type was suggested, but the paralysis was not of the ascending type; the limbs were not flaccid and helpless, the reflexes were not entirely abolished, and implication of the cranial nerves at so early a date would be most unusual.

I am inclined, therefore, to regard the case as one of myasthenia gravis, accompanied by hypertrophy of the thymus.

The sense of muscular weakness and tiredness, the implication of the facial and faucial muscles, the absence of sensory symptoms, of altered reflexes, and of muscular wasting are characteristic. The only difficulty that presents itself is the extreme rapidity of the progress of the disease, the whole period covered by the history being only thirteen days. The average duration of sixty cases collected by Campbell and Bramwell¹ is one and a half years from the first appearance of symptoms, but in one fatal case the disease lasted only fourteen days, and in another only a month.

Possibly the fatal termination was hastened by the presence of the catamenia, for it has been noted that patients are generally worse at this period. A complete *post-mortem* examination was not allowed, and consequently no examination of the nervous system could be made, whilst owing to the patient's brief stay in the hospital the myasthenic electrical reaction was not tested.

Such pathological changes as were found at the *post-mortem* examination were, however, confirmatory of the diagnosis of myasthenia gravis, for in a very large proportion of such cases there have been found hyperplasia of the thymus, also of the thyroid and the spleen, with dilated capillaries, haemorrhages, and blood debris, not only in these organs, but also in the liver, kidneys, and muscles. The muscles were not examined microscopically, but in the other organs no typical lymphorrhages were found, only dilated and engorged capillaries.

With regard to the causation of the condition and its relationship to the status lymphaticus little can be said. Buzzard thinks the symptoms of myasthenia "are best explained by assuming the presence of some toxic agent which has a special influence on the protoplasmic (as opposed to the fibrillar) constituent of voluntary muscle," and in this case the presence of numerous minute haemorrhages in the gastro-intestinal tract is certainly very suggestive of an infective process. The relation of such an infective process to the thymic alteration is not clear. There is no reason to think that this patient had at any time previously suffered from an enlarged thymus, but the death symptoms, asphyxia, and reflex cardiac failure are like those of status lymphaticus. We can only conjecture that the enlargement of the thymus and spleen were compensatory to some lymphoid exhaustion brought about by an acute toxæmia, probably of gastro-intestinal origin.

REFERENCE.
¹ *Brain*, vol. xxviii.

THE ANTIHAEMOLYTIC ACTION OF ARSENIC.

BY

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In a former number of this JOURNAL one of us (Gunn, BRITISH MEDICAL JOURNAL, July 18th, 1908) has pointed out that very dilute solutions of arsenious acid exert on the red blood corpuscles *in vitro* a distinct protective action against haemolysis by hypotonic saline solutions. The conclusion was also drawn that arsenious acid is rapidly fixed to the red blood corpuscles, and the suggestion was made that an action of arsenic of this nature may, in part at least, explain the benefit which results from the medicinal administration of arsenic in blood diseases, especially in pernicious anaemia, on the ground that it may for a time protect the erythrocytes from destruction by physiological or pathological processes. Further experiments have been made to determine whether this antihaemolytic action of arsenious acid is manifested by other compounds of arsenic and against haemolytic agents other than hypotonic solutions.

As it is probable that arsenious acid, after its absorption exists in the blood partly as sodium arsenite and partly as sodium arsenate, experiments were made with both these salts. Haemolytic agents of diverse nature were employed—namely, distilled water, cyclamin, and sodium glycocholate.

The normal saline solution (N.S.) was in all experiments 0.85 per cent. of sodium chloride in distilled water. A 1 per cent. suspension of human blood corpuscles was obtained by adding 0.025 c.cm. of blood to 2.5 c.cm. of normal saline solution, and suspensions of this percentage were used throughout. In experiments in which washed corpuscles were used, the corpuscles were thrice centrifuged with fresh saline and the final sediment made up to 2.5 c.cm. in the usual way.

I. SODIUM ARSENITE.

(a) Protection of Corpuscles against Haemolysis by Distilled Water.

In each of two tubes, A and B, was placed 0.5 c.cm. of a 1 per cent. suspension of unwashed corpuscles. To A was then added 0.5 c.cm. of a solution of sodium chloride 1 in 20,000 in N.S.; and to B. 0.5 c.cm. of a solution of sodium arsenite 1 in 20,000 in N.S. They were allowed to stand at room temperature for fifteen minutes, whereupon 0.7 c.cm. of distilled water was added to each tube. This produced in four minutes almost complete haemolysis in A, but only slight haemolysis in B. The tubes were allowed to stand at room temperature for eighteen hours, when it was found that the corpuscles in A were completely haemolyzed, whereas in B there was still a considerable sediment of unhaemolyzed corpuscles. In this experiment the corpuscles in B were suspended in normal saline solution, containing sodium arsenite in the proportion of 1 in 40,000. The corpuscles in A were suspended in a normal saline solution containing an additional quantity of sodium chloride in the proportion of 1 in 40,000, which was added to the saline in order to render the osmotic concentrations of the two solutions as nearly as possible the same. After the lapse of fifteen minutes the same amount of distilled water was added to each tube, and this produced a distinctly greater haemolytic effect on the control corpuscles than on those corpuscles which were under similar conditions, apart from the influence of sodium arsenite.

The conditions and results of this experiment may be stated briefly in the following table. As other experiments to be described were performed in a similar manner, they will be detailed in tabular form only.

TABLE I.

Tube A.	Tube B.
(1) 0.5 c.cm. blood suspension (unwashed corpuscles).	(1) 0.5 c.cm. blood suspension (unwashed corpuscles).
(2) 0.5 c.cm. sodium chloride 1 in 20,000 in N.S.	(2) 0.5 c.cm. sodium arsenite 1 in 20,000 in N.S.
Stood for 15 minutes at room temperature.	
No haemolysis.	No haemolysis.
(3) 0.7 c.cm. distilled water.	(3) 0.7 c.cm. distilled water.
<i>Result.</i>	<i>Result.</i>
In 4 minutes almost complete haemolysis.	In 4 minutes slight haemolysis.
In 18 hours complete haemolysis.	In 18 hours incomplete haemolysis.

A series of similar experiments was made and repeated, in which the corpuscles were subjected to solutions of sodium arsenite varying from 1 in 20,000 to 1 in 200,000. The same qualitative effect was obtained in all, though the antihaemolytic effect of the more dilute solutions was less pronounced. No protective effect was detected with solutions more dilute than 1 in 200,000.

Of course for such experiments it is necessary to add to the tubes not much more distilled water than is sufficient to haemolyze the control corpuscles, otherwise complete haemolysis will occur in both tubes.

(b) Protection of Corpuscles against Haemolysis by Cyclamin.

To ascertain whether sodium arsenite protects the corpuscles against haemolysis by saponin substances, experiments were made with cyclamin, which is one of the most active haemolytic agents of the saponin group. A strength of cyclamin solution convenient for the amount of corpuscles taken was ascertained by preliminary experiments and found to be 1 in 100,000 in normal saline solution.

The following experiment illustrates the kind of result obtained:

TABLE II.

<i>Tube A.</i>	<i>Tube B.</i>
(1) 0.5 c.cm. blood suspension (washed corpuscles).	(1) 0.5 c.cm. blood suspension (washed corpuscles).
(2) 0.5 c.cm. sodium chloride 1 in 50,000 in N.S.	(2) 0.5 c.cm. sodium arsenite 1 in 50,000 in N.S.
Incubated for 15 minutes at 38° C.	
(3) 0.15 c.cm. cyclamin solution.	(3) 0.15 c.cm. cyclamin solution.
Reincubated.	
<i>Result.</i>	<i>Result.</i>
In 5 hours complete haemolysis.	In 5 hours considerable haemolysis.
	In 18 hours incomplete haemolysis.

This experiment shows that an amount of cyclamin which will in five hours completely haemolyze a certain number of corpuscles in saline solution fails, even in eighteen hours, to haemolyze completely the same number of corpuscles when the saline solution contains sodium arsenite in the proportion of 1 in 100,000.

Many experiments of this nature were carried out in which the corpuscles were subjected to concentrations of sodium arsenite varying from 1 in 20,000 to 1 in 500,000. When the concentration of arsenite was 1 in 100,000 or greater there was a varying amount of absolute protection against haemolysis; when the concentration was 1 in 200,000 to 1 in 500,000 there was considerable delay in the onset of complete haemolysis in the arsenite tube as compared with the control tube, but within twenty-four hours all the corpuscles were haemolyzed also in the former tube.

In some other experiments the following variation was introduced. After the sodium arsenite had been allowed to act on the corpuscles at 38° C. for fifteen minutes in the usual way, the arsenite solution was removed from the corpuscles by thrice alternate centrifuging and replacement by normal saline solution, the final replacement bringing the blood suspension up to the original bulk of 1 c.cm. The control tube went through all the same processes apart from the exposure to sodium arsenite. The arsenite corpuscles, as compared with the control corpuscles, were now found to manifest an increased resistance to the haemolytic action of cyclamin, similar to that which had been found in the preceding series of experiments. From this it follows that the interference with the haemolytic action of cyclamin is due not to the presence of sodium arsenite in the saline solution, but to some combining action of sodium arsenite with one or other constituent of the corpuscles.

(c) *Protection of Corpuscles against Haemolysis by Sodium Glycocholate.*

It is well known that salts of the bile acids are haemolytic agents. To determine whether arsenic protects against haemolysis by bile salts, experiments were made with sodium glycocholate. A strength of solution of this substance convenient for these experiments was found to be 1 in 5,000 or 1 in 10,000 in normal saline solution. The former concentration was used in the following experiment, which illustrates the kind of result obtained.

TABLE III.

<i>Tube A.</i>	<i>Tube B.</i>
(1) 0.5 c.cm. blood suspension (washed corpuscles).	(1) 0.5 c.cm. blood suspension (washed corpuscles).
(2) 0.5 c.cm. 1 in 10,000 sodium chloride in N.S.	(2) 0.5 c.cm. 1 in 10,000 sodium arsenite in N.S.
Incubated 30 minutes at 38° C.	
(3) 0.3 c.cm. sodium glycocholate solution.	(3) 0.3 c.cm. sodium glycocholate solution.
Reincubated.	
<i>Result.</i>	<i>Result.</i>
In 3½ hours complete haemolysis.	In 3½ hours no haemolysis.
	In 20 hours incomplete haemolysis.

It is evident from this experiment that the presence of sodium arsenite in the proportion of 1 in 20,000 renders the corpuscles markedly less vulnerable than the control corpuscles to the haemolytic action of sodium glycocholate.

Many such experiments were made in which the corpuscles were subjected to varying concentrations of sodium arsenite, and it was found that solutions at least as dilute as 1 in 100,000 exerted a distinct protection of the red cells against haemolysis by sodium glycocholate.

II. SODIUM ARSENATE.

Series of experiments of the same kind as have been described with sodium arsenite were performed also with sodium arsenate. They showed that sodium arsenate acts in the same way as sodium arsenite in protecting the red blood corpuscles against haemolysis by distilled water, cyclamin, or sodium glycocholate.

According to Binz, blood has very little oxidizing power on arsenious acid, but acts in a strongly-marked manner as a reducing agent on arsenic acid. It is probable, therefore, that the major part of arsenious acid, after its absorption, will exist in the blood as sodium arsenite, and for this reason we have described in detail the experiments with arsenite.

CONCLUSIONS.

The conclusions we draw from these experiments are that arsenic, whether in the form of sodium arsenite or sodium arsenate, exerts on the red blood corpuscles an action antagonistic to that of certain haemolytic agents. The experiments, therefore, afford additional proof in favour of the view that a protective action on the formed red blood corpuscles against normal or abnormal haemolytic processes may, in part at least, account for the as yet imperfectly explained benefit which results from the medicinal administration of arsenic in blood diseases.

Memoranda :

MEDICAL, SURGICAL, OBSTETRICAL.

MENINGOCELE OF SKULL CAUSING DIFFICULTY IN DELIVERY.

READ in connexion with Dr. Robinson's case reported in the JOURNAL of December 3rd, 1910, p. 1773, the following may be of some interest:

In August I was called to attend a primipara, but, on arrival, I found that delivery had taken place, and that it only remained for me to remove the placenta, about which there was no difficulty. The nurses then asked me, with consternation, to tell them what had been delivered. The creature was uncovered, and I found the following remarkable conditions:

There was a frontal meningocele—perhaps as large as the head—drooping over and concealing one side of the face. It was tense and the skin appeared to be thin. There was a certain amount of exophthalmos of one eye, a double harelip, and a cleft palate. Otherwise there was no apparent malformation, but the child was quite vigorous and—perhaps owing to the latter circumstance—presented an appearance more horrible and repulsive than anything I have seen before, not excepting museum specimens.

It was necessary to conceal it from the mother, and so appalling was the appearance that even the nurses' feelings had to be taken into consideration. Obviously it was unsuitable for private guardianship, and, imagining that its existence must be brief, I induced a public institution to take charge of the child. However, on inquiry about six weeks later, to my great surprise, I learnt that the infant was thriving, crying for food, and showed no indication whatever of failing. I can follow the history no further, but what the future of such a creature must be, should it survive, requires little imagination.

I was informed that the delivery occurred normally and without assistance, the tumour, of course, presenting, and from the appearance of the skin I have no doubt that any manipulation would have caused the meningocele to burst.

The only statistics of congenital meningocele with which I am acquainted are those of Z. Laurence. He quotes 39 cases, of which 6 reached adult age. I am not aware that he gives the dimensions.

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