

## THE TREATMENT OF ANIMALS POISONED WITH SNAKE VENOM BY THE INJECTION OF ANTIVENOMOUS SERUM.<sup>1</sup>

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### FURTHER EXPERIMENTS.

THE importance of the treatment of snake bite, though comparatively slight in this country, assumes much greater proportions in connection with the Indian, Burmah, Australian, and African colonies, as in India alone there is an annual death-rate from snake bite of between twenty and thirty thousand people, whilst the financial loss through the death of cattle, due to the same cause, is very considerable. For this reason it is obvious that any treatment of snake bite which offers reasonable promise of diminishing this mortality should be seriously considered by those who are responsible for the health administration of districts in which snakes are found.

For some time past I have devoted considerable attention to the production of antivenomous serum, and after many experiments I succeeded some time ago in placing in the hands of doctors in India and Australia a serum, the value of which has now been proved in a small number of cases in which the snake which has bitten the patient has been identified and captured. Many of my observations have been confirmed, some in this country by Professor Fraser, others by observers in British Colonies, but the importance of the serum method of treatment has even now not been fully realised.

I have to-day, however, the opportunity of giving you the results of experiments that have been performed under Dr. Woodhead's licence, but under my direct personal supervision, so that they may be relied upon as affording direct proof of the value of my method. Those animals that have been successfully treated you may examine for yourselves; others that have been poisoned with the snake venom, but have not received the serum, have succumbed. These latter serve as control experiments with which to compare the results obtained when the serum has been given.

These experiments are easily carried out, and are absolutely painless; in rabbits, as in the case of the human subject, the first symptom indicating the action of snake poison is slight somnolence, which, becoming more and more marked, is gradually succeeded by a condition of unconsciousness associated with, first, muscular contraction, and then with loss of motor power, which, commencing in the hind limbs, passes forwards until the respiratory centres are affected, the cardiac centre being the last attacked. When the animal dies the heart is found in a condition of diastole. The venom may be injected in two ways—intravenously, when a comparatively small dose acts with great rapidity; subcutaneously, when the dose also acts powerfully, but more slowly. A lethal dose of cobra poison injected subcutaneously is about 1 mg. of dried substance, which proves lethal in about twelve hours. Twice this quantity, injected into the veins, kills a rabbit of about 1,500 g. in sixteen minutes. Five times as much, introduced subcutaneously, proves fatal in about three and a half hours. I may, however, give you the results of experiments devised to bring out the exact action of the antivenomous serum, which experiments have been followed by those who are working in the laboratories.

### PROTECTIVE INJECTIONS.

At 9 A.M. on the day the lecture was delivered, four rabbits, weighing between 1,450 and 1,770 g., were injected intravenously in the lateral aural vein, each with 3 c.cm. of the antivenomous serum. This afternoon these rabbits have been injected intravenously with 2 mg. of dissolved dried venom, sufficient to kill the animal in sixteen or seventeen minutes. None of these animals show any symptom of sleepiness, and it is evident that the venom will have little if any effect upon them. At the time that these animals were injected with the two lethal doses, two control rabbits weighing 1,340 and 1,275 g. respectively were similarly injected intravenously with 2 mg. of the venom; these both succumbed with the

symptoms above mentioned, one in about sixteen minutes and the other in seventeen minutes. We have here, then, ample evidence of the great protective power that this serum exerts when injected into the body before the venom is introduced.

### CURATIVE PROPERTIES OF THE SERUM.

In a second series of experiments carried on to demonstrate the curative properties of this serum six rabbits were similarly treated with 5 mg. of venom injected under the skin. Half an hour afterwards two of these animals received 3 c.cm. of the serum intravenously; neither of them showed any symptoms of poisoning, and remained perfectly well. One hour after the venom had been introduced two others of these poisoned animals were similarly injected intravenously with 3 c.cm. of the serum; they also remained well. Two of the other rabbits should have been left for a hour and a half, but the dose of poison was so large that one of the animals succumbed at the end of an hour and twenty minutes; the other animal was immediately injected with the same dose of serum as above, with the result that it is now well, although the dose of venom was so large, and had been allowed to act for so long a time, long enough, indeed, to kill the other animal injected at the same time. This is a very striking proof of the efficacy of the serum.

### MODE OF ACTION OF THE SERUM.

Although the antivenomous serum does not act directly upon the toxin, but only through the cells, it begins to exert its influence immediately it is introduced into the body. This fact is well brought out by the following experiments: 3 c.cm. of the serum were injected into the lateral vein of the left ear of a rabbit, weighing 1,280 g.; 15 minutes later this animal received into the lateral vein of the right ear 2 mg. of the venom (sufficient to kill it in less than twenty minutes had it not received the serum); the animal has remained perfectly well, and still shows no evidence of poisoning by snake venom. A more striking experiment still is one of which I give a description. A rabbit having received intravenously 2 mg. of venom, two minutes later was injected with 5 c.cm. of the antivenomous serum in the vein of the opposite ear. The animal has remained perfectly well.<sup>2</sup> Such an experiment shows that the venom does not destroy the cellular elements at once, and that even when the poison has already found its way to the circulation these cells may be rendered insensible to the action of the poison by means of the action of the serum.

[Dr. Calmette then gave extracts from his paper that he intended to bring forward at Carlisle, and concluded by asking Dr. Woodhead to read the following:]

### NECESSITY FOR GUARANTEES OF THE EFFICACY OF THE SERUM.

The experiments that have been described to you concerning the efficacy of the "antivenomous serum," the results of which you have before you, prove that the said serum really constitutes a specific remedy against venomous snake bites. The use of this serum must necessarily become generalised at no distant date in all countries where venomous snakes are found, in order that both men and domestic animals may be protected. Is it not advisable, therefore, for the British or Colonial Governments, which are deeply interested in this matter, to take rigorous measures in order to prevent the sale in England and in its Colonies of serums for which no absolute guarantee of efficacy and purity is given?

I have the honour to propose that you will adopt the following proposition, and bring it in some way before the Government at as early a date as possible:

1. That there be instituted in London and in each British Colony where there are found venomous snakes a Sanitary Committee to be entrusted with the duty of testing the efficacy of antivenomous serums offered for sale or sent out to be delivered gratuitously by druggists and others.

2. That no bottle shall be sold or distributed unless bearing the mark of such control.

3. That this control be effected according to the sole simple and rapid method which alone presents every guarantee of accuracy.

<sup>1</sup> A lecture delivered in the laboratories of the Conjoint Board of the Royal Colleges of Physicians (Lond.) and Surgeons (Eng.).

<sup>2</sup> All these animals were still alive and in excellent health eight days later.

4. The method proposed is the following: A standard solution of type venom will be placed at the disposal of the appointed experts. The toxic unit of this solution will be based on the quantity of venom necessary to kill a rabbit of 2 kilos. in twenty minutes by intravenous inoculation in the marginal vein of the ear; the above quantity corresponding on an average to 2 mgs. of cobra venom (weighed dry) and to 4 mgs. of rattlesnake venom. An antivenomous serum to be sufficiently active for therapeutic use must be a preservative in a minimum dose of 2 c.cm. on intravenous injection into a rabbit of 2 kilos. against an intravenous injection of the toxic unit of venom. The preventive inoculation must be made fifteen minutes only before the inoculation of the venom. The testing of the serum is thus effected in less than half an hour.

5. That stations provided with serum and all the necessary apparatus for its application be established in the principal centres of agriculture and in the mining and forest districts of the Colonies infested with venomous snakes, such as Australia, Burmah, and India, so that every person bitten may be able to come at once and receive treatment.

[Dr. Calmette spoke in French.]

#### VOTE OF THANKS.

At the close of the lecture, which was listened to with great interest by a large number of experts, including Professor Michael Foster, Professor Ray Lankester, Drs. Lauder Brunton, P. Carmody (Trinidad), Liveing, Rose Bradford, Washbourn, Arthur Stradling, F. W. Mott, Buckmaster, Slater, Starling, H. E. Durham, and Macfadyen, the members of the Laboratories Committee, and many of those carrying on investigation in the laboratories, Dr. Pye Smith proposed a vote of thanks to Dr. Calmette for the very lucid and convincing manner in which he had handled the subject; he was sure all those present wished Dr. Calmette success in his efforts to treat a condition so important to us, especially as it affects our colonial brethren. This vote was adopted most cordially.

### THE ASSOCIATION OF FELLOWS OF THE ROYAL COLLEGE OF SURGEONS OF ENGLAND.

A MEETING of the Committee of the Association of Fellows of the Royal College of Surgeons of England was held at 25, Grosvenor Street, W., on August 7th. In the unavoidable absence of the President, Mr. George Pollock, the chair was taken by Mr. TIMOTHY HOLMES, Vice-President.

The minutes of the last meeting having been read and confirmed, Mr. PERCY DUNN, the Honorary Secretary, reported the result of the election at the College on July 2nd, when the President of the Association, Mr. George Pollock, received 206 votes, which placed him fourth on the poll. The following resolution was then proposed, seconded, and unanimously carried:

That the best thanks of the Committee of the Association of Fellows be accorded to Mr. George Pollock for coming forward as the candidate of the Association at the College election on July 2nd, 1896.

A discussion then arose with respect to the election of direct representatives of the profession on the General Medical Council, and whether it would be expedient for the Association to identify itself with the support of the claims of any particular candidate. In view of the pressing questions relating to the reform movement at the Royal College of Surgeons, together with the efforts which were being made to redress the professional wrongs suffered by Mr. Anderson as a Fellow and Member of the College, in which the whole profession were concerned, the proposition was made that Mr. Walter Rivington, Vice-President of the Association, member of the Council of the Royal College of Surgeons, and of the Senate of the University of London, should be invited to come forward as a candidate, and that the Society and Members of the College should be asked to join in this invitation. The following resolutions were then proposed by Mr. HOLMES:

1. That the Society of Members be requested to unite with this Association in inviting Mr. Walter Rivington, as a reformer who has consistently supported the claims of the Members to the franchise of the College, in accordance with the views of this Association, to permit himself to be nominated a candidate for election to the General Medical Council.

2. That the following objects of mutual advantage to Fellows and Members of the College be adopted by this Association, and be put forward as grounds for this invitation:

A. The effectual promotion on the General Medical Council, the Senate of the University of London, and other bodies corporate represented on the General Medical Council, of the principle recently acted upon by the Council of the Royal College of Surgeons of England—that the representatives of bodies corporate on the General Medical Council should effectively represent the rights and interests of those bodies on whose behalf they are chosen, and of the constituents of those bodies so far as those rights and interests have relations to the functions of the General Medical Council in carrying into execution the Medical Acts, a principle which, as soon as the Members of the College obtain the franchise, will have the effect of giving to the body of general practitioners of England and Wales an additional representative on the General Medical Council, and which, if adopted by other bodies corporate, will give on that Council twenty-five representatives of large constituencies, comprising the whole profession in the place of five representatives as at present.

B. The affirmation of the principle that under Section XIII of the Medical Act, 1858, the funds of the General Medical Council should be applied impartially to carrying into execution every portion of the Medical Acts.

C. The affirmation of the principle is of vital interest to the public and the empire in order to secure for the service of the profession and the public the most eligible men of each generation, the inducements held out to men to enter the medical profession should be strictly observed and made good; and especially the right to practise the profession for a living under Section xxxi of the Medical Act of 1858, re-enacted by Section vi of the Medical Act of 1886, and that it is, therefore, the duty of the General Medical Council to resist any violation by any person or authority whatever of these or other sections of the Medical Acts.

D. The recognition of the fact that in the cases of Marshall and Wife v. Anderson, and Anderson v. Gorrie and others, the said inducements have been totally violated, and that it is the duty of the General Medical Council to take steps by way of appeal from the decision to have them made good to Mr. Anderson, and to secure them against similar violations in the future.

3. That this Committee heartily supports the invitation of the Civil Rights Defence Committee to the Society of Members to co-operate in defence of Mr. Anderson's rights as a Fellow and Member of the College, by which defence the principles and objects adopted as grounds for inviting Mr. Rivington to permit himself to be nominated as a candidate for election to the General Medical Council are illustrated and may be established and secured.

In seconding the resolutions Mr. GANT said it afforded him great pleasure to support the invitation to Mr. Rivington to come forward as a candidate for the General Medical Council. He had been associated with Mr. Rivington for a great many years, both on the Committee and elsewhere. He had observed that Mr. Rivington possessed three special qualifications which were invaluable for anyone holding a public position, namely, great fidelity to any cause which he espoused, extreme conscientiousness, and conspicuous honesty. He expressed a particular wish that these remarks should be recorded in the minutes.

The above resolutions were then put and carried unanimously, and the Honorary Secretary was instructed to forward a copy thereof to the Society of Members of the College.

This completed the business of the meeting, and the Committee adjourned.

THE Stepney Guardians recently adopted a plan for providing medical assistance for the outdoor sick poor in cases of emergency. They decided to pay any duly qualified doctor who might be called, and owing to its success the scheme has now been made permanent.

THE BRITISH LARYNGOLOGICAL RHINOLOGICAL, AND OTOLOGICAL ASSOCIATION.—The following gentlemen have been elected office-bearers for the ensuing year:—*President*: Dr. W. Milligan (Manchester). *Vice-Presidents*: Dr. J. Middlemass Hunt (Liverpool), Mr. F. Marsh (Birmingham), Mr. E. C. Wilkin (London). *Council*: Dr. George Stoker (*ex-officio*), Dr. Dundas Grant, Mr. Mayo Collier, Mr. Wyatt Wingrave, Dr. Hemington Pegler, metropolitan; Dr. James Dawson (Bournemouth), Dr. A. Bronner (Bradford), extra-metropolitan. *Treasurer*: Dr. McNeill Whistler. *Hon. Secretaries*: Mr. R. Lake, Mr. St. George Reid.