

Clinical and Physiological Notes on the Action of Cannabis Indica

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Cannabis Indica has been before the profession for many years as a remedy to be used in combating almost all forms of pain, yet, owing to the variations found to exist as to its activity, it has not received the confidence which I think it now deserves. At present certain improvements made in the method of obtaining the extract from the crude drug have very materially increased its reliability, so that by selecting an article made by a responsible firm we may be fairly sure of receiving a preparation in which we can place confidence. Within a few years this drug has become particularly prominent in connection with its use in migraine, particularly when used in conjunction with gelsemium, although of the two remedies the hemp is by far the most active agent in subduing the pain and preventing other attacks.

Heretofore the profession has used the remedy in such cases purely from an empirical stand-point, but I shall in a moment explain more fully its true physiological action. Aside from this, however, I have certainly seen very severe and intractable cases of migraine successfully treated by this remedy, not only in regard to the attack itself, but by acting as a prophylactic. The best use of the remedy under such circumstances is as follows, in case the drug obtained be fairly active.

If the attacks are frequent then the remedy should be used constantly in small doses, in such a way that the patient is not conscious of any influence of the drug, and about

one-eighth of a grain of the solid extract may be taken night and morning, or, if this produces any tendency to sleep, the whole amount may be taken at night. At the beginning and during the attack it should be freely administered, until either the pain is diminished or very marked symptoms of its physiological action assert themselves; and that this line of treatment is not one calculated to produce serious results is proved by my own experiments, and by the fact that so far no case of fatal poisoning from its ingestion has been recorded as occurring in the human being.

I myself have taken as much as one grain of the solid extract of a very active preparation without producing any disagreeable symptoms other than that of a deep sleep, which lasted for nearly eighteen hours, preceded by a period of great hilarity, which did not pass into any sensation of dread, such as has been described by some persons.

When gelsemium is used in addition to the hemp, its usefulness is limited only to its action in warding off an immediately impending attack, and I do not believe it possesses much power for good unless it be given when the first symptoms of the malady appear. Its exceedingly poisonous properties necessarily prohibit any repetition of a dose, and for this and the reasons above stated the drug should be administered in one single dose of fifteen to twenty drops of the tincture at the first sign of an attack.

Cases of migraine treated in this way, when the disease does not depend on any distinct organic lesion, are in a large proportion of instances either entirely cured or greatly benefited, the attacks even when they recur being considerably farther apart.

In neuralgias depending on a condition of debility in nursing women and in overworked men cannabis indica alone acts very favorably; not by acting in any way as a stimulant to the system, but rather by allaying any irritability of the nerve-trunks. Again, in many cases of irritative cough, depending either upon some nervous irritability or upon some actual irritated condition of the air-passages, cannabis indica will be of service in allaying the troublesome symptom, and is often found useful in the chronic winter cough of old people, provided no great outpouring of mucus or liquid is in the lungs.

In certain stages of phthisis it is a very valuable remedy,

not on account of any influence possessed by it on the pathological processes, but by quieting restlessness and anxiety, and by turning the mind of the patient to other channels. Indeed, in cases of advanced phthisis I believe it would be justifiable to push the drug almost to the condition known as euthanasia, and this has been done quite frequently by many practitioners. Under these circumstances, the patient, whose most painful symptom has been mental trepidation, may become more happy or even hilarious.

The advantages in its use over that of opium consist chiefly in the absence of prostration and nausea after its ingestion, and in the partial lack of soporific power which it possesses as compared to the opiate, for in certain cases sleep is not always desirable when pain is to be removed. That cannabis *indica* has, however, marked powers as a soporific is not to be denied. Added to these advantages is the fact of its failure to produce serious symptoms even if very large doses be taken, although I have found the efficient dose of a pure extract of hemp to be as powerful in relieving pain as the corresponding dose of the same preparation of opium.

That it is capable of producing a habit there can be no doubt, although whether its devotees are as devoted as are those of opium I cannot say. In my own practice I have seen a case of a young man who took his first dose as an experiment, and who afterwards had such a constant desire for its repeated use that he was forced to abstain from it entirely. He also said he could readily understand how the drug might have devotees, and that the pleasurable sensations excited were far preferable to those of alcohol.

During the time that this remarkable drug is relieving pain a very curious psychical condition sometimes manifests itself; namely, that the diminution of the pain seems to be due to its fading away in the distance, so that the pain in a delicate ear would grow less and less as a beaten drum was carried farther and farther out of the range of hearing.

This condition is probably associated with the other well-known symptom produced by the drug, namely, the prolongation of time.

Turning from the clinical stand-point of the drug to its physiological effects, we find that its clinical uses rest on a scientific basis, and I shall, therefore, detail one or two experiments showing in what manner the drug acts.

If a considerable quantity (10 minims)* of the fluid extract be given to a twenty-pound dog, by the jugular vein, in the course of two or three minutes he becomes very playful and happy, and gambols over the floor. In the course of about five minutes more there appears a slight stagger in the walk, which gradually increases, and is most marked in the forelegs, the condition of mental exhilaration continuing. Soon after this equilibration is partly lost, for the animal, sitting on its haunches, places its forefeet wide apart; nevertheless, in the course of ten minutes more he seems to partially recover his balancing powers, and to be as happy and frolicsome as ever, barking and running. In the course of twenty or twenty-five minutes more he vomits, and the swaying and staggering reassert themselves, now affecting both hind and front legs. This condition rapidly passes into a drowsy state, which, in turn, deepens into a profound sleep, from which it is difficult to arouse the animal to consciousness, although the reflexes are markedly accentuated, particularly to sounds. This sleep lasts for many hours, and finally the dog wakes up himself again. In some instances a lack of co-ordination, due evidently to failure of sensation, appears, so that the animal places his feet on the floor as if it were uneven, or higher or lower than it is.

That the drug may be given in enormous amounts by the jugular vein in the dog without producing death is proved by the fact that I have injected as much as 10 c.c. of the fluid extract without producing serious symptoms. Thus, at 1:20 P.M. the injection was given. At 1:25 the dog was sound asleep and groaning, as if having bad dreams. At this time pinching the ear called out no sign of discomfort, and the respirations were eight per minute.

At 5 P.M. the animal was as sound asleep as before, but was unfortunately killed by the laboratory assistant, owing to a misunderstanding of my orders. Just before death the respirations had risen to ten per minute, and several movements had been made by the dog.

Again, I have given by the jugular vein 22 c.c. of a fluid extract, which I knew to be active, without producing death or any marked change in either arterial pressure or pulse-rate, as may be seen from the following condensed table:

* A minim is a sixtieth part of a dram, which is in turn an eighth of a fluid ounce. It is thus a small drop.

DOG; ETHERIZED; WEIGHT, 40 POUNDS; PULL GROWN

Time	Drug	Pressure	Pulse	Remarks
3.01.10	114-144	186	
3.01.20	114-142	180	
3.01.30	116-142	192	
3.01.40	2 C.C.	144-100	192	Injection begun.
3.01.56	86-136	198	Injection ended.
3.02.06	118-154	168	
3.02.16	134-154	150	
3.02.26	132-150	162	
3.07	126-138	156	
3.09	126-142	144	
3.09.10	126-140	146	
3.09.20	126-142	144	
3.09.38	128-148	150	Vagi cut in order to determine if the slowing was due to pneumogastric stimulation.
3.09.48	136-164	168	
3.11	134-166	180	
3.12	168-194	162	
3.12.23	5 C.C.	168-190	150	Injection begun.
3.12.35	110-190	162	Injection ended.
3.12.45	78-112	162	
3.13.05	164-178	180	
3.13.25	176-184	162	
3.25	154-172	186	
3.35	148-170	162	
3.37	148-168	180	
3.37.12	8 C.C.	162-174	144	Injection begun.
3.37.22	166-88	132	Injection ended.
3.37.32	56-84	156	
3.39.00	88-136	180	
3.41.10	126-156	174	
3.41.20	126-150	174	
3.41.37	7 C.C.	138-150	144	Injection begun.
3.41.42	136-154	138	Injection ended.
3.41.52	148-118	168	
3.42.02	90-140	150	
3.42.12	104-70	168	
3.42.22	98-68	156	
3.42.5	88-116	96	
3.44	118-92	102	
3.44.16	10 C.C.	98-124	105	Injection begun.
3.44.20	74-146	88	
3.44.40	54-34	96	
3.45	28-24	66	
3.45.10	26-22		Pulse imperceptible; heart stopped; respiration continued for ninety seconds after heart.

The only influence exercised on the circulation by the drug consists, as is seen by the above table, in a slight slowing of the pulse and fall of arterial pressure. That the slowing is

due to direct cardiac depression and not to stimulation of the vagal centres is proved by the failure of the pulse to return to its normal rate when the vagi were cut. The fall in arterial pressure seems to depend entirely on the failure of cardiac power.

The 22 c.c. were given between 3:01 and 3:41, in four doses, ranging from 2 to 8 c.c. At 3:44, 10 c.c. more of the extract was given rapidly into the jugular, producing death in about sixty seconds. In other words, it required 32 c.c. of the strong fluid extract, by the jugular vein, to produce death in a dog weighing forty pounds.

When we consider that this extract was active in doses of 8 minims to man, it must be conceded that this drug has but slight lethal power.

Respiration continues after the heart ceases to beat in those cases in which the drug is sent into the cardiac apparatus en *masse* through the jugular vein; but when death is not due to this cause, there seems to be a simultaneous failure of heart-power and respiration.

The action of the drug on the nervous system is, of course, the most interesting part of the investigation, and we find that in the frog, as in the dog, the greater portion of its action is on the brain.

When a very large dose of the fluid extract (5-20 minims) is given hypodermically to the frog, it immediately becomes quiet, and in a moment or two will lie flat on its back, apparently in a deep sleep, with slow and full respirations. That the condition of relaxation is due to sleep or cerebral depression was proved by oft-repeated experiment, reflex action being increased very markedly, proving that the motor and sensory nerve-trunks were unaffected, as well as the motor and receptive centres in the cord. Reflex action, however, rapidly diminishes after remaining for five or ten minutes, and total relaxation comes on. That this is not due to motor-nerve or spinal palsy is proved by electric stimulation of the cord and nerve-trunks, which is always followed by contractions of the tributary muscles.

The loss of reflex power, therefore, must depend on depression of the sensory apparatus, and further experiment confirms this reasoning, for, as was again and again proven, the drug, when applied locally to the exposed sciatic, invariably prevented the passage of the most powerful impulses

from the foot to the cord. The poisoned foot could be burnt off without any response, while if the opposite leg was burned the batrachian instantly leaped away, using both the poisoned and unpoisoned leg, showing again that *cannabis indica* does not have much effect on the motor nerve-filaments even when directly applied to them.

Under these latter circumstances, however, the poisoned leg is not moved quite as rapidly as its fellow, showing that the motor nerve has not escaped absolutely the direct application of the drug. That the sensory tract of the cord is affected was proved by tying the common iliac in order to protect the nerve-trunks of the posterior extremities, and then injecting the poison into the body. Under these circumstances there is, as usual, the first stage of heightened reflex action, followed by corresponding depression of the same, and irritation of the protected sensory nerve fails to call forth any response from the spinal cord.

To summarize these conclusions, we find that *cannabis indica* produces in the lower animals a period of happiness followed by more or less deep sleep, according to the amount of the drug. That in both the dog and frog we have a stage of heightened reflex action following the dose.

That this increased reflex action is replaced by reflex palsy which is not due to motor-nerve or motor-spinal-tract palsy, but to failure of the sensory side of the cord and nerve-trunks.

That the chief action of the drug is upon the centres in the cerebrum, that the action on the sensory tract of the spinal cord and nerve-trunks is secondary to its cerebral action.

Before closing this paper I desire to call the attention of practitioners to the local anaesthetic action of this curious substance. As already detailed, when applied directly to the nerve-trunks it paralyzes them, and I have found that when applied to the mucous membrane of the tongue in considerable quantity it diminished sensibility to a considerable degree. Dentists, I am told, constantly use it for sensitive dentine. The drug is too irritating to be used on delicate membranes such as the eye, for I have proved in the dog that it is apt to bring on severe inflammation.
