glycerine, and atropine. Dr. Hay and Dr. Hunt watched him for two hours, and by that time the attack had passed away.

I cannot tell you in millimetres of mercury what the blood pressure was, as at the time I was otherwise occupied, but I can tell you that his little heart was taxed to its utmost capacity. In a case of tachycardia thus induced no one, I presume not even Dr. Mackenzie, would consider it an "absurdity" if Dr. Oliver's instrument had been used and had shown a raised pressure.

I have told you that this form of tachycardia is entirely different from that associated with exophthalmic goitre. Some years ago the surgeons invaded this territory of medicine, and treated the disease by the ablation of a lobe of the thyroid gland. I have seen some very successful cases, but I have also seen a few where death followed very severe tachycardia. This is now supposed to be due to removal of the parathyroids. In such cases the extreme rapidity of the heart's action is associated with low arterial blood pressure, the veins are engorged, and the patient bathed in perspiration. Happily the surgeons have again left the field.

In my explanation of this case in the *BRITISH MEDICAL JOURNAL* I associated the tachycardia with direct injury to the epigastrium, but in the light of the two subsequent attacks I am induced to ascribe the attacks to acute cardiac strain. In a scrimmage at football the respiratory muscles would be fixed and the arterial pressure would be raised; the same conditions would occur in carrying a heavy load upstairs, or in sprinting before a policeman. If in such conditions the chest were fixed in the state of expiration the respiratory pump would be thrown out of action, and no assistance would be thus given to the right side of the heart. It is easy to perceive how such acute strain would raise the blood pressure and lead to hyperdistension of the right side of the heart. The case of adrenalin tachycardia supports this view of the case. The right side of the heart and the great veins were distended with blood to their utmost capacity, so the cardio-splanchnic phenomenon of Abrams could not be elicited. The reserve force of the heart was drawn on almost to its utmost capacity, as shown by the slight difference between the mean and systolic pressures. The relatively high arterial pressure enabled the patient to walk to the hospital, maintained the nutrition of the heart, and prevented any risk of syncope.

TREATMENT.

Put the patient in bed, freely use such agents as amylnitrite, nitro-glycerine, etc., to lessen peripheral resistance and equalize the amount of blood in the two sides of the heart. Encourage the patient to take long, deep breaths, so as to aspirate the blood from the right side of the heart into the lungs, and thus give a better supply to the left ventricle. Counter-irritation might call into play the reflex cardiac contraction of Abrams. If, after the preceding measures have been carried out, the hyperdistended right ventricle does not properly contract, then the addition of digitalis or of digitalin and strychnine is required. A good brisk purgative to clear the portal circulation. The diet should be as dry as possible, so as to avoid the addition of fluid to the over-repleted veins and right side of the heart.

Professor Wood, of Nashville, Tennessee, informs me that he has a lady patient subject to tachycardia, whose attacks are cut short by vomiting or by passing a stomach tube. In neurotic cases many remedies will no doubt succeed. In our case vomiting had no such effect. In many cases after the injection of adrenalin into the peritoneal cavity the stomach contents are ejected.

THE SANITATION OF THE DWELLING-HOUSE.—The first International Congress on the Sanitation of the Dwelling-house, organized under the auspices of the French Society of Hygiene, will be held at Paris, October 15th to 20th, 1904, under the presidency of M. Janssen, Member of the Institute. Among the honorary presidents, in addition to the leading hygienists of France, are the Prime Minister, and the Ministers of Public Instruction, Agriculture, Commerce, and Marine. The object of the Congress is to study the sanitary conditions of the building and installation of dwelling-houses, to urge the reforms in these conditions that appear to be required, and to discuss the practical means of inducing municipalities, owners, architects, engineers, builders and tenants, to apply the principles of hygiene to the construction of dwelling-houses.

FURTHER FACTS IN FAVOUR OF AN INFECTIVE ELEMENT IN GOUT.

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IN the *BRITISH MEDICAL JOURNAL* of January 9th, 1904, I recorded the results of a *post mortem* examination of a fatal case of acute gout in a fowl. This record indicated that we had to deal with an acute general infective process. As acute gout is rare in lower animals, it may be some time before these observations are confirmed and extended. In the meantime the recorded facts indicate the importance of investigating anew the histological appearances of chronic gout. If the histological appearances in the acute disease point clearly to an acute infective process, the histological appearances in chronic gout ought similarly to point to a chronic infective condition. The following facts support the view that there is an infective element in chronic gout, and they show the importance of investigating the disease from the standpoint of a chronic infective disorder. It may, in the first place, be advisable to give a brief summary of the views at present held as to (a) the histological appearances in gouty tissues, and (b) their interpretation. The dominant opinions in this country are those of Sir A. Garrod, whose classical work on the subject was published in 1876. Garrod's views on these subjects may, I think, be correctly summed up in the following statements extracted from his work:

I. "It has long been known that changes in and around the joints occasionally take place in gout owing to the deposition of a chalk-like material, principally urate of soda."

II. "The other morbid appearances seen in joints affected with gout are comparatively unimportant, being similar to those observed after other forms of inflammation, as redness, thickening, and dryness of the synovial membrane, and occasionally effused blood."

III. "The establishment of the fact that gouty inflammation is invariably accompanied with the deposition of a peculiar salt is of the highest importance, inasmuch as it proves the inflammation to have a specific character and to differ entirely from other morbid affections of the joint."

IV. "I am of opinion that not only is the deposit of urate of soda constantly found in gouty inflammation, but that it stands to it in the relation of cause rather than effect; that is to say, the deposition of the salt first takes place in the synovial membranes, cartilages, and tendinous structures of the joint, and by its presence gives rise to inflammatory action."

The view that the deposit of urate of soda is the primary event (No. IV) has been stoutly opposed by Ebstein and other writers, who maintain that a necrosis of tissue is the primary incident and the crystalline deposit a later phase in the pathological process. Ebstein, however, agrees with Garrod in regarding uric acid as the primary irritant; the former believing that the uric acid causes the necrosis by its presence in excess in the tissues in the form of a soluble compound. In my opinion neither of the theories held by Garrod or Ebstein adequately explains the histological appearances as revealed by modern methods of examination.

The knowledge that we have of late years attained *re* bacterial influences, and the reaction of tissues to microbic infection, indicates that "the other morbid appearances seen in joints affected with gout" (No. II above) are of the highest importance for the correct interpretation of the appearances. This increased knowledge of bacterial processes in my judgement necessitates a modification of Garrod's views, marked I and II ante; on the other hand, it merely confirms his masterly deduction as to the "specific character of the inflammation No. III." In the following record the grounds for these opinions will be shortly stated. Little reference is here paid to the microscopic appearances of articular cartilages, as these have been very fully described by Sir A. Garrod and Sir Dyce Duckworth; attention is more particularly directed to certain histological changes, which appear to have received inadequate recognition.

Fig. 1 shows characteristic gouty deposits in the subcutaneous tissue of a phalanx in an untreated section. Fig. 2 is from the same section after treatment by ordinary staining methods. The chemical agents employed (haematoxylin and eosin) have effected the removal of the crystalline deposit, the complete absence of crystals being attested by the use of the polariscope. The gouty deposits are now seen in the form

of foreign bodies presenting a hyaline-looking appearance in their centre with striation at the periphery. This striated appearance is the result of separation of the crystals from the tissue in which they have been embedded. It is thus seen that uric acid is only one constituent of these foreign bodies.

Fig. 1.—Deposits containing urate of soda in the subcutaneous tissue. Untreated. ($\times 60$.) Cf. Fig. 2.

The appearances of this tissue warrant the statement that we have no more right to assign etiological significance to uric acid than to other substances of an unknown nature present in the structureless material left after removal of the crystals.

Fig. 2.—Same section as Fig. 1, treated by ordinary staining methods (haematoxylin and eosin), which have removed all traces of crystalline deposit. ($\times 60$.) Note that the "foreign bodies" are of the nature of hyaline-looking tissue, in which the uratic crystals were embedded. Observe also the small cell invasion.

In connexion with these necrotic areas in extra-articular tissues, my observations lead me to accept Ebstein's teaching as to a necrosis of tissue preceding the deposit of crystals. There is, however, one point of importance *re* these deposits to which I wish to draw special attention. I find from examination of gouty tendons that the necrotic areas have a definite relation to the vessels of the part. The appearances in the tendons indicate that the necrotic areas are to be accounted for by an infection by the blood stream.

Fig. 3 is of special interest, as it is a section of the great toe-joint. On the left of the field the articular cartilages have disappeared and bony ankylosis is present. A study of these

sections does not support the view that the uratic deposits *per se* are in any way responsible for the bony changes. In the articular cartilages on the right of the field crystalline deposits are seen a little distance from the surface of the cartilages—in the usual position as pointed out by Garrod. The erosion of cartilage is seen to be due not to the presence of the crystalline deposits, but to the action of small round cells of a granulation tissue type. In the centre of the field a pale area of myxomatous tissue is seen surrounded by uratic deposits in a cellular and vascular matrix.

Fig. 3.—Great toe-joint in chronic gout. Observe: (1) Bony ankylosis on the left side. (2) Disappearance and erosion of cartilage. (3) In the centre of the field a pale area of myxomatous tissue surrounded by uratic deposits in a cellular and vascular matrix. (4) The opposing articular surfaces with crystalline deposits are seen to the right. ($\times 20$.)

The special points to which attention is directed in Fig. 4

Fig. 4.—Section of phalanx in chronic gout. Note: (1) To the left of the field urate of soda in necrotic tissue. (2) A great accumulation of small round cells outside (1). (3) To the right of the field is seen bone (stained dark) and tendon. (4) The tissue between the necrotic tissue and the tendon and bone contains numerous large engorged blood vessels. ($\times 50$.)

are: (1) The great accumulation of small round cells of a nature commonly associated with the action of bacterial toxins, and (2) the richness of the blood supply.

In connexion with Figs. 5 and 6, taken from sections of bone, the footnotes appended will suffice for description. It is advisable to state that we have clear evidence from the sections that the absence of crystals from different parts is not simply accounted for by a solution in course of preparation.

I have examined a large number of sections of soft tissues and of bone, and have found that in the former the crystalline deposits are readily removed by various chemical agents, for example, haematoxylin and eosin staining, alum, acidulated alcohol, etc.; in the latter the crystalline deposits were

Fig. 5.—To show the manner in which some of the necrotic areas are produced. Note: (1) In the upper part of the field six giant cells are seen surrounding a necrotic area which contains a crystalline deposit in its centre. (2) Beneath (1) a second necrotic area is seen, in which the outlines of the nuclei of the degenerated connective-tissue cells are still visible. No deposit has yet taken place at this spot. (3) The large number of cells of an inflammatory type—proliferated connective-tissue cells—in the rest of the field.

unaltered by similar treatment. Reference has previously been made to the rich blood supply of parts of the affected tissue. Fig. 6 further illustrates this feature.

Fig. 6.—Necrotic area with a central deposit of crystals, surrounded by small round cells and giant cells. Observe two large capillaries full of blood immediately outside the giant cells.

Particular attention is directed to Figs. 7 and 8. It has long been known that gouty bones contain an excess of fat. Garrod writes on this point as follows: "Although I have not quantitatively determined the amount of fat in the bones of patients who have died from aggravated forms of gout, I am convinced that it often exists in large quantities, but whether this change is related essentially to the disease or is merely dependent on imperfect nutrition requires further observation and determination."

The histological appearances in Figs. 7 and 8 are a striking confirmation of the results obtained by chemical analysis.

With reference to those changes it is of great interest to note that Ebstein claimed for bone marrow "an essential participation in the development of primary articular gout," this opinion being based on the theory that the marrow is a site of production or uric acid.

Fig. 7.—Section of phalanx to show the structure of the bone and marrow. ($\times 12$.) Observe: (1) The bony trabeculae are very much thinned. (2) The "red" marrow characteristic of this bone has disappeared. Cf. Fig. 8.

I agree with Ebstein as to the probable importance of the bone marrow in gout, but on entirely different grounds, which may be briefly summarized as follows:

Fig. 8.—Higher magnification of marrow in Fig. 7. ($\times 200$.) Observe: (1) Complete disappearance of the normal marrow cells, which are replaced by fat. (2) A distended vessel.

1. A study of the clinical features of an acute paroxysm of gout—the manner of onset, the temperature chart, the local appearances, liability to relapses, etc.—suggests an acute infective disorder: the paramount importance of the bone marrow in all acute infections is universally recognized.

2. In the BRITISH MEDICAL JOURNAL of January 6th, 1900, I recorded a striking change in the histological appearances of the blood (white blood corpuscles) in acute gout. While the interpretation of these changes was not clear, their existence confirmed in my mind the existence of an infective element causing a strain on the bone marrow function. In a later paper by Dr. W. Bain a similar appearance of the blood has been described.

3. In the course of an investigation on the comparative

pathology of chronic articular disease, involving the examination of over 200 subjects, I was impressed by the fact that the gross changes in the bone marrow exceeded in severity the lesions in the articulations.

The fuller consideration of these points is beyond the scope of the present paper, the main object of which has been to prove that the *tout ensemble* of the pathological picture of chronic gout is strikingly similar to that seen in chronic infective diseases. From this point of view the presence of uric acid is regarded as the feature which gives "the inflammation its specific character" (Garrod).

Let me, in concluding, draw special attention to the subject title of this paper, which I trust is sufficient to show that the author regards the bacterial element in the disease only as one of the factors in its production.

I have pleasure in acknowledging my indebtedness to Mr. Alexis Thomson, F.R.C.S.E., for the tissues which have formed the basis of this investigation; and also to Mr. Richard Muir for assistance in the examination of the sections, and for the reproductions from the microscopic slides.

ON THE DIACETIC ACID REACTION IN THE URINE,

WITH ESPECIAL REFERENCE TO GASTRIC ULCER.

BY

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It has long been known that, while the presence of diacetic acid in the urine may be of the gravest import in such diseases as diabetes and grave acid intoxication, it may also occur under certain other conditions without serious significance. Litten,¹ Lorenz,² Payne,³ von Noorden,⁴ and others have drawn attention to the occurrence of this reaction in conditions of gastro-intestinal disturbance, gastric ulcer, and inanition and starvation. It is also known to occur in certain febrile diseases, and Windle⁵ long ago described it in pneumonia. In this note we wish to deal specially with the occurrence of this reaction in cases of gastro-intestinal disturbance, and more particularly in gastric ulcer.

As a rapid clinical test for the presence of this body, Gerhard's reaction, namely, the production of a port-wine colour on the addition of a solution of perchloride of iron to the urine, is extremely simple; a few drops of liquor ferri perchloridi are added to the urine, and in the majority of cases a whitish-grey phosphatic cloud forms. If diacetic acid be present, the urine assumes a port-wine colour, which is largely masked, however, by the phosphatic cloud. It is best, therefore, to filter this off and add a few more drops of the reagent to the filtered solution. The colour of the solution, if diacetic acid be present in appreciable amount, is a dark cherry-red when viewed by transmitted light. By reflected light it has more of a purplish tint. In some cases where the reaction is very marked the phosphatic cloud does not form. The colour is at once destroyed by the addition of a few drops of a solution of citrate of potash. Previous boiling of the urine, which converts much of the diacetic acid into acetone, diminishes the colour reaction, but boiling for half an hour is not sufficient to convert all the diacetic acid.

A somewhat similar colour reaction is produced when the solution of ferric chloride is added to the urine of patients taking salicylic acid, or any of the numerous compounds of this body, such as salol, aspirin, salicin, or diuretin. Ordinarily the colour thus produced, which is said to be due to salicyluric acid, is of a deep purple colour, rather than the cherry-red produced by diacetic acid. But by altering the degree of dilution or by increasing the amount of ferric chloride solution added to the salicylic urine a colour can be produced which is indistinguishable from that due to the presence of diacetic acid. The colour produced by salicylates is also entirely removed by the addition of a little citrate of potash. The distinction between the diacetic reaction and that due to salicyl compounds is, however, perfectly simple. Previous boiling for five minutes causes a great diminution in the colour, if dependent on diacetic acid, but the colour remains unaltered if due to salicylates. The detection of acetone, either by Legal's, or preferably by the iodoform test, is distinctive. To determine the presence of the

diacetic acid in the urine of patients taking salicylates, etc., the urine must be boiled and then tested for acetone. The colour produced by diacetic acid is not likely to be confused with the brown or black colour following the addition of ferric chloride to urines containing melanin. The urines of patients taking sulphocarbolates, iodides, and phenacetin do not give this reaction. In a recent case of fatal carbolic acid poisoning the urine gave no reaction with ferric chloride. This agrees with a statement of Dr. Garrod's,⁶ though the contrary is often stated. It may be pointed out that, although acetates are said to be excreted as carbonates, the urines of individuals, even when in ordinary health, may give a cherry-red colour after liquor ammonii acetatis has been taken, and that since this drug is often given to patients with a raised temperature, this factor must be borne in mind in estimating the significance of febrile diaceturia.

The observations to which we shall refer have been made on the urines of patients under our care during the last three years. Attention has been paid specially to cases of gastric ulcer, most of which have been treated by starvation or rectal alimentation. The occurrence of this reaction in diseases other than those involving the gastro-intestinal tract has been far from frequent, and it is evident that in any febrile case presenting this colour reaction in the urine the influence of practical starvation from non-absorption must always be borne in mind.⁷ Care has, of course, been taken to exclude cases where the administration of salicylate compounds might be a source of error. Although the reaction has been present in several cases of diabetes—in two of them for prolonged periods, up to a year in one case—this subject will not be considered here, as its occurrence and significance are so well recognized.

GASTRIC ULCER.

The total number of cases tested was 44; of these, 3 were cases of perforated ulcer treated by operation and suture, and the remaining 41 were cases treated by purely medical measures. Of the 44 cases, 40 were women, including the 3 cases of perforated ulcer; the remaining 4 were men. As the incidence of the reaction shows well-marked differences in the two sexes we shall consider them separately.

Of the 40 female cases 2 only were allowed food by the mouth from the commencement of treatment, and the reaction was absent in these cases. In the remaining 38 food by the mouth was withheld for periods ranging from two to twelve days, and in all but five of these diaceturia was definitely present. Most of these 5 cases, in which the reaction was not obtained, were among our earlier cases, and the urine was not examined very systematically, so that it cannot be said that diacetic acid was constantly absent. In one case, however, in which careful daily examination was made it was absent throughout. It may be stated here that it appears to make no difference, so far as this reaction is concerned, whether the patient be absolutely starved or nutrient enemata be given, and for the sake of brevity we may refer to the period during which food by the mouth is withheld as the period of starvation.

The reaction usually appears quite early in these cases; in 19 cases in which the urine was tested regularly from the time of admission, it appeared on the day of admission in 2 cases, on the second day in 12, on the third in 1, and on the fourth in 4; it was found to be present when the urine was tested on the third or fourth day in several others. The average date of its appearance after the commencement of starvation would seem to be about the second or third day. The diacetic acid tends to disappear sooner or later after the return to mouth feeding, but the exact date of its disappearance is extremely variable. In our cases it varied from one day to a fortnight, the average being about five days. We have also been unable to establish any relation between the length of time of its persistence after the return to mouth feeding and the duration of starvation. One can only surmise that its disappearance coincides with the restoration of the balance of metabolism.

In the few cases of gastric ulcer in men this reaction either did not occur at all or only appeared after long periods of starvation. In one patient, who was admitted to hospital for chronic gastric ulcer on four separate occasions, it appeared on the first occasion on the ninth, on the second on the tenth day of starvation, and disappeared rapidly; on the third occasion there was a transitory reaction on the fifth day only, and on a fourth it was entirely absent. In a second patient with chronic ulcer we found it present on the eighth day of starvation only. In a third patient in whom food by the mouth was withheld till the ninth day, it was entirely absent.