Miller (W. D.)

EXPERIMENTS RELATIVE TO THE FORM IN WHICH ARSENIOUS ACID MAY BE BEST APPLIED FOR DEVITALIZING THE PULPS OF TEETH.

By W. D. MILLER, M.D., D.D.S., Berlin.

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The question of the action of arsenious acid upon the human economy has long been a subject of investigation among pharmacologists and physicians. Nevertheless, the way in which the complex of symptoms characteristic of arsenic-poisoning is brought about remains to the present a subject of dispute.

According to the theory of Liebig,* arsenic acts upon living tissue in a manner similar to sublimate, the tissue being converted into an albuminate of arsenic; at the same time, of necessity, losing its vitality. This theory received little credence because it does not accord with the most common observations regarding the local action of arsenic, and because all attempts to produce an albuminate of arsenic have thus far failed.

The oscillation theory of Binz,† which has attracted much attention, notwithstanding its ingeniousness seems to meet with a great deal of adverse criticism.

By a series of experiments on animals, Binz arrived at the following results:

1. In the living organism arseni*ous* acid is converted into arsen*ic* acid, and arsen*ic* acid into arseni*ous* acid.

2. These two transformations are brought about in a short time by protoplasmatic tissue, within as well as without the animal body.

3. Those tissues which during life are most affected by the action of arsenic are the ones to most readily give up their oxygen to arsenious acid outside of the organism.

From these results Binz came to the conclusion that the conversion and retro-conversion of these two acids into each other bring about a violent oscillation of the atoms of oxygen within the protoplasm, and this is the cause of the poisonous action of arsenic. It acts only as the carrier of oxygen.

Binz compares the action of arsenic to the destruction of organic matter by iron in the presence of air and moisture. Ferric oxid gives up an atom of oxygen to the organic matter, becoming thereby reduced to ferrous oxid; but this compound cannot exist in the presence of air and moisture, ferric oxid being formed almost immediately, which then again gives up its oxygen to the organic matter. This process, continued indefinitely, brings about an oxidation or combustion of the matter. In this way iron nails in wood become quite

* Die Chemie in ihrer Anwendung auf Agricultur und Physiologie, 1843.
† Pharmacologie, 2. Aufl., 1891, p. 417.

loose in time, and iron-stains eat holes in linen. Husemann,* who is the most outspoken opponent of Binz, points out that in accordance with the oscillation theory arsen*ic* acid should exert the same action or as strong an action upon living tissue as does arseni*ous* acid. This, however, does not agree with the results of experiments or clinical observations.

The discordance of the views regarding the local action of arsenic is still more pronounced. Some designate it as a violent escharotic, others assert that it has no escharotic action whatever. Some claim that it acts only upon diseased tissue. How this opinion was ever arrived at is to me incomprehensible. Some find it to act upon the central nervous system, others upon the peripheral nerves.

In regard to the patho-histological changes brought about by local applications of arsenic, I know of no investigations more worthy of consideration than those of Arkövy :†

"1. As_2O_3 brought into contact with the tooth-pulp acts in the following way : A certain degree of inflammatory hyperæmia, total or partial, depending upon the quantity of the agent applied, sets in ; the blood-vessels become expanded, and here have a tendency to thrombosis. This latter effect may also be in connection with embolism of the capillaries, when the agent is quickly taken up into the blood-vessels.

"2. As_2O_3 produces no coagulation of tissue whatever.

"3. It has a specific influence upon the blood-corpuscles, combining with the hæmoglobin to form a compound of arsen-hæmoglobin, and of this chemical process there seems to be evidence in the profuse yellowish tinge of the whole pulp-tissue, and in the discoloration of blood in several of the blood-vessels.

"4. In nearly every case it is taken up in substantia (in form of molecules) into the blood-ways ; when there it produces, besides the above-mentioned changes, granular detritus of the contents and anæmic collapse, shrinkage,—the latter effect being brought about nearly exclusively in cases where greater doses were used.

"5. The bulk of the pulp-tissue—viz, connective-tissue fibers and odontoblasts—undergoes no change whatever ; not so the connective-tissue cells, which increase three to four times their normal size.

"6. The special action of arsenic trioxid upon the nerve-elements consists in the following : The neurilemma is only so far influenced that its nuclei are somewhat increased ; a more essential change takes place in the axial part, where, after the application of more than one mgrm., granular detritus of myelin sets in, and the axis-cylinder commences here and there to disappear. As a very surprising alteration may be regarded the notchy tumefaction of the axis-cylinder, described heretofore almost only in cases of central lesions.

"7. All these alterations occur in and among normal-looking tissue.

"8. The action of arsenic trioxid is macroscopically exhibited by a brownish-red tinging of the whole or of certain parts of the pulp-body, as well as of the neighboring dentine and cementum, this latter in cases treated with greater doses,—viz, two to five mgrms. This alteration is most expressed at the top of the crown-pulp and at the apical one-fourth to one-third part. This circumstance may

**Deutsche med. Wochenschrift*, 1882, Nos. 48–50.

† Transactions Internat. Med. Congress, Dental Section, London, 1881.

be considered as an external evidence of the devitalization being completely attained to."

In view of the results obtained by Arkövy, I thought that I might be spared the labor of extending my investigations to the histological changes which are produced by local applications of arsenious acid, devoting my time chiefly to the clinical aspect of the question, and in particular to the question, In what form should local applications to the dental pulp be made?

In applying arsenic to the pulps of dogs' teeth, it is impossible to bring about the same conditions in every case; either the pulp is more exposed in one case than in the other, as it is more wounded, or the bleeding may interfere more in one case than in the other. Again, the quantity of arsenic applied cannot be *absolutely* the same in all cases, etc.

To eliminate these and various other sources of error, it is necessary to make a large number of experiments, which, as every one knows who has experimented upon dogs, is a matter of great difficulty. Experiments upon pulps have the further inconvenience that it is impossible to study with the naked eye changes which are going on in the pulp *intra vitam*, and which may be of great aid in determining the nature of the process. Chiefly, however, for the reason that my experiments dealt with the comparative action of various forms of the paste, I found it desirable to choose a subject for experimenting upon which was more easily accessible than the pulp of dogs' teeth. A few trials only were made on frogs and rabbits, as these animals soon proved to be ill adapted to the purpose.

The greatest number of experiments was made on the tails of white mice. This organ presents in so far a similarity to the pulp, as it is comparatively long and narrow, and traversed in the direction of its length by central blood-vessels and nerves.

To make the similarity greater, I passed, in some cases, a glass ring over the tail, fitting closely at the root, to take the place of the constriction at the apical foramen.

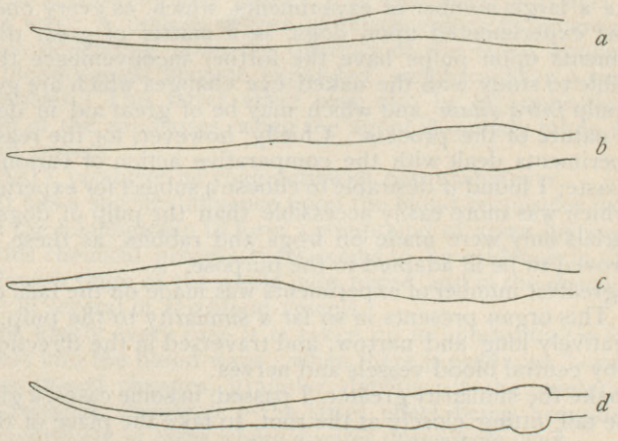
Again, in a number of cases I inclosed the tail, after applying the arsenic, completely in a plaster cast. This was accomplished by filling a proper-sized glass tube with a thin mixture of plaster of Paris and drawing it over the tail, or rather drawing the tail into it by means of a thread tied to the tip of the tail. Finally, for this operation, tubes were used which were broken through on one side about an inch from the end. As soon as the cast had hardened, the plaster was removed through this opening sufficiently to expose the tail, at a circumscript point. The slit was then made, arsenic paste applied, protected by gold foil, and the opening closed with plaster of Paris.

To whatever part the arsenic was applied, the most prominent symptom manifested was the enormous swelling and œdema (except where the tail was inclosed in a cast). Applied in a skin pocket above the root of the tail, the whole rump and the hind legs became intensely swollen and appeared yellowish, and semi-transparent on holding the mouse toward the light.

On incision, a large quantity of yellowish serum escaped. Complete anesthesia and paralysis of the hind legs usually resulted, the mice sometimes gnawing them off. Death frequently followed the application, unless very small quantities were used.

When arsenic was applied to the ear, after slightly scraping or cutting it, the ear appeared in twenty-four hours swollen, red, and succulent; later a portion of the ear, or sometimes the whole of the external ear, was thrown off.

In working upon the tail, a longitudinal slit was made through the skin about one-quarter of an inch long, being careful to avoid the blood-vessels, which in white mice are distinctly visible. The skin-flaps were slightly raised and the paste inserted. In twenty-four hours marked swelling extending about one-half an inch in each direction from the point of application, sometimes over the whole tail. In the vicinity of the wound the tissue appeared reddish to bluish-red; farther removed there was sometimes no reddening whatever, the tail appearing swollen, waxy, and œdematous. In forty-eight hours the whole tail was intensely swollen, bluish-red; in many



Showing the action of arsenious acid on mouse-tails. *a*, normal tail; *b*, tail thirty-six hours, *c*, forty-two hours, after application of arsenic paste; *d*, tail with glass ring.

cases the skin was found cracked open and drops of serum exuding. A free flow of serum followed an incision. In seventy-two hours tail blue and wilted (dead). Complete anesthesia of the greater part of the tail was found to be present in about forty-eight hours.

The action of the arsenic appeared somewhat accelerated in those cases where a closely-fitting glass ring was put on the tail near the root, and the arsenic applied one-quarter to one-half an inch below the ring. These rings were set on the root of the tail with gum arabic or plaster of Paris, and allowed to remain for twenty-four hours before the arsenic was applied. This precaution was taken in order to make sure that the ring was not tight enough to produce any disturbance in the circulation.

In more than forty cases, there was not one in which the action of the arsenic extended beyond the ring.

One of the most pronounced symptoms produced by the arsenic is the œdema. This fact suggests the thought that the death of the pulp might be due in part to a strangulation brought about by the pressure within the rigid walls of the pulp-chamber. If this were the case,

we should expect tails in a plaster cast to be devitalized more quickly than when they were free to expand. The experiments did not, however, furnish much evidence in favor of this view. The difference was so slight that I was obliged to repeat the experiments fifteen times before I could come to a conclusion, which is, that the action of the arsenic is not appreciably influenced by enveloping the organ in a rigid cast. In some cases the action appeared to be more diffuse, in some loss of sensibility appeared to occur sooner, but no constant pronounced difference could be detected.

From these results we cannot, however, with certainty, conclude that the pressure within the pulp-chamber has no part in bringing about death of the pulp, since its effect may be compensated for by a diminished absorption of the arsenic, resulting from the increase of pressure within the tissue. That the death of the pulp is not due solely to a strangulation of the vessels at the apical foramen will be evident from the fact that arsenic acts locally upon tissue that is perfectly free to expand. The action of arsenic is of a progressive nature, beginning at the point of application and extending gradually in each direction. The peripheral portion of the tail, of course, dies *in toto* as soon as a complete stagnation is brought about at the point of application of the paste.

The view formerly entertained by many, that arsenic acts only upon diseased tissue, is untenable.

Arsenic is still described by many as a powerful escharotic, although nearly all who have experimented with it have pointed out that it has no action of the nature of the well-known escharotics, such as carbolic acid, chlorid of zinc, etc.

The local application produces no immediate visible effect whatever.

It is well known that different tooth-pulps show very great differences in their susceptibility to the action of arsenic. The age of the patient, the size of the pulp, the freeness of the exposure, and particularly the condition of the pulp as to calcifications, have a marked effect upon the rapidity of absorption of the paste, so that, while in many cases death of the pulp occurs within twenty-four hours, in others again repeated applications may be necessary to accomplish the purpose. The rapidity of action naturally depends to a certain extent upon the amount of arsenic applied, and upon the action of the substances with which it is incorporated.

The form in which arsenic was for many years solely applied to the pulp is in connection with creasote or carbolic acid and morphia; in later years we hear much of the essential oils and lanolin as base, with addition of iodoform, cocain, etc., to prevent the pain often attendant upon the devitalizing process.

I have experimented upon mice, and to some extent upon dogs, with the following combinations:

1. Arsenious acid; chlorid of zinc.
2. Arsenious acid; carbolic acid.
3. Arsenious acid; oil of cloves.
4. Arsenious acid; lanolin.
5. Arsenious acid; thymol; oil of cloves.
6. Arsenious acid 1; thymol 2; oil of cloves.
7. Arsenious acid; glycerin.
8. Arsenious acid; 5 per cent. aqueous solution of common salt.
9. Arsen*ic* acid.

In each case a sufficient quantity of the liquid was added to form a paste. No. 9, being deliquescent, soon formed a paste of itself when exposed to the air.

No. 1 applied to the ear produced shriveling at the point of application, caused by the chlorid of zinc. This prevented the absorption of the arsenic, and consequently the characteristic arsenic effect did not appear at all.

On the tail the *escharotic* action of the *chlorid of zinc* was very pronounced, in half an hour a white patch having formed one-fourth to one-half inch long and extending half-way around the tail.

At the same time a marked contraction or constriction of the tail was produced. This constriction apparently retarded the absorption of the arsenious acid, the rapidity of action, on the whole, being less than where the mixture No. 2 or 3 was used.

Application of No. 2 to the ear produced more or less redness and swelling, with death of a limited portion of the ear.

No. 3 produced a much more powerful action than either 1 or 2, when the application was made to the ear or to the tip of the tail. When applied under a skin-flap near the root of the tail, it did not act so very much more promptly than No. 2, though, on an average, there was still a difference in its favor.

No. 4 produced but very slight action in all cases; usually it was little more than zero.

In the DENTAL COSMOS for 1893, page 805, I called attention to the fact that the pain which is so frequently produced by applications of sublimate to the teeth may be in a great degree or entirely avoided by the addition of thymol. This led to the thought that thymol might be a valuable ingredient of arsenic paste.

Experiments were accordingly made with the mixture No. 5. As was anticipated, the action was much milder than that produced by No. 3, since a given quantity of the paste contains only about half to two-thirds as much arsenic as an equal quantity of No. 3. It was, however, equal to that produced by an application of a mixture of morphia and arsenious acid in oil of cloves, and we have reasons for thinking that the local anesthetic action of thymol exceeds that of morphia. Many, indeed, deny that morphia has any local anesthetic action at all. Thymol has, further, the decided advantage of a considerable antiseptic action. At the Dental Institute I have been making use of a paste having the following composition:

℞—Thymoli,
Acidi arsenicosi, āā x;
Ol. caryoph., q.s. ut ft. pasta.

We have no reason thus far to be other than satisfied with the results. One disadvantage of this mixture lies in the fact that part of the thymol separates from the arsenic in crystalline form, rendering it necessary to stir the paste from time to time. This difficulty might no doubt be overcome by a slight alteration in the composition of the mixture, possibly by the addition of glycerin.

The effect produced by applications of No. 6 was decidedly less than that by No. 5. Further dilution of the paste was not attempted, although we are perfectly safe in concluding that by increasing the proportion of thymol we may reduce the strength of the paste to any desired extent.

A paste made of arsenious acid with water acted quite as promptly as when oil of cloves was used. Nos. 7 and 8 were tested each only four times. They produced the impression of acting at least as promptly, if not still more rapidly, than the paste with oil of cloves. The action of *arsenic* acid was very marked. A small quantity of this taken upon a glass slide deliquesces immediately, so as to form a thin paste. An amount of this about equal in size to the head of a pin, applied to a slit in the tail of a mouse, caused death in four cases out of five inside of four hours; paralysis of the hind legs, diarrhea, and, in one case, convulsions, being the chief symptoms.

Arsenic acid also produced a local escharotic action, similar to that of carbolic acid, though in a much less degree.

In the fifth case, the mouse showed the symptoms just stated to such an extent that it was expected to die at any moment; it recovered, however, and on the following day appeared perfectly well; the local action was scarcely visible.

The results recorded above point to the following practical conclusions:

1. The rapidity and intensity of the action of arsenious acid depends, under certain circumstances, to a very considerable degree upon the substance or substances with which it is incorporated.

2. Where there is but a small point of exposure, and in particular where extensive calcification has taken place in the pulp, escharotics should be avoided, since the contraction of the tissue retards the absorption of the arsenic. This retardation is but slight where there is a broad surface of exposure.

In stubborn cases where applications of the ordinary paste fail to effect the devitalization, a paste consisting of arsenious acid in oil of cloves, glycerin, or salt solution should be employed, undiluted by any third constituent.

3. Thymol is worthy of a trial as a substitute for morphia, on account of its anesthetic and antiseptic properties.

4. For devitalizing pulps of milk-teeth or remains of pulp-tissue in root-canals, arsenious acid, if employed at all, should be diluted by two to three parts of some other constituent (thymol, oxid of zinc, morphia, iodoform).

In fact, in all cases where, for any reason, a milder action of the arsenic is desired, it may naturally be employed in this diluted form. In these cases Arkövy recommended the use of pepsin for devitalizing the pulp.

The question naturally arises whether results deduced from experiments on mice apply equally well to the pulps of human teeth. It is my impression that such is the case. Nevertheless, it would undoubtedly be well to supplement the above experiments by experiments on the pulps of teeth, although it will always be found very difficult to secure the variety of conditions in dogs' pulps which we meet with in the pulps of human teeth. Experiments on nine teeth (three dogs) gave results which fairly correspond with those reported above.

I give the results of my experiments to the profession at this time because I am about to interrupt my work for three months, and do not care to delay so long with the publication.