"Some introductory notes concerning the nature of Rheumatism."

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Some introductory notes concerning the nature of Rheumatism.

Most authors and investigators commence their writings on the subject of rheumatism by objecting to the name given to the complaint. When the condemnation is so universal, little need be said here: the question of the undesirability of the term is well set forth by the late Dr. T. D. Miller Fothergill in his "Practitioner's Handbook" (3rd Ed., p. 259). "The term 'rheumatism' ought to be expunged from our vocabulary. It is a crotchet to those who are diagnostically weak, and has given a false sense of security in many grave diseases, and tended to hide the real nature of the malady."

For our present purpose, we may briefly describe the complaint under discussion as an arthritis, characterised in its acute form by pyrexia, diaphoresis, and a special tendency to visceral implication.

Various theories have been enunciated - especially during the last 65 years, - to explain the actual nature of rheumatism; and these theories we may divide or classify in four principal groups: I. the Nervous; II. the Chemical; III. the Neuro-chemical; and IV. the Bacillary, or Infective (including the Viralistic). A fifth theory, which ascribes the affection to a disturbance of the heat-centre...
can scarcely be seriously entertained, as it in no way explains either the joint troubles, or the cardiac lesions. [The actual author of this theory I have been unable to discover, but in Cullen's "Practise of Physic", published in 1784 (chap. xiii.) the articular lesions are attributed to the direct influence of cold upon the joint structures, which were thought to be especially exposed to this influence, because of their thinner covering.]

1. The Nervous Theory. - Dr. T. K. Mitchell, in the Amer. Jour. Med. Science, (1831. vol. viii. p. 56. and 1833. vol. xii. p. 361.) first suggested that rheumatism is due to a lesion of the spinal cord or medulla oblongata, where it is supposed that the centre concerned in joint nutrition exists. The lesion is said to be due to irritation conveyed by the different nerves from an area exposed to a chill or damp - Caußtalt (Die Specielle Pathologie und Therapie. vol. i. p. 604.) thinks that vasomotor changes alone are sufficient to account for this; and Buzzard (Diseases of the Nervous System. 1862. p. 256.) considers that the joint nutrition centre is situated in the immediate neighbourhood of the sweat-controlling centre in the medulla. Mr. Jonathan Hutchinson has expressed his acceptance of the Nervous Theory of Rheumatism, which, he says, is, in short, a catarrhal neuritis, the exposure of some tract of skin or mucous membrane to cold or

The chief objections to this theory are, that it, in no way, accounts for the visceral lesions; that it regards cold as the principal, if not the only, factor in the etiology of the disease; whereas as Sir B. N. Dalton has pointed out in the Brit. Med. Jour. (1890. Vol. I. p. 472) rheumatism may be acquired by breathing the emanations of foul sewers. Further, the use of alkalies and salicylates—al present—the popular drugs given in cases of rheumatism—is totally at variance with an unqualified acceptance of the theory. It is quite possible, as we shall see shortly, that the nervous system is involved; but it is hard to see how the various phenomena can arise entirely from a lesion of this nature.

II. The Chemical Theory—or theories, for there are at least two (a) Prout's Lactic Acid and (b) Harvey's Urac Acid Theory.

(a) The Lactic Acid Theory was first enunciated by Dr. Prout in a lecture delivered at the College of Physicians. D. E. A. Garrod, in his Treatise on Rheumatism (1890. p. 15) says, "Probably the theory which has obtained the most general acceptance, in this country at least, is that which attributes the disease to the presence in the system of an excess of lactic acid, which is supposed.
to play a part analogous to that of uric acid in gout."

In 1858, Dr. Steny W. Richardson ("The causes of coagulation of the blood," 1858, p. 377) in experiments performed on dogs by the injection into the peritoneal cavity of a 10 per cent. solution of lactic acid produced endocarditis, accompanied in some cases by pericarditis, in some by arthritis. Discredite has been thrown on these results by Rayfer, (Virch. Archiv. 1861, vol. xxv, p. 285) who shows that, in over thirty dogs examined by him, in which no experimental injections were made, there were no changes in the endocardium similar to those obtained by Richardson. And this objection is upheld by the researches of the Müllers. Still it must be noted that Richardson detected the gradual incidence of cardiac murmurs during life, and found arthritis in some cases.

A second series of results, this time obtained from the human subject are those of Dr. Ballhazan (now Sir Walter) Foster, of Birmingham (Brt. Med. Jour. 1871, vol. xi, p. 720. "The Synthesis of Acute Rheumatism.") He found that when he administered the lactic acid in doses of m.xv-ixxx, 15 patients suffering from diabetes, he caused painful swellings in the joints, and shooting pains travelling about the body. This was especially noticeable in one case, where the drug having been stopped, at the patient's request it was repeated owing to the relief from the diabetic
Troubles which it afforded. The pains returned again on the second day, and six successive arthritic attacks accompanied by pyrexia and diaphoresis were thus produced. In confirmation of these results, Küly (Beiträge zur Pathol. und Therap. des Diabetes, 1872, vol. ii. p. 166) describes a case in which pain in the left hip and thigh followed the use of the same drug.

We must however not lose sight of the fact that both the drug acidum lacticum and sarcobactic acid found in muscle, although both are ethylidene lactic acids (CH₃CH(OH)COOH) and therefore isomeric, differ essentially from one another, the animal acid having a distinct rotatory power over polarised light which is not possessed by that obtained by the fermentation of sugar.

There have doubtless been many cases where the administration of lactic acid has not been followed by joint troubles, but as Senator says (Ziemess's Handbuch, 1879, vol. xiii. i.), “negative cases do not count for much, for there is undeniably always a “personal susceptibility” with which we must reckon.”

An objection to the deductions drawn from the above cases of Foster and Küly, might be made by those who agree with the theory of Dr. Haig, to which we shall shortly allude. To put it briefly, Haig considers uric acid to be the “materies morbi,” and
he states that anything which reduces the alkalinity of the blood will cause arthritis. Acids will do this, and, of course, lactic acid falls under this category. But we cannot overlook the fact that so does salicylic acid, which, although not such a powerful acid as lactic, weighs for weight, in neutralising an alkali, is still one both physically and chemically according to Cechardt’s definition, and containing equally the carboxyl group (COOH); and further, we shall see it is one of the most valuable and potent remedies for the disease.

Dr. Hilton Fagge, in his ‘Practice of Medicine’ (vol. ii. art. ‘Rheumatism’), when speaking of this theory, wrote: ‘The lactic acid from muscular exertion is not oxidised or excreted, but accumulates, and acts as an irritant to the joint tissues.’ A strong argument against this view has been carried by Dr. Fuller (‘On Rheumatism, Rheumatic Gout, and Sciatica’, 1860), and by Dr. Macleod (‘Rheumatism’, 1881). They protest — and with reason, that it is unlikely that all the poison would be thus produced at the commencement of the attack, and not slowly given off during its prevalence. Dr. Fuller (op. cit.) considers it probable that the lactic acid continues to be produced during the faulty conditions of assimilation which obtain.

Forringill (‘Practitioner’s Handbook’, p. 260) wrote: ‘When glycopen is given off into the general circulation, it is
converted back again into sugar. This sugar is broken up into lactic acid, which unites with the alkalies in the body and forms lactates. Headland supposed that it is the oxidation of lactates which gives rise to the body heat, and these views are borne out by the researches of Ludwig and others. Each molecule of soda turns off many molecules of lactic acid during its residence in the organism. This is, however, a point to which we shall have occasion to refer later on.

It must be stated that Salomon ('Charité Auslese', 1850, vol. i. p.137) actually failed to detect lactic acid in the venous blood of rheumatic patients, although he did find it in the blood of those who suffered from leucocytocrasia. We must remember that the method of analysis employed, depending on the crystalline form of the lactate of zine, is complex, and might possibly be a source of error.

This naturally brings us to the question: 'Is the sweat of rheumatism acid?' and 'Is the acidity, if present, due to lactic acid?' It was owing to a belief that an affirmative answer was to be given to these questions, that Poulet first evolved the lactic acid theory. M. Favre ('Arch. gén. de Méd. 1853, vol. ii. p.1') did actually detect the acid, and was even able to turn the lactate
of zinc which he obtained; but more recent investigators have not been so successful. In fact, Sir Alfred Garrod ('Repertorium Sientae Medicinae', vols. i. and II. 'Rheumatism'), Dr. A.E. Garrod ('Treatise on Rheumatism'), and M. E. Bannier ('art. 'Rheumatism' in Dider. Encyklop. des Sci. Méd. ) deny that the sweat is particularly or invariably acid; whilst M. Salomon (op. cit.) goes further, and affirms that the sweat is never acid if freshly collected from an absolutely clean surgoce.

Dr. Percy Childs, in his recently published book, 'Rheumatism: Some Investigations respecting its Cause, Prevention and Cure' (1892, p. 22) says that the salivary as well as the sweat is acid in the condition which he calls "arthropenia", which he states is always to be found preparatory to, and accompanying, rheumatism. Dr. R. W. Lathms also, in the Grosham Lectures for 1886 ('Some Points in the Pathology of Rheumatism, Arthritis and Diabetes', p. 36) says, "The more acute and severe the case, the more profuse and acid is the perspiration, and the larger the amount of lactic acid it contains." To both these authors we shall have occasion to refer again, but what we have quoted now is sufficient to show that recent authors still believe in the acidity of the sweat, which acidity they regard as due to lactic acid.

(3.) The Uric Acid Theory. Dr. Haig (Wood's 'Medical and Surgical Monographs', Feb. 1890; 'Salicylic compared with
Salicylate of Soda as to effect on the excretion of uric acid, etc. Med. Chin. Trans. vol. lxxiii. p. 297. "The causation of acute rheumatism," Practitioner. Feb. Med. Apr. 1891; and "Uric acid as a factor in the causation of disease." 2nd Ed. 1894. p. 197. has been very zealously working for some years past to prove that rheumatism, like gout, is due to uric acid. He considers that we may have "uric acid storms" (which manifest themselves as migraine, eczema, chorea, rheumatism, gout, etc.) when the blood becomes less alkaline, and uric acid circulates in the system. In this way, he says, the uric acid is brought to the joints and synovial membrane, which are less vascular, and consequently less alkaline, and in consequence the uric acid is precipitated.

In the same way the valves of the heart become affected and when once a small window is formed, the alkalinity of the neighbouring tissues may be decreased, and a permanent lesion may result. The effect of the administration of alkalis and salicylates is to increase the alkalinity of the blood, and, at the same time, to eliminate the uric acid.

Dr. Haig has shown (Med. Chin. Trans. vol. lxxiii. p. 200) that, "roughly speaking, salicylate of soda has about thirteen times the excretory power of salicin, weight for weight, and that salol is intermediate, much weaker than a salicylate, but stronger than salicin." It seems a
Only that he did not experiment also with salicylic acid, for in the "Report on acute rheumatism written of the Collective Investigation Record of the Brit Med Assoc." (vol. iv. p. 75) we find that, whereas the average duration of the whole attack treated with salicylates was 1903 days, and with salicylic acid was 23.92 days, the duration when salicylic acid was used was only 10.7 days. This seems the more extraordinary, because Dr. Haix regards an acid as an exciting cause.

Thus the quote (Med. Afr. Trans. vol. lxxxiii. p. 203) from the "Lady" (1874. vol. i. p. 231) "a case in which Dr. Wilson gave dilute nitric hydrochloric acid, &c. by antiseptic means, with milk, bread and beef tea as a diet," and the patient's temperature on the ninth day was still 101° F., and it was not until the fourteenth day that the joint swelling was gone, and the urine alkaline. This should be compared with the table given by the late Dr. Hilton Fagge ("Lancet," 1881. vol. ii. p. 103). Here we find their patient treated with nitric complain well on the 7th-11th day, with alkalies on the 4th-9th, and with salicylates on the 2nd-6th day.

Again, in "The causation of acute rheumatism" ("Practitioner," Apr. 1891. p. 271.) Dr. Haix refers to the statement that Dr. Shawl, of Cardiff, by injecting phosphoric acid into the blood was able to produce "undoubted evidence of Endocarditis Acid." (Ibid. Med., p. 193) he explains Dr. Foster's results from the administration of lactic acids to diabetics — to which we
have already referred (p. 14) — by stating that “any acid would have done, provided it raised the acidity of the urine and diminished the alkalinity of the blood.”

Lastly, our author refers to the personal experience of Dr. Samuel Brunton (ibid. p. 191) who suffered from an attack of gout when in the Riviera. This attack Dr. Freeman of San Remo, who was consulted, rightly attributed to the use of red wines, which are always acid.

These examples would all show that an acid, by diminishing the alkalinity of the blood, may increase the amount of uric acid present, and so cause arthritis.

But, as we have seen, one acid at least, viz. salicylic, does not do so; in fact, according to the Investigation Record (quoted above) it forms the most potent remedy. Dr. Latham (Goon. Lectures, 1866, pp. 91-95) explains its action in detail, and insists emphatically that it should always be administered in full doses to produce the physiological effects, and without any alkali or base.

Before passing to the next theory on our list which we shall find resembles this one in many ways, I would give a quotation from Halliburton (Text book of Cream, Pulpit, and Pathol. 1891, p. 307) which bears upon the question: “Although we have no positive knowledge of the poison, we at any rate possess the negative information that it is not uric acid, and so rheumatism and rheumatic arthritis are easily distinguishable
from gout, where undoubtedly sodium urate is the poison. (Good.)

The Neuro-chemical Theory, associated especially with the name of Dr. Lathams of Cambridge, and in the most able manner, enunciated by him in the Croonian Lectures for 1886. It is a difficult matter to describe this theory in detail, without transcribing the major part of his volume, but we will here attempt merely a brief résumé.

It is a well-known physiological fact, that when any part of the animal body is exposed to cold, we find a constriction of the cutaneous vessels of the area, and reflexly through the vasomotor centre in the medulla oblongata, a dilatation of the deeper vessels of the muscles. This increased blood supply means increased tissue metabolism, and therefore we get a greater production of heat, and of lactic acid (CH₃CHOH.COON) and glycotic acid (CH₂OH.COON).[Speck. p.72]. Their formation from glycogen (C₆H₁₀O₅). [Sheridan, Chemical Bodies of the Animal Body. p.129] uses up all the available oxygen, and instead of being completely oxidised to carbonic acid gas (CO₂) and water (H₂O), they pass into the circulation in their present form.

At the same time (Croon. Lect. p.32) there is an increased production of glycotine (amido acetate acid, CH₃NH₂.COON) from which uric acid is formed, which, in turn, during its circulation stimulates the vasomotor centre, causing a vascular constriction in the muscular area, and thus we may get
a return to the normal state of affairs. This cycle of events Laithwaite considers to be the explanation of an ordinary feverish cold.

Uric acid, our author regards as the real poison of rheumatism as well as of gout; in the latter, it is formed in the liver from the excess of the glycocine produced there, either from imperfect metabolism due to a want of harmony between the vascular dilatation and the activity of the liver cells, or from too great a supply of nitrogenous material by the portal vein (ibid. p. 71). In rheumatism, on the other hand, the glycocine is produced in the muscles from imperfect metabolism (ibid. p. 76). It is conveyed by the blood to the liver and spleen where it becomes hydrocyanate (glycochyl urea, \( \text{NH}_2\text{CO} \)), and finally (ibid. p. 62) uric acid (\( \text{CO}_2 \text{NH} - \text{CH}_2\text{NH}_2\text{CO} \)).

Returning to the consideration of the phenomena of a feverish cold, we saw that uric acid stimulated the vasomotor centre. But, granted for a moment, that this centre is impaired (either by heredity, or acquisition), it no longer reacts to the stimulation by the uric acid, the vessels in the muscular region become more dilated, more heat is evolved; and more lactic acid is produced which, in its turn, stimulates the sweat centre, and thus aids its own elimination by the skin. Such an explanation completely
agrees with the symptoms, fever and diaphoresis. We shall see how it accounts for the arthritis and visceral lesions.

Dr. Latham (ibid. p. 79) considers that the uric acid in excess acts on the nerve cells concerned in joint nutrition — these cells being now generally regarded as being situated close to the origin of the vasa (Russell's "On affections of joints in locomotor ataxia," Brit. Med. Journ. 1861. vol. i. p. 333). Their natural function is thus impaired, and inflammation of the joints results.

The shifting character of the rheumatic affection is best accounted for in Dr. Latham's own words (ibid. loc. cit. p. 33):

"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." (Laddie and Sterling's "Physiology," 1885, p. 354). 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" (ibid. p. 898). Some of the nerve cells, or some portion of the dominating centre may be more readily exhausted by the continued stimulus 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 irritation exhaustion, first in these particular cells, and in 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 will be lessened, and simultaneously will the symptoms which were associated with this increased blood supply be modified or removed."

The visceral lesions as well as tonsillitis, chorea, and erythema which have all a definite relationship to rheumatism are all explained by Latham, on the same reflex principle and need not detain us now. The theory is a beautiful one, and is worked out with the greatest skill and ability - the one great objection brought against it being that one cannot find either the lactic acid, or the excess of uric acid in the blood. In some respects, it resembles Hay's theory, but it differs from it because Hay thinks the excess of uric acid is lodged in the joints, Latham that
The Miasmatic and Infective Theories.

The first of these which is now associated with the name of Dr. Maclean, is first hinted at in 1809 in a letter written by Dr. Saunders to Haqqart, in which rheumatism is described as "an ague in disguise." Dr. Maclean, in his work on "Rheuma" (1831) includes the lactic acid theory in his explanation, for he states that this acid is produced by the disintegration of the miasmatic micro-organisms.

Some support is afforded by the researches of Th. Kemp, in Amsterdam ("Rheuma: acute. acuti: Nederlandse Tijdschr. voor Geneeskunde, 1836, Aug. 6. p. 143") in which he shows that the prevalence of rheumatism varies inversely with that of ague in that city.

There seem to be, at least, three great arguments against this theory: first, that in the "Reports on acute rheumatism cases" made to the Collective Investigation Committee of the Brit. Med. Assn. (Record, vol iv. p. 74) the greater number of cases by far occurred in "high, dry and exposed" localities, and only 2 out of a total of 646 cases in "damp, confined" localities. (It is true, however, that Dr. Syme, who wrote the report, says that "no facts of real value come out under this head," and 47.66 percent occurred in a "cold, damp, cold, and cloudy atmosphere")
Secondly, Quinine, the great remedy in ague, has but little power in rheumatism: in fact, owing to the reduction in the amount of nitrogenous excretion which follows its use (Mitchell Bruce, "Materia Medica and Therapeutics", p.263) it is probably injurious. Since writing the above, I found in Haig's "Uric Acid" (2nd Ed. 1894, pp.22-23) the statement that he finds that quinine increases the excretion of uric acid, which, he believes, it accomplishes "by contracting the spleen, a well known reservoir of uric acid." The statement of Haig and others that quinine diminishes the uric acid in the urine, he explains by stating that "sulphate of quinine has a double action on uric acid; that is to say, it has the action of a sulphate which causes retention of uric acid, and cleans it out of the blood, and then it has the action on the spleen, causing uric acidemia, and a plus excretion of uric acid." That quinine is an antiseptic, and, at the same time, is not an efficient remedy for rheumatism, seems to show that the disease is not due to a micro-organism circulating in the blood.

Thirdly, as Dr. Haig also says (ibid. p.324) "no satisfactory explanation of the value of alkalis among drugs, or of milk and farinaceous diets, or again of hot baths, blisters, and other sudorifics in general management, can be given on the theory that acute rheumatism is due to a micro-organism or microbe." These latter two objections apply equally to the
Infective Theory, which has always been a favourite in the continent, and has been advocated by such well known men as Klebs (Archiv. f. exper. Path. 1875. vol. iv. p. 409, and 1876. vol. v. p. 52) and Ebner (Vieh. Arch. vol. xixii)

In 1885, Friedländer (Ueber Rheumatismus, Verhand. der Cong. f. innere med. vol. iv. p. 203) regards arthritis as the peripheral manifestation of a lesion of the central nervous system, causing irritation of a sensory centre in the medulla. (In which relation, he contrasts Lësch’s paranen, bulla paranen, exophthalmaic goitre, tetany, diabetis mellitus and vispidus.) The central nervous lesion he considers is due to a definite micro-organism.


More recently, Dr. Mantle (Brit. Med. Journ. 1887. vol. i. p. 1281) draws attention to the occurrence of tonsilitis in connection with rheumatism and infective fever alike, and regards the coincidence as suggestive of cause. M. Jaccoud (Gaz. des Hôp. 1886) states that endocarditis is always infective, and that as rheumatism is the chief cause of the heart affection, it must be infective also.

Dr. S. N. Dalton in a paper to the Brit. Med. Journ. (1890
vol. i. p. 472) states this belief (to which we have already referred) that rheumatism may be caused by breathing foul air of drains and sewers. In this relation, Dr. Hy. Dwight Chapin, of New York, ("Med. Ann. 1892, p. 432") writes: "The probable bacterial origin of rheumatism brings it into relationship with other diseases due to micro-organisms, and renders clear the following points of likeness: (1) its tendency, if untreated, to run a quite definite course lasting about nine weeks in adults, and two weeks or less in children; (2) a tendency to relapse, as seen in typhoid, and to a less extent in scarlatina and diphtheria; (3) the hyperpyrexia, which occurring most frequently in rheumatism, occurs also in typhoid and septic peritonitis; (4) the affection of the same parts in rheumatism and pyrexia, and the survivals common to each; (5) the greater incidence of the disease on the young, and the comparative immunity of the old, in this resembling all other members of the group; (6) its greater prevalence at certain seasons; (7) a liability to repeated attacks, in this respect resembling most erysipelas, and (8) a marked hereditary tendency as with tuberculosis."

Recognition of the bacterial nature of the disease throws light on the influence of those drugs which have been found most useful, namely, iodoform, quinine, and salicylates. That the disease is a special one renders it possible that the disease should co-exist with others; that it may enter the system by the inhalation of sewer-gas renders possible its
co-existence with others that may be contracted in the same way. Sewages is a variable mixture, containing numerous kinds of disease-producing germs, which leads to results varying according to the soil it meets and the relative proportion of the organisms present. The author holds, therefore, that rheumatism is an addition and not a part of the disease with which it occurs. If two poisons are absorbed at once, the one having the shorter incubation develops first, hence Rheumatism follows tonsillitis.

All the above points are perfectly compatible with the chemical or neo-chemical theories, and we are inclined to object to the comparison of rheumatism with pyrexia, for suppuration never occurs in a pure case of rheumatism. Further, neither iodine nor quinine can be said to be of much use in the treatment of the acute form of the complaint; and the infective theory offers no explanation of the nature of chronic rheumatism.

Halliburton ("Text-book of chemical pathology and pathol." (1891. p.307) remarks: "In all probability, the disease is produced by a special poison of a chemical (i.e. non-bacterial) nature."

It only remains for us to mention, while discussing this theory, that in 1892, Sahl ("Deut. Arch.f. Klin. Med. p.148), and Licatelet ("Proc. Intl. Cong. '92) have shown specimens of bacilli which they have cultivated from the articular fluid of rheumatic patients.
Such are the chief theories which have been published to explain the nature of the complaint. My attention was first directed—especially to the chemical (lactic acid) theory—by the teachings of Prof. Gannett Peabody, and Dr. J. O. Affleck. After carefully considering the subject in many ways, I thought there possibly some light might be thrown upon it by the discussion of the following questions: (1) Is there anything peculiar or noteworthy in the geographical distribution of the disease? (2) Does the mode of operation of the disease, now named or which has been recommended in the past, show anything? (3) Can we explain the formation of lactic acid (if there is any) during the disease? and (4) Can we detect any increase of lactic acid anywhere in the suprarenal? [Regarding the last question, I may say that a recent severe illness has prevented the performance of the necessary experiments, which, however, I hope I may soon be able to accomplish.]

Early in my investigation I was struck with various 'connecting links' not only between rheumatism and gout, but also between rheumatism and diabetes, gallstones and calculus. I had not then any knowledge of St. Lattouf's 'Romanian Lectures,' or of Gannett's 'Treatise on Rheumatism,' in which some of these points are mentioned; and I draw attention to it now in order to explain any subsequent allusions.

(1) Geographical Distribution. This I found to be a subject very hard to investigate, and it was only after great thought that I determined to use the death-rates returned by the
Registrar General for England and Wales. The obvious fallacy is that we do not exactly know the rate of mortality in the disease; thus Dr. Perry Cooke in his new book on Rheumatism, Its Cause, Prevention and Cure (1893, p. 9) states that, out of 1137 cases treated at St. Bartholomew's Hospital during six years, only 1.32 per cent. died, but no less than 70.86 per cent. developed heart disease as a result of the attack, whilst in the Report on Acute Rheumatism Returns (Collective Investigation Record of the United Kingdom, vol. iv, p. 31) out of 655 cases the death rate was 3.60 per cent. Of course, the death rate in a hospital would naturally be lower than obtaining in general practice where the patients are treated in their own homes with varying skill and possibly in poor and insanitary surroundings. Still the Registrar General's returns seemed the only ones I could give, and I determined to calculate the average deaths per 10,000 living (Rutland having only 20,000 odd inhabitants) for each county for a period of five years, 1890-94. Unfortunately, the Report for 1894, for some reason, is unusually late in publication, and even to-day (Apr. 27th 1894) it has not reached me.

The government returns are made under the headings: (1) Rheumatic Fever, Rheumatism of Heart, and Rheumatism. This arrangement has been in force since 1891, but for want of a more precise definition of the terms, I have included them all under the one word 'Rheumatism.' The tables which embody the results at which I have arrived will be found for greater
convenience - as an appendix, and to them I have added a couple of diagrams and a map of England and Wales shaded according to the death rate for rheumatism per 10,000 living.

The first point which is striking on looking at this map is the far greater prevalence of the disease on the west side of the country. This is directly opposed to the views of Sir Ayl Gannott, expressed in Reynolds 'System of Medicine' (vol. i. p. 940). There we read: 'In England, the occurrence of rheumatic fever appears to be much more common in the eastern than in the western counties: this is usually accounted for by the exposure of the former position of the country to the cold north-east winds.'

My own observations confirm my results for I found the disease very common in Lancashire, less so in Worcestershire, and comparatively speaking rare in the North Riding of Yorkshire and even in Essex, in spite of its warmish nature.

A second point well seen in the map and county curve diagram is that Lancashire is the worst county for the disease, and not Cumberland as we might possibly have presumed from its great rainfall. South Wales again stands high, but not Cornwall.

We note also that proximity to the sea appears to be a factor with which we must reckon, for the death rate in inland counties is, as a rule, below the average. It is also hard to blame the industries of the country, for why should Dorset stand so high?
Looking now at the three curves, we notice a marked general agreement between the curves for gout and diabetes, one less pronounced between rheumatism and gout, and lastly, that the curve for rheumatism has little in common with that for diabetes. In fact, speaking generally, gout and diabetes seem rather to prevail in the midland counties and especially in those in the south. One might have expected gout to be prevalent in Surrey and Middlesex, owing to the greater wealth and high living of the inhabitants; but why do Somerset and Hertfordshire appear so far up on the list? and why are Cambridgeshire and Cornwall so prominent as counties where diabetes prevails?

It is possible that observations carried over a longer period might give better results, and these I propose making in the future, but I think we are justified in denying that rheumatism affects especially the eastern counties. I have further added a table (p. 37) which, I consider, shows that neither the mean annual rainfall, relative humidity, nor temperature has much effect on the death-rate from the disease.

(2) Turning to the second question which I set myself, namely, the possible light thrown by the action of drugs used in times past, and at the present day, I first searched such old works on medicine as I could find,
and then took the modern text-books, and the Medical Annuals for the years 1889-94.

The earlier works provided but little of importance, partly because I knew nothing of the pharmacology of the remedies. Thus in Sydenham's works (1840, vol. i. Medical observations, p. 156) I find the following prescription for acute rheumatism:—

* Rx: Calcit. g. v. calcei.

Phren.: water.

Lettuce: water, 2:3 v.;

Sup. of lemons, 3½ x; Sup. of violeta, 3½.

Mix and make into a julep; to be taken ad libitum."

A calamine leaf is to be put on the part to allay pain.

Dr. John Mason Good, who published 'The Study of Medicine' in 1825, advises (vol. ii. p. 507) copious bleeding and Dover's powder. He thinks aspirin was of little service, although he admits that small doses of calomel (combined with opium by Dr. Hamilton) "have occasionally seemed to shorten the term of the disease." He considers that rhubarb may be useful at times; it was employed by Dr. Hume in Edinburgh Infirmary in 1780. The advisability of bark was questionable. Dr. Cullem found it "absolutely improper, and manifestly hurtful." On the other hand, it was much lauded by Dr. Morton, Sir Edward Hulse, Dr. Forde, Dr. Guthrie, Dr. Haygarth, of Chester, and others of renown.
In a letter to the 'London Medical Gazette' (1833, vol. xi., p. 596) Edward Copeman ('Apothecary to the Norfolk and Norwich Hospital') strongly urged the use of the common arnica (Ageratum Scoparianum) which was suggested to him 'from having accidentally witnessed its effects in the case of a lady who had suffered from chronic rheumatism.' He knew how that any urine in the substance is really due chiefly to the potassium bicarbonate in which it was given.

Dr. Thos. Watson, in his 'Lectures on the principles and practice of Physic, delivered at King's College' (1845, vol. ii., p. 628) does not recommend phlebotomy, or Down's powder. Colchicum, he says, sometimes 'acts like magic', but it is often disappointing. He further speaks highly of the use of emulsion and opium given in the method which Dr. Hope described in 1837, and which he learned from Dr. Chalmers. He affirms that colocynth is 'only beneficial in cases, during the convalescence'. In the sub-acute form, when the urine is almost always loaded with calculous matter, and strongly acid, alkalis are to be given, and 'more has been praised of late' (bid. p. 628).

The above extracts give a good idea of the line of treatment fifty years ago, and I only propose to give a very brief list of the remedies introduced since that period.

Blistering was advocated by Herbert Davies in 1864, and we are told that in one case the blister even covered 297 square inches. Dr. J. K. Mitchell, believing in the nervos theory, ordered dry cupping over the spine.
Perchloride of iron was recommended by Dr. Russell Reynolds (Brit. med. Jour. 1859, vol. ii. p. 649, and 1876, vol. ii. p. 417), its use being based on its value in erysipelas.

In 1849, Dr. Owen Rees published his well-known method of treatment, this was much extolled in many quarters; but the resulting benefits are now regarded as being due rather to the careful diet and hydropathic measures employed. Quinine, pellagra, and veratrum viride are recommended by Sir Alg. Garnod (Reynolds' Systems) more as useful adjuncts than specific remedies.

Cinchona and potassic nitrate, which, as we have seen, have been long used, hold much the same place as when Cottle wrote about them (vide supra). Very few practitioners would rely on their use only to cure an attack of rheumatic fever.

The alkalies were introduced by Bright in 1847, and are recommended by Sir Alg. Garnod (med. chir. trans. 1855, vol. xxxvii. p. 11) and by Dr. Fuller (On Rheumatism, &c. 1860). Their use was strongly advocated — in opposition to the salicylic treatment — by Dickson, Senators, Chambers and others, owing to the lesser risk of cardiac mischief which follows their administration.

A combination of quinine with the alkalies, especially with the addition of the salicylates, found a warm supporter in Garnod (Reynolds' Systems, vol. i. p. 876), and Sir Dyce Duckworth and Dr. E. A. Garnod strongly endorse these views.

Trimetaphosphate, which was first employed by the Russian physician Ouvenewius (Schmidt's Jahrbücher, 1859, vol. xci. p. 21.)
Dujardin-Beaumetz (Paul. gén. de Therap. 1873. vol. XXXIV. p. 337)
may be said to have re-introduced by bringing forward the
use of the hydrochlorate (N(CH3)3HCl). It relieves congestion and
cases pain in the same manner as veratrum viride, and arsenite
which was recommended by Bordard of Geneva in 1834 (Paul. de
Therap. 1707. p. 53).

Unquestionably the introduction of the salicylic compounds has
been the greatest achievement in the history of the Therapeutics of
Rheumatism. In England, the credit of their introduction is entirely
due to Sir Macleod who used salicyum in 1874, on the supposition
that the remedy for a disease is always to be found where the disease
is most common: as Persian foxes abound where ague prevails, so
the willows grow where rheumatism is most to be found.

The salicyl group, in which we count salicylic acid (CH3
\text{COOH})
sodium salicylate (CH\text{COOH}\text{Na}) , salicin (CH\text{COOH}\text{C6H4OH}) , salol (CH\text{COOH} \text{C6H4OH})
on saliven (CH\text{COOH} \text{C6H4OH}) and oil of wintergreen (which
contains 9072 methyl salicylate (CH\text{COOH} \text{OH})) are all decomposed to
salicylic acid in the system. This acid, according to St.
Latham (Gom. Act. 1896. p. 91), unites with the glycine (amido-
acetic acid CH\text{NH2} \text{COOH} and forms salicylic acid (CH\text{COOH} \text{C6H4OH})

by which means the formation of uric acid is prevented.

This seems to me to reach the root of the matter, but
in order to be clear and impartial I have tabulated all the
drugs recommended during the past 8 years, according to their pharmacological action.

1. Antiseptics. The Salicyl group. (Salphen being recommended by Guttman and Köhler.)

Quinin.

Benzonat (more useful in gout (2. Latham's Accid., p. 87)

Béot (inferior to Salol (2. Latham's Pharmacy, 5th Ed., p. 154))

Eucalyptol


Quinin.

Benzonat.

Béot

Eucalyptol

Acouit.

Cimicifuga

Antipyrin.


3. Cardiac-depressors. Salicyl group. Vaso-dilators

Quinin (slight).

Benzonat.

Acouit.

Cimicifuga

Veratrum viride

4. Diuretics. Salicyl group. Cimicifuga

Quinin (slight).

Acouit.

Benzonat.

Acouit.
5. Diaphoretics

- Salicyl group
  - Acoula
  - Cimicifuge
  - Kaolin
  - Tartar emetic
  - Pot. nitric


- Sod. salicylate
- Lithium
- Magn. Sulph

7. Aperient

- Pot. tartaro
- Sulphur
- Bryonia
- Spigelia

8. Hepatic Stimulant

- Quinaeum
- Colchicum
- Mercury

*Antitumour: produces profound changes in hepatic cells especially in the nuclei (iv id p.261)*

9. Tonic

- Iron salis
- Cascara
10. Specific drugs: Rheu Esauadron recommended by S. Ault in *Tramph Gazette*, Oct. 1890 (p. 104)


11. Alternatives (a) diminishing metabolism

Salicyl group:   Sulphur,

Quinine:        Iodine,

Kainin:          Ammoni, Chlorid.

(b) Increasing metabolism


Quisacum (2):   Tannin emetic

Mercury:         Arsenic.

I have taken the trouble to draw up this tabular list even at the risk of being one-sided, because I think it does throw light upon the nature of the complaint. A careful study of it shows us that it is not by destroying bacteria or other micro-organisms, it is not by acting on the nervous system and it is not by merely raising the alkalinity of the blood, the most valuable drugs give us help. It is by a specific action on some product of a chemical nature circulating in the system and of an acid nature. Hence the value of the athers, which in their turn are inferior to salicylic acid; for the latter, from its chemical nature prevents the formation of the particular poison and destroys it where already formed.
3. The chemistry of lactic acid. There are, as we have already seen two isomeric forms of ethylene lactic acid (2) the ordinary inactive lactic (3) the active, right-rotatory form known as para- or racemolactic acid. The isomer of these is produced by the diastatic fermentation of sugar through the agency of a ferment. (according to Pasteur and others the "Penicillum glaucum", D. Ferron "Organic Chemistry" (8th. p.324)

In the human stomach there is a ferment (Hamburger) which swiftly acts on the carb. hydrates (C_{6}H_{12}O_{6} = 2 C_{3}H_{6}O_{3}) [Landor & Stirling "Physiology" (3rd Ed. p.242-251). This acid is found in the stomach immediately after taking food, together with hydrochloric acid, whilst after an hour only hydrochloric is to be detected. (Ewald and Bozès). Many suggest that the lactic acid is evolved by the action of the former on the soda lime chloride (ibid. p.246). The presence of lactic acid prevents the diastatic action of phytalin continua in the stomach. (Cl. Bernard) 

The bacillus acid lactic and its spores exists everywhere in the atmosphere, but the common household observation that milk keeps better in a dry cool place than in a damp warm one, may as regards atmospheric humidity, be compared with the prevalence of chemist's acids.

Finally we are told that the faeces are often acid in consequence of lactic acid being developed from the carbohydrates of the food (ibid. p.293) and further that lactic acid is absorbed in the intestines (ibid. p.299).
A important point bearing on the essential difference between gout and rheumatism and opposing Dr. Haig's view is to be found in the statement that Berenger-Fraud, acting on the suggestion of Dr. Foucoul, of Orleans, gave lactic acid as a prophylactic in gout. (Bull. gén. de Therap. Dec. 30, 1891) and "Fraud believes that it is a valuable remedy, which will be placed high in the list of drugs which possess distinct anti-arthritic powers" (Med. Ann. 32, p. 2812).

(2) Sarco-lactic acid. Prof. Rutherford (Text-book of Physiology, fasc. i. p. 42.) says this form "is produced in muscle during contraction; the mode of its formation is unknown." It is found in the muscles, and also in the urine after muscular activity, and after extirpation of the liver in birds and frogs (Huckerski, Arch. v. exp. Path. und Pharmakol. bull. XXI, 1893, S. 10). When blood is perfused through a freshly excised liver (or through kidney, lung, or muscle) an increase of lactic acid is found (Ehrlich-Koch and Quaglies, Arch. f. Physiol. Jahrg. 1886, S. 403). And furthermore sarcolactic acid is found in the liver cells when the food contains much fat. (Landois, Ibid. p. 264.)

I think in the first place, that we are justified in excluding ordinary lactic acid from the list as a possible 'matrizes morbi'; for if rheumatism were due to it, our first indication would be to condemn the diet (milk and fatty food) which has been always found to be the only one
which should be allowed.

Regarding rancid lactic acid the question is much more difficult to answer. Latham has shown (Graubr. Lectures 1896, p.21) that Allomann \((\mathrm{C}_7\mathrm{H}_3\mathrm{Ni}_6\mathrm{O}_{29})^+\) is built up of cyan. alcohols united to a benzene nucleus, the molecules held together by some vital force or otherwise. The cyan-alcohol molecule may by hydration or decomposition give off free ammonia and the corresponding acid (p.23).

E.g. \(\text{CH}_3\text{CHONCN} + 2\text{H}_2\text{O} = \text{NH}_3 + \text{CH}_3\text{CHONCOOH}\) (lactic acid or if the molecule \(\text{CH}_3\text{CHONCN}\) were detached and the portion \(\text{CH}_3\text{CHON}\) )

CNONH then liberated, the latter would, with \(\text{H}_2\text{O}\), be decomposed at once into \(\text{CO}_2\) and \(\text{NH}_3\), and the remainder hydrated into lactic acid.

\[
\text{CH}_3\text{CHON} + 4\text{H}_2\text{O} = \text{CH}_3\text{CHONCOOH} + \text{CO}_2 + 4\text{H}_2\text{O} \\
\text{CH}_3\text{CHONCN}
\]

We have already traced (p.12) the role which Latham considers is played by lactic acid after its formation. We have also seen that he regards it as chiefly acting in rheumatism by increasing indirectly the formation of uric acid which again acts on the nerve cells concerned with the nutrition of the joints. We have further seen how beautifully Dr. Latham accounts by this theory for all the various symptoms of rheumatism and its allied complaints.
We have already seen the objections raised to it.

Before bringing these notes to a close we must refer to the investigations described by Dr. Perry Wilde in his book "Rheumatism" (1893). He considers that the acids, manufactured in the tissue, owing to imperfect oxidation, remain there at first owing to a want of oxygen to ensure their perfect combustion (p. 17). Further, he states that the lactic acid forms a chemical compound with the muscle (p. 24) which compound can only be broken up by more oxygen being brought to the parts. For treatment therefore he advises that the heat of the parts should be raised locally, so that the disturbing compounds are destroyed "in situ" (p. 33). Salicylates and quinine, which diminish metabolism he condemns entirely (p. 31). The visceral lesions are explained as follows: when the partially oxidised compound (lactic acid) is in such quantity that the tissues are saturated it overflows into the lymphatic and so reaches the heart, producing there changes similar to those found in the muscles. A better supply of good arterial blood if soon obtained would remove these effects also, but when much change has taken place full repair is impossible.

Sir Alg. C. Beer (med. Anz. Trans. vol. Ixxxv. p. 139) has shown that at the beginning of an attack of rheumatism the blood corpuscles and haemoglobin diminish, and of course this means that the supply of oxygen which
such blood carmin is reduced; this affords support to Dr. Wilder's view, which however requires more evidence in their favour, before we can entirely abolish the use of salicylates in the treatment of rheumatism.

The problem still remains unsolved, but I trust that the digest I have given, and the notes I have made may not be entirely without value.

P.S. Dr. Anthony Todd Thomson in a Clinical Lecture delivered at the Dispensary of the London University on Oct. 22. 1831, said as follows: "I would venture, m'rs. gentlemen, to throw out an hypothetical conjecture, which, if it do not enlighten you, may afford an exercise for your minds: knowing that much hydrogen is evolved in fogs, it is not probable that this is also the case whenever the atmosphere is surcharged with aqueous vapour, and as Pry-met with certainty that the process of cooling proceeds more rapidly in hydrogen than in atmospheric air, how far is this likely to operate as a cause of rheumatism? It is a well-known fact that the disease is often produced at sea, by frequent washing the deck, a custom now judiciously frequently dispensed with."

This is a gem which I thought worthy of reproduction from the 'London Medical Gazette' 1832. vol. 9. p. 132.)
Table showing death rates per 10,000 living estimated to middle of each year.

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Table showing meteoroological conditions for several years.
Diagram showing average death rates (per 10,000 living) from Rheumatism, Gout, and Diabetes in registration counties of England and Wales, during the years 1898, '99, '00, and '01.

Explanation of coloured lines:
- Death rate from Rheumatism per 10,000 living.
- Death rate from Gout per 10,000 living.
- Death rate from Diabetes per 10,000 living.
- (Dotted) Average death rate per 10,000 living from these diseases in England and Wales.
Diagram showing average death-rate (per 10,000 living) from Rheumatism, Gout, and Diabetes in registration divisions of England and Wales during the years 1898, 1899, 1900, and 1901.

Explanation of coloured lines:
- = Death-rate from Rheumatism per 10,000 living.
- = Death-rate from Gout per 10,000 living.
- = Death-rate from Diabetes per 10,000 living.
- = Coloured average death-rate per 10,000 living.

- - - = Death-rate from Rheumatism, Gout, and Diabetes in England and Wales.
ENGLAND & WALES

Showing Death rate (88-91)
from Rheumatic per 10,000 living

Under 500

Over 500 - 1,000

1,000 - 1,100

1,100 - 1,200

1,200 - 1,300

Over 1,300

GEORGE PHILIP & SON, LONDON & LIVERPOOL.