Infirmary in vain and the opening came at last not by conviction, but as those things so often do, by chance. The chance came in an attack of eczema in one of the managers, and had Daniel Rutherford Haldane, the uncle of the Minister for War, not been cured of his eczema by Dr. Jamieson, we might not have been here to-day.

In 1884, permission was grudgingly given for the opening of an out-patient department, and for some years this was carried on in what is now our male ward, and was then the ear and throat, dental and skin out-patient department. Gradually the clinique grew, patients got more numerous, and students began to find out the advantages of learning something about skins. The numbers grew so great that it was found necessary to move to the extramural clinical theatre, where for some years Dr. Jamieson taught the greatest number of English-speaking students that have anywhere assembled to learn dermatology. All this was a labour of love; but as the students grew more and more numerous it was obvious that further advances required to be made and a regular class established. This last ditch took a long time to carry; the vested interests fought hard. Ultimately the managers gave permission to institute a class, and shortly after the University capitulated and appointed Allan Jamieson Lecturer in Dermatology.

Six beds were allotted to him in 1891, and the numbers have gradually increased to sixteen. When the re-drainage scheme is completed the number will be twenty-four.

Thus at last Bennett's ambitions were fulfilled, and, so far as dermatology is concerned, "the Edinburgh School of Medicine is complete in all the means necessary for studying every kind of disease at the bedside."

In 1886 Sir Henry Littlejohn, in whose gift the post is, offered to Dr. Jamieson the Consulting and Visiting Physicianship of the Edinburgh City Hospital for Infectious Diseases, then established independently. This afforded him the opportunity of pointing out, among other things, the diagnostic features of the exanthemata and the characteristics of erysipelas, and during the five years he held office there he found the hospital most valuable for teaching purposes, as well as for research. He resigned on the opening of wards for dermatology in the Royal Infirmary.

This is not the time to dwell on what Allan Jamieson has done for dermatology at large—to have established the subject on a firm footing in the greatest British school of medicine is a triumph which might make the humblest man proud.

One personal word. We have worked together for fourteen years, his kindness and generosity to me have been beyond praise, and the only cloud on my natural gratification on my promotion to this proud position is the fact that it involves his retirement.

In the college honours that will before long be offered him we all, I am sure, wish him much enjoyment and happiness.

And now, Gentlemen, I have dealt with the past, and we look forward to the future. It shall be my ambition to follow Bennett's principles and to endeavour to teach you to observe for yourselves. This, I believe, can only be done in small classes, and, though I shall deliver lectures here, I shall regard the limited classes which I shall teach on the other days of the week as at least as important parts of the course.

In the anonymous articles on the teaching of medicine which are appearing in the *Scottish Medical and Surgical Journal*, and which it is my editorial duty and privilege to peruse in their unabridged form, you will find a striking unanimity in the view that students waste their time at operations. Between the hours of 11 and 12 there are many departments of the hospital where time may well be spent. I can assure you that in your after-career you will not regret the three or four hours a week which I ask you for the next ten weeks to devote to dermatology.

ANTWERP EXPOSITION.—An international exposition is to be held at Antwerp in April, May, and June, 1907, under the patronage of Her Royal Highness the Countess of Flanders. There will be a Medico-Pharmaceutical Section, including within its scope exhibits relating to hygiene, food, and beverages (wine, liqueurs, beer). Full particulars can be obtained by application to the Secretary's Office, 30, Rue d'Arenberg, Anvers (Antwerp).

A Clinical Lecture ON THE ACTION OF SALICYLATES IN ACUTE RHEUMATISM.

By RALPH STOCKMAN, M.D.,

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SALICYLIC ACID had been well known to chemists for about half a century when Kolbe, in the course of a research on chemical constitution, succeeded in making it on a large scale from phenol, and announced in a series of papers published in 1874-5 that it was a powerful antiputrefactive and antifermentative, capable in dilute solution of killing low organisms and of annulling the action of yeast, pepsin, emulsin, and similar ferments. He recommended its use in medicine as an antipyretic and antiseptic, with the result that Buss, while investigating its action in various febrile conditions, observed that it was specially valuable in acute rheumatism—a discovery which was amply confirmed by Stricker in 1876. In the same year J. T. MacLagan published an account of his successful treatment of rheumatic fever with large doses of salicin. Since then salicylic compounds have been universally relied upon for the treatment of acute rheumatism, most authorities regarding them as exercising a specific action on the cause of the disease, which is now generally assumed to be a microbe. Previous to the introduction of salicylates such drugs as aconite, veratrum, colchicum, quinine, alkalis, opium, and a host of others, had been in vogue, but they had for the most part come to be regarded as either quite useless, or at best very unsatisfactory in their curative effects. Under the administration of these, cases of acute rheumatism probably all ran their normal course until a natural cure resulted, but with the difference, as compared with many other fevers, of having no definite limit of duration. From three to six weeks used to be a common computation, but many cases lasted much longer either with successive exacerbations or with continuous slight fever, while others recovered in two or three weeks, or even in a few days. Whether the natural cure results from an antitoxic or from an antibacterial substance formed in the body is unknown, but it is evident that this hypothetical body is of satisfactory amount and potency in some cases, while in the majority it fails to rapidly and completely cut short the disease. During the fever there is a moderate leucocytosis, and one attack predisposes to others instead of acting as a protective.

In the absence of any certain knowledge regarding the specific microbe of acute rheumatism and its toxins, it is impossible to determine experimentally whether salicyl compounds act as bactericides or as antitoxins in the disease. When we try to solve the problem indirectly by studying their effects on known organisms and ferments, we find that salicylic acid and its sodium salt are capable of preventing the action both of living ferments and of enzymes outside the body, so that in the body their action might conceivably be exerted in either or both directions. These are questions, however, of which the settlement can be attained only by further research, and which cannot be profitably discussed in a clinical lecture. When salicylates are given in sufficient dose in an uncomplicated case of rheumatic fever, the pain in the joints and the temperature begin to be favourably affected at once, the former subsiding in twelve to twenty-four hours and the latter within forty-eight hours. The joint swelling disappears in two to four days, and the frequency of pulse and respiration diminishes with the fall of temperature. The course of events closely resembles a crisis in fever.

The Charts 1 and 2 show the immediate and continuous drop of temperature, accompanied by cessation of pain and the fall in pulse-rate which characterize the successful action of sodium salicylate. In Chart 2 the accidental omission of three doses was followed by a slight rise which quickly subsided on resuming the medicine.

In Charts 3 and 4 the course of the temperature resembles the "pseudo-crisis" which is so common in pneumonia, and, like it, is followed by a definite termina-

tion of the fever, although in Chart 4 it has taken some days to settle down finally. It is quite evident that in all four cases there has been a radical interference with the *materies morbi*, and that the salicylate has either killed the organism or neutralized its toxin.

In other cases the effect is not so rapid. In Charts 5 and 6 the reduction of temperature is by lysis rather than by crisis, while in Chart 6 an exacerbation occurred which was only overcome by substantially increasing the dose. In all these cases the resemblance of action to that of quinine in malaria, or to the natural curative body in pneumonia, is very marked. In some cases the temperature can only be brought to a settled condition by increasing the original dose or by giving one large additional dose (40 to 60 gr.) on one or on several days in succession (Chart 7).

In many cases the results of salicylic treatment are not so satisfactory. Thus, it not uncommonly happens that the patient has a relapse or exacerbation while still taking salicylate, or on reducing the daily dose. This can usually be rapidly overcome by giving an increased amount, as shown in Chart 8. In other cases the condition becomes subacute, or chronic with a slight temperature and ceases to be visibly influenced by salicylates alone (Chart 9).

In cerebral rheumatism with hyperpyrexia (Chart 10) and in severe endocardial and pericardial infection with hyperpyrexia (Chart 11) salicylates have little effect, cold bathing being the only efficient way of reducing temperature. In certain cases of rheumatic pericarditis, however, the action is as decided and rapid as it is on the joints (Chart 12). These charts illustrate fairly well the different ways in which cases of acute rheumatism may react to salicylic treatment, and a fuller consideration of the results may help us to understand these differences and the reasons for them.

In many cases of acute rheumatic infection, pain and swelling of the joints are the most prominent symptoms, and it is always described as a very characteristic feature of the disease how different joints are affected in turn, and how in each, after a few days, the pain and swelling subside very rapidly without causing any permanent damage. This used to be called a metastasis, but there is no transference of the disease from joint to joint, and it

simply means that all the joints are not invaded simultaneously by the morbid agent. The most probable explanation of the rapid subsidence of the swelling and pain is that locally in the joint an antitoxic or antibacterial substance is formed which powerfully antagonizes the poisonous agent, and does it so rapidly that the joints are very seldom injured. The closed cavity of the joint probably favours the accumulation of the antibody until it reaches a highly active degree of concentration. This view is supported by the circumstance that while the fibrous tissues of the joints, tendons, and aponeuroses are also very often the seat of rheumatic infection, it is well recognized that in these places the inflammation is usually very persistent,

and apt to leave behind permanent fibrous thickenings; and this, I think, is owing to the antibody being in much less quantity in the body serum than in the joint effusion.

The explanation of the rapid action of sodium salicylate on the pain and swelling of the joints is that it is excreted into the joint-cavity from the blood in comparatively large amount, as can be readily shown by its detection in the fluid withdrawn by means of a hypodermic syringe. On the other hand, colonies of microbes settled deep in the fibrous tissues, or in the valves of the heart, are more or less sheltered from the action of the salicylate, and are probably scarcely reached by it; or, if reached, the solution in the serum is too

dilute to exert much action.

I suggest this as the explanation why valvular rheumatic infections, and infections of the fibrous tissues generally, are not nearly so amenable to the action of salicylates as the joints are. The important practical deduction to be drawn from this is to treat the patient at once and with large doses, so as to kill off the microbes while they are still in the blood stream or joints, and before they have had time to establish themselves in the fibrous tissues. Early treatment with sufficient doses greatly lessens the risk of acquiring valvular disease and chronic fibrositis. It also diminishes the frequency of prolonged sub-

Chart 1.—Sodium salicylate, 20 gr. 3-hourly.

Chart 2.—Sodium salicylate, 20 gr. 4-hourly.

The fall of temperature is continuous and resembles a crisis.

Chart 3.—Sodium salicylate, 20 gr. 4 hourly.

Chart 4.—Sodium salicylate, 20 gr. 2 hourly.

The permanent fall of temperature is preceded by a pseudo-crisis.

Chart 5.—Salicylate. 20 gr. 2-hourly and 3-hourly.

Chart 6.—Sod. salicylate, 10 gr. 4-hourly and methyl salicylate on joints.

In both the temperature falls by lysis.

acute fever and of relapses, as these are due to organisms surviving in the fibrous tissues. Both in adults and children the rheumatic infection frequently manifests itself first in the fibrous tissues, whence it may or may not spread to

the joints and heart, and in these cases it has long been recognized that salicylates do not act so rapidly or so satisfactorily as in cases where the joints are chiefly involved. Nevertheless the internal administration of sodium salicylate together with free local application of methyl salicylate gradually subdues the infection. In

Chart 7.—Sod. salicylate, 20 gr. 4-hourly. The temperature fell only when 40 gr. was given in addition in one dose.

these protracted cases the prolonged irritation is apt to give rise to considerable reactive proliferation of the fibrous tissue locally, hence the valves of the heart and the aponeurotic structures very frequently do not return *ad integrum*, while the joints practically invariably do so. Under the administration of salicylates, the tendency to

Chart 8.—Relapse while taking sod. salicylate. It came on when the dose was reduced, and subsided on increasing the dose again.

rheumatic hyperpyrexia and to cerebral rheumatism is undoubtedly diminished. In spite of frequent assertions to the contrary, I believe also that endocarditis is often prevented, although it is still deplorably common. When one considers that under the action of salicylates certain cases are aborted, that many others are at once diminished

Chart 9.—Chronic feverish condition not subsiding under salicylate of sodium.

in severity, and that along with the fall of temperature the number of heart beats may be reduced to the extent of 15,000 to 30,000 in the twenty-four hours, it is apparent that the strain on the valves and their liability to infection must be greatly lessened.

As regards dosage, 15 or 20 gr. of sodium salicylate

every three or four hours usually suffices (90 to 160 gr. daily), but similar amounts or more may be given every two hours for the first twelve or twenty-four hours, so as to get as much as possible into the system in a short time. From one-half to nearly the whole of it is quickly converted into salicyluric acid, which is an inert substance,

Chart 10.—Cerebral rheumatism. Chart 11.—Rheumatic pericarditis and endocarditis.

In both cases the temperature is unaffected by sodium salicylate.

and the remainder is rapidly excreted, hence the necessity for frequent administration.

It is often impossible to push it owing to the production of deafness and other well-known poisonous effects. These are chiefly due to an action on the nerve centres, the heart and pulse being scarcely affected. Mendel has given sodium salicylate intravenously and Bouchard

Chart 12.—Rheumatic pericarditis. Rapid cure under sodium salicylate.

hypodermically, and both say that the results are very satisfactory if proper precautions are observed.

Methyl salicylate can be given internally, as an emulsion or in milk, in 10 to 20 minim doses. It is very active, and it has not the unpleasantly sweet taste of sodium salicylate, but it is often very irritating to the stomach. It also acts well when applied over the joints or limbs, and thus applied is especially useful in acute

muscular rheumatism. Chart 13 shows the course of a case treated with it.

Salicin, saligenin, and aspirin (acetyl-salicylic acid) form salicylic acid in the body, and in virtue of this have an antirheumatic action; while besides these there are numerous other compounds of salicylic acid which are active, but for the most part inferior to sodium salicylate.

There can be no reasonable doubt that compounds of salicylic acid, or substances from which it can be formed in the body, have a specific action against the poison of acute rheumatism. The number of such specifics is small in medicine, comprising quinine in malaria, mercury in syphilis, a few serums and arsenic in malaria, in pernicious anaemia, in chorea, in lymphadenoma, and in sleeping

Chart 13.—Action of methyl salicylate.

sickness. The action of arsenic in all these diseases is comparatively feeble. In all it requires prolonged administration, in some it merely lessens the vitality and virulence of the parasite, and hence improvement is often slight and relapses are very common. In the same way it is evident that salicylates in acute rheumatism frequently exert an action too feeble to satisfactorily cut short that disease, and that this is most apparent when the inflammation is seated in the fibrous tissues connected with the muscles and joints, or in the valves of the heart. It would certainly be an advantage to have a new remedy acting similarly but more powerfully, and, if possible, without its toxic effects on the central nervous system. There is no reason why such specific remedies should not be discovered for all the ordinary fevers if a large series of likely substances was systematically tested in our fever hospitals.

THE RECOGNITION OF MYELOPATHIC ALBUMOSE IN THE URINE.

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THE detection in the urine of the peculiar substance first described by Bence Jones in the year 1847, is one of the most significant clinical observations which it can fall to the lot of the physician to make. Its presence is one of the few signs of disease which can be strictly called pathognomonic, admitting, as far as our present knowledge goes, of only one interpretation, and it is usually for many months the only indication of the true nature of the disease from which the patient is suffering, and may for a long time be the sole evidence that he is seriously ill at all.

Multiple myeloma, the morbid condition of which it

is the sign, goes on to a fatal termination with the certainty of malignant disease, and no measures hitherto attempted appear to have the slightest influence in retarding its progress. In fact, a correct diagnosis has seldom been made until the disease has become pretty widely distributed, and clearly beyond the reach of any local measures which might conceivably be employed to arrest it. We may be certain that in this, as in other forms of new growth, any remedial measures that may hereafter be devised will be only applicable in the early stages of the disease, and their success will depend upon an early diagnosis. As this is only possible by the detection in the urine of the body which is the subject of the present paper, I think it is of the highest importance to have a clear understanding of the means by which it may be recognized.

Myelopathic albumose, as, for reasons set forth in former contributions, I designate the body in question, is a member of the great group of nitrogenous colloid substances known as proteids. Elaborate investigations have been made during the last few years, especially in Germany, with a view to determining its exact position in the group; but, as might be expected in view of our scanty knowledge of the constitution of the proteids in general, no great progress has been made in this direction. This much, however, may be taken as established—it differs essentially from all other proteids which have ever been met with either in health or disease. It is closely related to the native albumins, but at the same time presents characters which bring it near, if not within, the group of albumoses. It is remarkable in this that it is the only simple proteid derived from the human body that has ever been made to crystallize artificially. Further, it shows a remarkable readiness to undergo what I can only describe as molecular changes under conditions not easy to determine, changes which make its detection difficult if we are not aware of the possibility of their having taken place.

Myelopathic albumose is physically and chemically closely related to the albumins, and when present in urine generally gives a positive response to the common tests for albumin, for which it is consequently most likely to be mistaken. Thus it is thrown out of solution by heat in the presence of a trace of acid, by ferrocyanide of potassium and acetic acid, by picric acid, and by mercurio-potassic iodide. On the other hand, its response to these tests is, as a rule, not identical with that of albumin, the most noticeable points of difference being with regard to its solubility or otherwise at various temperatures and the greater or less readiness with which it is precipitated by various mineral acids. Some of the points of distinction can only be properly demonstrated by somewhat tedious chemical methods, and will only be briefly alluded to here. The object of this paper is to point out simple methods of analysis which are within the reach of every practitioner who pays attention to the urine at all, which require no complicated apparatus, and which, if carried out with ordinary care, may be relied on to distinguish myelopathic albumose from all other possible constituents of the urine.

I. Heat Test.

Myelopathic albumose coagulates at a much lower temperature than albumin—namely, at 58° C., or thereabouts (while serum albumin coagulates at about 75° C.)—the exact point varying a little in both cases according to the degree of acidity of the fluid, the concentration of the solution, and other conditions not thoroughly understood. Thus, in the case of albumose coagulation is sometimes accelerated by agitating the fluid. The best way of applying the heat test is on a water bath, which can be easily improvised by placing the test tube with the urine inside another of larger calibre containing water. When thus used the test is very striking, the whole column of urine becoming suddenly opaque at about 58° to 60° C., and the coagulum running together to form flakes at two or three degrees higher. Occasionally some turbidity is noticed at a much lower temperature, especially if the acidity is somewhat high. The recognition of this low coagulation point I consider conclusive evidence of the presence of albumose. I have never failed to find it in myelopathic albumosuria, and it never occurs in albuminuria. Care must, however, be taken to add only enough acid to ensure coagulation. A slight excess of acid may prevent its taking place altogether.