mitted to confess that the proudest moment of my life was when the late Mr. Bailey told me that a book, of which I was the humble author, had been purloined from the College Library? Would it, thought I, be possible for an intelligent reader to pay a writer a higher compliment?

THE LENGTH OF PAPERS.

With societies, as with individuals, age brings tolerance. But a century and a quarter ago the Medical Society regarded diffuse communications with intense horror; they would not have them at any price. Even Lettsom had his manuscript on Intussusception taken back to him for abridgment. And, if such treatment of communications was desirable when the Society was small and when there was sometimes a dearth of communications, it is positively necessary now. Let me beg, therefore, that everything brought before the Society be short, sharp, and to the point.

Our Society was always anxious that the papers read before them should be discussed. And to see that they had the right sort of material for their meetings the Council used to read through every communication before sanction was given to its being brought before the Society. For obvious reasons this desirable course can no longer be pursued, and responsibility in this matter now rests chiefly with the Honorary Secretaries. It is intended, however, during the coming session to relieve the Secretaries of much of this inconvenient responsibility by more generally referring proposed communications to the various Committees of Reference.

In the infancy of the Society the procedure in connection with each paper was as follows: The paper was read by the Council, and, if approved, was ordered to be brought before the Society. On the first occasion of its being read before the Society, however, it was not discussed, but on the conclusion of the reading, a vote was taken as to whether it should be publicly read a second time. If this was declared in the affirmative, the discussion took place after the second reading, and a vote of thanks was then passed to the reader. It is impossible to go back to that plan, but we must all feel that it had much to commend it. The Fellows of a Society derive more benefit from the full discussion of a few papers of high merit than from hearing many papers of lesser value.

A SURGICAL CONFESSIONAL.

In the oration which I had the honour of delivering before this Society about eighteen months ago, I made a suggestion, in all seriousness, that it might be advantageous if we set apart one meeting in the session for the discussion of unsuccessful cases, or those which had ended in disaster. I now ask how it would fall in with the views of the Society to make the last meeting in this year a "Surgical Confessional evening?" I do not know if my own experience differs widely from that of other surgeons, but I am the unhappy possessor of considerable wealth of clinical material for such an evening, which, in the silent watches of the night—and at other times—is apt to thrust its records before my inward eyes. I would be willing, therefore, to start the business of the evening. There would, of course, be no report of that meeting; possibly, indeed, the reporters would themselves like to bring forward a case or two of their own. At any rate, I should be glad to hear what my surgical *confères* think of the idea.

ADVANTAGES OF THE SOCIETY.

In conclusion, permit me to make a request of each one of you, namely, that you specially endeavour to bring recruits into the Society. We want particularly young men, though, of course, we shall gladly welcome those who can no longer claim the privileges and advantages of youth, for we have no age limit. But young men are those who are going to do and to carry on the work of the Society, so we must have a fair proportion of young recruits. As you well know, you can safely advise your friends to join our Society, whatever their line of practice is going to be—medical, surgical, obstetric, general, or special. In our rooms they will make the acquaintance of men in all lines of practice, and they will soon find acquaintanceships ripening into friendships. At our meetings they will hear all subjects treated of in turn and discussed in a bright and practical manner; I am glad to say that the discussions are sufficiently informal not to create weariness or inspire awe.

Lastly, the annual subscription is small, and it entitles one to a copy of the *Transactions* of the Society, a work which seems steadily to be increasing in value and interest. But beyond all this, and beyond the various and manifold benefits offered by the Society, the working Fellow will discover advantages in our Library which, considering the smallness of his annual payment, certainly cannot be offered by any other Society in London and probably are without equal in any other city in the world.

May this, the 126th year of the useful life of the Medical Society of London be as happy as any one of those through which it has already passed; may there be no falling off in practical value of the work done in it, and may the spirit of tolerance and fraternity which Lettsom breathed into that little group of medical friends in the month of May, 1773, continue to increase amongst our Fellows not only for the session which is now beginning, but until time itself shall be no more.

THE NATURE OF THE ANTAGONISM BETWEEN TOXINS AND ANTITOXINS.*

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In the *Deutsche medicinische Wochenschrift* for 1894 a controversy appeared on this subject between Behring and Buchner. Behring maintained that the antagonism was of a chemical nature, and that the antitoxin neutralised the toxin much as an alkali neutralised an acid. Buchner, on the other hand, adduced results opposed to this view, pointing to the interpretation that the action was an indirect one, due to the antitoxin operating in some indirect way through the medium of the cells of the organism. Since this controversy many investigations have been made with the object of deciding this fundamental point. At the present time, however, opinion is still divided; Behring, Ehrlich, and Kanthack being principal exponents of the direct chemical view, whilst Buchner, Roux, and Metchnikoff still maintain that the interaction takes place only through the intervention of some cells in the body.

We will briefly review the more important observations which bear directly upon the subject of our paper.

I.—OBSERVATIONS FAVOURING THE INTERPRETATION THAT THE ACTION OF ANTITOXINS IS INDIRECT.

Calmette¹ in 1895 made experiments with the toxin of cobra poison and its antitoxin, which he had recently succeeded in producing. Cobra poison is not apparently attenuated by heating its solutions to 68° C. for ten minutes. The antitoxin is, however, completely destroyed by this treatment. Mixtures of cobra poison and antitoxin which produced no symptoms when injected into a rabbit killed similar rabbits in a few hours if after the mixture had remained in contact for ten minutes it were heated for another ten minutes to 68° C. before injecting. From his experiments Calmette concluded that the toxin of snake venom does not interact with its antitoxin *in vitro*, but only *in corpore*, and therefore that its action cannot be explained as a simple chemical operation between the two.

Wassermann² found that the toxin produced by the bacillus pyocyaneus was not destroyed by boiling, whereas its antitoxin was. The amount of toxin and antitoxin which neutralised each other was first determined by experiment, then the same quantities and proportions of these substances were allowed to remain in contact and afterwards heated to boiling. The animals receiving an injection of this heated mixture died, whereas the control animals which received an equal dose unheated recovered. From these experiments Wassermann concluded that the toxin of pyocyaneus does not interact with its antitoxin *in vitro*, but only *in corpore*, and therefore that it cannot be explained as a simple chemical operation between the two.

Nikanorow³ discovered that the precipitate formed by the

* Read before the Royal Society, June, 1898.

addition of a 1 per cent. solution of cupric acetate was possessed of antitoxic properties and the filtrate not. A 1 per cent. solution of cupric acetate does not, however, precipitate the toxin. Mixtures of the two could thus be separated by the use of this reagent. Experiments conducted along the lines mentioned in the experiments above led to identical results.

Marengi⁴ made some observations with the toxin and antitoxin of diphtheria which were identical in principle with those of Calmette and Wassermann. In this case, however, it is the toxin which is destroyed at the lower temperature (60° C., Roux and Yersin), whereas the antitoxic properties still remained after heating the serum to 70° C. Mixtures of the two in such proportions as to cause no symptoms when injected into a guinea-pig were made. After heating such mixture to a temperature sufficient to destroy the toxin, the mixture was discovered now to possess antitoxic properties which could be titrated against a fresh amount of toxin.

II. OBSERVATIONS FAVOURING THE INTERPRETATION THAT THE ACTION OF ANTITOXINS IS DIRECT.

The view that the operation is a direct one has always received support from the general truth of the "law on multiples," on which indeed the antitoxin notation has been founded. It is further strengthened by the observations of Kanthack and Ehrlich.

Kanthack,⁵ in 1896, demonstrated that the influence of cobra poison in preventing the coagulation of *shed* blood, observed by Cunningham, was prevented by the previous admixture of some of Calmette's antivenomous serum to the solution of cobra poison.

Ehrlich⁶ found that if a solution of ricin be added to defibrinated blood (? animal) the corpuscles are precipitated in a clump. A ricin solution of the same strength, but containing a little serum from an animal immunised against ricin, failed to produce this result.

Within the last few days we have received a short account of some experiments by Stephens and Meyers,⁷ bearing upon the same point. Cobra poison exercises a hæmolytic action upon blood *in vitro*. After admixture of the poison with antivenomous serum this hæmolytic action was absent. The necessary precaution of making the solution of the venom with saline solution approximately isotonic with blood serum was taken.

Before relating the results of our own experiments we may point out one source of fallacy in the conclusions drawn by Wassermann, Calmette, Nikanorow, and Marengi—namely, that they take no account of the factor, time, which may be a very important element in any possible chemical interaction between toxins and antitoxins. Every chemical reaction has a certain definite velocity coefficient, and the rapidity of action under any circumstances where the reacting compounds are in solution depends upon this coefficient, and also upon the product of the active masses of the reacting bodies present. Temperature will also exercise an important influence.

As we shall later show, the experiments quoted by these observers can easily be repeated and the same results obtained. Nevertheless, their conclusions are quite unjustified, and by modification of the factors—time, temperature, and active masses—exactly opposite results may also be obtained.

EXPERIMENTAL RESULTS OBTAINED BY THE AUTHORS.

Our experiments have been conducted with the toxin of diphtheria, and one of the constituents of the poison of the Australian tiger snake *hoplocephalus curtus*.

The diphtheria toxin was prepared by cultivating the organisms in broth made from well-hung beef, after the method of Spronck.⁸ It was filtered through a sound Pasteur-Chamberland filter, and the toxin strength of the filtrate determined by injection into a series of guinea-pigs. That with which most of our experiments were conducted had a minimum lethal dose of 0.12 c.cm. per kilogram in forty-eight hours.

The antitoxins used were Behring's No. 1 and serum from the Pasteur Institute, Paris.

The constituent of the venom used was the one which is not destroyed by heating a solution of venom to 90° C. This

constituent resembles most closely, if indeed it be not identical with, the principal constituent of cobra poison; and, as shown by one of us,⁹ Calmette's antivenomous serum possesses a small but decided counteracting action upon it. This action, although unfortunately of little or no practical importance, is sufficient for our present purpose, for in our experiments we could mix comparatively large quantities of the serum with small fatal doses of the venom *in vitro*. Under these circumstances one could easily neutralise the poison.

The antitoxin was the antivenomous serum prepared by the Pasteur Institute at Lille, and bore date November, 1896.

We endeavoured at the outset to determine whether the action of antitoxins upon toxins were chemical or physiological, by a direct physical method. In 1896 one of us¹⁰ published an account of a method of separating substances of large molecular size from those of smaller, in solutions containing both. This method was simply by filtering through a film of gelatine, supported in the wall of a Pasteur-Chamberland filter. The filtration was accomplished by a pressure of 50 atmospheres.

A standardised solution of diphtheria toxin was filtered through such a filter. The filtrate was found to contain diphtheria toxin. This filtrate was then tested to ascertain whether it were as toxic as the original solution. As will be seen from the protocols it was somewhat diminished in toxic power (Protocol I).

The antitoxin of diphtheria, as was shown by Brodie,¹¹ does not pass through such a filter. When antitoxic serum is filtered through gelatine, the whole of the proteids, and together with them all antitoxic virtue, are absent from the filtrate (Protocol II). As the toxin is not held back by the filter, whereas the antitoxin is, one is provided with a simple physical means of separating them, provided they have not reacted upon one another.

We mixed a solution of toxin containing eight fatal doses per kilogram of guinea-pig in each c.cm., with sufficient Behring's antitoxin to more than completely neutralise all the toxin. This mixture was allowed to remain in contact at 30° C. for two hours, and then filtered through the gelatine filter. Varying quantities of the filtrate were injected into guinea-pigs up to nearly 4 c.cm. per kilogram of body weight, that is, a quantity originally containing thirty-two fatal doses. The filtrate was quite innocent. The guinea-pigs suffered no inconvenience, and gained weight while under observation in small cages. The injections produced no local oedema.

If the toxin had remained unaffected beside the antitoxin there was nothing to prevent it passing through the filter in virtue of its relatively small molecular size. As, however, it did not do so, we can only conclude that it had entered into some sort of chemical relationship with the relatively large molecules of the antitoxin during their sojourn together prior to filtration.

Having obtained results so definite, and in apparent contradiction to those of the authors quoted in the beginning of this paper, we next experimented with snake venom in order to repeat Calmette's¹² observations.

We took a series of rabbits (Protocol V) and injected them with mixtures containing one constituent of the venom of *hoplocephalus curtus* and Calmette's antivenomous serum. On reference to the protocols of this series of experiments it is seen that 2 c.cm. of this sample of serum was sufficient to counteract an amount of the poison contained in 0.002 g. of the dried venom. This amount killed control rabbits in about eight hours (Protocol IV).

In some of the experiments this amount of venom and serum was allowed to remain in contact for fifteen minutes at the laboratory temperature (21° C.), and then heated to 68° C. for ten minutes to destroy the antitoxin. In Calmette's experiments the rabbits injected with this heated mixture died, whereas the controls injected with the mixture which had not been heated lived. From this he concluded that the serum and venom were merely existing side by side, and had not reacted upon one another. In our experiments, on the contrary, the rabbits injected with the heated and unheated mixtures of venom and serum alike lived, nor did any of them suffer from symptoms such as loss of appetite, loss of weight, or diminished temperature. The only conclusion to be drawn from these experiments is that during the time which elapsed between the mixture of the venom and serum

the latter had acted upon the former, so that there was no longer a fatal dose of venom present. The protocols will show that heating for ten minutes to 68° C. has no influence upon the venom.

These results, while they lead to results in entire agreement with those drawn from the filtration experiments with diphtheria toxin and antitoxin, are diametrically opposed to the results obtained by Calmette. As the experiments are so simple as not to leave any possibility of experimental error, we turned our attention to any existing difference in the conditions under which Calmette and ourselves worked. As previously pointed out, Calmette absolutely neglected the possible influence of time, temperature, and the relative proportions of the active masses of the toxin and antitoxin present in his mixture. Up to the present we have investigated the value of the factors, time and proportion of active masses, and have shown that these are most important. Indeed, by altering either the one or the other we can produce results which, if these factors be neglected, would lead to diametrically opposite conclusions.

The toxin and antitoxin of this venom are both of great molecular size and complexity. The former is a deuteroalbumose and the latter probably a globulin,¹³ or at any rate its molecular size is of the same order. *A priori* one would expect the velocity coefficient of any reaction between such complex molecules to be a high one, and in addition, from their great molecular weight, the solution will contain relatively few molecules: so that it is not surprising that any chemical operation in which they are concerned should occupy a very appreciable time.

The value of the factors time and influence of proportion of active masses will be best seen in reference to the table below, which is compiled from Protocols VII, VIII, IX, and represents the results of twenty-one experiments. On reading along any horizontal line will be seen the influence upon the result of the time during which the toxin and antitoxin were allowed to operate upon each other, with proportion of active masses constant. On reading any vertical line the influence of varying proportions of active masses with time of operation constant is indicated. The thick line separates off the fatal results from those in which the rabbits lived. All other factors were kept constant. The solutions were mixed in the varying proportions and stood at laboratory temperature (20-23° C.). At stated intervals, by a stop watch, portions were pipetted off, and the reaction terminated by rapidly raising the temperature to 68° C. in a water bath. They were kept at this temperature for ten minutes, cooled, and kept for injection.

Proportion of Toxin to Antitoxin per kilo.		Time allowed for Interaction of Toxin and Antitoxin, Temp. 20-23° C.						
Anti-toxin.	Toxin.	Control Venom only.	2 mins.	5 mins.	10 mins.	15 mins.	30 mins.	Injected unheated 8 mins.
1 c.cm.	2 fatal doses	Died 15 hours	Lived; (very ill for 2 days)	Lived; ill 1 day	Lived; no symptoms	Lived; no symptoms	Lived; no symptoms	Lived; no symptoms.
1 c.cm.	3 fatal doses	Died 12 hours	Died 20 hours	Died 23 hours	Lived; ill 2 days	Lived; ill 1 day	Lived; no symptoms	Lived; no symptoms.
1 c.cm.	4 fatal doses	Died 9 hours	Died 13 hours	Died 15 hours	Died 23 hours	Lived; very ill 2 days	Lived; no symptoms	Lived; no symptoms.

In our experiments with diphtheria we allowed abundance of time (two hours) for the reaction between the toxin and antitoxin to take place. The surplus of antitoxin was also large, so that the active masses were considerable and the temperature was favourable, namely, 30° C. (Protocol III). We have not yet

determined the influence of temperature upon the rapidity of the reaction, but our results so far seem sufficiently conclusive to decide the question, and leave no room for doubt that the antagonism between the toxins of diphtheria and snake venom and their relative antitoxin is due to a direct chemical action which takes place between them. Further, that the opposite conclusion came to by Calmette, and presumably those of Wassermann, Nikanarow, and Marengli, were due to their disregard of the value of time as a factor in such chemical action.

PROTOCOL.

A.—EXPERIMENTS WITH DIPHTHERIA TOXIN.

I.—Experiments to ascertain whether the Toxin of Diphtheria passes through a Gelatine Filter.

The toxins were prepared by the method stated above, and filtered through a Pasteur-Chamberland filter to free them from bacilli. The minimal fatal dose calculated for one kilogram weight of guinea-pig was 0.12 c.cm. of toxin No. 1, and 0.6 c.cm. of toxin No. 2. Portions of each of these toxins were filtered through gelatine, and afterwards injected into guinea-pigs. As seen below, the filtrates in each case contained toxin, but in less amount than the original solutions.¹⁴

Toxin No. 1.

	Amount Injected.	Weight of Animal in Grms.	Result.
Before filtering through gelatine	0.25 c.cm.	562	Died under 36 hours.
" " "	0.5 "	540	" "
" " "	1.0 "	655	" "
After filtering through gelatine	0.12 "	187	" in 41 hours.
" " "	0.24 "	176	" in 30 hours.

Toxin No. 2.

	Amount Injected.	Weight of Animal in Grms.	Result.
Before filtering through gelatine	0.5 c.cm.	377	Died in 56 hours.
After filtering through gelatine	0.5 "	275	" 72 hours.

II.—Experiments to confirm Brodie's¹⁵ Statement that the Antitoxin of Diphtheria does not pass through a Gelatine Filter.

0.5 c.cm. of Pasteur Institute antitoxin was mixed with 1 c.cm. of toxin No. 1 (=8 fatal doses per kilo.), and injected into a guinea-pig weighing 260 g.

The animal remained well, and gained 26 g. during the four days it was kept under observation. The same sample of antitoxin was passed through the filter. Of the filtrate 0.6 c.cm. was mixed with 0.6 c.cm. of the same toxin, and injected into a guinea-pig weighing 163 g. The animal died in 22 hours.

III.—Experiments to show that when Diphtheria Toxin is mixed with Diphtheria Antitoxin in sufficient quantity, and allowed to remain in contact for a sufficient time, the filtrate which has passed through a Gelatine Filter is free from Toxin.

Sixty c.cm. of toxin No. 1 (containing approximately 500 lethal doses per kilogram) was mixed with 2.5 c.cm. of Behring's antitoxin (=600 units). The two were well mixed and allowed to stand at 30° C. for two hours before filtration.

The filtrate was injected subcutaneously into guinea-pigs as under:

Weight in Grammes.	Amount Injected.	Amount per Kilo. of Body Weight.	Result.
460	1.0 c.cm.	2.5 c.cm.=20 fatal doses	No symptoms.
340	1.25 c.cm.	3.6 c.cm.=30 "	" "
318	1.25 c.cm.	3.9 c.cm.=32 "	" "

The animals were absolutely unaffected. They never failed in appetite, nor was there any local cedema.

B.—EXPERIMENTS WITH SNAKE VENOM.

IV.—Experiments to determine the Minimal Fatal Dose of the Poison Used.

The venom employed was that of *hoplocephalus curtus*. This had been procured free from admixture with saliva by making the reptiles bite into a watch glass covered with thin rubber sheeting. The liquid poison was rapidly dried at ordinary temperatures (15° to 20° C.) over calcium chloride, powdered, and stored in a stoppered bottle. All weights of venom mentioned below refer to this dried venom. About 2 to 3 milligrammes were weighed out for each experiment, and dissolved in 0.9 per cent. NaCl solution, so that 1 c.cm. contained 0.0001 g. of dried venom.

The solution was then heated momentarily to 90° C. in order to destroy one of the poisonous constituents of the venom of this snake, a proteid which coagulates at 85° C.¹⁶ This was done because Calmette's serum possesses little or no immunising action against this constituent.¹⁷

In all our experiments the same sample of venom was used, and it was treated in the way described above. The injections were always made subcutaneously into the flank.

Animal.	Weight in Grammes.	Amount of Original Venom per Kilo. of Body Weight in Grammes.	Result.
Rabbit ...	1,360	0.0004000	Died in 5 hours.
" ...	1,020	0.0002000	" 8 "
" ...	910	0.0002000	" 9 "
" ...	1,250	0.0001500	" 10 "
" ...	1,705	0.0001500	" 10 "
" ...	1,250	0.0001000	" 10 "
" ...	1,240	0.0000800	" 12 "
" ...	1,030	0.0000750	" 10 "
" ...	1,220	0.0000500	" 16 "
" ...	1,370	0.0000360	" 24 "
" ...	1,300	0.0000300	" 48 "
" ...	1,380	0.0000300	Lived. Very ill 3 days.
" ...	1,820	0.0000275	Died in 24 hours.
" ...	1,430	0.0000250	" 3 days.
" ...	1,140	0.0000200	Lived. Very ill 3 days.
" ...	1,300	0.0000200	" " "

From the above series it appears that 0.000025 g. per kilo. of body weight is about the lowest fatal dose. In the present paper, in speaking of so many fatal doses, this has been taken as the unit.

V.—Experiments to ascertain the value of Calmette's Serum in counteracting the Poison after it had been deprived by Heat of One Constituent.

The solution of venom was prepared as in Series III. Calmette's serum bore date November, 1896. The two were mixed together in varying proportion, as stated below, and allowed to remain at laboratory temperature (23° C.) for fifteen minutes. They were injected subcutaneously in amounts corresponding to the body weight of the animal.

Animal.	Weight in Grammes	Amount of Venom in Grammes per Kilo.	Amount of Serum in c.c. per Kilo.	Result.
Rabbit	1,350	= 16 fatal doses.		
"	1,370	0.0004	None.	Died 5 hours.
"	1,330	0.0004	0.25	" 6 "
"	1,370	0.0004	0.5	" 10 "
"	1,370	0.0004	1.0	" 12 "
"	1,375	0.0004	1.5	" 16 "
"	1,240	= 8 fatal doses.		
"	1,220	0.0002	1.0	" 38 "
"	690	0.0002	1.5	Lived. Ill 2 days.
"	1,380	0.0002	2.0	No symptoms.
"		0.0002	3.0	" "

Two c.cm. of the serum completely counteracts 0.0002 g. of the venom deprived of one of its constituents.

VI.—Experiments to determine whether Mixture of Venom and Serum (in such proportions as to completely deprive the former of any toxic properties) regained Toxic Properties after destroying the antitoxin by heating to 68° C. per 10 minutes, subsequent to admixture.

The venom solution and serum were mixed in the proportion of 1 c.cm. of serum to every 0.0001 g. of venom. This proportion was found by the previous series of experiments to be adequate. The two solutions were mixed together, and allowed to remain thirty minutes at a temperature of 23° to 24° C., after which the mixture was heated to 68° C. for ten minutes to destroy the antitoxin. They were then cooled, and injected subcutaneously in varying quantities per kilo. weight of the animal. The injections had no effect upon the animals, although they contained originally eight fatal doses of venom. This must, therefore, have been neutralised by the antitoxin during the time which elapsed before its destruction by heat.

Animal.	Weight in Grammes.	Amount of Venom per Kilo.	Amount of Serum per Kilo.	Result.
i. Rabbit	1,140	0.0002	3 c.cm.	Lived. No symptoms.
ii. "	710	0.0002	2 "	
iii. "	1,210	0.0003	3 "	
*iv. "	1,020	0.0002	None.	Died in 9 hours.
v. "	1,160	0.0002	None.	" 8 1/2 "

* In Experiment No. iv no serum was mixed with the venom, but the venom solution was heated alone to 68° C. for 10 minutes to show that this treatment has no influence upon it.

VII.—Experiments to determine the influence of Variations in the Time during which Venom and Antivenomous Serum operated upon one another.

In this series of experiments the same samples of venom and serum were employed as before. The relative proportions of the two were kept constant. The venom solution and serum were mixed together in the proportion of 0.0001 g. of venom to 1 c.cm. of the serum and well stirred. After they had remained in contact at the temperature of the laboratory (21° C.) for times varying from two to thirty minutes, portions were pipetted off, and rapidly raised to 68° C., at which temperature they were kept for ten minutes. The portions were then rapidly cooled, and injected subcutaneously in quantities proportionate to the body weights of the animals. Amounts of venom and of serum equivalent to 0.0001 g. and 1 c.cm. respectively per kilo. of body weight were injected in each case, except the control, when this quantity of venom was employed.

Animal.	Weight in Grammes	Time during which Venom and Serum were in contact before heating.	Results.
i. Rabbit	1,370	Venom only (control)	Died in 9 hours
ii. "	1,320	2 minutes	" 13 "
iii. "	1,340	5 "	" 15 "
iv. "	1,400	10 "	" 23 "
v. "	1,220	15 "	Lived. Very ill 2 days
vi. "	1,160	30 "	" No symptoms
vii. "	890	Not heated at all	" " "

VIII.—Similar to VII, except that the Preponderance of Antitoxin was greater, namely, 0.000075 g. of Venom and 1 c.cm. of Serum per kilo. of Body Weight in each Case.

Animal.	Weight in Grammes.	Time during which Venom and Serum were left in contact before heating.	Results.
i. Rabbit	1,025	Venom only (control)	Died in 12 hours.
ii. "	1,190	2 minutes	" 20 "
iii. "	1,130	5 "	" 23 "
iv. "	1,060	10 "	Lived. Very ill 2 days.
v. "	1,250	15 "	" Ill 1 day.
vi. "	1,210	30 "	" No symptoms.
vii. "	1,070	Not heated at all	" "

IX.—Similar to VII and VIII, but the Preponderance of Serum is still greater, namely, 0.00005 g. of Venom and 1 c.cm. of Serum per kilo. of Body Weight in each Case.

Animal.	Weight in Grammes.	Time during which Venom and Serum were in contact before heating.	Result.
i. Rabbit...	1,070	Venom only (control)	Died in 15 hours
ii. " ...	1,200	2 minutes	Lived. Very ill 2 days
iii. " ...	1,170	5 "	" Off feed 1 day
iv. " ...	1,130	10 "	" No symptoms
v. " ...	1,030	15 "	" "
vi. " ...	1,450	30 "	" "
vii. " ...	1,050	Not heated at all	" "

NOTES AND REFERENCES.

- ¹ Ann. de l'Inst. Pasteur, 1895, p. 250. ² Zeit. f. Hyg., 1896, B. xxii, p. 521. ³ Vratel, 1896, vol. xxxi, abstracted, Jour. Phys. Chem., 1896, p. 983. ⁴ Cent. f. Bakt., 1897, vol. xxii, p. 521. ⁵ Demonstrated at the meeting of the Physiological Society, October, 1896, not published in Proceedings. ⁶ Fortschritte der Med., 1897, No. 2. ⁷ Report of Proceedings of Pathological Society of London, Lancet, March 5th, 1898, p. 644. ⁸ Ann. de l'Inst. Pasteur, 1895. ⁹ C. J. M., Intercolonial Medical Journal of Australasia, August, 1897. ¹⁰ C. J. M., Journal of Physiology, vol. xx, 1896. ¹¹ Journal of Pathology, 1897, p. 460. ¹² Loc. cit. ¹³ Brodie, loc. cit. ¹⁴ This small diminution in toxic power by filtration may possibly be due to the action of oxygen at high tension (50 atmospheres of compressed air) or to the size of the toxin molecule being of the order of the molecular size of albumoses. Albumoses as shown by one of us (Journal of Physiology, 1896) passed through gelatine, but less readily than water, and the filtrate is consequently less concentrated than the original solution. ¹⁵ Loc. cit. ¹⁶ C. J. M., Proc. Roy. Soc. N.S.W., 1896. ¹⁷ C. J. M., Intercol. Med. Jour., August, 1897.

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CASE OF EXCISION OF A MASS OF ENLARGED CERVICAL GLANDS (TUBERCULOUS) WITH A PORTION OF THE INTERNAL JUGULAR VEIN.*

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OWING to the frequency with which tubercle primarily manifests itself in the lymphatic glands there is no subject more important to the surgeon and the general practitioner than its treatment. Upon this point a good deal of controversy has taken place, especially (and this for æsthetic reasons) in relation to cervical tuberculous lymphadenitis, but I think most surgeons have now come to recognise the fact that, as tuberculous glandular disease manifests itself clinically in many ways, so the line of treatment must vary to meet these different morbid conditions. Broadly speaking, the main groups under which cervical tuberculous lymphadenitis presents itself are three in number.

1. A single movable gland.

* Patient was shown on April 1st, four weeks after operation, at the meeting of the Glasgow Medico-Chirurgical Society.

2. A bunch of movable glands, all of which remain separate and distinct from one another.

3. A large mass of glands matted together and embedded in dense, fibrous tissue. When grasped it is felt that the mass, though movable as a whole, has firm and deep attachments, and that the individual glands composing it are blended one with another.

My own line of practice as regards the first two groups is rather to rely on constitutional treatment, but if resolution does not take place, and caseation and softening are imminent, to proceed to incision with complete evacuation of the tuberculous contents by the sharp spoon, followed by stuffing with Berlin wool (Stiles) impregnated with iodoform. Very careful subsequent dressing gives excellent results, and the small incisions made become in time very slightly noticeable.

It is a different matter when one has a case that belongs to the third group, where the anterior and also the posterior triangle of the neck is occupied by a large and fixed tumour of considerable size, which is not yielding to the constitutional measures of treatment that have very properly been advocated in the earlier stages of the disease. The first thing to be done in such a case, of course, is to be sure that what we are dealing with is a local tuberculosis of the lymphatic glands; a condition unquestionably of an infective nature, as shown by its passing from gland to gland, and yet not necessarily part of a general tuberculosis. We must also be satisfied that the swelling is not of the nature of a lymphadenoma, that is, a special affection of the lymphoid tissue throughout the body, nor either of those forms of sarcoma known as lymphosarcoma and lymphatic gland sarcoma. This point having been cleared up (if necessary, by a preliminary incision to remove a small gland or a portion of a larger one) we have then to decide what should be the treatment of so extensive a local tuberculous lymphadenitis.

One point that must always weigh with us is the age of the patient. In young children excision is not to be recommended. Reliance must be placed on caseation and softening of the glands with subsequent incision and scraping. No doubt some risk of general tuberculosis is run, but very young children do not bear well the lengthy and severe operative measures that such cases undoubtedly entail. It is different, however, with young adults. If they are otherwise in good health excision is, I consider, the best treatment for any big mass of enlarged cervical glands that, notwithstanding constitutional treatment, is rather increasing in size and extent. It was on these grounds that I decided to operate on a case that was sent to me by Dr. Moorhouse of Stirling.

She was a young girl of 17 years of age, of slight build and rather delicate appearance. She stated that for some time, even as far back as March, 1897, she had had pain in the left side of her neck, but it was not until last November that she noticed any swelling. Since then there has been a great increase in its size and also in the local uneasiness. When I first saw her at the end of January, the enlarged glands not only occupied part of the anterior triangle of the neck on the left side, but also extended under the sterno-mastoid muscle into the posterior triangle, forming a continuous mass along the posterior border of that muscle and the anterior border of the trapezius as far down as the clavicle. When grasped they felt firmly anchored down to the deeper structures, and I had no doubt they were adherent to the carotid vessels and the internal jugular vein. I advised a further trial of constitutional measures, but towards the end of February it was clear no improvement was taking place and that the case could only be met by operative measures. The operation that seemed to me called for was the removal of the glandular mass on the lines recommended by Mr. Watson Cheyne in Vol. i of *King's College Hospital Reports*, one of the distinctive features of which is the excision of any portion of the internal jugular vein involved in the swelling. This was accordingly done on March 2nd. The incision chosen was the S-shaped one that has been recommended by Senn. (See Fig. 1). The first part of it runs parallel to the body of the lower jaw, and it then passes backwards towards the occiput. After describing a good curve it is carried forwards again towards the clavicle, to be continued backwards in a second curve, if necessary, and then end at the acromion.

When this flap was reflected forwards, I found that the sterno-mastoid muscle was adherent in its full extent to