

Wood (H. C.)

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CLINICAL PROFESSOR OF NERVOUS DISEASES, UNIVERSITY OF PENNSYLVANIA; NEUROLOGIST TO THE  
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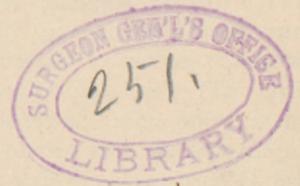


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# Hyoscine.--Its Physiological and Therapeutic Action.



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Every reader of therapeutic literature must have noticed the great diversity of experience and sentiment which exists in regard to the therapeutic action of hyoscyamia. By some physicians it is believed to be of great value as a calmative and hypnotic remedy, whilst others have found it almost inert; and others, equivalent in its influence to atropia. Its commercial form is almost as various as its action; it occurs both crystalline and amorphous, and when it is stated, as by Dr. Judson B. Andrews, Superintendent of the Buffalo State Insane Asylum (*New York Med. Journal*, June 14, 1884), that very extended trial shows that the most reliable form is Merck's *uncrystallized* hyoscyamine, suspicion is at once aroused, because crystalline principles are, as a rule, much purer than amorphous ones; and such statements suggest that it is not the hyoscyamine itself, but some other active cohering body, to which the uncrystallized hyoscyamine owes its virtues.

It is very curious that the profession, and especially alienists, have so universally ignored the labors of Ladenburg, although his results were fully set forth in the last edition of the United States Dispensatory. This German chemist has shown that the so-called *amorphous hyoscyamine* is a more or less impure alkaloid, essentially distinct from true or *crystalline hyoscyamine*; this second alkaloid, *hyoscine*, affords crystallizable salts, of which at least two are now commercially prepared by Merck.

It is plain that our older clinical and experimental records in regard to these alkaloids are of value chiefly as suggestions, and that to get definite results, investigations must be made with the crystallized, and, therefore, presumably pure salts. The present article is offered as a study of one of these alkaloids, namely, *hyoscine*. The salt used was Merck's crystallized hydrobromate, or in a few trials, hydriodate. It will be understood, therefore, that throughout this memoir the word hyos-

cine is used as meaning the hydrobromate, or hydriodate of hyoscine.

The first series of experiments were made upon the frog. It was found that this animal was sensibly affected by  $\frac{1}{20000}$  of its weight of hyoscine, but in none of the nine experiments made to ascertain the minimum fatal dose, did less than  $\frac{1}{5000}$  part of the frog's weight cause death. The symptoms were very uniform. They consisted of an increasing sluggishness with a progressive loss of voluntary movement, and a corresponding depression of the reflex activity; but without marked loss of sensibility. The respiration seemed to suffer *pari passu* with the general muscular power.

In numerous trials I was not able to make out a distinct stage of reflex excitability at any time; but in one or two experiments without section of the spinal cord, when the frog laid absolutely quiet upon his back, making no effort to regain the natural position, touching him would cause violent universal movements, which seemed to be purposive, but were so wild, ungainly and repeated that I was not sure that they were not convulsive. There was at no time any tetanus. During the recovery from the effect of large but non-fatal doses, the normal muscular power was gradually restored without any convulsive manifestations, such as occur in the frog after atropia-poisoning.

Death was brought about by failure of breathing, the heart beating for a considerable time after the arrest of respiration. When a strong solution of the alkaloid was placed upon the exposed heart it exerted only a very slow and feeble depressing influence.

After death the muscles and the motor nerves were found to respond to the feeblest galvanic currents in a normal manner: tying the femoral artery so as to isolate a leg, did not affect the supervention of the palsy in that leg, when the poison was injected into the anterior part of the body, and after death the motor nerves and muscles of the protected leg were found not to be more sensitive than those to which the alkaloid had access.

These experiments were sufficient to demonstrate that upon the *frog hyoscine* acts as a *motor spinal depressant, killing by arresting respiration probably through a centric influence; that when recovery occurs there is no stage of tetanus following the palsy; and that any influence the alkaloid may exert upon the circulation is of a depressive character, but is so slight as to be of no importance.*

The next series of experiments were made

upon mammals. Hypodermic injections were given to three mice, the doses being respectively 0.002 grm. (0.03 grain.), 0.004 grm., and 0.006 grm.; only after the last dose was any distinct effect perceptible. This mouse became very quiet and lethargic, but finally recovered.

On a subsequent occasion 0.025 grm. injected into a mouse caused in three minutes violent general tremblings, and a minute later the animal suddenly expired. The injection of 0.006 grm. produced in fifteen minutes in a white mouse, quietness, with a marked loss of jumping power. 0.012 grm. was then injected, and in one and a half minutes the breathing became sensibly affected and the animal had nearly lost the power of crawling. Four minutes later the respiration was very slow and labored; in four minutes more the red eyes had become black-cherry colored and the mouse was gasping; a few seconds subsequently convulsions came on and the animal soon died. A very large white mouse was killed by 0.012 grm. in one hour and seven minutes.

In all of these cases, as well as in some not detailed, the symptoms were similar, except that distinct convulsions occurred in one case: the manifestations were progressive weakness and quietude, great disturbance of respiration, the movements becoming distant, slow and very labored, but afterwards more shallow, asphyxia, (as shown by the red eyes of the white mouse becoming black and extraordinarily projecting,) convulsive movements and death; the heart continuing to beat forcibly after the extinction of the respiratory function.

Owing to the great costliness of the drug, but one general experiment was made upon the large mammals. 0.17 gramme of the hyoscine injected into the jugular vein of a small dog caused him in a few minutes to seek out a corner, and curling himself up, go to sleep. The pupils were widely dilated, and during the sleep there was repeated purging of yellowish watery stools.

The general effects of the alkaloid upon mammals seem to coincide with those caused by it in frogs; but in order to determine more positively its influence upon the functions of respiration and circulation, special experiments were performed.

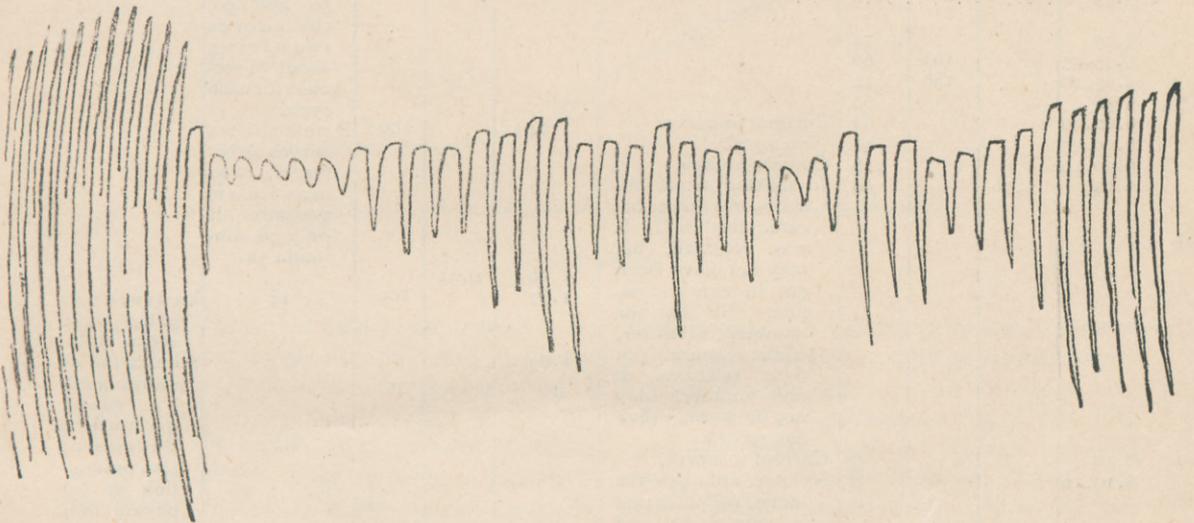
The first series were directed to the respiration: In experiment 1 (upon a rabbit) the respiration-rate under the influence of the doses used, fell from 90 per minute to 25. The amount given altogether was

0.096 gm., or nearly  $1\frac{1}{2}$  grains of the salt. In experiment 2 (upon a rabbit) the results were not so simple; the respiration-rate fell for a time, but afterwards became more frequent. At this period it took on a markedly Cheyne-Stokes character, as shown in the tracing (A) herewith given. Finally the breathing became very shallow, with intervals during which it was so nearly imperceptible that the animal was several times thought to be dead. In experiment 3 the respirations seemed to be increased in number by the drug, but were rendered very shallow and irregular. The cause of the markedly

and in half an hour rose to 168, as far above the normal as it had fallen below.

In Experiment 4 four injections of 0.05 gm. each into the jugular vein of a dog weighing 15 pounds (in all, 3 grains of hyoscine), failed to have any distinct effect upon the blood pressure, which was, in fact, a quarter of an hour after the last injection, a little above the normal.

When an injection of hyoscine is first thrown into the jugular vein, there is a slight temporary fall of the arterial pressure, which comes on so immediately that it is probably due to a direct action upon the



TRACING A.

Cheyne-Stokes respiration it is impossible at present to determine, but it is very plain that the alkaloid has a markedly depressing influence upon the respiratory function, and in all probability upon the respiratory centres.

The next two experiments were made upon unmutated animals in order to test the action of hyoscine upon the arterial pressure. They proved that the alkaloid exerts only a very feeble influence upon the heart or vasomotor system. In experiment 3 two injections of a half-grain each into the jugular vein of a rabbit, caused a fall of the arterial pressure in about 10 minutes from 140 to 112; the pressure, however, rapidly recovered itself,

heart. The slight rise of the pressure which occurred near the close of each of the experiments may very plausibly be explained as the result of asphyxia. This is strongly corroborated by the fact that in an experiment (5) made upon a young pup, the pressure rose throughout. Such inconstancy of action indicates the existence of one or more indirect influences exerted by the poison. In order to get rid of any asphyxiating action and consequent secondary circulatory phenomena, manometrical studies were next made upon curarized animals, kept alive by artificial respiration.

The experiments were two in number, as follows:

EXPERIMENT 16.

A young cat, about seven weeks old; section of pneumogastrics; woorari; artificial respiration; canula in carotid.

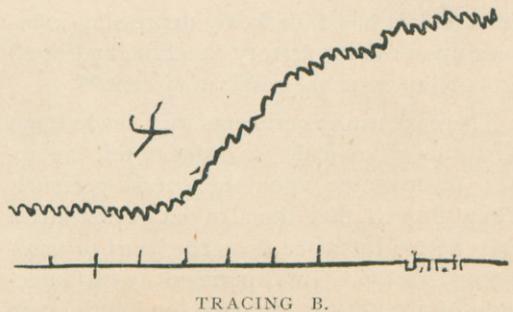
Time. H. M. S.	Drug. Grains.	Pulse.	Art. Press.	Remarks.
5		240	120	
.10			122	
5.04	0.76			
5.04.10			100	
5.04.27		204	78	
5.04.35		204	60	
5.05.00			60	<i>Tracing B.</i>
5.10.00			100	
5.20.00			100	
5.21		240	100	Galvanization of a brachial nerve.
5.21.03			120	
5.21.05		180	140	
5.21.07			150	Current broken.
5.25	0.77		100	
5.25.10			88	
5.25.15			74	
5.45	0.76	216	110	
5.45			74	
5.45.05		168	60	
5.45.10		180	42	
5.51			60	
6.00.00			68	Current to nerve.
6.00.05			94	<i>Tracing C.</i>
6.00.10			116	Current broken.
6.04	0.76		60	In shifting drum, abscissa needle became displaced. It was replaced, but may not have been put in exact position. So that the numbers hereafter, whilst accurate in their relations to one another, may not be so to previous record.
6.10			8	Current to nerve.
6.10.10			8	No rise, although the individual pulse rate is very large and full.
6.20			8	<i>Tracing D.</i>
6.20			8	Current to nerve.
		156	14	No effect. <i>Tracing D</i>
6.31.30			28	
6.32				Artificial respiration stopped. No rise in the arterial pressure followed. During all this period of low pressure after the 4th injection, the pulse has been very large and regular; the individual waves being fully twice as large as those before any of the drug was given.

EXPERIMENT 17.

A large dog. Woorari and artificial respiration; section of pneumogastrics; injection in jugular vein.

Time.	Drug. Grains	Pulse.	Arterial Pressure.	Remarks.
12.51.30		96	74	
12.51.35	0.91			
12.51.39		80	60	
12.51.45		90	72	
12.51.52			56	
12.52	0.91			
12.55.56		85	40	<i>Tracing E.</i>
12.56.05		85	40	
12.56.09		85	40	
I.		80	56	
I.00.04			48	
I.00.12		88	56	
I.03		88	70	
I.04			64	
I.10				The pressure at this time is slowly and regularly rising and falling between 56 and 90, the curves requiring about 16 seconds for each cycle.
I.24		100		Pressure curves as before, but maximum pressure is only 46, minimum 32.
I.26	0.91			
I.27		100	14	Individual pulse wave seems full.
I.29				Stimulation of crural nerve by strong galvanic current; also production of asphyxia failed to cause rise of pressure.

In experiment 16 just detailed 0.75 grain of the alkaloid injected into the jugular vein of



a kitten caused in 35 seconds a fall of the arterial pressure to one-half its norm, 120.

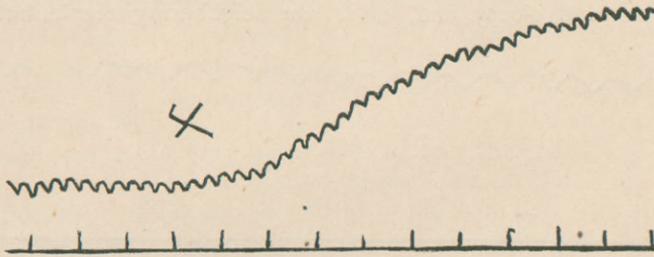
Five minutes later the pressure had steadied itself at 100. Two subsequent injections reduced this to 60, or thereabouts, but a fourth injection was required to depress the pressure nearly to zero. In Experiment G, two injections of 0.91 grains each into the jugular vein reduced the arterial pressure only from 74 to 60, and a third injection was required to bring the pressure down to 14.

The two experiments show that when hyoscine is given under such circumstances as to eliminate all respiratory disturbance, it steadily depresses the arterial pressure, but that to produce any decided effect enormous doses are required.

The comparatively large immediate depression which follows injection into the

produced before the administration of the drug. Both experiments (16 and 17) show, however, that finally the drug does cause a vaso-motor palsy; for in each there came a time in which, while the heart was still beat strongly, galvanization of a sensitive nerve failed to cause rise of pressure; also in experiments 17 and 18, asphyxia failed to cause any rise of the arterial pressure at a time when the heart was sending pulse waves fully as large as those that had come from it before the administration of the drug.

The persistency at this time of the pulse wave indicates, also, that that the drug does not fully paralyze the heart until very late in the poisoning; not, indeed, until after the vaso-motor system. When the drug was ad-

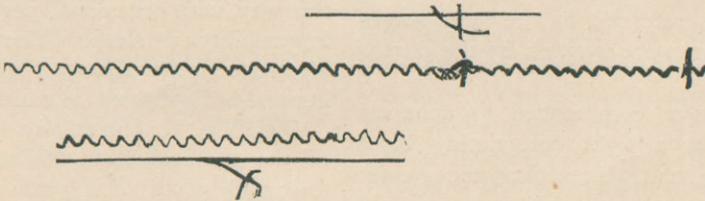


TRACING C.

jugular indicates that cardiac depression is at least one cause of the fall, and the two experiments lend some countenance to this view.

During the course of experiment 16, trials as to the effect of galvanizing a sensitive nerve were made, and it was found that even after the injection of two and a quarter grains, the rise of arterial pressure, and consequently

ministered to the uninjured animal, the pulse was usually, but not invariably, slowed, sometimes it was quickened. This would seem to indicate that the indirect actions of the drug upon the heart were sometimes, but not always, more powerful than any direct influence. When sections of the pneumogastrics and the use of woorari and artificial respiration had been practiced, the pulse was slowed



TRACING D.

the vaso-motor spasm, followed very promptly upon the stimulation. This comparative immunity of the vaso-motor centre was corroborated in another experiment (Exp. 18) which it is not necessary to detail, in which after the injection of three grains into the jugular vein of a rabbit the stoppage of the artificial respiration apparatus caused a rise of pressure, which was nearly equal to that similarly

by the drug. In no case was there any sign of influence upon the pneumogastrics. In two experiments, trials by stimulating their nerves galvanically were made in different stages of the poisoning, and neither augmented nor diminished excitability was found.

The experiments which have been detailed show that *hyoscine* acts upon mammals chiefly as a *spinal depressant*; that it is a *centric respi-*

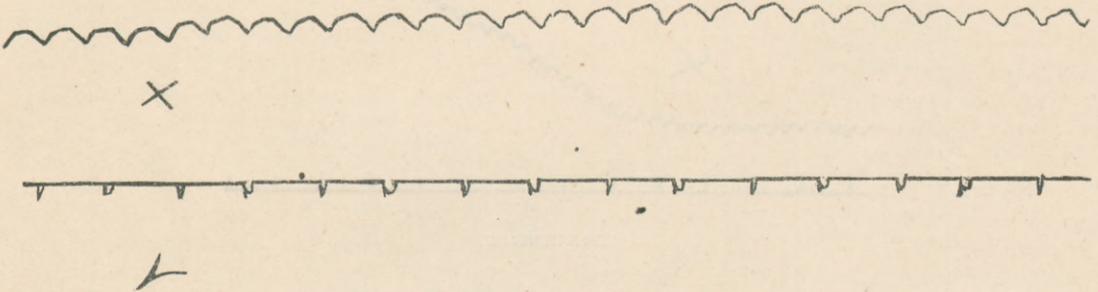
ratory depressant, causing death by asphyxia; that it has very little effect upon the circulation, what influence it exerts being in the normal animal set aside by the asphyxia it produces; that it does not paralyze the pneumogastrics; that in enormous doses it paralyzes the vasomotor system; that on the heart itself, its influence is very feebly depressant.

The final series of trials were made upon human beings. Whilst assisting me in the laboratory, Dr. F. E. Stewart accidentally swallowed a small quantity of a strong solution. The following statement is condensed from his account: The first symptoms were dizziness, dimness of vision, and inability to walk straight, due as described "to a want of coördination in my movements." About an hour later supper was taken, when the doctor became "very stupid and sleepy, and, as it

to hear the clock go on striking several times more, at which I was somewhat surprised.

The desire now took possession of me to go to bed and sleep off the effects of the drug. One of the gentlemen of the house just then came in to inquire my condition, but I could not realize his presence in the room. It seemed as if I were dreaming, and that my answers to his questions were part of the dream.

I now staggered into the next room, partially undressed, and got into bed, when I immediately fell asleep. I was awakened sometime afterward with no difficulty, by an inquiry for my health, but the presence seemed but a dream, and I again sank into a profound slumber, which lasted for an hour or more. I then partially roused and again attempted to count the strokes of the bell in the neighboring steeple, but lost the number



TRACING E.

were, a heavy weight hanging on my eyelids, which I found quite difficult in opening." The pulse was 60, slightly interrupted. There was also a sense of swimming in the head, and in a little while the desire to doze became irresistible, but the sleep was light and dreamful; a little later there was a distinct sense of suffocation, with pain in the forehead. The following notes referring to the later stages of the poisoning, were written by the doctor himself:

"My head now commenced to ache as though there was a tight constricting band around my forehead. Breathing, though not difficult, did not seem to relieve a sense of suffocation that now came over me, and every few minutes I was obliged to take a long breath for relief. I now began to wonder whether the stupor might not become too profound, so I attempted to rouse myself from the trance-like condition that appeared to be stealing over me, but the efforts were only partially successful. The clock now commenced to strike 8 o'clock, and I attempted to count the strokes, but arrived at eight only

before it was through striking, and it again seemed as though the clock struck a number of times too many.

I now became oppressed with a feeling of general uneasiness and unrest, and I tumbled in bed from side to side, vainly trying to move the load from my chest that seemed crushing me, and I spent the remainder of the night in this way, with occasional periods of complete insensibility in sleep. There has been no after-effect other than a slight headache, and general indisposition to exertion."

Drs. Wm. L. Abbott and Geo. B. M. Free, of the medical staff, Philadelphia hospital, took each  $\frac{1}{100}$ th of a grain of hyoscine hydrobromate hypodermically. Their report is as follows, largely, of course, made out from the notes of their fellow-resident physicians:

Effects were first noticed in about ten minutes, as a slight dizziness. This rapidly increased, so that it was almost impossible to walk straight. The feeling of lightness and giddiness was exactly like that produced by excess of alcohol. About half an hour after administration, dryness of throat came on. There was a sensation of restlessness, so that

it was difficult to remain quiet in spite of the giddiness. Extreme sleepiness soon developed after this. F. had a slight feeling of nausea. One hour after administration Dr. A.'s condition was as follows: "Face flushed; voice thick; mouth very dry; can scarcely speak; very sleepy; will hardly answer questions; said he felt as if he had had about eight beers, and as if he were slightly drunk." Pulse, 60. Dr. F.'s condition was noted: "Seems in a very deep sleep; not aroused by considerable noise in room; on being aroused, complains of great giddiness and looks pale." Pulse at 9:15 P. M., 48. A.'s at same time was 54. F. remained sleeping until some one aroused him and gave him an apple, he ate it, and lying down slept until morning; on awakening had no recollection.

Under my direction and supervision careful trials of the drug were made by Dr. Edward Martin, then resident physician in the University Hospital. There were in all eight cases, suffering, except in one or two instances, from diseases entirely indifferent to the drug, such as traumatic musculo-spiral paralysis, granular lids, etc. In order to avoid the fallacies of observation, so prone to occur when real or alleged hypnotics are given in the evening, the drug was administered near the middle of the day. The dose used was from  $\frac{1}{360}$  to the  $\frac{1}{120}$  of a grain, always administered hypodermically. The tabulated reports of the cases are before me, and I select one as typical, except in the effect upon the pulse and respiration.

MUSCULO-SPIRAL PARALYSIS (TRAUMATIC).

Time.	Dose.	Pulse.	Resp.	Remarks.
3:45 P. M.	Hyoscine Hydrobrom, gr. $\frac{1}{120}$	76	19	Has had some frontal headache for two weeks.
3:55		76	20	Feels "light" in head. Headache worse.
4:00	gr. $\frac{1}{360}$	84	19	Pulse feels stronger and fuller.
4:05		96	21	Drowsy.
4:15	gr. $\frac{1}{360}$	96	19	Throat and mouth dry.
4:25		100	20	Dizzy. Gait unsteady. Lay down. Headache much worse.
4:30		102	18	Face flushed.
4:35		120	19	Sick at stomach. Slightly delirious.
4:50		102	20	
5:00		90	18	Sleeping.
5:10		90	18	Throat not so dry.
5:30		90	02	Sleeping at times.
6:00		84	18	Dizzy and a headache.
7:00		80	18	At about 8 P. M. the patient fell into a heavy sleep, from which it

MUSCULO-SPIRAL PARALYSIS (TRAUMATIC).

Time.	Dose.	Pulse	Resp	Remarks.
				was difficult to rouse him. This lasted the greater part of the night. The next day he complained of an exacerbated headache, but had no other symptoms.

An analysis of all the cases shows that in every one except that just detailed, the pulse rate was reduced; in No. 2, from 78 to 60; in No. 3, from 84 to 60; in No. 4, from 84 to 70; in No. 5 (hysteria), from 150 to 72; in No. 6, from 108 to 86; in No. 7, from 96 to 80, or in a second trial from 128 to 80; in No. 8, from 64 to 60.

The respirations, in four cases were not distinctly affected; but in case 2 they were reduced from 24 to 18; in case 3, from 27 to 20; in case 4, from 24 to 20; in case 7, from 27 to 20. The tendency to sleep was very marked; usually the sleep during the afternoon was light and doze-like, precisely as described by Dr. Stewart, but in one or two instances it was heavy from the beginning and it was always profound the following night. There was often slight nausea, but in no case vomiting. Dryness of the throat and mouth, giddiness, flushed face and some wandering of mind during the condition of dozing seem to have been nearly universal. No action upon any of the secretions was noted, and in no case were there any unpleasant after-effects. The hypodermic injections gave no more pain than do those of morphia, the drug appearing to be free from irritant properties.

These studies of hyoscine are sufficient to show that the relations between its actions upon the lower animals and upon man are in obedience to the law which I formulated some years since, that as a nerve centre is more and more differentiated it becomes more and more susceptible to the action of drugs. Thus we find the cerebral symptoms produced by the alkaloid in the dog are much more decided than those caused in the mouse, whilst in man the cerebral effect predominates over the spinal. It is plain, however, that in man hyoscine acts as a very feeble sedative on the circulation, a more decided sedative to the spinal and respiratory nerve centres, and a dominant hypnotic upon the brain.

The case of Dr. H. A. Hutchinson, (*Alienist and Neurologist*, Vol. III., p. 539) who experimented upon himself with a quarter of a grain

of amorphous hyoscyamine, illustrates the effects to be expected from toxic doses of an impure hyoscine; the symptoms were dryness of the throat and mouth, great loss of muscular power and of co-ordinating power, until finally the doctor was scarcely able to walk; then profound, quiet coma, lasting eleven hours, and associated with entire relaxation of all the muscles. It will be seen at once that the symptoms were those of deep narcosis and spinal sedation.

The peculiar therapeutic value which this physiological study leads us to look for in hyoscine arises from the union of decided hypnotic powers with a spinal sedative influence and a very feeble depressant action on the circulation. The experiments so far indicate also freedom from disturbance of the secretions and unpleasant after-effects. The calmative influence of conium in certain cases of mania is well known, but such action appears to be indirect and due to the motor-depressant influence of the drug. From hyoscine we have reason to expect both a direct and an indirect beneficial action.

The first person to use a pure crystalline salt of hyoscine in medicine, so far as I know, was Prof. Edlessen (*Centralb. f. Med. Wissensch.*, 1881, 416), who administered it in six cases of whooping cough with advantage in three cases; in six cases of asthma always with advantage, and in two cases of severe enteralgia with relief to the pain.

Dr. Rudolf Gnauck (*Centralb. f. d. Med. Wissen.*, 1881, 801. *Charité Annalen*, 1882, 448), has used the crystalline hydriodate in a number of cases, and reports complete accord with Prof. Edlessen in finding great diversity in the susceptibility of various people to its influence.

In some cases it caused so much general distress, headache, weakness, numbness, etc., as to forbid its use. Failure of appetite, and feebleness he appears to believe the chief contraindication to its use. He gave it in twenty-eight cases of various forms of insanity with sleeplessness at night. Sleep usually came on in from one-half to one hour, and continued through the night. In four cases no good effect was achieved. In delirium tremens and dementia paralytica its influence was least happy. Given during the day in eighteen cases of great excitement and delirium it had marked effect in inducing sleep or at least calmness; the quietude continued after each dose from one to eight hours. Dr. Gnauck gave the alkaloid hypodermically in doses of from 0.005 grm. to 0.001 grm. On

account of varying susceptibilities the smaller amount should at first be employed.

I have used the hyoscine in five cases of violent mental disease:

Case I. was a lady suffering from *acute dementia*, with maniacal outbreaks. At times the restless sleeplessness was very marked. Twenty-two grains of chloral with three-eighths of a grain of morphia repeated twice had no perceptible effect upon this insomnia. A  $\frac{1}{100}$  grain of hyoscine was given by the mouth, and in a few moments the patient went to sleep. On four successive nights the hyoscine ( $\frac{1}{100}$  gr.) produced from four to six hours of very quiet sleep, the patient, when not under its influence, continually getting out of bed, wandering aimlessly around the room, etc.

On the afternoon of June 16 date, there were numerous fine subcrepitant râles in the lungs (evidently congestion with some œdema). The  $\frac{1}{100}$  grain of hyoscine was given about 9 P. M., and repeated about 2 A. M. No sleep was induced, but there was very pronounced dyspnoea, with livid flushing of the face, distress and great restlessness. The next day there was general œdema of the lungs, and the patient was supposed to be dying, but under treatment the attack subsided. After this the patient slept much in the day time, but at night wandered about in a demented delirium. Chloral and morphia again entirely failed of effect.

June 21, she was given, at 10 P. M.,  $\frac{1}{80}$  of a grain of hyoscine by the mouth, and at 11.15 she went to sleep; the breathing was slightly labored, the face a little flushed. The sleep was very heavy and quiet, and lasted two hours. A day or two subsequently the patient was seized with a second sudden attack of œdema of the lungs, dying in twenty-four hours. This attack, and the fact that the râles in the first attack appeared before the administration of the daily dose of hyoscine, show that the drug was not the cause of the œdema, although it, probably, by depressing the respiratory center, augmented the distress. There was also chronic interstitial nephritis.

Case II.—M. C.—, aet. 25, had been in the University Hospital for several months, suffering from long-continued and violent hystero-epilepsy with rare outbreaks of mania, lasting only a few hours. During the latter part of May, not having had a fit for an unusual length of time, she became much depressed and markedly erotic.

June 6. She was suddenly seized with

most violent mania. She was in a condition of the wildest excitement, with a furious expression of face, loud, incoherent, incessant lascivious talk, and great muscular restlessness and effort. She endeavored to injure herself and others around her, jumped out of a window, and did many lewd and violent acts. Various remedies were employed, *inter alia* an ice-water bath, without effect, and finally, screaming, yelling and fighting, she was tied fast in the bed. She had no sleep that night, and the next twenty-four hours raved incessantly in spite of blistering the head and the administration of twenty grains of bromide of potassium and 10 grains of chloral every 2 hours.

June 7. She was in a very marked typhoid state without abatement of her delirious fury and erotism.

By 3 P. M., June 9, she was in an alarming condition, having since the beginning of the attack absolutely refused food, and having had no sleep. Her fury was only interrupted by long-continued spells of muttering delirium. Milk and whisky had been forced down her, but the tongue was brown and dry; the teeth covered with sordes; the voice lost in huskiness from incessant use; the pulse failing; the whole muscular system affected by repeated, irregular twitchings. A hypodermic injection of  $\frac{1}{100}$  grain of hydrobromate of hyoscine was now given; in five minutes her face was flushed. She gradually became more and more quiet, talked only in a whisper, and in twenty minutes was perfectly at rest, though not sleeping. She now took her milk punch readily, and remained in this condition for about six hours, when she commenced to rave and struggle as before.

About 6 o'clock in the morning of June 10,  $\frac{1}{80}$  of a grain of hydrobromate of hyoscine was given hypodermically; in ten minutes her face was flushed, five minutes later she became cyanosed—so much so that artificial respiration was deemed necessary. The drug seemed to have no action on the rapidity of the respirations, but made them more and more shallow. The muscular twitching seemed to be aggravated, which prevented the action on the pulse being noted. In a very few minutes, however, she became very quiet and easy, and so remained, though sleepless for eight hours.

At 2.30 A. M. of June 11, she was in a raging delirium.  $\frac{1}{100}$  grain of hyoscine was given hypodermically, which kept her quiet until 10 A. M. She was then given another hypodermic of  $\frac{1}{100}$  grain. She went to sleep

and slept till 4 o'clock, then took  $\frac{1}{100}$  grain by the mouth, and again slept for three hours, when she again became noisy;  $\frac{1}{80}$  of a grain by the mouth then kept her quiet about five hours.

By 2 A. M., June 12, she had become again maniacal, and  $\frac{1}{80}$  grain was given by the mouth; in half an hour she was again asleep and slept for four hours, then gradually grew more and more talkative until 10 A. M., when 1-90 of a grain was given by the mouth, which produced a quieting effect in 30 minutes. She remained quiet until 9 P. M., when she became slightly excited, then another  $\frac{1}{80}$  of a grain was administered and she rested quietly all night. The next two days she was entirely irrational but not wild or delirious. She was then removed to an insane asylum.

Case III.—M. E. *Religious melancholia*, with maniacal excitement. Had not been in bed for several nights. One-sixth grain morph. given hypod. produced only dosing in chair. 2:20 P. M.,  $\frac{1}{100}$  gr. hydrobrom. hyos. hypod. Resp., 24. Pulse, 77.

3:20 P. M. R. 19. P. 69, patient quiet. 4 P. M. Right face flushed; patient wants to sleep. Slept for one hour. Awoke quiet. 8 P. M. Went to bed. Slept soundly all night."

From this time forward hypodermics were repeated as required. They kept the patient quiet and produced sleep.

Case IV.—J. M., aged 75; with marked general arterial atheroma, and said to have been *insane* for many years; was admitted to my ward in the Philadelphia Hospital, in a furiously maniacal condition, requiring him to be strapped in bed.\* He had not slept for 48 hours, notwithstanding the use of narcotics. I ordered hyoscine. The following report was furnished by the resident physician, Dr. G. E. Day: "He was given  $\frac{1}{100}$  gr. hydrobromate of hyoscine hypodermically at 2 P. M., and in less than half an hour he quieted down and fell asleep. At 8 o'clock he was still asleep, when another  $\frac{1}{100}$  gr. was given. At 12 o'clock he was still sleeping, and fearing unpleasant results, I did not give him any more. He slept until six o'clock the following morning, and then was transferred to the insane department. Neither pulse nor respirations were noticeably affected by the drug."

Case V.—*Senile dementia*, with sleepless-

\* Owing to the foolish formalities of the law, several days are required to get a man into the insane department of the hospital, and in cases of violent mania, being without means of otherwise controlling patients, we are forced to treat them by strapping, until they can be transferred.

ness. I saw the lady only in consultation, and have only had the report the hyoscine at first failed, but afterwards acted most happily.

For the reports of the following cases which occurred in the Philadelphia Hospital I am indebted to Drs. Wm. L. Abbott and Geo. B. M. Free, Resident physicians, who used the drug at my suggestion:

Case VI.—M. K., *delirium tremens* with persistent wakefulness, 40 grains of chloral, 80 of bromide of potassium, and  $\frac{1}{4}$  grain of morphia having entirely failed,  $\frac{1}{100}$  of a grain of hyoscine was given at 7 P. M. At 8 P. M. was awake, but quieter; at 9 P. M. was asleep and snoring. Soon after this awakened, but seemed comparatively rational; complained of giddiness. During the rest of the night, was awake and delirious. The next day was quiet and had no return of delirium at night.

Case VII.—G. C., aged 40, *delirium tremens*. Received at 6 P. M., and again at 8 P. M. a hypodermic injection of  $\frac{1}{100}$  of a grain of the alkaloid; no effect was produced upon the restless, talkative delirium, the pulse and respiration-rate being respectively reduced 15, and 2 per minute.

Case VIII.—M. K., *senile dementia*, with almost complete insomnia. A mixture containing 60 grains of the bromide of potassium, 20 grains of chloral, and  $\frac{1}{4}$  grain of morphia given at bed time having failed entirely of effect, on the three successive nights  $\frac{1}{100}$  grain of hyoscine caused from 4 to 5 hours sleep, with reduction in the pulse and respiration rate.

Case IX.—J. M., *maniacal dementia*, without sleep for four nights; patient so furious at night that he had to be strapped in bed. During each of these nights he had received 40 grains of chloral, 180 grains of the bromide

of potassium and  $\frac{1}{4}$  grain of morphia, without effect.

Administered at 3:10 P. M.  $\frac{1}{100}$  grain hyoscine hypodermically. Patient went to sleep in about ten minutes, and did not wake up until after midnight, then took a drink of milk and slept until morning. Before administration, 3:10 P. M., pulse was 81, respirations, 20; 3:30 P. M., pulse, 100, respirations, 15; 4 P. M., pulse, 88, respirations, 16; 5:30 P. M., pulse, 74, respirations 13. Next day he was in the same condition as usual, that is, wandering around in a demented condition. In the evening administered the same dose hypodermically. Before administration, 6:45 P. M., pulse was 84, respiration 18; 7:25 P. M., pulse 96, respiration 13; 10:50 P. M., pulse 85, respiration 17. The patient went to sleep as before, and remained quiet all night, respiring somewhat jerky; patient sleeping uneasily, twitching and jerking the limbs.

The clinical results which so far I have had with this drug in cases other than maniacal, are very meagre, but so far as they go are correspondent with physiological results, which indicate little value for the relief of pain, but much for the removal of spasm.

In one case of violent facial neuralgia of paroxysmal type,  $\frac{1}{100}$  grain was given hypodermically; at my instance, by Dr. Farnham, at that time my resident physician in the Philadelphia Hospital. In a short time the patient complained of giddiness, numbness in the legs and arms, and staggering on attempt to walk. This was followed by vomiting, the pain continuing without abatement for an hour or more, when a hypodermic injection of morphia was administered. The vomiting may or may not have been due to the hyoscine, as the patient sometimes vomited spontaneously in her attacks.





