

XIV.—ON THE CHEMICAL CAUSE OF THE POISONOUS NATURE OF ARSENIC.

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It appears that Liebig has hitherto been the only author who has proposed a theory of the poisonous action of arsenic. It is to be found in the first edition of his work on the applications of chemistry to agriculture and physiology, and is essentially as follows: Arsenious acid and corrosive sublimate possess, in the highest degree, the capacity to form solid compounds with albumen. By internal administration, the albumen of living tissues loses the capacity to undergo the transformations necessary to their existence. The life of important parts is thus destroyed, and the death of the whole organism follows. Latterly, Liebig has not maintained this view; it is, however, still to be found in certain chemical works. It is untenable, for the reason that a solution of arsenious acid, or of its salts, does not form the solid compounds or albuminates which Liebig assumed, although this is undoubtedly the case with corrosive sublimate and certain other substances. Moreover, there has not been observed a single instance of a precipitating action produced by arsenious acid on the constituents of the animal body, stronger than that which would be produced by carbonic acid. This non-existence of an arsenious albuminate is proven by the fact that one can, for instance, poison an animal by dropping an arsenical solution on the extremely sensitive conjunctiva of the eye, without producing, on the place where the poison has been introduced, any other appearance than a slight reddening. In the interior of the body, however, the destructive effects are most distinctly visible. They centre in the stomach, even in those cases when not a trace of the poison has directly come in contact therewith. Anatomical investigations have shown us that precisely those tissues in the body, which are specially endowed with the capacity to receive and utilize the oxygen of the blood, such as, more particularly, the glandular protoplasm, form the principal seat of the destructive action.

The neutral salts of arsenic acid are just as poisonous as those of the arsenious acid. According to some accounts, they are even more so.

Arsenious acid changes readily to arsenic acid, and the transformation proceeds still more readily in the inverse sense. This latter

process is effected by albumen in general, the former by the living albumen of animals and plants.

These facts were proven first outside of the organism, with separate parts of the same. Arsenic acid was reduced, when treated at the temperature of the body, with egg albumen and fibrine of warm-blooded animals. Fresh brain substance had the same effect. The tissue of the pancreas, of the liver, and the undecomposed protoplasm of vegetable organs, not only reduced arsenic to arsenious acid, but also oxidized the latter to the former. If those tissues which oxidize arsenious to arsenic acid, be previously heated in boiling water, they lose this property. Blood, hæmoglobuline and fresh fat possess neither the former nor the latter property.

This double action may also be observed on the living animals. The two stages of oxidation of arsenic are reciprocally changed by the action of the glands of the intestinal canal, which also belong to those parts of the organism which experience soonest and most severely the effects of poisoning. Those portions of the organism which are not, or only secondarily, affected during life, are not capable of effecting the oxidation of arsenious acid. The careful consideration of all of the individual results of our experiments, leads to the conclusion that the reciprocal transformations of these two acids (which we were the first to prove in the case of *animal* bodies) produce within the living albumen molecule, in which they take place, a violent oscillation of the oxygen atom, whereby the tissues are corroded to the extent of their complete destruction.

An exact parallel exists between arsenic and nitrogen in this respect. Nitric oxide is extremely poisonous; it is transformed by reception of oxygen into the powerfully oxidizing hyponitric acid. The latter destroys the tissues, while it is, in part, transformed back into nitric oxide. Throughout the whole process, the nitrogen is without direct action; it is merely the inert carrier and distributor of the powerfully aggressive, active oxygen atoms. Arsenic fulfils the same functions where it appears as the carrier of active oxygen, *i. e.*, every moment arsenious acid is converted into arsenic acid, and this back again into arsenious acid.

The differences existing between arsenic and nitrogen are those of degree only. The oxides of nitrogen corrode those portions of the organism where they are first introduced; the oxides of arsenic develop their activity only within the organism, and, as is well known, are externally corrosive only by prolonged action. The active oxygen of the oxides of nitrogen is detached in an instant; that of ar-

senic acid requires some time, and that is the reason why the latter completes its destructive action only within the organism. That such oxygen atoms possess poisonous properties, is evident from the well-known deleterious effects of ozone, when it enters the system in any other state than that of extreme dilution. The case has, furthermore, recently been proven to be the same with the salts of chloric acid. They give up to certain constituents of the body their three atoms of oxygen, become changed to chlorides, and thus exert a corrosive and destructive influence on the cells and the blood.

Viewed from this standpoint, there becomes apparent a remarkable correspondence in poisonous, and in chemical, behavior among the other members of the nitrogen group. It is already known that they exert in the body a poisonous action similar, in its minutest details, to that of arsenic, differing therefrom only in degree.

This rapid change in the state of oxidation has been proven in the case of antimony, bismuth and vanadium. No known facts are opposed to the assumption of a similar transformation, such as we have shown to take place in the body, in the case of arsenious acid. Phosphorus passes, as such, dissolved in fat, into the circulation and into the tissues. Within, as well as outside of, the body, it acts as an ozonising agent. There results therefrom a violent disintegration of the living albumen molecules, which manifests itself, precisely as in the case of the administration of arsenic in suitable medium doses, in a considerable increase in the production of urea, in the diminution of glycogen, in the disorganization of important cellular groups, etc. All the effects produced in the body by phosphorus and arsenic, and, as far as has been investigated, the different stages of oxidation of the other members of the nitrogen group, and the benefits which have been obtained by their cautious administration, may be explained by the local excitation of oxygen.

The details of these experiments, and the conclusions drawn therefrom, have been published in the *Archiv fuer experimentelle Pathologie und Pharmacologie* (Leipsic, July, 1879), **II**, 200-230.