GULSTONIAN LECTURES

ON THE

PHYSIOLOGICAL ACTIONS AND THERAPEUTICAL
USES OF CONIUM, BELLADONNA, AND
HYOSCYAMUS, ALONE AND IN
COMBINATION WITH OPIUM.*Delivered at the Royal College of Physicians, London.*By JOHN HARLEY, M.D., F.R.C.P.,
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MR. PRESIDENT AND GENTLEMEN,—It must be admitted that a knowledge of the actions of medicines within the body, in its healthy and diseased conditions, is the highest attainment of the physician, inasmuch as it lays large tribute upon each and all of his scientific attainments, and sooner or later becomes the practical expression of his professional skill. There is no word, perhaps, which so well expresses the necessary acquirements of the therapist as the word physician; for to know how a medicine acts within the body is to know Nature as manifested in both vegetable and animal kingdoms, and to be familiar with her subtlest operations.

If an apology were needed for bringing forward the subject proposed in this course of lectures, I might very well have pleaded the neglect of therapeutics, which, in this country at least, has resulted in so much scandal to our profession. But such an apology for thus making use of the rare opportunity which I have the honour of possessing would be most unbecoming in this place and before this assembly, where the importance of therapeutical inquiry is so fully recognised.

In selecting four of our longest used, best known, and most useful medicines, I must claim your indulgence while I direct your attention to a few points concerning which our knowledge is still imperfect. In the short space allotted to these lectures, time will fail me to refer otherwise than very incidentally to the labours of others; and I feel that it will be necessary to confine myself almost exclusively to the details of my own inquiries. As, however, these are essentially of an experimental nature, they will carry with them the force which attaches to such a mode of inquiry, without theoretical enforcements of my own.

The first plant that engages our attention is *Hemlock*. The history of Conium presents a most discouraging view of the progress of medical knowledge. It is clear to me that the ancient Greek physicians possessed an accurate knowledge of the physiological action of this plant; and it is equally clear that this knowledge has become grossly obscured in after-times, and that error from time to time has crept in, until at last the truth with regard to this plant has been so overclouded by it as to be at last and in our own day almost indistinguishable. A glimmering of the ancient light has occasionally appeared to those who have undertaken to investigate the properties of this plant; but the general state of our knowledge may be summed up in the words of two of our most eminent therapists. Ten years ago, Pereira wrote: "In the present state of uncertainty with respect to the real physiological operation of hemlock, it is obviously impossible to lay down indications or contraindications for its use which can be much relied on." (Vol. II, part ii, p. 202.) Dr. Christison closes his admirable investigations upon the active principle of this plant with the following remarks. "I wish I could have added to these observations on the poisonous effects of conia and hemlock some account of their physiological action in small doses. This branch of the inquiry into their action I have not yet been able to investigate; it cannot be pursued with any accuracy by experiments on the lower animals. The phenomena must be ascertained in the human subject chiefly, which I have not hitherto been able to accomplish. On this head, it may merely be observed that, if any physicians or physiologists would acquire definite information as to the physiological effects of hemlock in small or medicinal doses, they must begin the inquiry anew. Little importance can be attached to anything already done in this field, as I have no doubt whatever that by far the greater proportion of the preparations of hemlock hitherto employed have been of very little energy, and, in the doses commonly used, are absolutely inert." (*Edinburgh Philosophical Trans.*, vol. xiii, p. 398.)

Since these words were written, little or nothing has been done in the direction which they indicate; and they are as generally applicable at the present time as they were when they were first uttered. Reference to the most modern and approved treatises on the actions of medicines shows how little, apart from its bare toxic effects, is known of the

physiological action of hemlock; and a critical examination of the preparations most recently provided for our use, and of their doses, prove, as I shall hereafter have occasion to show, that, as a medicine, we are practically ignorant of the virtues of this most valuable plant. I do not here speak of the toxic effects of hemlock, which have been well illustrated in one or two fatal cases that have occurred in the last few years. Experiments, too, on its toxic effects on the lower animals, are most exhaustive and complete. Leaving, then, the *corpus vile* nearly altogether out of consideration, I shall devote myself almost exclusively to a consideration of the subtle agency of this plant in man, and, generally speaking, in the able-bodied.

Having assured myself of the effects of Hemlock in my own person, I have been thus able to fully appreciate its operation in others, and to proceed much more boldly than I could otherwise have done without such personal knowledge.

PHYSIOLOGICAL ACTION OF HEMLOCK.—The first effect of hemlock is a depression of the motor function; and its last is the complete obliteration of all muscular movement derived from the cerebro-spinal motor tract.

The earliest effects of hemlock are determined by the condition of activity of the individual. If, after a dose of conium, he should continue to use his legs, the effect will most probably be first felt in these parts. If he remain in a state of comparative rest, the effects will be first declared in the eyes.

After taking three drachms of the succus of the *British Pharmacopæia*, I set out walking; and, three-quarters of an hour after the dose, I felt a heavy clogging sensation in my heels. There was a distinct impairment of motor power. I felt, so to speak, that "the go" was taken out of me. After walking about a mile uphill, this sensation was very decided; and, on putting a foot on the scraper at the door of the hospital, the other leg was shaky, and felt almost too weak to support me. My movements appeared clumsy to myself, and it seemed necessary that I should make an effort to control them. At the same time, there was a sluggishness of the adaptation of the eye. My vision was good for fixed objects; but, when an uneven object was put in motion before the eyes, there was a haze and dimness of vision, producing a feeling of giddiness. The pulse and pupils were unaffected. These were the whole of the effects; and, after continuing for an hour, they rapidly disappeared, and left me in the possession of my usual vigour.

If a strong, active individual take five or six drachms of the succus on getting up in the morning, and start off for a long walk, he will be overtaken in the course of half or three-quarters of an hour with a feeling of general tiredness, and a special weakness of the knees, as if he had been regularly tired out by walking all day to the full extent of his powers. If he be unusually active and strong, he will not, perhaps, yield to the inclination to rest, but will proceed slowly on his way, feeling a strange lightness and powerlessness of the legs, with a tendency to drop forward on his knees. This will be associated with some giddiness, and a feeling of heaviness over the eyes. At first, the feeling of languor will be most oppressive, but it will soon become more tolerable; and, if he should continue his journey for an hour, he will find that the feeling of fatigue has by this time nearly passed off. In the course of another hour, he will be as active as ever.

The following were the effects produced in my own person during a period of rest, and they contrast well with the foregoing. Three-quarters of an hour after taking five drachms and a half of the succus conii, on raising my eyes from the object upon which they had been fixed to a more distant one, the vision was confused, and a feeling of giddiness suddenly came over me. That these symptoms were due to impairment of power in the muscular apparatus employed in the adaptation of the eye, was obvious to me; for, so long as my eyes were fixed on a given object, the giddiness disappeared, and the definition and capacity of vision for the minutest objects were unimpaired. But the instant that I directed the eyes to another object, all was haze and confusion, and I felt giddy; and, in order to recover my vision and dismiss the sense of giddiness, it was necessary to lay hold upon some object, as it were, with my eyes, and rest them securely upon it. It was clear to me that the adjusting muscular apparatus of the eye was enfeebled, and its contractions so sluggishly performed that they could no longer keep pace with the more active movements of the external muscles of the eyeball. Within ten minutes of the appearance of this disorder of vision, a general muscular lethargy affected me, and the eyelids felt as heavy as if they were oppressed with the deepest drowsiness. The pupils were considerably dilated. I sat down to note these observations; but, being afraid to maintain this posture, lest the rapidly increasing muscular lethargy should get the better of me, I rose up again and tried to shake it off. An hour and a quarter after taking the dose, I first felt decided weakness in my legs. The giddiness and diminution of motor power continued to increase for the next fifteen minutes. An hour and a half

after taking the dose, these effects attained their maximum; and at this time I was cold, pale, and tottering. The pulse, which had been emotionally excited by the sudden accession of the foregoing symptoms, was now 68, quite regular, and of undiminished force and volume. The legs felt as if they would soon be too weak to support me. There was a positive diminution of voluntary power in every part of the muscular system, and this nearly amounted to complete paralysis as far as the hamstring and levator palpebræ muscles were concerned. At one time, the greatest exertion was required to elevate the eyelids. The mind remained perfectly clear and calm; the brain active throughout; but the body seemed heavy, and well-nigh asleep. After continuing for about half an hour at their maximum, the symptoms began rapidly to decline, and within three hours and a half of taking the dose they had totally disappeared. As a proof of this, I may mention that, for the hour following the disappearance of the conium symptoms, I was engaged in writing letters; I then walked briskly a distance of three miles, and finished the day's work by drawing a microscopic object.

In order to illustrate the further effects of conium, I select the following examples.

First, I gave to a man, aged 57, of powerful muscular development, the succus conii, in doses increased from three drachms to an ounce. The medicine produced no appreciable effect until the quantity was increased to six drachms. This dose was followed, twenty minutes after taking it, by sudden giddiness, and so much weakness of the legs as rendered the patient incapable of walking; so that he was obliged to lie down. There was an aching pain across the eyebrows, and mistiness of vision. He could hardly raise the eyelids, which seemed pressed down with a heavy weight; and he was disposed to fall off to sleep. After twenty minutes, he got up and walked a mile; but the legs were so weak that they could hardly support him; the knees tended to fall forwards; and his gait was tottering. An hour and a half after the dose, the effects had almost entirely passed off, and he felt as if nothing unusual had happened to him. On another occasion, after taking an ounce, these symptoms were repeated; but the accession of the giddiness and weakness was so rapid, that he would have fallen, but that he caught hold of a support. In this case, the symptoms continued a little longer than when only six drachms were taken.

Secondly, a delicate young woman, of inactive habits, took four drachms of the succus. Twenty minutes afterwards, and while attending to her usual duties, she experienced nausea and giddiness. She dropped an inkstand which she was holding in her hands, and was unable to walk; and she was placed in the recumbent posture. These symptoms came on with alarming swiftness, and the pulse went up to 120 from emotional excitement; but in a few minutes the heart regained its usual quietude, and she remained perfectly composed and calm, but without power to move the arms or legs. An hour after taking the medicine, there was nearly complete muscular paralysis; the eyelids were closed, the pupils widely dilated; and the mind perfectly clear, calm, and active. She tried perseveringly to raise the eyelids when I requested her to do so, but she was quite unable to separate their margins. The pulse and respiration were normal; the surface warm. At the end of an hour, these symptoms passed off; and after three hours she had completely recovered her activity, and resumed her duties. The next day, she complained of slight wearisome pain in the muscles of the legs.

Such are the general and constant effects produced by hemlock when administered in full medicinal doses. When the dose falls short of producing any of the above mentioned symptoms while the individual is in a state of ordinary activity, then we have absolutely no indications of the action of hemlock.

In my own person, I have sometimes thought that, in the absence of any appreciable symptoms, a feeling of dullness and depression might be attributed to its use; but, from my observations in others, I am rather inclined to attribute this to the anxiety about the expected operation of the medicine. When the eyes and legs are both at rest, then a feeling of languor will be the only effect of a dose of hemlock just sufficient, when these organs are in active play, to produce slight and transient giddiness and weakness of the legs. The operation of hemlock is uniform and invariable in man; and the same remark doubtless applies to the lower animals also. All animals, I believe, who possess voluntary motion, may be brought within its influence.

It has sometimes been doubted whether the horse is liable to its influence; but this doubt is solved by the following experiments made by Mr. Frederick Mavor, of Park Street, and myself, upon a thoroughbred two-year-old colt. At intervals of a week, we gave the succus conii of the *Pharmacopœia*, in doses of six, eight, twelve, and sixteen ounces, by the mouth. No effects followed any but the last dose. He continued lively, and eating his food as usual, until twenty-five minutes after the last named dose, when he was observed to remain

standing stockstill, with the ears fallen, and the head and neck hanging down; the upper eyelids swollen and drooping, so as to nearly cover the eyes. He presented at the same time a dull, heavy, tumble-down appearance. The pulse, pupils and tongue were unchanged. An experienced veterinary surgeon happened to come in at the time; and, observing the general expression of languor exhibited by the animal, and the swollen and nearly closed eyelids, said, "That horse has the influenza, so prevalent just now." Five minutes afterwards, and as he was standing stockstill, the animal dropped upon his knees, and, in recovering his position, nearly tumbled down. After a little stumbling, he regained his legs, and continued for the next twenty minutes in the same state of dullness and perfect quietude as before, excepting that now and then, when a fore or hind leg gave way, he was obliged to exert himself and regain his equilibrium. At the end of this time, he was walked out. After a little stumbling, he went along slowly and languidly, with the ears down, the head and neck depressed, and the eyelids half-closed, swaying a little as he went. Two hours afterwards, the effect had entirely passed off, and he was as active and lively as before the dose. The head and ears were erect; the swelling (from muscular relaxation) and drooping of the upper lids had disappeared; the pulse was of good volume and power, and unchanged. No excreta were voided during the action of the medicine.

[The lecturer next proceeded to inquire more particularly into the action of hemlock upon particular parts of the nervous system—the third nerve, the hypoglossal, the reflex function of the cord, and upon the cerebrum itself. He contrasted its effects with those produced by alcoholic intoxication, and sought in the physiological action of hemlock some explanation of the phenomena of sleep. He then continued.]

The whole motor function of an individual under the full influence of conium is actually asleep; and this is the simplest view that we can take of the physiological action of hemlock. It is to the corpora striata, to the smaller centres of motion, and to the whole of the motor tract, precisely what opium is to the brain of a person readily influenced by its hypnotic action; and just as opium tranquilises and refreshes the over-excited and weary brain, so does conium soothe and strengthen the unduly excited and exhausted centres of motor activity.

At first sight, we should be apt to regard conium as a depressor of the motor function, and consequently of the muscular vigour; but this, I am convinced from repeated observations, would be a very erroneous view of its action; and I am prepared to say that, in repressing and removing irritative excitement of the motor centres, conium is a tonic to these parts of the nervous system in cases which require its use. I have administered conium for months—in one case, for more than six months—daily, and in such doses as have usually produced its full physiological effects; and the result has invariably been an improvement in the general nutrition and vigour of the body. It is doubtless by removing sources of central irritation of the nervous system that conium acts thus indirectly in improving the nutrition of the body.

The influence of conium appears to be in proportion, not to the muscular strength of the individual, but to his motor activity. This is a very important conclusion. It is derived from the following facts.

1. The operation of hemlock in the same individual varies in degree according to his motor activity. A dose of conium, which in the ordinary condition of the patient shall be just sufficient to produce the peculiar effects of the plant in a mild degree, will, during the exhaustion following a profuse seminal discharge, operate much more decidedly and intensely.

2. Those leading a sedentary inactive life are more readily affected by conium than those of active habits. A delicate person of active habits will, therefore, bear a larger dose of hemlock than one possessing abundance of strength with but little energy.

3. An active restless child will often take, with scarcely any appreciable effect, a dose of conium sufficient to paralyse an adult of indolent habits; and such as would reduce a powerful muscular man to a tottering condition, and force him to assume the recumbent position, and retain it for a quarter of an hour or more.

The general inference from these observations is that the dose of conium must be proportioned, not to the muscular strength of the individual, but to the degree of his motor activity, functions which the operation of conium indicate to be so far distinct from each other. Indeed, it appears that by means of conium we may comparatively measure the bodily activity of the individual. Having completed his investigation of the phenomena and sensible effects resulting from the operation of hemlock, the lecturer, in seeking an explanation of the *modus operandi* of the active principle of conia, was brought to consider the questions of its effects upon the sympathetic system and of its elimination from the body. With regard to the first of these questions, he failed to recognise any effect upon the sympathetic nervous system, and consequently upon the heart and the secretions.

Fully recognising the beneficial influence of conium upon nutrition and pain, he attributed these results to its power of allaying the nervous irritation, to which the continuance, at least, of the morbid process, might fairly be attributable. Its anodyne power in cancer of the stomach or bowel he considered to be the result of muscular relaxation in the diseased parts, rather than to any direct influence upon the sensory nerves—the conium being to the muscular parts involved in the cancerous disease, what the knife is to the sphincter muscle of the bowel when in a condition of irritable ulceration.

With regard to the elimination of conia, he had failed to observe it in the pulmonary and cutaneous exhalations, or in the urine. The latter excretion was searched most carefully and by different processes, but no trace of conia could be obtained. The urinary secretion remained unchanged during the action of the medicine, as shewn by the analysis of the urine of a male patient, aged 51, secreted during the half hour immediately preceding a dose of one ounce of the succus conii of the *British Pharmacopœia* (Urine A), and that which was secreted during the next two hours and a quarter, the period occupied by the full operation of the medicine and its decline, so as to leave the patient in his usual condition (Urine B). Both specimens of urine had precisely the same physical characters—a full sherry colour, clear, naturally acid, and a specific gravity of 1023·2.

1000 grain measures of the Urine	1000 grain measures of the Urine
A contained	B contained
Chlorine 5·5 grs.	Chlorine 5·66 grs.
Urea 16·0 grs.	Urea 16·6 grs.
Phosphates & sulphates 10·2 grs.	Phosphates & sulphates 10·5 grs.
Uric acid, normal amount.	Uric acid, normal amount.

In some cases, the solid constituents were more abundant in the urine passed before the action of medicine; in others, more abundant in that passed after the operation of the drug; the variations in all cases having reference to the time of ingestion of the last meal, and being altogether independent of the action of the conium.

In treating of the second part of his subject, viz., the therapeutical uses of conium, the lecturer brought forward several interesting cases of nervous disease, and showed the power which conium possesses in controlling and subduing the convulsive diseases of children in particular. He advocated its use in chorea, cramp, tetanus, and in some forms of epilepsy. In pertussis, laryngismus stridulus, and other spasmodic affections due to derangement of the vagus nerve, he stated that his experience of conium had been exceedingly satisfactory. In all cases of irritability of the spinal cord, and especially in cases of undue excitement of the sexual organs, the beneficial action of conium was very marked. I cannot too strongly insist, he observed, on one point, viz., that a dose of hemlock which falls far short of producing the peculiar physiological effects of the plant, is of no more use in the treatment of the diseases to which it is adapted, than an ordinary dose of quinine would be in the treatment of ague. Having satisfied myself, by careful observation of the patient, as to the quantity required to produce the earliest indications of hemlock action, viz., slight and transient giddiness with a little weakness of the knees, I prescribe a repetition of this dose every other, or every day, or even twice a day.

In tetanus it will be necessary to administer from three drachms to one ounce of the succus conii, and repeat it at intervals of two or three hours. If there be any difficulty in giving it by mouth, it may be administered by rectum.

Our ignorance of the therapeutical use of conium is declared in the preparations which have been, and still are, furnished for our use, and in the doses in which these are recommended. The extract of conium, when most carefully prepared, does not contain more than one per centum of conia; and of this preparation five grains would generally be insufficient for a child two years old, while not less than twenty or thirty grains would be required to produce in a slight degree the physiological effects of conium in an adult of moderate activity. The dried leaf and the preparations derived therefrom are absolutely inert, and the tincture of the fruit lately introduced into the *Pharmacopœia* is equally useless. If two ounces of either the tinctura conii *P.L.* or of the tinctura conii fructus be taken, absolutely no conium effects will result. The only reliable preparation is the succus conii. From two drachms to one ounce of it will, according to the motor activity of the individual, invariably produce the full physiological action of hemlock, and the beneficial effects which may be expected to follow. I usually give a child, six months old, twenty or thirty drops of the succus conii; a child over two years old, one drachm; one ten years old, from one to two drachms. For a woman, I prescribe two or three drachms; and for a man, four or five drachms. From these initial doses I ascend until the peculiar effect of hemlock is declared. Having once attained this, it is rarely necessary to increase the dose, for the system rarely manifests any considerable toleration of hemlock, and a dose which produces a given effect will,

after six months' continuance of the medicine, usually influence the patient to the same extent at the end of that time. The succus is not liable to any appreciable variation, and it will keep unimpaired for years. But, for a complete examination of the medicinal value of the preparation of hemlock, I must beg to refer you to some papers which I contributed last year to the *Pharmaceutical Journal*.

FURTHER OBSERVATIONS ON THE CÆSAREAN SECTION.

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IN the present communication, it has been my object to register all cases of Cæsarean section, published and unpublished, which (as far as I have been able) have occurred in Great Britain and Ireland since the publication of my former observations (*BRITISH MEDICAL JOURNAL*, 1865, vol. i, p. 211), to which I beg to refer my readers, as it is quite impossible, and indeed unnecessary to enter, at the present time, upon all those subjects which are legitimately concerned in the consideration of this operation, as one of election, or even as one of necessity. The concentration of, or reference to, all cases of this important operation, especially as it is not universally adopted, or even recognised, is most valuable to those members of the profession who are desirous to analyse and compute the risk and dangers of it, in comparison with the results of those alternative operations which are recommended to supersede its performance, and thereby to satisfy themselves whether the unfortunate results of this (the Cæsarean section) are really attributable to it, or to other factors of mischief not necessarily belonging to it.

The annexed tables are very limited when compared with those from which they have been extracted, and which embrace the following points; the number and kind of previous labours; the mode of delivery; the tangible state of the os uteri; the situation of the placenta; the line of the incision; the previous and present constitutional state; the administration of chloroform; the application of ether-spray; the reputed cause of death; and the results of the *post mortem* examination. I have enumerated the above points, which head the columns in the said tables, in order that the reader may understand upon what plan I have based my deductions.

I take this opportunity of returning my sincere thanks to Dr. Frederic Bird and to Dr. J. Braxton Hicks, for their great kindness and liberality in furnishing me notes of three unpublished cases of Cæsarean section; and also to Dr. Greenhalgh, Dr. Eastlake, Dr. Pirrie, and Dr. John Taylor, for having supplied me with additional and important particulars relative to their published cases.

There are nineteen cases tabulated, of which number seventeen have occurred in England, one in Scotland, and one in Ireland. I may again remark, that it is a remarkable fact that there is no case recorded from Wales. The causes which have rendered the operation necessary in these nineteen cases are as follows. In two the pelvis was distorted from mollities ossium; in four it was caused by rickets; in one the pelvic bones were undeveloped, and the apertures diminished—characteristically partaking of the oblique shape described by Naegelé, only differing in having both sides, although not equally, affected; in four cases the obstacle was caused by pelvic distortion, but the character of the deformity is not mentioned; in one a large exostosis, springing from the upper portion of the sacrum, caused the difficulty; in one it was produced by a large fibrous tumour impacted in, and blocking up, the pelvic cavity; in four cases carcinomatous degeneration of the cervix and os uteri, and in one case of the rectum, rendered the operation necessary; in one case the operation was performed on account of a large hydatid cyst, which had passed from the abdomen into the pelvis, and was placed before, and compressed by, the advancing head of the infant; it was so hard as to be mistaken for a bony growth. Although the diminution of the pelvic apertures has been deemed sufficient in these cases to prevent the delivery *per vias naturales*, yet it must ever be borne in mind that the cause of mischief in most of them is not stationary, but progressive, so that ultimately the pelvis might be as nearly as possible completely blocked up. In one case (79) the error of diagnosis which was made, was proved by the *post mortem* examination. It might have been obviated by an earlier examination, before the cyst had been so firmly compressed. Puncture of it at an early stage of labour would doubtless have removed the cause of obstruction. In some of the cases the os uteri could not be felt; whilst in others it could only