pupillage, though they have not ceased to be students, may study the variations of disease.

I ask the more boldly for contributions to the pathological collection, because of its present satisfactory condition, and the activity of work in it. You will soon see it in the repaired and renovated building. Looking at the number and value of the specimens, and the wide range of pathology which they illustrate; looking at the interest of the history of our science which is told in many of them; at the memorials of Hunter and Matthew Baillie, of Astley Cooper, Liston, Howship, Lawrence, Hammond, Fergusson, Hilton, and many more; looking forward to what the museum will tell of the researches and skill of those who are still with us; and among whose names, I venture to feel sure, Mr. President, that none will take precedence of your own, while men study the specimens with which your skill and just audacity in operating have enriched the series of diseases of the ovaries and uterus. Looking at all these things, and then at the perfect order and condition in which the specimens are preserved, I feel that the collection is one in which all we members of the College may feel personal pride in calling our own, and should feel a personal duty to enrich. And its utility is being constantly more appreciated. I have been often made happy by the contrast which I have seen while working at the new edition of the catalogue. While I was writing the last edition, between thirty and forty years ago, scarcely a student ever entered the museum. Hour after hour, I sat alone; I seemed to be working for no one but myself, or for nothing but the general propriety that a museum ought to have a catalogue, though no one might ever care to study with it. Now, and for some years past, a day rarely passes without many pupils and others being at work in every part of the museum.

All this is good, but much more is to be done. Our museum should be, even more than it is, the centre in which all pathologists may find help in searches after that which is not yet known; in such searches, for example, as may lead to a complete knowledge of the variations of diseases. For many years, even from the beginning, the anatomical and physiological departments of our museum have been not only a noble collection of specimens, but, through the renown and learning of its conservators, a great centre of teaching. Scientific men, especially comparative anatomists and anthropologists, have known that here, if anywhere, they could find whatever help a museum and a master in those sciences could give. A fortnight ago the President of the Royal Society, presenting one of the royal medals to Professor Flower, said: "Professor Flower has been for more than twenty years conservator of the museum of the Royal College of Surgeons, and it is very largely due to his incessant and well directed labours that the museum at present contains the most complete, the best ordered, and the most accessible collection of materials for the study of vertebrate structures extant."

It is not for me to praise the pathological collection with similar words. But great as may have been its utility hitherto, we may be confident that it will henceforth be more useful than ever. In the vast increase of the biological sciences it became impossible that one man should be nearly complete in the knowledge of both natural and pathological anatomy, I say impossible. I believe there is not such a one living; if there could have been one it might have been Mr. Flower. Now, we may hope that labours as "incessant and well-directed" as his will be devoted especially to the pathological collection.

It is known to many of you that Sir Erasmus Wilson, in his usual liberality, gave the College £5,000, of which the interest should be spent in the promotion of pathology; and he agreed that this would best be done by helping to the appointment of a curator of the pathological department of the museum; and we have an admirable one. Mr. Eve is a worthy colleague and helper of Mr. Flower, excellent like him not only in knowledge, but in that which is even more rare, the love of museums, and of all that belongs to their maintenance and illustration, even to the making of catalogues. In all these good qualities he has distinguished himself at St. Bartholomew's. I believe that we may rely on him for making so good use of the museum, and of all that can be brought to it, that the College shall be the chief centre for the study of pathology, even to the furthest point at which it can be studied in specimens of diseased structure. I beg your help that it may be so; and if I shall have helped to-day to this good result, the first Bradshawe lecture in our College will have well fulfilled the purpose of its founder.

RIDES FOR INVALIDS.—A society in Boston has engaged itself in the work of providing free rides for invalids during the warm months. From last May to the present month, 1,343 persons were given rides. In addition, 1,400 car tickets, and 640 round tickets on the harbour steamers, were distributed.

OBSERVATIONS

ON

THE PHYSIOLOGICAL AND THERAPEUTIC ACTION OF THE ELEMENT ARSENIC IN THE FORM OF ARSENITE AND ARSENIATE.

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AND

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[Continued from page 1138.]

The results set forth in the tables may be summarised thus.

As to the comparative action of arsenious acid and arsenite of soda, the series of both salts are perfectly parallel, the same doses of each drug being administered in each experiment; hence the comparative action may be read off at once in the "time" columns. If these numbers be individually compared, it will be seen that there is considerable variation, but certainly not more than one would expect with the individual differences which must exist between frogs, however carefully selected; added to which, there must be taken into consideration the range of variation necessitated by the mode of experimentation. If, however, the results be taken in the aggregate, the agreement is certainly as close as one could expect. Thus, the tables show seventeen experiments with arsenite of soda, and sixteen with arsenious acid. Of these, thirteen are available for comparison, since in each case definite results were obtained. If the double series of numbers be summed up, we get as follows:

Death of Central Nervous System.		Average.	Death of Muscular Tissue.		Aver.
Arsenious acid	266 hours	20.5	290 hours	23	
Arsenite of soda	223 hours	17	278 hours	21.5	

The numbers representing the death of the muscular tissue were obtained by adding up the "anterior limb column." It was thought unnecessary to repeat this operation for the other two columns, though, of course, each column, or all three, may be used for comparison.

The numerical agreement which thus appears, requires no further comment. In addition to this, however, the agreement qualitatively between the arsenite of soda and arsenious acid was throughout the experiments so very marked, that one could scarcely doubt that one had to do with equally active preparations of arsenic.

The solution of sodium arsenite used was strongly alkaline; hence it would appear that the element arsenic is equally active, whether in the form of arsenious acid (the aqueous solution would probably be represented by the formula H_3AsO_3), or of a further combination with sodium as sodium arsenite, Na_3AsO_3 . This being so, it was thought unnecessary in the further experiments to continue the parallel series of threes, and accordingly the arseniate of soda and arsenious acid were thenceforth alone contrasted.

Proceeding at once to the consideration of the arseniate series, the experiments recorded in the table may be divided into three parts. In part I, the arseniate dosage is the same as that of the arsenious acid and arsenite of soda. The results here obtained show that, whilst these latter caused death after a maximum of 24-26 hours, the arseniate frogs were not only alive after 48 hours, but appeared quite normal. In part I, then, we have the results of "equal dosage."

In part II, the dosage of arseniate was at first increased by one half, then brought back again to the original dosage of part I; but all the experiments included under part II in the parallel series corresponded to a dosage of two parts of the element arsenic as arseniated against one part as arsenite and arsenious acid—i.e., in part II, we have double dosage of arseniate.

Of seven experiments with the arseniate, the dose was fatal in two cases, at the end of 29 hours and 64 hours respectively. In a third case, the experiment was discontinued at the end of 57 hours. The frog at this time was severely affected, and ultimately died; but beyond this period of 57 hours, the comparative observations were not continued, and the time of death was not noted. Accepting, however,

57 hours as the interval after which death occurred, we should have the numbers 29, 64, 57. The remaining four frogs appeared normal after periods of 46 hours, 48 hours, 31 hours, and 72 hours respectively.

Of the six corresponding experiments with arsenious acid, death occurred in five cases; in the sixth, the experiment was ended, and the frog killed at the end of 29 hours. At this time, however, the frog was severely affected, the voluntary movements being helpless, and the respirations markedly irregular, so that there is not the least doubt but that the frog would have died. However, leaving this frog out, we have the times of death, ranging between the extremes of 36 and 12 hours, with an average death-interval of 29½ hours.

Of the seven experiments with arsenite of soda, death occurred in six cases, whilst, quite unaccountably, in the seventh, the frog appeared normal after an interval of seventy-two hours. In the six cases of death, the times varied between the limits of eleven hours and a half, and fifty-two hours, with an average death-interval of 24½ hours.

The arseniate series of part II, showing three deaths against four survivals, would seem to indicate that one had come near the limits of the toxic dose; the three deaths are too few to strike an average from, even were this not inadmissible on the grounds of inconstancy of result. In part II, then, we have a marked contrast between the toxic effects of the arseniate on the one hand, and of the arsenite and arsenious acid on the other; the former not only yielding an inconstant result, but also in those cases where death did obtain, a considerably higher death-interval than the two lower oxides. This contrast is the more striking that the dose of metallic arsenic, as arseniate, is in this series twice as large as that in the form of arsenious acid and arsenite of soda.

In part III, we pass to the consideration of larger dosage, and here the experiments were between arsenious acid and the arseniate alone.

Under (a), the experiments represent equal dosage of metallic arsenic. The doses being large, death occurred in each case, but the time differences are very striking here. Thus, for the four experiments in this series, we have, for the arseniate, the following results:

Death of Central Nervous System.

9 hrs. 40 min.
8 " 45 "
9 " 30 "
9 " 20 "

37 hrs. 15 min.; Av. = 9 hrs. 20 min.

Death of Muscular Tissue.

9 hrs. 40 min.
21 " 15 "
22 " 30 "
9 " 20 "

62 hrs. 45 min.; Av. = 15 hrs. 40 min.

Against these, we have for arsenious acid the following:

Death of Central Nervous System.

1 hr. 10 min.
— 40 "
— 50 "
— 50 "

3 hrs. 30 min.; Av. = 50 min.

Death of Muscular Tissue.

9 hrs. 30 min.
5 " 10 "
5 " 30 "
4 " —

24 hrs. 10 min.; Av. = 6 hrs.

The ratios stand, then, arseniate to arsenious acid as 9 hrs. 20 min. : 52 min.; and as 15 hrs. 40 min. : 6 hrs.

Thus we see that, death being effected in each case, the death-interval varies greatly with the preparation used: arsenious acid causing death of the central nervous system in one-tenth of the time taken by the arseniate, whilst, with regard to the muscular tissue, the very lowest estimate makes the arsenious acid two-and-a-half times as active in point of time. It must be remarked here that the two numbers with the asterisk against them represent the times, not of death of the muscular tissue, but of systemic death, and that at these times in question the muscles all acted powerfully. Through some mischance, the time of destruction of muscular irritability was not noted; however, the error is in the direction of making the arseniate more active than is actually the case, probably very considerably so; this is borne out by the results obtained in part III (b), in which, with larger arseniate dosage, the death-intervals of the muscular tissue in no case fell as low as ten hours.

In part III (b), the arseniate was given in doses containing five times as much metallic arsenic as the arsenious acid doses; these latter were maintained the same as in part III (a). The results obtained here give as follows:

Arseniate of Soda.

Death of Central Nervous System.

3 hrs. 20 min.
2 " —
3 " 20 "
5 " 15 "
6 " 15 "

20 hrs. 10 min.; Av. = 4 hrs.

Death of Muscular Tissue of Anterior Limb.

27 hrs.
22 "
17 "
19 "
15 "

110 hours; Av. = 22 hrs.

Arsenious Acid.

0 hr. 45 min.
— " 50 "
— " 35 "
— " 50 "
— " 50 "

220 min.; Av. = 46 min.

7 hrs. 15 min.
5 " 40 "
3 " 15 "
4 " 45 "
6 " 10 "

27 hrs. 5 min.; Av. = 5 hr. 25 m.

Here, the dose being fatal in each case, the arsenious acid caused systemic death in one-fifth of the time taken by the arseniate; and this, though the dosage of metallic arsenic, as arseniate, was five times as great as that in the form of arsenious acid. The contrast between the times of death of the muscular tissue in the two cases is almost as marked, the arsenious acid acting four times as quickly.

We may point out here a result of some interest. On referring back to the tables with smaller dosage, it will be seen that the muscular tissue outlived but by a short time the central nervous system. Thus we have the average numbers 20.5 and 17 for the latter, against 23 and 21.5 for the former; whilst in these latter tables, we find very considerable difference between the death-intervals of these two tissues; this is well marked for the arseniate, but is much better marked for the arsenious acid; here, indeed, the ratio, one to six, is within the mark. We see, then, that, as we increase the intensity of our poison, the action on the two tissues does not keep equal pace, but affects the more delicately balanced structure at a relatively increasingly growing rate; indeed, the action on the delicate structures of the cardiac and respiratory centres is so sudden as almost to be of the nature of shock. The loss of reflex excitability of the spinal centres is possibly considerably accelerated indirectly through the impairment of the circulation.

The results may be advantageously recapitulated. It will be remembered that the element arsenic is here given in various forms of combination; and that the dosage refers, in all cases, to the amount of metallic arsenic present. We find, then, that in its lower grade of oxygen combination, whether in the form of arsenious acid, or in further combination with soda, as arsenite of soda, metallic arsenic manifests equal activity; that, in its higher grade of oxygenation, as arseniate, metallic arsenic manifests considerably less activity than in its lower grade of oxygenation.

The latter proposition rests on twofold evidence.

1. We have the fact, that, taking equal dosage of metallic arsenic, the doses may be so selected, that the lower oxide shall cause death, whilst the higher oxide is ineffectual.

2. The further fact, that, increasing the dosage so as to cause death in each case, the difference between the action of the two oxides appears as difference in rate of action, the lower oxide acting much more speedily; and this, even when the dosage of metallic oxide, in its higher combination, is five times as great as in its lower.

So much for the quantitative comparison of the action of different forms of arsenic combination. With regard to qualitative comparison, it is perhaps a little difficult to avoid classing difference in degree of action amongst qualitative differences; but certainly much of the difference in effect witnessed is rather in degree than in kind. The lower oxide is the more active; and, especially with the larger doses, there is observed a degree of rapidity of action which scarcely allows of the completion of the injection before its appearance. Amongst these appearances are: the violent attempts at escape during the first few seconds following the injection; the subsequent quiescence, the frog scarcely moving unless stimulated; the frequently observed attempts at vomiting; the early and marked effect on both respiration and circulation, the latter being judged of by the abdominal pulsations; the paralytic symptoms appearing towards the end; and, finally, the desquamation. All these have been more fully described elsewhere. (*Loc. cit.*, *Jour. of Physiol.*, vol. i, no. 4.)

Passing to the action of the arseniate, the absence of sudden violent action, with the gradual supervention of respiratory and cardiac failure, and finally of paralytic effects, is what one observes. But, with the larger doses, together with the more rapid accession of symptoms, retching and vomiting were witnessed; whilst desquamation, which, even with doses of 0.5 c.c. (8.45 minims) of a one per cent. solution of metallic arsenic, was not a well-marked symptom, became strongly marked when the same dose of the five per cent. solution was employed. Amongst other symptoms, frothing was observed, both with arsenious acid and arseniate, as an occasional symptom, and early in the action. Fibrillation of the muscles was observed on a few occasions with the arseniate.

It is clear that, qualitatively, but little distinction between the two oxides of arsenic can be made out; in fact, comparing them together, the contrast is to be found in the suddenness of the onset and violence of the symptoms, in the one case; in the delay and gradual accession of the symptoms, in the other.

The very concentrated solutions of arseniate of soda, employed in the end experiments, containing, viz., 5 per cent. of metallic arsenic, caused a certain amount of shock, following directly on the injection; this occurred in three out of the five cases, but recovery soon followed, and in all a stage of comparative well-being preceded the onset of symptoms.

It having been shown that there is a very decided difference in action between the two oxides, the question yet remains: How does the element arsenic act? The fact of the immediate onset of symptoms, with the lower oxide, proves that one has here an arsenic combination having a direct and powerful affinity for the tissues. The fact of the delayed action of the higher oxide bears two interpretations; the arseniate may still affect the tissues directly, and as such, the affinity, however, being much more feeble; or, it may not act as such, but only after it has suffered reduction to the state of the lower oxide—reduction, of course, involving time.

With reference to this last view, there are certain facts of importance, viz.:

1. The fact that the arseniate is a body which, not unready, suffers reduction to the state of arsenite, under suitable conditions.
2. The fact that the process of reduction is constantly obtaining in the tissues.
3. The fact, according to Binz and Schulz, that such reduction from arseniate to arsenite is actually effected in the tissues.
4. The fact of the qualitative similarity in the symptoms of arseniate and arsenite poisoning—a similarity which might exist truly, though either salt acted as such, but which *à fortiori* must obtain if the arseniate act only after reduction.

It is true that Binz and Schulz also state that the reverse process, viz., reconstruction of the higher oxide from the lower, also obtains in the tissues; but having shown, as these experiments undoubtedly do, that the lower oxide is by far the more active preparation, we should regard such reconstructive process as obviating, rather than as constituting, poisonous action; and we should hold that, if such double process do occur, the explanation of the arseniate action on the reduction-theory will have to be found in that the process of reduction considerably outbalances that of reconstruction. This, according to Schulz (*op. cit.*, Band xv), actually is the case; in the papers just quoted, he gives tables showing the relative powers of reduction and oxidation of certain of the tissues; the former process is there seen to outbalance by far the latter.

These points are by no means mere points of contention; they have obvious practical issue. The element arsenic is a most important therapeutic agent, and a very widely used one; it is clear, therefore, that a scientific use of such demands, in the first place, a knowledge of the relative activities of the various preparations employed. These experiments here relate to the frog, it is true, and, moreover, they refer to toxic doses; but there can be no question as to their indicating which is the more active preparation when thus employed. It may be objected that the rate of tissue-change in the amphibian organism is no measure of that obtaining in the tissues of the warm-blooded animal; and also that the argument from toxic doses to medicinal doses is not necessarily valid. It is precisely these objections which give practical importance to the reduction theory; for, if the arseniate do not act as such, but only after reduction to the lower oxide, why use it at all? It may be that in the small doses employed, therapeutically, the arseniate is practically all converted into arsenite, and the equal dosage, now in use, justified; but we are distinctly dealing with an unknown quantity, for of our definite arseniate dose administered we cannot say how much precisely will suffer reduction, how much will be eliminated as such. Next to qualification, the scientific demand is quantification; and how, in the reduction theory, is this possible? On the other hand, are there any advantages to be claimed for the therapeutic use of this drug such as might outweigh these disadvantages? Garrod states the arseniate to be far less irritant than the arsenite, and these experiments are certainly in favour of this; but, in the very large use of the arsenite now obtaining, is this irritant action practically a source of much trouble? Does it justify us in employing unknown quantities when we have known quantities at hand?

To conclude this subject, the result of some experiments of a different nature may be briefly stated.

The isolated ventricle of the frog's heart was fed with an artificial circulating fluid, and by means of Roy's tonometer the contractions were registered on a revolving blackened cylinder. To the circulating blood-mixture, solutions of arsenite and arseniate of soda were added. The following are the results obtained, given in tabular form. The quantities of arsenite or arseniate employed in each experiment represent the quantities requisite to destroy the contractility of the cardiac tissue.

Both solutions were distinctly alkaline, the arsenite indeed strongly so.

Arsenite of Soda 1 per cent. metallic arsenic=2.5 per cent. about, Na ₃ AsO ₃ .	Arseniate of Soda, 5 per cent. metallic arsenic=11 per cent., about, Na ₂ HAsO ₄ .
May 9th T. of Room=17°C. 29c.c.	Aug. 29th T. of Room=18°C. 24c.c.*
" 10th " " =15°C. 38	" 30th " " =15°C. 32
" 11th " " =18°C. 44	" 31st " " =17°C. 28
" 11th " " =18°C. 34	Sept. 1st " " =17°C. 32
" 12th " " =22°C. 32	
" 13th " " =18°C. 44	

* Av.=37c.c.

221

* Av.=29c.c.

* This number, 24c.c. was below the mark. The beats on this occasion not being completely abolished.

Again, we see in these experiments a similar relationship between the two oxides to that already found, for, to produce the same effect, viz., abolition of contractility, far larger quantities of the arseniate (compare the percentage strengths) are required than of the arsenite. The arseniate, indeed, is scarcely, if at all, more poisonous than the neutral salts of sodium, the chloride, bromide, iodide*; it behaved, moreover, just like these salts in other respects, and after the contractions had been reduced to a minimum, the substitution of fresh blood for the poisoned blood restored the contractility of the muscular tissue.

These results tend rather to confirm the reduction theory, for the reduction which is effected by the small amount of tissue represented by the ventricle must be very minute, and, when effected, if such do occur, it will be most probably swept away and diluted with the whole mass of circulating fluid, so that, practically, the ventricle would be in contact with the unreduced arseniate, and this these experiments show to be almost inert.

On the other hand, we note that the arsenite is decidedly more poisonous; and, moreover, in two experiments, in which, after reduction of the beats to a minimum, fresh blood was substituted, the contractility showed no recovery.

It will be unnecessary to recapitulate; it is sufficient to say that these last experiments with a single tissue confirm those with the entire organism in their results, and, in particular, they render more probable the reduction theory by showing the absence of direct affinity of the arseniate for certain, at least, of the tissues, ganglionic and muscular.

REPORT OF THE TREATMENT OF A VERY EXTENSIVE OUTBREAK OF RINGWORM OF THE HEAD, IN A SCHOOL: EIGHTY-FIVE OUT OF NINETY-TWO CHILDREN BEING AFFECTED.

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The following is a summary of the management of one of the largest outbreaks of ringworm of the head hitherto recorded. It shows the result of treatment by the compound carbolic acid, citrine, and sulphur ointment (described in the BRITISH MEDICAL JOURNAL, February 25th, 1882), and by oleate of mercury; also the great value of croton oil, when applied to small places of disease which have resisted treatment for some months.

On May 2nd, 1882, I visited a school consisting of ninety-two children, between the ages of nine and eleven years; and, on inquiry, learned that there had been some chronic cases of ringworm in the school, and that an extensive outbreak of cutaneous and scalp ringworm had recently developed.

On careful examination, it was found that forty-six out of forty-seven boys, and thirty-seven out of forty-five girls, had ringworm of the scalp. Some of the cases were chronic and extensive, others were moderate and more recent, while some were only one or a few days old. By far the majority had body-ringworm as well; but, as the scalp-disease was the cause of the cutaneous outbreak, and the latter was of very secondary importance, we did not tabulate the number of the spots on the bodies, nor the results of the treatment. I may just mention that the cutaneous patches were all cured during the first two or three weeks, either by Coster's paste, acetic acid, or the compound ointment; and that, after the heads were well under treatment, and the clothes fumigated, no fresh spots appeared. This leads me to remark that an outbreak of body-ringworm, in a school, is generally due to scalp-ringworm—probably overlooked.

The first precaution taken on May 2nd was the isolation of the nine unaffected children; and the following preventive ointment was ordered to be rubbed into all their heads every day: B Hydrargyri oxidum rubri

* See paper, *Transactions of the Medical and Chirurgical Society*, vol. lxx, p. 151.