the use of the electric light spreads, their number might not improbably be multiplied. The limit of safety could hardly yet be said to be known; and, on this point, it had been remarked by Mr. Cunningham that the Board of Trade were still sadly at sea.

Alterations in Disease.—It had been generally assumed (Dubois-Reymond, Muncel) that the human body acted as a fluid-conductor, but Dr. Stone had made a few observations which cast doubt on this assumption. In dropsy, resistance was diminished. In one case, where determinations were made before and after the sudden onset of dropsy, the resistance fell to one-half. In degenerated tissues, where muscle was replaced by fibrous tissue, resistance fell. In six cases of old hemiplegia, Dr. Stone found that the hemiplegic side offered less resistance—that is, was a better conductor than the sound side. The difference in the several cases was 420 ω , 350 ω , 380 ω , 120 ω , 550 ω , 730 ω —far too large a divergence for mere observational errors.

Alterations in Metallic Impregnations.—The effect of metallic impregnations had been tested. It was found that lead had a slight, and mercury a marked, influence in diminishing resistance. In a case of copper-impregnation, observed in a coppersmith, whose right arm was chiefly exposed to the impregnation, the right side conducted better than the left. From the urine of this patient, three milligrammes of metallic copper were recovered by electrolysis, and kindly measured by Dr. Bernays in the chemical laboratory of St. Thomas's Hospital.

Alterations in Pyrexia.—In conclusion, Dr. Stone said that he was not yet prepared to speak positively with regard to the influence of temperature. In one case of ulcerative endocarditis, the resistance had been observed to be greater during periods of pyrexia; but opportunities of making such determinations under favourable circumstances, without unkindness to the patient, were obviously very rare.

At the second lecture, Dr. Stone proposed to take up the subject of Polarisation; and at the third, that of Induced Currents and their peculiarities.

BRITISH MEDICAL BENEVOLENT FUND.—The applications for relief, which came before the Committee of this Fund, at their monthly meeting, held on March 30th, presented some features of unusual interest. The number of cases submitted for consideration was twenty-seven, rather above the average; and of these, twenty-two received grants varying from £18 to £6, according to circumstances; £15 was voted to the honorary local Secretary at Liverpool to aid a subscription, now in course of raising, for a medical man, aged 61, temporarily incapacitated by illness. A lady, aged 70 (London) received a grant of £18 in equal monthly instalments of 30s.; £10 was given to a member of the Committee, to be used for clothes, to enable a medical man, who had been for some months laid up with obstinate sciatica, to obtain a situation as assistant (London); £10 to enable a lady to return to her situation as a governess in Russia; £12, at the rate of £1 a month, was voted to a lady, who has been a helpless invalid from paralysis for over three years; £10 was voted to a widow, whose son is completely invalided by chronic abscesses (Stratford-on-Avon); £18 was sent to the honorary local Secretary at Bradford, for a widow with six children, whose ages run from 15 to 2; £12 to the wife of a medical man, who has been deserted by her husband (London). Valuable aid was given to the Committee in deciding applications by the able and exhaustive reports furnished by the various honorary local secretaries, whose local knowledge enabled them to really sift cases, and inform the Committee of the exact position of the applicants, and the best mode of administering relief. In all, £260 was ordered to be distributed, and the number of applicants suffering from real distress relieved by these grants amply justifies the existence of this charity, and appeals most strongly to the profession for aid in its objects. The Committee would draw attention to the cosmopolitan nature and reach of the fund; cheques were sent to various parts of London; to Manchester, Liverpool, Oxford, Torquay, Southsea, Goolse, Oldham, Glasgow, Alfreton, Blisworth, Crail in Fifeshire, Stratford-on-Avon, and Bradford. A glance at the report shows that the amount annually distributed to the objects of its benevolence has grown from nothing in the first year, to a sum only just short of £3,000 in the year ending December 30th, 1885, in grants and annuities; and the Committee wish to point out that no distinction is made by them, help being freely given to any applicant who may be eligible and properly recommended; and they earnestly and confidently appeal for increased subscriptions to enable them to render this, the jubilee year of the fund, the most remarkable since its foundation in 1836.

The Earl of Powis has been re-elected President of the Shrewsbury Dispensary for the ensuing year.

THE CROONIAN LECTURES OR SOME POINTS IN THE PATHOLOGY OF RHEUMATISM, GOUT, AND DIABETES.

Delivered at the Royal College of Physicians, London, April, 1886.

By P. W. LATHAM, M.A., M.D., F.R.C.P.,

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LECTURE III.

MR. PRESIDENT AND GENTLEMEN,—The metabolic function of the liver may be interfered with in diverse ways. From the stimulating effect of food during digestion in the stomach or duodenum, two things should take place in the liver: dilatation of the vessels of the gland, and certain changes in the gland-cells—results which may be compared to those obtained from the submaxillary gland by stimulating the chorda tympani; the metabolic events being dependent upon the absorption and transformation of certain constituents of the blood by the hepatic cells, and this action controlled by the nerve-fibres in connection with these cells. But these two processes, vascular dilatation and metabolic activity, are independent of each other. The vessels may dilate; but, if the terminal portions of the nerves of the secreting cells be paralysed, the blood will pass through the gland more or less unchanged; and the same effect will be produced by paralysing the nerve either at its central origin or along its course.

We know that, as regards the innervation of the tongue and the sense of taste, there are nerve-filaments which respond only to particular kinds of stimuli; so it is not unreasonable to assume that distributed to the liver-cells there are various nerve-filaments, one set regulating the transformation of saccharine, the other the nitrogenous elements conveyed to the cells by the portal circulation; and, if either set were paralysed, we should have the metabolism of the corresponding elements interfered with. How far the secretory power of the liver-cells is influenced by the vagus, is not very clear; but the vessels are under the control of the dominant vaso-motor centre which is located in the medulla oblongata, where also we have the nucleus of the vagus. If, then, there be a want of harmony between the vascular dilatation and the action of the liver-cells, if blood containing the products of digestion be passing through the liver in larger quantity than the cells can act upon (whether that inaction be due to exhaustion of the cells themselves, or to exhaustion of the secretory nerves in connection with them), then there will be imperfect metabolism, and consequently the formation of uric acid in the manner which I have described. So far as the imperfect metabolism of the saccharine elements is concerned, we have illustrations of what I mean in the results which take place from the "diabetic puncture," or, as shown by Dr. Pavy, from section of the sympathetic filaments ascending from the superior thoracic ganglion, or from the removal of the superior cervical ganglion.

There may be also imperfect metabolism of nitrogenous material, in another way; namely, if too much be introduced into the portal vein from the alimentary canal. The portion then which is least readily acted upon (namely, the glycocine) will not be transformed, and so the formation of uric acid is promoted. We see the same thing constantly, even when the liver is in a healthy and normal condition, if it have too much work imposed upon it; that is, if more nitrogenous material be introduced into the portal vein than can be transformed in the gland. And so an occasional indulgence at the table is very generally succeeded by the appearance of urates in the urine. If the liver-cells be already exhausted by long continued over-stimulation, with how much greater difficulty will the perfect metabolism of nitrogenous food be effected!

In either of these modes, then, arising from defective changes in the liver, uric acid may be formed in excess, and then eliminated, or it may circulate as a poison in the blood. Why, in some cases, is it eliminated as urates or as uric acid in the urine, or as renal or vesical calculi, without any arthritic symptoms? Why, in others, does it develop the arthritic symptoms to which we give the name of gout?

If the kidneys are sound, as in the majority of people below middle

age, the uric acid, unless in large excess, will be excreted; it is thrown off directly it is formed, and there is little overflow of the product into the circulation. If the urine have a neutral reaction, it will appear as urates of ammonia, soda, etc. If, however, other acids, such as lactic acid, be formed at the same time, and eliminated by the kidneys, the base will be separated, and uric acid, as such, be excreted, and, according to the amount, will give rise to gravel, or to renal or vesical calculi. But gradually the kidneys may become weakened or diseased; and then, as the blood passes through them, the acid is formed, a portion passes on, and is not eliminated. As it is an abnormal product, we are making no violent assumption in saying that it will act as an irritant upon some portion of the nervous system. We have seen how distinctly the similar body, caffeine, acts as a stimulant to certain portions of the nervous system. According, therefore, to the susceptibility or sensitiveness of different portions, will be the outward manifestations of this irritation. Such a susceptibility or sensitiveness of the nervous system is constantly observed in different individuals. In some, the nerve of smell is much more easily stimulated by certain odours than in others. In some, again, the nerves of taste recognise differences in flavour which are totally imperceptible to others. In children, too, and in persons in enfeebled health, how readily is pyrexia developed by irritation of the nerves of the intestine or of the digestive glands, from improper diet.

If the nucleus of the vagus be the sensitive spot, then gastric uneasiness, asthma or cardiac irregularities might be developed.

Dr. Buzzard has suggested that in locomotor ataxy "the frequency of the coincidence of gastric crises with the osseous lesions gives reasonable ground for the hypothesis that the latter may depend upon an invasion of a part of the medulla oblongata closely adjacent to the roots of the vagi. It is only as a working hypothesis that I make the suggestion. Is there something which we may call provisionally a trophic centre for the osseous and articulatory system in the immediate neighbourhood of the roots of the vagi?"

"As I have suggested on a previous occasion, the discovery of such a centre would materially help us to explain the remarkable association of cardiac complications with the joint-affection of acute rheumatism, as well as the sweating characteristic of this disease, and the occasional hyperpyrexia which occurs in it. And it might also help to throw light upon the obscure pathology of arthritis deformans."¹

In a subsequent paper he further adds: "In a communication brought before the Pathological Society of London, in February, 1880 (*Transactions of the Pathological Society*), I made the suggestion that the gastric crises depend upon irritation of the nuclei of the vagus by sclerosis. At that time, I had no anatomical evidence to offer in support of the hypothesis, which was based upon the paroxysmal character of the attacks, so completely in accord with that characterising the attacks of lightning-pains. It appeared evident to me that if sclerosis, which, when it attacked nerves of common sensation, produced pain, came to invade the nucleus of the vagus, it might be expected to give rise to symptoms like those of the gastric crises. During the meeting of the International Medical Congress in London, Professor Pierret, of Lyons, has shown me sections of the medulla oblongata which he has lately made from a case of tabes with gastric crises. I was greatly interested in his demonstration that the fasciculus gracilis, in immediate relation with the nuclei of the vagus, exhibited distinct sclerosis."²

Professor Roy and Dr. Graham Brown have recently stated³ that, "In the curarised dog stimulation of one uncut vagus with an induced current, causes contraction of the bronchi of both lungs, the contraction being usually powerful, but to this there are exceptions. Section of one vagus usually causes a marked expansion of the bronchi of the corresponding lung, which may be preceded by a slight temporary contraction, apparently due to the stimulus of the section. Stimulation of the peripheral end of one cut vagus always causes a much more powerful contraction of the bronchi of both lungs, than when the uncut nerve is stimulated with the same strength of induced current." They have also stated that these and other experiments enable them to understand how asthma may be produced.

If portions of the spinal cord in connection with the nerves distributed to the joints be more than usually sensitive, this sensitiveness or susceptibility being either inherited or acquired, then stimulation or irritation of these portions would lead to changes in the respective joints similar to those which result from nerve-wounds, or from injuries to the spine. At first, the uric acid might produce little effect; but,

with repeated or constant stimulation, these portions of the spinal cord would become more susceptible to the action of the morbid products, and so nutritive changes or inflammation would be developed in the joints connected therewith.

Suppose for a moment that the portion of the nervous system most susceptible to the action of the uric acid is the vaso-motor centre, the domination portion of which, as we know, is located in the medulla oblongata, what effects should we expect to follow? The most powerful vaso-motor nerves are those which act upon the blood-vessels of peripheral parts, for example, the toes, fingers, and ears, while those that act upon central parts seem to be less active; consequently, we should expect the toes and fingers to be first affected; and, just as by stimulating the sympathetic nerve of the sublingual gland we have contraction of the vessels and altered secretion from the gland, so in the toes and fingers we should have contraction of the vessels, and the metabolism of the parts more or less modified. In addition to contraction of the vessels caused by impulses affecting the blood-supply, there are impulses affecting directly the activity of the protoplasm. The constructive metabolism about the joints is stimulated, whilst the blood-supply and destructive metabolism are lessened, and so there is increased development or growth about the part. Further, the blood which goes to the part contains sodium urate; consequently, this deposited along with the other substances, in the metabolism of inflammatory changes which take place in the tissues around the affected part.

But, whilst the vaso-motor centres may be directly stimulated by the irritant, they may be also stimulated by irritation of the efferent or sensory nerves. Stimulation of the centripetal end of a divided efferent nerve causes increased blood-pressure. Have we not here, then, an explanation of the phenomena of a gouty paroxysm? The uric acid stimulating both the sensory nerve, and, through it or independently, the more active portion of the vaso-motor centre, causes pain in the joint and contraction of the vessels; the pain increases with the continued stimulation, but, after a time, the nerve is exhausted or paralysed (as we know to be the case from continued stimulation of other nerves, as, for instance, in tetanising a muscle). The vessels now dilate, destructive metabolism is stimulated; there is relief from pain, and, with the relief, another indication of paralysis of the sympathetic shows itself, namely, more or less perspiration.

A similar explanation may, I think, be given of the mode in which arthritic symptoms result sometimes from nerve-wounds. The wound may be such, that the sensory or efferent fibres in the nerve are injured, whilst the vaso-motor and other fibres are intact. From the irritation set up, either by the cicatrix or otherwise, the sensory fibres are stimulated, and, through it, the vaso-motor centres in the manner I have just described as occurring in gout; but, as uric acid is not the irritant, and is not circulating in excess in the blood, there is no deposit of this substance in the metabolic changes taking place in the joint.

And further, if irritative, inflammatory, or degenerative changes take place in the spinal cord anywhere along the course of the sensory nerves, by which the sensory nerves are stimulated, this would lead to stimulation of the corresponding portion of the vaso-motor centres, and so to the development of those symptoms which we know under the name of arthritis deformans, or rheumatoid arthritis. In this way, we can easily understand how dysmenorrhœa may be the starting point of this joint-affection, a clinical fact which has been recorded by Dr. Ord.

Among the peculiar local affections in connection with gout, we have, as pointed out by Dr. Graves, congestion of the lobes of the ear; a singular affection of the teeth, which consists in an insuperable desire to grind them; the occurrence of *tic d'olercux* of several branches of the fifth pair; daily paroxysms of intense heat of the nose, which continues for three or four hours, the part becoming first of a bright and then of a purplish red colour. All these symptoms may, I think, be ascribed to irritation in that portion of the nervous system where the roots of the fifth nerve and the vaso-motor centre are in close proximity, namely, in the medulla oblongata. To this spot I shall have to refer again.

But, independently of any functional or organic change in the liver or in its nervous connections, there is a third way in which uric acid may be developed. And that is from the excessive formation of glycochine in the muscular tissue—in the manner I have already referred to as the result of what is commonly called a feverish cold. This glycochine, passing in the blood to some glandular organ—the liver or spleen it may be—is there conjugated into hydantoin, and afterwards further transformed into uric acid. When the nervous

¹ "On the Affection of Bones and Joints in Locomotor Ataxy, and its Association with Gastric Crises," by T. Buzzard, M.D., *BRITISH MEDICAL JOURNAL*, 1881, vol. i, p. 333.

² *Transactions of the International Medical Congress*, 1881, vol. ii, p. 27.

³ *Proceedings of the Physiological Society*, May 10th, 1885.

⁴ Landois and Stirling, *Physiology*, 1895, p. 493.

system and the kidneys are sound, this product is eliminated by the kidneys, and the attack subsides.

But suppose the individual who is exposed to damp or cold has been previously reduced in strength, is tired out or exhausted, that is to say, his vaso-motor system, or some portion of it, is in a weak state, the weakness being either developed from bodily or mental exhaustion, or it may be, inherited. Then, following the chill, there would be the same effects produced as I have described when referring to the effect of cold applied to the skin; but, the vaso-motor centre being enfeebled, the nerves regulating the vessels of the muscular area would be more completely paralysed by the external cold; and when reaction, induced in some degree by the lactic acid, set in on the surface of the skin, there would be less power in the muscular nerves to recover from that paralysed condition. More than this—so far as these vaso-motor elements are concerned—the morbid products are still circulating in the system; and, the vaso-motor centre not having recovered itself, the continued stimulation by glycochine or uric acid on that exhausted centre, no longer excites it, but gives rise to further exhaustion, and consequent further dilatation of the vessels in the vascular area connected with it, and more complete falling asunder of the molecular elements of the tissue.

Let me illustrate what I mean by reference to the sciatic nerve.

"Division of the sciatic nerve of a mammal causes dilatation of the small arteries of the foot and leg. Where the condition of the circulation can be readily examined, as, for instance, in the hairless balls of the toes, especially when these are not pigmented, the vessels are seen to be dilated and injected, and a thermometer placed between the toes shows a rise of temperature amounting, it may be, to several degrees."⁵ "But the dilatation so caused, after a few days, disappears; the foot on the side on which the nerve was divided, becomes not only as cool and pale, but frequently cooler and paler than the foot on the sound side. If the peripheral portion of the divided nerve be stimulated with an interrupted current immediately, or very shortly, after division, the dilatation due to the division gives place to constriction; the sciatic nerve acts then quite like the cervical sympathetic, except perhaps that this artificial constriction cannot be maintained for so long a time, and is very apt to be followed by increased dilatation. If, however, the stimulation be deferred for some days, until the dilatation has given place to a returning constriction, the effect is not constriction, but dilatation; the nerve then acts, so far as its vaso-motor fibres are concerned, like a muscular nerve, and not like the cervical sympathetic."⁶ So also with regard to the mylohyoid muscle. Section of the nerve produces dilatation, but the dilatation is transient. The vessels speedily return to their former calibre; and then it is found that stimulation, of whatever strength, of the peripheral portion of the divided nerve, brings about not constriction, but dilatation.

If, then, the vaso-motor fibres of the muscular nerves have been weakened, the result would be that the normal stimulating effect of uric acid on the vaso-motor elements connected with motor nerves generally would be transformed into a depressing or paralysing effect, the vessels of the muscular area would be still further dilated, the molecular constituents of the tissue would be loosened, hydration and oxidation would go on causing fresh development of heat, there would be the continuous formation of glycochine and lactic acid, the glycochine giving rise to uric acid, which, accumulating in the system, produces its deleterious effect in modifying the function of the nervous system; the lactic acid dilating the smaller arteries,⁷ and stimulating the sweat-centres, passing off in part by the skin. With increased stimulation of the paralysed centre of the muscular nerves, complete dilation of the vessels in the muscular area will take place; the molecular constituents of the tissue now fall completely asunder, the $\text{CH}_2\{\text{OH}\}\{\text{CN}\}$ and $\text{C}_2\text{H}_4\{\text{OH}\}\{\text{CN}\}$ being entirely hydrated into glycollic acid and lactic acid, with the rapid production of heat, and the heat is further developed by the ready oxidation of these products. In this way, to some extent, the so-called hyperpyrexia of rheumatic fever is produced.

But, whilst uric acid affects in this way the vaso-motor fibres of muscular nerves, it also affects the nutrition of the joints. I have endeavoured to explain how it does so in gout, producing first of all contraction of the arteries and constructive metabolism, by the stimulating effect of the poison on the sensitive nerve-centres, followed by dilatation of the arteries, and destructive metabolism when the centres are exhausted. In rheumatism, however, the dominant centre is exhausted, to begin with, and so we have destructive metabolism and

vascular dilatation, preceded by very slight, if any, constructive metabolism and contraction of the vessels. In gout, the uric acid is the result of modified innervation of the liver, or exhaustion of the hepatic cells, and so there are non-transformation of the glycochine, and the consequent formation of uric acid. In rheumatism, the glycochine results from changes in the vascular area, and in the metabolism of the muscles; and, along with its formation, there is also the formation of lactic acid, by hydration, both from the cyan-alcohol $\text{CH}_2\cdot\text{CH}_2\{\text{OH}\}\{\text{CN}\}$ and the cyan-alcohol $\text{CH}_2\cdot\text{CH}\{\text{OH}\}\{\text{CN}\}$. The nutrition of the joint is modified, as above described, by the uric acid, but the nutrition is further modified by the presence of the lactic acid in the blood, producing dilatation of the arterioles, more particularly of those in the cutaneous area.

In this manner, then, I venture to suggest, are the characteristic changes about the joints in acute rheumatism developed.

Again, if the dominant vaso-motor centre be in an enfeebled or exhausted state, and irritative, inflammatory, or other changes take place in the spinal cord along the course of or adjacent to the sensory nerves by which these nerves are stimulated, we should have, quite independently of the presence of uric acid in the blood, destructive metabolism and vascular dilatation about the joints; the extreme effects of which are seen in Charcot's disease accompanying locomotor ataxy. Regarded in this light, Charcot's disease bears the same relationship to arthritis deformans that rheumatism does to gout.

In a similar way, also, I would explain the joint-affection known as gonorrhoeal rheumatism. Here we have prolonged irritation of the sensory nerves of the urethra, acting through an enfeebled or weakened vaso-motor centre; and, in this way, the nutrition of the joints in connection with that centre is modified.

I have referred to that portion of the sensory tract in the medulla oblongata in the neighbourhood of the nucleus of the vagus, the root of the fifth nerve, and the dominant vaso-motor centre, as the part which controls the nutrition of the joints, and which is more particularly affected by external cold. The following facts give support to this view, and can be explained on the same hypothesis.

Cases occur in which the solitary local affection, associated with a feverish cold, is an outbreak of herpes on the lips, nose, or buccal mucous membrane, the so-called *Febria herpetica*. "We find a sharp attack of fever in a child or young person, without any local cause; we expect the onset of some serious disease, but our anxiety is soon allayed; in a few days, there unexpectedly appears on the lips, nose, or cheeks, a closely packed group of vesicles, which at once removes our uncertainty, and shows us that we have to do, not with the early stage of one of the more serious fevers, but with a feverish cold, which will end favourably in a day or two."⁸ Here we have, as the result of "catching cold," disorder of nutrition, showing itself in parts supplied by branches of the fifth nerve, namely, the labial and nasal branches of the superior maxillary nerve.

Rheumatism not unfrequently, after a short interval, follows tonsillitis. Attention was prominently called to this, a few years ago, by Dr. Kingston Fowler, and I have seen several instances where it has occurred. Now, we may assume either that the condition of the central nervous system in the individuals so affected is such that slight injurious influences, such as the effect of a slight chill, or exposure to cold, acting upon the central nervous system, will produce an attack of quinsy, whereas more severe injurious influences will cause rheumatic fever; or we may assume that, in quinsy, the continued irritation of the sensory nerves distributed to the tonsils produces exhaustion of some portion of the dominant vaso-motor centre; and as, in quinsy, uric acid is largely developed, this, acting on the enfeebled centre, exhausts it still more, and develops the arthritic symptoms of rheumatism in the manner which I have described. Either hypothesis will illustrate my argument. The tonsillar nerves are derived from the fifth nerve—the middle descending branch from Meckel's ganglion—and from the glosso-pharyngeal portion of the eighth nerve. This branch of the fifth, to which I have referred, is derived from the larger root of the nerve, which may be traced back to the lateral tract of the medulla oblongata immediately behind the olivary body, and is connected with the grey nucleus at the back part of the medulla between the fasciculi teretes and the restiform columns. The deep origin of the glosso-pharyngeal may be traced through the fasciculi of the lateral tract to a nucleus of grey matter at the lower part of the floor of the fourth ventricle, external to the fasciculi teretes. Both these nerves receive filaments from the superior cervical ganglion of the sympathetic.

The occurrence of arthritis in the course of hemiplegia, a point to

⁵ Foster's *Physiology*, 4th edition, p. 199.

⁶ *Ibid.*, p. 209.

⁷ Gaskell: *Journal of Physiology*, vol. iii, p. 18.

⁸ Ziemssen's *Encyclop.*, vol. xvi, p. 241. London. 1877.

which I referred in my second lecture,⁹ would at first sight appear antagonistic to a theory which ascribes the joint-symptoms to neurotic changes in the medulla oblongata. But it only requires a little reflection to show that it gives the strongest support to the theory. Following apoplexy, there is descending sclerosis of the lateral columns, which proceeds slowly. When it shows itself in the medulla, irritation may be set up around the degenerating portion; and this, extending to the grey matter and anterior cornua, may set up the arthritic symptoms which sometimes show themselves in from fifteen days to a month after the apoplectic seizure.

As regards megrim, Dr. Edward Liveing¹⁰ writes: "There can be no question, then, I think, as to the frequent connection of megrim, whether in its blind, sick, or simply hemicranial forms, with a gouty diathesis, and its occasional replacement by fits of regular gout." Some years ago, I endeavoured to prove¹¹ that megrim was due to vaso-motor disturbance—to uncontrolled action, or, as I should now say, to stimulation of certain branches running from the superior cervical ganglion of the sympathetic followed by exhaustion. Dr. Haig, in a recent number of the *Practitioner*,¹² asks the question: "May not excess of uric acid in the blood cause such vaso-motor irritation?" Certainly; and in persons who are subject to megrim, whose sympathetic ganglia have this sensitive constitution, the causes which will lead to the formation of uric acid in the system, will, with tolerable certainty, develop an attack of this particular disorder.

Again, with regard to chorea: if the vaso-motor fibres proceeding from the upper cervical ganglion to form the carotid plexus have, through prolonged stimulation, become exhausted or weakened, there would be, as the result of that exhaustion, vascular dilatation and circumvascular change in the track of the middle cerebral artery. But there would also be nutritive changes in the nerve-cells of the brain, and exhaustion of their metabolic powers. We should, in fact, have a similar condition produced to that of the submaxillary gland, when the chorda tympani is stimulated after the injection of atropine; and, as far as the nerve-cells are concerned, the same result would be produced as ensues from embolism. Their co-ordinating action would be paralysed in both cases, and such changes would produce the inco-ordinated movements of chorea. Nor is it difficult to suppose that sudden shock would give rise both to vaso-motor paralysis, and to inhibition of the assimilating power of the nerve-cells. Dr. Dickinson has made out very clearly that it is in the tract of the middle cerebral artery, and in the posterior and lateral parts of the grey matter, and in the upper portions of the spinal cord, that vascular dilatation and circumvascular change take place both in chorea and diabetes; and I venture to suggest that they are induced in the manner I have indicated.

Will the theory I have here advanced offer any explanation of the shifting character of the rheumatic affection? My application of the theory is as follows. Vaso-motor centres are distributed throughout the whole spinal axis. "They can be excited reflexly, but they are also controlled by the dominating centre in the medulla oblongata."¹³ "Now this general vaso-motor centre in the medulla oblongata is really a complex composite centre, consisting of a number of closely aggregated centres, each of which presides over a particular vascular area."¹⁴ Some of the nerve-cells or some portions of this dominating centre may be more readily exhausted by the continued stimulation of an irritant circulating in the blood than the others; and, after the development of the irritant (uric acid) in the system, it will, of course, produce exhaustion, first in these particular cells and in the subsidiary ganglia in connection with them, and so lead to dilatation in the vascular area directly under their control. The other cells in the dominating centre, and the subsidiary ganglia in connection with them, possessing a healthy tone, will be stimulated to action in the normal manner, and contraction will take place in the vascular areas connected with them. This action itself would have the effect of driving more blood to the paralysed vascular area, and intensifying the symptoms there. But, with continued stimulation of these healthy centres, exhaustion will sooner or later be induced; further stimulation increases the exhaustion, and then dilatation of the vessels under their control will be induced; with this dilatation in a new area, the amount of blood in the parts primarily affected will be lessened, and simultaneously will the symptoms which were associated with this increased blood-supply be modified or removed.

If at any time a joint has suffered injury in any way, this joint will be more sensitive than natural, perhaps more easily fatigued; and

we can readily understand that this condition must be associated with some change in that part of the central nervous system which controls the nutrition and sensation in the joint; that this spot in the central nervous system will be more sensitive—more easily acted upon by irritating causes than other parts; that, by the irritation, the nerve-cells in the part will be more easily exhausted; and therefore, in rheumatic individuals, this particular joint will be the one first affected, and perhaps solely affected, in all attacks of rheumatism.

The following most interesting case, which recently came under my observation in Cambridge, illustrates, I think, very well the development of arthritic mischief from irritation of the central nervous system, the irritation being chiefly localised in the medulla oblongata, and affecting the vaso-motor centre.

J. W., aged 54, a labouring man, was working on a stack in the dusk of early morning on December 24th, 1885, when he fell, dropping about eight feet, on to his left side. He walked home, with pain and difficulty, a distance of over a mile; he went to bed, lay there drowsy and without appetite, very helpless, and only just able slowly to move his limbs. After remaining a week in this condition, he was carried into Addenbrooke's Hospital on December 31st, 1885, under Mr. Wherry, to whom I am indebted for an opportunity of seeing the patient, as well as for the notes of the case.

When admitted, he was drowsy and stupid, and answered questions in a dull manner when roused; cutaneous sensation seemed everywhere perfect; movements of the limbs were very slow, difficult, and painful; turning over in bed was a struggling, tedious process. The grip of the hands was very feeble, especially the right; no rigors, no sweats; no bladder symptoms. Bowels confined.

His health had always been good, and he was working daily up to the date of his accident.

January 1st, 1886. Some swelling of the left wrist and fingers, and both ankle-joints, with pain on movement, and tenderness; relieved by an opiate. Heart-sounds normal. Evening temperature, 101.6° Fahr.

January 2nd. Marked swelling and redness of left wrist-joint, and of the joints of the first and second fingers, with oedema, and angry red appearance of the back of the wrist. Slight swelling also of the right wrist and finger-joints. It was extremely tender, and looked as if it would suppurate. Beads of sweat on left forehead; a few small herpetic vesicles are seen along the course of the left supra-orbital nerve; tears and secretion excessive in conjunctival sacs of left eye; pulse 80; considerable oedema of both ankles. Patient is drowsy, and sleeps, except when roused by pain. No general sweating; urine, acid. Bowels open by calomel. Evening temperature, 101.4°.

January 3rd. Redness and swelling in left wrist continues, as well as in both ankles; drowsiness and stupor; mucus in conjunctival sacs of left eyelids, not in the right. The knees usually drawn up in bed, of which movement he does not seem conscious; he can put them down by an effort. Morning temperature, 100.2°; evening, 101.8°.

By Dr. Latham's suggestion, he was cupped at the root of the neck behind, in two places, about two ounces of blood drawn; no relief that night. Evening temperature, 101.6°.

January 4th. He seemed better, and in less pain. Morning temperature, 100.2°; evening temperature, 101.6°.

January 5th. Less pain and tension in the joints; morning temperature, 99.2°. His manner still stupid and dull. Two cups were applied near the lower cervical vertebrae, and two near the lower dorsal vertebrae, and about four ounces of blood drawn. He was ordered to take at once five grains of calomel, and one grain of opium, and a black draught the following morning, if necessary. Evening temperature, 101°.

January 6th. Better. Morning temperature, 100°; wrists and ankles less swollen. Bowels open three times after the calomel. Evening temperature, 101°. Ordered tinct. opii $\mathfrak{m}\mathfrak{x}$, at bedtime.

January 7th. Wrists and ankles better. Complaints of pain in right knee, with some tenderness, but there is no swelling. Morning temperature, 100.4°; evening, 100.8°. Ordered four blisters, $1\frac{1}{2} \times 1\frac{1}{2}$, to four spots along the spine, to be kept open with savine ointment. Opiate to be taken every night.

January 9th. The right foot and ankle more painful and swelled. The other joints better. Morning temperature, 101.2°. Ordered a blister, 4×3 inches, over the lower dorsal vertebrae. Evening temperature, 101.8°.

January 10th. Feels better; has had a good night, has no longer the dull stupid manner, mind clear; was ordered tinct. opii $\mathfrak{m}\mathfrak{x}$ three times a day; the blister to be kept open with savine ointment.

From this time, continuous improvement took place. The evening and morning temperatures fell daily until the 19th, when the evening

⁹ BRITISH MEDICAL JOURNAL, April 10th, page 676.

¹⁰ On Megrim and Sick-headache, 1873, pp. 404-5.

¹¹ On Nervous or Sick-headache, Cambridge, 1873.

¹² March, 1886, p. 181.

¹³ Landois and Stirling's Physiology, London, 1885, p. 854.

¹⁴ *Ibid.*, p. 898.

temperature reached the normal point, and the blistered surfaces were allowed to heal.

There was some oedema about the affected joints after the redness and pain had passed away, but this entirely disappeared by the 23rd. There was still at this date a little tenderness and thickening about the left wrist. The unilateral sweating of the face was noticed from time to time.

February 2nd. The patient's condition much improved. Is sitting up. Has lost all pain, except now and then in left wrist. There is some thickening and stiffness about the joints which were affected, and his grip is still weak, though very much stronger than before.

Dr. Dyce Duckworth, in an extremely suggestive and able essay,¹⁵ contends that gout is a primary neurosis, and that the portion of the nervous system specially involved is situated in some part of the medulla oblongata. I hope that what I have advanced will tend not only to confirm this view, but also—to use the words of Sydenham, which he quotes—to clear up and explain some of “the difficulties and refinements of the disease itself.”

Having indicated the way in which the symptoms of rheumatism and gout may be produced, let me now appeal to clinical experience, and show how far the results obtained from the practical treatment of these disorders supports the view I have here advanced as to their pathology.

If uric acid is the poison, the treatment for both diseases resolves itself into this: to prevent the formation of this substance, and, when formed, to promote its elimination from the system. The kidneys will in time effect the latter if we satisfy the first condition, and we may do this by seizing upon or eliminating the glycochine from the system; for, as this is an essential constituent of uric acid, by removing it we prevent the further formation of that body, and so remove the irritating substance by which the action of the central nervous system is perverted.

In gout, this may be effected, in some measure, by benzoic acid. When benzoic acid is swallowed or introduced into the alimentary canal of a mammal, whether herbivorous or omnivorous, it appears in the urine as hippuric acid, $C_9H_9NO_3$. The urine of adult herbivorous mammals contains no uric acid, this substance being replaced by hippuric acid, which varies in quantity both according to the food of the animal, and according to the amount of work or exercise it has taken. Hippuric acid is also found, though in much smaller quantity, under normal circumstances, in human urine. Now hippuric acid may be decomposed, by boiling it with strong hydrochloric acid, into benzoic acid and glycochine.¹⁶

This action may be reversed; and, by heating benzoic acid and glycochine in a sealed tube to 160° C., hippuric acid is formed.¹⁷ It may also be formed by injecting benzoic acid and glycochine, or bile, into the blood of a living animal.

According to Kühne and Hallwachs¹⁸, benzoic acid, injected alone into the jugular vein, is not converted into hippuric acid, but it is if injected into the portal vein. Meissner and Shepard,¹⁹ however, state that, after injecting benzoic acid into the jugular vein of a rabbit, at first benzoic acid alone appeared in the urine, then more and more hippuric acid, and lastly hippuric acid alone. These experimenters maintain that hippuric acid is formed in the kidneys alone; but benzoic acid appearing first alone in the urine in the above experiment would hardly bear out that view, and Salomon,²⁰ after introducing benzoic acid into the stomach of a nephrotomised rabbit, obtained a decided amount of hippuric acid from the muscles, liver, and blood. Again, when benzoic acid is injected into the portal vein of some animals at least, it appears as hippuric acid in the hepatic vein.²¹ Hippuric acid also appears in the urine, when benzoic acid is swallowed or introduced into the alimentary canal. Here it meets with the glycochine in the bile; and, as they pass into the liver, these are conjugated with elimination of water, forming hippuric acid.

¹⁵ *Brain*, vol. iii, 1880, pp. 1-22.

¹⁶ *Watt's Dict. of Chem.*, vol. iii, 1865, p. 158.

¹⁷ *Ibid.*, p. 156.

¹⁸ *Jahresb.*, 1859, S. 638.

¹⁹ Meissner and Shepard, *Untersuchungen über das Entstehen der Hippursäure*. Hannover, 1866.

²⁰ W. Salomon, *Zeitschr. für phys. Chemie.*, S. 365, 1879.

²¹ *Foster's Physiology*, 4th edition, 1883, p. 441.

The molecule $\text{CO} \cdot \text{NH}$, when the substance forms part of the tissue, is transformed²² into CNOH , and then living hippuric acid would be represented by the formula

having a constitution of the same character as that of the molecules of living albumen. But benzoic acid, after passing through the liver, may be transformed in the tissues in two ways, into hippuric acid, either by being conjugated there with glycochine, or combining with the antecedent of glycochine.

In my previous lecture, I endeavoured to show that this antecedent of glycochine is methene cyan-alcohol $\text{CH}_2 \left\{ \begin{array}{l} \text{OH} \\ \text{CN} \end{array} \right.$, which, acted upon by acids, would form glycollic acid; but, if first treated with ammonia, forms a cyan-amide, and then, hydrated with acids or alkalis, forms glycochine.²³

When this substance and benzoic acid, therefore, are brought together in the tissues we should have

the latter of which, when dehydrated, being converted into benzonitrile,²⁴ this becomes

the formula which I have just shown to be that for living hippuric acid.

It is in this way that benzoic acid acts. It seizes upon the glycochine or its antecedent, and so prevents the formation of uric acid; it passes out in the urine as hippuric acid, and gouty patients undoubtedly derive benefit from its use. Dr. Golding Bird prescribed it in conjunction with phosphate and carbonate of soda, with cinnamon water, as a vehicle in gout. Dr. Garrod says, “I can confidently affirm that I have already obtained great advantage in the treatment of these diseases (gout and gravel) from the employment of the benzoates.”²⁶ Doubt has been expressed whether the benzoates do diminish the uric acid excretion or not. Cook²⁷ states that in a healthy individual the administration of benzoic acid does not stop the formation of the normal amount of uric acid, but masks its presence in the urine and interferes with the murexide test. The later experiments of Dr. Noel Paton,²⁸ however, clearly demonstrate “that benzoate of soda really does diminish the uric acid secretion.” In an abnormal state of things, when there is an excessive amount of

²² See *BRITISH MEDICAL JOURNAL*, April 3rd, page 632.

²³ See page 635.

²⁴ *Watt's Dict. of Chem.* vol. i, p. 563.

²⁵ Glycollic acid and benzonitrile can, in the laboratory, be transformed into hippuric acid, by converting the benzonitrile in benzoic acid and ammonia, this combining with the glycollic acid to form ammonium glycolate, which, when heated, is transformed into glycochine; and then, on combining this with benzoic acid, hippuric acid is formed in the usual way.

²⁶ *Lancet*, April, 1883, p. 673.

²⁷ *BRITISH MEDICAL JOURNAL*, July 7th, 1883, p. 9.

²⁸ *Journal of Anatomy and Physiology*, January 1886, pp. 26-32.

glycocine passing unchanged into the blood, the benzoic acid seizes upon this and converts it into hippuric acid; and so, if glycocine be necessary for the formation of uric acid, the amount of the latter must be correspondingly lessened. The remedy, however, must be given in sufficiently large doses, doses large enough to absorb all the glycocine, and then it may not only prevent the further formation of uric acid, but, as Cook's experiments show, it may render the uric acid already existing in the blood more soluble, and therefore more readily eliminated by the kidneys.

Salicylic acid, or oxybenzoic acid $C_6H_4 \begin{Bmatrix} OH \\ COOH \end{Bmatrix}$ is another remedy which acts like benzoic acid, and this also has been found by Dr. Noel Paton²⁹ to diminish the excretion of uric acid. When administered internally, it passes off by the urine as salicyluric acid—that is, it combines, in its passage through the system, either with glycocine or its antecedent, fer, on treating salicyluric acid with fuming hydrochloric acid, it is resolved into salicylic acid and glycocine.

Consequently, in the system, by seizing either upon glycocine or its antecedent, salicylic acid takes away an essential constituent of uric acid, and so prevents the formation of this body.

As the salicyluric acid passes into the living system, the $CO \cdot NH$ would be transformed into $CNOH$, and the above formula for salicyluric acid would become

or, if salicylic acid combine with methene cyan-alcohol, the antecedent of glycocine in the tissues, it would then undergo similar changes to those I have described for benzoic acid.

In gout, uncomplicated with contracted kidney or albuminuria,³⁰ salicylic acid is often of service.³¹ But it is in acute rheumatism that it shows its special power, acting truly, when properly administered, as a distinct specific. Here is a disorder which, under different treatment, may exist for weeks stationary, so to speak, in its intensity, the great heat and nervous and vascular excitement, and pain and swelling exactly of the same amount to-day as they were weeks ago; a disorder which, less than fifty years ago, was said to be "often such in itself, and such in its appalling incidents, as to need, from time to time, that medicine should put forth the full compass of all its powers. Every organ, or system of organs, which either directly or indirectly can receive the impression of remedies, are, from time to time, called to bear all that they can possibly endure; and it is often only when the powers of medicine are pressed even to the verge of destroying life that life is saved."³²

And now, with or without the administration of a purgative, as the occasion requires, the patient is placed fully under the influence of salicylic acid, and in from forty to sixty hours, not unfrequently in a shorter time, the pains in the joints have subsided, the limbs can be freely moved, and the bodily temperature has reached the normal condition. But more than this—and here the remedy shows its signal power—in no case of rheumatism that has come under my care during the last six years, either in hospital or in private practice, has there been developed, where the heart was previously sound, any cardiac complication, such as endocarditis or pericarditis. If this

can be maintained and ensured, we have, indeed, in our hands, a most potent remedy. Cardiac complications constitute the chief danger of acute rheumatism, and the danger, if the disease is taken in hand soon enough, may, with our new remedy, be averted.

But certain conditions must be observed to ensure success in the administration of the remedy. They are as follow.

First, the true salicylic acid obtained from the vegetable kingdom must alone be employed. If you have to give large doses, avoid giving the artificial product obtained from carbolic acid, however much it may have been dialysed and purified. An impure acid will very quickly produce symptoms closely resembling delirium tremens.

Secondly, give the acid without any alkali or base. A very good form is to mix 100 grains with 15 of acacia powder and a little mucilage. Allow the mass to stand and harden, and then divide into thirty pills.

Thirdly, place the patient fully under the influence of the drug—that is, let him have sufficient to produce cerebral disturbance—that is, buzzing in the ears or headache, or slight deafness; with the development of these symptoms, the temperature and the pain in the joints will begin to decline. To an adult, I generally administer three doses of 20 grains (six pills), at intervals of an hour, and, if the head remain unaffected, a fourth dose at the end of another hour; and then repeat the 20 grains every four hours, until the physiological effect of the remedy shows itself. In the majority of cases, from 80 to 100 grains are enough. In severe cases, 140 to 150 may be required. Afterwards, about 80 grains a day are sufficient; and, as the temperature declines, smaller quantities will develop their physiological effects, 60 or even 50 grains being then sufficient to produce cerebral disturbance. It would appear that, as long as the rheumatic poison is circulating in the system, the physiological effect—that is, the effect it produces in the healthy organism—does not show itself; acting as an antidote, the greater the amount of poison, the larger must be the dose of the remedy; but, as soon as the formation of the *materies morbi* is stopped, then the excess of the remedy acts as it would in the healthy organism, and its peculiar physiological effects are developed. It is a very striking illustration of the difference between the therapeutic effect of a remedy and its physiological action.

Fourthly, give the patient from 40 to 80 grains daily for ten days, after all pain and pyrexia have passed away.

Fifthly, let the patient's diet consist entirely of milk and farinaceous food for at least a week after the evening temperature has been normal. On the other hand, if the patient have meat and soup, you may look forward with fair probability to a relapse.

Sixthly, take care to maintain a daily and complete action of the bowels. Calomel is the best purgative, from 2 to 5 grains at night, followed in the morning, if necessary, with a saline draught. This is the most important adjunct to the action of salicylic acid, and I will presently explain to you why this is the case.

Seventhly, let the patient be enveloped in a light blanket, and with no more bedclothes than are sufficient to keep him from feeling cold. The object of the treatment now is to cool the patient—not, as in former times, to sweat the poison out of him; and the cooler he is kept, the sooner will the temperature be lowered. In fever, increased heat increases the metabolism, just as in a cold-blooded animal.³³

These are the seven rules upon which I act. I have given the true salicylic acid, where there have been both aortic and mitral mischief; and I have also given it in rheumatism complicated with pericarditis, and, as yet, I have seen no bad result from it. Of course, in cases of pericarditis, accompanied with delirium, the use of the remedy requires caution; you cannot tell when the system is saturated with the remedy, and you must therefore trust to smaller doses and other means for controlling the disease. Further, if pericarditis or endocarditis, pneumonia, or pleurisy, have been developed, the remedy is powerless over the mischief which is done; it will neutralise the poison producing the mischief, so as to stop its extension; but the inflammatory exudations will undergo their usual changes, unabbreviated in their course. We see the same thing in tonsillitis. Given early enough, salicylic acid will stop the mischief; but, if exudation of lymph have taken place, salicylic acid is powerless to cause its absorption.

There is another important point to be noticed here. In my first lecture I showed that, from condensation of two molecules of

$CH_2 \begin{Bmatrix} OH \\ CN \end{Bmatrix}$, lactic acid and carbonic acid could be formed.³⁴ By seizing, therefore, upon this antecedent of glycocine, salicylic acid lessens the formation both of uric acid and of lactic acid.

During the administration of even large doses of salicylic acid in

²⁹ Loc. cit., p. 25.

³⁰ Paton's experiments show "that this drug has really an irritating action on the kidneys," loc. cit., p. 25.

³¹ See Dr. Dyce Duckworth's remarks on the use of salicylate of soda in gout. *Year-Book of Treatment for 1884*, p. 81.

³² Dr. P. M. Latham's *Works*, New Sydenham Society, vol. i, p. 112.

³³ Stirling and Landois, *Physiology*, page 451.

³⁴ See BRITISH MEDICAL JOURNAL, April 8rd, page 635.

rheumatism, a certain amount of uric acid is still sometimes excreted by the kidneys. How is this to be explained?

As the molecular constituents of albumen fall asunder, the molecule $\text{CH}_2 \begin{Bmatrix} \text{CNOH} \\ \text{CNOH} \end{Bmatrix}$ may become detached, and, as it passes from the living tissue, the CNOH would be transformed into CO-NH, consequently the above molecule would be converted into hydantoin $\text{CH}_2 \begin{Bmatrix} \text{CO-NH} \\ \text{NH-CO} \end{Bmatrix}$ which, having little affinity for salicylic acid, would pass on to the glands, and, conjugated with urea or biuret, pass out of the system as uric acid.

I have referred to the necessity of keeping up daily and sufficient action of the bowels. The benefits resulting generally, in rheumatism, from the so-called purgative plan of treatment, have always been recognised by the older physicians as striking and satisfactory. By the judicious use of cholagogue purgatives, we eliminate the bile from the intestines, and so remove from the system a quantity of glycocine, which, if re-absorbed, would lead to the consequent formation of uric acid. Calomel is unquestionably of service here. Doubts may exist as to whether it promotes the flow of bile from the liver, or not; but when the bile gets into the intestine, calomel will cause its evacuation. "The conclusion seems inevitable, that mercurial purgatives given to healthy persons cause the escape of large quantities of bile from the alimentary canal."³⁵ Referring to the three modes of treatment—by venesection, by opium, and by purgatives—which were in vogue at the time, Dr. P. M. Latham says, with regard to the last: "As this plan of treatment works prosperously day after day in its immediate effects, so day after day it gives an earnest of the remedial impression it is exercising upon the whole disease. It abates the fever, it softens the pulse, it reduces the swelling, and it lessens the pain. In short, in subdues the vascular system like a bleeding, and pacifies the nervous system like an opiate; and often, in the course of a week, the acute rheumatism is gone. In three days, there is often a signal mitigation of all the symptoms; and in a week I have often seen patients, who have been carried helpless into the hospital, and shrieking at the least jar or touch or movement of their limbs, risen from their beds, and walking about the ward quite free from pain.

"Of this plan, often so striking in its operation, and often so satisfactory in its results, I have some further remarks to make. It is called the purgative plan; yet its purpose is achieved by calomel and purgatives conjointly. The purgatives would not answer the end without the calomel; of that I am quite certain; neither would the calomel answer without the purgatives, unless it produced of itself ample evacuations from the bowels. It is probable, in short, that the remedial efficacy of the plan resides essentially in the calomel; in calomel, however, not as mercury, but as itself—calomel. If the specific effect of mercury—salivation—arise, it is not only beside our purpose, and against our wish, but it begets a serious hindrance to the use of calomel in sufficient quantity for the end in view. Thus the whole plan is frustrated. Having begun one plan of treatment, we are obliged to take up with another: Time is lost, the case is perplexed, the disease is prolonged, and the patient perhaps injured."

"Now, if in the treatment of acute rheumatism, you were to choose one indication and abide by it, and were to trust one class of remedies, and to it only, you will find more cases that admit of a readier cure by the method now described, than by either of the two former. You would find the aggregate of morbid actions and sufferings, which constitute the disease, more surely reached and counteracted, and more quickly abolished by medicines operating upon the abdominal viscera only, than by those which influence either the blood-vessels only, or the nerves only. You would find in calomel and purgatives, a better remedy than either venesection or in opium."³⁶

In the earlier attacks of gout, too, I have often seen marked relief follow the administration of calomel and a saline cathartic. Where there is high arterial tension, as in the gouty paroxysm, this may be distinctly lowered by these remedies. They check the further formation of uric acid, which is stimulating the vasomotor centre, and causing the increased arterial tension, by eliminating the bile from the intestines. In some persons, calomel has a depressing effect, and, when the kidneys are unsound, is injurious in its action. Where calomel is inadmissible, a gentle laxative, such as rhubarb, is often of service. When the object is simply to unload the bowels in a debilitated subject, it is the best purgative. It is said to act chiefly by increasing the peristaltic action of the bowels throughout their entire

extent, but especially that of the duodenum. According to Rutherford, it is a cholagogue. Sir Henry Hallford recommended, as a prophylactic remedy against gout, a few grains of rhubarb, with double the quantity of magnesia every day; or some light, bitter infusion, with tincture of rhubarb, and about fifteen grains of bicarbonate of potash.

The saline cathartics probably act only by causing serous evacuations, and, in that way, carry off from the blood some of the poison contained in it. They may also act beneficially, perhaps, by relieving a congested liver.

The diet is another important point to be attended to in the treatment both of gout and of rheumatism. It should be simple and nutritious; jellies and food containing gelatine should be avoided, as this substance furnishes glycocine. Animal food will not, itself, produce uric acid in a healthy system, as is shown in its absence in the urine of the carnivora; but from all kinds of meat a certain amount of glycocine will be produced, and, even if all the rest of the nitrogenous portion, after being absorbed into the system, were converted into urea, this would necessitate an increased elimination of urea, and consequently a greater tax on the powers of the kidneys. If these powers be weakened, there will be, with an increased call upon the organs, less power to act; and not only will the urea, but, still more, the uric acid, accumulate in the blood. The striking benefit and increased urinary secretion, which result in some forms of albuminuria from a skimmed-milk diet, that is, the simplest of all diets, very well illustrate what I mean here. The presence of urea in the blood may, by its action on the nerve-centres, determine an increased blood-supply to the kidneys, and so, in a healthy state of things, an increased secretion; but, if the secretory portion be damaged, or the nerve-force controlling it defective, an increased flow of blood to the part, producing a congested condition of the organ, would not expedite, it would rather hinder, the work of the secretory portion. The simpler the diet, then, the less tax there will be upon the kidneys, and the better they will do their work. Let the diet, then, be chiefly farinaceous, with just sufficient nitrogenous food to satisfy the wants of the system; and, in the acute attacks, let that be in the form of milk, diluted even, if necessary.

The explanation which I have here offered of the symptoms of a gouty paroxysm, helps us to understand the beneficial action of colchicum in this disorder. According to Dr. Lauder Brunton,³⁷ this drug paralyses the sensory nerves, the motor nerves and muscles being unaffected. It seems to act best when the bowels are previously acted upon. If in gout, then, uric acid during the paroxysm be stimulating the sensory nerves, and, through them, the more active portion of the vaso-motor centre, and we paralyse the sensory nerves with colchicum, the uric acid no longer produces its effect, and the paroxysm ceases; but colchicum has no effect in preventing the formation of uric acid, and, after the paroxysm, we must endeavour to prevent its recurrence, by putting a stop to the formation of the poison, which we may effect by eliminating the bile from the intestines by mercurial or other purgatives, by giving benzoic or salicylic acid, and by suitable diet. In large doses colchicum will cause purging, but marked symptoms of collapse supervene, so that it is not safe to administer the remedy in this way.

It remains for me to say a very few words with regard to the pathology of diabetes, and to explain why I have classed it together with gout and rheumatism. If the function of the liver be interfered with, so that there is imperfect metabolism of glucose as it passes through the organ, this would be a satisfactory explanation of the origin of the disease, and we should expect in such cases that the urgency of some of the symptoms would be lessened by careful diet, abstention from saccharine and starchy food. But there are other cases in which the diet seems to have much less effect in controlling the symptoms; it is this form that I wish briefly to discuss.

I have endeavoured to show that in acute rheumatism, by the separation of the cyan-alcohols $\text{CH}_2 \begin{Bmatrix} \text{OH} \\ \text{CN} \end{Bmatrix}$ and $\text{C}_2\text{H}_4 \begin{Bmatrix} \text{OH} \\ \text{CN} \end{Bmatrix}$ from the rest of the albuminous chain, we have glycocine, and glycollic and lactic acids formed; the glycollic acid being oxidised into CO_2 and water, the lactic acid, in some measure, being oxidised into these products, and in some measure passing off by the skin. But suppose that, whilst the vaso-motor fibres of the muscular nerve are paralysed and the vessels dilated, the molecules $\text{CH}_2 \begin{Bmatrix} \text{OH} \\ \text{CN} \end{Bmatrix}$ are detached and hydrated into glycollic acid, but only partially oxidised, the result would be that the glycollic acid would be transformed into carbonic acid and methyl aldehyde and water.

³⁵ H. C. Wood, junr., *Treatise on Therapeutics*, 2nd ed., 1877, p. 435.

³⁶ Dr. P. M. Latham's *Works*. New Syden. Soc., vol. i, p. 123, 124.

³⁷ *Pharmacology*, 1853, pp. 968-9.

Condensation of six molecules of the aldehyde may then take place, as in plants, forming glucose

By urari, as I have already stated, we can put a stop to muscular contraction, that is, to the oxidation of the muscular elements and to formation of CO_2 when the muscular nerve is stimulated. If then the tissue be, so to speak, partially urarised, the aldehyde is not oxidised, but condenses into glucose. In urari poisoning, sugar appears in the urine, though "the exact way in which this form of diabetes is brought about has not yet been clearly made out."³³

Let me carry you one step further in the comparison between rheumatic fever and diabetes. If in rheumatic fever the central part of the nervous system connected with the muscular nerves be so enfeebled that there is complete dilatation of the vessels in the muscular area, and a falling asunder not only of the molecules $\text{CH}_2 \begin{cases} \text{OH} \\ \text{CN} \end{cases}$ but also of the molecules $\text{C}_2\text{H}_4 \begin{cases} \text{OH} \\ \text{CN} \end{cases}$ and $\text{C}_3\text{H}_6 \begin{cases} \text{OH} \\ \text{CN} \end{cases}$ then, by the hydration and oxidation of these, hyperpyrexia would, in some measure as I have suggested, be developed. But if the complete oxidation of these molecules were interfered with, the $\text{CH}_2 \begin{cases} \text{OH} \\ \text{CN} \end{cases}$ would give rise in the manner

above indicated to glucose. By hydration, $\text{C}_2\text{H}_4 \begin{cases} \text{OH} \\ \text{CN} \end{cases}$ would be converted into lactic acid, which, if not completely oxidised into carbonic acid and water, would be first oxidised into carbonic acid and aldehyde.

the aldehyde by condensation forming para-aldehyde, a remedy recently introduced as a hypnotic. Hence the commencing drowsiness in some stages of diabetes.

If the molecules fall still more completely asunder, and the molecule $\text{C}_3\text{H}_6 \begin{cases} \text{OH} \\ \text{CN} \end{cases}$ become detached and hydrated into oxybutyric acid, but only partially oxidised, then from one form of this acid, acetone would be formed

which appears in the urine towards the termination of the disease. So, then, in hyperpyrexia, there is detachment of the molecules from the benzene nucleus, with their hydration and rapid oxidation; whereas, in acetonaemia, there are detachment and hydration, but imperfect oxidation of the molecules. That is to say (if this theory is correct, and such experiments were possible), by urarising an individual suffering from rheumatism with pyrexia, the urine would become saccharine; if hyperpyrexia were present; by urari the disorder would be transformed into acetonaemia.

Now, you will find that, in some forms of diabetes, salicylic acid is of the greatest service; whereas, in others, no good results from its use.

Given in doses of from ten to twenty grains three times a day, I have frequently seen it produce marked improvement; and Dr. Holden, of Sudbury, has shown me notes of cases, about to be published, where rapid amelioration of the symptoms has resulted from its use.

The urine in these cases contains often, in addition to glucose, an excess of uric acid, and the patients suffer from neuralgic pains in the joints and limbs. It also, not unfrequently, contains some substance which dissolves cuprous oxide, and so more or less interferes with the application of Fehling's test. What this is, has not yet been determined. My friend, Mr. Pattison Muir, kindly examined some specimens, and made out that it is some substance which readily dissolves calcic phosphate. Possibly it may be glycollic or lactic acid. If further examination should prove this to be the case, it would go a long way to support my view of the origin of this form of diabetes.

I have thus endeavoured to indicate some of the changes in the nervous system, the blood, and the tissues, which may take place in diabetes, rheumatism, and gout, and to enlarge upon the text furnished by a far-seeing pathologist,³⁴ when he wrote: "Disturbance in the nervous system, in some part and form, may be regarded as a factor in every case of gout. There are reasons enough for thinking that changes in the nervous centre determine the locality of each gouty process, while changes in the blood and tissues determine its method and effects; and that thus we may explain the symmetries of disease in gout—sometimes bilateral, sometimes antero-posterior—and thus its metastases."

My task is done. It only remains for me to thank you, Mr. President, and the Censors, for giving me an opportunity of placing my views before the College; and to thank the distinguished Fellows and Members who have listened to me. I have brought together a number of facts, and endeavoured to draw certain inferences from them. The inferences may be wrong, but the facts remain; and I trust that in this way, at least, I may have helped to a better understanding of these disorders.

ON THE DIFFERENTIAL DIAGNOSIS OF DISTENSION OF THE FALLOPIAN TUBES.

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THE title of Dr. Horrock's paper "A Pelvic Tumour," seemed to invite friendly suggestion or criticism. But the further consideration of a particular case, the exact nature of which may probably never admit of absolute proof, will be unprofitable: while the broad question of the differential diagnosis of a distended Fallopian tube from uterine myoma is an important one, and its discussion may be eminently profitable.

And because I do not quite agree with Dr. Horrocks in the leading features of this differential diagnosis, I desire to point out what, in my experience, are the chief marks of similarity and difference between the two diseases.

1. Menorrhagia may be common to both diseases, but in uterine myoma it is painless, in tubal disease it is very painful.

2. Moderate enlargement of the uterus (from 3 to 3½ inches) is present in tubal distension accompanied by hæmorrhage (as in most cases where metrorrhagia is a prominent symptom); an enlargement beyond this may generally be expected in myoma.

3. The tumour formed by distension of the Fallopian tube is always single or double, and is always posterior to the uterus; nodular myoma is usually multiple, and the situation of the outgrowths variable.

4. The tumour formed by a distended tube, even when chronic and quiescent, is always very tender to touch, whether that touch be from the examining finger of the surgeon, or from the passage of scybala through the rectum; a myomatous nodule, unless inflamed, is comparatively insensitive. Probably, for a similar reason, dyspareunia is a very general symptom of tubal disease, but is almost unknown in myoma.

5. The outline or shape of a distended tube is fairly constant, in possessing a longer and a shorter axis; that of nodular myoma is round or quite irregular.

6. The tumour caused by a distended tube varies in its firmness or consistency, and at some time or other will show signs of elasticity or fluctuation; that of nodular myoma remains hard.

7. Both a distended tube and myoma of the posterior uterine wall may sink lower in the pelvis by causing retroflexion of the uterus; but, apart from this, the former, although adherent, tends to sink slowly by its own weight; the latter reaches a lower point only by increased growth.

8. When pregnancy occurs, the uterine enlargement being caused chiefly by the development of the muscular tissue of the uterus, a myoma of this tissue will be much more likely to be raised by the growing uterus than a distended tube, which is only adherent, and often but lightly, to its peritoneal investment.

In the case referred to in my paper of March 20th, the tube has remained in its original position during the progress of the pregnancy.

The only other condition that is likely to be confounded with distension of the Fallopian tube is cyst or abscess of the ovary. A special form of cystic disease of the ovary is often, perhaps generally, combined with occlusion and distension of the tubes; and if the latter

³³ Foster's *Physiology*, 4th edition, p. 425.

³⁴ Sir James Paget, *Clinical Lectures and Essays*, 1879, p. 332.