Remarks ON ACUTE ARTHRITIS OF DOUBTFUL ORIGIN.*

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WE must all have met with cases which, at first assumed to be rheumatic fever, have failed to react to salicylates, and yet, as shown by the sequel, were not pyæmic, gonococcal, or due to any other obvious infection. It is in connexion with these cases of acute arthritis of doubtful origin that I propose to speak. But as a preliminary consideration it may be worth while to refer briefly to the value of a reaction to salicylates as evidence of true rheumatism. There is no doubt that one of the main clinical characters of acute rheumatism or rheumatic fever is that it reacts to salicylates; a case which reacts permanently, as regards fever and articular pain and effusion, may for practical purposes be regarded as one of rheumatic fever. But cases occur, particularly in young women, in which full salicylate treatment fails to produce any effect for two or more days, so that the question arises whether the fever and joint disease are not of a more severe nature than was thought, and yet persistence in treatment is eventually followed by a complete reaction and recovery. The delayed reaction has in some instances appeared to me to depend on constipation.

On the other hand, vigorous salicylate treatment may produce a reaction, more especially as regards the fever, in cases of arthritis due to other causes. The fall of temperature, which, no doubt, is largely due to the profuse perspiration induced by the salicylates, is, it is important to remember, temporary. Further, the remarkable power of aspirin in relieving pains due to such widely different causes sufficiently proves that it is unsafe to argue that everything relieved by salicylates is necessarily a manifestation of rheumatism.

ARTHRITIS OF DOUBTFUL ORIGIN (a) COMPLICATING OR (b) DIRECTLY SUPERVENING ON RHEUMATIC FEVER.

In these cases, which are not very rare, the sequence of events is somewhat as follows: (a) An attack of multiple arthritis clears up under salicylates except in one or two joints which progress in spite of treatment, and at first suggest suppuration, which, however, does not occur, and eventually the joint or joints present some fibrous ankylosis. When seen for the first time in the later stage of fibrous ankylosis these cases seem incompatible with the history that the primary affection was rheumatic fever, as it is generally agreed that rheumatic fever never induces fibrous ankylosis. But when the progress of the disease is watched from the outset it must be admitted that there is no reason, except the unusual sequels, to doubt that the primary disease was rheumatic fever. (b) In other cases the primary attack yields satisfactorily to salicylates, and after an interval is followed by what at first appears to be a relapse, but the arthritis does not subside under salicylates, and signs suggesting suppuration, and subsequently fibrous ankylosis, follow. The explanation of these cases leaves much room for discussion. The most obvious view is that a primary rheumatic synovitis becomes complicated by a secondary infection. Thus a patient with rheumatic fever who has oral sepsis may recover from the rheumatic attack and subsequently suffer from arthritis due to infection derived from the mouth. I have long considered that patients with oral sepsis are specially prone to relapses of rheumatic fever. In the following case rheumatic fever was followed after an interval of quiescence by inflammation of a joint not affected in the primary attack.

A woman, aged 27 years, was admitted to St. George's Hospital with pain and swelling of fourteen days' duration in both shoulders, elbows, shins, and the back. She had tonsillitis and several decayed teeth. On full salicylate treatment she rapidly

recovered, and was about to leave the hospital, when she was attacked with pain and swelling of the left wrist. This was at first regarded as a relapse of rheumatic fever, but salicylates entirely failed to relieve the pain and swelling. The joint became more swollen, the skin over it red, and the movements very greatly restricted. With local treatment—an icebag followed by a Watson's splint—the inflammation subsided, and subsequently passive manipulations and massage restored the power of movement. Dr. E. L. Hunt found that the blood serum agglutinated a laboratory culture of *Bacillus coli* in a dilution of 1 in 50 in one hour.

In the following case it is possible that there was a double infection at work, first that of rheumatic fever, later that of syphilis.

A married woman, a barmaid, was admitted to St. George's Hospital with what was thought to be acute rheumatism, and was treated with salicylates; the joint pains and fever disappeared, but one ankle and one elbow became painful and red, and suppuration was so far suspected that arthrotomy was discussed, though not carried out. The movements of these joints became restricted, and the adhesions in the ankle were broken down under an anaesthetic. Some months later a cutaneous syphilide appeared and iodide of potassium was given, with the result that the movement of the elbow greatly improved. Was this a case in which syphilitic arthritis supervened on rheumatic synovitis?

On the other hand, it might be argued that in group (a) the joint or joints persistently affected are the primary site of an infection which gives rise to a transient and secondary toxic arthritis in the other joints, and that the toxic joint affections, being essentially transient, subside while salicylates are being taken, though not because of the influence of this treatment.

A man, aged 50, was admitted under my care with what appeared to be multiple rheumatic arthritis. He had been treated at home with salicylates for a month without any improvement. In the hospital he was again put under salicylates, and the joints improved with the exception of one knee, which steadily got worse and was thought to be suppurating. Puncture failed to bring away any pus, but from the few drops of blood removed a coliform bacillus was cultivated; the patient was then treated with a vaccine, and slowly recovered.

OTHER ARTHRITIDES OF DOUBTFUL ORIGIN.

Acute non-rheumatic arthritis may conveniently be divided into two groups: (1) Infective, in which micro-organisms are present in the affected joints; (2) toxic, in which the joints are sterile, and in which the inflammation is presumed to be due to poisons brought from some other part of the body.

I.—Infective Arthritis.

Besides the recognized forms of infective arthritis, such as gonococcal, pneumococcal, streptococcal, and staphylococcal, there are others which are less often seen, such as that due to the *Diplococcus intracellularis* of cerebrospinal meningitis. A rare form of infective arthritis is that due to *B. coli* or allied organisms. I have seen two cases in which coliform organisms were obtained from the joints; in one of these, in which the articular effusion was purulent, the same organism was obtained in a blood culture.¹ Suppurative arthritis due to the colon bacillus has been observed as a result of appendicitis (Sevestre and Thomas²), and the *B. coli* has been found in two cases of arthritis occurring in dysentery (Salle³). As an exceptional occurrence arthritis is seen in some common acute infective diseases, such as measles, mumps, and diphtheria; this arthritis is so rare that it seems probable that some added infection, rather than that responsible for the primary disease, has given rise to the joint affection. It is less rare in enteric fever.

It is rather remarkable that influenza, which so commonly gives rise to arthralgia and is so prolific in complications and sequels, has very rarely been proved to give rise to arthritis. It is true that arthritis complicates or follows conditions called influenza; G. A. Wright⁴ has collected seven cases in point, but bacteriological proof that the joint affections were due to the influenza bacillus was not provided. Dudgeon and Adams⁵ however, have recorded the case of a child, aged 10 months, with multiple arthritis and meningitis; pure cultures of *B. influenzae* were obtained from all the sites of infection except the lungs. Thursfield,⁶ who quotes Slawky's case of pyæmia and purulent arthritis due to *B. influenzae*, suggests that Dudgeon and Adams's case was due to Cohen's bacillus or the organism which is found in cases of so-called influenzal meningitis and resembles

* The first Hunterian Society's Lecture, delivered on October 12th, 1910.

B. influenzae morphologically and culturally, but can be differentiated from it by its pathogenetic effects upon rabbits and guinea-pigs.

It is noteworthy that in pyaemia, apart from purulent arthritis, the joints may become painful and swollen without anything further taking place; this synovitis, for such it appeared to be in the few joints I have examined after death, may pass off during life. Possibly the synovitis is due to small quantities of micro-organisms in the synovial membrane, which do not manage to multiply sufficiently to set up suppuration. Another possibility is that the synovitis is toxic and not due to microbic invasion of the articular tissues.

An example of pyaemic arthritis, fortunately somewhat rare, is that seen in cases of acute epiphysitis in children; the condition is exactly the same as acute infective periostitis or acute necrosis of the long bones, except that instead of attacking the shafts of the long bones it falls on their epiphyses, and thus spreads into the adjacent joint. The mention of acute periostitis reminds me of a case in which acute necrosis of both fibulae near the ankle-joint and a temporary reaction to salicylates led me for a time to make the mistake of regarding the disease as rheumatic fever.

Perhaps this is the best place to mention cases of multiple arthritis which do not react to salicylates but respond well to injections of polyvalent antistreptococcal serum. In a case under my care reported by my house physician, Dr. H. Robinson,⁷ there was multiple arthritis with fever which went on for a month in spite of full salicylate treatment. The state of the joints did not justify aspiration so there is no proof as to the exact cause of the arthritis, but the rapid improvement after injections of polyvalent antistreptococcal serum strongly suggests that the condition was due to streptococci.

Acute synovitis in generalized *miliary tuberculosis* must be extremely rare.

A man aged 52 was admitted to St. George's Hospital with a temperature of 103° F., pain and swelling in the wrists, knees, and ankles, and delirium. He was at first treated as a case of rheumatic fever and given salicylates freely, with a temporary fall of temperature. The temperature, however, rapidly rose, and remained between 101° and 105° F. until his death, which occurred five days after his admission to the hospital. After death he was found to have generalized miliary tuberculosis. The left knee-joint contained an excess of fluid, and the synovial membrane showed petechial spots; unfortunately no bacterial examination of the synovial fluid or of the synovial membrane was made.⁸ Poynton⁹ has recorded the case of a boy aged 5 years, with tuberculous meningitis and acute tuberculous arthritis of the left knee, the synovial membrane of which was swollen. It does not appear that the arthritis was proved to be tuberculous. Dr. S. J. Ross of Bedford has given me the details of a case of acute arthritis of the knee-joint in a man aged 21, which came on three weeks before death from generalized miliary tuberculosis. Clear fluid aspirated from the joint was sterile on various culture media.

Although none of these cases have been proved to be due to an eruption of miliary tubercles in the synovial membrane, this would seem the most probable explanation.

Reference may be made here to a different form of arthritis supposed to be connected with tuberculosis; by the term "*tuberculous pseudo-rheumatism*" French writers—Poncet,¹⁰ Bezançon,¹¹ Griffon—describe an acute synovitis resembling that of rheumatic fever, which does not react to salicylates and may eventually go on to ankylosis or to a typical tuberculous joint. There are two views as to the relation of tuberculosis to this form of joint affection: (a) That toxins absorbed from tuberculous foci in other parts of the body are carried to the joints, and there induce lesions; in other words, that it is a toxic arthritis. (b) That tubercle bacilli are present in the articular tissues. On this hypothesis of an infective arthritis, the resulting condition would be regarded as comparable to acute tuberculous pleurisy with effusion. By examination of the fluid in a case of tuberculous pseudo-rheumatism, Griffon¹² found that the cytological formula was the same as in the fluid of tuberculous pleurisy—namely, a great predominance of lymphocytes, and that injection of the fluid into guinea-pigs induced experimental tuberculosis.

Still's disease,¹³ or the special form of chronic arthritis with enlargement of the spleen and lymphatic glands, has been thought to be a tuberculous manifestation, and to represent in children the tuberculous pseudo-rheumatism of adults. But it is not yet decided whether it is due to an actual invasion of the joints by tubercle bacilli, as was

suggested by a local arthritic as well as a general reaction to tuberculin in Edsall's case,¹⁴ or whether it is a toxic result, as is suggested by the occurrence of a general reaction only to tuberculin injections in Parkes Weber's case.¹⁵ An obvious difference between tuberculous pseudo-rheumatism of adults and Still's disease is the relatively acute nature of the former and the chronicity of the latter. This may perhaps be paralleled by the more acute course of tuberculous meningitis in children than in adults. It is also interesting to compare the hyperplastic tuberculosis of the intestines, which is so different from ordinary intestinal tuberculosis, with Still's disease, which is equally unlike tuberculous arthritis. It is conceivable that the changes in Still's disease are due to a mixed infection, of a low grade of virulence, of tuberculosis and some other micro organism.

II.—Toxic Arthritis.

The first point to establish is that such a condition really occurs. In support of its existence we can point not only to gout, but to the occurrence of articular pain, and in a few cases of effusion, after the subcutaneous injection of antitoxic serums. It has been mainly noted after the use of antidiphtheritic serum. McClure¹⁶ points out that, whilst this is rare in patients confined to bed, it is common in patients who, having had prophylactic injections, are up and about. He also refers to its occurrence after injections of Yersin's anti-plague serum. The pain of this toxic form of synovitis is not relieved by salicylates.

It should, however, be borne in mind that the deduction that a given case of joint disease is toxic rather than infective, because the fluid aspirated from the joint is sterile, may be fallacious, for the micro-organisms may be in the inflamed serous membrane, or be so intimately connected with it that they are not obvious in the fluid. This is fully recognized as regards the effusion of acute tuberculous pleurisy, and may well be true in the rare cases of acute arthritis in generalized tuberculosis referred to above.

As is well known, two forms of arthritis may complicate scarlet fever: (a) The suppurative form due to pyaemic infection, which does not concern us here; and (b) the form usually called rheumatic. With regard to the latter, McClure, from an analysis of 170 cases, disagrees with the general opinion (Osler,¹⁷ Garrod,¹⁸ Caiger¹⁹) that the joint affection is rheumatic and is relieved by salicylates. He considers it toxic, and supports this on the negative results of blood cultures and cultures from the joints of 30 of his cases. In its toxic origin he compares it with the arthritis due to serum disease.

Intermittent hydrarthrosis, in which attacks of pain and swelling occur so regularly that they can be accurately foretold is a rare condition, but is of special interest in that the obscurity of its pathogeny has led Garrod²⁰ to formulate the notion of articular erythemas. There is much that is attractive in the view that intermittent hydrarthrosis, which has occurred in patients who have had angioneurotic oedema, and in others who have had urticaria, is an affection of the synovial membrane analogous to a cutaneous erythema. As skin eruptions, and especially the erythemas, are so commonly due to toxæmia, it is tempting to assume that the toxins which commonly induce cutaneous erythema may, when the synovial membranes are a place of diminished resistance, give rise to congestion and effusion.

Here we may recall the association between arthritic manifestations on the one hand, and purpura and other skin eruptions, such as urticaria and erythema nodosum, on the other hand. Originally the presence of the arthritic lesions was given undue prominence and was regarded as evidence that the whole syndrome was essentially rheumatic fever; this is shown by the old names *peliosis rheumatica* (Schönlein's disease) and *purpura rheumatica*. Doubt has been thrown on this conclusion. Osler's²¹ description of the erythema exudativum multiforme group, which includes cutaneous, arthritic, visceral, and cardiac lesions, was perhaps the first step in this direction; and more recently Pratt,²² after examining all the evidence, cannot find any reason to believe that the arthritis of purpura is rheumatic in origin.

The characters of toxic arthritis are that the manifestations are more transient and less severe than in

infective arthritis; that pus is not produced, and that the inflammation is apt to flit from joint to joint.

Arthritis associated with Lesions of the Alimentary Canal.—In some rare instances there may be evidence that a micro-organism has been absorbed from the alimentary canal and carried to the joints, so that an infective arthritis is set up, as in the cases of dysentery in which a coliform organism has been isolated from the joints (Salle). Apart from these exceptional cases the arthritis associated with lesions of the alimentary canal may, perhaps, be assumed to be toxic and due to the action of poisons, usually of microbic origin, absorbed from the alimentary tract. Oral sepsis is well known to be an antecedent in some cases of a disease closely resembling, and often said to be, rheumatoid arthritis; the joint changes are usually chronic rather than acute. But occasionally attacks of acute arthritis are seen in patients who have pyorrhoea alveolaris or suppuration draining into the mouth. I have seen recovery follow removal of such an infective focus. Acute arthritis in association with the common disorders and lesions of the stomach and intestines is extremely rare. According to Salle,⁸ dysentery is accompanied by some degree of arthritis in about 4 per cent. of the cases. Ulceration of the rectum has in some instances been noted to be associated with acute arthritis, which has been observed to disappear when the bowel condition was cured (Wallis²³).

Considerable interest attaches to the association of appendicitis with arthritis, for it has been interpreted in two different ways: it has been thought that the appendicitis is a manifestation of rheumatism (Grant²⁴), and conversely that the joint manifestations are secondary to absorption from an inflamed vermiform appendix. The association is undoubtedly rare, but it is worth bearing in mind.

Similarly there is considerable scope for discussion as to the relation of the association of arthritis with the various forms of colitis. The French school regard mucous colitis as a manifestation of the arthritic diathesis, on the grounds that the subjects of mucous colitis have a hereditary or personal history of joint affections. On the other hand, arthritic lesions may follow in the wake of colitis, and may be explained as due to the absorption of intestinal toxins. This arthritis is commonly chronic, an acute form is rare. I have seen two cases in which acute arthritis was associated with colitis, but in both instances the two conditions were probably independent of each other and due to some common infection. Both began with fever, at first thought to be influenza.

In one, a woman aged 50, widespread peripheral neuritis was first observed, then oedema of the legs, and then arthritis and severe mucous colitis with the passage of intestinal sand. Recovery was very slow, the movements of the joints being much impaired for more than a year after the other symptoms had disappeared.

In the other case, a man aged 32, sore throat and multiple arthritis first appeared, accompanied by constipation; this was followed by diarrhoea and the passage of blood and mucus from the bowels. About a week later a large round worm was discharged from the bowel. After a long convalescence he recovered completely.

In conclusion, acute arthritis may be a manifestation of various diseases; but whilst some fevers are so constantly characterized by obvious cutaneous changes as to be grouped together as the exanthemata, the occurrence of arthritic changes are less constant in well-recognized diseases. I do not know if it has ever been suggested from a teleological point of view that the object of cutaneous rashes is to give warning that the individual is infectious; but the same spirit of final causes might urge that the reason why certain diseases, such as acute rheumatism and in some instances scarlet fever, affect the joints is that, by limiting movement, rest for the heart may be ensured. Teleological explanations though attractive are dangerous, and this one will not stand much criticism.

The other point on which I wish to insist is that a weakness in resistance on the part of the joints, whether inherited or acquired, may determine inflammation in the joints in certain persons when attacked by an infection or disease which in ordinary persons is not characterized by arthritic manifestations. This probably accounts for the rare form of arthritis exceptionally seen in hemiplegia and paraplegia.

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EXPERIMENT AND OBSERVATION IN MEDICINE.*

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IN selecting a subject for the presidential address, it is sometimes the practice to take one definite subject and to follow it out fully, but in other cases a retrospective view is taken, recalling some points of interest that have occurred in the president's own career, or a general survey of the progress of medicine or some branch thereof. It is my intention to take the latter line, and to put in order some of the reflections that have from time to time engaged my attention.

When we compare the advances made in the strict sciences with those made in medicine, we must admit that, brilliant as are the latter, they cannot compare with those of the pure sciences. We have to remember that medicine is not only a science but also an art, and it is with the latter that most of us are chiefly concerned, and art is long. The laboratory worker is concerned with science, but the clinician is almost wholly concerned with the art or practice of medicine. Much of this distinction in results is due to the nature of the material we deal with. The personal equation of the patient is so variable, there are so many difficulties in the way of making adequate controls. The human factor is a variable and not a constant, and so the equation never works out accurately.

"Science is measurement," but measurement with the accuracy of a chemical balance or a Kelvin electrometer is impossible to apply to clinical methods. We can, it is true, count pulses and respirations, and record temperature and weight, and these observations are very useful. But other measurements, such as sphygmographs and haemomanometers, have many sources of error, and the error of experiment bears such a large proportion to the actual measurement as to render the latter of dubious value.

And our observation, as a rule, does not take the form of measurement, but of signs that have not an absolute value, but only a relative one. A resonant note in one person would be a dull one in another. The note elicited over the lung of a thick-set, muscular, or fat subject would, if heard over the lung of a thin patient, suggest disease. There is a great variability in the standard of resonance in different patients, and for each patient it is necessary to have a standard of normal resonance. I believe that in the early stages of phthisis, where the signs at each apex are exactly the same, there is a danger of overlooking the signs, owing to our habit of comparing the resonance of one apex with the other, instead of relying on a standard of absolute resonance.

In all scientific operations the element of control is largely represented. Two substances of exactly the same composition, weight, and appearance can be placed side by side, one experimented on and the other retained as control, and the two can be compared at every stage. This can be done in testing urine and laboratory work, but in treating patients it is very difficult. The scientific method of study would be to have two patients exactly

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