THE PHYSIOLOGICAL EFFECTS

AND

THERAPEUTICAL USES

OF

HYDRASTIS.

BY

ROBERTS BARTHOLOW, A. M., M. D., LL. D.,

Professor of Materia Medica and General Therapeutics in the Jefferson Medical College of Philadelphia; Author of "A Practical Treatise of Materia Medica and Therapeutics," of "A Treatise on the Practice of Medicine," of "A Manual of Hypodermic Medication," of "A Practical Treatise on the Application of Electricity to Medicine and Surgery," etc., etc., etc.

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But little attention has, heretofore, been given to the physiological actions of hydrastis. It is true Schatz,* Felluer, Sclavatinsky, and some others,† have made some studies, but their results differ so widely from those herein detailed that it may be questioned whether they operated with sufficiently good specimens of the drug. The alkaloid hydrastine with which the following experiments were made was sent to me by Prof. J. U. Lloyd, of Cincinnati, who is, I hope I may be permitted to say, unimpeachable authority. As hydrastine is quite insoluble, a solution of the hydrochlorate was prepared for me by Messrs. John Wyeth & Bro., which contained thirty-three per cent. of the salt. The effects of the alkaloid were compared with those of the fluid extract. As the actions of hydrastis consist of the sum of the effects of its active constituents, it is necessary to know how far each contributes to the results. It was soon ascertained that the alkaloid hydrastine is the true active principle—for the very characteristic effects of this were simply repeated by sufficient doses of the fluid extract. The latter is, as might be expected, slower in action, but in respect to the manner of action there was between them no appreciable difference. Three grains of the hydrochlorate caused the death of a frog in four minutes, whilst forty minims of the fluid extract proved fatal in twelve minutes, the mode and character of the action being the same. The results in rabbits were corresponding. In general terms, the effects of hydrastis are those of hydrastine in both classes of animals, but minute differences may hereafter be detected on closer examination.

General Effects of Hydrastine Hydrochlorate in Cold-Blooded Animals.—When ten minims of the 33 per cent. solution are injected into the abdominal cavity of a frog, the following phenomena ensue: In two minutes, muscular rigidity is manifest, with extension of the limbs and inability to move; in three minutes the cutaneous reflex is so heightened that the gentlest tap on the skin causes a tonic convulsion from above downwards; successive tonic convulsions then ensue, with fibrillary trembling between, until at the end of

* Centralblatt für gesanute Therapie, Band 2, p. 82.

† Meditz. Horz. No. 16, 1884. Quoted from the London Med. Record for November 15, 1884.

four minutes death occurs in a strong tetanus. On opening the chest, the heart is still found in action, but in a few minutes more ceases in diastole, all the cavities being full of blood, and its muscular tissue is found to be irresponsive to electrical irritation.

In a rabbit weighing about fifty ounces, forty minims of the same solution, or thirteen grains, caused death in five minutes with the same phenomena—that is, with successive tetanic convulsions, the head drawn forcibly back, the limbs extended, and the respiration fixed, with increasing cyanosis of the ears and mouth. The heart continues in action after respiration has entirely ceased, and on opening the chest then it is still found in slow movement, the auricles most active and all the cavities distended with blood. The muscular tissue of the heart, does not respond to electrical or mechanical irritation.

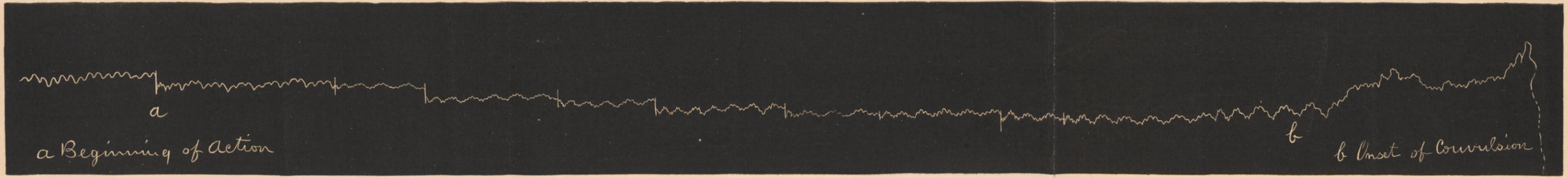
It follows from the foregoing that hydrastis belongs to the group of excito-motor agents. It heightens preception, the cutaneous excitability and the reflex functions, and it causes death by tetanic fixation of the respiratory muscles.

Determination of the seat of the actions, whether spinal or peripheral.—A frog weighing about twelve ounces was pithed. After division of the medulla, the whole length of the spinal cord was carefully destroyed. No other injury was done, and very little blood lost. Ten minims of the hydrastine solution were then thrown into the peritoneal cavity. The frog remained perfectly limp and flaccid, and no spasm or convulsion of any kind occurred. The heart, on opening the chest some time after the death of the frog, was no longer in movement, the action having ceased in the diastole, and the cavities, as in other instances, were distended with blood.

The spasms and convulsions caused by hydrastine are, therefore, central or spinal, and not peripheral.

Has hydrastine any effect on the peripheral nerves and muscles?—To ascertain this, the left sciatic nerve was dissected out, isolated and a strong ligature applied around the limb the nerve excluded, thus cutting off the circulation from the parts below. Ten minims of the hydrastine solution were now thrown into the abdominal cavity. The usual effects followed—stiffness, rigidity and spasm of the muscles, general tonic convulsions, and intermediate fibrillary contractions. On stimulating the sciatic of the ligatured limb, contractions, not active, of the gastrocnemius followed; but on direct excitation of the unpoisoned muscles of the calf, they responded readily. In the other, the poisoned limb, feeble contractions of the calf muscles ensued on stimulation of the nerve, and similar contractions took place when these muscles themselves were directly acted on. After a time when the influence of the hydrastine had attained the maximum, and immediately after suspension of respiration, both nerves failed on stimulation to excite muscular contractions, and the poisoned muscles became entirely inexcitable.

The foregoing experiments prove that hydrastine exhausts the irritability of motor nerves and muscles.


a
a Beginning of action
b
b Onset of Convulsion

Action of Hydrastine Hydrochlorate on the Heart.—A freshly removed frog's heart suspended in the solution, rapidly loses its electric excitability, and in a minute no longer responds to a strong current. Applied to the exposed heart *in situ*, the same effect is produced more slowly, and in five minutes an arrest of the movements takes place in diastole, the cavities being fully distended with blood. The auricles resist the action somewhat longer.

The pneumogastrics being divided, ten minims of the solution are injected into the abdominal cavity. The heart is acted on more slowly, and its excitability to stimulation, electrical and mechanical, although much feebler than the normal, still persists. On excitation of the peripheral end, the heart is rather lazily arrested. In the previous experiments, the heart undisturbed in its anatomical relations, it was found that the excitability of the vagus, just before the cessation of respiration, was entirely destroyed, and at the stoppage of the heart's movements, its muscular irritability was lost.

From these experiments we learn that hydrastine acts both on the inhibitory and motor apparatus, destroying their power of response to excitation, but the former function yields later, or after the latter.

To determine more precisely the nature of the action exerted on the cardiac motor and inhibiting apparatus, the vagus was first paralyzed by atropine, and then the usual dose of hydrastine administered. The increased movement caused by atropine was soon lessened by hydrastine, and the heart, after the cessation of the respiratory movements, was ultimately arrested in the diastole, the cavities fully distended as before described. The effect of the atropine was now exhibited in the preservation of the irritability of the heart muscle. In the experiments before detailed, it was found that hydrastine destroyed the irritability of the heart muscle, but when atropine was administered, the response to mechanical and electrical irritation was retained.

The Action of Hydrastine on the Blood Pressure.—A chloralized rabbit weighing about fifty ounces was used for the purpose. The right carotid artery was connected with the manometer and the revolving cylinder in the usual way. The attached tracing exhibits the effects of hydrastine. Up to the point *a* the pressure was at the normal for a rabbit under the influence of chloral, and then began the effects of the drug. It causes, as the tracing shows, some lowering of the blood pressure. The sudden rise at *b* was due to a convulsion, the quantity of chloral not being sufficient to prevent them entirely.

Antagonism between Hydrastine and Chloral.—The number of experiments has been too small to formulate positive conclusions, but enough has been learned to indicate that chloral antagonizes to a large extent the increased reflex excitability and the tonic convulsions caused by hydrastine. It is probable, indeed, that the antagonism will be found as extensive in range as between chloral and strychnine. Thus far I have not had the opportunity to ascertain the lethal dose of hydrastine. Until that is determined, the power

of its physiological antagonists can not be measured with accuracy. Further experiments are making on this point, and will be announced hereafter.

Strychnine and Hydrastine.—A remarkable correspondence can be traced between the actions of strychnine and hydrastine, but the power of the former seems to be the greater, whilst in extent of action the latter seems far more. Both exalt the reflex function of the cord; both induce tetanic convulsions, and both cause death by arrest of the respiratory movements in a tonic spasm. Hydrastine more affects the peripheral nerves and muscles, and to a much greater extent impairs the contractility of the cardiac muscle.

The Therapeutical Applications of Hydrastis.—As the results obtained from the administration of hydrastis constitute the sum of the actions of its several constituents, it may be best to consider the powers of the active principles separately, before treating of the effects of the drug as a whole.

The plants containing berberine are, as a rule, members of the tonic and reconstituant group. Hydrastine being peculiar to hydrastis, much of the effect produced by this agent must be due to the presence of this principle. Prescribed alone, hydrastine has been supposed to have the effects of a tonic, antiperiodic, and to some extent alterant—a term used to signify the power to promote the waste and excretion of morbific materials. The physiological study of hydrastine, as made by Schatz, Fellner, Slavatinsky, and others,* has not contributed to the subject of its therapeutical power, although it forms a groundwork for the therapy of the future. If, however, the physiological actions as detailed in this paper be confirmed by subsequent researches, quite a new phase will be given to its therapeutical applications.

As the fluid extract contains all the constituents of hydrastis, it is the most concentrated form available for administration and, therefore, will be the best preparation for procuring the effects of the remedy as a whole, whether given by the stomach or applied externally.

Hydrastis in Gastro-Intestinal Disorders.—As a stomachic tonic, when the condition of the stomach is that of debility, as we find it in atonic dyspepsia, so-called, and in convalescence from acute diseases, hydrastis serves a useful purpose. In common with the bitters, it stimulates appetite and increases the secretion of the gastric glands. Disposing thus of an increased supply of aliment, the constructive metamorphosis is promoted. For this purpose, it is best to administer ten to twenty drops of the fluid extract a few minutes before meals.

Both the alkaloids of hydrastis, exerting an inhibitory influence on fermentation, the fluid extract can be given with excellent effects in cases of catarrh of the stomach accompanied with fermentative changes in certain foods, whether or no, the *Sarcina Ventriculi* be present. The result of the action will be more permanent than the above remark implies, seeing that this remedy can modify, if not remove, that alteration of the mucous membrane

* Centralblatt für die gesammte Therapie, Band 2, p. 82, and Meditz. Obozr. No. 16, 1884. The latter, quoted by London Med. Record, Nov. 15, 1884.

which is accompanied by an outpouring of pathological mucus. To effect this purpose it were better to administer the fluid extract, two or three hours after meals, and the dose should range from fifteen to thirty minims.

As a tonic and reconstituent in the classes of cases above mentioned, quinine is now largely used: it is quite certain that hydrastis can be substituted for the most part with advantage.

The experiments of Rutherford* have confirmed the belief, founded on empirical observations, that hydrastis is an hepatic stimulant, although not one of the most active. As he operated with "hydrastin" so-called, which consists for the most part of berberine, it is probable that the results which he obtained are not equalled by those produced by the exhibition of the fluid extract. Hydrastis has been found useful in gastro-duodenal catarrh, associated with catarrh of the bile ducts—a morbid condition in which the output of bile is lessened by the mechanical obstruction, and the intestinal digestion is impaired in consequence of the insufficient supply of bile, the fermentative changes set up by the mucus which plays the part of a ferment, and the consequent absorption of imperfectly prepared materials. In this state of things we find the true explanation of some cases of jaundice, of most cases of "biliousness," and the initial changes of lithaemia.

The gastro-duodenal catarrh of chronic alcoholism is a condition in which the use of hydrastis has a decidedly beneficial effect, and the improvement in the digestion has seemed to lessen the appetite for alcoholic stimulants. This statement, made by several observers,† has been rather sarcastically commented on by the authors of the National Dispensatory, ‡ who are, however, pessimistic if not nihilistic in their therapeutical conceptions. The new facts, demonstrating the effects of hydrastine as a spinal stimulant, are additional reasons for supposing it to be possessed of the powers claimed.

For the relief of the intestinal troubles above mentioned, the fluid extract of hydrastis should be given in the interval between the meals, and the dose should be larger (℥ss—℥i) than in the case of the corresponding stomachal troubles.

As an antipyretic and antiperiodic, the alkaloid—hydrastine—has had no adequate clinical study. Twelve years ago, I made some experimental trials at the Hospital of the Good Samaritan, in Cincinnati, in seven cases of tertian intermittent. White hydrastine in crystals was furnished me by Prof. E. S. Wayne, M. D., of Cincinnati, the well-known chemist and pharmacologist. Two of the cases were recent, uncomplicated, and but a few paroxysms had occurred. Twenty grains of hydrastine, administered in three doses, in anticipation of the seizure, merely modified its violence, but did not prevent it in either case. The second attempt proved successful. Three of the cases more chronic in character required sixty, sixty-five and eighty grains respect-

* The British Medical Journal, 1879, Vols. I. and II. Report of the Committee of the British Med. Association, etc.

† The Practitioner, London, Vol. XVI., p. 121, *et seq.*

‡ Third edition, p. 798.

ively. The two remaining proved still more rebellious, and the patients becoming uneasy, I was forced to resort to quinine. The supply of pure hydrastine was not sufficient to carry on further experiments, and a suitable opportunity to resume the investigation not occurring, I have no further clinical experience in this direction to report.* Nevertheless, these trials, whilst not numerous, are at least significant. They indicate the possession of real antiperiodic power, inferior to quinine, it is true, but apparently inferior only to the great antiperiodic. Since that time, the chemist's skill has produced by synthesis various products approaching in composition closely to quinine, and possessed of powers very similar but still inferior. It may be that under these circumstances, hydrastine will never rival quinine or its analogues, but the powers which it is now shown to possess may require a different statement hereafter.

Topical Applications.—For local use, the best mode of applying hydrastis is in the form of the fluid extract, which may be employed undiluted or diluted with glycerine. Its staining power is an objection, since the color which it imparts to cotton cloth, if not permanent, is at least not readily washed out. This fact suggests the possibility of using this pigment or coloring matter as a dye-stuff.

The fluid extract of hydrastis is an excellent topical application in cases of catarrhal inflammation of the mucous membranes. In nasal, faucial, uretheal and vaginal catarrh, and in otorrhœa and conjunctivitis, there can be no doubt of its good effects. It may be applied freely in the undiluted state without fear of injury, if no good be accomplished by it. It has proved to be a very efficient injection in gonorrhœa, more especially after the acuter symptoms have subsided. For this purpose it may be diluted with glycerine or mucilage, or both, to the required extent. Formerly when I used to see these cases in considerable numbers, I found it a capital application in cervicitis. I had, also, excellent results in such cases, and in gonorrhœa, from "hydrastine" suspended in mucilage.

To express a final judgment as to its therapeutical value, my conviction is that hydrastis is a useful remedy, and well deserves a trial in the various conditions in which it is recommended above.

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* The remarkable activity of the pure hydrastine furnished me by Prof. Lloyd, necessitates caution in its administration, until its lethal power in man can be determined. It is now evident that the hydrastine used by me formerly in the treatment of diseases was not pure. I must therefore caution my readers in respect to the administration of the pure alkaloid, and especially its salts, and warn them not to employ this active agent, as they have heretofore been giving berberine, or a mixture of hydrastine and berberine.