Thesis

by

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Part 1

51 Queen Street
Edinburgh, April 1801
On
The Physiological Actions
of
Extractive Hyoscyamine
and
its employment in the
Treatment of Insanity.
A Thesis submitted to the
University of Edinburgh
on application
for the Degree of Doctor of
Medicine by
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57 Queen Street,
Edinburgh.
April 1881.
Part 1.

On the Physiological Actions of Extractive Hyoscyamine.
The drug which I have used in making the observations which I am about to detail and comment upon is that which is known as Merck's Extractive Hypoxyamine. I have obtained from the manufacturer of it an account of its prominent characteristics. It appears as a dark brown syrup with a strong and disagreeable tobacco-like smell. The consistency though pretty thick under normal circumstances may easily become thinner in warmer climates or when heated. When it is spread out in a thin layer the Hypoxyamine though of a dark colour will be seen to be
transparent. In well-stoppered bottles it will keep for years without deleterious changes having occurred. During manufacture there is no risk of its being spoiled. It is prepared from Hymenopus Tiger-nut, parts of the plant—roots, leaves, or even stalks of the plant being employed.

My own observations have made me a better judge of the taste of the drug than Mr. [illegible] claims to be. The taste of the extractive resembles that of the fluid accidentally sucked from the stem of a foul tobacco-pipe with that added flavour for which we have no better descriptive term than "mooziness." It dissolves readily in Ether and Alcohol. One grain of the substance in eight minims of Ether, 2 or 4 drops of Alcohol, and 200 parts of water up to one ounce forms a brown-coloured
solution which retains the "moxy" and sedent taste of the extractive and has been aptly characterized by a female lunatic as lasting like "the washings of spittoons.

There is now no doubt that samples of the drug which have been more recently imported are much stronger than those originally used by me and when I come to speak of the therapeutic actions of extractive amygdamine I shall make special reference to the nature and extent of this variation. Merck himself states that the quality supplied at former times cannot have been quite so pure as that which he now supplies and it may have contained about 10 per cent of impurities which, only improvements in the manufacture of it were able to eliminate. He asserts however that the drug in its
present state may be considered as of the utmost purity that such a form can be brought to.

It is necessary also to state that in addition to this increase in the potency of the drug, I discovered early in the course of my observations that the full physiological and the necessary therapeutical actions could be induced by much smaller doses than those first used by me.

I believe that the largest quantity of extractive Hyoscyamus ever taken at one time by any individual was three grains. The dose taken by myself previously to entering upon the investigation of its therapeutical uses. When I began to administer the extractive to the patients in the West Riding Asylum the common dose I employed was two grains. This was soon diminished first to a grain and a half, then to one grain or afterwards to
Three-quarters of a grain. Three quarters of a grain was for a considerable time regarded as the fixed quantity necessary for the production, by a single administration, of all the physiological actions of hyoscynamine which could be turned to therapeutical account. Subsequently, however, I came to regard half a grain of infraactive hyoscynamine as being sufficient to produce that result, and upon many constitutions a quarter of a grain has been found capable of causing mental quiescence and muscular prostration. I have never heard of a single fatality from the larger doses though owing to forms of maladministration in my own hands and those of others I have seen and heard of cases in which great anxiety was caused by the dangerous condition to which the patient was reduced by a single dose. To these instances of mal-
administration I shall advert farther on. In the meantime I may state that having taken on one day two grains and, on the fourth day following, three grains more, I was so little affected after the first main action of the medicine had passed off, that I was able to resume my occupation on the following mornings.
In making a prolonged series of observations upon animals in order to determine the physiological actions of Extractive Hyoscyamine employed guinea-pigs, rabbits, cats, dogs and pigeons. Guinea-pigs were soon abandoned because it was found that a considerable portion of the somewhat viscid alkaloid, when injected subcutaneously, remained unabsorbed.

The following signs usually followed the injection of a small dose of hyoscyamine as for instance a quarter of a grain into a rabbit:—

Dilatation of the pupils beginning in about 2 minutes after administration, and advancing till a maximum was reached in about 15 minutes.
Unsteady movements and rubbing of the face with the paws.
Drowsiness of the mouth and nostrils.
Fall of pulse,
Frequently cessation,
Fall of temperature, continuing till the diminution had reached about 1/2.
Slight alteration of respiration the tendency being to fall.
Interludes of sleep alternating with ataxic helpless movements, nodding of the head and apparently delirious excitement.
Sleep
Renewed excitement and
Recovery.
During the progress of the symptoms paralysis of ocular accommodation was a permanent symptom and was frequently shown by the animal trying to lay hold of objects or jump upon projections and invariably falling
sting the distance of the object as being much less than it was in reality.

Somewhat larger doses very slowly wi producing these signs somewhat markedly and up to at least half a grain of the extractive hyoscyamine the general action of the drug is to depress the pulse and subdue the respirations while slightly reducing the temperature. These doses of a grain are administered. An important change occurs in the progress of the symptoms and this will be subsequently commented upon. In the meantime a glance at the following chart recording the effects produced by the injection of half a grain of the extractive hyoscyamine under the skin of a rabbit weighing 7½ ounces will convey an idea of the typical action of doses confined to this limit.
Half a grain of Extractive Hypoxyamine to a rabbit weighing 6.5 ounces.

### Table 1.

<table>
<thead>
<tr>
<th>Time</th>
<th>Temperature</th>
<th>Respiration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:15</td>
<td>105</td>
<td>135</td>
</tr>
<tr>
<td>1:30</td>
<td>103</td>
<td>135</td>
</tr>
<tr>
<td>2:00</td>
<td>102</td>
<td>135</td>
</tr>
<tr>
<td>2:30</td>
<td>101</td>
<td>135</td>
</tr>
<tr>
<td>3:00</td>
<td>100</td>
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</tr>
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<td>3:30</td>
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<td>135</td>
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<td>4:00</td>
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<td>135</td>
</tr>
<tr>
<td>5:00</td>
<td>96</td>
<td>135</td>
</tr>
</tbody>
</table>

This table indicates what my observations lead me to regard as nearly a typical schema of the changes produced in animals by doses not sufficiently large to produced any decided amount of central disturbance or motor helplessness. The relations respirations and temperature were taken at 1:45 P.M. immediately previous to the administration of the drug. To begin with, the
Pulsations were 168 per minute.
In half an hour after the injection of half a grain of hyoscynamine they had fallen to 148, in another quarter of an hour they were counted at 140. In three quarters of an hour more they were found to have risen to 160—almost the starting point; during the next half hour there was a perceptible fall which continued, till, in another half hour, the pulsations reached a minimum of 132 after which time they gradually rose till next morning they had reached within 6 beats of the starting point.

In this case the injection of the medicine was followed by dilatation of the pupils, dryness of the mouth and throat, a tendency to nod the head forward to allow the tongue to strike the floor; muscular torpor rather than paralysis and little or no appearance of hallucinations.
The cerebral symptoms appeared not to have gone beyond mere sleepiness as shown by the tendency to nod and to squat piggily upon the floor.

The temperature sank only one degree Fahrenheit; the respirations were as usual irregular, but if anything were slowed.

This rabbit passed urine 36 times during the course of the observation, both times being during the course of the first two hours. The significance of free urination during the action of hyoscynamine will be referred to farther on.

Somewhat similar symptoms were produced by the administration of a quarter of a grain to a rabbit. At first however the animal was much more excited, thought to all appearance the exact无人机
and—more the effect of terror than of the drug, and this agitation was rapidly followed by profound sleep. The visible signs of the action of the drug were, in their order: (1) Four minutes after the administration, complete dilatation of the pupils; (2) After an interval of ten minutes—great excitement and restlessness without loss of motor power; (3) In other ten minutes, urination. At this time also the kitten showed decided weakness of the hind legs and its mouth was so dry as not to smother blotting paper; (4) In twenty minutes more the motor capacity was much diminished but the kitten could still walk with moderate precision though with evident effort. (5) Next it began to sleep in a restless manner and then profoundly. After an interval of an hour it was awake but quiet—composed and next
day it was healthy and active.

It will be seen by the foregoing examples that doses of extractive hypoxamine which are scarcely potent enough to produce the characteristic actions of the drug are still capable of influencing materially the action of the heart and of the vaso-motor system, reducing the number of the pulse beats and diminishing the temperature of the body. The characteristic feature in the record of experiments with doses under one grain of the extractive hypoxamine administered to animals is that the heart's action is during the operation of the drug persistently reduced, the pulse, not even during excitement, never rising beyond the initial point. It will be seen that in this respect doses of 1 grain downwards produce entirely different effects.
When 1 grain of ox
Bacillus staphylococci is administered to a full grown cat the first
symptoms manifested by the animal is dilatation of the pupils and
dryness of the mouth, nostrils and throat. The pulse persists for nearly
half an hour and then rises with a sudden bound to a
point about 240 beats above his
starting point. For more than
an hour it continues to rise and
then falls with a suddenness
almost equal to the change
already mentioned. After the
sudden elevation it continues
to rise by degrees till, in about
half an hour from the time of
the pronounced elevation the
initial point is reached.
From this beginning the temper-
atture falls and neither the
sudden rise of the pulse, the
accession of cerebral excitement
ment nor the equally sudden rise of pulsation, modifies their pronounced decline of temperature. The fall may be as great as 3° or.

The accession of cerebral excitement and mental ataxia, movements of motor paralysis is generally synchronous with the marked rise in the pulsations; the animal falls into a sleep which is frequently interrupted evidently by delusional or hallucinatory stimuli and on making vigorous efforts to run or leap, only succeeds in perfectly or rolls about in a helpless manner. The visible condition of the animal is at this period almost exactly what it would be if it were in a state of alcoholic intoxication.

The following table will show the simultaneous actions on pulse, temperature, and respiration.
of a 1 grain dose of the extractive

Table 2

Effect of one grain of extractive Hyoscyamine
upon a cat.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Temperature</th>
<th>Pulsations</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.99</td>
<td>100</td>
</tr>
<tr>
<td>10</td>
<td>0.97</td>
<td>100</td>
</tr>
<tr>
<td>20</td>
<td>0.99</td>
<td>100</td>
</tr>
<tr>
<td>30</td>
<td>0.96</td>
<td>100</td>
</tr>
<tr>
<td>40</td>
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<td>0.97</td>
<td>100</td>
</tr>
<tr>
<td>100</td>
<td>0.95</td>
<td>100</td>
</tr>
</tbody>
</table>

The following Table will serve to show the uniformity with which doses of this poison act upon animals. The similarity of the appearance presented by the two Tables is striking. On comparing them it will
be seen that in the one case the maximum elevation of temperature took place in 35 minutes and in the other in 34 minutes from the time of administration.

Effect of one grain of retroactive hypophyamine upon a fat
(Table 3)

Temperature

Pulse rate
The marked feature in the action of Extractive Hypophosphin is upon the pulse, when it is given in doses up to a grain, is that in the case of small quantities the pulse falls and remains below the starting point; in the case of one-grain doses it at first falls and rises about half an hour rises with a bound. When however more potent doses are given—quantities sufficient to produce all the most powerful actions of the drug—short of fatal dose the pulsations are found to be quickened from the beginning. In fact, after the injection of three grains under the skin of a cat great agitation at once ensues and the pulse is too tumultuous to be counted. When it becomes possible by the
quieting action of the drug itself to estimate the pulsations they are found to have risen about thirty beats per minute, and continued observation shows that they remain with moderate steadiness at this point for a period of about six hours. The respirations, at first exceedingly rapid, sank to 24 per minute, during the stage of complete prostration and simultaneously the temperature reached its minimum point which was 12.4° below that registered at the beginning of the experiment. This animal recovered and on the following morning the pulsations were found to have regained the point at which they were when the examination was made previously to the administration of the drug.
The following chart will illustrate these changes in a perceptible form.

Effect of three grains of Extractive Hyperparanime on a Cat

<table>
<thead>
<tr>
<th>Time</th>
<th>Temperature</th>
<th>Pulsations</th>
</tr>
</thead>
<tbody>
<tr>
<td>11:15</td>
<td>195</td>
<td>140</td>
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<tr>
<td>10:30</td>
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<td>120</td>
</tr>
<tr>
<td>9:00</td>
<td>160</td>
<td>105</td>
</tr>
</tbody>
</table>

The chart shows a decrease in temperature and an increase in pulsations over time.
This animal was under observation for 8 consecutive hours. In two minutes after the injection of the drug the pupils were fully dilated. The animal was much agitated. In five minutes the mouth and nostrils were dry and hot. In a quarter of an hour loss of muscular power became evident and the cat lay down upon the plaxa table. Almost immediately afterwards it crawled languidly towards the edge and fell over like so much dead matter. At times it attempted to walk but swayed from side to side and its attempts were short but frequently repeated. It showed great underestimation of distances and when it tried to reach for jump upon objects fell much short of them. There
was little or no sensory impairments till the narcotic influence of the drug had been fully established which occurred in about two hours after its administration.

Before the occurrence of narcosis the mental condition had been one of good-natured quiescence interrupted by little outbursts of excitement in which the animal made vague and impotent movements evidently instigated by some delusional notion or some hallucination. Even when subsequently the cat slept most soundly the sleep was broken at intervals by spontaneous movements and accompanied by short angry cries. At this stage sensation was dulled even during the intervals of excite
ment. So touch and to pain the animal was almost indifferent. For about two hours this was mental and bodily prostration. Continued and by degrees the cat became again more wakeful. Sleep was more easily disturbed and the spontaneous walking were more frequent. It was noticed in this instance as in many others that the animal when, at this stage, it attempted to walk, pushed itself backwards. It seemed that the hind legs were the most completely paralyzed part of the body. And that the animal in struggling to use muscular power pushed itself away from the point at which its paws were pressing with relative strength of impulse. I have seen this backward movement so strongly marked that
with an energetic show the animal has thrown itself over in a backward somersault. All the phenomena which have been mentioned I have frequently seen to be shown by man when under the influence of Hypoxyamine except this tendency to backward movement. This I have never seen, nor anything which would correspond to it.

This animal emerged gradually from its state of stupor and by degrees regained the use of its limbs after much ungraceful effort and numerous falls during its attempts to walk. Eight hours after the administration of the drug the cat was almost well and walked with moderate firmness but with a swaying carriage. On the following morning it was
well but timed.
Doses of Hyoscyamine which are sufficient to cause death have been frequently seen by me to act in two distinct ways. The first is by syncope, when the animal dies suddenly, probably during a struggle with the observer. In such cases the animal usually shows few symptoms of narcotism and, while medicated, has usually passed urine freely and frequently. In this class of cases the brain is generally somewhat anemic and the sinuses not unnaturally full.
The second mode of death is by exhaustion and coma most frequently after retention or more frequently suppression of urine. In such cases death is preceded by protracted heavy sleep, gasping respirations and a gradual
fall of temperature to the extent of about 10°. Post-mortem examination shows the existence of great engorgement of the cerebral sinuses; and the vessels of the brain are full of blood; at least in the neighbourhood of the membranes, though the brain substance itself may be.

The liver and kidneys are generally suffused with dark thick blood, and the bladder is not unfrequently empty.
I have tried to convey some idea of the facts which I discovered while making observations as to the effect produced on animals by different more or less powerful doses of extractive Hyoscyamine. I have still to speak of the action of frequent by repeated doses and of the physiological action on man.

I administered to a Rabbit one grain of Hyoscyamine daily for three weeks. Rabbits were found to have no exemption from the poisonous effects of Hyoscyamine and I have more than once known them to die from doses of about two grains. This rabbit h weekly one grain was given daily showed some noticeable divergences from the ordinary actions of the drug. The pulse rose persistently, the respirations
also rose, and the temperature without the exception of a single day was always higher after the ten than it had been previous to the administration of the first dose of the drug. The animal lost weight during the first week but subsequently worked its way up gradually towards its initial weight. At the end of three weeks the effect of isolated doses of 1 grain each was to raise the pulse 70 beats per minute. Their respirations also rose 12 per minute and the temperature was increased by 1.2° but it regained its starting point in 3/4 hours. The effects, in short, of one-grain doses after frequent repetition was found to be resembled in all respects except in the modifications of temperature, similar to those
produced by much smaller doses when administered to various animals. In reality there seems to be to a considerable extent a tolerance established, and I have had frequent occasion to observe that this also is the case when the drug is persistently administered to man. In the cases of men and animals from which I drew this conclusion there was no variation of results from cellularity or other inflammatory action.
When administered to man, extractive hyoscyamine has very pronounced physiological effects. The cerebral actions are either more early manifested than in animals or as perhaps is more probably the case, are more immediately perceptible. The dilatation of the pupils and the dryness of the mouth and throat are quite as pronounced as in the lower animals. With doses of two and three grains respectively the pulse had a maximum rise of about 20 beats and the temperature fell about half a degree. It will be seen that both these changes are much less marked than when the drug is given to cats and rabbits in similar quantities.

I believe that I was the first to take the extractive...
Hyoscyamine in such quantities as were sufficient to produce the full physiological actions of the drug. At first I took two grains believing that this quantity might be regarded as a small dose; after I had safely administered five grain doses to dogs. The first symptoms produced were dilatation of the pupils, dryness of the mouth and giddiness, all of which were observable almost simultaneously. I made a point of walking about the room without interruption and in exactly minutes from the time that the drug was taken I noticed that the pupils were still more dilated and that motion was impaired there was decided drowsiness. In ten minutes more motion was much impaired. For an
hour and a half the progress of peculiar symptoms developed itself in the following series: drowsiness, increased impairment of voluntary motion, slowness of articulation, intense dryness of mouth and nostrils, interrupted sleep, active dreams and involuntary exclamations accompanied by illusions of sight and paralyses of accommodation and followed by incoherence and aphasia. On this occasion it was impossible to take further reliable observations of the progress of the cerebral symptoms. During the following night, sleep was disturbed by dreams and by exclamations evidently meant as a response to interrogations which had only a subjective existence.
Next morning I experienced no disagreeable sensation beyond a glutinous stickiness of the mucous membrane of the mouth. The dilatation of the pupils continued for several days. Four days afterwards in order to test both the action and the safety of the drug previously to commencing a course of observations on the use of Extractive Hyoscyamine in the treatment of various forms of Insanity I placed myself under the care of two observers and took three grains of the drug. Dilatation of the pupils, giddiness, drowsiness, loss of motor power ensued as before. The voice became husky and there was interrupted sleep. In about an hour and a quarter after the drug was taken I was unable...
to walk without help even but throughout the course of the observation motor impairment was not so marked as it had been in the animals experimented on. During intervals of walking there were great incoherence and restlessness.

As I have had no occasion to hope, I shall never again, have to take such a large dose; I am not likely ever to administer such a quantity of the drug to any other person. I shall quote from the Fifth Volume of the West Riding Asylum Medical Reports in which, from my own recollection and the notes of others, I wrote of the symptoms produced after the development of maniacal restlessness. “During a long continued display of delirious excitement the pulse fluctuated irregularly.
between 104 and 120 the respirations fell to 14 and the temperature reached a minimum of 78.4° and a maximum of 79.2° in the axilla. During this stage of the action of the medicine the patient manifested all the symptoms of simple mania. He mislooked identities, spoke incoherently, acted irrationally, and was frequently under the influence of delusions and hallucinations. Early in this period there was marked paralysis of ocular accommodation. Chairs which were five or six feet distant were grasped as if within reach and repeated efforts were required to rectify the mistakes originating in the aberration of vision. The full cerebral effect of the drug was
Manifested two hours after administration. The first symptom was the inability to fix the attention on any given subject. The patient, though rising from his seat for a definite purpose immediately forgot what his own intentions were. He talked in incoherent snatches, and after commencing to express an idea passed suddenly on to the statement of another and apparently unconnected one which also he left obscure and unexplained. While under the combined influence of delusions, hallucinations of sight and paralysis of accommodation he attempted to step from a window about thirty feet from the ground stating that he was going out upon the causeway which was upon he was convinced, not on a level with the
window. He had numerous hallucinations of sight: A picture which under the influence of a delusion he had taken from the wall and placed on a sofa he in mediately afterwards sat upon in the belief that it was an embroidered cushion. He pointed to cats which he said were standing on their hind legs & making fantastie movements when no such animals were visible to others. Friends at a distance were spoken to as if sitting in parts of the room which were quite unoccupied. Female faces and heads were pointed at in the air as examples of perfect grace and beauty. The mistakes in identity were to complete that interrupted conversation was carried on.
with persons who had temporarily assumed the identity ascribed to them by the patient. During the persistence of these personal delusions, statements which were either unreservedly sincere or ludicrously inappropriate were freely elicited by suggestion. The patient several times changed his clothing with the intention of going out for special purposes to work, to walk, to dine but every new suggestion led to a modification of dress till actuated in a totally different manner he left his toilet in complete and directed his attention to new and equally absurd pursuits.

Latterly the motor in partment became less marked but the cerebral condition was characterized by greater incoherence in speech and
extravagance in action. The emotional condition was one of quiet satisfaction and comparative good humour. When the influence of delusions required the use of personal restraint, the patient met it more by illogical argument and expostulation than by force. The cerebral condition during the time following upon the short period of drowsiness was characterized by wakeful restlessness all, nine hours after the administration of the medicine, the patient in a comparatively brief interval undressed and went to bed. Throughout the night he experienced numerous hallucinations of sight. Snakes and other animals crawled on the bedclothes. Always the same.
itself by the hollows and elevations of the cornea but this delusion could be dispelled by mental analysis. The sides of the room appeared to form the two pages of a book separated by the intervening angle; and by the disturbance of vision it seemed to rest upon the bed and lie open before the patient; but after fixed attention the vision appeared to recede till the elements of the delusion were fully determined by their relation to surrounding objects. After a short period of interrupted morning sleep no traces of the operation of the drug remained except with dilatation of the pupils some dryness of the throat and slight cassitude. × × ×

Though during the greater part
of the time. Consciousness was not affected. scarcely a single incident anterior to the time of going to bed was remembered by the patient; neither could the events recorded be recalled to his memory by any attempt to associate the vagaries which he had forgotten with those of which he had a clear recollection. While the physiological action of the drug lasted there was free diarrhea but no vomiting or nausea.

In most of the cases in which I have witnessed in others the operation of doses of Extractive Hyoscyamine there has been more pronounced muscular helplessness than I experienced. Very soon after the administration of a three-quarter gram dose
to an adult man it was usual to see him in a state of complete prostration in which he is able to move his hands or his head to a very small extent while standing erect becomes an impossibility. This extreme prostration however is usually short lived in duration and the patient is soon able to make hallowing hallucinatory pickings at the bedclothes in his attempts to pick up delusional sheets of dust, or vermin. This is a very common form of hallucination. Or he may crawl around the room bent on a delusional search and quite neglectful of those who may be looking on. While the drug is in action the voice and method of articulation are peculiar. The patient may commence in a moderate
Strong but husky voice to answer a question but before he has proceeded many words it sinks gradually till it becomes inaudible. The speech is like that of a man woken from a drunken sleep. While the drug is in action both in men and in animals the emotional condition is one of great good humour and amiability. In a condition which is highly useful when thymamine is used in the treatment of aggressive forms of Mania.

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At Cameron of Lochgilphhead Kilmuir observes that the effect of the drug on excited Maniacs often resembles that of a glass of whisky on an irritable Scotchman.
There are two main points which require to be considered regarding the physiological action of Extractive Hyoscymamine. The first is the action on the Heart; the second, the action on the Brain.

My belief is that the main action on the heart of small doses of the drug is slowness produced by irritation of the Pneumogastrics distributed to that organ; and of large doses, first, slowness from irritation of the Pneumogastrics followed by great and sudden quickening resulting from paralysis of the inhibitory nerves to the atria and of the heart. The influence exercised upon the heart may be more complex, but I think that there is at least evidence for the belief that that primary irritation and secondary paralyses of the
Pneumogastrics occur.

The Cardiac changes produced by extractive hyoscyamine would be explicable by such a modification of the Pneumogastric distal function by whatever cause produced. I shall shortly point out that action of the pneumogastrics when an animal is almost recovered from a large dose of hyoscyamine throws the rapidly failing pulse suddenly up almost exactly to the point which had been reached during the period of the entire action of the drug. I shall show that direct poisoning of the isolated pneumogastrics with extractive hyoscyamine produces precisely the same action upon the heart as narcosis is produced by the constitutional administration of a large dose. I shall also be able to reconcile this action upon the pneumogastrics with the changes produced by the drug.
upon the pulse, respirations, and the temperature.

There is some difference of opinion regarding the interpretation of the fact that when the heart is acting quickly under the influence of the active principle of the myocardials, section of the pneumogastrics does not cause further acceleration. It is simply stated that as the heart is acting as much as it possibly can, section of the pneumogastrics can make no perceptible difference to it. As far as hyoscyamine is concerned, my observations militate against this view. In the use of large doses it is seen that the period at which the heart's action suddenly rises with a well-marked bound is not during or after the excitement of the administration of the drug but during the period when by
the accession of drowsiness the
hearts action would naturally
be lower than it had been at
the period of preliminary examin
ation and the time of the
Subcutaneous injection of the
drug. The precision also
with which the rapidity of the
hearts action returns to the
after section of the pneu
mogastries to the point which it had and
reached during the operation of
hyperamine points clearly I
think to the conclusion that
the pneumogastries are actively
affected by the medicine. It is
clear however that this precision
of recoil would be distinctly
in favour of the view that the
quickening of the hearts action
is independent of any influ
ence exerexised by the drug upon
the vagus of this maximum
always corresponded to the
highest rate of pulsations to which
the healthy heart could be urged. This however is not the case in animals labouring under the influence of hyoscyamine, that the preening of the isolated pneumogastric plexus should produce all the modifications of pulse, respirations, and temperature characteristic of the drug. Evidence that the vagi are specially singled out for as a field for the operation of the drug when it is constitutionally administered, and that the cardiac and respiratory movements are affected through palsy of their peripheries and not as a vague accompaniment of its constitutional action. It is highly probable that there is also a stimulation of the accelerator cardiac nerves during the first action of the drug and I believe that when the drug has been administered...
for a considerable time. To the same animal it continues to act on the sympathetic after it has ceased to act on the pneumogastries. In as much as after the administration of each dose to an animal which has been having repeated quantities for a fortnight the temperature instead of falling rises nearly a degree and the respirations also rise. The pulse, as in animals employed for the first time, rises considerably.

I represent in the following tables the effect of cutting the pneumogastrics in a rabbit rapidly recovering from the action of a low one-grain dose of Extractive Hypogastria.
Table 5.

Showing the effect of one grain on a rabbit and the effect of cutting the Pneumo gastrics when the action of the drug has begun to diminish.

<table>
<thead>
<tr>
<th>Time</th>
<th>Temperature</th>
<th>Pulsations</th>
</tr>
</thead>
<tbody>
<tr>
<td>11:30</td>
<td>102.5</td>
<td>200</td>
</tr>
<tr>
<td>11:40</td>
<td>102.5</td>
<td>195</td>
</tr>
<tr>
<td>11:45</td>
<td>101.5</td>
<td>190</td>
</tr>
<tr>
<td>12:00</td>
<td>101.5</td>
<td>195</td>
</tr>
<tr>
<td>12:25</td>
<td>99.5</td>
<td>190</td>
</tr>
<tr>
<td>12:45</td>
<td>98.5</td>
<td>185</td>
</tr>
</tbody>
</table>

Temperature  Pulsations
Showing the action of one and a half grains on a cat and the effect of cutting the stomach after the effect of the drug has begun to pass off.

Table 6.
Table 7.

Showing the action produced by smearing the isolated pneumogastrics with retroactive hyoscynamine.

<table>
<thead>
<tr>
<th>Dose</th>
<th>Temperature (°F)</th>
<th>Pulses</th>
</tr>
</thead>
<tbody>
<tr>
<td>27.0</td>
<td>185</td>
<td>102</td>
</tr>
<tr>
<td>26.5</td>
<td>180</td>
<td>101</td>
</tr>
<tr>
<td>26.0</td>
<td>175</td>
<td>100</td>
</tr>
<tr>
<td>25.5</td>
<td>170</td>
<td>99.5</td>
</tr>
<tr>
<td>25.0</td>
<td>165</td>
<td>98</td>
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<tr>
<td>24.5</td>
<td>160</td>
<td></td>
</tr>
<tr>
<td>24.0</td>
<td>155</td>
<td></td>
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<tr>
<td>23.5</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>23.0</td>
<td>145</td>
<td></td>
</tr>
<tr>
<td>22.5</td>
<td>140</td>
<td></td>
</tr>
<tr>
<td>22.0</td>
<td>135</td>
<td></td>
</tr>
<tr>
<td>21.5</td>
<td>130</td>
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</tr>
<tr>
<td>21.0</td>
<td>125</td>
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<tr>
<td>20.5</td>
<td>120</td>
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</tr>
<tr>
<td>20.0</td>
<td>115</td>
<td></td>
</tr>
<tr>
<td>19.5</td>
<td>110</td>
<td></td>
</tr>
<tr>
<td>19.0</td>
<td>105</td>
<td></td>
</tr>
<tr>
<td>18.5</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>18.0</td>
<td>95</td>
<td></td>
</tr>
<tr>
<td>17.5</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>17.0</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>16.5</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>16.0</td>
<td>75</td>
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<td>15.5</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>15.0</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td>14.5</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>14.0</td>
<td>55</td>
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<td>13.5</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>13.0</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>12.5</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>12.0</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>11.5</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>11.0</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>10.5</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>10.0</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>9.5</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>9.0</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>8.5</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>
The observations recorded in the first two of these tables were undertaken to determine whether cutting the pneumogastriæ when an animal was fully under hypnogenic amine would lead to further acceleration of the heart's action. As it is quite impossible to know definitely at what stage the heart has reached its maximum activity, I considered it best to wait till a decided fall in the number of pulsations an indication was afforded that the influence of the drug was beginning to pass off. Then by cutting the pneumogastriæ I could observe to what extent the pulsations returned towards the maximum which they had reached during the action of the drug. In the first two
Stance; the pulse immediately after section of the pericardium,
gastrics had never till it was within 10 beats of the highest
pulsation recorded during the operation of the drug.
In the second instance it rebounded to within 10 beats
of the maximum record, but may at first have been higher
because 10 minutes elapsed before the pulsations could
be reliably counted. One cannot expect that the pulse
after section of the pericardium gastrics will rebound com-
pletely to the maximum
point because during the prolonged operation of the
drug both the sympathetic
and the substance of the heart
are more or less exhausted by
the strain known upon them.
I do not claim that
the observations recorded
in the first two of these three tables are given themselves conclusive evidence that the pneumogastrics are specially acted upon by hyoscyamine but taken in conjunction with that recorded in the third of these tables (No. 9) I think they can leave no doubt that the pneumogastric distribution controlling the action of the heart and lungs is powerfully acted upon by the drug to an extent which accounts for almost all the modifications of respiration and temperature produced by the drug. Nothing could be more striking than the resemblance between the changes following on the administration of one grain to a cat and those produced by Smaeury the isolated pneumogastrics.
with solution of hypseyamine.
In both cases the pulse rose with a bound through about which left it about 100 beats higher than before. In both cases this rise was followed by a fall of from 65 to 75 and the fall was succeeded in both instances by a secondary rise. In both cases the temperature fell during the first hour close upon 3°.

The action of the drug upon the respirations and temperature confirm the impression that the pneumogastrics are powerfully affected by the drug. This is best seen when large doses are administered. Such doses as that given to a dog (Tables III and IV) produce the same effects upon the number and nature of the respirations as section of
the vagi. The respirations are diminished in number by one half, they are deep, jerky or heavesy and marked by diaphragmatic in inspiration. The expirations are short and followed by a long pause. If in an animal under the influence of a dose sufficient to produce this effect on the respirations the vagn are cut an addition the consequences is only to intensify the condition and to kill the animal sooner than would have been the case if the vagn had been cut in an animal unaffected by hyoscynamine. The marked and persistent decline in temperature is also an evidence of the affection of the vagn explicable by the great unipediment which paralysis of the pneumogastrics places in the
way of the proper arteriolarization of the blood.
I think I am justified in concluding that the most important action on the heart and the mechanism of respiration produced by the extractive hypsoeramine is that which is brought about by (1) irritation and (2) paralysis of the peripheral branches of the pneumo saphes functionally connected with them.
Dilatation of the pupils is much more rapidly and decidedly produced by the tractive Hyoscyamine when administered internally than when applied locally. The dilatation is neither prevented nor removed by Calabar Bean. The alvine and urinary excretions of an animal under the influence of the drug produce dilatation when applied to the eye of another animal but the liquor amnii does not and the drug does not affect the foetus in utero. One seventh of a grain was found to produce cerebral symptoms and motor helplessness in pigeons but neither dilatation of the pupils nor dryness of the mouth was ever noticed in these birds though they were
carefully looked for.

It was determined that the motor nerves were
especially affected as was
proved by the fact that an
animal to which a sufficient
dose had been given retained
power longer in a limb of
which the femoral artery
had been tied than it did in the limb of the other
side.

In proceeding to speak of the action of Extractive
Hyoscyamine on the central
nervous system it may be
stated generally, that the drug
acts powerfully as a delirio-
narcootic. In small doses
drowsiness may be the only
condition induced though
as a rule this drowsiness
is accompanied by a slight
disturbance of ideation amount-

ing...
to dreaminess and transitory delusions. Usually also this condition is associated with restlessness and a feeling of muscular inactivity and weariness like that experienced after prolonged and severe exercise. If a larger dose is administered sleep occurs almost at once and as a rule is not prolonged and a short period of repose is followed by a succession of delusions and hallucinations alternating with periods of drowsiness and slumber. The condition is one of exactly resembling Simple Mania with motor more or less motor inactivity super added. At the same time the voice is husky and sentences properly commenced cannot be successfully finished. This peculiar mode altogether cessation of speech is not due...
to drowsiness, as it is sometimes very marked during periods of active wakefulness. It seems to be a combination of ataxic and amnesic aphasia.

During the action of the drug, the mental condition is one characterized by good nature and sometimes hilarity, and the tendency to loquacity contrasts strongly with the inability to maintain conversation. I have frequently caused patients to speak by inducing in them the action of extractive hyposy or acute dementia had not been heard to do so for prolonged periods; and in some cases, by breaking the spell of silence, have induced them for a time, at least to resume this the fraction of speech.

I make no attempt to explain
the method in which the drug produces these marked mental changes. When so much doubt exists regarding the manner in which normal ideation is associated with normal cerebral changes it would be futile to speculate as to the modes of operation of this artificial modification of intellectual life. Consequently I shall proceed to speak of the result of my investigations in their bearing upon the treatment of various forms of Insanity by Extractive Hyoscyamine.
Thesis
by
Robert Lawson M.B.

Part II

Therapeutic Actions of Intrauterine Hypoglycemic
In the London Practitioner for July 1876 I published "A contribution to the investigation of the therapeutic actions of Hypocyamin." This paper was devoted to the statement of the effects produced by the drug in the treatment of recurrent, acute, and chronic mania, monomania of suspicion, and the excitement of senile dementia. Illustrations were given of the good results obtained by the administration of extractive Hypocyamin in one grain and one and a half grain doses in cases of these forms of mental derangement. Special attention was paid to the observations which were recorded in that paper to the
section of single large doses and it was stated that: "in about fifteen minutes the most violent and excited patient can be thrown into a comparatively deep sleep by about one grain of the amorphous alkaloid (which would be equal to about one-quarter of a grain of the present perfect specimen of the drug). And on waking from his slumber almost invariably frees him self—also from the delusions and hallucinations which have bewildered him."

In that paper the usefulness of the drug in what is everywhere known as "refractory cases" in which the voluntary perpetuation of injury to persons and property is a common accompaniment of or probably a direct result of the insane condition was strongly commented on and
the subsequent observations made by myself and others have confirmed in my mind the belief that in extractive hyoscynamine we have a drug to which no other drug can approach, for usefulness when the arrest of such cases is aimed at. It was said that there is one class of cases of mania in which hyoscynamine is particularly useful. In the refractory wards of an asylum outbursts of excitement are constantly manifested which present more of the features of voluntary abandonment to angry passions than of pure insanity. Such patients are very aggressive, very loud in their denunciations and very destructive of clothes and furniture. To such a patient a one-grain dose (one-quarter grain 1
The present preparation of Hyoscyamine is a very ready and serviceable means of treatment. The violence and the alarming manifestations of muscular force which precede the administration of the medicine stand in very strong contrast with the helplessness, the absolute and conscious impotence which follow shortly upon its exhibition. The vigorous rupture of rugs is succeeded by involuntary twitching of a superlative heroic character. The mind directed from the stimulation of surrounding excitants is fooled by delusions and hallucinations which the limits are too weak to take action on and a period of oblivious sleep is followed by a tendency...
not to waste energy on the annoyance of others but to count the most absolute retirement or inaction. The sensations produced by the immediate action and after effects of the drug are such as to lead the recalcitrant lunatic to exercise a certain amount of self-control in order to avoid the employment of what such patients speak of as "the silly medicine." Many circumstances render such cases the most suitable ones for the use of the drug. Such patients are usually in robust health, have been eating well and are not likely to suffer much from a temporary derangement of digestion and none feel more keenly the inconvenience of being reduced to a state of helplessness."

* p. 136 for further discussion of this subject.*
Subsequent experience made me more certain than I then was that this primary prostration produced by hyoscynamine and which was stigmatized under the name of "chemical restraint" was very frequently followed by partial or complete recovery from Insanity. In this first contribution to the therapeutics of ataractic hyoscynamine I also dwelt especially upon the value of the drug as a means of treating patients labouring under recurrent or constant symptoms of mania with suspicions of a delusional nature; so that I am of opinion that from the beginning I selected for treatment the cases which my own observation and the more prolonged investigations of others showed to be most amenable to successful treatment by this drug. I lay great stress on this fact and cannot too strongly repeat th
Statement that it is in cases of these two classes—the one in which there is a tendency to preventible mischief, and the other in which violence is apt to originate—chronic, delusional suspicions, that the Extractive Hypoxyzamine is and will be found to be most useful.

In this paper also I pointed out the disadvantages associated with administering the drug to cases of furious, or what is sometimes called acute delirious, mania: so that in my first series of observations I differentiated two important classes of cases in which extractive hypnoxyzamine was found to be useful and one class in which it was liable to be prejudicial.

At this stage it may be useful to examine into the significance of two objections which have been raised to the use of narcotics in the treatment of lunacy. The first is that
which is significantly embodied under the phrase "chemical restraint"; the second is that the constant or frequent use of stupefying drugs for the suppression of excitement is greatly productive of consecutive dementia. Now if the prostration of a violent lunatic by drugs is in itself and absolutely an objectionable measure, then the administration of hyoscyamine in large single doses or in such objectionable; for nothing could more complete than the absolute prostration produced by that drug. But I do not think that anyone will be found to support so extreme a view as would be embodied in the assertion that nothing would justify the employment of that "chemical restraint" which peremptorily overpowers a dangerous lunatic. Surely a fairly definite prospect of even a temporary arrest of serious excitement would not only
justify the employment of either chemical or physical restraint. In fact no argument could in such a case be advanced against chemical restraint which could not bear with equal validity be advanced against fixing an insane patient in bed to prevent him retarding or preventing recovery from a surgical injury or operation. The aim of an asylum physician should be to apply the means best fitted for the restoration of his patients to reason and there could in my opinion be nothing more illogical than to denounce the use of strong narcotics in the treatment of Insanity simply because they are strong narcotics. It would be quite as reasonable to object to the employment of spirits in the treatment of fractures because they enforce upon a limb an approach to absolute rest.
Consider the argument more valid which would suppress the employment of strong narcotics because they are liable to gross abuses. The major part of such an argument is one could be advanced against the use of many of the most valued articles of the pharmacopoeia, but surely one is not assuming too much when he trusts that physicians in asylums will endeavour to qualify themselves in the employment of any therapeutic agent so as to be able to secure its benefits and minimize its prejudicial qualities; and if it is further advanced that strong narcotics may be abused so as to suppress that excitement which they are not qualified to cure I distinctly decline to receive without definite evidence a statement which is labelled in the highest degree ungenerous.
With regard to the second argument so often brought against the use of narcotics in asylum practice, namely that it leads to a great amount of consecutive dementia, I would remark that if the supporters of this charge could assert that the treatment of excitement by narcotics was followed by dementia and that the course of excitement without narcotics was followed by none they would have a strong case. But surely those whose knowledge of Insanity rests upon a physiological basis will readily admit that any kind of excitement is more likely to lead to dementia than any kind of rest and that the continued excitement of a maniac representing as it does the continued waste of imperfect renewed brain elements is the most likely of all things to lead to consecutive dementia.
The onus of proving that the continuous use of narcotics increases this physiological tendency to dementia rests upon the accuser and on the other hand, the physician who by the use of a powerful narcotic subdues the mania and brings his patient round without impairment of his mental faculties has not only cured the excitement but has counteracted one of the most direct effects of excitement, the tendency to dementia. Those who advance this view about the mental impairment produced by narcotics do not specify the method in which the impairment is produced. They cannot believe that the bad effect is produced by the withdrawal of the brain from active ideation, from volition or involuntary agitation. So they [then] hold the idea that the dementia is produced by
direct action of the drug upon 
the brain tissues. If they do 
so they must certainly exclude 
from their index expressatories 
the important analgesic-narcotic 
opium or much demonstrate 
the existence of Dementia in 
two of our greatest men who 
are not surpassed for that 
subtlety of thought and 
language which is usually 
regarded as being at the 
opposite extreme of mentality 
from that at which dementia 
rests. They must exclude 

d'e Quinsey and Samuel Taylor 
Coleridge among the number 
of those who should be regarded 
as drug-made dements, for 
without doubt they consumed 
more opium than is usually 
administered to the most violent 
manie or the most agitated 
Melancholie.

I cannot see therefore that there 
is any more reason for exclud
extractive hydrocyanic acid from the
pharmacopoea of all nations
simply on the ground of its
potency than there is for forbidding
the use of Hydrocyanic Acid,
Aconite, Strychnia, 
Staphyria on
the same grounds. If the
drug can be shown to be
beneficial it is all the better
for being potent; but those who
employ it must make themselves
all the more certain of its
properties and of the cases in which
it is likely to be beneficic in
directing its benefit. It may also
be added that anyone who would
venture to employ a drug which
himself or others had found
useful simply because he dis
approved of the theory upon
which it was supposed to act
has yet to acquire the first element
of scientific method— that which
authoritative subordinates the
mode by which an end is attained
to the attainment of the end.
the one being an indubitable phenomenon, the other a meta physical diagram.
In the Sixth Volume of the West Riding Asylum Medical Reports I published a second contribution to the Therapeutics of Hyoscyamine. In that paper I related the results of my employment of extractive hyoscyamine in single and continued doses in Manic with delusions of Suspicion, in simple and recurrent mania in Manic with Logomania and in cases characterized by apparently involuntary or at least uncontrollable destructiveness of clothing. I also referred to its use in the Epileptic Status, and in the excitement of General Paralysis. I have reason to believe that in no class of cases with the inception of refractory patients whose violence is more or less voluntary and controllable is extractive hyoscyamine more useful than in the excitement of General Paralysis of the Insane.
Paroxysms of excitement which occur during the progress of that malady are of the most absolutely fatuous nature. In one form of mania is the reason to completely destruendo. The patient is aimlessly restless,racklessly destructive and seems absolutely oblivious of the phenomenal world and completely absorbed in a delusional existence. Such paroxysms of excitement when left untreated almost invariably leave the patient more demented than he had been and in fact constitute well marked stages in the progress of the malady. The following instance shows that these paroxysms may be successfully treated with extractive hypnotamine:

For a whole month the patient had been excited and restless and though means were employed to subdue his excitement he had had only short snatches of
sleep. In the intervals he was employed in tossing about, re-
arranging and tearing his bedclothes and in soiling the
walls and swabbing the floor with his excretions. After three
repetitions of a 1/4 grain dose of
extractive hyoscyamine (1/10ths of the present preparation) even
on alternate nights his excitement was completely removed.
He also became clean in his habits, had been there remained
well and was transferred
to a quiet and comparatively
comfortable ward where he
remained pleasantly for many
months.

In this second contribution another
class of cases of Mania was
referred to for which extractive
hyoscyamine is a most useful
remedy. These are cases of
logorrhoea in which patients
cause disturbance and dis
order by their incessant worrying.
conversation. I had frequently seen a large single dose equal to one quarter of Marchi's present preparation throw off a headache of this kind or materially add to the dose of a patient who had been continuously talkative much more reticent and much more industrious than he had previously been. For an instance of this kind I may refer to page 177 of the West Riding Asylum Medical Reports Volume vi. The patient referred to in that record has been frequently seen by me and I have always found him more rational and reticent than he had been before the administration of this his only dose of the medicine. In administering extractive hyoscyamus at first I endeavoured to select such cases as could be scientifically regarded as best cases namely such as had for sometime been uninterrupted characterised by the features which I proposed
to remove by the administration of hyoscyamine. In the paper above quoted I referred to a patient who in his second attack of insanity had been very violent and destructive for a fortnight before and three days after admission and to whom 1/4 of a grain (1/60th of the present preparation) were given. He had almost succeeded in strangling himself. After a single dose he was perfectly quiet and rational, was employed in the kitchen and was discharged recovered six weeks after his admission, having exhibited no appearance of insanity after the first four days. This was not an alcoholic case.

The employment of any extractive hyoscyamine has met with unmerited reproach from on account of some observers
having administered the drug in a class of cases in which and in full doses which were from the beginning shown by me to be susceptible to the influence of hyoscyamine. My subsequent experience and that of others indicate that in excitement associated with shock, in that of locomotor ataxy associated with cerebral symptoms and in the form of disease which is generally called acute dementia but which is in reality more allied to catalepsy than dementia, Extractive Hyoscyamine instead of being productive of benefit is apt to lead even when it is administered in small doses to alarming prostration. My experience in connection with this class of cases has been such as would lead me to discourage strongly the employment of Extractive Hyoscyamine in the treatment of them.
The following case will show the activity of the drug and also the rapidity with which alarming symptoms pass off.

N.B. had been in a state of acute dementia for eight months in which she had rarely spoken. She hung about the day-room and corridors in an aimless manner and the saliva dribbled from her mouth perpetually. It was at first thought that a small dose of extractive hydrocyanic acid would break the spell by which she seemed to be bound and by inducing her to talk might lay the foundation of permanent improvement. She had hypodermically a dose equal to $\frac{1}{52}$ of the present drug and she talked a little, expressing principally a desire to go away from the institution. After the third or fourth injection of this dose she at first became very restless and excited and afterwards fell into
a very prostrated condition. She was comatose and her pulse was feeble and so quick as to be uncountable. In this extreme state she remained for over an hour when her sleep became gradually less profound her pulse slackened and gained strength, she again became very restless and erect, talked a good deal and her sleep naturally. Next day she had resumed her old condition of total dulness, silent dementia with beneficial effect having been produced on her mental state. It is worthy of notice as a remarkable fact and one which may explain the dulness of acute dementia and the physiological cause of the production of the dryness of the throat and mouth by hyposeyamine that the dulness of solva continued unabated during the progress of the activity of the drug though the action of hyposeyamine was perhaps more profoundly induced in this case than in any instance
which has ever been under my observation. The continuance of the
dribbling in this case points to the
opinion that the state of the mouth
and throat in both acute dementia
and the action of hyoscynamine is
not due to local causes and that
the central pathological condition
present in acute dementia is not
one which is likely to be counter
acted by hyoscynamine. Stavuy
has also observed this potent action
of the drug in cases of chorea,
and Aubertes expresses his expe-
tence in the following words.
"In the case of chorea my exper-
ience agreed with Dr. Lawson's: the
even half of a grain produced
most severe symptoms and caused
me great alarm." (On the
Treatment of Insanity more especi-
ally by Drugs p. 26.) I am disposed
that it should be understood that
an excitement associated with
acoemotor alaxy & chorea and in
so-called Acute Dementia Sabsou
hyoscynamine should never be used.
In his second contribution to the Therapeutics of Hypnoamine I was able to advance still stronger evidence of the value of the extract in the treatment of aggressive and almost voluntary excitement. I recorded one case which as it appears to me to fulfil every requirement of scientific demonstration I am induced to reproduce. This patient was admitted in July 1875 and up to January 1876 his history in the refractory ward of the asylum was one of almost continuous excitement, pugnacity, violence and destructiveness. It was at first believed that he would turn out to be a General Paralytic and he was literally treated with Calabar Bean and at his excited times with large doses of Chloral—sometimes as much as 145 grains. This diagnosis was at first and he was soon recognised to be a simple maniac with exalted delusions. In the
beginning of January 1876 after a six months course of unsubdued excitement he had one grain of hypodermine (equal to a quarter grain of Mercuri’s present perfected preparation). In a quarter of an hour he was asleep. For several hours his sleep was profound and subsequently he was for some time either in the same condition or during intervals was awake but helpless. On the morning of the second day after the administration of the dose he was quiet and rational and remained quieter ever afterwards and soon requested to be removed from the refractory ward and employed at his own trade as a mechanic. His wish was gratified and for several months he made himself exceedingly useful, and showed no trace of excitement and while laughing at the tentative suggestion of
of his exalted ideas he expressed his conviction that he must have been very bad and was willing to work under supervision till his cure was regarded as complete. He was discharged recovered on August 8th 1876. He had only one dose of the active hypsizygamine and the protracted period of convalescence was considered advisable on account of the excessive gravity of his former condition previous to the administration of the drug. On account of his own anxiety to have his recovery absolutely secured.

The conclusions at which I had arrived when in 1876 I published in the West Riding Asylums Reports the result of my observations on the therapeutic employment of hypsizygamine in Asylums were that in single large or repeated small doses it was especially useful in cases of mania...
of which violence and destructiveness, apparently voluntary were a decided feature; that it was useful in subacute and chronic, especially, recurrent Mania with delusions of Suspicion in the excitement of General Paralysis of the Insane; that it required to be used with great care in the excitement of Chorea or of Locomotor Ataxy and in any form of disease in which any senile forms of excitement much vascular degeneration might be suspected; that it was inadmissible generally in acute especially delirious Mania.

The observations which I have since then been personally able to make and the communications which I have received from others from who have employed the drug widely in English and Scotch Asylums have convinced me that there is but little to add to or withdraw from these early
propositions but as I have already stated I am now so fully convinced of the prejudicial action of extractive hyoscynamine in the excitement associated with choreag locomotor ataxy & in so-called acute dementia that I would strongly recommend that the drug be never administered to patients suffering from these maladies. In the excitement associated with epilepsy, however though I have great reliance on the liberal administration of para liebreich's chloral in controlling that disorder, extractive hyoscynamine will, in cases in which chloral may be inadmissible be found to be highly useful. It is absolutely necessary however that all who on my previous or present recommendation desire to try the usefulness of the drug should very clearly apprehend three things 1st that I always have employed Merck's extractive
hyposyphamine, that the perfection of the process of manufacture and the result of a gradual diminution of the dose during the course of experimental research have led me to the conclusion that all the good effects produced by extractive hyposyphamine can be obtained by doses equal to one-fourth of those originally given by me: Also that Merck has stated that the extractive hyposyphamine now manufactured by him "may be considered as of the utmost purity such a form can be brought to."

I consider therefore that the proper dose of Merck's extractive hyposyphamine is and should continue to be from \( \frac{1}{16} \) th to \( \frac{1}{8} \) th of a grain when subcutaneously given hypodermically and \( \frac{1}{8} \) th to \( \frac{1}{4} \) th of a grain by the mouth, and that these doses may be repeated not more than twice in twenty-four hours. I would also recommend that the drug
Should if possible be given as to be absorbed with a meal and that if it is absolutely necessary to administer it to a patient who has not had food for some time the dose should be somewhat diminished.

A formula which is suitable for either hypodermic or oral use is

Extractive Hyoscyanine (Murchison)
Ether n. 100
Alcohol n. 10
Water ad n. 10

M. (Dose from 3 to 12 minims)
Dr. Prideaux, Assistant Medical Officer at the Friends' Retreat, York, published in the Journal for September 27th and succeeding numbers some interesting observations on the use of extractive hyoscynamine in the treatment of Insanity. In almost every respect he was able to confirm the conclusions to which I had previously come. Both he and Mr. Swanson of York had numerous cases in which the drug was employed with marked benefit and in doses much smaller than those which I had used. One of Dr. Prideaux's cases shows that the extractive hyoscynamine when administered simultaneously with other sedatives surpassed them in the alleviation of the symptoms of mania. It is reported by him as follows.

Mrs. aged 29, admitted on November 19, 1878. She had been ill for three days and her condition was far worse than on either
of the two previous occasions. Her temperature was 100.2°.
She was much excited, crying, laughing and talking in a wildly incoherent manner. Her
skin was flushed, hot and dry, with a rapid pulse. She remained up to Dec. 20, 15 days without
any improvement. She had become much fatter, very
difficult to feed, wildly maniacal and very violent. On that day
she was much excited had had
very little sleep for three nights
and none at all the previous
night, in spite of comparatively
large doses of chloral and
bromide of potassium. Namely,
from xxx of each, whilst opium
made her far worse. She was ordered 40th of a grain of
hyoscynamine early in the
afternoon. After its admin-
istration she was still excited
for a short time but in half
hour time went to sleep
and slept for two hours. She woke up much quieter. At night she had 20 grains of chloral, and passed a quiet night and slept for two hours.

The following morning she was again excited but a dose of 1/6th of a grain of hyoscyamine gave her again two hours sleep in the afternoon. At night she had 30 grains each of chloral and bromide of potassium but although quiet had no sleep. On the 21st as the hyoscyamine seemed to have given her sleep and rest then nothing else would she was ordered 1/6th of a grain twice a day at 2 p.m. and 9 p.m. with the result that she slept two hours with the first dose and four hours after the second at night twice as much sleep as she had had any night since her admission. On
the 5th she was much quieter and decidedly improving, showed
hands and for the first time appeared to have some idea
of where she was. During the
afternoon and night with the
two doses she slept 7 hours. The
treatment was continued and
every day she gradually im-
proved. She was quieter took
food better and had from six
to eight hours sleep. On the 8th
1/6th of a grain of hyoscyamine
was given 3 times in the 24
hours once in the afternoon and
twice in the night if she
awoke early. It was found
that a certain amount of
tolerance had been established
and that one dose at night
was not always sufficient.
With this increase the patient
slept well every night. She
was quiet, took her food well
gave little trouble, was com-
paratively lucid in her con
Vernation and improved in every way. The treatment was continued and as it was found she slept so well at night with the two doses of Hyoscynamine the afternoon dose was omitted. She progressed very favorably and on Dec. 16th had become perfectly rational in her conversation, and from that time convalesced rapidly and returned home recovered.

A case of Mania with delusions of suspicion and special hallucinations, treated by Dr. Swanson reached an equally successful issue. Previous to his treatment with Hyoscynamine he had been otherwise dealt with, from the 22nd January to the 17th of March. Up to that date he had not improved and 1/20th of a grain of extractive Hyoscynamine was administered to him. In about an hour he became much excited and
said he had been poisoned. He could not stand & his pupils were considerably dilated. Three hours afterwards he was quite quiet and composed, had lost all his delusions and conversed in a rational manner. One-sixteenth of a grain was then ordered to be given every three hours. On the 13th after four doses he was slightly incoherent but made no reference to his delusions. On the 13th the treatment was still continued; still improving; traces of former delusions; complained of dryness of throat. On the 22nd he was somewhat depressed, slight traces only of his delusions still existing. On April 2nd the treatment was still continued, delusions had entirely gone and from this time he rapidly improved and became convalescent."

Dr. Prideaux reported that his experience of the drug in a large number of cases seemed to him
to justify his coming to a series of conclusions virtually the same as those at which I had arrived and which I have earlier in this essay recorded.

My published observations attracted the attention of practitioners not engaged in asylum practice and some physicians had the interest to employ the drug in what seemed to be suitable cases.

At renewal of Knottingley writing to the Lancet of July 1876 it is stated that having seen an article in The Practitioner of July 1876 having a case of mental derangement accompanied by fits of violent mania he determined to give hyoscynamine a trial and one draught proved so efficacious that the patient was very quiet for some months. Sometime afterwards having a case of hysterical convulsions in a young girl which increased in violence to such an extent
as to make it almost impossible for any number of people to
be able to manage her notwithstanding the administration of
the largest dose of chloral & which
Percival
did and even gave a similar
draft and with such good
results that she has never had
another fit since.
Dr. J. G. Sinclair Coghill of Ventnor,
apparently confounding the extractive
hyoscyamine used by myself and first
spoken of by me as the amorphous
alkaloid as distinguished from the
crystalline forms of hyoscyamine and
some of the latter preparations expressed
astonishment that S. Percival could
have safely given such large doses
as one grain (equal) to 7/4 grain of
Merck's present manufacture. But
in a later letter (Augt. 3 1878) Dr. Coghill states
that though alarming symptoms were produced in a female patient
suffering from Mania by the
administration of a half grain
close yet he was so much encouraged by the ultimate results of the hypopyraine treatment in this case that he would not scruple to employ this powerful remedy. Stoghill's communication induced me to write to the Lancet pointing out plainly the distinction between the amorphous alkaloid which I had all along used and the crystallised hypopyraine which after several observations in which it was employed was abandoned as being at that time unreliable. I do not think however that if my papers had been read with reasonable care any confusion should have arisen as to the difference between the drug used by me and the crystallised form as I specify both in the Practitioner for July 1876 and in Volume 17 of the West Riding Asylum Medical Reports that the drug I employed was an amorphous form manufactured by Merck. In the latter paper
I contracted (page 82) the amorphous form with the Sulphate in such a manner as could leave no reader in doubt.

In the communication to the Lancet for Aug. 31, 1878, I also gave an illustration showing how much the potency of the drug was influenced by the character of the mental malady which it was used to counteract. I had administered from the same bottle and almost simultaneously a quarter of a grain of hyoscyamine to each of two patients. In the one case there ensued complete freedom from long continued and destructive excitement, followed by quiet sleep in which the pulse remained regular and normal in rapidity. The ultimate result was the continuance of a state of quiescence for several days. In the other case there was much frustration accompanied by occasional outbursts of restless excitement which after a time...
were followed by prolonged sleep. No bad consequences ensued, the patient having resumed her usual state on the day of administration. The first case was one of pure mania; which in the second was one of acute dementia (so-called) in which there were frequent repeated attacks of mania. These last observations have led me to conclude that hyoscynamine is not commendable. I have already referred to this subject.
Thesis by
Robert Lawson M.B.

Part 2
Therapeutic Actions (Cont.)
In July 1879 Dr. G.H. Savage, Medical Superintendent of Bethlehem Hospital, published in the Journal of Mental Science a paper which was read by him before the Medico-Psychological Association. In this paper he recorded the results of his experience of the products of Hypocyamine, as given in the form of Merck's Extractive Hypocyamine. His observations with Hypocyamine were not such as encouraged him to continue to use it. His opinion of Merck's Extractive Hypocyamine may be gathered from the following sentence in his paper: "In the whole I like the drug as a producer of quiet, without much injury to the patient as well as of can like any medicinal Rehaut." The result, he says, of my present
Present experience, more especially in acute manic-depressive cases is that the extractive is the most potent form of the drug and is useful as a means of quiet restraint in violent and dangerous cases, especially those that are very homicidal and that seeming to have lost common sensibility dash themselves about and run serious risk of injuring themselves. Again "I believe the drug to be useful in violent recurrent cases such as Dr. Lawson recommends it for." Dr. Savage adds "I dislike the Crystalline Hyoscyamine in many particular cases which it has & found the Tincture of Hyoscyamus to be nearly useless." Considering that Dr. Savage in the cases which he quotes namely one of acute mania with in temperance & two of acute Mania administered the deep-oxidated
to deal with instances in which I would not have recommended the drug at all. Certainly I would not have employed it in the cases and remembering in addition that Dr. Savage does not "consider any of the above-named drugs as curative in any sense" that his "feeling is strongly against all nauseotics and most so called nerve drugs" in his opinion of their capabilities of Enafracting hyspsy may be interpreted as amine Routhe regarded as not being on the whole favourable to the drug, that he disapproves of it on a principle which he had formed before employing it.
It was somewhat unfortunate that during 1878 when the demand for
extractive hyoscynamine had
been much increased, mainly by
the publication of my observations
of its usefulness a supply of
the drug was imported which
was either comparatively inert
or different in its action from
what had already been investigated.
It Prudeaux was most active in
drawing attention to this fact and
his energy has been the means
of stimulating the manufacturer
to a more uniform and to all
appearance a perfect manufacture
of the drug. It Prudeaux
wrote on September 11, 1878 that
he had found a grain of a
recent preparation to kill a
rabbit in 30 minutes and for
the last ten minutes "it was
in violent convulsions and
one of which it died." He found
that the sample referred to had
not nearly the same power

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as former ones in producing dilatation of the pupil and that though it produced a certain dilatation of the corneal pupil its effects in that respect were not equal to those formerly manifested. These features point to the suspicion that the preparation was most notably not the extractive form of hyoscynamine at all but rather the Hyoscynamine distillation which Harnack describes as being a pale yellow movable fluid having a pleasanter smell than the extractive consisting of only a very small portion of Hyoscynamine in an extract form. Such being the case administering about 20 mgs of this distillate of Hyoscynamine to frogs brought on convulsions a phenomenon which had not been produced by 20 mgs of the crystallized form. Harnack states that during all his experiments with
Hyoscyamine is an extract from
the resin of different sorts of plants.
He never witnessed convulsions
though his experiments were
numerous and the dose widely
varied. My own observations,
extending over a prolonged
period and dealing with guinea
pigs, rabbits, pigeons, cats, dogs,
thrummen beings, with doses of all
admirable effects. One being is
confirmatory of the belief that
sound extractive hyoscyamine
never though it is more powerful
than the distillate form does not
cause convulsions.
It is to be feared, therefore, that
during a year when much
activity was shown in testing the
truth of my statements
about extractive hyoscyamine
a drug was frequently used
which differed in the two most
important elements from that
preparation itself, being much
less powerful and much more
dangerous.
I cannot therefore too strongly re-
new my assertion that if observers
assign to themselves the task of
testing the reliability of my observ-
ations with the drug they should
satisfy themselves to begin with
that they are dealing with
Merritt's Extractive Hyposeygamine.
Recognize the truth of the charge
that the value of a medicine
is diminished when narrowing
restrictions have to be placed on
the manner in which it is to
be procured, but these restrictions
could only be regarded as
temporary if they would
become altogether unnecessary
when the scientific employment
of the drug had been com-
pletely formulated and the
process of manufacture were
uniformly adopted by all
Manufacturing Chemists.
After the publication in the sixth volume of the West Riding Asylum Medical Reports of the results which I had obtained from the use of Hyoscyamine, I continued to differentiate as far as possible the cases for which Hyoscyamine was suitable and those which were better treated by other drugs. I confirmed my impression that not much benefit could be expected from extractive Hyoscyamine in pure Manoecholia and that as a rule cases of Manoecholia were almost invariably better treated with Morphia.

The following is an illustrative case:

P.W., aged 37, was when admitted suffering from intense excitement. He had had a severe bout of drinking, and before admission had been very destructive. When he was taken after having for three hours caricaded himself against the admission of the police, for they knew that they were going to
he was found not to be under the influence of drink but be much excited. He believed that the police intended to shoot him and had hallucinations of sight, but no suicidal propensities. The attack had lasted a week. On the night of admission he was very nervous and he had a full dose of Extractive Hysoscyamine (equal to 3/6 of a grain) and slept all night. He was quieter next morning but when officially visited he was found barricaded in such a way as to ward off all comers. He was still somewhat under the influence of Hysoscyamine, being dazed and when spoken to remained serious of having piled up the chairs in front of him. He had hallucinations and showed general muscular tremor. The Hysoscyamine was continued in small doses and almost
from the first he fell into a state of intense terror, trembled all over, refused his food. I made sudden attacks on attendants, while at other times he was excessively timid. The Hypocyanine was stopped and Morphia in half grain doses was ordered. After the first dose he was quiet and ate food. At bedtime he had a second half grain dose of Morphia and had a good night. In the morning he was perfectly calm, appreciated his hallucinations as such, was firm on his limbs and angry. His tongue was only slightly tremulous. Next day without further medication he was quite composed, expressed a wish to work, and from that time was quite convalescent.

I would not again consider it necessary to use Hypocyanine and Morphia against each other for the treatment of Alcoothee.
excitement. Prolonged experience and frequent trials of potent medicines in the treatment of prominent forms of Insanity have led me to the conviction that in three forms of disease — Simple Melancholia, Mania and the excitement of Epilepsy or the Epileptic Status there are three definite methods of treatment which will generally be found more effective than in any other methods. I say "generally" because special circumstances of individual cases might necessitate a change of management. The first special form is the combination of Sulfate of Magnesia with large doses of Morphia in most forms of Melancholia the second is the use of large doses of Morphia with two drachms of Liquor Hemiodecaline and concentrated preparation of Lecythes Chloral.
in the Epileptic Status and in Epileptic excitement. It is only in the instance of Epileptic excitement that I would be inclined to think that Hyoscyamine would be likely to be a profitable substitute for these formulae in the treatment of the special forms of disease which I have specified and in that I should always be disposed to give the Volatile Hydrate a first and free trial. 

Though I found, as a rule, that the extractive Hyoscyamine was not so useful in cases of simple recent mania as in tuberculous chronic or recurrent cases. Yet it sometimes happened, in my more recent experience, that good results have been produced by the drug in such instances. At the same time it holds and my opinion is confirmed by other highly qualified observers whom it shall subsequently
quote that they are by no means the most appropriate cases for the exhibition of the drug. When the drug is employed in recent cases of simple mania it should certainly be only when the patient is young and robust and when it can be given either along with or shortly after food. The following instance will show the value of the drug under such circumstances.

R. M., aged 24, was on admission very much excited and for about a year previously he had been showing some peculiarieties of manner and much given to repetition of his words in talking. Latterly he became low spirited in consequence of domestic trouble. About a week before admission he had come home from a religious meeting in a state of intense excitement. He developed the idea that he was Christ and had been preaching in that character.
He had heard soldiers around his dwelling. He had the idea that he had thousands of money and was a powerful preacher. He has lately lost much sleep and not taken food well. When his case was taken he was much excited and stated that a certain phrase employed by a preacher suggested to him instantaneously his identity with Jesus Christ and he afterwards had a pain in the side which he connected with the spear-wound. There was no defect of articulation and his case was evidently one of simple mania. He had 360s. of a grain of Hyoscynamine and the effect was good. He threw off his delusions and in two days without any repetition of the dose he was rational and free from delusional ideas, began to eat and sleep well, showed no tendency to relapse and in three days he was com
valessent. There was no alcohol
in this case.
I at first had an impression
that in these somewhat rare cases
of mania in which there is an
unnatural reluctance extractive
hyoscymamine would be beneficial
in initiating the patient a
new method of behaviour. This
seemed a reasonable assum-
ton because I had more than
once observed that a lunatic is
apt to continue a fixed line of
conduct which had begun even
pronounced insanity even when
an improved mental tone is
given to the patient.
I gave the patient a control over
his or her actions which is not
taken advantage of. This is in
some cases due to habit and in
others to the disinclination to give
up by a voluntary and un-
caused act the past which the
patient has been enacting in the
presence of others. I think that
in some cases I have by the
administration of hyoscyamine given before it is possible to begin the programme and I have been also inclined to think that this is one of the uses of the drug in cases of mania with destructiveness and violence.
valerene. There was no alcoholism in this ease.

I do not consider it necessary to draw from my own experience other cases showing the value of the drug in Mania with apparent voluntary violence, in recurrent exacerbations occurring during the course of Chronic Mania with delusions of apprehension leading to destructiveness and regression and in the excitement of Paralytic. It is much more interesting to be able to detail the independent experiences of others whose unbiased observations regarding the use of Extractive Hypoglycine make their evidence upon the point much more satisfactory than that of one who may have come to be prejudiced in its favour.

But before leaving this part of my subject I would like to confirm the statement which I made in my paper in the Sixth Volume,
of the West Riding Asylum Reports regarding the use of Extractive Hypsoamine in that spasmodic form of retention of urine which is common in organic brain diseases especially general paralyses of the insane and which more frequently than is generally supposed is the cause of much bewildering excitement.

The following case, will supplement what I have already recorded on this head.

A.M., a General Paralytic, had not passed water as far as was known for nearly a week. He had a single full dose of extractive hypsoamine and during its operation he passed water freely. He then had small doses continuously and could urinate freely while he was taking the drug. In a few days the use of the drug was given up and again his water had to be drawn, but the medicine being resumed
he was again able to urinate freely. In a few days more he was able to dispense with the drug and his excitement was much abated. He never had the physiological action fully restored. Previously to the employment of Hyoscyamine he had been catheterised twice a day and chloral had been given without effect. The first dose of Extractive Hyoscyamine given was equal to 1/16ths of a grain of Merck's present preparation. This is one of many instances in which I have employed the drug in this affection with benefit.
The communications which several Asylum Superintendents and assistant medical officers in both English and Scotch Institutions have addressed to me shew that their experience more or less confirms my own; and the fact that the manufacturer of the drug has great difficulty in obtaining sufficient material for the manufacture of all that is now ordered from is evidence that Extractive Hyoscyamine is now undergoing an extensive trial.

To Mitchell, Medical Superintendent of the South Yorkshire Asylum, speaking of Extractive Hyoscyamine he says:—We have found the preparation of fairly conform strength; as now prepared it is a most powerful drug; so that it never has failed in having a sedative effect on the patients taking it when administered in sufficient quantity. Our
experience is that patients are variously affected; some being able to resist the effects of 1/8th of a grain and even 1/6th by mouth and others being completely brought under the influence of the drug by doses of 1/20 of a grain, in rare instances even 1/100th daily by mouth. We only use it hypodermically in very strong patients and then begin with not more than 1/1000 of a grain, scarcely ever giving more than 1/100 in this way. We consider it a very dangerous drug when there is heart or lung disease and in old patients though they may seem strong. I do not like to give it, except to allay temporary excitements in curable cases. If long continued in such cases it seems rapidly to reduce the bodily condition of the patient. We have found it most useful in the excite
ment of Chronic mania and of General Paralysis and that the best way of giving it is by mouth, say from 1/12th to 1/4 of a grain, twice daily—an average dose being about 1/8th. In such instances the patients continued to take their food well, never became excited and some of the most troublesome General Paralytics here have become very quiet manageable patients without having grown at all more demented than they were.

I am inclined to think that the drug is much more potent when it is given to a patient who has been for sometime without food than it is when administered with or shortly after food. A case of Dr. Cameron of Hockliffe head asylum supports this idea as will be seen when his cases are subsequently referred to.

Dr. Evan Lewis writing from
the West Riding Asylum states the result of his recent experience in that Institution to be that a dose which wholly modifies a heavy muscular individual with all the usual physiological accompaniments can be obtained in one-eighth of a grain of the preparation at present manufactured by Merck and supplied by Harvey Reynolds and Co. Seeds. This is given hypodermically. Dr. Lewis adds that the 1/10, 1/20 or 1/60 of a grain are the usual doses he administers thus. In Chronic Mania, with destructive propensities and in the most acute stages of General Paralytic the 1/6 of a grain subcutaneously administered twice daily is generally sufficient to produce the desired result. In epileptic Mania as in the case of Mrs. 1/8th of a grain given by the mouth twice daily has proved invaluable in arresting
her reckless and troublesome excitement. It has a most injurious effect in Mania associated with Chorea and in most cases of acute Insanity with the exception of the early excitement of General Paralyses. In alcoholic cases its curative or palliative action is very doubtful.

Dr. Cameron, Medical Superintendant of the Argyll Rhute County Asylum states that he has found extractive hyoseyamine most useful in the intercurrent excitement of Dementia and in acute Mania. In one case of Mania et poeta, it did not seem to do much good when given in doses of 1/4 of a grain. "I usually," he adds, begin with 1/40 of a grain in the case of women and 1/32 in the case of men subdermally and give double the above quantities by mouth. The largest dose I have given
by the mouth was half a grain in a case of chronic mania.
M. Cameron in forwarding to me some cases illustrating his method of using the drug states further that in his experience Extractive Hyosephamine promotes recovery in new cases, that it has prevented death from exhaustion in acute mania and that its beneficial effects have been very well marked in chronic mania with violence and delirium tremens even when recovery did not take place. We consider the drug a remarkably safe narcotic and have never seen any untoward effects from its use.

The following selection from Mr. Cameron's cases will show how effectively the drug may be employed in mania with violence and other conditions similar to those referred to.

J. M. F. a dement aged 25, a re
Markably strong man was excited and refused to remain in bed and had all but smashed out the door of his room. Three-sixteenths of a grain of Extractive Hyoscyamine, Maduraad, administered hypodermically produced deep sleep which lasted for 6 hours and cut short the excitement which never returned. Dr. Cameron adds: "This patient has been free from excitement for two years."

K.K. A male patient aged 52, demented. He was much excited and showed his excitement by jumping over walls and fences and by ditching about the shades and other tools used in the garden grounds. The first day he went out to work in the garden he smashed half a dozen strong wheel barrows in quick succession through their front 10 rod. A quarter of a grain quieted him for about six hours; he slept for about two hours. He
was about 9 months in the asylum and never afterwards required the use of the drug. He frequently asked what it was and when he was excited on other occasions exercised self-control to avoid a repetition of the use of it. It was given by the mouth in this case but Dr Cameron states that subsequent experience leads him to believe that half that the quantity would have sufficed if given hypodermically.

The following instance shows the less satisfactory working of the drug in an extreme case—a case in which perhaps it would be absurd to expect that any drug could produce more than temporary benefit:—Miss A, a female patient aged 31, an aggravated case of chronic mania. When actively excited it is difficult to believe that she possesses any of the attributes of humanity beyond
the outward semblance. Half a grain is required to calm the patient and to produce sleep. Dr. Cameron observed that the periods of sleep lasted from an hour to four hours. When the effect of the drug passed off the patient was much the same as before. On one occasion a quarter of a grain produced about six hours uninterupted sleep. This was unusual and on enquiry it was found that the drug had been administered on an empty stomach.

Similar instances of the successful and unsuccessful use of Extractive Hyoscynamine have with the kind permission of Dr. Mitchell been supplied to me by Dr. MacInnis of the South Yorkshire County Asylum. The last case which I have copied from the copious notes of Dr. Cameron (that of J. B.) shows how the potency
of the drug may be influenced by the fasting condition of the patient. That such a drug would be more potent and less commendable during a state of fasting could be predicted from what is already known about other delirio narcotics. I would strongly recommend that extractive hyoscyamine should be given if possible sometime after a full meal has been taken and if it is considered advisable to use it in a case where food has been persistently refused. Some highly nutritive substance should first be supplied to the patient through the stomach tube. Another case (that of H.H.) raises a point about which there might be much discussion. It is whether or not a drug which when once administered has such an effect upon the destructive patient as to lead him to exercise great self-control rather than be obliged to
take another dose of it is not really a form of restraint and a reprehensible agent. The question can be argued out. There are three varieties of excitement with destructive habits; one in which the destructiveness is without doubt or qualification due to involuntary and uncontrollable, insane impulses; a second in which a certain insane tendency to agitation and irritability is on certain occasions supplemented by an outbreak of violence and destructiveness which is largely if not altogether voluntary and controllable; and a third in which violence and destructiveness are altogether voluntary. The first class of cases are subdued only while they are under the direct influence of Exaeretic Hyoscynamine or other narcotic. Cases of the second class divide themselves into two varieties one in which destructiveness is believed to be l
Such an extent the result of insane irritability that a drug may remove the destructiveness by curing the irritability; and a second variety in which the destructiveness is so evidently surpassed all that could reasonably be regarded as directly symptomatic of the mental disturbance that any attempt to suppress it by drugs would appear to be directed more to the punishment of the misconduct than to the removal of disease. It would be using a drug as a penal agent. This is still more true of the third class of cases. It is highly probable that in those cases where among asylum patients violent and destructive habits are either voluntary or less completely controlled than they might be, much good might be done by making violent lunatics much more amenable to the action of
of the laws than they are at present. There are large numbers of lunatics who, though their insanity may be unquestionable, have as much self command as would enable them to refrain completely from all acts of violence and destructiveness. But the violent lunatic is generally an ardent advocate of the doctrine of the irresponsibility of the insane and in fact he often, reveling in his insanity, boasts of being able to commit with impunity voluntary acts of outrage from the proper punishment of which his own reputation for insanity exempts him. It is necessary to deal with them as the berserkers of their cases which gives rise to assaults by attendants and errors of management by Medical Superintendents by placing the former in the position of policemen and the calling...
when the latter to assume the
functions of magistrates.
If these cases were punishable or, what is virtually
the same thing, removable from
Comparatively peaceable asylum,
to be treated as criminal
lunatics till they showed
a greater regard for lawful
conduct there would be
fewer abuses in our asylums,
fewer assaults by attendants,
a diminished employment
of narcotics and an unlimited
extension of that humane
and only sensible method
of asylum administration
which extends to the insane
the greatest possible amount
of freedom while maintains
in asylum life as many of the
conditions & associations of
every-day existence as are
compatible with the safety of the
dane and the interests of the
insane. I hold that no
no narcotic whatever should be employed merely for the purpose of suppressing destructiveness or violence; that the proper employment of narcotics is in removing the mental aberrations which may have led to such untoward symptoms; and that in well selected cases no narcotic is so beneficial in producing this enviable result known as sedative hyoscynamine.
Summary.
The following summary will perhaps express in a form the leading facts brought out by my investigations regarding the properties and uses of Atropine.

Physiological Summary:
1. The smallest active doses—say one quarter of a grain of the substance as now manufactured by Merck—when administered to animals cause slowness of the pulse and increased arterial tension, reduce the temperature, dilate the pupils, and have little effect on the respirations.
2. Small doses (say 4th of a grain of the present preparation) cause slowness of pulse alone with increase of arterial pressure followed by quickening and subsequent fall to the normal point.
During the action of the maedume there is restlessness, impairment of vision, followed by motor paralysis, diminution of respiration and reduction of temperature about 1°. Dryness of the mouth and throat and dilatation of the pupil are also produced. Large doses (from 3/4 to 1/2 grn. of the present preparation) cause the pulse to rise from the first and it continues to beat with rapidity for 6 or 8 hours. There are great fall of temperature diminution of respirations, loss of motor function, delirium, excitement, sometimes prolonged but interrupted sleep, followed by a sudden return of the pulse towards something below the starting point. After this the effects of the drug disappear completely. Lethal doses cause death rather by syncope.
During excitement or by coma due to non-elimination of the drug by the urine and in perfect evaporation of the blood through the interference with respiration.

In birds extractive hypnotic and the prevents no dryness of the fauces and no dilatation of the pupils.

Long continued administration of the drug causes loss of weight quickened pulsation respiration and increase of temperature.

The characteristic actions of the drug are primarily produced by (1) irritation of the pneumogastric supply in the heart and lungs (2) paralysis of these by some independent stimulation of the sympathetic and by direct action on the cerebral tissues.

Internal use yields dilatation of the pupil more rapidly.
than local application. This delirium is not counteracted by Calabar Bean.

(8) When extractive Hyoscynamus is given to man the principal effect is the drowsiness in ability to think, speak or move accordingly to one's inclinations. Hallucinations, principally of sight, an under estimate of light, fall of temperature, elevation of pulsation, mentally, a condition of self satisfaction and good humour.

Larger doses, (say 1/2 grain of the present preparation) injected hypodermically, cause great frustration, coma, fluttering pulse, excited movements of the limbs, and, when the action of the drug is beginning to pass off, mental excitement followed by gastrick reversion which is wonderfully rapid & complete.
In two cases in which large doses (3/8 and 1/2 grain of the 33 per cent. preparation were given) there was haematemesis which however was followed by no bad results.

B. Therapeutic Summary

1) That extractive mepacrine is useful and safe in the treatment of chronic mania in which there are delusions of suspicion and hallucinations of the special senses; in destructiveness and violence due to mental irritability curable by the removal of the mental disturbance; in the excitement of general paralyses of the insane, in simple mania occurring in robust men or women.

2) That the treatment of such cases is best carried out by the use of single large doses 1/6 to 3/16 drachm.
of a grain when given hypodermically and 1/4 to 1/2 of a grain when given by the mouth.

(3) That considerable intervals should elapse between the times administrations of such doses and that they should not be given more than once in 24 hours and not more than 3 days连续.

(4) That intravenous hydroydine has also been found to be useful (a) in the excitement of epilepsy (b) in the retention of urine common in organic diseases of the brain (c) in cases of "acute" mania et alcohholique mania although in such instances it requires to be employed with great care.

(5) That in subacute or simple mania where there are no evident contraindications small continuous doses
(not more than 32 per cent. a day by the mouth divided if convenient so as to keep up the action day and night) Sometimes produce gratifying cures.

(1) That in the excitement associated with Chorea, Ataxia, and Locomotor Ataxy, in "Acute Dementia" and generally speaking in Acute Mania, Cholia, Extractive Hysteria, etc., has been shown to be in the case beneficial and in most cases prejudicial.

(2) That small continuous doses control the destructiveness often associated with imbecility and dementia, such destructiveness being quite involuntary and uncontrollable; but that great care is required in giving even small doses continuously to aged dements.
That the drug is inadvisable where there is decided heart disease, renal disease, aneurism or atheroma and, that, generally speaking, the use of Intermediate Hyoscine amine amongst patients of over 60 years of age is associated with many risks and few real advantages.