softer bone tumour from Miss H——'s ear, with a thin section under a low power, 75 diameters, shows that the growth is made up of material similar in structure to newly-formed bone. The free surface is bounded by fibrous membrane raised into small papillæ, and covered by squamous epithelium. In the substance of the tumour trabeculæ of bone form a sort of spongy tissue, in the meshes of which a vascular medullary tissue is contained. Magnified 350 diameters, the fibrous membrane shows no nerves or glands, and only a few small vessels. The layer of bone immediately beneath it is more condensed and thicker than the central portions. Its lamellæ are parallel to the surface, and contain but few bone corpuscles. In the central portion of the growth the trabeculæ are thinner and limit irregular oval spaces. These are filled in some parts with a richly nucleated fibrous tissue containing numerous spindle and round cells. In other parts there is but little fibrous tissue scattered in the midst of round cells. No giant-cells are seen anywhere. The vessels consist chiefly of very large thin-walled tubes, resembling dilated capillaries. They are well filled with blood. Here and there a few arterioles are visible.

The tumour differs from a true ivory exostosis in containing cavities filled with medullary tissue, and hence it may be termed "a spongy osteoma," as defined by Cornil and Ranvier. Some exostoses of pedunculated form may be removed by wire; in these suppuration is generally plentiful, and occasionally a polypus arising from the exostosis precedes its appearance, as in a case I published.⁴ Kramer has described an interesting instance of a polypus in the form of a stalactite, so hard that a knife could not cut it. Clark of Bristol has removed by electricity an exostosis, which followed the growth of a mucous polypus, from the right ear of a girl nineteen years of age. But Bonnafont, I believe, was the first surgeon who dealt successfully with an ivory exostosis causing complete closure of the meatus. This was accomplished by means of graduated styles, and by the use subsequently of nitrate of silver. I have found this method of treatment almost unbearable, from the intense pain to which it gives rise. Trötsch has successfully used laminaria to enlarge the opening between the growth and the wall of the auditory canal. Miot adopted another plan; he trephined the tumour with a very fine instrument in two or three places, set up suppuration, and dead bone afterwards came away in sufficient quantity to allow the membrana tympani to be seen.

(To be concluded.)

ON SOME POINTS IN THE PATHOLOGY AND TREATMENT OF ACUTE RHEUMATISM AND DIABETES.¹

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I PROPOSE to consider four questions:—

1. What is the starting-point of the morbid process in acute rheumatism?
2. Is there any pathological relationship between it and diabetes mellitus?
3. Will any remedy cure acute rheumatism; and
4. If so, how does the remedy act?

I think it will be conceded that these are questions of considerable interest, and well worth attention. The solution I am about to offer of the problems may not be altogether complete; but if there is no unreasonable improbability about the theory, it may at least be suggestive, and perhaps lead to further investigation.

1. What is the starting-point then of the morbid process? Let us turn our attention to the muscular tissue and consider for a moment the physiological changes which take place in that tissue in a state of health. The hæmoglobin of the venous blood as it passes through the lungs becomes wholly, or almost wholly, oxyhæmoglobin. Hurried to the tissues, the oxygen of the arterial blood passes from the blood into the muscular tissue; immediately it has passed it is then

fixed in some way at present unknown to us; the tissue packs away at every moment each molecule of oxygen which it receives from the blood so as no longer to be removable by diminished tension. Out of the body the tension of oxygen in the muscle is *nil*, none can be obtained from it from the air-pump. The oxidation takes place in the muscle itself, oxygen passes into the tissue, but we cannot trace its sojourn there. On the other hand, the muscle is always producing and discharging carbonic acid, and when it contracts there is a sudden and extensive increase of the normal production of that gas. With much but not all of its oxyhæmoglobin reduced, the blood passes on as venous blood, and with its carbonic acid tension increased it arrives in the lungs, where the gas is discharged.²

This change now in the muscular tissue, the fixing of oxygen and exhalation of carbonic acid, must be regulated by some nervous mechanism, in the same way, for instance, as the blood is prevented from coagulating in its vessels or the stomach from digesting itself; and this power must originate in some nervous centre, which we may call the "inhibitory chemical centre," or, using a more applicable term, the "coördinating chemical centre"—the centre which restrains chemical action and regulates the production of heat. "And, indeed, we have some positive evidence of the existence of such a mechanism."³

Suppose this "coördinating chemical centre" has undergone functional or organic change, and that this regulating action is consequently weakened or removed, what would be the result? Instead of the muscle absorbing and fixing oxygen and giving out carbonic acid, some intermediate changes in the tissue would show themselves; the tissue would be disintegrated and oxidised more vigorously, and those changes would take place, in some degree at least, which in the laboratory are seen to result from decomposition or the action of oxygen or ozone. And what are those changes? One of the first is that the reaction of the tissue becomes acid. "Whilst muscle is alive and in a physiological condition it possesses a neutral reaction to test-paper; so soon as it dies this reaction becomes acid, and this takes place so rapidly in warm-blooded animals, as to render it almost impossible to ascertain the normal reaction."⁴ The acid produced is lactic acid. Whence is it derived? Muscle we know contains a small amount of glycogen, which by hydration may be converted first into glucose and then into lactic acid.

Again, lactic acid may be derived from alanine, a substance metameric with urethane and sarcosine, $\text{C}_3\text{H}_7\text{NO}_2$.

Sarcosine, though not found in a free state in the body, is obtained in the laboratory from dead muscle. Nor is it inconceivable that under the action of chemical and *vital* forces acting upon the muscle, urethane or alanine, or it may be some other compound metameric with sarcosine, may be formed in the muscle as it passes from a state of health and activity to one of disintegration and death. At any rate, whatever be the source of lactic acid, whether from glycogen or other compounds in the muscle, we know that it appears in the muscle as the result of disconnection with the nervous centre, and I therefore suggest that if the "inhibitory" or "coördinating chemical centre" be weakened, as in acute rheumatism, by the effect of cold or other cause, lactic acid instead of being oxidised in the muscle will pass from the tissue into the blood; and independently of its own conversion into carbonic acid and water in the blood, there produce its effect on the smaller arteries, and, by determining a larger amount of blood and oxygen to the part, cause more rapid oxidation of tissue, and develop considerable heat or pyrexia.

That the presence of lactic acid in the blood will determine a larger amount of oxyhæmoglobin to the tissue and cause more rapid transformation of tissue than normal, is a natural inference from the researches of Dr. W. H. Gaskell, who

⁴ Brit. Med. Jour., Feb. 2nd, 1878.

¹ The substance of two papers read before the Cambridge Medical Society, Nov. 5th, and the Cambridge Philosophical Society, Nov. 22nd, 1880.

² Text-book of Physiology by Dr. Michael Foster. 2nd edit., pp. 384-7.

³ Foster, loc. cit., p. 376.

⁴ Gamgee: Physiological Chemistry, vol. i., p. 359.

found that the injection of a solution of lactic acid (1 to 1000) into the circulation caused dilatation of the smaller arteries.⁵

But if lactic acid is derived from some variety of $C_3H_7NO_2$, or from glycogen, whence comes the glycogen, or that other substance? Again, in acute rheumatism there is a large elimination of lithates—whence are they?

Let us turn our attention to the constituents of dead muscle. Creatine in dead muscle by hydration may be resolved into sarcosine and urea; and four molecules of sarcosine, together with nine atoms of oxygen, contain the elements of uric acid, glycogen, carbonic anhydride, and water.

But as sarcosine is not found in living tissue, if urea, uric acid, &c., are products of living tissue, then there must be some undetermined compound of $4C_4H_9N_3O_2$, from which in

By taking this as the living representative of $4\text{C}_3\text{H}_7\text{NO}_2$, we have a formula which, when oxidised, can theoretically be split up into uric acid, glycogen, &c., and gives a molecular formula for them, and which, if there was a change in the constitution of the molecules, could produce sarcosine. The chief difficulty in accepting such an antecedent for sarcosine is that it involves the conversion of (NH_2) compounds into those of NO ; and yet, from the researches of Dr. Bence Jones,⁶ such a change does take place in the system, acetate of ammonia, when given internally, being eliminated as nitrates.

By combining cyanic ether with urethane we should probably have a compound somewhat like living muscle, which, as was shown by the observations of Kühne and Eberth,⁷ who had the good fortune to see a living nematode freely moving about in it, is semifluid. Cyanic ether also combines with urea, forming a crystalline substance, which does not possess the characters of an ordinary ammonium compound.

It is not improbable that $4C_3H_7NO_2$ may exist in the tissue before hydration, as,

and so resembles uric acid in requiring hydration and oxidation to convert it into recognised substances. In order to convert uric acid into urea it must be combined with water and oxygen, the results differing according as an alkali or an acid is employed for the conversion. If hydration in the living body is performed in the liver, and oxidation in the muscular tissue, the following intermediate compounds between uric acid and urea would be developed. If hydrated in the liver—

In alkaline fluid this substance would be oxidised in the tissue into allantoin $(\text{NH}_4)(\text{CNO})(\text{NH}_2)(\text{CN})(\text{CO})_2 + \text{CO}_2$, and the allantoin would then be hydrated in the liver into urea $(\text{NH}_4)(\text{CNO})$, and allanturic acid $(\text{NH}_4)(\text{CNO})(\text{CO})_2$ to be again oxidised in the tissue into urea and 2CO_2 .

If the blood had a different reaction uric acid after hydration in the liver would be split up into urea (NH_4CNO) and $(\text{NH}_2\text{CN})\text{CO}_3$, the urea passing off to the kidney, the other substance being oxidised in the tissue into alloxan $(\text{NH}_2\text{CN})(\text{C}_3\text{O}_4)$, to be further hydrated in the liver, and split up into urea and mesoxalic acid $(\text{H}_2\text{O})(\text{C}_3\text{O}_4)$.

If these substances, however, are formed by oxidation in the tissue, and by hydration in the liver, how is it that in health they appear only to a comparatively small extent in the blood? I will illustrate this by reference to electro-

living muscle these substances are produced, and from which in the process of dying sarcosine results.

Now, $C_3H_7NO_2$ represents sarcosine, urethane, and alanine, to which I will add a fourth, an entirely hypothetical compound—cyanic ether + H_2O .

To form the representative of sarcosine in the living tissue I want a very unstable compound, and one that is clear and fluid. Cyanic ether is a transparent, colourless, very mobile liquid, and is decomposed by water.

And taking the other ether which the formula represents—viz., urethane—I have

lysis. In the decomposition of water by electrolysis oxygen appears at one pole, hydrogen at the other, and though the fluid between them appears to be at rest, we know there is a molecular change all along the line. In the transmission, likewise, of the current along the telegraph or telephone wire, there is a molecular change through the whole length of the wire, but the result is seen or heard only at the end. So it probably is in these transformations of the tissues. The blood acts as the conducting medium. It contains substances differing in their properties, but closely allied in chemical composition to those contained in muscle. Creatine, then, we may assume, is hydrated in the liver into urea and the representative of living sarcosine; these products are not set free, or only to a very small extent, in the blood, but there is an interchange of molecules in the blood between the liver and kidney on the one hand, and the liver and the tissue on the other. The change effected in the liver in this way shows itself only in the kidney and the tissue; the urea is eliminated, the living sarcosine appears in the tissue to be immediately oxidised, and to show itself in the liver as uric acid, glycogen, and carbonic acid gas, the last being liberated in the blood, and passing in the stream to be exhaled by the lungs. The uric acid and glycogen are now hydrated in the liver, the results showing themselves in the tissue and in the kidneys.⁸ According as the blood is alkaline or otherwise will uric acid pass through the changes I have above referred to.

Now, a very interesting point arises. In considering the changes of uric acid above described we see that urea is formed both in the muscle and in the liver, and we may assume that when it is formed it passes at once by intermolecular change direct to the kidneys. So also we may assume that carbonic acid, whether formed in the muscle or in the liver, directly it is formed passes at once into the blood, to be eliminated by the lungs. Glycogen $(C_6H_5O)_2C_2O_3$ by hydration is transformed into glucose $(C_6H_6O)_2(CO_2)_2$, and, like uric acid, may, under different circumstances, undergo different transformations. If the blood is normal and alkaline by hydration in the liver it may become $(C_2H_6O)_2 + 2CO_2$, the carbonic acid at once entering the blood, the alcohol $(C_2H_6O)_2$ appearing in the tissue, to be oxidised into $4CO_2 + 6H_2O$; passing, perhaps, through the stage of $(C_2H_4O)_2$ acetic acid, and $2H_2O$.

But if the blood is in an abnormal condition the interchange of the molecular elements may be modified (and the alkaline reaction of blood becomes, like muscle, changed when the power of the coordinating centre is removed, as shown in the process of coagulation), the glycogen $(C_2H_5O)_2C_2O_3$ may then be hydrated in the liver and, as the result of the

⁵ Journal of Physiology, vol. iii., p. 18.

⁶ Philosophical Transactions, London, 1851.

⁷ Gamgee, *op. cit.*, p. 320.

⁸ Assuming such an interchange of molecular particles, does not this offer a simple explanation of one mode of nutrition and disintegration of the tissues?

variation in the molecular interchange in the blood, appear in the tissue either as glucose $2(C_5H_6O)CO_2$, or as lactic acid $2C_3H_6O_3$, which last we know does appear in muscle when the power of the coördinating centre is removed.

The following substances, with others, would exist in the liver and tissue (urea and carbonic acid being eliminated as formed), according as the blood had a normal alkaline or abnormal reaction :—

IN LIVER.		IN TISSUE.	
$4C_4H_9N_3O_2$	hydrated into Urea + $\left[\left\{ CO(NH_2)C_2H_5O \right\} \left\{ CN, C_2H_5O, H_2O \right\} \right]$	oxidised into	Uric acid, glycogen, carbonic acid, and water.
TABLE I. — Blood Normal.			
$(NH_2)_2(CN)_2(CO)_3$ Uric acid.	into	$(NH_4)(CNO)(NH_2)(CN)(CO)_3$ Pseudo-uric acid.	into Allantoin and CO_2
$(C_2H_5O)_2(C_2O_3)$ Glycogen.	into	$2C_2H_6O$ Alcohol.	into $\left\{ \begin{array}{l} 4CO_2 + 6H_2O \\ \text{or } 2(C_2H_4O_2) + 2H_2O \end{array} \right.$ Acetic acid.
$(NH_4)(CNO)(NH_2)(CN)(CO)_2$ Allantoin.	into Urea +	$(NH_4)(CNO)(CO)_2$ Allanturic acid.	into Urea + $2CO_2$
TABLE II. — Blood Abnormal.			
$(NH_2)_2(CN)_2(CO)_3$ Uric acid.	into Urea +	$NH_2(CN)(CO)_3$	into $(NH_2)(CN)(C_3O_4)$ Alloxan.
$(C_2H_5O)_2(C_2O_3)$ Glycogen.	into	$2(C_2H_6O)(CO_2)$ or $2C_3H_6O_3$ Glucose. Lactic acid.	into $6CO_2 + 6H_2O$
$(NH_2)(CN)C_3O_4$ Alloxan.	into Urea +	$(H_2O)(C_3O_4)$ Mesoxalic acid.	into $3CO_2 + H_2O$ or $(H_2O)(C_2O_3) + CO_2$ Oxalic acid.

Consequently, if the power of the coördinating centre is removed or impaired, we should have, as shown in Table 2, simultaneously in the liver, and as the last stage in the process, glycogen about to be transformed, and appear in the tissue as lactic acid or as glucose, and alloxan about to be split up into urea and mesoxalic acid; and to this point I shall refer when dealing with the action of remedies.

It would seem from these hypotheses that in a state of health glycogen and glucose are abnormal constituents of muscle, the liver glycogen appearing in the tissue as $2C_2H_6O$, to be at once transformed into CO_2 and H_2O . But, if the controlling power is weakened, glycogen is transformed, and appears in the tissue as lactic acid or glucose, according to the extent to which that power is weakened, and according to the variation in the molecular change along the blood line; and these substances may also, from the same causes, appear in the blood itself. If lactic acid produces the same effect on the smaller arteries of the kidney as was seen in the experiments of Dr. Gaskell to be the effect on those of muscular tissue, and so (under certain conditions of the red blood-corpuscles to be presently referred to) act as a diuretic, the experiments of Claude Bernard seem to support very strongly the view I have here advanced as to the common origin of glucose and of lactic acid. "When we prick the mesial line in the floor of the fourth ventricle, in the centre of the space between the origins of the auditory and pneumogastric nerves we at the same time produce an exaggeration of the hepatic (saccharine) and of the renal secretions; if the puncture be effected a little higher, we very often only produce an augmentation in the quantity of the urine, which then frequently becomes charged with albuminous matters; while if the puncture be below the indicated point, the discharge of sugar alone is observed, and the urine remains turbid and scanty. . . . As these two points are very near one another, it often happens that if the instrument enters obliquely they are simultaneously wounded, and the animal's urine not only becomes superabundant but saccharine."⁹

⁹ Med. Chirurg. Review, Jan. 1857, p. 42.

Lastly, though it is most probable that in health the various substances are oxidised in the tissues and not in the blood, yet where there are morbid changes and abnormal products appearing in the blood, if the energy of the red blood-corpuscles as carriers of oxygen from the lungs is not lessened it seems hardly possible that oxidation of oxidisable substances should not take place there. How else can the conversion of vegetable acids be explained, which, when administered internally, are eliminated as carbonates? In acute rheumatism it would seem probable, therefore, that there is increased heat or pyrexia, partly by increased oxidation in the tissue from the smaller arteries dilating, owing to the presence of lactic acid in the blood, and partly also by the oxidation of the lactic acid in the blood itself; and that from the increased oxidation in the tissue an excessive amount of uric acid is formed, which the liver is unable to act upon; it escapes into the blood unchanged, and is eliminated by the kidneys.

If the energy of the red blood-corpuscles was in any way diminished or inhibited, and there was no increased oxidation going on from lactic acid being present in the blood, but merely dilatation of the minute arteries, then if the vessels of the kidney were affected in the same way we should have simply increased flow of urine—diabetes insipidus. Again, in diabetes mellitus as there is no rise of temperature, and the glucose is not oxidised in the blood, is the energy or number of the red blood-corpuscles inhibited or modified?—and if the energy were unrestrained, would this give rise to hyperpyrexia? We know that during the progress of disease intercurrent with diabetes the sugar does sometimes disappear from the urine, but this may be only from the introduction of some zymotic element into the blood.

Is it possible, then, that altered intensity of the "coördinating chemical centre" presiding over the changes in the tissue and in the liver, and a variable energy in the action of the red blood-corpuscles, may express the pathological relationship between hyperpyrexia, diabetes mellitus, acute rheumatism, and diabetes insipidus?

(To be concluded.)

ON RICKETS.

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At the discussion on Rickets at the Pathological Society it was necessary to compress what I had to say into the last five minutes of an unusually long sitting, and to this was added the knowledge that the opener of the debate had still to occupy more time with his reply. Such conditions were conducive more to vigour than to precision of statement; some things that I wished to say had to be omitted, and others were too shortly put to make my full meaning in-

telligible. But though obscurely stated, the points themselves are not unimportant, and considering that so few facts have been added to our knowledge, I venture to put on paper in a more detailed manner what I should have said elsewhere had time permitted me, and while attention is still directed to the subject.

My text is visceral rickets, if there is such a thing. Three propositions concerning this branch of the subject have been put forward at one time or another.

1. That the spleen and liver are not enlarged in rickets—the seeming increase is due to displacement.
2. That the enlargement of the spleen and liver is as much a part of the disease as the changes in the bones—an opinion advanced by Sir Wm. Jenner and supported by Dr. Dickinson.
3. That the viscera are enlarged, but present no distinct-