

The formula,  $C_{17}H_{24}O_{10} = 388$ .

*Methoxyl Determination.*—Quantitative estimation of methoxyl was made by the method of Zeisel,<sup>1</sup> using the modified apparatus recommended by Perkins.<sup>2</sup>

1. 0.2752 Gm. *cornin* gave 0.1524 Gm. AgI = 7.33%  $OCH_3$ .
2. 0.2429 Gm. *cornin* gave 0.1404 Gm. AgI = 7.63%  $OCH_3$ .
3. 0.2966 Gm. *cornin* gave 0.1708 Gm. AgI = 7.59%  $OCH_3$ .
4. 0.5401 Gm. *cornin* gave 0.3256 Gm. AgI = 7.95%  $OCH_3$ .
5. 0.5751 Gm. *cornin* gave 0.3481 Gm. AgI = 7.98%  $OCH_3$ .

The formula  $C_{16}H_{21}O_9(OCH_3)_3$  requires 7.98%  $(OCH)_3$ .

#### SUMMARY AND CONCLUSIONS.

From the data so far obtained *cornin* appears to be neither an acid nor a base, but a  $\beta$ -glucoside having dextro-glucose as its carbohydrate nucleus.

Analytical data show that its molecule contains one methoxyl group. There are indications that it either contains a free aldehyde group or is easily hydrolyzed with the formation of an aldehyde.

It is an extremely bitter substance, readily soluble in water, but sparingly soluble or nearly insoluble in all of the ordinary organic solvents.

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#### ANTIVENIN (NEARCTIC CROTALIDÆ).\*

BY JOSIAH C. PEACOCK.

The production recently of serum antidotal to the poisons of North American snakes in quantity that permits its distribution through the drug stores of the United States warrants the heralding of that achievement and of other reference to this antivenin that will serve the pharmacist in interpreting to the physician and public the importance and value of this specific treatment.

Since until a short time ago the average annual supply of such serum was only about fifty packages, which were distributed gratuitously by those studying its effectiveness, the present commercial availability of this remedy as well as its adequacy for protection are matters which deserve wide publicity, especially by way of revising and clarifying many impressions and statements that now pertain only to the past.

As a votary of the welfare of health, the pharmacist can render a distinct service to the community by giving an understanding of these facts to all whose pursuits or pastimes take them into rural surroundings.

A brief account of the development and application of anti-snake-bite serums in general and of this North American one in particular seems opportune; but what the pharmacist will certainly want, in order to be prepared to discuss this new addition to his stock of specific medication is a concise comprehension of this serum in its many practical aspects.

<sup>1</sup> *Monatsh.*, 6 (1885), 989; 7 (1886), 406.

<sup>2</sup> *J. Chem. Soc.*, 83 (1903), 1367.

\* Scientific Section, A. P. H. A., St. Louis meeting, 1927.

With the recognition of the chemical behaviors and physiological actions of the bacterial toxins, a striking resemblance in these properties to those of the poisons of snake venoms was quickly noted. And, with the discovery and production of diphtheria antitoxin, it was found that immunity could also be established against the venom of snakes, even though, as then appreciated, the constituent principles and the action of the venoms and corresponding antitoxins or antivenins are more complex than those of the bacterial analogues.

Accordingly, as a class of antitoxins, the practical preparation of antivenins dates from the publications of Calmette in 1894.

Prior investigation by Mitchell and Reichert (1883) and by others had shown considerable variation in the composition of venoms of different kinds of serpents, and subsequently experience soon proved that it is necessary to administer an antivenin which has been prepared from the venom of the particular species, if full value of treatment is to be realized; in other words, true specificity was worked out and demonstrated through actual therapeutic application.

Immediately following the original production of antivenins, they were put to use in some countries in Europe, Asia and Africa; and though more or less clearly understood as fully specific only to the poisoning by the species that furnished the venom for their production, these serums were offered for any help they might give in case of bite by another kind of snake, since in some instances, a serum was expected to show what is known as paraspecificity in correcting or favorably influencing some part of the symptoms. This latter application of the antivenins has made an opportunity for them to be commented on as both useful and useless.

As these serums were made from venoms that exert poisonous effects which are distinctly different from those characteristic of the poisons of our native snakes, in the Western Hemisphere such antivenins were neither accepted nor used with implicit confidence in their sufficiency.

Until about 1898, the preparation of antivenins was carried out as a secondary consideration by a few bacteriological laboratories, when a laboratory at Sao Paulo, Brazil, became interested in antivenin production.

Indeed from the earliest days of antivenins, the Government of the State of Sao Paulo, had studied these specifics and was now ready to specialize in the production and distribution of serum made from the venoms of native snakes.

And although our Brazilian friends have had this big task of producing enough serum for the needs of their own country, they have not been oblivious to the hazard under which some of their neighbors live, for it has been entirely through their sympathy and good graces that the people of the United States have for several years past been favored with a limited supply of serum that is specific against North American species. These experimental lots have been made possible by Dr. Raymond L. Ditmars, Curator, New York Zoölogical Society, he not only collecting the necessary venom but personally supervising the delivery of the serum which he has distributed gratuitously, as mentioned, for a Federal Public Health law of 1902 forbids the sale of viruses, serums, toxins and analogous products not made specifically for the United States by methods approved by its inspector, the product declared sterile, and the producer duly licensed, as required by the terms of the Act.

Dr. Ditmars has not only been the unknown hero in the saving of many lives; he has long been an ardent and persistent pleader for the manufacture of North American anti-snake-bite serum within the United States. For a number of years past he and other herpetologists have been noting the annually increasing fatalities from snake-bites, and have emphasized the need to protect our outdoor people against this growing danger, which arises both from the conservation of the forests and the development of tillable land, these two influences fostering a notable increase in rodents and other small creatures upon which the snakes depend for food.

Thus with the promotion of enterprises located in rural districts snake-bite had come to be a matter of much economic importance, a menace to industry that must be offset as fully as practicable.

But even snakes are not totally devoid of compensating virtues, for they help the agriculturalist by killing rodents, and other crop-destroying creatures. Besides the complete obliteration of snakes in a country as large as ours appears to be a matter entirely out of the question; consequently, since they are to remain, protection against their poisonous effect must be provided and placed within the reach of everyone. It is a matter of practical note that, while in Brazil death from snake-bite has been reduced from several thousand a year to a very few cases in which serum is not used or not used soon enough, in India where the English authorities have a system aimed at eradication by paying for dead snakes, the yearly toll in life is 20,000 to 25,000 or more.

Conferences were held by students of this problem and business interests concerned with the need to protect the lives of workers and others who are exposed, and it was found advisable to make a complete survey of the poisonous snakes of the United States and of other parts of this continent, and thereafter prepare such specific antivenins as would be needed for secure protection.

As an encouragement to this undertaking, the Brazilian contribution toward the improvement of the specific snake-bite treatment as the result of the work of Dr. Afranio do Amaral and his predecessors over a period of twenty-five years stood out both as a scientific accomplishment and as a most practically applied success.

Accordingly, a little over a year ago, Dr. Amaral, once chief of the Serum Therapeutic Institute at Sao Paulo, was officially invited through international diplomatic circles to come to the United States as director in all of this effort. The Brazilian Government generously granted him a leave of absence to permit him to organize and establish in the United States a laboratory for the routine production of antivenins.

Dr. Amaral at once took hold of this problem with the grip of a thorough familiarity with the subject and a determination to make it practical as well as possible for every inhabitant of North America to protect himself; and on June 1, 1926, the Antivenin Institute of America was opened at Glenolden, Pennsylvania.

After collecting snakes and extracting venom, horses were immunized and, under joint study with the Hygienic Laboratory of the United States Public Health Service, serum has been refined, concentrated and standardized to make antivenin.

On April 25, 1927, a license was issued by the Secretary of The Treasury authorizing the manufacture of Antivenin (*Nearctic Crotalidæ*) and the sale of it in interstate traffic.

For further understanding of the urgent need for this remedy, some thought may next be given to the seriousness of snake-bite and to the uncertain value of non-specific treatment, for in spite of the fact that there may appear to be some authorization of the latter, in reality all authorities agree that specific serum is so far as known "the sole means of neutralizing the poisons and averting the noxious action which the toxic elements exercise on the tissues of the body."

If not given specific serum, from fully 10% in the northeastern section of the United States to about 35% in the southwestern section of those who are bitten die; of the others, some suffer from more or less injury, occasionally resulting in impairment of body. As many as 200 to 300 deaths within a year in the United States due to snake-bite have been reported, and this seems to be far below the actual number.

Writing recently on the occurrence and habits of our native poisonous snakes, Dr. Ditmars said that practically every portion of the United States is infested by them and that the one curious thing in the distribution of them is "that they are so thoroughly in our midst." That poisonous snakes may be encountered without having to go into the wilds or far from the cities is revealed in his further statements that "venomous snakes extend their domains to within a few minutes motor ride of Main Street." "For instance, one may stand on fashionable Riverside Drive in New York City, and without a field glass look northward and across the Hudson to rocky areas inhabited by copperhead snakes." "From records at hand we believe that copperhead snakes still exist within the actual northern boundaries of New York City." "During the past two years we received more than three dozen large copperheads captured within the city limits of a thriving community about twenty minutes' motor run from the boundaries of the Bronx."

While there has always been a need in the United States for Anti-Snake-Bite Serum, to-day there is a greater need than ever before, not only because of the economic situation already mentioned but also of a social necessity, for the population's frequent trips to the country make it necessary to protect the lives of those who have the misfortune to be bitten by poisonous snakes. As is evident to all, outdoor sports, hiking, camping and automobile camping are phases of diversion that have become nation-wide and are gathering tens of thousands of recruits each year, thus adding steadily to all hazards of the past, with the result that there has been a marked increase in the reports of snake-bites and queries relating to antidotes.

Clearly then the elimination of the danger of snake-bite is an important problem for city dwellers as well as for inhabitants of the country.

Taking the States as an entirety, there are four types of dangerous snakes, the rattlesnakes (in a dozen or more varieties) the copperhead, the moccasin and the coral snake; all of which bear names likely to vary with locality.

The coral snake has a deadly venom, but owing to its burrowing habits as also the arrangement of its head and fangs, it is not apt to be the cause of a bite, unless actually handled because someone is attracted by its gaudy colors. For this reason there is but little general concern regarding it. The other three kinds are, therefore, the more likely cause of bites, the principal danger being from bites by rattlesnakes.

Rattlesnakes, large or small, may readily be identified by the characteristic

tail appendage—the rattle. Possession of the rattle shows the snake to be a poisonous one. Rattlesnakes, copperheads and moccasins all belong to the family of pit vipers, having a deep pit on each side of the head between the eye and the nostril. This alone plainly marks a snake as poisonous; its rattle may have been broken off.

Until recently there has been no systematic attempt made to record snake-bites or fatalities resulting therefrom in such manner as to accurately reveal these happenings; instead, in some sections, there appears to be a decided reluctance to reporting these occurrences. But, with specific serum now available, it can safely be predicted, that, before long, state and federal health bureaus will be dealing with snake-bite as a separate classification in their reports, instead of listing it under miscellaneous maladies.

Pharmacists have heard less of snake-bite cases than have hospitals and doctors in private practice, because surgery rather than medicine has been resorted to both as immediate and later treatment of those who survive the first effects of the bite.

The importance, the value of having a specific remedy at hand when a bite occurs is well known to all who understand the sometimes very quickly destructive effect of the venom on the blood, other tissues and the nerves.

The activity of the venom of our pit vipers is due mainly to a hemorrhagin, its most important toxin, which destroys the endothelial or inner lining of the blood vessels, causing death through hemorrhage in the vital organs. Such local destruction of tissue, followed by paralysis of respiratory center, is the effect of these venoms. Venoms may also contain proteolytic ferments, accounting for the softening of muscles and other tissues which is experienced. The venom easily penetrates, causing rapid infiltration. The toxic action of the venom occurs without appreciable incubation period, which is a difference from bacterial toxins. The venom of certain foreign snakes acts in a somewhat opposite manner to that of ours in regard to blood coagulation as they increase the coagulability of the blood with production of intravascular thromboses.

The observed fact that some individuals suffer so much more quickly and more seriously than others following a bite is likely to incline one to a belief in varying degrees of natural immunity, although this is not the case, this variation depending upon the actual amount of venom that the snake injects.

Until a few weeks ago, if someone had come into the drug store and asked for a remedy for snake-bite, unless one had been following the development of North American anti-snake-bite serum, it is likely that the table of antidotes to poisons would have been consulted; and in some of these tables poisoning by snake-bite is considered. Perhaps the dispensaries or first-aid manuals would have been carefully perused.

But whatever might have been turned to, it is probable that but little in the way of information as to remedies was found, and any mentioned would likely have been commented on as of uncertain value.

A popular notion to be dispelled is the value of a free use of whisky, for alcohol helps the poison, not the patient, facilitating the penetration and absorption of the venom; consequently all alcoholic liquors should be avoided.

As the greater number of snake-bites are received on the extremities, the poison

may be retarded in reaching the general circulation by immediate application of a tourniquet between the bite and the body. To fully compress the blood vessels and lymphatics this bandage must be applied where there is but one bone. But the use of a tourniquet demands much attention and care in order not to injuriously affect the circulation in the limb.

Just as diphtheria was once treated with non-specific substances, snake-bite has had a like therapeutic history, including the use of many secret formulas, the reputed value of which are very much favored by chance; for, as everyone will understand, a snake may bite a person when its poison glands are empty or nearly so, as for example, just after having killed prey. Therefore, as in case of exposure to diphtheria, there may or may not be infection, but, since it is not feasible to determine whether much or little bacteria or venom has been received, only the administration of specific serum satisfies as proper protection.

Most non-specific treatment are oxidizing agents aimed at the destruction of the poison in the wound. While it is true that some of these substances will destroy all venoms if actually mixed together, as in a test-tube, the fact remains that the poison is usually absorbed by the tissues beyond reach of these agents by the time they can ordinarily be applied. Their use is usually preceded by application of a tourniquet and making of incisions; sometimes suction with the mouth or by cupping is made after these measures, with or without the use of such substances.

Unfortunately, these methods do not assure protection, because the poison having a pronounced affinity for cell elements rapidly fixes itself in the tissues, and for that reason is not readily extractable by these mechanical means nor accessible to non-specific agents, either liquid or solid. As a comparison of the rapidity with which venom acts it is well to recall the rapidly accomplished interactions that normally go on in the blood and other tissue functions of the body.

For the foregoing and similar reasons the uncertain value of non-specific treatment has long been acknowledged.

Indeed, reference to a serum might have been met under such names as Anti-venin, Antivenene, Antivenine, Antivenom, Antivenomous Serum, Anticrotalus Serum, Anticrotalidic Serum, Antiophidic Serum, etc., but only to learn that it was not specific for the poisons of North American snakes. And there would be gathered the impression that no accurate or dependable method of standardizing specific serum has as yet been found, and even the plain statement, that an anti-venin against the venoms of the poisonous snakes of the United States has not been successfully prepared.

And, it is true that, except for the limited supply mentioned elsewhere, until the present commercial supply of fully specific, stable and standardized North American Anti-Snake-Bite Serum become available, these statements faithfully reflected the situation as regards the needs of the United States. But the helplessness of that yesterday is now banished forever.

Coming now to a consideration of the serum itself as an item of materia medica, it is to be regarded in such practical aspects as those of its production, nature, action, standardization, safety, range of usefulness, certainty and promptness of effect, sufficiency, convenience of package, regulation of dosage, simplicity of administration, etc., several of which matters are closely interwoven, and one or

more of which will probably be a concern in most of the questions to be answered to physicians and public.

Since North American Anti-Snake-Bite Serum (Antivenin, Nearctic *Crotalidæ*) is a true antitoxin, although complex, in all of these practical features it may be regarded as like diphtheria antitoxin. If that compact thought is called to mind, it will well qualify a pharmacist to answer almost any question that is asked concerning this serum.

It has the appearance and other sensible properties of a concentrated diphtheria antitoxin. Like the latter, it is a colloid suspension in (isotonic) physiological solution of sodium chloride of certain antitoxic substances obtained from the blood serum or plasma of the immunized horse.

Antivenin (Nearctic *Crotalidæ*) is its definite title under the license of the Treasury Department. It is called antivenin to signify that it is an antitoxin to antidote the toxins of venom. It is a purified and concentrated serum globulin obtained from the blood of horses which have been highly immunized against the venom of the most poisonous North American species of serpents of the family *Crotalidæ*, and contains antibodies which neutralize their venoms.

It is described as nearctic, a term combining neo, new, and arctic, northern, to indicate that it is for use in the United States, Northern Mexico and Canada, the northern part of the new hemisphere according to the zoögeographical zoning system.

The combined descriptive words, Nearctic *Crotalidæ*, definitely designated it as protective against the venom of the poisonous North American species of serpents of the family *Crotalidæ*, and to adapt it to general use against the snakes likely to be encountered in the United States, it is made to antidote the venom of the copperhead and the water moccasin as well as that of the rattlesnakes. It therefore contains antibodies which neutralize the venoms of the three kinds.

This distinction is important because of the fact that this antivenin is not completely effective against a Central and South American species of rattlesnake which has a somewhat different type of venom, not for the venoms of coral snakes, nor for those of other families which may be met with in our museum collections.

The polyvalency of this serum is noteworthy as indicating its sufficiency for so large a part of North America, and permits the employment of the synonym, North American Anti-Snake-Bite Serum. This antivenin is appropriate for any part of Canada and Northern Mexico. Specific serums for use in Southern Mexico and Central America are in course of development.

This Antivenin, like others, is prepared under much the same method as that used in the preparation of diphtheria antitoxin, the active constituents of the venom inciting in the animal the mechanism of natural resistance with resultant formation of specific antibodies or antitoxin.

For this purpose quantities of venom must be provided; accordingly venom is extracted from snakes, desiccated and stored for use. In the extraction of venom the snake is made to imitate the natural "strike" upon an easily penetrated diaphragm of parchment or rubber that covers a vessel to receive the venom; the resistance that the membrane offers to the poison glands which are connected with the fangs serves to induce the snake to expel the fluid into the receptacle beneath.

Snakes which have ejected venom may be corraled, and after about two weeks extracted again.

The dried venom is prepared for injection into the horses, following again the procedure for antitoxins, the initial dosage being but a fraction of a milligram of venom. In some European laboratories, as also by some other investigators, before the venom is injected, its toxic activity is reduced by admixture with chemical substances in order to destroy the toxophorous group. That plan is not followed in the production of this Antivenin; instead the venom is used unaltered from its natural effects.

As the process of immunizing the horse is proceeded with, the amount of venom in the successive doses is cautiously increased until a dosage about 1000 times as large as the initial one is readily tolerated. From time to time, trial bleedings are made to determine progress in development of antibodies. A period of six months or more in which to build up this tolerance is preferable to a shorter term.

When such marked degree of resistance or immunity has been developed, blood is drawn from the animal in the customary manner, and, after separation of the red cells, the plasma or serum is purified by the usual salting-out process employed to separate the useless protein constituents from the antitoxin, and by such method this antivenin-like diphtheria antitoxin is globulinized and concentrated. The fact that the antibody or antitoxic properties are attached to the pseudoglobulin enables a refinement and concentration of this serum which not only reduces the bulk of the finished Antivenin to a fraction of the volume of the blood serum that it represents, but also allows it to be freed of much valueless horse-serum protein. Thus the dosage of 100 cc., that is commonly advised in the directions pertaining to serums previously offered, referred to an unconcentrated serum, the value of which is now equalled by the very much more acceptable bulk of 10 cc. of this concentrated and standardized product.

To make antivenin suitable for injection, it is sterilized by filtration through bacteria excluding filters; it is also subjected to the usual tests for purity, sterility and safety, as is done with other antitoxins.

One of the outstanding accomplishments in the progress that has marked the work of the Brazilian laboratories was the devising of an accurate and therefore dependable method for assay and standardization. The results by this improvement are mathematically accurate, as shown by their concordance when multiple proportions of venom and antivenin are taken for test; so that in this very important respect the standardization of this remedy parallels that of other substances which combine in definite ratio; and again diphtheria antitoxin comes to mind.

This method of standardization is a direct titration method in which a fixed amount of antivenin, say 1 cc., is mixed with different amounts of venom, the mixtures kept at body temperature in an incubator for at least thirty minutes and then injected into the venous circulation of pigeons which is readily accessible in the wing. One cc. of antivenin must neutralize at least two milligrams of the venom used in producing it, as demonstrated by the pigeon showing no symptom of poisoning. Following this, test controls are made on mice, rabbits and other animals for evidence of both preventive and curative action, thus warranting the assumption of life-saving effectiveness in mammals. Certainty and promptness of effect



are thus determined. A long experience with this method in Brazil has convincingly demonstrated that the indications of this direct titration are entirely trustworthy in treatment of humans. And it is a fortunate fact that the neutralizing effect of the antivenin shows as marked an avidity for the toxin as the venom manifests toward the blood and other tissues.

While the potency of antivenin can be expressed in terms of the amount of venom which it will neutralize, 10 cc. of the concentrated and standardized product as now marketed is a proven ordinarily sufficient dose.

This Antivenin is marketed in the syringe container so well known in this country for packaging biological products, with sterile needle and accessories for attachment at time of use, which arrangement is a marked advantage over the sealed ampuls in which foreign antivenins are put up, making a separate syringe necessary. This convenience greatly facilitates promptness in administration, prevents loss of material and obviates contamination.

As to the matter of safety, Antivenin (Nearctic *Crotalidæ*) is as fully entitled to every acceptance and confidence as is diphtheria antitoxin and is just as safe and as harmless as the dose of diphtheria antitoxin given to a child to protect it against diphtheria to which it may have been exposed.

The dependability of this remedy as an insurance against loss of life will cause it to be purchased, carried and used by many who are exposed. It must, therefore, be looked upon as a weapon of protection which a layman is justified in using in defense of himself or another, and will use when occasion demands.

Accordingly, in each package there is placed a sheet of exact directions for use, written in simple language that a layman may clearly understand how to administer it to himself or to another. So thoroughly practical are these directions that every drug store should keep a copy convenient for ready reference.

While the likelihood that a person will be alone when bitten fully warrants the informing of everyone who may be exposed on both the urgent need to give Antivenin at once and on the manner of injecting it into himself or another, attention by a physician should always be had as promptly as possible thereafter.

If one is certain of receiving Antivenin within a day's time after a bite there need be no fear, merely on account of such delay.

Like diphtheria antitoxin, Antivenin should be given as soon as needed, which implies as soon as a bite is received or recognized. As with that antitoxin, so with Antivenin "early and enough" is the rule for dosage; the earlier it is given, the more completely effective it is and the quicker the recovery from ill effects.

Usually the contents of one syringe (10 cc.) is sufficient as that quantity is enough to protect against the average amount of venom secreted at any one time by our poisonous snakes; but additional such doses may be given if the symptoms through persistence or relapse suggest the need for further treatment. Extreme symptoms at any stage would warrant larger doses. The knowledge that an unusually large snake gave the bite or an exceptionally large amount of venom being injected would also call for larger amounts. The entire contents should be given as a dose, rather than in divided portions.

The age of the person bitten has an important bearing on the dosage: since the amount of venom to be antidoted is the same whether a child or an adult is bitten, it is only a matter of common sense to give the former (child) more Anti-

venin, because the venom works in proportion to the body weight (the smaller the body the more complete the destruction of the tissues).

With further reference to dosage, directions in books and elsewhere which mention 100 to 300 cc. as the amount should now be understood as pertaining to an unconcentrated serum, and very likely to a non-specific one or to a serum that is not standardized.

While Antivenin is usually administered subcutaneously, in desperate cases, a physician will give it intravenously. In any case, the relatively small dose of this standardized Antivenin may be injected intramuscularly by physicians. In some early cases it is necessary to inject part of the serum in close proximity to the wound.

Convenient sites for injection under the skin when administering to oneself are the thigh, or the side of the abdomen where there is loose flesh, or the outside of leg just above the knee where the flesh can be gathered up. A very convenient location through which to inject another, and a most advantageous one from the standpoint of prompt effect, is between the shoulder blades.

The technic of each mode of injection is exactly that for a similar administration of diphtheria antitoxin.

Systemic symptoms may call for cardiac stimulants (but not alcohol, which brings about further depression), application of warmth to the body, maintenance of a quiet position, and diuretics and saline laxatives if needed.

Again, like diphtheria antitoxin, Antivenin if applied in time simplifies the whole procedure of treatment, doing away with the need of bandaging, incision and all purely local treatment, as these are made entirely unnecessary when Antivenin is used at once in sufficient dosage. If a tourniquet has been applied it should be released completely as soon as Antivenin is injected. Indeed, if Antivenin is at hand, it is far better to spend the first few minutes in giving this remedy than in applying a tourniquet.

In this comparison with diphtheria antitoxin, there likely comes to mind the question of practicability to immunize persons with venom as is done with the bacterial toxins, such as the well-known use of diphtheria toxin-antitoxin mixture. An answer has been found in the observation of the horses under development of Antivenin: there is a recognized tendency toward rupture of the liver, which contraindicates such undertaking.

There is no such effect, however, from the Antivenin, which contains no toxic substance, but only antitoxins.

Being a serum globulin from the horse's blood, Antivenin like all such antitoxins, may possibly cause serum reaction in exceptionally sensitive individuals, but with no more likelihood than does diphtheria antitoxin. Should such hypersensitive person be encountered, there may still be opportunity to hyposensitize by the method of Besredka, or in the event of it being first necessary to save the life of the person by immediate injection, the serum may be administered under supervision of a physician and desensitizing attended to later.

While Antivenin is a remedy of mathematical precision when face to face with the toxin which it neutralizes, like diphtheria antitoxin, it is not looked to for any effect except the correction of symptoms which arise directly from the respective poison used to produce it in the animal.

Antivenin is best preserved at ice-box temperature, but does not need to be so kept indefinitely. Kept at moderate temperatures, anti-snake-bite serum has been known to remain good for more than five years. The package protects the Antivenin from light. When carried, some thought should be given to guarding it from unnecessary heat and exposure. Actual experience has shown that Antivenin may be trusted for five years for full effect, and may be used even after that period, allowance being made for some depreciation. This makes it cost but a very nominal insurance expense to such as provide it for their emergency outfits.

Antivenin is entirely appropriate for use on animals. In some sections there seems to be need for such use of it. It is estimated that the State of Texas alone loses over a million dollars a year through livestock dying as the result of snake-bites. A special serum, called Veterinary Antivenin, is being produced for this demand.

As a concluding thought let it be fully understood that Antivenin is as dependable in snake-bite as diphtheria antitoxin is when life is threatened by diphtheria. It is the best known form of protection against unnecessary suffering or untimely death from such cause.

This assurance against serious consequences, this idea of "insurance" in having Antivenin on hand unquestionably available within easy reach will be quickly grasped and greatly appreciated by all who are likely to encounter snakes; and, since for those most practical of reasons, certainty and sufficiency of effect, all specific medication deserves the widest possible recognition, pharmacists may with every propriety fully inform their clientele on this recent addition to rational *materia medica*.

#### ABSTRACT OF DISCUSSION.

**Walter C. Jones** asked how long the serum would retain its potency. The author replied that it had been used ten years after its preparation. That Dr. Amaral experimented with the venom of North American rattlers during a number of years and quantities of the serum had been produced at the instance of Dr. Raymond L. Ditmars, Curator of the New York Zoölogical Society, and on the basis of experience in the preparation of these particular lots they felt assured that the serum would retain its potency for ten years. However, a five years' dating is placed on the package so as to keep within the bounds of safety.

**Secretary Pittenger** inquired whether the serum was a mixed antitoxin and that the same serum serves for all three classes of poisonous snakes met with in this country.

The author stated that the serum answers for the rattlesnake, copperhead and moccasin poisons and that these were the three poisonous snakes which would likely be encountered in this country.

**J. C. Munch** stated that he had quite a discussion with Dr. Amaral and learned of him some of the difficulties he had encountered in Brazil and he desired to compliment him on the remarkable work done in bringing out the serum. He asked about standardization of the serum and the author replied that it is standardized by tests on pigeons and afterwards proven on larger animals.

A member inquired of the author of the paper whether any serum had been developed which had proven satisfactory for the bite of the California black spider. The author replied that, as far as he knew, no serum has been developed but studies were going on.

The author again emphasized the fact that alcoholic liquors were not antidotal because he thought that information had a cautionary value, because of the dependence which had been placed in alcohol as an antidote.

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