

**MULTIPLE NEURITIS IN WOOD ALCOHOL POISONING.**

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IN view of the recent bringing to light of the fact that many deaths have been caused by the use of methyl alcohol, and further, by reason of the renewed interest taken in the subject of methyl alcohol optic neuritis as evidenced by the more recent work of Buller and Wood,<sup>2</sup> it

<sup>1</sup> Bertarelli, Centralblatt f. Bakt. XXXVII. Bd., Heft 6.

<sup>2</sup> Some Problems in the Life History of Pathogenic Organisms, Science, December 16, 1904.

<sup>3</sup> Introduction to a discussion held at the New York Academy of Medicine, January 17, 1905.

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has seemed pertinent to inquire if types of neuritis other than that affecting the optic nerve may be caused by the use of methyl alcohol taken internally, either as a liquid or as a vapor.

It is well known that ethyl alcohol—ordinary grain alcohol—produces as a result of long use not only optic neuritis (first brought into prominence by Eichorst in 1876), but also the familiar type of peripheral multiple neuritis, first described in this country by James Jackson,<sup>2</sup> of Boston, as far back as 1822 as "A Peculiar Disease Resulting from the Use of Ardent Spirits."

Up to the present time, however, I have been unable to find any record of multiple neuritis induced by methyl alcohol. My search through literature has been extensive but not exhaustive, and at first sight it would seem highly improbable that attention had not been called to this condition, but it appears to have been overlooked, or I have overlooked it.

Inasmuch as the optic neuritis of wood alcohol poisoning has been thoroughly covered by some scores of investigators, Ward Holden,<sup>3</sup> Birch-Hirschfeld,<sup>4</sup> Rymowitzsch,<sup>5</sup> de Schweinitz,<sup>6</sup> among them, I have limited the present note to some personal observations on peripheral neuritis resulting from the use of wood alcohol.

Of this affection *per se* three patients have come under my observation. By reason of the time limitations for this discussion their histories are presented very briefly.

The first patient was seen in 1898. He was a business man, thirty-four years old, and a moderately constant drinker. Sprees were not frequent but he drank small quantities, particularly at night before going to bed. During business hours he rarely indulged. He drank a special brand of whisky which was sold to him by an enterprising druggist, a friend of his, for 25 cents a quart or a dollar a gallon. His friend told him that it was tax-free whisky (moonshine whisky), that he bought on the quiet from some friends in the country. As a matter of fact it was a 35 per cent. Columbian spirits whisky with suitable flavors to make a "richly blended article." He was proud of his ability to "get next" to such a bonanza.

My notes made at the time do not cover the question of the length of time of his indulgence, but he had been drinking this whisky, and other whiskies also, the latter, however, in comparatively small quantities, for at least three months, if not six.

He began to suffer from severe gastric irritability and marked hyperesthesia in the upper extremities, particularly in both arms and hands. This was followed by incomplete paralysis of the extensors and typical drop-wrist. He also had a mild grade of ptosis.

I saw him while in the early stage of paralysis and also found that he had a partial amblyopia. It was very restricted. The patient recovered after four months of treatment, but he still complained of some blurring of vision. Since that time I have lost sight of him.

My notes are not extensive in this case but they are sufficiently explicit to enable me to exclude practically all other causes of neuritis. He was not a beer drinker. Arsenic may be eliminated. Other metal toxemias were excluded, as were also the posttoxic affections of the infectious diseases, malaria, grippe, typhoid, diphtheria, etc. The dyscrasias were also excluded. It is true that he occasionally drank good whisky, but most of his drinking was done in the evening at his own home from his own private special stock. I have always felt that this was a distinct example of neuritis from wood alcohol. The neuritis did not differ in any particular from neuritis due to ethyl alcohol. Both caused by same agent.

Two other cases may be of interest in this connection, as showing a much lighter grade of affection and a different mode of ingress of the poison.

Both of these patients were painters, particularly varnishers. They did nothing but shellac work, on desks, furniture, etc., and they worked long hours and in comparatively small rooms.

The shellacs that they used were for the most part dissolved in wood alcohol and they were exposed to the evaporating fumes. They were comparatively unaware of any distinct action of the alcohol. As for one of them I never could make up my mind that he did not use the diluted alcohol to drink. Indeed, instances of drinking the wood alcohol washings from shellac barrels are not unknown. One of the patients reported on by Buller and Wood indulged in this manner.

Both of these patients suffered from the hyperesthetic form of the disease. The involvement was also of the upper extremities alone. There were the familiar paresthesias, numbing, pricking and shooting pains in the back of the hands and forearms. The pains were at times severe and there was intense pain upon pressure over the nerve trunks. The joints were involved to a slight extent only. There was also a certain amount of edema or puffiness.

These were instances, I believe, of beginning peripheral neuritis due to breathing the fumes of wood alcohol. It might be recalled that de Schweinitz<sup>7</sup> and others have described typical optic neuritis and blindness as a result of breathing the fumes of wood alcohol.

Both of these patients were intelligent men, and noting similar symptoms they were led to seek medical aid before serious consequences arose. It is true that the involvement was slight only, but it seemed at one time in the disease, particularly in one of the patients, that paralysis might develop. There was distinct motor weakness in both instances, and it might be added that they seemed more anxious about the impairment of their muscular power than they were about the sensory symptoms.

In so far as this whole question of wood alcohol poisoning is of comparatively recent development it might prove of service, particularly in opening a discussion, to recapitulate, in a re-

stricted sense, somewhat concerning our knowledge of the comparative toxicity of the different alcohols, particularly the peculiar characteristics of wood alcohol.

The alcohols that interest us are hydroxides of the marsh gas series: Methyl,  $\text{CH}_3\text{OH}$ ; Ethyl,  $\text{C}_2\text{H}_5\text{OH}$ ; Propyl,  $\text{C}_3\text{H}_7\text{OH}$ ; Butyl,  $\text{C}_4\text{H}_9\text{OH}$ ; Amyl,  $\text{C}_5\text{H}_{11}\text{OH}$ . Wood alcohol, grain alcohol, and amyl alcohol or fusel oil represent the most familiar.

Pharmacologists are in practical accord that from the lowest to the highest of the series there is for acute poisoning a gradual increase in the toxic action of these alcohols, and the early figures of Joffroy and Serveaux<sup>8</sup> have been practically confirmed by a large series of experiments with various animals. In general it may be said that the comparative toxicity in acute poisoning is: Methyl, .5 to .7; ethyl, 1; propyl, 2 to 3; butyl, 3 to 5; amyl, 5 to 8. These figures are not absolute for all species, but they represent a mean of the results of many investigations.

Thus Dujardin-Beaumetz and Audigé,<sup>10</sup> almost the earliest observers, working with dogs, showed that the toxic doses in grams per kilo of animal were arranged as follows: Wood alcohol (ordinary), 5 to 6; pure wood alcohol, 7; ethyl, 7.75; propyl, 3.75; butyl, 1.85; amyl, 1.50. Joffroy and Serveaux's<sup>8</sup> figures for the equivalents in toxic power for rabbits were as follows: Methyl alcohol, 25.25; ethyl alcohol, 11.70; propyl alcohol, 3.46; butyl alcohol, 1.45; amyl alcohol, .63; furfural, .24, and Bär's experiments on guinea-pigs to control the figures of the earlier French writers showed practically the same results. Poisoning increased with the boiling point of the alcohol. He would arrange them as follows: Methyl, 8; ethyl, 1.0; propyl, 2; butyl, 3; amyl, 4. Less than one per cent. of higher alcohols added to ethyl alcohol does not seriously modify its toxicity, but four per cent. causes a distinct rise in toxic power. One to two per cent. of furfural also increases the poisonous action of ethyl alcohol.

Reid Hunt's<sup>11</sup> more recent and exhaustive work on dogs shows somewhat similar results. He raises the question, however, that the results as observed in acute intoxication of the lower animals may not be applicable to man.

It may thus be seen that, dose for dose, for lower animals, including monkeys, and possibly also for man, although there are reasons why this may not be true, methyl alcohol is slightly less toxic than ordinary alcohol.

But the matter is distinctly different when repeated dosage is concerned. Here experimentation with the lower animals has shown that wood alcohol differs in its action from other alcohols. It is markedly cumulative in its action while the others are not or distinctly less so. The action of a single toxic dose, moreover, is much more prolonged than for any of the other alcohols, for Pohl and others have shown that the maximum output of decomposition products following wood alco-

hol doses does not occur until the third or fourth day. Thus lower animals may take ethyl alcohol or the higher alcohols for considerable periods of time, weeks, months or even years, and if the doses are not too large there is soon established a balance between absorption and elimination, and the animal continues to live and develops slowly the characteristic tissue changes of alcoholic degeneration. This is also true for fusel oil and for furfural, two of the most poisonous ingredients of many intoxicating drinks.

Under methyl alcohol, however, even if the doses given are not distinctly toxic, after a comparatively short time, two or three weeks, the animal dies, usually of coma, inanition, fatty degeneration of the liver, and almost invariably develops changes in the nervous tissues of the eye. It is thus very evident that the type of poisoning is different with methyl alcohol, and that probably the products of decomposition of methyl alcohol in the body are different from those of the higher alcohols.

Just what the exact steps are in the oxidations, more particularly of ethyl alcohol and wood alcohol, we are not yet in a position to state positively. Pohl<sup>12</sup> has shown that the probable course of the oxidation of ethyl alcohol is into ethyl aldehyde, to ethyl acetate, acetic acid, carbon dioxide and water; thus in the urine, beyond the small amount of unchanged alcohol, there are no traces of the decomposition products. For wood alcohol the oxidations are probably into formic aldehyde and then to formic acid, and the latter acid has been found in considerable quantities in the urine by Pohl, by Reid Hunt and others who have worked on this side of the problem. Pohl failed to find any increase of formic acid in the blood or tissues, however.

Pohl, Hunt and others have concluded then that in view of the prolonged action of methyl alcohol and the high toxic action when given in small repeated doses, it is probably very slowly oxidized and hence probably remains, first as methyl alcohol in contact with the tissues for a long time, and that probably formaldehyde and formic acid play some part in the poisoning. Hunt has said that formic acid is probably six times as toxic as wood alcohol.

It is not therefore necessary to say that it is because of the impurities in wood alcohol, furfural, acetone, etc., that this body is toxic; it is because of its very slow oxidation processes, and its own characteristic decomposition compounds.

Before wood alcohol was put upon the market as an odorless substitute for grain alcohol, as it was about 1896, under the name of Columbian Spirits, its very penetrating odor prevented, in large part, its use for adulterating whiskies and other alcoholic preparations, tinctures, essences, colognes, flavoring extracts, etc., but at the present time, if we are to take the statements of many competent analytical chemists that a large percentage of all these preparations is adulterated, and that largely by wood alcohol, the

Herbivores can survive

Good!

Good!

situation is not reassuring. The Board of Pharmacy in this city at one time found an extensive use of wood alcohol in the manufacture of the tinctures of official preparations, to be used in serious illness, and, be it accorded to their credit, they have been indefatigable in their efforts to stop such highly reprehensible practices—and with success.

Why then do we not find a number of patients suffering from methyl alcohol peripheral neuritis, and why are there not more reported cases in literature?

There are a number of reasons why! One is that death occurs so promptly in many instances that there is not enough time to develop the lesion in the peripheral nerves; or because of the greater susceptibility of the ganglion cells of the retina, partial or complete blindness appears so promptly that the methyl alcohol mixtures are not taken for a greater length of time.

As for the reasons for this relatively greater susceptibility of the retinal ganglionic structures it can be accepted at the present time only as a fact, bearing in mind that the alcohols as a class affect the more complex nervous elements of the cerebrum and highly differentiated special senses more rapidly than the comparatively more primary spinal neurons of the peripheral nervous system.

Peripheral neuritis from wood alcohol does not seem to have been observed in any of the animals experimented on. Here again the early death precludes the development of the lesion, and, moreover, most of the investigators had in mind solely the effects to be observed in the retina and optic nerves. The more general subject of experimental wood alcohol peripheral neuritis is therefore in need of investigation.

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#### LITERATURE.

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