

This is what we must look forward to and aid with all our powers as physicians.

The objection has been raised that the treatment has in some cases caused a spreading of the disease and acute tuberculosis. Liebmman has stated that he has found tubercle bacilli in the blood of patients treated with the fluid. These examinations have been repeated by Professors Ewale and Guttman in a number of cases, and no bacilli found. A careful examination of Lippmann's slides have revealed the fact that the glasses used contained traces of old sputum. They had not been sufficiently cleaned.

To the charge that the fluid contained tubercle bacilli, and that we were in danger of giving our patients acute tuberculosis by its use, Dr. Libbertz has replied that there were a few tubercle bacilli in the preparation, but that they had been killed by repeated boiling.

Inoculation experiments have confirmed this statement.

The injection of 2 cg. under the skin of the speaker gave rise to the following symptoms:

Four hours after the injection of 2 cg. under the skin of the left forearm, I experienced severe headache, backache, malaise and nausea. The temperature rose to 99.8, pulse full, 108. The rate of breathing was also increased to about 30. These symptoms continued for four hours, when the thermometer registered 98. That night I slept comfortably; the following morning the arm was sore and tender and swollen. There developed a lymphangitis which lasted for 48 hours. During this time the thermometer reached 102. I suffered from severe headache and malaise. The trouble subsided, however, leaving absolutely no symptoms whatsoever. The effect of the fluid had passed off after twelve hours. The subsequent lymphangitis I attribute to the fact that the syringe used was not sterilized, and secondly that the forearm was not a well chosen place for the injection.

I have learned these points from this experience:

1. To adhere to the Koch syringe, rather than the ordinary hypodermic which I had used in my own case.

2. To appreciate the wisdom of Koch's recommendation to use the interscapular region as the site of the injection.

3. That the injection of tuberculin does not produce any deleterious effects in healthy people. I would like to state that mine was the only case in my experience in which there occurred any trouble at the site of the injection.

Perhaps in a number of cases where acute tuberculosis was found, the remedy had lighted up a number of latent tubercular points, rather than that they had been produced by a scattering of the bacilli from the older lesions. Further study and observation may lead us to avoid such cases

in the future. Above all, we are to remember the work and instruction of Professor Koch, and that the chapter on the treatment of tuberculosis is not a closed one by any means.

ON THE CHARACTER OF THE EVIDENCE AS TO THE INJURI- NESS OF ARSENIC AS A DO- MESTIC POISON.

Read in the Section of Practice of Medicine and Physiology, at the Forty-second Annual Meeting of the American Medical Association, held at Washington, D. C., May 5-8, 1891.

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This communication is an attempt to place in as clear a light as possible, the credibility of the evidence that symptoms of arsenical poison may occur as a result of the ordinary exposures, such as are met with in domestic or civic life.

I shall not try to indicate the frequency with which such poisoning occurs, but only the possibility that it may occur; for the question as to frequency can only be satisfactorily answered when a large body of facts have been accumulated, especially those relating to the obscurer forms of chronic poisoning. The first thing to be done, would seem to be to disprove the opinion which has so much weight, even among those who would otherwise credit the evidence of domestic poisoning, that not enough arsenic could possibly reach the tissues to cause serious effects.

For this purpose I shall show: first, that urine analyses indicate beyond cavil that the exposures of civic life are a very frequent cause of arsenical contamination; next, that our knowledge of the laws of elimination indicates that the excretion of the small quantities which pass off with the urine day after day for months and years, in the case of many persons in the community, implies the presence by accumulation of much larger quantities in the tissues. The dangers attending domestic exposure might, in fact, be fairly compared with the dangers attending the medical use of arsenic, and I shall show that these dangers are usually underestimated. If in the cases of domestic exposure, the single doses are smaller, yet on the other hand, the period of exposure is much greater; the patient is not under the watchful care of a physician; the character of the arsenical compounds sometimes brings special dangers; the place of absorption is often the lungs and not the stomach; and there is some reason to believe, that there are certain very chronic and exceptional forms of poisoning, following the repeated use of minute doses, with which we are not yet thoroughly familiar, and which, in the absence of signs of acute poisoning, are likely to be overlooked.

The dangers attending the medicinal use of arsenic have been underestimated by physicians, partly because of their relative infrequency; partly because the first indications of them (œdema of the face, irritation of the mucous membranes, etc.,) are so familiar, and usually so amenable to treatment, that they are hardly looked upon for what they are, namely, imperative signs that symptoms of more serious import are not far off (as shown by the experiments of Vaudrey).

Again, the effects of habituation, the storage of the arsenic in a temporarily innocuous form (albuminoid compounds of arsenic; Dogiel, International Congress, Copenhagen, 1886), and constitutional indifference to the poison confer as a rule such complete immunity, that those not so fully protected by nature, or with whom the protection ceases after a time, for one or another cause, stand in all the greater danger on account of the false impression of security which is spread abroad, and which makes physicians impatient of studying the obscurer indications of poisoning.

The most important collateral facts bearing on the question of the quantity of arsenic absorbed in domestic poisoning cases, are, as above stated, those obtained by urine analyses, of which large numbers have been made by the chemists associated with Harvard University.¹

To speak of only the most recent and conclusive series of experiments, Dr. C. P. Worcester, of Harvard University, a skilled chemist and with large experience in this particular analysis, has examined for my brother and myself one hundred and fifty urines, taken from patients most of whom presented certain obscure symptoms, but not such as would have justified the diagnosis of arsenical poisoning, and has found arsenic in more than thirty per cent., in quantities varying from a trace to upwards of .05 mg. to the litre.

About half of these patients were private, while the other half were from the clinic for Diseases of the Nervous System of the Massachusetts General Hospital, and many of the latter were chosen as presenting no arsenical symptoms.

These results conclusively show: *first*, that the community is exposed to arsenical contamination on a very large scale, so that the occasional occurrence of poisoning, due perhaps to special susceptibility, unusual exposure, failure of elimination, etc., need occasion no surprise, and ought to be carefully sought for by every physician; *second*, that the mere finding of arsenic in the urine in a doubtful case does not prove that the symptoms were of arsenical origin.

What does the elimination of these small quantities indicate as to the amount present in the tissues?

It was formerly believed that arsenic differed from lead in being eliminated rapidly and in not uniting with the tissues. Both of these opinions are now disproved. Arsenic has been found in the liver bones (Gibb) six months after the cessation of a course of arsenical treatment (which, by the way, led to the patient's death); it has been found in the urine even nine months after the apparent removal of the patients from exposure in "domestic" cases; and Prof. E. S. Wood has recently found traces in the urine as long as three months after cessation of a short course of arsenical treatment (these experiments are not yet concluded, and I quote a verbal statement only as relating to one or two cases).

Arsenic does then, in some cases at least, tend to accumulate, and the daily elimination of .03 to .3 mg. (gr. $\frac{1}{3000}$ to $\frac{1}{1000}$, computed by supposing two litres of urine to be excreted daily, and to contain two-thirds of the whole elimination of the arsenic), must indicate the presence in the tissues of quantities quite large enough to cause poisoning, provided it should become active all at once, or provided that for any reason the elimination should be checked.

That the effects of arsenic—like those of lead, and phosphorus—are in a measure dependent upon the action of the stored up poison, is shown by the fact that the symptoms of medicinal poisoning often appear only when a given dose has been taken for some time, after which the patient is apt to show an increased sensitiveness (though this is not regularly the case). In the case of lead it is a matter of common knowledge that sudden outbreaks may occur after lead drinking water has been used for a long time, as well as among the workers in lead mines. In the case of arsenic, it is quite common to find the paralytic symptoms breaking out days or weeks after a single large dose or repeated smaller doses.

Is the use of arsenic in maximum therapeutic doses unattended with danger?

This is by no means the case, although the doses used are far less, at their largest, than those taken by the Styrian peasants with impunity.

Habituation to large doses may by care be brought about, but in the attempt to do this the lesser symptoms of poisoning are frequently excited, and the graver symptoms occasionally.

No doubt there are but few physicians who have had these graver symptoms in their own practice, but this is certainly because they have taken pains to avoid them, for the experiments of Vaudrey upon himself and others, have shown that by increasing a little further the doses which excite the lighter symptoms, serious prostration and local symptoms regularly follow. A few years ago I collected a number of the severer cases of medicinal poisoning,² and I give here a few of them in brief outline. The cases of

¹ Especially Profs. E. S. Wood, C. Harrington, W. B. Hills, C. R. Sanger, (now of Annapolis Naval Academy), H. B. Hill, C. P. Worcester, A. M. Corney.

² Boston Medical and Surgical Journal, March 7, 1889.

paralysis are especially noteworthy because these are now known to occur frequently in arsenical poisoning of a certain grade, and, as we shall see, they reappear among the cases of "domestic" poisoning.

1. Gaillard: Typical arsenical paralysis following full doses of Fowler's solution, increased to the limits of tolerance and administered for five weeks.

2. Canada Med. and Surg. Journ., 1886-1887, v. 15, p. 716. Arsenical paralysis, ending fatally, after large doses (\mathcal{M}_{xx} to xxx) of Fowler's solution. The autopsy showed the presence of neuritis.

3. Hastings: Arsenical paralysis with neuritic symptoms, following \mathcal{M}_{ij} to v of Fowler's solution continued for some weeks.

4. Gibb: Long course of arsenical treatment ending in neuritis, causing disorders of sensibility, pain, and paralysis. The patient died six months later, having taken no arsenic in the interval, and traces of arsenic were found in the liver and bones.

5. Dublin Quarterly Jr., v. 36, p. 474. \mathcal{M}_{ij} of Fowler's solution, were taken daily for ten or twelve months, at the end of which time "symptoms of acute arsenical poisoning" came on, ending rapidly in death.

6. C. L. Dana: Arsenical paresis with ataxia. \mathcal{M}_{xxx} of Fowler's solution three times daily, in spite of the fact that the dose had been gradually increased.

7. Hooper: \mathcal{M}_v of Fowler's solution were given three times daily for eight months. Toward the end of this time the following symptoms came on and increased, ending three months later in death;³ conjunctivitis with œdema, tachycardia, tremor, excessive and progressive prostration, insomnia, irritation of the trachea and larynx.

8. Jones: \mathcal{M}_v to xv of liquor arsenicalis given three times daily; at the end of a month, intense gastro-intestinal irritation, scanty urine, trophic changes in the legs, sensory and motor paresis.

9. Burne, cited by Taylor: Gr. $\frac{1}{10}$ of arsenious acid daily for four days; then, inflammation of the stomach, delirium, debility and exhaustion.

10. Taylor: Gr. $\frac{1}{10}$ of arsenious acid taken twice daily for seven days, then, "sickness," irritation of the skin, and eczema over the whole body.

11. Taylor: \mathcal{M}_x of liquor arsenicalis chloridi (said to be a very poisonous preparation) taken three times in the course of twenty-four hours; then, constriction in the throat, pain and irritation of the stomach and bowels, tingling and

numbness of the hands and feet, with paresis; extreme depression; gradual recovery.

12. Personal Observation: \mathcal{M}_{iv} to v of Fowler's solution taken three times daily for six weeks; then there came on extreme prostration, pains of severe character in the extremities, widespread muscular atrophy, and paralysis, so severe that the patient was helpless for many months. During the worst of his illness he inhabited a room with a highly arsenical paper. I consider this case as especially important because it was possible to eliminate, as satisfactorily as this can ever be done, all the other causes of neuritis. The patient was a gentleman in good circumstances, not syphilitic, not tuberculous, with no lead in the urine. He had had no acute diseases, no grippe, no anæmia; and the symptoms came on during the pleasant weather of June.

Of course this handful of cases does not prove that arsenical paralysis is common from medicinal doses, but only that it occurs.

There are, however, three obvious reasons why we do not have more such reports: 1. The watchfulness of physicians; 2. The failure to recognize the nature of the cases seen; 3. Unwillingness to report unfavorable results.

Imbert Gourbeyre says that many cases of paralysis occurred in the last century when arsenic was used so freely in the treatment of intermittent fever. He does not give references, however, and I have not yet fully studied this point.

Dr. Winkler, of Altenburg, writing in 1811, quaintly reports a case of paralysis of the legs occurring in the practice of a colleague, after an arsenical treatment of intermittent, but "does not believe" it was due to arsenic, and is obviously wholly unfamiliar with the characteristics of arsenical paralysis, now so well known.

This would be a suitable place to introduce, by way of comparison, the recorded cases of paralysis due to domestic exposures.

I have not, however, undertaken, in this paper, to bring forward the clinical evidence indicating the frequency with which arsenical symptoms occur, but only such as would present as strongly as possible the fact that they do occur.

For this reason I shall confine myself to my own experience in speaking of arsenical paralysis (and other signs of neuritis). I will note, however, that a number of such cases are on record. Alexander, of Breslau,⁴ for example, in a recent pathological monograph on arsenical paralysis (1889), considers nine cases to have been of "domestic" origin, out of fifty-eight which he selected from a much larger number of general analysis.

The cases which I have seen myself, several in number, were mainly light cases, as might be expected, and for that reason less conclusive. I

³ It has been abundantly shown by the history of acute arsenical poisoning that symptoms once inaugurated may continue and increase, though no more arsenic is taken. The paralysis, for example, often fails to appear for days or weeks, and even months.

⁴ Boston Medical and Surgical Journal, March 7, 1889.

therefore report but two, one of which has been published.⁵ (Atwood.) This is the case of a lady 43 years old, and of naturally good health,⁶ except that for a year or two she had suffered from severe colds and from "indigestion."

The new symptoms began about six weeks after her return from a vacation, at which time she had moved into new rooms, which were afterwards found to be papered with a highly arsenical paper.

The symptoms consisted, first, in severe abdominal neuralgia, recurring every morning and passing away in the afternoon, and not attended with signs of indigestion. This continued for nine months, but before the end of this period she began to lose sleep and appetite, and to notice tingling sensations in the fingers, lips, tongue and feet. The hands and wrists became sensitive on pressure, and whenever she was recumbent the arms used to "go to sleep." Writing, formerly easy, became a labor.

The dynamometer registered R. 55, L. 17, instead of 30 to 50 as might have been expected; hyperextension of the right hand and fingers was very poor; there was tremor of both hands; the electrical reactions of the extensors, especially those of the right arm, were markedly impaired.

The patient has been under observation for the past two years, and had been known to me for several years before. Arsenic (but no lead) was found in the urine three or four times at intervals of many months, at first in relatively large amounts, afterwards in traces, until finally it disappeared.

The health gradually improved after removal from exposure, except that a moderately severe facial spasm has been present ever since. The general health has once or twice given way to some extent under hard work, but the special symptoms have never returned. I omitted to say that at one time the sensibility of the right finger tips was found slightly less than that of the left. The dynamometer finally registered $\frac{R}{L}$ 35.

I consider this case of special value for the reason that while evidently an instance of neuritis, the morbid conditions would certainly have been overlooked but for careful examination. Careful electrical examinations in doubtful cases would very likely reveal slight changes of great diagnostic importance, since we know, both from experimentation with animals, and from clinical observation, with both lead and arsenic, that there is a period when neuritis is latent as regards paralysis, and yet is discoverable by electrical tests and by the microscope.

Far more numerous than these characteristic cases of arsenical neuritis, are of course the lesser

and obscurer symptoms, and they are also really of far greater importance just because they are obscure. I shall not occupy space by discussing them, because physicians at large are not yet in the mood to consider them without prejudice, and my present object is solely to allay that prejudice. I will only remark that we have good reason to believe, not only from the history of domestic poisoning, but from medicinal, and accidental, and homicidal cases, that in chronic arsenical poisoning, or in the chronic remains of acute poisoning, two tendencies are occasionally manifest; one to relatively isolated impairment of special organs or functions (tachycardia, sexual impotence, loss of voice, irritation of the kidney, localized neuralgia, herpes zoster and other affection of the skin, etc.); the other to anæmia, or the impairment of the general nutrition, without marked local symptoms.

This latter tendency has seemed to me especially important as occurring among infants. I have, however, also seen, in consultation, in a child of two years, a generalized neuritis, with impairment of the electrical reactions, apparently due to arsenical poisoning. What is the source of the arsenic in the cases of domestic poisoning; and in what form does it act?

These questions are still unanswered, but no candid person can doubt that papers (mainly those of older date) and fabrics are mainly responsible. Probably it comes little by little from many sources and acts after accumulation. In the case of a lady, under my own care, a severe eruption, of inflammatory vesicular character, broke out all over the face and neck. She was seen by an experienced dermatologist who pronounced the eruption not eczematous, and found traces of arsenic in the scales removed from the skin. I found traces of arsenic in the urine and a large quantity in the covering of a reclining chair in which she habitually sat. The patient was subject to universal eczema, and had proved susceptible to arsenic given internally. Perhaps for these reasons the skin was unusually sensitive.

The theory that the arsenic sometimes occurs in a gaseous form cannot yet be set aside; and the mode of introduction (i. e., by the lungs) may perhaps increase its immediate violence, just as Alexander (l.c.) found that when injected under the skin of the shoulder in animals it had more constitutional effect than when injected into the peritoneal cavity. At any rate, the urine analyses prove that it comes from somewhere and accumulates in quite a quantity; and the clinical analyses prove that it may cause serious and characteristic symptoms, and a great many more slight but very troublesome and often chronic and obscure effects.

⁵ Inaugural Diss. on Arsenical Paralysis. 1889.

⁶ For details see the published report. Boston Medical and Surgical Journal, March 7, 1889.