method of staining that the pyramidal axis cylinders end in an arborescence which merely comes into contact with the spinal cell or interlaces with its dendritic processes, there being no actual continuity.

[11] Leçon sur l'Appareil Vaso-moteur, 1875.

[12] Maladies du Vieillard, second edition.

[13] Brit. Med. Jour., vol. ii., 1893.

is primarily concerned in the nutrition of the motor nerve and its correlated muscular fibre, while the dendritic processes serve to convey incitation and functional activity. He also states that lesion of these processes may cause paralysis with all the symptoms of a spinal paralysis, but with no muscular degeneration. If such a condition can exist might we not consider it possible, nay, probable, that by the action of a toxic body the cell's action might by itself be so lowered or held in abeyance that nutritional changes in the muscles would ensue without much disturbance of the conductive faculty of the processes, and also without any degeneration of the muscle beyond wasting? In progressive muscular atrophy we have a slowly progressive lesion of the ganglion cells, and their prolongations in the axis cylinders of the nerve fibres. Might we not, on a modified scale, have such symptoms if, instead of a complete destruction of these cells, we have only a depression of their function? In fact, such a condition must exist, as we cannot otherwise account for the atrophy either by reflex or direct toxic action. The cells' activity must be lowered. In one class of case, of which those mentioned by Dr. Spender[14] may be taken as typical examples, we must assume that the action on the cells has been so great as actually to give rise to a distinct lesion, and this, spreading upwards in the pyramidal tract, has finally come to affect the bulbar nuclei. Folli's[15] discovery of atrophy of the motor cells goes a long way to confirm this theory. What was probably only at first a depression of function due to the changes set up by the rheumatoid toxine had apparently in the long run become actual organic change. With regard to the selective site of the muscular atrophy, we find Dr. Ferrier[16] saying "It is not unreasonable to suppose that the degree of representation, and therefore the trophic strength, of the extensors in the anterior cornua is less than that of the flexors, while such extensors as have the most numerous connexions with the spinal segments would have a greater vital resistance than those whose segments are fewest." From this we may deduct that those muscles with the lowest trophic representation will be those which are first and most affected in any disease which lowers the vitality of the nerves and nerve centres. Duplay and Cazin[17] have suggested that it is due to the anatomical relationship between the nerves which supply the joints and those which supply the affected muscles. This does not explain it all, however, and Dr. Ferrier's explanations seem the more probable and the more easily intelligible, especially if we add that reflex impulses may possibly help in the selection.

It has been proved that certain toxines have the power of producing changes in the vaso-motor system and also in the trophic condition of the skin. It is thus that we account for the local sweatings and pigmentation. We know that normal pigment arises from a particular product of metabolism of the cutis, being formed both in the ordinary epithelial cells and in the connective tissue cells. These connective tissue pigment cells are the regulators of the metabolic process, as they consume the surplus pigment-forming substances. The abnormal pigmentation of rheumatoid arthritis is probably due to a local increase in the formation of the normal pigment consequent upon some abnormal trophic innervation and to a deficient consumption of the surplus by the connective tissue cells. The vaso-motor changes are in all probability due to the centre situated in the cells, in the intermedio-lateral tract being affected in a similar fashion to those in the anterior cornua. One of the chief points of interest is the tachycardia. Bezançon[18] states that tachycardia may in some cases be due to pressure on the vagus, but he suggests that more often it is due to the absorption of certain toxines. He cites the case of the bacillus tuberculosis and also of certain staphylococci, streptococci, &c., of the secondary purulent infection so common in phthisis. Bouchard obtained from tuberculin a substance to which he gave the name ectasine, which had the property of producing dilatation of the vessels. Toxines with similar powers have been obtained from the product of the bacillus pyocyaneus by Charrin and Gley, and from those of the staphylococcus aureus by Arloing. By acting as vaso-dilators these substances would tend to produce tachycardia, since the heart's action becomes more rapid as the peripheral friction diminishes. In other cases the toxines, by giving rise to a neuritis of the vagus, may cause it. Vierordt in a case of phthisis found such a neuritis as was evidenced by a great number of vagus fibres having undergone degeneration and atrophy. With regard to the local sweating, it is probably due to paresis caused by the toxines acting on the sudoriparous and vaso-motor centres of the bulb. Similar action is seen in influenza (Semmola[19]). It has been found by Hunter[20] that in all probability pernicious anæmia is caused by the presence of bacterial poisons, just as it has been found to occur from the presence of cadaveric poisons and analogous ferments. Such being the case, it requires little imagination to conceive that a similar process may occur in rheumatoid arthritis. These bacterial poisons would seem to act by a hæmolytic process which is specially limited in its actions to the portal blood.

[14] Brit. Med. Jour., 1893.
[15] Il Policlinico, December, 1894.
[16] Loc. cit.
[17] Loc. cit.
[18] Revue de Médecine, January, 1894.

DR. BLAXALL'S BACTERIOLOGICAL REPORT.

(From the Laboratories of the British Institute of Preventive Medicine.)

This investigation was undertaken at the request of Dr. Bannatyne of Bath, who stated that he with Dr. Wohlmann had arrived at the conclusion from the clinical aspect of cases suffering from rheumatoid arthritis that the disease was due to a micro-organism; and, further, that by microscopic examination of the synovial fluid from affected joints they had found an organism constant and distinct. This micro-organism they considered to be specific. Synovial fluid from affected joints was sent me from Bath. The fluid was aspirated with antiseptic and aseptic precautions, with such success that out of eighteen cases which have been submitted to me, only twice have I found it contaminated. My first attempts to stain organisms in the synovia and to obtain cultivations from it resulted in failure. I adopted the ordinary methods of bacteriological procedure, staining films of the synovial fluid for a few minutes with aniline dyes and inoculating serum tubes and all ordinary culture media, as well as making plate cultivations of nutrient agar-agar and gelatin, after Koch's method. But I was unable to observe any organisms in the microscopic specimens or to recognise any appearance of growth upon any of the culture media. I then varied the staining methods, leaving the specimens in the dyes for a prolonged time in the cold, applying heat, and using concentrated solutions. By these means organisms could be perceived in the specimens corresponding exactly to those described by Dr. Bannatyne and Dr. Wohlmann, and morphologically identical with those seen in their microscopic specimens. But their recognition was unsatisfactory owing to several causes. In the first place, it was evident that the organisms took up the stains with great difficulty and only by their prolonged action or by the application of heat, but these means resulted in a very dense colouration of the synovial film; secondly, they were decolourised with great ease, for attempts to decolourise the substratum left the organisms unstained. Again, the microbe being very minute, it was exceedingly difficult in heavily stained specimens to discriminate it from débris or from precipitate of the dye used. It was necessary then to find a method by which the organisms should be well stained, should retain the stain and yet allow the synovial film to be sufficiently decolourised, and one that should obviate all precipitation of the dye. I cannot claim to have attained this result, but after many trials I have adopted the following procedure as being most satisfactory. A thin film of synovial fluid drawn out between two cover-glasses is dried over the flame and fixed in the usual way by passing through the flame five or six times, as otherwise the organisms are apt to be washed out. The cover-glass is then immersed in dilute acetic acid for about two minutes, well washed with water and dried again, this second drying being to prevent the cover-glass sinking in the staining fluid. The stain which I have found most useful is aniline methylene blue. The cover-glass is placed specimen-side down on a watch-glassful of the stain and the whole placed in a moist chamber in the dark for from three to five days. It is then washed in gently running water for some hours, rinsed in distilled water, dried, and mounted in the usual way. More expeditious, though not giving such clear and well-defined specimens, are aniline gentian violet and carbolic fuchsine. This latter stain I have found it advantageous to dilute one-third with distilled water. From twelve to thirty-six hours is sufficient for these in a moist chamber. The cover-glasses are washed in running water in

[19] Trans. of the Académie de Médecine, 1891-92.
[20] Practitioner, 1890 and 1893, and Brit. Med. Jour., vol. ii., 1892.

the same way, then well rinsed with 30 per cent. alcohol, washed in distilled water, dried, and mounted. The acetic acid clears the synovial film, and allows the dye to penetrate more readily, the prolonged staining deeply colours the organisms, so that the washing process leaves them well stained, though the film is decolourised, and the moist chamber, by preventing evaporation of the dye, obviates the precipitate. Microscopic examination of the specimens reveals an organism possessing peculiar characteristics. At first sight it appears to be a diplococcus, the two cocci being distinctly stained, but separated by a clear unstained interval about equal in length to the diameter of either stained end. This interval I have never succeeded in staining. But careful observation will show, especially where the substratum is faintly coloured, that the intervening portion is nearly as broad as the diameter of either stained extremity, and that it has parallel contours. I therefore consider the organism to be a bacillus which exhibits very marked polar staining. The average length is 2 μ and the average breadth 0·6 μ, but this latter measurement varies greatly with the intensity of the staining. But the organism, as seen under the microscope, appears much smaller than these measurements would indicate, owing to the limited portions stained. The number of organisms met with in a cover-glass specimen of synovial fluid from a joint affected with rheumatoid arthritis varies greatly. Sometimes the field is crowded with them; at other times they are scattered and hard to find. These differences appear to follow very closely the acuteness or chronicity of the disease. The organisms are generally evenly distributed through the film, showing, however, a tendency to congregate around leucocytes. Their arrangement is always discrete. I have never seen chains or masses formed.

Though the staining methods mentioned above have given me the most satisfactory specimens, yet the organisms can be seen when stained for a much shorter time, especially with gentian violet, methyl violet, or carbolic fuchsine. But it is found that these stains if allowed to evaporate deposit upon the cover-glass a precipitate of dye which so closely resembles the organism that it is by no means easy to recognise them when but few are present in a preparation so obscured. For this reason I have quite discarded heating the stains, because after such a brief staining attempts to remove the precipitate by washing and the use of reagents bring about more or less completely the decolourisation of the organism, whereas after a longer contact with the stain the microbes are coloured more firmly and are less easily decolourised. But there is one exception to this statement in a method which I have devised and found useful. Impressed with the small size of the organism and the minute portion stained, it occurred to me that the protoplasm might take up dyes more readily if it came into contact with them while moist. With this in view I mixed a drop of synovial fluid with a few drops of the stain (aniline methylene blue being best) on a cover-glass and rubbed out with a platinum needle. The cover-glass, with the stain and synovial fluid together, was then dried slowly over a burner and when quite dry fixed by passing several times through the flame, then freely washed with water, dried, and mounted. In this way I obtained very fair results, the greater part of the stain being washed off, leaving the organisms well coloured. For rapid diagnosis this method is very useful. Treated by Gram's method the organism is almost completely decolourised. I have been able also to detect the organisms in the synovial fluid in the hanging-drop specimen, but this is far from easy unless they are present in large numbers. I have now stained and examined the synovial fluid from various joints from eighteen cases affected with rheumatoid arthritis, and in every one have observed the organism which I have described above, but in fluids from distended joints due to other causes, as chronic synovitis, gonorrhœal and tubercular affections, I have entirely failed to find them. (Fig. 1. Synovial fluid, stained gentian violet. × 900.)

Cultivation.—At first all attempts at cultivation, both aerobic and anaerobic, yielded apparently no result; but I imagined that this might be due in part to the small size of the organism—so that if it formed colonies they might be scarcely perceptible, and, judging from the scattered distribution in synovia, that the tendency to a free growth might be small—and in part to a slow development. Keeping these points in view I resolved to try it upon a large scale and in such a manner that any change in the medium might be easily detected. Into litre or half-litre flasks were put 250 c.c. of peptone beef-broth, filtered repeatedly until it presented a perfectly clear and bright appearance. Great care was taken over this to avoid the slightest obscuration. The flasks were sterilised and placed in an incubator kept at blood heat for several days, to prove their sterility and also to be sure that the fluid remained perfectly clear. If these conditions were fulfilled the flasks were carefully opened and a drop or two of synovial fluid from an affected joint allowed to enter. The flasks were then incubated at blood heat. Similar flasks, but *uninoculated*, were also incubated at the same time to serve as controls. I was fortunate enough to attain success with the first experiment. The first point noticed was that for three days the beef-broth remained perfectly clear, pointing strongly to the conclusion that the synovial fluid contained no ordinary organism. But from the fourth day and onward there could be seen floating in the clear fluid very minute particles, and these increasing gave rise to an appearance resembling "gold dust." This effect was enhanced by lightly shaking the flask. Sometimes the growth seems to stop at this "gold dust" stage, but at other times it may become slightly flocculent, recalling to mind the appearance of a commencing growth of tubercle bacilli in glycerine beef-broth. The beef-broth never becomes turbid, but always retains its bright appearance. The control flasks showed no such development. Microscopic examination of such a culture, stained as before, displays the organisms in considerable number; but it can be readily understood, from the delicate nature of the cultures and the imperfections of staining methods, that a too great reliance on stained specimens was not advisable, and that additional evidence would be helpful. Verification was obtained by making hanging-drop specimens, and this is the easiest method of demonstrating the presence of the organism. In the hanging-drop the microbe appears precisely as in the stained specimens, with two bright refractile ends and an intermediate part much less obvious. They may occur in zoogloea masses, or as discreet individuals hugging the edge of the drop. They are non-motile but have a marked oscillatory movement. I have been fortunate enough to see them undergo division in the hanging-drop specimen. The intervening portion lengthens out, the ends appearing to pull against one another energetically, the whole organism oscillating the while uneasily. The middle part lengthens out more and more, so that the organism appears to be almost twice its ordinary length, then suddenly the link snaps and the freed ends fly off in contrary directions and are lost amidst their fellows. This phenomenon helps, I think, to explain some variations in length frequently noticed in stained specimens from cultures. In these, some bacilli will be seen very short, the stained ends quite close together, with a minute unstained connecting link, very suggestive of a diplococcus. These I take to be quite young organisms. Some, however, are much longer, attaining a length of 3μ or possibly 4μ, the stained ends widely separated, and a clear, unstained sheath faintly visible with the highest powers. These I imagine to be the older forms soon about to divide. In these older forms, too, the staining is sometimes somewhat different. Instead of the stained portion being more or less spherical at the ends of the organism the coloured part is in the form of a conical cap, the base towards the centre of the bacillus, and spreading faintly down the edges of the sheath. These forms show best the claim of the organism to be considered a bacillus. It will be obvious, however, that it is very difficult to bring out these subtle differences in a photograph, and, indeed, the limited staining of the organism and its minuteness render the production of good photographs by no means easy. (Figs. 2 and 3. Fig. 2 shows a beef-broth culture, stained fuschin. × 1200.) If beef-broth cultures are inoculated on tubes of sloping nutrient agar-agar and incubated at blood heat, growth takes place in about three days and in a very characteristic manner. This growth is exceedingly delicate. It appears no more than as a fine transparent film, which under a lens can be seen to consist of minute colonies no larger than a pin point and perfectly transparent. To the naked eye it bears a very close resemblance to condensation water, though control tubes and the obvious tests show that this is not the case. It grows also on Löffler's serum, but here the growth is even more difficult to recognise owing perhaps to the opalescence of the medium. It occurs as minute points, least difficult to observe at the lower part of the tube, where the condensation water has washed off the cholesterin. Stained cover-glass specimens and hanging-drop specimens made from such cultures reveal

an organism identical morphologically with that described as present in the beef-broth cultures and synovial fluid. I have also grown the organism in milk, where it appears to flourish, but without causing curdling or precipitation of the casein. On nutrient gelatin, however, at 22° C. I have never succeeded in getting a growth, and in liquid gelatin, incubated at 37° C., there is no visible growth. Examination of the blood in cases affected with rheumatoid arthritis has also afforded me positive results of the presence of the organism. I have examined the blood taken near to an affected joint and also that from a distance, and in both have been able to detect the organism in microscopic specimens. Out of five specimens of blood submitted to me I have been successful in three, and these were the most severe cases. But further proof of the presence of the organism in the blood is the fact that twice I have been able to obtain cultures from it. The method was the same as previously described. The blood was inoculated into flasks of clear sterilised beef-broth and incubated at blood-heat temperature. Sub-cultures were also made from these flasks on to agar-agar and blood serum. The organism found was identical in every respect with that which grew from the synovial fluid and with that which was observed in the stained specimens. Some animal experiments have been made for which I am indebted to the Council of the Royal College of Surgeons of England and to Dr. G. Sims Woodhead. Two cubic centimetres of a beef-broth culture were injected subcutaneously into mice, guinea-pigs, and rabbits, but without a fatal result. There is some reason to think, however, that the cultures set up a disease in rabbits which affected the joints, but further experiments are necessary to arrive at the truth with regard to this matter.

As far as I am aware, only one organism has been previously associated with rheumatoid arthritis which it is necessary to discuss. This was described by Schüller.[21] He writes of a bacillus 2·6 μ long and 0·75–0·995 μ broad which exhibits polar staining. It is easily coloured by ordinary stains, especially carbolic fuchsin, but very easily decolourised. It is noteworthy that Schüller thinks it incumbent on him to point out the distinction between his organism and tubercle bacilli. It grows readily upon gelatin at 25° C. In 2–3–6 days small white grains or knobs appear. The gelatin is liquefied, and eventually the organism grows to such an extent that the whole mass becomes an opaque white. On agar-agar it grows as greyish-white flecks or films. It is obvious that the organism described by Schüller differs markedly from the one under discussion; in fact, the only points of resemblance are the polar staining and the easy decolourisation. It therefore appears to me to be indisputable that the organism of Schüller is not that which was discovered by Dr. Bannatyne and Dr. Wohlmann.

To sum up. 1. In the synovial fluid of eighteen cases of rheumatoid arthritis an organism has been demonstrated which is constant in its characteristics. 2. The organism is a minute bacillus exhibiting marked polar staining. It is difficult to stain and easily decolourised. 3. The organism can be grown in culture media and presents striking characteristics. In beef broth it gives the appearance of gold dust and on agar-agar and serum its growth is almost invisible. It does not grow on nutrient gelatin at ordinary temperature. 4. It is present in the blood in severe cases. 5. It has not been found in the synovial fluid from distended joints due to other causes. It should be added that it has been impossible to examine sections of the synovial membrane owing to the want of pathological specimens. In conclusion, I should like to record my thanks to Mr. Barnard for the care and skill he has expended on the photographs.

[21] Max Schüller: Untersuchungen über die Aetiologie der sogen chronisch Rheumatischen Gelenkentzündungen (Berliner Klinische Wochenschrift, Sept. 4th, 1893).

MEDICO-PSYCHOLOGICAL ASSOCIATION. — The spring meeting of the South-Western Division was held at Bailbrook House, Bath, on the 14th inst., the President being in the chair. There was a large attendance of members and several important resolutions were passed. The report of the Committee on Criminal Responsibility was ordered to lie on the table. The discussion on the "nursing staff" was taken part in by several members. Dr. Stewart contributed a useful note on Section 38 of the Lunacy Act, 1890. The members afterwards dined together at the Grand Pump Room Hotel.

COLOUR VISION.[1]

BY W. G. LAWS, M.B. EDIN., F.R.C.S. ENG.,
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THE speaker pointed out that the subject lay in the debatable region between mental states and physical processes, where so many interesting problems remained unsolved. The eye was the end organ which brought us into direct relation with the ether, that ultimate form of matter as to which it became possible to doubt whether it was material at all, and which probably entered closely into the processes of thought itself. Before speaking of the theories of colour vision it might be asked what was there in colour vision that so many scientific minds had felt required explanation. It would be noticed that every theory contained the same fundamental idea that there must be a certain number of colours, varying with different observers, but always few, which were to be regarded as pure or simple colours, all others being considered as compounds or mixtures of these. On looking at the perfectly continuous series of colours which we see in the spectrum there seemed to be no obvious physical reason for this distinction. It was, indeed, a psychological rather than a physical one. We had an innate disinclination to conceive of an infinite number of different causes for the infinite number of different sensations of which we were conscious; it was a principle deeply rooted in our reason, expressed long ago by William of Occam, whose famous Razor, "*Entia non sunt multiplicanda*," was employed by us nowadays as constantly in the solution of physical problems as it was by the Invincible Doctor in the division of the sophistries of Rationalism. Mr. Laws hoped to show, however, in relation to one at least of the theories that it was possible to cut too close with it. Many theories of colour vision had been proposed during the last 200 years, some of them interesting and original, but two only had gained any general acceptance and to these the discussion would be confined. He then described the theory of Young as it was published in 1801, its modification by Helmholtz more than half a century later, with his proof of the mathematical possibility of reducing all our colour sensations to three. Hering's theory was next described, mainly in extracts from his original papers, Mr. Laws considering that none of the published accounts of it in this country did justice to the simple conception, the logical development, and lucid expression of the theory as stated by Hering himself. What we might fairly demand of a theory of colour vision was that it should give a reasonable explanation of our everyday experience with regard to our sensations, and also should furnish us with a trustworthy guide when the conditions were modified by pathological processes. As it was impossible for him to discuss all the phenomena in the light of these theories he would make the appeal only to an experiment made for us by nature, namely, the condition of congenital colour-blindness. Of this Mr. Laws considered that practically only one type existed, admirably described in Dr. Pole's account of his own case; that other types had been described was due to the attempt to make the facts of observation fit with an erroneous theory; the rare cases of monocular colour-blindness were quoted as highly conclusive on this point; finally, the verification was at the hand of each one in the colour-blind zone of his own retina. He summed up the evidence from colour-blindness as showing that whenever there is a diminution of the number of our colour-perceptions it is not *one* that disappears, but always a *pair* of complementary colours. Here was the reason that the trichromic theory of Young failed—it was not in harmony with the essentially paired character of our colour sensations. Further examples of this character were given in the phenomena of successive and simultaneous contrast, and it was pointed out that we have only to look at a colour in order to call up the sensation of another as definite and (under proper conditions) as brilliant as the former, and having the constant psychical character that it is the greatest possible contrast to the former that our minds can conceive. The physical relationship of the two was such that if the spectrum be divided into two halves, and the more refrangible be superposed on the less refrangible half, then colour by colour and shade by shade the one will neutralise the other and a colourless band result. The

[1] Abstract of a paper read before the Nottingham Medico-Chirurgical Society on April 15th, 1896.