REMARKS ON ARTHRITIC GOUT.

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FROM a clinical point of view we may usefully divide the cases in which gout appears in connection with the joints into three classes.

1. The acute attack of regular gout. A description of this, based on that of Sydenham, may be found in every treatise on the practice of medicine, and does not therefore need to be reproduced here.

2. Chronic gout—possibly a sequela of an acute one, with much deposit of urates in a solid or semiliquid state. In this, with more deformity, there is much less pain and tenderness. Though these, with redness and superficial swelling, may from time to time be superadded with an increase of deposit within the joint.

3. Pains referred to the joints of a more or less fugitive character or tenderness felt, chiefly on use, which latter may, if excessive, be followed by increase of pain and even some redness and swelling; or even an attack of No. 1.

The current explanation of these phenomena is that there is an excess of uric acid in the blood. This excess is variously explained. First, as being due to excessive formation, or, secondly, as being due to deficient excretion, or, thirdly, as being due to storage within some organ—for example, liver or spleen—of uric acid. This, it is alleged, is, from causes we need not stay to inquire into, suddenly released and poured into the blood, which then contains an excess. It may be that two or all of these causes may be combined.

However this may be, we find therein no explanation of why the uric acid should pounce upon a joint. And, if possible, less why this joint should be the great toe, as it is in a vast majority of first attacks. Various explanations have been offered of this curious fact. The latest authority on gout, Dr. W. Ewart, reviewing these explanations in his excellent treatise,¹ says: "None of the alleged reasons are satisfactory, and the question remains one for speculation."

In a disease which has been so long and so attentively studied by physicians of the greatest eminence, it might seem improbable that any of its clinical features had escaped recognition. Yet some years ago I had the temerity to assert that such was the case.² It is a matter of much satisfaction to me to find that Dr. Ewart has been able to confirm the accuracy of these observations. He says: "The facts observed by Sir W. Wade, and confirmed by others and by the writer, possess great theoretical importance." Let me proceed to summarise them.

An acute attack of gout in a great toe will in due course begin to subside. The pain and tenderness, and swelling and redness, will be less. If at this epoch the toe be touched it will be found that, although the redness and swelling have lessened equally all over the joint, this is not the case with the tenderness. Some spots will be found which are not in the least tender, others where the tenderness is intense. Either then or subsequently it will be found that this tenderness is linear. It extends in a narrow line from the base of the great toe slantingly across the foot to the outer side, and may reach as far as the ankle. On either side of this narrow line tenderness there is none. This line is the site of a nerve trunk, which is distributed to the periphery of the great toe. If the covering of the first phalanx is sufficiently free from tenderness to permit it to be grasped it will be found that the joint may be moved without giving any pain. But care must be taken not to induce pain by stretching the nerve above mentioned. If the first phalanx is still too tender, the second may be seized and the tarso-metatarsal joint tested.

A similar experiment may be made with the thumb when that is the seat of the disease, and very often at an earlier stage of an attack. At whatever stage in either toe or thumb it may be made, it will almost always be found that the

tenderness—that is, the pain elicited by movement—is in the soft parts and not in the joint. To return to the toe. Tenderness will be found in the sole in a line running nearly parallel to the inner margin of the foot. Here is situated a nerve trunk, distributed to the great toe-joint. Tenderness will also be found in two nerves running, one near the outer and the other near the inner margin of the under side of the great toe; and this before reaching the joint, over the joint, and probably also beyond the joint.

In cases of Class No. 3 we find similar tenderness, in some one or other of these nerves perhaps constant or perhaps inconstant. The same thing will be found in the wrist, hand, and fingers, and it is needless to enlarge further upon it.

What is this nerve condition? Why does it arise? And what is its connection with the arthritis? The occurrence of neuritis in gouty persons has long been known. Dr. Buzzard points out in his interesting Harveian Lectures³ that in neuritis "sometimes the motor, at other times the sensory, and perhaps, on the whole, least commonly the vasomotor fibres bear the brunt of the attack, with a corresponding contrast in the symptoms. To gain a true idea of the frequency of neuritis it is necessary to remember this fact, and we shall otherwise be liable to overlook the true character of affections because they do not display all the characters of a typical neuritis" (p. 21). The context shows that Dr. Buzzard includes the trophic influence of nerves under the head of "vasomotor."

Is the nerve affection in gout a neuritis? Certainly in many instances it may well be assumed to be, but in others it bears more resemblance to neuralgia. For example, a gouty person walking quietly, perhaps about his room, is seized suddenly with intense pain about the ankle, he cannot move the foot; but in a few minutes the pain may have entirely ceased and he can walk comfortably. This is by no means uncommon, and has happened to myself several times. The transient, momentary pains of various parts are well known to gouty persons. It was these considerations which led me to write of "Gout as a Peripheral Neurosis," and not as a peripheral "neuritis." It is not easy to get opportunities of examining *post mortem* the changes undergone by the nerves in gout; but till this has been done it is impossible to say whether they are of an inflammatory nature or not, still less whether the inflammation affects one or more of the various layers of connective tissue, or the primitive sheath, or the medullary sheath, or the axis cylinder, or the lymphatic spaces, and, if more than one of these, in what order they are attacked.

Why does this arise? Probably there are two factors. First, injury. This may be of a very slight character, the pressure on the nerves of the foot in walking, the use of the thumb in writing, which has occurred to me twice whilst writing this paper. More severe injury. A gentleman, who had had repeated attacks of gout, whilst walking about Naples sprained his ankle and was immediately laid up by gout in that ankle, then in the other ankle, and in a few days with it in both knees. The whole attack lasted about six weeks. Whilst no doubt an acute attack of gout in one joint will often clear up the system and remove previous ill-health, on the other hand, as in this case, it is often the precursor of attacks in other joints, and seems not to remove, but to start, a state of goutiness.

The second factor is a something in the system, which enfeebles the nerves and prevents those of the gouty man resisting influences which non-gouty people, or, indeed, he himself when free from goutiness can, and do, encounter without any bad results. The equilibrium of the nerves is unstable. We can scarcely doubt that there is some toxic agent in the blood, and it is probable that some persons inherit such instability, or they may only inherit an instability of some organ which ought to prevent the formation of the toxic agent, or of one which should favour its excretion. It is quite easy to conceive that some persons inherit all three weaknesses. Inasmuch as nerves depend for their integrity upon the nerve cells from which they originate, it is conceivable that in gout the primary fault may be in these nerve cells. I should not refer to this but for the fact that some important authorities⁴ regard gout as having its *primum mobile* in some nervous centre. Till this view receives more definite support than it can at present command, let us recognise

and appreciate that which we can feel and handle, namely, the peripheral neurosis.

The third question is, What is the connection of this neurosis with the arthritis? Let me recall some of the facts. Pains about joints may precede acute gout. These pains can be demonstrated to be in nerves and not in joint. Pains, redness, and swelling round a joint which is intact—that is, not painful on being moved; best seen in thumb. Pain, redness, and swelling, with tender nerves, remaining after joint has ceased to be tender; best seen in great toe. Without disputing that the joint may have been tender, it is quite impossible to prove it. Dr. Ewart says: "*The extent of the arthritis associated with the periarticular swelling is matter of doubt.*" Sir. W. Wade's observations go far towards proving that there is much less arthritis than had hitherto been supposed—at any rate, that the *pain and tenderness* have not their seat inside, but *outside* the joint, and apparently in the nerves themselves." (Page 319. The italics are Dr. Ewart's.)

The patient's opinion is valueless in this respect; for a patient will refer the pain to the joint, when it can be demonstrated by proper examination that it is not there. All this goes to show that the essential element of the attack is to be looked for in the local nerves. But it is answered, and truly, Many years after a single attack, a uratic deposit may be found in a joint. If the attack is due to the deposit, how is it that the joint recovers before the deposit has been removed? A joint many times attacked may be found after death free from any deposit. It may have been absorbed. True; but it equally may have never been there.

The assumption that the attack is due to uratic deposit leaves unexplained why it is deposited. The neurotic theory, if it does nothing more, offers an explanation. The current view is curiously paradoxical. In an acute attack the deposit is so small that the joint quickly recovers. Yet it is acutely painful. In many chronic and subacute attacks the deposit is very copious, whereas the pain and tenderness are very small. This, then, is the paradox. In a painful disease which depends upon the deposit of urates, the greater the deposit the less the pain. It would seem that so long as the nerve is in a condition to become painful, it does not promote—perhaps retards—the deposit of urates. When by some further, at present unknown, changes it has lost the faculty of becoming painful, it does not retard, perhaps accelerates, such deposition. The inference to be drawn from all these facts is, I submit, as follows. The neurosis is the primary and essential element. If a sensory nerve is attacked we get pain and tenderness, if a vasomotor one we get redness and swelling; if the nutritive nerve of a joint, we get changes in the joint, one result of which may be a deposit of urates. I submit from this that this theory, more completely than any other, brings into line the various manifestations of gout. But it may be asked how it is that one toxin (uric acid) affects now an external, now an internal, sensory nerve; now a motor, now a vasomotor, now a trophic nerve, now an excretory one. This raises an important question, on which Dr. Ewart says (p. 143), "We still hesitate, then, to admit, without further investigation, that gout is primarily dependent upon uric acid as a cause, or that uric acid necessarily exerts any exclusive influence on the production of the phenomena of goutiness." Dr. Ewart's hesitation is shared by many. It is enhanced in my mind by the fact that different toxins have an elective affinity for different nerve tracts. Conversely we perhaps may infer that affections of different nerve tracts imply different toxins. That such may be the case in gout receives strong support from the ingenious and laborious researches of Dr. Haig.⁵ This uncompromising advocate of the uric acid theory claims to have proved that other bodies chemically allied to, but not identical with, uric acid resemble it in their action upon the human body. This, then, is a matter which, like the state of the local nerves, deserves a much more critical investigation than either have as yet received.

REFERENCES.

- ¹ *Gout and Goutiness and their Treatment.*
- ² *Gout as a Peripheral Neurosis.*
- ³ *On some Forms of Paralysis from Peripheral Neuritis of Gouty, Alcoholic, Diphtheritic, and other Origin.*
- ⁴ Sir Dyce Duckworth's *Treatise on Gout.*
- ⁵ *Uric Acid as a Factor in the Causation of Disease.*

Of 19 persons on whom the degree of Doctor of Medicine was conferred by the University of Geneva during 1896, no fewer than 7 were women.

ANTIPNEUMOCOCCIC SERUM.

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In the year 1891 the researches of G. and F. Klemperer, Bonome, Foà and Carbone, Emmerich and Fowitzky, proved that the blood serum of rabbits immunised to the pneumococcus possessed the property of protecting other rabbits against infection with this micro-organism.

G. and F. Klemperer, Foà and Carbone, Foà and Scabia, and Janson have since treated cases of pneumonia in the human subject with the serum of immunised rabbits; while Andeoud has used for the same purpose the blood serum of patients convalescent from pneumonia. In these cases the quantity of serum used was of necessity small, and no exact determination of its strength was made.

To obtain a sufficient quantity of serum it is necessary to immunise large animals, such as the horse; and, to estimate its strength, it is necessary to use more reliable methods of cultivating the pneumococcus than have hitherto been employed.

In this paper I propose to give an account of the immunisation of a pony, to describe the method I have adopted for estimating the protective power of the serum, and to report two cases of pneumonia treated with the serum.

IMMUNISATION OF PONIES.

In January, 1895, a pony was placed at my disposal by Professor Ruffer, then Director of the British Institute of Preventive Medicine. I take this opportunity of thanking the Council of the Institute for generously providing me with most ample opportunities for carrying out this work. The expenses of the purely scientific part of the investigation were defrayed by a grant from the Royal Society, but the greater expenses incurred in purchasing and keeping the ponies were borne by the Institute. I would also heartily thank Professor Ruffer for most valuable advice, and Dr. Bulloch for the great assistance he has rendered in carrying out the necessary manipulations. To both I am deeply indebted for freely giving me the results of their large experience in the immunisation of horses.

The pony was first injected with broth cultivations of the pneumococcus which had been heated to 60° C. for one hour, and subsequently with living cultivations. In October, after being under treatment for nine months, it was suddenly seized with intestinal obstruction, and died after a few days' illness. This was especially unfortunate, as a fairly high degree of immunity had been attained, and the blood already possessed some protective power.

The immunisation of a second pony was commenced in November, 1895. The pony was first injected with broth cultivations heated to 60° C. for one hour, then with living agar cultivations, and lastly with living broth cultivations. The injections were made into the subcutaneous tissue of the shoulder.

The temperature chart has unfortunately been mislaid and the record of the temperature has thus been lost. In a few instances a note of the temperature was also made in the report.

November 21st, 1895; 70 c.cm. broth cultivation heated to 60° C. for one hour. The temperature rose next morning to 103.5°, but soon subsided.

November 30th; 170 c.cm. broth cultivation heated to 60° C. for one hour. No pyrexia and no local reaction.

December 7th; a small loopful of a living agar cultivation. No local reaction.

December 13th; the whole of a living agar cultivation. No local reaction.

December 19th; two living agar cultivations. No local reaction.

January 4th, 1896; 6 living agar cultivations. A swelling appeared at the spot of injection and lasted five days.

January 13th; 50 c.cm. living broth cultivation. A swelling of the size of an orange appeared at the spot of injection and lasted a few days.

January 21st; 82 c.cm. living broth cultivation. A large