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Original Article



HYDROBROMIC ACID: ITS ACTION ON THE CIRCULATORY AND NERVOUS SYSTEMS.

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THE several papers which have been recorded on the therapeutical use of hydrobromic acid indicate that this new drug possesses sufficient promise to call for a close study of its physiological properties, and especially so because of the asserted similarity of its physiological action and that of the alkaline bromides, together with the noticeable absence of the disagreeable digestive derangements which are known to so often follow the extended use of the alkaline salts. In a review of these papers it is found that this agent was first employed by Wade, who states that it fully represents the action of bromine on the system, and that it modifies the action of both quinine and morphia on the brain, the same as the potassium bromide. These statements have been corroborated by other observers, some of whom have further claimed that its effects are more intense, but less permanent, that it lacks the action of the potassium bromide on the heart and muscular systems, that it has been used with marked success in the treatment of tinnitus aurium, supposed to be due to labyrinthine congestion, that it is a tonic to the digestive organs, and that it readily becomes decomposed in the stomach.¹

This is the sum of the knowledge we possess of the action of this acid on the economy, and it certainly is sufficient to indicate, if the above statements be true, that we have a valuable addition to our materia medica. In order, however, to conclusively determine whether the acid possesses the peculiar physiological properties of the alkaline bromides, the following investigation was made, and since the recognized therapeutical properties of the alkaline salts are conceded to depend upon their peculiar actions on the circulatory and nervous systems, my researches were confined to this special study. One difficulty, however, to contend with in a comparison of the actions of this acid and alkaline bromides is that no thorough manometrical study of the action of the latter has yet been made, and even the papers so far published present conclusions which are at variance on many points.

In my experiments on the *circulation* it was found that the *arterial pressure* was affected in one of three ways, evidently depending upon the dose given. Thus, after very small doses it was wholly unaffected or a slight rise, which was almost inappreciable, occurred. After larger doses the pressure generally fell a little (making a tracing similar to that produced by stimulating the cardiac inhibitory nerves), and was followed by a return to or above the normal, and if the arterial tension was increased above the normal, it frequently remained so for six, eight, or ten minutes. In experiments when the pressure did not primarily fall, it increased from the first, and usually equaled, when it reached its greatest height, about one sixth of the normal pressure. After very large or toxic doses, the

blood pressure fell from the first, and continued to sink until it reached zero. In animals with cut vagi nerves, doses which would cause a primary fall of pressure in normal animals would induce a rise, and it was also noticeable that the rise of pressure, as a rule, was more marked in animals thus operated upon. This clearly indicates that the drug exerts some action on the pressure through the vagi nerves. After isolation of the heart from any centric nervous influence by severing the vagi nerves and cervical portion of the spinal cord, essentially the same results followed as occurred in normal animals. This, therefore, shows that outside of the action on the vagi nerves, as just referred to, these changes in the arterial tension must be dependent upon the action of the acid on either or both the heart and vaso-motor peripheries. In order to determine if the drug had any effect on the latter, microscopical examinations of the web of the frog's foot were made, and it was found that the local application of the diluted acid caused a distinct capillary contraction. A marked pallor was noticed after the local application of the acid to muscular tissue, but just how far this was due to capillary contraction or to probable myosic coagulation is unknown; the same pallor was also noticeable in some instances about the lips and eyes of animals under the influence of toxic doses. I think, therefore, from the above results, that it is fair to conclude that the peripheral vaso-motor mechanism is stimulated.

When the drug is applied locally to the heart the cardiac power becomes at once diminished, and the pulsations are soon arrested.

It is evident from the above results that the rise of pressure was due to a stimulation of the peripheral vaso-motor mechanism, and the fall to a direct depressant action on the heart muscle. The reason why a rise of pressure occurred during a consentaneous depression of the cardiac power was probably and simply because of a comparatively more intense action on the vaso-motor peripheries, the diminished capillary lumen being sufficient to more than compensate for the diminished power of the heart.

The *pulse-rate* was not appreciably affected by very small doses. Larger doses sometimes caused a momentary slowing, with a diminution of the arterial pressure (making a tracing similar to that caused by inhibiting the heart), and after the subsidence of this inhibition the pulse, to a various extent, recovered, not, however, reaching the normal, and it then became slowly diminished; at other times a momentary rise occurred (accompanied by a consentaneous diminution of the arterial pressure, but differing in character from that above noted) which equaled about one tenth to one fifth of the normal in excess, and this rise was followed by a diminution equaling about one third to one half of the normal. The increase of the pulse-rate was marked by pulse-curves, which were lower and less abrupt in their line of ascent than those of the normal, and the diminished pulse-rate by curves which were higher and more abrupt in ascent. After large and repeated doses (thirty drops in dogs) the pulse-rate fell below, but remained near, the normal until after the second, third, or fourth doses, and it then either rapidly fell to zero, or rose very rapidly (in one instance from thirty-three to seventy-eight pulsations in forty seconds); or, in a third lot of cases it rose gradually to the normal (taking in one instance six minutes to do so), and sometimes continued to in-

¹ Wade (Peninsula Journal of Medicine, February, 1875, p. 62); Fothergill (British Medical Journal, 1876, i. p. 42); Forrest (ibid., 1877, p. 398); Campbell (ibid., p. 480); Fry (ibid., p. 480); Woakes (ibid., p. 773); Hamilton (Philadelphia Medical Times, 1877, p. 31); H. C. Woods (Therapeutics, 1879, p. 333); Browne (British Medical Journal, 1877, ii. p. 13).

crease considerably. If the doses are still repeated in cases like the last two the pulse-rate may rise at every dose, being followed by a diminution, and finally, a last dose will cause it to rise to a considerable height, near which point it may remain a few seconds, when the heart fails and the pulsations become slowed and gradually diminish until death ensues; or, instead of the final injection causing such a very marked rise, it may so affect the heart that its movements are at once arrested. In these several instances the increased pulse-rate was always accompanied by a diminution of the blood pressure, deep and labored respirations, and often struggles, and the pulse-curves were equal to only about from one tenth to one eighth of the normal size.

After section of the pneumogastric nerves, no change from the above results occurred, except that the very transient inhibition of the heart immediately following an intravenous injection was not present. The same may also be said of the results of experiments made on animals with cut cervical spinal cords and pneumogastric nerves, by which the heart was cut off from impulses originating in or reflected from the nervous centres. It is obvious, then, that with the exception just made, the changes in the pulse produced by hydrobromic acid are due to a direct action on the heart, and that this action is one of paralysis is evident from the fact that the increased pulse-rate was accompanied by a diminished size of the pulse-curves and diminished arterial pressure (notwithstanding an attendant condition of capillary constriction). It is obvious, then, that the increased pulse-rate was not an evidence of cardiac stimulation, but of depression, and was no doubt, in a measure, but a compensating action of the heart in endeavoring to overcome by increased frequency of pulsation, the results of its diminished power. It has been further found that the heart is less irritable after death than normally, and that the exposed heart of the frog was paralyzed by a direct application of the diluted acid.

Upon the *nervous system* hydrobromic acid seems to act as a universal depressant, producing in frogs, in toxic doses, a diminution and final extinction of all reflex and volitional phenomena, and the early induction of narcotism. In dogs, cats, and rabbits the action on the brain is comparatively feeble, while the same is equally as true as regards the action on reflex and voluntary movements, although not so marked. In frogs reflex activity is slowly and gradually diminished until a certain period is reached, varying from seven to twenty minutes, when it suddenly and completely disappears, at which time neither mechanical stimuli, nor the strongest current obtained from a Léclanché cell and a Du Bois Reymond induction coil would induce the least response. It was also noticeable that failure of reflex movements occurred first in the posterior extremities, and that after stimulus, when applied to them, would elicit no reflex response whatever, response would still be called forth by stimulus applied to the anterior extremities; and in several instances, not only were these movements present in the anterior extremities when they were stimulated, but also in the posterior, indicating that the cause of failure of reflex movements in the posterior extremities when stimulus was applied to them was on account of a paresis of either the sensory nerves or sensory portions of the cord. For the motor nerves and motor portions of the cord must be capable of transmitting impulses else reflex phenomena would

not have occurred in the posterior extremities in those cases where the anterior extremities alone were irritated. On account of the interest centred in these experiments, the results of one of them is given in detail:—

Experiment. Frog; normal. 1.53 P. M. Reflex action occurred in one and a half seconds after immersion of posterior extremities in a two-per-cent. solution of sulphuric acid; the frog's legs were then completely washed of the acid solution by a gentle stream of water. 1.55. Ten minims of hydrobromic acid, properly diluted, were injected into the posterior lymph-sac. 2.00. Reflex action, tested as above, occurred in two seconds, the frog's legs being washed as before. 2.05. No reflex movements occurred even after a minute's immersion of the posterior extremities; reflex movements occurred in the anterior extremities in three seconds after being dipped in the acidulated solution, and were accompanied by feeble reflex movements in the posterior extremities.

Although in my experiments with this acid voluntary movements were never observed to occur after the suppression of reflex activity, such as have been so frequently observed after poisoning with the alkaline bromides, yet the above result certainly indicates that the action of these two poisons on both reflex and voluntary movements is identical; and this has been found by further experimentation to be the case, for in animals in which the abdominal aortas were ligated for the purpose of preventing the access of poison to the posterior extremities, reflex movements failed in the unpoisoned limbs as soon as they did in the others, indicating that the failure of these movements must have been due to a direct action of the acid on the spinal cord. Farther, by applying a galvanic current to the exposed spinal cord in the dorsal region of poisoned animals, no movements occurred in the anterior extremities, but pronounced movements were induced in the posterior; certainly showing that the inability of the cord to convey impulses upward must have been due to a paralysis of its sensory portions, while the motor portions must still have been intact, as was evident by the contractions caused in the posterior extremities. It is obvious from this that the seat of reflex paralysis lies in the sensory (reception) portions of the cord, and that if the motor portions of the cord and motor nerves still remain sufficiently intact to convey impulses, after complete paralysis of the sensory portions of the cord, the possibility of the occurrence of voluntary movements, or at least of movements the impulses of which have their origin in the cerebral ganglia, is readily conceivable. And it is probable that with small doses such phenomena will occasionally occur. Whether the peripheries of the sensory nerves are affected or not early in the poisoning I have been unable to decide, on account of the early depression of the sensory portions of the cord; I, however, do not think they are, because in animals in which all the blood-vessels of the left leg were ligated it was found that the unpoisoned nerve failed to respond to stimulus just as soon as the other; but that they are ultimately affected seems proven by the fact that the local action of the dilute acid rapidly destroys their activity. The motor portions of the cord as well as the motor nerves are also depressed, as determined by definite strengths of electric currents, and are ultimately paralyzed—the former succumbing first; since the motor nerves will still transmit impulses even after a complete abolition

of the functional activity of the motor portions of the cord. Consciousness in the higher vertebrates was maintained until almost death ensued, although in frogs narcotism seemed early induced.

In the early part of this paper it was stated that it was claimed that the acid "possesses all the more valuable properties of the potassium bromide, but lacks its influence on the heart and muscular systems;" but whatever it may possess of the aforesaid valuable properties, it certainly does affect the heart the same as the potassium bromide, as has already been conclusively proven; it depresses the skeletal muscles and ultimately paralyzes them (as I have also satisfactorily decided, although it is here unnecessary to give the detailed results of this research), and acts on the nervous system markedly similar.

A summary of the conclusions drawn from the results of the present research is placed for the convenience of reference in a parallel column with the conclusions arrived at by the different investigators on the action of the potassium bromide, which represents the physiological action of the alkaline salts.

HYDROBROMIC ACID.

The Circulation: Arterial Pressure. The arterial pressure is unaffected by very small doses, or a slight rise occurs; moderate doses cause an increase from the first, or a diminution of pressure, followed by a return to or above the normal; large doses cause the pressure to fall, and if sufficient cause it to fall to zero.

The fall of pressure is due to a depression of the heart muscle.

The rise of pressure to a constriction of the vaso-motor peripheries.

Pulse. The pulse-rate is not appreciably affected by very small doses; moderate doses sometimes caused a momentary slowing by inhibiting the heart, the pulse then recovering to a variable extent, and being followed by a gradual fall; or, a momentary rise occurs accompanied by a diminution of arterial pressure, this being followed by a diminution to below the normal; or, after large and repeated doses the pulse falls below normal and then becomes exceedingly rapid, or becomes rapid from the first, or may be depressed from the first. All these effects being due to a direct cardiac action, with the above single exception. The increased pulse-rate being attended with a diminution of pressure and small pulse-curves.

Nervous System: Cerebrum. Consciousness in the higher mammals present until near death. *Spinal Cord.* The sensory portions of the spinal cord

POTASSIUM BROMIDE.

Arterial Pressure: Administered hypodermically it causes diminished arterial tension, with increased pulse frequency. Large doses paralyze the heart, and thus reduce arterial pressure (I. G. Schonten, *Archiv der Heilkunde*, xii., 2, 1871; Schmidt's *Jahr.*, Bd. c. liv.).

(See above.)

Vaso-motor peripheries irritated, causing constriction (Lewisky, *Virchow's Archiv*, Bd. xlv., p. 191; Amory, *The Phys. and Ther. Action of Bromide of Potassium*, Boston, 1872; Meuriot, *L'étude de la Belladone*, p. 49; Saison, *Schmidt's Jahr.*, Bd. cxliii.) This action on the capillaries has been denied.

Pulse. After slow intravenous injection of a two per cent. solution of the potassium bromide, the pulsations become slower and feebler, the blood pressure falls, and the heart is finally arrested. Hypodermically injected, the pulse-rate is increased with diminished arterial pressure and diminished pulse-curves. Large doses paralyze the heart (Schonten, *loc. cit.*; Eulenberg and Guttman, *Virchow's Archiv*, xli., 1867).

Cerebrum, Spinal Cord and Nerves. "The evidence is, I think, sufficient to prove that bromide potassium affects all parts of the nervous system of

are the first portions of the reflex apparatus to be paralyzed, and reflex paralysis is due to this cause. The motor portions of the cord are also depressed, as well as both the sensory and motor nerves.

Muscular System. The muscular system is depressed.

the lower animals, but that the cerebrum, the motor tract of the cord, and the efferent nerves are the last portions to be affected; that the most sensitive is the receptive [sensory] portion of the cord . . . and next to this are the peripheral ends of the sensory nerves." (H. C. Woods' *Therapeutics*, 1879, p. 825).

Muscular System. Depressed. (Papers Quoted.)

A MEMBRANE-LIKE AFFECTION OF THE BOWELS.¹

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By the above title I refer to a disease which has been designated by a variety of names, among them, "Painful Affection of the Intestinal Canal," by Powell,² "Diarrhœa Tubularis," by Good,³ "Mucus Disease" by Whitehead,⁴ and "Membranous Enteritis" by Da Costa.⁵ The affection, though not remarkably uncommon, is not often described by medical writers or referred to in text-books. It is characterized by the discharge from the bowels of what appear to be membranes or skins, of varying size, in the form of shreds, strips, or tubes. This peculiar discharge is accompanied with uneasiness and discomfort, if not with actual pain. The malady is of long duration, the patients, during the period of weeks or months while suffering from the discharge, being invalids, often confined to the bed or house. They seldom so far recover as to be in robust health, and sooner or later are subjected to recurrences of the trouble with the accompanying physical weakness and suffering.

Powell, in 1818, appears to have been among the first of modern writers to have called attention to the disease. He describes the evacuations of his patients suffering from the affection to have "exhibited a large quantity of flakes mostly torn into irregular shapes, and appearing to have formed parts of an extensive adventitious membrane of no great tenacity or firmness." "In the first of the cases which came under my notice," he says, "this membrane was passed in perfect tubes, some of them full half a yard in length, and certainly sufficient to have lined the whole intestinal canal. In others, also, the aggregate quantity has been very large, and it has continued to come away for many days, but it has been in irregular, thin flakes of not more than two inches in extent." And he further adds, "The appearance which comes nearest to it, both in resemblance and situation, is the membrane formed in the trachea under croup." Powell observed four cases, all in adult females.

I have myself notes of the following cases, the first two of which have been under my observation a portion of the period of their sickness. They both occurred in ladies of more than ordinary intelligence, able to give an accurate account of their ailments.

¹ Read before the Boston Society for Medical Improvement, May 23, 1881.

² On Certain Painful Affections of the Intestinal Canal. *Transactions of College of Physicians, London*, vol. vi.

³ Good's Study of Medicine, vol. i. *Diarrhœa Tubularis*. Tubular Looseness.

⁴ Notes on Mucus Disease. By Walter Whitehead, F. R. C. S. Edin. *The Manchester Medical and Surgical Reports*, 1870, vol. i.

⁵ Membranous Enteritis. By J. M. Da Costa, M. D. *The American Journal of the Medical Sciences*. October, 1871.