A CLINICAL RESEARCH ON THE HYPNOTICS
AND THEIR USE IN MENTAL DISEASE.

THESIS
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by
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Hypnotic and sedative drugs play such an important role in the treatment of excitement in mental diseases, that it is no exaggeration to say that the difference between the mad-house of the past and the mental hospital of the present day is largely due to the rational exhibition of these drugs in conjunction with other therapeutic measures.

To say that a certain class of drugs has brought about such a great change for the better is to make a very extravagant claim, but it is also a statement which forms an equally strong plea for the more intimate knowledge of any such extremely useful group of drugs; and it is my excuse for making a clinical research on the hypnotics and their use in mental disease the subject of this thesis.

The aim of the thesis is to show, from my clinical experience of hypnotics which of these I have found satisfactory and to indicate in some measure their rational use.

To use any drug rationally many things have to be taken into consideration: indications for and contraindications to, its exhibition borne in mind, and its advantages and disadvantages carefully weighed; consequently /
ly the scope of such an investigation is proportionately wide.

Thus for the sake of clarity I have divided the thesis into the following sections:-

1. Introduction.
2. Insomnia in Mental Diseases.
3. Classification of Hypnotic Drugs:
   (a) The alcohol group
   (b) the chloral group
   (c) the Paraldehyde group.
4. Theories of the Action of Hypnotics.
5. Drugs used with Clinical Notes on Cases.

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INTRODUCTION.

Like the poor, the mentally excited patient we have with us always.

Excitement is one of the commonest symptoms met with in mental disease and the one which the medical officer is most often called upon to treat.

Professor G. M. Robertson of Edinburgh has classified mental excitement into two categories analysing it in the following way:-

1. Primary or essential excitement which is intimately associated with the disease, corresponding in intensity /
intensity and duration to the disease and amenable only to those kinds of treatment which have an effect on the disease.

2. Mental excitement which is a reaction to some irritation in the environment acting upon an excitable patient. This second excitement is secondary and non-essential, and its treatment resolves itself into the removal of the patient from the source of irritation, or the source of irritation from the patient, as for example when a patient is removed from the exciting and irritating environment of a noisy ward to the peace and quiet of a single room where he or she will be alone. In such cases the excitement passes over without further intervention on the part of the doctor.

The treatment of essential excitement, however, does not follow such simple lines. Still this excitement must be treated, for if it is prolonged the patient becomes exhausted physically, and to combat mental disease we must see to it that the patient's physical health is such that it will be our ally and not our enemy.

Essential excitement being, as it is, so intimately associated with the disease we can hope for little in the way of amelioration of its acuteness by the mere removal of the patient to a single or padded room without other steps being taken to allay the excitement.

Primary excitement, then, calls for the employment /
ment of hypnotic and sedative drugs.

To induce rest and quiet and prevent exhaustion is the first essential to be aimed at when using hypnotic drugs, but other strong indications for their employment are not lacking.

Sir Thomas Clouston ("Clinical Lectures on Mental Disease", 1904, Sixth edition, pp. 711-712) states

"The effects we may legitimately aim at and hope for in the treatment of mental diseases by hypnotics and sedatives combined with other treatments are:

1. To cut short a commencing attack of melancholia or mania in some cases.
2. To re-establish the sleep habit of the brain.
3. To tide over short attacks that have a natural tendency to recover, through making the patient manageable by nurses in an ordinary private house.
4. To enable cases with severe attacks to be kept at home long enough to satisfy the patient's relatives that the attack is a definite one.
5. To give needed sleep to relatives and nurses.
6. To combat temporarily dangerous symptoms.
7. To take the edge off the worse symptoms of cases who are being treated during a long attack, so allowing other measures to have full effect.
8. To subdue severe and exhaustive symptoms, and save the patient's strength and life."
9. To satisfy and soothe the minds of such patients as will have some drug.

10. To quiet screaming or noise for the sake of others."

It is admitted that the use of hypnotics and sedatives is, to a certain extent undesirable, and that in many cases their employment is the choice of the lesser evil.

But might one not say the same about all drugs? To take the instance of the use of morphia in general practice, we all know how vigilant and careful we must be in its employment and to whom we may give it. Yet this fact does not preclude the use of morphia and its derivatives.

On the contrary, the aphorism that "without morphia few men would be callous enough to practise medicine" proves beyond doubt its great usefulness.

Again, no medical man in the treatment of any malady will employ drugs if other measures such as general hygiene and dietary in themselves will suffice.

Instead his treatment proceeds with caution along the line of what may be termed a therapeutic crescendo.

In the treatment of mental excitement the doctor adopts similar tactics and the discriminate use of hypnotic and sedative drugs is good practice. It is not the use, but the indiscriminate use of these drugs that is undesirable.

It /
a sedative immediately he notices the change in the patient's conduct.

This procedure has the further advantage that when a sedative is administered at this point a much smaller dose will suffice, for only that amount of sedative is required which will take the edge off the attack, and tone down the excitement of the patient until it falls within manageable limits. If the patient be overlooked and left untreated till the excitement has reached the maximum, a much greater amount of sedative would be required.

The general practitioner, especially the old family doctor, stands in much the same relation to certain of his patients as does the asylum medical officer to the people under his care, and in just the same way the general practitioner can give a sedative in the case of a patient whom he knows, when that patient is about to become excited, and thus obviate the patient's being sent to an asylum on quite inadequate grounds.

The type of patient whom I have in mind to be treated in the above way by the general practitioner is that patient whose main symptom is periodic excitement of short duration, and who is neither dangerous nor suicidal nor in any way requiring to be certified.

These cases are met with in senile people with delusional excitement and such cases can be quite well treated /
treated at home by means of the judicial use of sedative drugs.

If one is treating a patient in a private house one must needs resort to sedative drugs under certain circumstances. No doctor who has to treat such a case can allow the patient to become noisy or to attract public attention.

In these cases sedatives are employed to control excitement in such a way as to alleviate the symptoms and diminish the duration of the excitable period.

To give an isolated example. Last month I had occasion to treat a case of noisy excitement disturbing to the other patients in the wards of the local infirmary. Apart from noisiness, in which an element of hysteria was prominent, the patient was perfectly sane, and paraldehyde 3 II in combination with sulphonial grains XV gave him rest and his fellow patients peace.

"In acute illness, however, when other measures such as cold sponging fail or are inapplicable, and in certain cases where symptomatic treatment is all that is possible for the time being, hypnotic drugs have been and doubtless will continue to be quite rationally employed."

"J. M. Fortescue-Brickdale.

The result from the exhibition of an hypnotic in the /
the form of Liquor opii sedativus in m xx to m xxx doses at the onset of an attack of influenza is little short of marvellous. So impressed is Dr. Leonard Williams by this line of treatment that he states he has learned to regard it almost in the light of a specific against the bacillus of influenza.

(Leonard Williams, M.D.
"Minor Maladies." 1923. 3rd edition. page 22.)

Lastly, the treatment of insomnia in general practice affords great scope for the rational employment of hypnotics in the encouragement of the return of the sleep habit.

Insomnia, if prolonged, is a causal factor in insanity; therefore if sleeplessness is treated and eradicated and the brain given a rest, it is at least feasible to believe that a mental break-down in certain cases would be averted.

"Rest the part or the organ" is a fundamental law in the treatment of any diseased part or organ, and Hilton in his "Rest and Pain" has emphasised the paramount importance of the application of this great truth to all injured parts and diseased organs.

In his book Hilton quotes a letter received from the late Dr. Hood, Bethlem Hospital, dated March 22nd, 1860, in which Dr. Hood writes: - "I may state that I am frequently applied to for the admission of lunatics into this /
"this hospital whose insanity is caused by overwork, anxiety and exertion, and for whose cases nothing is required to restore mental equilibrium but rest .........

I could give you many illustrations from the wards of this hospital where we are called upon to treat symptoms in the cases of governesses, students, clerks, and clergymen; and rest is all they require, and with that the most aggravated cases are restored."

John Hilton, F.R.C.S.


This doctrine of rest holds good for the mind as well as for the body, and when all other measures fail how can the general practitioner give rest to the wearied and fatigued mind suffering from insomnia except by the employment of hypnotics?

It is seen, then, that hypnotics and sedatives form an important portion of the drugs used by the asylum medical officer; but it is also obvious that these drugs are useful to the general practitioner, though less used by him.

The general practitioner knows the effects and the value of the old tried remedies, but with the action of the more recent ones he is not so conversant.

The reason is not far to seek.

Among the large number of new drugs which have recently been introduced by enterprising firms of manufacturing /
facturing chemists, a rather large proportion belongs to the class of hypnotics and analgesics. The reason for this may be twofold. Firstly, the importance of hypnotics and sedatives in treatment; but the more probable reason is the fact that hypnotics and analgesic properties are possessed by a very large number of carbon compounds, and every manufacturer who wishes to exploit this class of drug finds it very easy to prepare a modification of some previously existing hypnotic, and claim it as an entirely new drug under a new trade name.

Each new compound is boomed with plenty of advertisement and remarkable results are claimed by the makers for these drugs.

The result is that the practitioner becomes so bewildered at the claims made about each that he falls among them all and hesitates to use any.

There is no doubt, however, that some of the recent synthetic preparations of the hypnotic groups are really very serviceable, and it is my object in the present thesis to give the results of a series of clinical tests of the more important ones.

Mental diseases, par excellence, afford scope for an extensive trial of these preparations, and being the medical officer in a large asylum I have utilised several of these preparations. In the present thesis I will record my results and will endeavour to draw from them some /
some conclusions as to the scope of and indications for the principal hypnotics.
(1) Causes of Insomnia.

The term insomnia may be simply defined as the absence of the normal amount of sleep.

People vary considerably as to the amount of sleep they require, and some persons require varying amounts of sleep at different periods of life. Active people, as a rule, require more sleep than their less energetic brethren, and it is a matter of common knowledge that young growing people require more sleep than persons in the prime of life.

Everybody is acquainted with the fact that some people can do with comparatively little sleep, with such a small quantity as in other people would be incompatible with health and the carrying on of their daily work. Such people never have more than four or five hours' sleep in the twenty-four, yet they manage to do a hard day's work and never seem to feel any ill effects.

This is more often true of brain workers; so much so that it has become a platitude that it is not too much brain work that injures a person but the worry accompanying the work.

To take an instance from authentic history, we need only read Memoirs to learn of Napoleon's ability to do with very little sleep and yet live an amazing-ly /
ly energetic life. One could not say that he suffered from insomnia for he also had the ability to sleep under the most adverse external conditions.

That the intensity of sleep multiplied by the duration is a constant is a very attractive explanation of the varying amount of sleep required by different persons, and in point of fact this theory seems a very satisfactory one. The people who, as we say, sleep lightly require more sleep than the heavy sleeper; and sleep which is constantly broken by dreams is not so refreshing as repose free from such interruptions.

In the matter of hours of sleep the correct attitude to adopt is that a man must be a law unto himself in the matter, bearing in mind that a sufficiency of physiological sleep denotes an amount which is normal for a particular individual, although the actual duration and depth of sleep may vary with age and personal constitution.

Sleep may be deficient in quality as well as in quantity.

It will be seen, then, that insomnia is a very comprehensive term including all grades from simple restlessness to total loss of sleep.

The causes of insomnia are many and it is therefore necessary to adopt a classification.
Purves Stewart in his "Diagnosis of Nervous Diseases" (1910) divides insomnia into two great groups: (1) extrinsic and (2) intrinsic. Extrinsic insomnia includes those cases in which the sleeplessness is due to some outside cause not directly arising in the cerebrum and its blood vessels. For example, physical pain of any sort, cough, vomiting, frequent micturition, diarrhoea, pruritus, etc., may keep the patient awake. In this group he includes insomnia arising from or associated with the emotions.

The causes of intrinsic insomnia he attributes to vascular, toxic or nervous factors, or a combination of all three.

Dr. C. Worster Drought classifies insomnia in much the same way. He also divides sleeplessness into two groups:

(1) Physiogenic Insomnia - Insomnia resulting from physical discomfort or organic disease.

(2) Psychogenic Insomnia - Insomnia in which no definite physical basis is found.

(a) Anxiety states. (anxiety neuroses and anxiety hysteria) mental conflicts, apprehension, disturbing dreams.

(b) Neurasthenia - states of fatigue.

(c) Hysteria - Auto-suggestion, somnambulism.

(d) Compulsion Neuroses - Obsessions.

(e) The psychoses - Manic depressive states, paraphrenia.
(f) Dementia Praecox.

(g) Confusional states.

Gérard Séé has also drawn up a useful though less elaborate classification.

(Craig and Beaton: "Psychological Medicine."

All the three foregoing classifications are excellent, but probably the simplest and best classification of the causes of insomnia is that given by J.B. Bradbury in "Disorders of Sleep" in Allbutt and Rolleston's "System of Medicine", 1910: Volume VIII: pp. 791-803.

In this classification, to which I refer, the causes of insomnia are given as follows:-

1. Irritative Causes.
2. Toxic Causes.
3. Psychical Causes.
4. Causes arising from change in mode of life.

This is a classification which includes every causal factor.

Causes arising from change in mode of life are indeed very real, and one which must often be treated by the general practitioner. This cause could be fitted into Purves Stewart's classification as an extrinsic cause, but it is difficult to say whether it is a physiogenic or psychogenic factor.

Lastly /
Lastly, it should not be forgotten that heredity plays a part in insomnia.

"A tendency to sleep badly runs in families and is sometimes observed in the youngest infants." S. Gee.

2. Physiological Considerations.

It is a striking fact that it is those natural phenomena with which we are most familiar and which we observe every day, that present the greatest difficulty when we seek a satisfactory explanation for their occurrence.

Sleep is not an exception to this rule. It is even difficult to define sleep. McDougall gives the definition of sleep as "a condition of rest in which impressions on the sense organs are no longer interpreted in normal fashion," ("An Outline of Abnormal Psychology", 1926: page 76.) and this is probably the best definition at the present stage of our knowledge regarding sleep.

Of the exact physiological mechanism of normal sleep very little is known. We have been able only to investigate the conditions conducive to and the changes in the physical state which accompanies sleep.

From observation of the latter various theories of sleep have been propounded from time to time, and these may be classified as follows:-
1. Circulatory Theory.
2. Biochemical Theory.
3. Neurodynamic Theory
   \( (a) \) Demoor \\
   \( (b) \) Lugaro.
4. Psychological Theory.
5. Theory of "sleep regulating" centre.

For each of these theories there is a certain amount to be said in its favour, but each of itself is insufficient to account for the phenomenon of sleep.

1. The theory of brain anaemia is perhaps the oldest attempt at explaining the occurrence of sleep. More than two hundred years ago Mayow pointed out that "if a man takes a big dinner all vital spirits have to go down into the stomach in order to carry on digestion, and the man naturally goes to sleep and cannot easily think," and conversely he continues, "if the man will try and think after his dinner and succeeds in doing so, the vital spirits will go up to the brain to do the thinking leaving the stomach to its own devices, and consequently the food is not digested." We are all acquainted with Mayow's observation having all experienced the drowsiness and mental lethargy which follows a heavy meal, and these are explained by the fact that more blood being required in the splanchnic area for the purpose of digestion there is less blood going to the brain. In Mayow's /
Mayow's time all the functions of the body were supposed to be carried on by what were termed "vital spirits" and we have only to substitute the word "blood" for "vital spirits" in Mayow's statement to bring his theory into line with modern ideas of the physiology of sleep and digestion.

Friedlander, experimenting with isobutyl alcohol on the rabbit, found he was able to control the sleeping and waking of the animal by merely reversing the position. When the head was held down the rabbit awoke, while if the head was held up so that the blood left the brain the animal went to sleep. Clinically, the same idea underlies the practice of applying hot water bottles to the feet to aid the onset of sleep.

It is further demonstrated by the fact that if a body is carefully balanced in the horizontal position during the waking state the feet fall with the onset of sleep.

Other clinical observations, such as depression of the anterior fontanelles in children and trephine openings in adults, pallor of the optic discs and narrowing of the retinal arteries during sleep, indicate a diminished blood supply in the cranium.

2. The advocates of the biochemical theory hold that sleep is caused by chemical changes in the cerebral cells /
cells due to the accumulation of waste products which have a soporific action on the brain. These substances, in Obersteiner's opinion, were acid in nature and Preyer claimed a soporific action for one particular acid, namely lactic acid.

In favour of this theory its supporters point out the fact that vitiated atmosphere tends to drowsiness. The dog partially asphyxiates himself by burying his nose when he curls up, birds are believed to tuck their heads under their wings for the same reason and man hides his head under the bedclothes.

Histologically the biochemical theory has some support from the observations of Hamilton Wright who has demonstrated that owing to the action of anaesthetic drugs on the cortical cells the Nissls granules lose their affinity for methylene blue.

In extreme cases the nucleus and nucleolus disappear, the cells become mere shadows and present all the appearance of having undergone degeneration. That this change is not a real degeneration is proved by the fact that the cells regain their normal healthy appearance when the anaesthetic leaves the circulation.

The existence of fatigue products, however, has never been definitely proved.

3. Two sections hold opposing views of the neurodynamic theory of sleep.

Demoor /
Demoor found in animals under deep anaesthesia that the gemmules of the dendrites of the cortical neurons were refracted. He came to the conclusion that this withdrawal of the gemmules constituted an interruption in the path of nerve impulses, giving rise to blocking of nerve impulses themselves consequent upon which sleep ensued.

Lugaro, on the other hand, holds quite the opposite view, as he believes that during sleep the gemmules are protruding, resulting in a very intimate interlacing of the dendrites.

Owing to the universality of connecting paths, the definite and limited relationships which exist between the neurons during waking hours are abolished. Nerve impulses not being definite and clear-cut but general and vague receive less and less attention until finally there is the condition of sleep.

Interesting and instructive as the work of Hamilton Wright, Demoor and Lugaro may be it must always be borne in mind that their observations were made, perforce, on animals in which sleep was induced by narcotics and such sleep is not precisely analogous to normal repose.

The former is a pathological state due to the action of a poison by which the chemico-vital activities of the cells are reduced, and it is seldom or never accompanied by /
by repair - the constructive side of metabolism.

In natural sleep, on the other hand, the balance is always on the side of anabolism.

4. From the psychological point of view Claparède believes that sleep is an instinct or innate tendency occurring at birth, and later subject to modification and to some extent falling under the control of the will.

Also from its resemblance to the hypnotic state sleep has been considered a form of auto-hypnosis. Though the two states have certain points in common, they differ materially in other ways. For example, "In the deeper stages of hypnosis the patient entirely loses consciousness of the outer world", but "in spite of loss of consciousness the patient's eyes may remain open, he will rise, walk and carry out commands given by the operator and will answer when spoken to by him, but fails to reply to any other person." ("Hypnotism." A. M. Hutchison, M.D. 1919. page 31.)

5. Economo's assumption that sleep is controlled by a sleep regulating centre situated in the mid-brain has a great deal to be said in its favour. We know there are other controlling centres in the brain such as the heat regulating centre, vaso-motor centre, etc. Then why not a sleep regulating centre?

Neoplasms and encephalitic lesions in the region of the mid-brain very near to the centre for ocular movement /
ment have been found in patients who suffered from narcolepsy and attacks of drowsiness.

As a theory the postulation of a sleep regulating centre is admirable because by such a hypothesis most cases of insomnia can be satisfactorily explained.

As already stated, however, none of these theories can alone account for the onset of sleep. The probability is that more than one of the factors in these theories play a part in the production of unconsciousness; thus perhaps fatigue products carried by the blood to a sleep regulating centre and acting upon this focus can induce sleep just as CO₂ carried by the blood to the respiratory centre results in the production of movements necessary for respiration.
3. Clinical Aspects of Insomnia.

Sleep is a physiological function which is encouraged by regular habit, and by favourable conditions, consequently anything that upsets the regularity of one's daily life is likely to act adversely on that person's sleep.

General physical disease is one such factor and a brief glance is all that is necessary to convince us that insomnia is a symptom of many diseases.

Not only is insomnia present but the kind of insomnia is, in many cases, typical of the disease. Thus there is the sleeplessness which originates in alterations of the vascular system, e.g. the high tension type met with in arterio sclerosis and the low tension type associated with anaemia and neurasthenia. In the latter type the patient feels drowsy when sitting upright in a chair but cannot sleep when the head is lowered in the sleeping position because the brain becomes overfed with blood. This is a striking clinical analogy to the experiments carried out by Friedlander on the rabbit.

In chronic heart disease insomnia is a prominent and often very distressing symptom. Its form is typical taking the form of a sudden starting awake with a feeling of suffocation and gasping for breath just when the patient is dropping off to sleep.
In practice probably the commonest form of sleeplessness is toxic insomnia which is almost invariably associated with gastric and intestinal fermentation.

Among the toxic forms of insomnia may be placed also that due to chronic excess in alcohol, and the sleeplessness of the acute fevers.

In organic nervous diseases insomnia is often an early symptom. Thus in encephalitis lethargica insomnia may precede the lethargy, and it seems to be even more common in the convalescent stage, more especially in the Parkinsonian type of the disease.

Insomnia, which may or may not be accompanied by excitement and exaltation frequently occurs in the early stages of general paralysis of the insane.

Korsakow's Syndrome (Alcoholic Polyneuritis with Mental Disease) is sometimes heralded in by sleeplessness though here the factor of pain resulting from the neuritis may account for the insomnia.

But if insomnia is very often a concomitant of physical disease, its presence in mental disease is practically without exception.

In asylum practice one has only to note in the information schedule sent out to relatives how often the question as to whether the patient suffered from insomnia is answered in the affirmative. In 100 consecutive cases noted by myself insomnia has been present to a greater /
greater or lesser degree in 83.

In many cases it is the first sign of departure from normal noticed by the relatives.

The experience of all alienists is that sleeplessness is present in nearly every case of insanity, at some stage of the disease, and it is safe to say that hardly ever does an acute attack occur without some sleep disturbance.

Clouston has summed it up in the phrase "certainly sanity and sleep go together" ("Unsoundness of Mind, 1911: page 120) and he does not underestimate the number of cases in which insomnia is a premonitory sign when he says, "Sleeplessness frequently in prolonged and aggravated form is the prelude to at least three quarters of all the cases of unsoundness of mind." (Ibid Page 141).

Finally it must be noted that the restoration of sleep is of definite prognostic value.

In the first place the return of the sleep habit is an indication that the acute symptoms have passed away, and secondly, due consideration being always given to other clinical signs and symptoms, the increased amount of sleep is a valuable aid in determining whether the patient is on the road to recovery or is beginning to dement.

Still adhering to the classification of insomnia adopted in Allbutt's "System of Medicine" we may here
pay further attention to psychical insomnia.

Among the commonest causes of psychical insomnia are grief, shock, worry and mental anxiety. In many cases where there is a disposing factor, such as nervous temperament, neurasthenia, hysteria and hypochondriasis, the sleep habit may be easily lost.

Overwork, especially if accompanied by too little rest and too much worry, is another frequent cause of psychical insomnia.

Women at the menopause suffer from psychical insomnia, though in these cases the sleeplessness may also be considered in the light of toxic insomnia as it may to some extent be due to accumulation of toxic products not eliminated at the catamenia.

By far the greatest number of cases of psychical insomnia are associated with the various insanities.

The insomnia of insanity may be further subdivided as follows:

(1) Insomnia of
   (a) Acute mania
   (b) Acute melancholia.

(2) Insomnia of
   (a) Dementia Praecox
   (b) Milder forms of mania
       i. in young persons
       j. in middle-aged persons.
   (c) Milder forms of melancholia
       i. in young persons
       j. in middle-aged persons.
(3) Insomnia accompanying cerebral atrophy due to arterio-sclerosis.

**Insomnia in Acute Mania.**

In acute mania, when there is great excitement present, sleep may be absolutely abolished, and in such cases may only return when the patient becomes exhausted. In some cases of chronic excitement the patient may never be seen actually asleep. Sir Thomas Clouston has reported such a case occurring at the Morningside Asylum. The patient in question was suffering from chronic mania, and for eighteen months was never found asleep by the night nurse who visited her every two hours.

Clouston remarks that the patient must have slept but her sleep was so light and so short that she was always awake every two hours. (Sir Thomas Clouston: "Clinical Lectures on Mental Diseases", 1904. 6th edition. Page 197).

The fact that this patient was awake every two hours is not surprising because in the sleep of mania a periodicity is often noticed - in this case a short nap of two hours with regularly recurring waking times - but a more common periodicity is that of sleeping on alternate nights, or sleeping two consecutive nights and having no sleep the third night.

The sleep of the maniac is irregular in one respect namely that the duration of each night's sleep is extremely /
tremely variable.

These facts are well illustrated in considering and comparing sleep charts 1 and 2. The first sleep chart is a record of the hours of sleep of the patient for the first twenty-eight nights following her admission, during which time she remained greatly and persistently excited.

The second sleep chart shows the hours of sleep which the patient was having nightly six months after her admission, at which time all excitement had disappeared and the patient was on the road to recovery.

History of Patient to whom Charts 1 and 2 refer.

Caroline S. aet. 23. Single.

Date of admission 18th March, 1926.

Acute mania.

On admission - Very excited and talkative. Conversation quite nonsensical. Laughs in a silly fashion. Has delusions that she is very holy and that she has a halo round her head. There was great psycho-motor activity, and flight of ideas. Her affective state was that of elevation and she was morbidly euphoric. Orientation good.
Explanation of Sleep Charts.

Vertical row of figures refer to hours of sleep.

Horizontal row of figures gives dates upon which hours of sleep were observed.

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SLEEP CHART. No: 1.
Insomnia in Acute Mania.
Caroline S.
Act. 35 years.
In sleep chart 1 the variability in the nightly duration of the hours of sleep is very manifest. Then, during the whole twenty-eight days, the patient had 114 hours of sleep, or, on an average, a little over four hours per night.

The following September improvement in the patient's mental state was very marked. Excitement was quite gone. Conversation was coherent and rational. She was bright, sociable and employing herself. She was somewhat facile, but her mental state was perfectly stable. The second sleep chart shows hours of sleep from August 26th - about one week after all signs of excitement had disappeared. In comparing this second sleep chart with sleep chart No. 1 two striking differences are noticed.

Firstly, the nightly duration of the patient's sleep is much more regular. Secondly, the amount of sleep during the whole second period and the amount of sleep per night is very much increased. During this second period of twenty-eight nights' observation, the patient had not a single sleepless night as compared with five sleepless nights during the first twenty-eight days after admission. Her total amount of sleep during the second period was 222 hours, that is an average of nearly 8 hours per night which is approximately double the sleep obtained during the period of acute excitement.

The patient was discharged recovered on 15th February.
February, 1927, after being on probation outside for twenty-eight days.

As already mentioned, increase in amount of sleep is of diagnostic value but only when other factors in a patient's case are taken into consideration. Increase in the amount of sleep alone is no criterion of mental improvement, as will be seen from a study of the following case.

History of Patient to whom Charts 3 and 4 refer

Johan, S. or W.  aet. 27.  Married.
Date of admission  12th December, 1925.

On admission patient was restless and excited, chattering incessantly and quite incoherently, displaying great flight of ideas; Psycho-motor activity greatly increased. Has delusions regarding morality of her husband and neighbours. Mistakes the identity of persons, and was disoriented from time and place.
SLEEP CHART, No. 3.
Insomnia in Acute Mania
John S., or W.
Aet 27 years.
SLEEP CHART. NO: 4.
Insomnia in Acute Mania,
John S. or W.
Age 27 years
The first sleep chart shows the irregularity and scanty amount of sleep. In twenty-eight days she had 87 hours of sleep, or on an average a little over three hours per night. Twelve months later the patient's sleep chart shows disappearance of irregularity of sleep with increase of total amount of sleep for second period and increase in amount of sleep per night. In this second period of observation for sleep the patient had 163 hours, or almost 6 hours per night as compared with 87 hours or a little over three hours per night in the first period of sleep observation for a similar length of time. Despite this increase in amount of sleep, the patient's mental state showed no improvement. Acute excitement was absent, but she was very foolish in her behaviour, quite unable to occupy herself, incoherent in her speech, faulty in her habits, and enfeebled in mind. At the present time (October, 1927) the patient shows no sign of improvement, but is becoming more and more enfeebled.

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Insomnia in Acute Melancholia.

In acute melancholia, especially in the agitated type, insomnia may be as marked as in acute mania. The sleep of the melancholiac, however, differs from that of the maniac in two ways. The hours of sleep in melancholia do not tend to be so variable as in mania, the amount of sleep each night being fairly constant.
History of Patient to whom Sleep Charts Nos. 5 and 6 refer.

Duffy MacN.  act. 68.  Married.

Date of admission  28th February, 1926.

On admission patient was extremely depressed, morbidly introspective and completely self-centred. He was restless and very agitated, wringing his hands, bemoaning his unhappy miserable state, and apprehensive of impending disaster. He had delusions of persecution directed against his neighbours and believed he was going to be burnt.

On night of March 2nd - 3rd 1926 he had paraldehyde.

Again on night of March 8th - 9th he had sulphon-al grains XV with 0.3 of whisky. This same amount of sedative was repeated the following night.

The sleep chart shows his sleep continued to be very small in amount, and also somewhat irregular in duration each night, but this irregularity is not nearly so marked as in the cases of acute mania.

During the first month his mental state remained unchanged, but after this resistiveness shown especially in refusal of food was added to his agitation. Physically he began to go down hill. Agitation and apprehension continued and he sank gradually lower and lower and died on 13th April, 1926. His sleep chart for the last eighteen days still shows a fairly constant amount of sleep each /
Insomnia in Acute Melancholia

Sleep Chart No. 5

Duty 68 hrs.
SLEEP CHART NO: 6.
Insomnia in Acute Melancholia
Duffy McN.
Age 68 years.
each night, though the duration of each night's sleep is short.

**Insomnia in Dementia Praecox.**

I have been unable to detect anything distinctive about or characteristic of the sleep or sleeplessness of patients suffering from dementia praecox. Patients in whom the disease has been of long standing duration and who are grossly demented seem to do with comparatively little sleep - 3 to 4 hours per night. This fact, however, may be merely characteristic of their being grossly demented and has no bearing on the original disease which produced the terminal state of dementation.

All the cases which I have observed on admission have enjoyed an average amount of sleep per night. Patients in whom the process of dementation has not approached the terminal stage likewise have an average and constant amount of sleep.
HOURS of Sleep.

SLEEP CHART NO: 7.
Insomnia in Dementia Praecox
Annie Baillie E.
Aet 23 years.
History of Patient to whom Chart 7 refers.


Date of admission 17th October, 1925.

On admission patient was morbidly shy and retiring. No interest in her surroundings. Smiled foolishly and was slightly elevated. Orientation good. Conversed in a low monotone and resented being continually prompted.

Twelve months later patient was decidedly schizophrenic. Very impulsive at times. At the end of another year patient showed no improvement. Asocial and occasionally elevated. Attitudinising at times. Impulsive and preoccupied by phantasy.

Roderickina B.  single.  (Chart 8).

Date of admission 15th July, 1908.

Age on admission 25 years.

Age at date (December, 1927) 44 years.

On admission patient was depressed. "Wore a vacant look. Apathetic."

The patient at the present time is showing morbid signs of dementation. Does not answer when addressed, and is entirely shut off from reality. Talks to herself in a low monotone quite incoherently. Croons to herself. Is impulsive at times, and slightly elevated at rare intervals.
SLEEP CHART NO; 8.

Insomnia in Dementia Precox,
Roderickina Boston.
Age on admission 25 years.
Age at date 44 years.
David J. (Chart 9). Single.

Date of admission 14th August, 1894.

Age on admission 28 years.

Age at date (January, 1928) 62.

14/8/94. On admission patient was disinclined to talk. Apathetic and disinterested. At times very resistive.

1911. Delusional and hallucinated for sight and hearing. Impulsive and at times irritable.

1915. Greatly demented.

SLEEP CHART NO: 9.
Insomnia in Dementia Frazee
David J.
Age on admission 28 years.
Age at date 62 years.
Insomnia in Milder Forms of Mania.

(1) In young subjects.

Mary B. McK.  aet 20 years. Single.  (Chart 10)
Admitted 8th March, 1926.

Patient on admission was mildly excited, slightly restless and talkative. Inclined to be a little above herself. Well oriented.

Ten days after admission patient's excitement had passed away. She was up and going about. Was sociable and employing herself in the laundry. Slightly facile and simple.

During period of excitement, though talkative and restless during the day, her sleep at night was good. Variability in nightly duration of sleep was absent and during eleven nights' observation she had 87 hours of sleep, or about 8 hours of sleep per night.

On 13.5.26. she was discharged on probation until 7.11.26. up to which time she retained improvement with no relapses and was discharged recovered.

(2) In middle-aged subjects.

Annie McD.  aet 49 years. Single  (Chart 11)
Date of admission  4th January, 1926.

Patient on admission was mildly excited and elevated. Conversation tending to be amorous. Displayed marked /
marked flight of ideas. Well oriented.

Mild excitement and elevation continued for nearly two months. At times her actions were foolish and she was inclined to be impulsive: e.g. One day in church, about three weeks after admission, she rose and hurriedly left the chapel when the minister entered.

About 10 weeks after she had been admitted both excitement and elevation had vanished. She was discharged recovered on 29th April, 1926.
SLEEP CHART NO: 10.
Insomnia in Mild Mania in young persons
Mary Bell Mac.
Aet 20 years.
SLEEP CHART NO: II.
Insomnia in Mild Mania in Middle aged Persons,
Annie McD.
Age 49 years.
Insomnia in Milder Forms of Melancholia.

(1) In young subjects.

Malcolm B. aet 22. Single. (Chart 12)
Date of admission 24th June, 1925.

On admission patient was dull, apathetic and morbidly self-centred. Would scarcely answer questions put to him. Actions very slow and deliberate. Was slow in response to questions, and in carrying out any simple thing he was requested to do. Continued without any mental change for about a fortnight and then began to rouse himself. Displayed more interest in his surroundings and began to occupy himself.

In three weeks' time his condition was much improved. Lethargy and dullness had gone, but he was slightly depressed. He gradually improved, retaining ground gained, and was discharged recovered on 22nd August, 1926.
SLEEP CHART. No. 12

Insomnia in Mild Melancholia in Young Persons
SLEEP CHART No. 13.

Insomnia in Mild Melancholia in Middle aged Persons.

Edward T.

Age 45 years.
(2) In middle-aged subjects.

Edward T.  aet 48.  Single.  (Chart 13)

Date of admission  20th December, 1925.

On admission patient was morose and silent, dull, apathetic and indifferent. Would answer questions but in the most casual manner, and seemed better pleased when left alone to brood. Disoriented for place and persons. Patient continued in this mental state for over three weeks when he showed signs of brightening up. Began to occupy himself. Conversed freely but showed some mental retardation, and was lacking in initiative and enthusiasm.

He progressed gradually, retaining improvement, and was discharged recovered on 2nd February, 1926.

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On considering the sleep charts of these four patients we find there is absence of any great disturbance of sleep, which goes to prove that in the milder forms of mania and melancholia, both in young persons and middle-aged people, the sleep habit may not be greatly upset.

Sleep Chart No. 12, the case of Malcolm B., shows two sleepless nights immediately following admission, but this need not surprise us when we recall the well established fact that many normal people pass a sleepless /
sleepless first night in a "strange bed."

Further note in the two cases of mild mania the absence of the variability of the nighttime duration of sleep so obvious in the cases of acute mania.

**Insomnia in Post-Encephalitic Cases.**

Insomnia is a very common sequela of encephalitis lethargica. Of 128 patients suffering from encephalitis lethargica admitted to and treated in Belvedere Fever Hospital, Glasgow and examined a year after the onset of the disease 55 were found to be victims of insomnia.

(C. M. Smith, M.D. Clinical Officer, Public Health Department, Glasgow - "Sequelae of Encephalitis Lethargica - Notes on 128 Cases" B.M.J. 14th May, 1927. Pp. 872,873)

I have observed the hours of sleep of the only two post-encephalitic patients admitted to the asylum, but, as will be seen by their sleep charts, insomnia did not figure as a sequela in their cases.

**Margaret W. aet 19. Single. (Chart 14).**

Patient was admitted on 1st October, 1926 on one doctor's certificate and emergency certificate. The medical certificate stated that the patient was subject to fits of temper during which she had on several occasions shown violence towards her mother. The day previous to her admission patient had one such outburst of temper, and had thrown a knife at her mother, inflicting a wound on her head.

On /
On admission patient showed no signs of depression, excitement, elevation, or confusion. Oriented in all dimensions. Answered questions relevantly, and conversation was coherent and rational.

On expiry of emergency certificate the patient was discharged not insane.

There was a history of encephalitis lethargica two years previously, and she had been treated in Belvedere Fever Hospital, Glasgow for six months.

On 19th May, 1927 the patient was again admitted to this asylum. On admission she was somewhat simple and facile, but otherwise showed no gross psychotic symptoms. She remained a patient in this asylum for two months, during which time she was quite free from insomnia, and was discharged relieved on 22nd July, 1927.
SLEEP CHART NO: 14.

Insomnia in Post-Encephalitis Lethargica
Margaret W.
Aged 19 years.
The second patient was


Date of admission 13th October, 1925.

Suffered from encephalitis lethargica three years previously. Before admission to asylum she was said to have occasional sleepless nights.

On admission she was simple and facile in her conduct and speech. There was no confusion, depression, or excitement. Conversed freely but childishly; orientation was good. Her physical condition was weak, as she was suffering from active phthisis pulmonalis.

She gradually became weaker and died on 9th February, 1927.

Her two sleep charts show that she did not suffer from insomnia while in this asylum.
SLEEP CHART NO: 15.
Insomnia in Post- Encephalitis Lethargica.
MARY MoL.
Aet 24 years.
SLEEP CHART NO: 16.

Insomnia in Post-Encephalitis Lethargia.

MARY Mc. L.
Act 24 years.
Insomnia in General Paralysis of the Insane.

In the early stages of this disease the patient may suffer from a short period of insomnia.

As the disease progresses this insomnia gives place to a phase of excessive somnolence during which the patient not only sleeps heavily at night but often falls asleep during the day. Still further on in the disease when motor restlessness becomes a prominent and persistent feature of the case, insomnia again makes its appearance and this phase of sleeplessness persists until, in the terminal stage, sleep once more becomes excessive.

I have in this asylum observed the sleep in six cases of general paralysis of the insane. Four of these cases underwent a course of malaria treatment, while two of the patients, owing to our inability to obtain the proper strain of malaria were not so treated.

In these two cases:—George C. Admitted 29th July, 1925 and died 6th September, 1926, and Donald M. admitted 15th April, 1926 and died 31st December, 1926, the variations in their sleep conformed very much to what is generally observed in general paresis.

The four other cases require separate mention, though it may be said that in the case of three of these patients sleep showed marked improvement after treatment.

1. Charles R. aged 46 years. Admitted /
Admitted 13th March, 1926.

Malaria and Tryparsamide Treatment from 24th April, 1926 to 16th August, 1926.

His sleep was perfectly good and regular after malaria treatment - sleeping on an average 6 to 8 hours each night.

Discharged relieved on 9th February, 1927.


Malaria and Tryparsamide Treatment from 18th February, 1927 to 29th June, 1927.

This patient has improved mentally. He is still rather elevated, and has no real insight into his condition. Is still delusional about certain matters relating to his previous occupation, but he now never becomes excited. He remains a rather uncertain quantity. His sleep, however, is good and regular, and he shows no tendency to fall asleep during the daytime - in fact he is very bright and alert, always doing odd jobs to assist the nurses.


Was of the expansive type of general paralytic; extremely elevated at times. Very excited, with grandiose delusions of wealth and great possessions. Suffered from insomnia. Malaria and Tryparsamide Treatment from /
from 12th August, 1926 to 25th January, 1927. After treatment his sleepless condition showed improvement.

Discharged on 28 days pass on 9th February, 1927.

On 15th February, 1927 he returned from pass of his own accord - depressed and with a strong feeling of inferiority. Showed no physical signs of G.P.I., and one without knowledge of his previous history would have had to perform a very careful examination of the patient before arriving at the diagnosis of general paralysis. Insomnia continued for about ten days, but his sleep returned, and at present (February, 1927) he sleeps 6 to 8 hours each night.

Acute depression has gone but patient is inclined to be morose.


On admission he was a typical general paralytic - fat, facile and foolish. Expansive type with grandiose delusions. Owned all the newspapers in Britain. He is an interesting case in that his reaction to malaria was peculiar, and his sleep after treatment was also peculiar.

24.5.27. Injection 3 c.c. B.T. malaria blood subcutaneous-ly in interscapular region.

10.7.27. First rise of temperature.

Between 10.7.27. and 26.7.27. he had 8 rises of temperature /
temperature. During all the time he had malaria he had only one rigor (on 20.7.27.) prior to the rise of temperature.

Though rigors were absent save on only one occasion each rise of temperature was preceded by sickness and vomiting.

By 26.7.27. the patient was becoming extremely anaemic and the skin in the region of the sacrum showed signs of breaking down, so quinine sulphate was given to stop the malaria.

In August patient was very weak. Skin over sacrum broken down. Required catheterisation for retention of urine. Mental state unchanged.

By September his physical condition had improved, and on 9th September a course of tryparsamide and mercury was commenced.

After three weeks this treatment was discontinued, because after each weekly injection patient became violently sick.

Soon after this time he became very excited. His delusions were more prominent and more absurd, and his sleep became correspondingly poor. The interesting point in his case is that during the last two months, from the middle of December to the middle of February, he has had almost complete sleep reversal.

At nights, though lying quite peaceably, he does not /
not sleep at all, but on the contrary sleeps the greater part of the day, having to be wakened for his meals.

Insomnia that Accompanies Cerebral Atrophy due to Arteriosclerosis.

When brain atrophy due to arteriosclerosis occurs it is accompanied by dilatation of the perivascular spaces, increase of the glia and pigmentation of the ganglion cells, but the medullary fibres are intact. Sometimes small areas of softening occur. Such conditions are met with in many cases of senile dementia.

Probably this may explain why the senile dement is so apt to sleep through the day - often while sitting up in his chair, - reference to which has already been made in a previous portion of this thesis.

Again we note that the senile dement becomes restless after he has retired for the night, this restlessness taking the form of wandering about the house.

When considering, then, the sleep of people suffering from senile dementia one ought to bear in mind the occurrence of their naps during the day, thus making it probable that their hours of sleep are on an average about the same as an adult of middle life.

I have found that in cases of senile dementia where there is general senile decay and no mental distress, most of their time is spent in sleep. Even when dozing /
dozing quite a lot during the day, they sleep well also at night.

Christina L.  aet 75.  (Sleep Chart No. 17).
Admitted 10th December, 1927.

Patient is greatly enfeebled in mind. Garrulous, rambling and childish in speech. Disoriented for time, place and persons. She is bed-ridden, and spends a great deal of the daytime in light, short sleeps, but, as her sleep chart shows, she also enjoys a good amount of sleep each night.

In some cases of senile dementia, however, the sleep is neither regular nor great in amount during the night. In these cases there is very often an element of distress, more obvious on some nights than on others. The patient keeps worrying or fussing and becomes so restless that it is usually early morning before they obtain any sleep.
SLEEP CHART NO: 17.
Insomnia accompanying Cerebral Atrophy
due to Arterio-sclerosis.
Christine L.
Age 75 years.
SLEEP CHART NO; 18.
Insomnia accompanying Cerebral Atrophy due to Arterio-sclerosis.
Mallag M.D.
Aet 68 years.
Mallag M. aet 68. (Sleep Chart No. 18).
Admitted 10th January, 1928.

Patient was enfeebled and disoriented; dull, and depressed. Morbidly concerned about herself. Expressed ideas of unworthiness, and was worried about the state of her soul.

Some nights this patient becomes very distressed, crying softly to herself, and is very restless. On such nights she does not sleep till early morning and then obtains only a few hours' sleep. As will be seen from her sleep chart, the nights on which she has little sleep coincide with the nights when she is restless and distressed.

She also is confined to bed, and probably obtains an average amount of sleep, for though she is not so liable to doze in the earlier parts of the day and the afternoon, she often has a nap later on in the evening between the hours of 5 p.m. and 9 p.m.

In arterio-pathetic dementia insomnia is a very marked and prominent feature.

Charles Ross. aet 52. (Sleep Chart No. 19).
Admitted 23rd November, 1927.

On admission patient talked quietly and rationally for a few minutes. Then became confused and unable to say correctly where he was or what day of the week it was /
was. He became very emotional, weeping and expressing the delusion that he was going to be "put in a hole." He said also that he had to attend two funerals in the morning, (which was not the case).

His memory for both recent and remote events was extremely inaccurate, and he had no control over his emotions.

There was a history in his case of alcohol, and of having lived a very hard life. Since coming in there has been no change in the patient's mental state.

Sleep Chart No. 19 shows the marked insomnia present in his case.
SLEEP CHART NO: 19.
Insomnia accompanying Cerebral Atrophy due to Arterio-sclerosis.
Charles R.
Aet 52 years.
CLASSIFICATION OF HYPNOTIC DRUGS.

A. The Alcohol Group.
   a. The alcohols, ethyl alcohol, Amelyne Hydrate.
   b. The Sulphones, Sulphonal, trional and tetronal.
   c. The Substituted Amides.
   d. Urea derivatives, neuronal proponal.

B. The Chloral Group.
   Chloral Hydrate
   Chloralamide
   Chloralose
   Somnal
   Hypnal
   Isopral
   Chloretone
   Bromonal
   Brometone.

C. The Paraldehyde Group.
   Paraldehyde
   Hyprone
   Phenyl methyl ketone.
THEORIES OF THE ACTION OF HYPNOTICS.

Exactly how narcosis is brought about has never been properly understood, and consequently there are many theories put forward to explain it.

A great deal of experimental work in the elucidation of the phenomenon of narcosis has been carried out, and the drug most frequently employed in these experiments has been chloroform.

Now it should be noted that there is no hard and fast dividing line between the anaesthetics such as chloroform and ether, and the hypnotics such as paraldehyde and chloral. The matter resolves itself into a question of dosage. If paraldehyde or chloral be administered in sufficiently large doses complete anaesthesia will be induced. Conversely if chloroform or ether be given in such small quantities as to produce rest and sleep only, then strictly speaking these drugs may be termed soporifics.

Therefore a theory which would satisfactorily explain the mode of action of chloroform would also explain the action of hypnotics.

The fact that the administration of chloroform is attended by a phase of excitement following the first stage of diminished consciousness and prior to complete narcosis has given rise to the theory that chloroform first excites /
excites and then depresses, but this excitement may not be due to the stimulation of the nerve endings in question, but due to lessening of the functions of the inhibitory centres of the brain, with the result that the centres of motion being untrammelled and unrestrained, act more strongly than would normally be the case.

Moreover, this second stage of excitement is frequently absent in the onset of narcosis.

Moore and Roa have propounded a theory in which they give to chloroform the selective property of attaching itself to the protein of the cells of the body - and especially the nerve cells. In support of this they have demonstrated an unstable compound of protein and chloroform. According to these investigators this chloroform-protein compound is analogous in its mode of action to oxyhaemoglobin. Just as oxyhaemoglobin gives up its oxygen to the tissue cells, so the chloroform leaves the protein of the blood cells and enters into combination with the protein of the nerve cells, thus producing narcosis and anaesthesia.

Conversely when the administration of chloroform ceases, the tension of chloroform in the blood is lessened, bringing about dissociation of the combination between the cell protein and chloroform, and anaesthesia passes off.

In the foregoing theory the blood plays an important /
ant part as vehicle, but of recent years the view that narcosis was due to changes in the blood and anaemia of the brain is no longer tenable, because it has been demonstrated that anaesthesia can still be induced in a frog the blood of whose brain has been replaced by a saline solution.

It seems fairly patent that the action of the narcotics is a direct one on nerve tissue.

Verworm is of the opinion that narcosis is due to arrest of oxidation in the cells. Lessened oxidation has been observed in many cases of narcosis, but there are also cases on record in which no diminution of oxidation has been noted. Again the decrease of oxidation may be the result of the narcosis and not one of the causal factors. Against this theory, too, is the fact that narcosis can be induced in a cell in the absence of oxygen, for instance in intestinal parasites.

Lillie has put forward the theory that narcosis is due to diminished permeability of the cell membrane, consequent upon which the ions which are necessary for the activity of the cell can no longer penetrate.

Of late years investigators have been more inclined to the view that narcotic drugs may act in virtue of their physical properties rather than their ability to enter into chemical combination with the tissues of the body.

This /
This trend of opinion is not surprising when certain facts common to all narcotic drugs are taken into consideration.

There are a great number of chemically inert substances which when absorbed enter into no combination of any kind with the tissues of the body; they are excreted unchanged, and yet they exert a greater or lesser narcotic action.

Then the chemical composition of the different narcotics is extremely diverse, and consequently their action cannot be attributable to the presence of any one radicle common to them all, but on the contrary it would rather suggest that the action of these drugs is dependent on the molecule as a whole, and not on any chemical combination that they may form in the body.

Practically all the narcotics possess the common physical property of being much more soluble in oil and lipoids than in water.

This property is so consistently present as to give rise to a scientific law which states that "The most powerful narcotic substances are those which combine a very slight solubility in water with a very high either solubility in/oils or brain lipoids."

When one of these narcotics dissolved in water comes into contact with an oil or a lipoid the drug leaves the watery medium, passes to the oil or lipid and /
and remains dissolved in the latter substances.

Now the brain cells are much richer in lipoid material than any other cells in the body, and because of this the narcotics are more liable to accumulate in these and thus have a greater effect on these cells than on any others. Moreover, the composition of cerebral cells is more easily altered and affected than are the constituents of the other body cells.

Having regard to these foregoing facts Meyer and Overton have built up a very attractive theory to account for the action of hypnotics.

In the body the narcotics are taken up by the blood, and Meyer and Overton compare the blood to a watery medium so that when the blood comes into contact with tissues having a great amount of lipoid material the narcotics, in accordance with their behaviour outside the body, leave the watery plasma of the blood for the cells containing lipoids, - thus accumulating to a marked degree in the cells of the brain. Once within the cells Meyer believes that the narcotic makes the lipoids more fluid, bringing about an alteration in the relationship of the lipoid to the other constituents of the cells, with the result that there is lessened cell activity and consequent narcosis.

This is not a chemical change but a purely physical one, and the amount of the drug which leaves the blood /
blood is in direct proportion to the relative solubility of the narcotic in blood and in lipoid material.

This co-efficient of partition between oils and water is in many cases, though not in all, a good indication of the power of the narcotic. For instance, it is true of narcotic substances which are closely related as in the case of the simple alcohols in which the narcotic power is increasingly greater from methyl alcohol right up the series to amyl alcohol in direct proportion to the increasing solubility in lipoids and decreasing solubility in water of each member of that series.

Again in a group of alcohols such as ethyl alcohol, glycol and glycerine we find that the greater the number of hydroxyl groups in the substance the less is the difference between the solubility of that substance in water and in lipoid, and its narcotic power is correspondingly decreased.

When, however, narcotics not so closely related to one another as the above are considered the relationship existing between the co-efficient of partition and narcotic power is not so simple - thus the relative co-efficient of partition of alcohol, chloral and acetone is 1 - 2 - 1, while their narcotic action is 1 - 16 - 1.

Thus it would appear that the co-efficient of partition, though undoubtedly a most important factor, is not solely responsible for the action of narcotics, but it /
it would seem that there is another, and as yet undiscovered, factor which in all probability comes into play after penetration of the cell by the narcotic.

This hypothesis of Meyer and Overton does not quite fulfil all the demands of a satisfactory explanation, but it does intelligently make clear a great number of the peculiarities of the narcotics, such as their distribution in the tissues, and their accumulation in the nerve cells.

In the present state of our knowledge the Meyer-Overton theory of the action of hypnotics is the most satisfactory.
LIST OF DRUGS USED.

1. Sulphonal.
2. Paraldehyde.
3. Thymosene Compounds "A" and "B".
4. Hyoscine Hydrobromide $\frac{1}{75}$ grain with Morphine Sulphate $\frac{1}{4}$ grain.
5. "15" Mixture.
7. Amylene Hydrate.
8. Chloralamide.
10. Dial.
11. Allonal.
12. Luminal Sodium.
13. Theominal.
Sulphonal, paraldehyde, and hyoscine compounds "A" and "B", are the sedatives and hypnotics most commonly used in this institution. Consequently I have employed them and seen them used very many times and so, instead of giving a tabulated record of results from these drugs, I append temperature charts illustrating examples of cases mentioned in the text.
Sulphonal.

**Synonym.** Diethyl-methane-diethylsulphone.

Sulphonal is one of the members of the sulphone group, and is therefore chemically allied to methane, in which all the hydrogens are replaced by alkyl or alkyl sulphonic radicles, thus:

![Chemical structure of methane and sulphonal]

Chemically sulphonal is a very stable compound. It is produced by oxidation of a compound of ethyl mercapton and acetone and occurs in crystalline and powder form. It is colourless and without taste and odour. Its solubility in water is 1 in 450, and in cold alcohol 1 in 30, but it is freely soluble in hot alcohol, which forms a good vehicle for its administration.

On account of its insolubility sulphonal is absorbed very slowly and its excretion is even slower than its absorption. Two results follow from its delayed absorption and slow excretion. Its action is delayed and uncertain, and sleep is therefore late in following, while on the other hand its effect is apt to be prolonged, and depression, drowsiness and lack of energy are commonly seen.
seen the day after its administration. Sulphonal is slowly decomposed in the body and excreted in the urine mainly as ethyl-sulphonic acid.

This breaking up of sulphonal takes place very slowly and Kast has found sulphonal in the blood many hours after administration of the drug. It is not completely decomposed in the body, as some unchanged sulphonal is found in the urine.

The hypnotic action of the drug is not due to ethylsulphonic acid, but to the unchanged molecule of sulphonal. Pharmacologists are not in entire agreement as to its action on the heart and circulation.

Lauder Brunton states that the drug has little action upon the circulation.

Dixon says: "It is less dangerous than chloral in that it has no depressant effect on cardiac muscle." (W.E. Dixon: "Manual of Pharmacology." Sixth edition, 1925. P. 69).

Cushing, however, says that although it has no immediate action on the circulation even in large doses, it is stated that the prolonged use of sulphonal is deleterious to the heart, and it appears to be more uncertain in its narcotic action in cases of heart disease than in other conditions.

Experimentally the late Sir Frederick Mott and Drs. D.W. Woodhouse and F.A. Pickworth have shown that sulphonal /
sulphonal causes morbid disturbance of nutrition in growing animals. In cats and monkeys where the hypnotic was continued for longer than a week numerous mucinoid particles were discovered throughout the central nervous system, sometimes within the nerve cells.

After intensive treatment with sulphonal chromatolysis, loss of Nissl substance and signs of degeneration were found in the nerve cells of the cerebellum, mid-brain and spinal cord. These investigators are of opinion that the mucinoid substance is a metabolic product of the nerve cells which have been damaged by hypnotics.

Again, some investigators are quite definite that an individual may acquire a tolerance for sulphonal, while Dixon states that the habitual use of the sulphonal group does not lead to tolerance. Personally I believe that a tolerance for the drug is undoubtedly acquired.

The use of sulphonal, especially if administered continuously for more than two or three weeks, gives rise to a series of symptoms indicative of poisoning.

When large doses are employed toxic symptoms are not at all uncommon.

But even moderate doses in old and debilitated persons may cause poisoning and it must always be borne in mind that certain persons are predisposed to sulphonal poisoning, in which cases very moderate doses of the drug give rise to alarming symptoms.

On /
On the other hand some persons can take sulphonal for a long time with impunity.

Among the earliest toxic symptoms is weakness of the muscles. There may be incoordination of gait and speech, so that words are slurred and indistinct - thus somewhat resembling general paresis. Digestive disturbances, such as vomiting, diarrhoea or constipation, accompanied by abdominal pain may be present. Very soon the urine turns a port-wine colour due to the presence of haematoporphyrin. The presence of haematoporphyrin in the urine is the most characteristic sign of sulphonal poisoning.

It is especially liable to occur in anaemic women. Haematoporphyrin was first recognised by Hoppe-Seyler. It has the chemical formula $C_{68}H_{72}N_{3}O_{12}$. The pigment is present in traces in normal urine, but in sulphonal poisoning it is greatly increased in amount and gives the urine a more or less red colour. It is an iron free derivative of haematin and is isomeric with bilirubin. After treating the urine by Garrod's method it may be examined with the spectroscope, when it shows a distinct and characteristic spectrum.

The amount of haematoporphyrin in the urine varies very much in different individuals.

In one case Tyson and Crofton found that the quantity /
tity passed in one day indicated the destruction of one-seventeenth of the total haemoglobin of the body.

Its formation is due to some obscure change in the liver and has an injurious effect upon that organ, for the relation of urea to the total nitrogen of the urine is changed. Metabolism of the purine bodies is also affected.

Sulphonal does not seem to cause any alteration in renal function although in some animals after prolonged administration of the drug albumen and casts were found in the urine, while haemorrhages into the kidneys have been observed after giving only a few doses.

When sulphonal was first brought to the notice of the medical profession in 1887, and for a considerable time afterwards, it was regarded as the hypnotic for which doctors had been looking for years.

Afterwards its bad effects and the occurrence of haematoporphyrimuria were more and more thrust upon the notice of the profession and to-day opinion as to whether or not sulphonal ought to be employed is very divided.

It is true that enormous doses of sulphonal have been taken by people - severe toxic symptoms supervening without fatal termination. In one case 250 grains sulphonal together with one ounce chlorodyne were taken without fatal results. (Campbell. "Lancet." 1897. J. Page 661).

Morris /
Morris reports a case of a man aged 68 who took 245 grains of sulphonal in the form of tablets of 5 grains each. The patient was in a state of stupor for 120 hours but at no time did his condition present symptoms to cause alarm.

The treatment adopted was purely expectant, and the patient ultimately made a recovery. The interesting point in this case is that at no time did the urine show haematoporphyrin. (Morris. "Brit. Med. Journ." May 22nd, 1909. Page 1235).

On the other hand, death has occurred after the ordinary medicinal dose.

With this drug, as it is not readily excreted, cumulative action occurs. Also the minimal toxic dose varies greatly in different individuals. Perhaps these facts help to explain the wide divergence of opinion held by different doctors with regard to sulphonal.

Professor W.A. White of Washington, states that he has found sulphonal an excellent hypnotic. Stoddart obtained good results from the exhibition of sulphonal in senile melancholiacs who, he says, are less liable to haematoporphyrinuria than younger patients. Nevertheless, he also says sulphonal is not to be recommended in cases of melancholia.

Craig and Beaton are not in favour of the use of sulphonal.

Professor /
Professor G.M. Robertson of Edinburgh is very averse to using sulphonial at all on account of its after effects.

During the nine years Professor Robertson was at Stirling District Asylum he only gave it once, to a female patient, and among the male cases he employed it only in cases of general paralysis of the insane. He further states that he has seen death occur in one case after only three doses of sulphonial.

In my own employment of sulphonial I have, from the very commencement, been most careful in choosing the cases in which I have given the drug, and nowadays I am still more careful on this point.

Exercising due discretion as to the cases in which to exhibit the drug, and proper precautions being taken, I have, on the whole, found sulphonial a very useful hypnotic.

First, then, one should always carefully choose one's cases. In old people doses like grains XXX or grains XV of sulphonial should never be employed.

Two aged patients, in my experience, succumbed to cerebral haemorrhage which occurred within eight hours of the administration of sulphonial grains XV. The occurrence of cerebral haemorrhage in two such cases may, of course, have been coincidental, but since then I have never given sulphonial for maniacal excitement in aged people /
people.

I have, however, found sulphonal most efficacious in evening restlessness giving rise to simple insomnia in elderly people when administered in 10 grain doses combined with half an ounce of hot whisky. Ten grains have always proved quite sufficient to procure the desired effect and consequently I never employ larger doses in such cases.

The warm alcohol serves two useful purposes. It is firstly the best vehicle in which to administer sulphonal, and the patient has also the benefit of the hypnotic action of the alcohol itself.

For such a case as the foregoing see appended chart of Mallag M.
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Sutley & Silverlock Ltd
92, Blackfriars Road, London.
Sulphonal has the advantage of being a motor sedative and therefore is ideal in the motor excitement of acute mania. There again one must choose one’s cases and I never use sulphonal in acute excitement if there is the slightest suspicion of heart disease. Moreover, with more experience I have changed my method of administration. In motor excitement in healthy adults I used to employ sulphonal in single doses of grains XXX sometimes, in cases where quick action was desired, combined with half an ounce of "15" mixture.

Nowadays, except in fairly rare cases whose physical condition I am quite sure is very good, I am not inclined to use sulphonal in single doses of grains XXX.

In a case where motor restlessness is the predominant feature and there is little or no noisiness, I give sulphonal grains XV in the morning between 9 a.m. and 10 a.m., and if necessary repeat the dose in the evening between 6 p.m. and 7 p.m. I think this method of administering sulphonal in divided doses of XV grains night and morning is much better than giving a single dose of sulphonal grains XXX. In a case where there is great noisiness combined with motor excitement, and quick and prolonged action is called for, I give usually paraldehyde drachms two and a half with sulphonal grains XV, the paraldehyde acting quickly and the sulphonal coming into action as the effect of the paraldehyde is wearing off, the /
I never use sulphonal on two successive nights unless I find that sulphonal gives the patient more rest than any other hypnotic.

I never use sulphonal continuously for more than a week and each patient to whom I administer sulphonal is carefully watched. On one occasion I have seen a patient who had had sulphonal continuously for one week collapse. General stimulation was the treatment adopted and the patient recovered. There was no haematoporphyrin in the urine.

There is one most important point which must always receive attention in patients to whom sulphonal is administered, namely the bowels must be kept open.

On the morning following the day on which sulphonal has been administered to a patient, I always give that patient an aperient and strict vigilance is kept to see that the bowels have moved.

Beyond drowsiness and lack of energy on the day following the administration of sulphonal, I have never seen any untoward symptoms with the exception of the case of collapse already mentioned.

A case of haematoporphyrinuria has never fallen within my experience.

For examples of cases in which sulphonal has been used by me, see appended temperature charts.
I have tried to come to some conclusions regarding the effect of sulphonal administered to patients time after time during recurrent bouts of excitement.

With this end in view I made a careful perusal of the cases of five patients who have been in this asylum for a period of time ranging from twenty-five years to fourteen years.

All these patients I know have had many recurrent periods of excitement which were frequently treated with sulphonal, but the fact that two of these patients suffer from dementia praecox while three belong to the manic depressive group, combined with the fact that I had no definite data as to the actual amount of sulphonal taken by each patient have complicated matters so much that I have been unable to come to any definite conclusions.
Paraldehyde.

Chemical Formula: $C_6H_{12}O_3$.

Paraldehyde is a polymer of ethyl aldehyde.

It is a colourless liquid of slightly less specific gravity than water. It has a most unpleasant odour and a hot burning taste.

Its boiling point is $230^\circ F$, and its freezing point is $50^\circ F$. During winter it is quite usual to see it freezing and forming crystals on the medicine measure as it is being poured from the bottle. It is unstable in the presence of light and must be protected in dark coloured bottles. Its solubility in water is 1 in 10 and it is very freely soluble in alcohol.

In its action it resembles chloral but it has not the depressing action upon the heart possessed by chloral. It possesses all the advantages of chloral without the disadvantages of that drug.

Paraldehyde also resembles alcohol in its effect, but it is such a powerful narcotic that it rarely induces any symptoms of excitement. I have never seen excitement produced by paraldehyde.

Being such a powerful hypnotic it acts very quickly, frequently within five minutes of its administration. Its usual time to take effect is from fifteen minutes to half an hour after being administered.

Paraldehyde possesses very great advantages as a hypnotic.
hypnotic. Its quick action makes it markedly superior to sulphonal, trional and veronal in this respect.

Again, it has no direct action on the heart and can therefore be given with confidence in cases of mania where there is cardiac weakness, debility and exhaustion either the outcome of prolonged excitement, or from such causes as refusal of food; thus being superior to chloral.

It produces sleep lasting several hours and causes no unpleasant after effects.

It is altogether a safe hypnotic to use, its range of dosage being very great.

The British Pharmacopeia gives the therapeutic dose as minims 30 to minims 120, but much larger doses have been administered without any more serious consequences than prolonged unconsciousness. Martindale and Westcott state that to their knowledge half an ounce has been given - which these authors think is probably a maximum single dose. But larger doses than half an ounce have been given - even in cases where no tolerance could possibly have been acquired.

Sir Thomas Clouston tells that a nurse of his once gave a patient, who had just begun to take paraldehyde, two ounces as a single dose, and the patient was none the worse.

Professor G.M. Robertson of Edinburgh states that one of his dispensers had dispensed two ounces of paraldehyde /
hyde to about half a dozen patients. The condition of the patients alarmed Dr. Robertson very much. He states that they appeared as if under chloroform, and that an operation could have been performed on them and they would not have moved. One of these cases died, but that patient was suffering from advanced phthisis and heart disease, which, no doubt, contributed to the death. Another case is recorded in which more than three ounces of paraldehyde were taken with no effect beyond prolonged slumber.

There is one fatal case of paraldehyde poisoning, however, recorded by Lovell Drage. The patient, a woman aged 46, was the victim of drug habits. In thirty-three hours she took at least thirteen drachms of paraldehyde and on the top of this a single dose of two ounces of this hypnotic which proved fatal in about three hours. The symptoms were unconsciousness, cyanosis, intermittent pulse, profuse sweating and shallow regular respirations.

In my experience I have never required to give more than three drachms of paraldehyde, though I have seen four drachms used in this asylum.

But if the drug is ideal from the point of view that it is safe and produces light, natural sleep very quickly, it possesses several unpleasant characteristics which are decided disadvantages, more especially in private practice.

The pungent odour and hot burning taste make it unpleasant.
unpleasant to take.

Moreover, it is practically impossible to conceal this taste. Various devices have been tried to this end. Strongly sweetened tea is said to act as well as anything.

The drug has been given in iced water or mixed with pounded ice, which has also the advantage that this prevents the burning sensation caused by irritation of oesophagus and stomach.

Some people administer it in capsules and as it is a liquid it may be administered by the feeding tube.

Stoddart advises Aqua menthae piperitae as a flavouring agent. I have always dispensed the drug in doses from two to three drachms in the form of a draught made up to two ounces with syrup aurantii and water, using the same amount of syrup aurantii as of paraldehyde in each draught. This serves two purposes, namely disguising the taste as much as possible and also diluting the drug.

Paraldehyde should never be administered unless well diluted, not only on account of its burning taste but also because it exerts an irritating influence on the alimentary tract.

Because of its being irritating to the mucus membrane of the stomach it is inadvisable to give paraldehyde to a person with digestive disturbance.

So much for its absorption.

Paraldehyde, though mainly excreted in the urine, is also in part /
part excreted by the lungs and consequently can be de-
tected in the breath for a considerable time after the
patient awakes. Owing to its being excreted by the lungs
it has an irritative effect on these organs more especi-
ally on the bronchial tubes. Therefore it is contrain-
dicated in respiratory disorders, though I have known
of a two drachm dose given in pneumonia with excellent
results.

I have read that when paraldehyde is prescribed
in pneumonia it should always be given per rectum, and
though this method of administration may overcome any
difficulty that may arise on account of the taste of the
hypnotic it in no wise obviates the deleterious action of
the drug upon the lungs, as it is not to its absorption
but to its excretion that its ill effects on these organs
are due. The respiratory diseases in which it should
never be given are acute and chronic bronchitis, as in
patients suffering from these diseases paraldehyde is apt
to set up bronchorrhea.

In spite of the nauseous taste of paraldehyde a
habit has been known to arise. I have come across three
cases, who, if they could not altogether be said to have
established a habit for paraldehyde, nevertheless had no
difficulty in taking it, but on the contrary evidently
enjoyed taking it. Because of the possibility of a hab-
it formation, and also the fact that a rapid tolerance
for /
for paraldehyde can be established, the hypnotic should on no account be given over prolonged periods.

Paraldehyde is not an analgesic and is consequently of little use where severe pain is a feature of the case.

A rare sequela of the exhibition of paraldehyde is the appearance of an erythematous rash.

It has been noted that paraldehyde resembles alcohol in its action and also tolerance for the drug is rapidly acquired in alcoholics; therefore it must always be borne in mind that alcoholic patients require larger doses of paraldehyde than do patients not addicted to alcohol.

Older patients whose blood pressure is above normal require larger doses of paraldehyde in order to produce sleep.

This may be seen from the following case.

Charles R. aet 52 years.
Admitted 23rd December, 1927.

Patient had a high blood pressure, and in his case there was a history of addiction to alcohol. His sleep was very poor as will be seen by Sleep Chart No. 19.

Given three drachms paraldehyde patient always obtained a good night's sleep.

It was decided gradually to lessen the quantity
of paraldehyde by fifteen minims per night, the actual amount of the draught remaining the same as originally given, namely two ounces.

It will be seen from the following table that less than two and a half drachms had little effect on the patient.

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<thead>
<tr>
<th>Date</th>
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<th>Sleep Duration</th>
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<td>6 &quot; &quot;</td>
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<td>2 &quot; 30 &quot; &quot;</td>
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<td>2 &quot; - &quot; &quot;</td>
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<td>6.2.23</td>
<td>3 &quot; - &quot; &quot;</td>
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For examples of cases in which I have employed paraldehyde see attached temperature charts.
1. Hyoscine Compound A. (Tabloid)

2. Hyoscine Compound B. (Tabloid)

The above two hyoscine compounds are preparations for hypodermic injection manufactured by Burroughs Wellcome & Co.

1. Hyoscine Compound "A" contains

- Hyoscine Hydrobromide  gr.\( \frac{1}{100} \)
- Morphine Sulphatis  gr.\( \frac{1}{6} \)
- Atropine Sulphatis  gr.\( \frac{1}{180} \)

2. Hyoscine Compound "B" contains

- Hyoscine Hydrobromide  gr.\( \frac{1}{100} \)
- Morphine Sulphatis  gr.\( \frac{1}{4} \)
- Atropine Sulphatis  gr.\( \frac{1}{50} \)

Atropine belongs to a series of very closely allied alkaloids of which the other principal members are hyoscyamine and hyoscine (scopolamine).

Hyoscyamine is isomeric with atropine and its action is very similar to atropine.

Hyoscine though not an isomer is very closely related.

Atropine consists of a mixture of an equal number of molecules of the two optically active hyoscyamines.

In its action on the central nervous system it first stimulates and then depresses. In man after a varying /
varying period of excitement drowsiness develops, followed by sleep. It diminishes secretions, dilates the pupils, accelerates the heart, and inhibits the movements of the intestines, i.e. it acts antagonistically to the parasympathetic nervous system (autonomic nervous system of Langley) i.e. it is a parasympathetic depressant. (Dr. M. Laignel-Lavastine: "The Internal Secretions and the Nervous System": 1909. Page XIII).

Hyoscine closely resembles atropine in its peripheral action, but it acts more powerfully, more quickly, and the effects are of shorter duration.

Morphine is an alkaloid derivative of opium, and of all such derivatives it is the most narcotic and analgesic.

Its main actions are depression of pain perceiving centres; depression of medullary reflexes and inhibition of peristalsis. It inhibits peristalsis in two ways, firstly while it is circulating in the blood by its action on certain nerve cells, and secondly, and more important, by its being excreted into the gut and having thus a direct action on the intestinal wall.

It thus causes constipation and that is one of its main disadvantages of its exhibition in mental cases.

Its depressant action on the various cerebral centres is in the reverse order of their development. Attention, self-control, and judgment, are early lost. Thus it /
it forms a good example of the law of dissolution. Hyoscine, atropine, and morphine form a good combination.

It may at first appear that morphine and atropine should not be combined as their actions on the pupil are opposite - atropine dilating the pupil while morphine contracts it. But these actions are not truly antagonistic because atropine dilates the pupil by acting on the peripheral endings of the third cranial nerve while the contraction of the pupil by morphine is induced by central action.

In using Hyoscine Compounds A and B one must be prepared to meet with idiosyncrasies towards the drug in different people. I have met with two such cases.

Mrs. R. or F. aged 67 years.

Admitted 31.1.21.

When I first came to this asylum I was warned not to give this patient a hyoscine compound for excitement as on one occasion when she did have such an injection she had collapsed and her condition had given rise to alarm. On 22.7.26. this patient had a very profuse haematemesis and was given by me ¼ grain morphine sulphate from which she displayed no untoward symptoms. On 25.7.26. she had recurrence of haemorrhage and again was given ¼ grain morphine with excellent results.

Patient made a good recovery. On 29.9.26. patient /
Patient was very excited. I gave her $\frac{1}{4}$ grain morphine sulphate with $\frac{1}{30}$ grain atropine sulphate and patient showed no signs of collapse or any toxic symptoms.

I therefore concluded that collapse when the Hyoscine Co. B. was used was due in part to the greater amount of depressant employed and in part to the presence of hyoscine hydrobromide in the injection.

Elizabeth S., aged 23 years.

Admitted 15.10.21.

Patient has recurrent bouts of excitement, is very noisy and will not stay in bed. Runs about and tries to escape. Several times she has had Hyoscine Co. "B" from me which has always had the desired effect as far as reduction of excitement is concerned, but always when the effects of the injection wore off she was sick and vomiting. The patient suffers from phthisis pulmonalis, and twice in my experience she has had severe haemoptyses, on each of which occasions I gave her $\frac{1}{4}$ grain morphine hypodermically, with good results.

Later, as in previous case, I once gave her for excitement $\frac{1}{4}$ grain morphine sulphate with $\frac{1}{30}$ grain atropine sulphate hypodermically, and she was neither sick nor vomiting when she woke up. Again the conclusion is that to some people the hyoscine hydrobromide in the compound is the toxic element.
I have found Hyoscine Compound A most satisfactory in the following case.

**John M. act 50 years.**

**Admitted 12.10.17.**

Recurrent excitement. Patient suffers from asthma.

When attack of excitement coincides with attack of asthma I invariably give the patient a hyoscine Compound A which affords him a good night's rest in two ways, by allaying the excitement, and by relieving the spasm of the bronchial muscles.

Patients sometimes object to the use of hyoscine as it gives them a feeling of constricting bands around the chest. The feeling is experienced by the patients soon after the administration of the drug and some people explain the excitement stage which is sometimes present before sleep supervenes as being the outcome of fear brought on by this sensation of imprisoning bands.

In my experience with hyoscine I have never observed an initial phase of excitement. In the great majority of cases the injection acts quickly, sleep coming on in from twenty to thirty minutes and lasting from five to eight hours, without the appearance afterwards of any toxic symptoms.

I have repeated the injection within twenty-four hours and have given it on as many as three successive days.
days without observing any signs of toxicity in patient. But if I give a hyoscine compound B. to a patient in the morning my usual practice, if a hypnotic is required at night, is to prescribe paraldehyde.

I have known hyoscine compound B. not only fail to produce sleep but fail to reduce excitement in any appreciable degree, and with this drug more than any other have I observed patients fighting against its effects.

When hyoscine compound B. fails to produce sleep or to reduce excitement I have used hyoscine in bigger doses combined with morphine sulphate — thus hyoscine hydrobromide grs. $\frac{1}{5}$ with morphine sulphate gr. $\frac{1}{4}$.

George A. aged 26 years.

Admitted 5.11.27.


On 6.11.27. had hyoscine compound B at 10 a.m. This had little or no effect. Repeated at 7 p.m. after which patient became quieter and had one hour's sleep.

On 8.11.27. excitement continued and he had hyoscine hydrobromide $\frac{1}{5}$ with morphine sulphate $\frac{1}{4}$ which gave him five hours' sleep — sleep coming on forty minutes after injection.

On 11.11.27. and again 17.11.27. he had similar injections /
injections with equally good results - having five and six hours' sleep on these respective nights.

**Alexander G.P.**  
*age 30 years.*  

Admitted 20.7.27.

Patient wildly excited in look and manner. Shouting loudly and incoherently. Totally disoriented. Mistaken identity. Extremely resistive, violent and aggressive. Had hyoscine Compound B at 1.30 p.m. on day of admission with no marked effect. Repeated at 10 p.m. same night, giving four hours' sleep, but patient awoke as noisy, violent and restive as ever.

At 7 p.m. on 21.7.27. was given hyoscine hydrobromide $\frac{1}{75}$ with morphine sulphate $\frac{1}{4}$ which gave him a good night's rest, but in morning shortly after waking patient was again as noisy as ever, and continued so throughout forenoon. He was very toxic looking, and towards afternoon showed signs of exhaustion. The bowels had not opened though he had had an aperient.

Enema saponis administered at 3 p.m. with very good result and patient almost immediately calmed down, confusion departed and he made a rapid recovery without once relapsing.

Discharged recovered on 8.11.27.
Louisa J.R.  

Admitted 3.4.24.

This patient had made a recovery and her mental condition had been stable for some time. She was discharged on twenty-eight days' pass on 1st February, 1923.

Returned on 5.2.23. having been very noisy, excited and sleepless during previous three days. Was very restive, violent and aggressive.

Had injection of hyoscine hydrobromide \(\frac{1}{2} \text{gr} \) with morphine sulphate \(\frac{1}{4} \text{gr} \) at 7.15 p.m. Half an hour afterwards patient was asleep and slept for eight hours.

In practice among sane people a doctor must always remember that for some people a hypodermic syringe possesses a fascination, consequently he must be most careful with regard to hypodermic injections, more especially of such drugs as give ease from pain or afford any sensation of temporary feeling of well being, excitement or elevation. In asylum practice an exact parallel scarcely obtains, save in cases who, prior to admission, had acquired the habit, but still the asylum medical officer does meet patients who ask for hypodermic injections.

Mrs. M. or C.  

Admitted 29.5.24.

A case of involutional insanity with delusions of unworthiness and of a hypochondriacal nature.

Patient /
Patient was most troublesome and noisy. At night her sleep was disturbed by terrifying dreams which persisted as visual hallucinations during the daytime.

She was most restive and would take no hypnotics by mouth, and was thus quite frequently given a hyoscine compound hypodermically. Ultimately she used to ask for "the needle."

On no account should one accede to such a request made by a patient.

On such occasions this patient refused all hypnotics by mouth and was so restive that none could be forcibly given by this route — yet patient was obviously distressed.

On several such occasions I have given this patient a hypodermic injection of 2c.c. sterile water and each time I have done so patient calmed down, went to sleep and enjoyed a good night's rest.

Because the morphine in the hyoscine compound tends to cause constipation, I always give an aperient the day following an injection of this compound.

For cases in which hyoscine compound A and B were employed see appended temperature charts.
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**Notes:**
- Feb 2: Afebrile, appetite very good.
- Feb 8: Usually good at noon, usually poor at night.
- Died of 11.29.20
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Name: John, J.  Age: 62 yrs  Disease:  
Result:  

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**Disease:**

- Feb 1: Diarrhea, temperature 98.6°F
- Feb 2: Diarrhea, temperature 98.6°F
- Feb 3: Diarrhea, temperature 98.6°F
- Feb 4: Diarrhea, temperature 98.6°F
- Feb 5: Diarrhea, temperature 98.6°F
- Feb 6: Diarrhea, temperature 98.6°F
- Feb 7: Diarrhea, temperature 98.6°F
- Feb 8: Diarrhea, temperature 98.6°F

**Remarks:**

- Feb 1: Diarrhea, temperature 98.6°F
- Feb 2: Diarrhea, temperature 98.6°F
- Feb 3: Diarrhea, temperature 98.6°F
- Feb 4: Diarrhea, temperature 98.6°F
- Feb 5: Diarrhea, temperature 98.6°F
- Feb 6: Diarrhea, temperature 98.6°F
- Feb 7: Diarrhea, temperature 98.6°F
- Feb 8: Diarrhea, temperature 98.6°F
| CENT. | FAHR. | MEM | MEM | MEM | MEM | MEM | MEM | MEM | MEM | MEM | MEM | MEM | MEM | MEM | MEM | MEM | MEM | MEM | MEM | MEM | MEM |
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| 40°   | 105°  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 39°   | 104°  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 38°   | 103°  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 37°   | 102°  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 36°   | 101°  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
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| 34°   | 99°   |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 33°   | 98°   |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 32°   | 97°   |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 31°   | 96°   |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |

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Sutcliffe & Silverlock Ltd.
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**Pulse**

- Dec. 1927: 68, 58, 52, 60, 72, 70, 70, 66, 68, 64, 64, 60, 68, 64, 66, 60, 68, 60, 64, 62, 60

**Resp.**

- Dec. 1927: 18, 18, 18, 18, 18, 18, 18, 18, 18, 18, 18, 18, 18, 18, 18, 18, 18, 18, 18, 18, 18

**Urine Oz.**

- Dec. 1927: 5, 3, 4, 5, 8, 6, 6, 0, 4, 3, 5, 6, 6, 6, 8, 6

**Reaction**

- Dec. 1927: Negative

**Albumen**

- Dec. 1927: 5, 3, 4, 5, 8, 6, 6, 0, 4, 3, 5, 6, 6, 6, 8, 6

**Sugar**

- Dec. 1927: Negative

**B. O.**

- Dec. 1927: 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0
| Date | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 |
| CENT. FAhR. | 41° | 40° | 39° | 38° | 37° | 36° |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | 106° | 105° | 104° | 103° | 102° | 101° |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | 99° | 98° | 97° | 96° |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

**Name:** Mary S.  
**Age:** 60 years  
**Disease:**

| Pulse |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Resp. | 40 | 44 | 46 | 50 | 20 | 65 | 20 | 40 | 12 | 40 | 12 | 40 | 12 | 40 | 12 | 40 | 12 | 40 | 12 | 40 | 12 | 40 | 12 |

**Urine OZ:**  
**Reaction:**

| Sp. Gr. | 2 | 2 | 2 | 2 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Albumen | 1 | 1 | 1 | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Sugar | 1 | 1 | 1 | 1 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| B. O. |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

**No. 2**

Sutles & Silverlock Ltd  
92, Blackfriars Road, London.
TABLE I.

( $\frac{3}{4}$ or $\frac{3}{8}$ = half ounce or 4 drachms

$\frac{1}{8}$ = 1 drachm)

"15" MIXTURE.

<table>
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<tr>
<th>Date</th>
<th>Dose</th>
<th>Patient</th>
<th>Time of Administration</th>
<th>When Asleep</th>
<th>Number of Hours of Sleep</th>
<th>Remarks</th>
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<td>1 3-4 April</td>
<td>$\frac{3}{8}$</td>
<td>Mrs. G.</td>
<td>11.5 p.m.</td>
<td>11.30 p.m.</td>
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<tr>
<td>2 5-6 &quot;</td>
<td>$\frac{3}{8}$</td>
<td>Mrs. G.</td>
<td>12.15 a.m.</td>
<td>12.55 a.m.</td>
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<td>3 12-13 &quot;</td>
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<td>12.50 a.m.</td>
<td>1.25 a.m.</td>
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<td>Mary R.</td>
<td>11.20 p.m.</td>
<td>11.50 p.m.</td>
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<td>5 14-15 &quot;</td>
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<td>John M.</td>
<td>7 p.m.</td>
<td>8.5 p.m.</td>
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<td>6 14-15 &quot;</td>
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<td>Mrs. G.</td>
<td>12.50 a.m.</td>
<td>1.25 a.m.</td>
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<td>7 15-16 &quot;</td>
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<td>8 16-17 &quot;</td>
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<td>10 18-19 &quot;</td>
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<td>11 18-19 &quot;</td>
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<td>7 p.m.</td>
<td>8.15 p.m.</td>
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<th>Number of Hours of Sleep</th>
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<td>66.15 p.m.</td>
<td>9.10 p.m.</td>
<td>6</td>
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</tr>
<tr>
<td>21</td>
<td>3m</td>
<td>Ann M.</td>
<td>7.20 p.m.</td>
<td>7.40 p.m.</td>
<td>9</td>
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</tr>
<tr>
<td>22</td>
<td>3V3j</td>
<td>John M.</td>
<td>11.40 p.m.</td>
<td>12.30 a.m.</td>
<td>4</td>
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</tr>
<tr>
<td>23</td>
<td>3V3j</td>
<td>Agnes B.</td>
<td>7.30 p.m.</td>
<td></td>
<td>0</td>
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</tr>
<tr>
<td>24</td>
<td>3m</td>
<td>Jessie McD.</td>
<td>7.15 p.m.</td>
<td></td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>3m</td>
<td>Jessie McD.</td>
<td>7.15 p.m.</td>
<td>11.40 p.m.</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>3m</td>
<td>George M.</td>
<td>11.20 p.m.</td>
<td>11.40 p.m.</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>
"15" Mixture.

This hypnotic mixture is called "15" mixture because it contains 15 grains potassium bromide, 15 grains chloral hydras and 15 minims Liquor opii sedativus to each half ounce of water.

Potassium bromide (K Br) acts by depressing the psychical functions, the motor area, the medulla, and cord.

Blunting of sensation and diminution of reflexes are found in the various mucous membranes, including the mucous membrane of the genito-urinary tract, and the latter is responsible for the loss of sexual feeling.

When using bromide several facts have to be borne in mind.

Its continued use over a prolonged period gives rise to a condition named bromism, which occurs more readily in some people than in others. The main signs and symptoms of bromism are cutaneous manifestations such as skin eruptions of various kinds, digestive disturbance such as loss of appetite; increased secretion of bronchial and nasal mucous membranes, and various mental symptoms. Small doses of liquor Fowleri given along with bromides will do much to prevent the occurrence of a bromide rash.

Most of the tissues of the body are unable to differentiate /
differentiate between bromides and chlorides and react to bromide in the same way as they do to common salt. The bromides supplant the chlorides in the body. Consequently with continued treatment bromides tend to accumulate.

After a single dose of thirty grains the urine was found to contain bromide for two months. (Cush: "Text book of Pharmacology and Therapeutics": 7th edition, 1918, pp. 268 269).

This inability of the tissues to differentiate between bromides and chlorides explains why the effect of bromides is enhanced when given to patients on a salt-free diet.

Lastly, it should be remembered that in old people bromides should be used with caution as even small doses may give rise to mental confusion and continued use of bromides may lead to permanent impairment of intellectual powers. (Leonard Williams, M.D. "Minor Maladies and their Treatment." 5th edition, 1923. pp. 336 - 337).

**Chloral Hydras.**

**Chemical Formula** - \( \text{C} \text{Cl}_3 \text{CH(OH)}_2 \).

Chloral hydrate is a crystalline solid with characteristic odour and a hot acrid taste. It is readily soluble in water. Its deliquescent properties preclude its use in most of the solid preparations, and its irritant effects /
effects contraindicate hypodermic injection. Its narcotic action being powerful, it acts quickly, and used with care is a most excellent hypnotic producing a condition identical with natural sleep, and lasting from six to eight hours. In its action it resembles chloroform, but unlike chloroform it rarely causes excitement. On the whole chloral is a remarkably reliable drug. Its main disadvantage is its depressant effect on the vaso-motor centre, which leads to another less important though nevertheless unpleasant sequela, of skin eruption. It also exerts a depressant action directly on the heart, and its use therefore is contraindicated in heart affections, renal diseases and general debility. Chloral is mainly excreted in the urine in the form of urochlorallic acid, but some unchanged is secreted into the stomach and this gives rise to the nausea and discomfort which some patients experience when they awake from sleep after chloral.

Chloral in therapeutic doses, and only in such doses should it ever be administered, exerts no analgesic effect, so that the presence of pain may prevent sleep after giving chloral.

Liquor Opii Sedativus (Battley) is a proprietary hypnotic and sedative. It is double the strength of tincture of opium and therefore contains 2% morphine. It acts quickly.
Patients treated with "15" Mixture.

Mrs. G. aet 56.

Admitted 8.7.11.

Patient suffers from paraphrenia.

On admission had delusions of suspicion. Imagines a man, Riley, had stolen her marriage lines. Had hallucinations of hearing. People shouting opprobrious names after her. Made accusations with no foundation against various people. At present date she is still very deluded. Believes Dick Whittington is her husband. At times acutely hallucinated hearing people abusing her. She becomes extremely noisy, shouting abuse at her imaginary tormentors. Her sleep on such occasions is bad. She falls asleep at beginning of night and very little awakens her, when she immediately becomes noisy and abusive. Her bouts of excitement last from ten days to three weeks, and during them I have found "15" mixture given occasionally affords her a good night's sleep, as will be seen from the following Table.

1927. April 3. four drachms "15" mixture 6 hours.

<p>| | | | | |</p>
<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>&quot;</td>
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<td>5 &quot;</td>
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<td>14</td>
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<td>4 &quot;</td>
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<td>7 &quot;</td>
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<td>6 &quot;</td>
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<tr>
<td>23</td>
<td>&quot;</td>
<td>&quot;</td>
<td>&quot;</td>
<td>5 &quot;</td>
</tr>
</tbody>
</table>
In a patient who has to have a hypnotic fairly frequently one must always ring the changes, and I find "15" mixture useful as a variant to other hypnotics, as in the following case:

John M. aet 35 years.

Admitted 15.3.27.

Suffering from Acute Melancholia.

On admission patient was perfectly oriented. Lucid in conversation, rational in speech and behaviour, save on the question of his delusions. Believed he was to be punished for previous misdeeds by being put in a coffin and buried alive. At times he suffered acute mental agony - his face betraying his emotion and his manner suggesting abject fear. At such times he was acutely hallucinated, hearing the footsteps of his persecutors coming for him and the sound of the coffin being placed on the ground outside the ward.

Expressed suicidal intentions.

He was having various hypnotics for during his acute hallucinatory periods his sleep was altogether gone "15" mixture in doses of six drachms was given.
1927. April 14th six drachms "15" mixture 4 hours' sleep

15th " " " " " 4 " " "
18th " " " " " 6 " " "
19th " " " " " 7 " " "
20th " " " " " 5 " " "
24th " " " " " 7 " " "
25th " " " " " 4 " " "

By giving six drachms of "15" mixture, the patient receives twenty-two to twenty-three grains of potassium bromide, a similar amount of chloral hydras, and twenty-two to twenty-three minims of liquor opii sedativus.

I do not, as a rule, prescribe "15" mixture in acute mental distress or extreme mental excitement, but in these cases I do employ it mainly as a change of hypnotic and always in doses of six drachms, as I find half an ounce of "15" mixture has little effect on acute excitement, as will be seen from the following two cases.

Jessie McD. aet 31.
Admitted 10.9.21.

On admission patient was very quiet, apathetic, introspective and shut off.

Suffers from Dementia Praecox. Has outbursts of katatonic excitement when she becomes very impulsive. During such an outburst on 29.4.27. she had half an ounce "15" mixture at 7.15 p.m., but it had very little effect /
effect on her and she got no sleep.

The same dose was repeated the following night at 7.15 p.m. The patient that night had four hours' sleep but did not fall asleep until 11.40 p.m., before which time excitement was not much reduced and probably the sleep in this case was not the result of the sedative.

Margaret McR. aet circa 40 years.

Admitted 20.3.27.

Involuntary insanity.

On admission patient was quiet, rather self-absorbed. Uncertain. Hallucinated for hearing.

Towards evening restlessness set in, going on to extreme motor excitement, singing, dancing, gesticulating. Became quite unmanageable. Continued thus for several weeks.

On 21.4.27. she was very acutely excited and very noisy. Given half an ounce of "15" mixture at 11.55 p.m. which had very little effect in reducing excitement. Patient slept at 3.45 and had one hour's sleep. Here again it is doubtful if sleep was induced by hypnotic, and patient continued to be noisy until after 3 a.m., three hours after the administration of the hypnotic. "15" mixture is a good hypnotic in cases where pain is the disturbing factor preventing sleep.

George M. aet 16.

Admitted 24.4.27.

On /
On admission patient was restless. Very unstable emotionally. Incoherent and confused. Acutely hallucinated and distressed. Had a tubercular condition of left elbow joint, with two discharging sinuses, which caused him considerable pain and prevented his sleeping.

On 24.4.27 was given half an ounce "15" mixture which gave him rest and six hours' sleep. This was repeated on 4.5.27, after which he had again six hours' sleep.

In patients who fall asleep in the early part of the night and then wake up after a little while and become restless, failing to go to sleep again, the exhibition of "15" mixture gives very good results as the potassium bromide has time to take effect and prolong the slumber.

In such cases "15" mixture should be given in the early part of the night just when the patient goes to bed.

James U. aet 70 years.

Admitted 15.4.27.

Senile Dementia.

Patient was very talkative. Quite incoherent, rambling, grossly confused and totally disoriented. He tended to fall asleep in earlier part of night and after a little while to wake up, becoming restless and attempting to get out of bed and wander about.

On 18.4.27, he was given half an ounce "15" mixture /
ture at 7 p.m.; he was asleep at 7.20 p.m., and slept eight hours.

It has been noted previously that care should be exercised in administering bromides to patients over sixty years of age as it tends to produce a state of mental confusion. In this case mental confusion was already a marked feature and on the following day patient was no more confused than he had been previously.
<table>
<thead>
<tr>
<th>Date</th>
<th>Dose</th>
<th>Patient</th>
<th>Time of Administration</th>
<th>When Asleep</th>
<th>Number of Hours of Sleep</th>
<th>Remarks</th>
</tr>
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<tbody>
<tr>
<td>31 Jan-1 Feb</td>
<td>Gyro</td>
<td>Catherine M.</td>
<td>7.10 p.m.</td>
<td>-</td>
<td>0</td>
<td>Restless and talkative</td>
</tr>
<tr>
<td>6-7 Feb.</td>
<td></td>
<td>Mrs. G.</td>
<td>11.45 p.m.</td>
<td>-</td>
<td>0</td>
<td>Restless and talkative</td>
</tr>
<tr>
<td>7-8</td>
<td>X</td>
<td>Annie J.</td>
<td>6.30 p.m.</td>
<td>7.15 p.m.</td>
<td>9</td>
<td></td>
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<tr>
<td>14-15</td>
<td>a</td>
<td>Jone S.</td>
<td>6.45 p.m.</td>
<td>7.20 p.m.</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>14-15</td>
<td>a</td>
<td>William R.</td>
<td>7 p.m.</td>
<td>8.30 p.m.</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>14-15</td>
<td>a</td>
<td>Mary Ann R.</td>
<td>12.35 a.m.</td>
<td>1.20 p.m.</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>17-18</td>
<td>a</td>
<td>Catherine M.</td>
<td>7 p.m.</td>
<td>8.15 p.m.</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>17-18</td>
<td>a</td>
<td>Alexander C.</td>
<td>6.45 p.m.</td>
<td>8.10 p.m.</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>5-6 March</td>
<td>a</td>
<td>Kenneth C.</td>
<td>8 p.m.</td>
<td>10.5 p.m.</td>
<td>6</td>
<td>Restless and talkative</td>
</tr>
<tr>
<td>5-6</td>
<td>a</td>
<td>James M.</td>
<td>8.15 p.m.</td>
<td>8.40 p.m.</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>6-7</td>
<td>a</td>
<td>Alexander C.</td>
<td>6.45 p.m.</td>
<td>10.20 p.m.</td>
<td>7</td>
<td>Restless and talkative</td>
</tr>
<tr>
<td>7-8</td>
<td>a</td>
<td>Alexander C.</td>
<td>7.15 p.m.</td>
<td>8.20 p.m.</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>9-10</td>
<td>a</td>
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<td>8.10 p.m.</td>
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<td></td>
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<tr>
<td>10-11</td>
<td>a</td>
<td>Angus M.</td>
<td>7.45 p.m.</td>
<td>9.20 p.m.</td>
<td>5</td>
<td>Distressed</td>
</tr>
<tr>
<td>14-15</td>
<td>a</td>
<td>Roderick M.</td>
<td>6.45 p.m.</td>
<td>10.20 p.m.</td>
<td>7</td>
<td>Impulsive motor excitement</td>
</tr>
<tr>
<td>15-16</td>
<td>a</td>
<td>Alexander C.</td>
<td>7.15 p.m.</td>
<td>10.5 p.m.</td>
<td>6</td>
<td>Restless talkative excitement.</td>
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<tr>
<td>16-17</td>
<td>a</td>
<td>Alexander C.</td>
<td>6.45 p.m.</td>
<td>3.30 a.m.</td>
<td>2</td>
<td>Very restless. Motor excite-</td>
</tr>
<tr>
<td>17-18</td>
<td>Gyro</td>
<td>Alexander C.</td>
<td>6.45 p.m.</td>
<td>9.50 p.m.</td>
<td>6</td>
<td>Restless. Motor excitement.</td>
</tr>
<tr>
<td>19-20</td>
<td>a</td>
<td>Alexander C.</td>
<td>7 p.m.</td>
<td>9.10 p.m.</td>
<td>6</td>
<td>Restless.</td>
</tr>
<tr>
<td>19-20</td>
<td>a</td>
<td>Angus M.</td>
<td>7 p.m.</td>
<td>9 p.m.</td>
<td>6</td>
<td>Distressed</td>
</tr>
</tbody>
</table>
Bromural.

Syn - A Brom-iso-valerianyl-urea.

Chemical Formula -

$$(\text{CH}_3)_2\text{CH} \quad \text{CH Br. CONH CONH}_2$$

Bromural is a white crystalline substance. It
has a rather unpleasant odour somewhat resembling valer-
ainic acid, and a slightly bitter taste. It is insoluble
in cold water but freely soluble in spirit and because
of this it is best administered in a little ($^\frac{1}{2}\text{oz}$)alcohol
half an ounce, and I have always given it in this way.

It is said that the dose cannot be extended beyond
$\text{Runcie}$ grains $X$ but $\text{Roeck}$ has given as much as 90 grains without
any toxic symptoms making their appearance.

Because of its rapid excretion, the hypnotic ef-
flect of bromural is not increased proportionately with the
dose. In this respect, therefore, there is a limit to
its usefulness. The rapidity of the excretion of the drug
is also the probable explanation of the fact that com-
paratively large doses of bromural can be administered to
children.

Bromural is an urea derivative containing 36% 
bromine. Its hypnotic effect is due to the combined urea
and bromine elements. There is no trace of bromine in
the urine, so that bromine does not seem to be split off
the compound in the alimentary tract, and therefore the
isolated /
isolated action of this element does not occur.

I commenced using bromural in doses of 5 grains, and found this amount gave no results. The patients did not go to sleep nor was restlessness in any degree reduced. On reference to the bromural sleep table it will be seen that Catherine M. has bromural grains five on 31.1.27 and had no sleep. On 6.2.27. Mrs. G. had five grains bromural with similar result. On 17.3.27. Alexander C. was given five grains bromural. The bromural table shows that he had two hours' sleep, but considering that the sedative was administered at 6.45 p.m. and patient did not sleep until 3.30 a.m. and having in mind the rapid excretion of bromural, it is not likely that these two hours of sleep were due to the sedative. 

In all these three cases mentioned there was a marked degree of excitement with talkativeness and restlessness. From the use of five grain doses of bromural I observed little or no sedative effect and therefore I always used the drug in 10 grain doses.

From a general consideration of the bromural sleep table (Table No. 2) it will be seen that bromural in 10 grain doses produces very constant results in the number of hours of sleep, the average being six to seven hours each night.

It acts fairly rapidly, my series of cases having on an average fallen asleep in about half an hour after the /
the administration of the sedative.

In cases where the action was delayed for longer periods, from one and a half to two hours, there was always motor excitement present or, as in the case of Angus M., acute mental distress.

Patients treated with Bromural.

-------------------

Alexander C.  set 38 years.


On admission was very emotional, spoke little and when questioned began to weep. Answers to questions irrelevant. Disoriented, and memory very poor. Shortly after admission expressed grandiose delusions of great wealth and extreme physical capabilities.

Examination revealed no physical signs of general paralysis of the insane. Wassermann reaction of blood and C.S.F. was negative.

History of alcoholism. Later on became noisy and talkative. Varied a great deal in his moods. Stubbornness restlessness and expression of grandiose delusions giving place to friendly facility which, in turn, was succeeded by periods of destructiveness and impulsive violence.

For very brief periods his memory cleared only to become clouded again.

He /
He was frequently excited, noisy and restless, and on such occasions suffered from sleeplessness.

Treatment adopted in his case was the following:

28.1.27. Amylene Hydrate minims 40 3 hours sleep.
31.1.27. Chloretone grains X (10) 7 hours "
5.2.27. " " X (10) 4 hours "
6.2.27. " " XX (20) 2 hours "
8.2.27. " " X (10) 4 hours "
11.2.27. " " XX (20) 4 hours "
14.2.27. " " X (10) 6 hours "
15.2.27. " " XX (20) 4 hours "
16.2.27. " " XX (20) 5 hours "
17.2.27. Bromural grains X (10) 7 hours "
6.3.27. " " X (10) 7 hours "
7.3.27. " " X (10) 3 hours "
15.3.27. " " X (10) 6 hours "
16.3.27. " " V (5) 2 hours "
17.3.27. " " X (10) 6 hours "
20.3.27. " " X (10) 6 hours "

On each occasion upon which the patient had bromural in ten grain doses a good night's sleep ensued. There were no ill effects noticed on the day following administration of bromural, and the patient complained of no discomfort or sickness - not even after he had had bromural on three successive nights, as see above 15th, 16th, 17th March.

The /
The patient continued to improve and was discharged on six months' probation on 11.9.27. Note in this case also the constant results obtained from ten grains of bromural as compared with uncertain results seen from the exhibition of chloroetone which in doses of ten grains produced on some occasions longer sleep than doses of twenty grains.

Angus M. aet 35 years.

Patient suffers from melancholia. The predominant features of this case were depression, hopelessness and apathy. Sits all day on a chair, hunched up, motionless, with downcast eyes. Entertained delusions that he was "possessed of devils." Oriented, lucid, and rational in conversation. Six weeks after admission he was much brighter, but gradually became restless, which restlessness developed into acute mental distress when his delusions obtruded themselves more prominently, and he believed himself lost. He would scream at the top of his voice, saying that devils were taking possession of him. He became intensely suicidal, asking for "something to put an end to" this unbearable existence.

These periods of psychalgia occurred at intervals of four or five months and his distress was such that he obtained little sleep during these attacks.

In one such period I gave him ten grains bromural on/
on two nights.

I found the drug took about two hours to have a complete hypnotic effect, but shortly after administration he became calm and on each occasion had a good night's sleep.

10.3.27. Bromural grains X  5 hours.
19.3.27. "    " X  6 hours.

I have given ten grains bromural in acute excitement in the following cases:

    William R.
    Catherine M.
    Kenneth C.
    James M.
    Roderick M.

and, as will be seen from reference to the bromural table, results have been constant and excellent.
<table>
<thead>
<tr>
<th>Date</th>
<th>Dose</th>
<th>Patient</th>
<th>Time of Administration</th>
<th>When Asleep</th>
<th>Numbers of Hours of Sleep</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>11-12 Jan.</td>
<td>40</td>
<td>Robert T.</td>
<td>7 p.m.</td>
<td>-</td>
<td>0</td>
<td>Heart embarrassment.</td>
</tr>
<tr>
<td>25-26</td>
<td></td>
<td>Jemima M.</td>
<td>7.30 p.m.</td>
<td>8.30 p.m.</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>28-29</td>
<td></td>
<td>Catherine M.</td>
<td>11.40 p.m.</td>
<td>1.30 a.m.</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>28-29</td>
<td></td>
<td>Alexander C.</td>
<td>7 p.m.</td>
<td>10.15 p.m.</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>29-30</td>
<td></td>
<td>Catherine M.</td>
<td>6.55 p.m.</td>
<td>8.10 p.m.</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>3-4 Feb.</td>
<td></td>
<td>Catherine M.</td>
<td>8.10 p.m.</td>
<td>8.30 p.m.</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>8-9</td>
<td></td>
<td>Mrs. F.</td>
<td>11.45 p.m.</td>
<td>12.10 a.m.</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>9-10</td>
<td></td>
<td>John McL.</td>
<td>7 p.m.</td>
<td>7.20 p.m.</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>4-5</td>
<td>60</td>
<td>Helen M.</td>
<td>12.45 a.m.</td>
<td>3.25 a.m.</td>
<td>2</td>
<td>Neuralgia.</td>
</tr>
<tr>
<td>4-5</td>
<td></td>
<td>Kenneth C.</td>
<td>11.55 p.m.</td>
<td>12.30 a.m.</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>5-6</td>
<td></td>
<td>Mrs. M. W.</td>
<td>12.45 a.m.</td>
<td>1.30 a.m.</td>
<td>2</td>
<td>Motor excitement. Noisy.</td>
</tr>
<tr>
<td>9-10</td>
<td></td>
<td>Christina C.</td>
<td>12.10 a.m.</td>
<td>2.45 a.m.</td>
<td>4</td>
<td>Very noisy.</td>
</tr>
<tr>
<td>11-12</td>
<td></td>
<td>John McL.</td>
<td>7 p.m.</td>
<td>7.20 p.m.</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>11-12</td>
<td></td>
<td>Robert G.</td>
<td>11.55 p.m.</td>
<td>-</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>15-16</td>
<td></td>
<td>Jessie R.</td>
<td>12.5 a.m.</td>
<td>1.20 a.m.</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>16-17</td>
<td></td>
<td>Christina C.</td>
<td>12 midnight</td>
<td>12.20 a.m.</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>22-23</td>
<td></td>
<td>John McL.</td>
<td>6.45 p.m.</td>
<td>10.10 p.m.</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>1-2 Mar.</td>
<td></td>
<td>Christina C.</td>
<td>7 p.m.</td>
<td>2.5 a.m.</td>
<td>3½</td>
<td></td>
</tr>
<tr>
<td>5-6</td>
<td></td>
<td>Christina C.</td>
<td>12.10 a.m.</td>
<td>12.20 a.m.</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>8-9</td>
<td></td>
<td>Christina C.</td>
<td>1 a.m.</td>
<td>1.20 a.m.</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>11-12</td>
<td></td>
<td>Christina C.</td>
<td>11.45 p.m.</td>
<td>12.20 a.m.</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>20-21</td>
<td></td>
<td>Christina C.</td>
<td>12.10 a.m.</td>
<td>1.45 a.m.</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>
Amylene Hydrate.

Synonym - Dimethyl-ethyl carberal Tertiary amyl alcohol.

\[
\text{CH}_3 \quad \text{C}_2\text{H}_5 \quad \text{C} \quad \text{OH} \\
\text{CH}_3
\]

Amelyne Hydrate occurs as a colourless liquid with a pungent taste and odour resembling a mixture of paraldehyde and camphor. It is very hygroscopic, and it decomposes when exposed to light, consequently it has to be stored in the dark. Its unpleasant taste is a disadvantage and therefore it is sometimes administered in cachets.

Its taste, however, may be masked by using suitable flavouring agents, the best of these being liquorice and orange. I have always administered amylene hydrate as a night draught using 40 to 60 minims of amylene hydrate made up to a draught of two ounces, using two to three drachms respectively of syrup of orange as the flavouring agent.

I have found this method convenient and satisfactory and experienced no difficulty in getting the patients to take the drug administered in this way. When using amylene hydrate in this way great care must be taken that it is two ounces of the draught and not two /
two ounces of undiluted amylene hydrate that is given.
An accident of this kind occurred at Bethlehem Hospital, London and caused the death of six female patients.

Two cases of poisoning from amylene hydrate are on record.

In one case reported by Anker 27 gms had been given, while in the other reported by Lederer 8 gms were taken. The symptoms were those of collapse. In the case reported by Lederer great intestinal irritation with vomiting were prominent symptoms.

The treatment adopted was general stimulation, after which both patients recovered.

Patients Treated with Amylene Hydrate.

Christina C. æt 33 years.
Admitted 27.6.24.

Patient suffers from dementia praecox.

On admission acutely excited, negative, and resistive. Garrulous, rambling and incoherent. Confused and did not properly recognise where she was. At present date (February, 1928) she is asocial, unfriendly, scarcely speaks and refuses to answer any questions. Smiles feebly and in superior manner when questions are put to her.

For several weeks she remained in this condition and then quite suddenly became excited, noisy and impulsive /
sive. Chatters incessantly - speech being a "word salad." Quite irrelevant and incoherent. Quite shut off from her surroundings. It is impossible to attract her attention, or to stop her chatter for even a moment. At night she sits up in bed and chatters.

Her circulation is very poor and she has had several syncopal attacks.

During her excited periods I have treated her with amylene hydrate, with following results:

9. 2.27. Amylene hydrate minims 60 3½ hours' sleep.
16.2.27. " " " " 5 " "
1. 3.27. " " " " 4 " "
5. 3.27. " " " " 5 " "
8. 3.27. " " " " 4 " "
11.3.27. " " " " 4 " "
20.3.27. " " " " 6 " "

John McI. aet 64 years.
Admitted 26.10.24.
Suffers from chronic mania.

On admission elevated and excited. Foolish and nonsensical. Delusions of persecution directed against relatives and neighbours. For most part patient is foolish in his talk and behaviour. Friendly, facile and elevated.

At irregular intervals, varying in duration from ten days to six weeks, he has bouts of noisy excitement lasting /
lasting two or three days, when he adorns his person with flowers, pieces of paper, string or any bright objects on which he can lay his hands. He gesticulates and rampages up and down the ward swearing, cursing and showering abuse upon all and sundry. His physical condition is precarious, cardiac action is disorderly and irregular. During the past year he has collapsed five times, recovering on administration of camphor in oil and application of warmth. These attacks are not of an acute cardiac nature but come on gradually, the patient first becoming drowsy, his temperature falling, and cyanosis making its appearance, until, if unnoticed, the patient passes into a state of collapse.

In his case when a hypnotic was required I usually gave paraldehyde, but I have found Amylene Hydrate acted quite as well.

9.2.27. Amylene Hydrate minimis 40 7 hours' sleep.  
11.2.27. " " 60 7 " "  
22.2.27. " " 60 6 " 

In the following case in which there was acute cardiac embarrassment I gave amylene hydrate without its having any effect.

Robert T. aet 66 years.  
Admitted 9.1.27.  
Senile dementia.  
On /
On admission extremely restless and talkative.
Grossly confused and disoriented for time, place and
person. Patient was in a very weak physical condition.
There was acute heart embarrassment, pulse 106, irregular
running, very feeble and easily compressed.

Heart sounds, on auscultation, could hardly be
made out.

Restlessness and insomnia continued.

On 11.1.27. patient was given 40 minims amylene
hydrate, but had no sleep.

Also
I have found amylene hydrate ineffective in one
case of very acute maniacal excitement.

Robert G. age 65 years.
Admitted 8.2.27.

Recurrent mania.

On admission patient was wildly excited, argumentative
and threatening, and friendly and sociable in turns.
Attention extremely fleeting. Great flight of ideas.

He continued to be persistently noisy, singing,
reciting poetry at the top of his voice, and extremely
restless.

On 11.2.27. he was given 60 minims amylene hydrate
at 11.55 p.m. This had no effect on the patient and he
had no sleep.
I have not found amylene hydrate very satisfactory where sleeplessness was due to pain.

Helen M. aged 28 years.
Admitted 10.2.21.

Congenital mental deficiency with mania.

On 4.2.27. this patient was suffering from severe neuralgia. I gave her 60 minims amylene hydrate at 12.45 a.m.

This did not reduce the pain and patient did not sleep till 3.25 a.m. when she dosed off into a fitful slumber lasting only two hours.
<table>
<thead>
<tr>
<th>Date 1927</th>
<th>Dose</th>
<th>Patient</th>
<th>Time of Administration</th>
<th>When Aslepp</th>
<th>Number of Hours of Sleep</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>26-27 Jan. G.R.XXX</td>
<td>Margaret M.J.</td>
<td>7.40 p.m.</td>
<td>8.20 p.m.</td>
<td>8</td>
<td>Easily disturbed and awakened</td>
</tr>
<tr>
<td>2</td>
<td>26-27</td>
<td></td>
<td>Annabella F.M.</td>
<td>7.40 p.m.</td>
<td>10.10 p.m.</td>
<td>$\frac{5}{3}$</td>
</tr>
<tr>
<td>3</td>
<td>26-27</td>
<td></td>
<td>Catherine M.</td>
<td>11.15 p.m.</td>
<td>1.30 a.m.</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>27-28</td>
<td></td>
<td>CARTOL, K.</td>
<td>12.20 a.m.</td>
<td>12.50 a.m.</td>
<td>2</td>
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<tr>
<td>5</td>
<td>28-29</td>
<td></td>
<td>Angela McK.</td>
<td>1.50 a.m.</td>
<td>2 a.m.</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>4-5 Feb.</td>
<td></td>
<td>Henry F.</td>
<td>7.5 p.m.</td>
<td>9.10 p.m.</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>6-7</td>
<td></td>
<td>Catherine M.N.</td>
<td>6.40 p.m.</td>
<td>7.15 p.m.</td>
<td>11$\frac{1}{2}$</td>
</tr>
<tr>
<td>8</td>
<td>7-8</td>
<td></td>
<td>Catherine M.N.</td>
<td>6.30 p.m.</td>
<td>7 p.m.</td>
<td>6</td>
</tr>
<tr>
<td>9</td>
<td>11-12</td>
<td></td>
<td>Ann M. L.</td>
<td>7 p.m.</td>
<td>9.5 p.m.</td>
<td>3</td>
</tr>
<tr>
<td>10</td>
<td>6-7   Mar.</td>
<td></td>
<td>Catherine M.N.</td>
<td>11.25 p.m.</td>
<td>12.10 a.m.</td>
<td>10</td>
</tr>
<tr>
<td>11</td>
<td>28-29</td>
<td></td>
<td>John M.</td>
<td>7 p.m.</td>
<td>9.5 p.m.</td>
<td>7</td>
</tr>
<tr>
<td>12</td>
<td>29-30</td>
<td></td>
<td>John M.</td>
<td>7 p.m.</td>
<td>9.20 p.m.</td>
<td>7</td>
</tr>
<tr>
<td>13</td>
<td>5-6   Apr.</td>
<td></td>
<td>John M.</td>
<td>7 p.m.</td>
<td>9.35 p.m.</td>
<td>4</td>
</tr>
<tr>
<td>14</td>
<td>5-6</td>
<td></td>
<td>Daniel V. M.</td>
<td>7 p.m.</td>
<td>1.10 a.m.</td>
<td>4</td>
</tr>
<tr>
<td>15</td>
<td>6-7   Feb.</td>
<td></td>
<td>Henry F.</td>
<td>6.30 p.m.</td>
<td>7.25 p.m.</td>
<td>7</td>
</tr>
<tr>
<td>16</td>
<td>6-7   Apr.</td>
<td></td>
<td>Daniel V. M.</td>
<td>7 p.m.</td>
<td>9.10 p.m.</td>
<td>1</td>
</tr>
<tr>
<td>17</td>
<td>6-7</td>
<td></td>
<td>John M.</td>
<td>7 p.m.</td>
<td>8.10 p.m.</td>
<td>8</td>
</tr>
<tr>
<td>18</td>
<td>12-13</td>
<td></td>
<td>John M.</td>
<td>7 p.m.</td>
<td>3.20 a.m.</td>
<td>2</td>
</tr>
<tr>
<td>19</td>
<td>21-22</td>
<td></td>
<td>John M.</td>
<td>7 p.m.</td>
<td>10.10 p.m.</td>
<td>6</td>
</tr>
</tbody>
</table>
Chloralamide.

Synonym - Chloral Formamide.

Chemical Formula

\[
\begin{align*}
\text{OH} \\
\text{C Cl₃} \\
\text{NH OCH}
\end{align*}
\]

Chloralamide is a white crystalline substance. It is a combination of chloral and formamide.

It is highly insoluble in water. It can, however, be dissolved in warm spirit but in that case care must be taken that it is not heated above 55°C otherwise the drug becomes decomposed.

If the powder is used the best solvent is spiritus aetheris nitrosi.

The most convenient form for use is the tablet, and it was in this form that I employed the drug using tablets of 5 grains each, manufactured by Burroughs and Wellcome.

Chloralamide is incompatible with alkalis and alkaline carbonates.

This fact explains one of the great advantages of this drug. When it is absorbed chloral is slowly split off by the alkaline body fluids, releasing ammonium formate which has a stimulating action on the circulation.

To this chemical decomposition does chloralamide owe its safety as a hypnotic in general, and especially when employed in patients suffering from any cardiac weakness.
Catherine M.N. aet 59 years.

Patient was labouring under senile dementia.

On admission she was somewhat confused and en-feebled in mind. She was approximately oriented for time and place, but was apt to identify individuals wrongly. She conversed agreeably and brightly but somewhat childish­ly. She believed that she was being persecuted because she recently had changed from one denomination of the church to another, and she had auditory hallucinations bearing on her delusions, hearing her persecutors come into her room to do her bodily harm.

She was pre-senile and her physical condition was weak. Auscultation showed both heart sounds heard in all areas but very feeble.

She was confined to bed because on two occasions when she had got up she had fainted. Her sleep was good up till the February after admission when she appeared more acutely hallucinated and obviously much distressed, moaning and weeping at nights.

On February 6th she had XX grains chloralamide and she slept for over eleven hours. She was given the sedative at 6.45 p.m. and was asleep at 7.15 p.m. Thus
the drug took 35 minutes.

The following night patient again had twenty grains chloralamide which took effect in thirty minutes and gave six hours' sleep. Sleep after this improved and patient had no more sedative until March 6th when she again had twenty grains chloralamide, after which she slept ten hours.

**Henry F. aet 67 years.**

*Admitted 22.6.21.*

Melancholia with hypochondriacal delusions.

This patient was able to get up for a little while during the day, his physical condition was, however, very weak as he had chronic failing compensation of the heart. Breathlessness came on with very little exertion and he was often confined to bed for several days as his feet and ankles used to swell.

He was troubled with simple insomnia.

On 4.2.27. he had twenty grains chloralamide and slept six hours. Thirty grains chloralamide were given and he slept seven hours.

In many cases I found chloralamide an unsatisfactory hypnotic from the point of view that it did not afford any or very little sleep. This was especially noticeable when there was acute mental excitement or acute mental distress present, as will be seen by referring to the chloralamide /
chloralamide table, in the cases of Cathol K. and Catherine M. and Daniel V.M. (I merely mention the first two patients without giving their history as later these two cases will be given in full in connection with other hypnotics. The case of Daniel V.M. has already been given under the section on insomnia in general paralysis of the insane.)

Catherine M. was given twenty grains chloralamide on 26.1.27. and slept only three hours. Moreover her sleep was light and broken, the least noise or disturbance being sufficient to wake her up. I have observed in several instances that a patient under the effect of chloralamide is very easily disturbed, the sleep induced being very light.


On admission was confused, rambling and incoherent in speech, and disoriented for all dimensions. Physical condition weak - subject to syncopal attacks.

On 26.1.27. the patient had twenty grains chloralamide at 7.40 p.m. and was asleep at 8.20 p.m., the hypnotic thus taking forty minutes to induce sleep. She had a total amount of eight hours of sleep, but the sleep was not continuous. Several times during those eight hours she awoke, turned or stretched herself, and went to sleep /
sleep again.

Very slight disturbance in her near environment was sufficient to waken her.

Chloralamide given at night following the administration of sulphononal in the morning gives very good results.

John M.  aet 55 years.
Admitted 15.3.27.

This patient's history is given fully in connection with "15" Mixture and so need not be repeated here.

On several occasions I treated this patient with sulphononal. Following my usual procedure of administration of this sedative, I used to give fifteen grains in the morning and fifteen grains at night, instead of a single dose of thirty grains. For the fifteen grains sulphononal at night I substituted chloralamide with the following results:

<table>
<thead>
<tr>
<th>Date</th>
<th>Chloralamide</th>
<th>hrs' sleep</th>
</tr>
</thead>
<tbody>
<tr>
<td>28.3.27.</td>
<td>&quot;</td>
<td>XX 7</td>
</tr>
<tr>
<td>29.3.27.</td>
<td>&quot;</td>
<td>XX 7</td>
</tr>
<tr>
<td>5.4.27.</td>
<td>&quot;</td>
<td>XX 4</td>
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<tr>
<td>5.4.27.</td>
<td>&quot;</td>
<td>XX 8</td>
</tr>
<tr>
<td>12.4.27.</td>
<td>&quot;</td>
<td>XX 2</td>
</tr>
<tr>
<td>21.4.27.</td>
<td>&quot;</td>
<td>XX 6</td>
</tr>
<tr>
<td></td>
<td>Date</td>
<td>Dose</td>
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</tr>
<tr>
<td>1</td>
<td>27-28 Jan</td>
<td>CRSX</td>
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<tr>
<td>2</td>
<td>28-29</td>
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<tr>
<td>3</td>
<td>31-1 Feb</td>
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<tr>
<td>4</td>
<td>1-2</td>
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<td>5</td>
<td>1-2</td>
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<td>6</td>
<td>3-4</td>
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<td>12</td>
<td>14-15</td>
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<tr>
<td>13</td>
<td>16-17</td>
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</tr>
<tr>
<td>Date</td>
<td>Dose</td>
<td>Patient</td>
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<td>----------</td>
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</tr>
<tr>
<td>14 5-6 Feb.</td>
<td>GRS XX</td>
<td>James M.</td>
</tr>
<tr>
<td>15 6-7</td>
<td></td>
<td>Alexander C.</td>
</tr>
<tr>
<td>16 6-7</td>
<td></td>
<td>James M.</td>
</tr>
<tr>
<td>17 10-11</td>
<td></td>
<td>Henrietta S.</td>
</tr>
<tr>
<td>18 11-12</td>
<td></td>
<td>Henrietta S.</td>
</tr>
<tr>
<td>19 11-12</td>
<td></td>
<td>Alexander C.</td>
</tr>
<tr>
<td>20 15-16</td>
<td></td>
<td>Catherine M.</td>
</tr>
<tr>
<td>21 15-16</td>
<td></td>
<td>Alexander C.</td>
</tr>
<tr>
<td>22 16-17</td>
<td></td>
<td>Alexander C.</td>
</tr>
<tr>
<td>23 19-20</td>
<td></td>
<td>Henrietta S.</td>
</tr>
<tr>
<td>24 19-20</td>
<td></td>
<td>Sarah I. M.</td>
</tr>
<tr>
<td>25 20-21</td>
<td></td>
<td>James M.</td>
</tr>
<tr>
<td>26 21-22</td>
<td></td>
<td>Catherine M.</td>
</tr>
<tr>
<td>27 22-23</td>
<td></td>
<td>Henrietta S.</td>
</tr>
<tr>
<td>28 6-7 Mar.</td>
<td></td>
<td>Henrietta S.</td>
</tr>
<tr>
<td>29 16-17</td>
<td></td>
<td>Henrietta S.</td>
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</tbody>
</table>
Chloretone.

**Synonym** - Chlorbutol

Trichlor-tertiary-butyl-alcohol.

**Chemical Formula** -

\[
C \text{Cl}_3 (\text{CH}_3)_2 \text{C OH}
\]

This substance occurs in white crystalline form. It has a very strong camphoraceous odour and taste. Its solubility in water is 1 in 200; in glycerine 1 in 10 and in alcohol 3 in 2. In using this drug I have taken advantage of its great solubility in alcohol and have always given it in some spirit. It may, however, be given in cachets or dispensed in powders, in which case it is important that chloretone should be wrapped in parchment powder papers. Its action as a hypnotic resembles chloral. Its dose is five to twenty-four grains.

Great care should be exercised in the use of chloretone and continual and constant supervision is necessary during its employment. A case of severe coma in a woman who took thirty grains of chloretone for toothache has been reported.

It is best administered in solution for if this is not done the insoluble drug tends to accumulate and is then absorbed in large quantities when any substance capable of dissolving it is taken by mouth. Therefore it is wise when not given in solution to limit the dose to ten grains /
grains and not to use the drug in repeated doses - thus obviating any chance of the sedative accumulating in the intestinal canal.

Patients Treated with Chloretone.

James M. aet 42 years.
Admitted 31.3.16.
Patient suffers from recurrent mania.

Three years ago when I first knew this patient his attacks of recurrent excitement came on at fairly regular intervals of three or four months. These attacks lasted about a week or ten days when the patient became gradually more settled and finally quite calm. During the intervals between the attacks of excitement, patient is friendly, civil and helpful, employing himself out of doors, and is an excellent and willing worker. He never shows any signs of depression. Recently his maniacal attacks have become more frequent in their occurrence, and tend to be longer in duration. While he is excited he displays great motor restlessness. He seems imbued with the spirit of mischief and, though never violent, interferes with every patient in the ward, and with everything in his vicinity.

He sings, shouts and dances, and if any attention is paid to him he cuts the most ridiculous capers with greater /
greater fervour than ever. His motor excitement of the
daytime, if untreated, persists throughout the night.

During one such attack he was treated with chlorem-
tone.

27.1.27. Grains X 4 hrs. sleep. (Asleep 3 hrs. 25 min. af-
ter administration)

28.1.27. " X 7 " " (Asleep 50 mins, after administra-

1.2.27. " X 7 " " (Asleep 3 hrs. 10 mins. after administra-

5.2.27. " XX 6 " " (Asleep 1 hr. 25 mins. after administra-

6.2.27. " XX 6 " " (Asleep 3 hrs. 5 mins. after administra-

20.2.27. " XX 6 " " (Asleep 50 mins. after administra-

Catherine M. aet 52 years.

Admitted 23.10.26.

Patient suffered from involutional insanity.

On admission patient was incoherent, babbling non-
sense and repeating snatches of nursery rhymes. Varied in
her moods from apprehensive supplication to abuse and
violence. Irrelevant and disoriented. Excited, and con-
tinued, with intervals of comparative quiet, and she was
at times very resistive, refusing her food. At other times
extremely noisy, talkative and restless.

Her sleep was very poor and during the month of
February, 1927 she was treated mainly with chloremtone.
1. 2.27. Chloretone Grs. X 5 hrs. sleep (Asleep 2 hrs. 35 mins. after administration)

3. 2.27. Amylene hydrate Minim 40 - 5 hours' sleep.

5. 2.27. Chloretone grs. X - 4 hrs. sleep (Asleep 1 hr. after administration)

15. 2.27. Chloretone grs. XX - 8 hrs. sleep (Asleep 50 min. after administration)

16. 2.27. Chloretone grs. X - 4 hrs. sleep (Asleep 5 hrs. 5 mins. after administration)

17. 2.27. Bromural grs. X - 7 hrs. sleep.

21. 2.27. Chloretone grs. XX - 3 hrs. sleep (Asleep 1 hr. 10 min. after administration)

Reference has already been made in the case of Alexander C. to the inconstancy of the amount of sleep induced by chloretone - in his case ten grains chloretone producing a greater number of hours of sleep than twenty grains.

In the case of James M. this fact is again noticed ten grains chloretone on each occasion giving longer sleep than twenty grains. In Catherine M's case the amount of sleep bears more relation to the dosage of the drug, but the time elapsing between the administration of the hypnotic and the onset of sleep is extremely variable, and this uncertainty of induction of sleep is also very manifest in the case of James M.

I have found chloretone most uncertain in its action /
action. In some cases of maniacal excitement it acted like a charm, inducing sleep which lasted five hours, within an hour of its administration, yet in other cases it not only failed to produce any effect at all, but actually caused the patient to become more excited.

The following cases will demonstrate this point.

**Sarah T. M.  aet 31 years.**
Admitted 31.12.25.

This patient's history has been given.

On 19.2.27. she was very excited, noisy, racketty and impulsive and was given twenty grains chloretone.

She calmed down very soon, was asleep within forty minutes of administration of hypnotic and slept five hours.

**Louisa Janetta R.  aet 38 years.**
Admitted 8.4.24.

During attacks of recurrent excitement this patient becomes extremely noisy, shouting and singing without cessation, marching up and down the ward, gesticulating wildly and refusing to be still for one moment.

On 3.2.27. at 11.40 p.m. she was given ten grains of chloretone. Instead of having any sedative effect upon patient, the hypnotic had, on the contrary, an exciting influence as her excitement and motor restlessness increased and continued throughout the whole night.
Patient suffers from General Paralysis of the Insane. On admission patient showed typical signs of general paralysis of the insane. Speech was slurring. Tongue, on protrusion, showed fine superficial tremor. Pupils unequal and did not react to light. Knee jerks exaggerated and unequal. Wrist and ankle jerks unequal. Wassermann reaction of blood and cerebro-spinal fluid markedly positive. No grandiose delusions but was distinctly elevated. Had delusions that his bed was a motor car the engine of which was continually getting out of order (this patient had been a motor mechanic by trade), and on certain nights he spent his sleeping hours in repairing the faulty mechanism.

On one such occasion (3.2.27.) he was given ten grains chloretone at 12.40 a.m. after which he became excited and more restless, and whereas prior to having the chloretone he had worked silently, he now kept up a continual chatter and did not sleep that night.

It may be argued that of these last three cases the first patient had twenty grains of chloretone while the last two had only ten grains of chloretone, and therefore the bigger dose induced sleep while the lesser dose produced not sleep but excitement. But it must be remembered that ten grains is more than the stated minimal /
minimal dose of chloretone and also that in several other cases ten grains chloretone were quite sufficient to induce sleep. And further the same uncertain action was observed in the following case where twenty grains chloretone was employed each time.

Henrietta S. aet 57 years.

This patient was suffering from secondary dementia following chronic mania.

At times this patient becomes greatly excited, restless, resistive and destructive - flinging whatever she can lay her hands upon across the room.

When prevented from putting her destructive desires into execution she struggles and fights, screaming and shouting at the pitch of her voice all the time.

10.2.27. Chloretone grs. XX 5 hrs. sleep.
11.2.27. " XX 1 " (Excited after administration)
19.2.27. " XX 4 "
22.2.27. " XX 1 " (Excited after administration)
6.3.27. " XX 5 "
16.3.27. " XX 0 " (Excited after administration)

From the above results it will be seen that on three /
three occasions the hypnotic in twenty grain doses in the same patient produced excitement. On the last occasion upon which chloretone was administered patient became very excited and remained so during the whole night, obtaining no sleep.
<table>
<thead>
<tr>
<th>Date</th>
<th>Dose</th>
<th>Patient</th>
<th>Time of Administration</th>
<th>When Asleep</th>
<th>Number of Hours of Sleep</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 28-29 Jan.</td>
<td>CrRusu</td>
<td>Caltol K.</td>
<td>7 p.m.</td>
<td>8.30 p.m.</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>2 29-30</td>
<td>&quot;</td>
<td>Caltol K.</td>
<td>7 p.m.</td>
<td>10.10 p.m.</td>
<td>6</td>
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</tr>
<tr>
<td>3 2-3 Feb.</td>
<td>&quot;</td>
<td>William G.</td>
<td>6.40 p.m.</td>
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<td>7</td>
<td></td>
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<tr>
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<td>11.20 p.m.</td>
<td>3.15 p.m.</td>
<td>2</td>
<td>Mental Distress.</td>
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<tr>
<td>5 3-4</td>
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<td>6 4-5</td>
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<td>7.45 p.m.</td>
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<td>5</td>
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</tr>
<tr>
<td>7 4-5</td>
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<td>6.45 p.m.</td>
<td>9.10 p.m.</td>
<td>5</td>
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</tr>
<tr>
<td>8 5-6</td>
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<td>6.50 p.m.</td>
<td>10.10 p.m.</td>
<td>3</td>
<td>Mental Distress.</td>
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<tr>
<td>9 5-6</td>
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<td>6</td>
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<td>9.5 p.m.</td>
<td>6</td>
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</tr>
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<td>11 6-7</td>
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<td>9.5 p.m.</td>
<td>5</td>
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<tr>
<td>12 17-18</td>
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<tr>
<td>13 24-25 Mar.</td>
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<td>7 p.m.</td>
<td>9.25 p.m.</td>
<td>6</td>
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<tr>
<td>14 29-30</td>
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<td>7 p.m.</td>
<td>9.15 p.m.</td>
<td>7</td>
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<tr>
<td>15 1928 12-13 Feb.</td>
<td>&quot;</td>
<td>Alexander M.</td>
<td>6.15 p.m.</td>
<td>8.10 p.m.</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>
Dial.

Synonym - Diallyl barbituric acid.

Chemical Formula -

\[
(C_3H_5)_2\text{CONH} \quad \text{CO}
\]

\[
(C_2H_5)_2\text{CONH} \quad \text{CO}
\]

From the chemical formula it will be seen that dial is a further homologue of veronal, the formula of which is:

Dial is manufactured by the Clayton Aniline Company, Ltd. and supplied in tablet form each tablet containing one and a half grains dial.

I first prescribed dial for insomnia in a sane person.

Mrs. F., a highly strung, nervous woman, easily excited and inclined to worry over trifles. In October, 1926 she sustained a bereavement by the death of her husband.

She was greatly upset and for some nights was unable to obtain any sleep.

After seeing her I prescribed three grains dial from which she had a good night's rest. The following night /
night she had no sedative but slept about two hours. Sleep was fitful and disturbed.

On the third night three grains dial were again taken, resulting in a restful sleep. The fourth night was passed sleeplessly, so on the fifth night three grains dial were again taken and patient slept well. After this her sleep improved for about a week or ten days when insomnia made its reappearance.

Dial was again employed for two alternate nights with as equally satisfactory results as when previously used, and since then Mrs. F. has required no further treatment for insomnia. No ill effects were experienced from the taking of dial.

**Nurse W.**

In May, 1927 Nurse W. of the staff of this asylum came to me with the complaint that for some time her sleep had been very bad, some nights she had no sleep at all, and such was the state of affairs for two nights previous to seeing me.

At nine o'clock on 15.5.27. this nurse took three grains of dial. She was asleep soon after and slept soundly during the whole night. At six o'clock next morning she was still under the effect of the hypnotic feeling very sleepy; as she herself said, she "could have gone on sleeping for another twelve hours." Apart from /
from drowsiness she did not in the least feel ill or out of sorts. That night she went to bed soon after going off duty; was asleep by 8.30 p.m. and slept soundly till six o'clock the following morning when she awoke feeling quite refreshed.

Since then I have twice prescribed for sleeplessness in this nurse's case and each time gave only one tablet (one and a half grains) dial which was quite sufficient to give a good night's rest in this instance without any feeling of drowsiness during the following day.

When used as an analgesic dial does not give such satisfactory results.

Attendant Roderick M.

In July, 1927 this man had a fluctuant swelling on left side of his neck which, when operated upon, proved to be due to actinomycosis.

Prior to operation the condition caused him such pain that he was unable to get any sleep at night.

On 25.7.27. I gave him three grains of dial, but this did not in the least mitigate the pain of his swollen neck and did not afford him any sleep, and afterwards I prescribed omnopon.

Bearing in mind my experience of dial among sane people /
people, I employed it in asylum practice in cases where there was not a great element of excitement, and little restlessness and mental distress.

The following two cases will serve to show that result from the exhibition of this sedative in such cases is satisfactory.

These two patients, Cathal K. and William G., resembled one another in several points. Both were about the same age. There was little difference in their physical conditions. Both suffered from melancholia and entertained delusions of a somewhat similar nature.

Of the two, Cathal K. suffered the more acute mental distress and proved the more intractable. In his case the suicidal element was at times very prominent, while William G. never gave direct expression to suicidal tendencies.

William G. aet 61 years.

Admitted 29.11.26.

On admission patient was very agitated, wringing his hands and moaning dolefully.

Most apprehensive, believing that he was to be punished for tampering with money belonging to his employers, (This was a delusion as he had been a scrupulously honest employee), and was profuse in his excuses for things going wrong.

Believed /
Believed he was lost to eternity and there was no hope for him. Very hypochondriacal - complaining of all sorts of vague illnesses for which there was no physical basis. He suffered from sleeplessness but restlessness was absent.

2.2.27. Dial grains III 7 hours' sleep.
3.2.27. " " 7 " "
4.2.27. " " 5 " "
5.2.27. " " 6 " "
6.2.27. " " 6 " "

His sleep improved and mentally he gradually became brighter and was discharged recovered on 24.5.27.

Cathol K. aet 65 years.
Admitted 15.1.27.
On admission was acutely depressed, morbidly preoccupied and introspective.

Uncommunicative, negative, extremely apprehensive. Disoriented for place but not for time or persons. Delusions of having committed unpardonable sin. Believed he was guilty of blasphemy in consequence of which his soul was lost, and he feared impending dissolution. Depression continued. Became very suicidal - refusing his food - considering it preferable to die of starvation to being cast into a fiery furnace which was being prepared for /
for him. Some nights he would bid me good-bye as he firmly believed "his end was at hand", and on such occasions, which coincided with complete insomnia, he betrayed great mental distress. At all times his sleep was very small in amount.

28.1.27. Dial grains III 7 hours' sleep.
29.1.27. '' '' 6 '' ''
2.2.27. '' '' 2 '' ''
4.2.27. '' '' 5 '' ''
5.2.27. '' '' 3 '' ''
6.2.27. '' '' 6 '' ''
17.2.27. '' '' 5 '' ''
24.3.27. '' '' 6 '' ''
29.3.27. '' '' 7 '' ''

2.2.27. and 5.2.27. were nights on which he was greatly disturbed, and on these nights it will be seen dial did not afford so much rest as on the nights on which he was comparatively free from mental distress.
<table>
<thead>
<tr>
<th></th>
<th>Date</th>
<th>Dose</th>
<th>Patient</th>
<th>Time of Administration</th>
<th>When Asleep</th>
<th>Number of Hours of Sleep</th>
<th>Remarks</th>
</tr>
</thead>
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<tr>
<td>1</td>
<td>29-30 Jan</td>
<td>1 tablet</td>
<td>James M.</td>
<td>6:15 p.m.</td>
<td>11:45 p.m.</td>
<td>4 1/2</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>29-30</td>
<td>1</td>
<td>George W.</td>
<td>6:10 p.m.</td>
<td>11:30 p.m.</td>
<td>1 1/2</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>29-30</td>
<td>2</td>
<td>Mary M.</td>
<td>6:30 p.m.</td>
<td>9:30 p.m.</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>29-30</td>
<td>2</td>
<td>Jessie R.</td>
<td>7:45 p.m.</td>
<td>9:15 p.m.</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>29-30</td>
<td>2</td>
<td>Kenneth M.</td>
<td>6:10 p.m.</td>
<td>10:45 p.m.</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>30-31</td>
<td>2</td>
<td>George W.</td>
<td>7 p.m.</td>
<td>8:40 p.m.</td>
<td>8</td>
<td></td>
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<tr>
<td>7</td>
<td>30-31</td>
<td>2</td>
<td>Kenneth M.</td>
<td>6:45 p.m.</td>
<td>9:50 p.m.</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>31-1 Feb.</td>
<td>2</td>
<td>George W.</td>
<td>6:45 p.m.</td>
<td>9:30 p.m.</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>2-3</td>
<td>2</td>
<td>George W.</td>
<td>6:45 p.m.</td>
<td>10:10 p.m.</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>6-7</td>
<td>2</td>
<td>George W.</td>
<td>6:45 p.m.</td>
<td>9:10 p.m.</td>
<td>7</td>
<td></td>
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<tr>
<td>11</td>
<td>7-8</td>
<td>2</td>
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<td>12:15 a.m.</td>
<td>12:35 a.m.</td>
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<tr>
<td>12</td>
<td>8-9</td>
<td>2</td>
<td>Ann M.</td>
<td>12:35 a.m.</td>
<td>12:50 a.m.</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>8-9</td>
<td>2</td>
<td>Mary M.</td>
<td>12:45 a.m.</td>
<td>1:35 a.m.</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>8-9</td>
<td>2</td>
<td>Malcolm M.</td>
<td>6:55 p.m.</td>
<td>8:10 p.m.</td>
<td>4</td>
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<tr>
<td>15</td>
<td>8-9</td>
<td>2</td>
<td>Christina ETM.</td>
<td>7 p.m.</td>
<td>9:10 p.m.</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>8-9</td>
<td>2</td>
<td>Catherine G.</td>
<td>6:45 p.m.</td>
<td>7:30 p.m.</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>9-10</td>
<td>2</td>
<td>Ann M.</td>
<td>11:55 p.m.</td>
<td>12:55 a.m.</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>9-10</td>
<td>2</td>
<td>Catherine M.</td>
<td>7:15 p.m.</td>
<td>8:15 a.m.</td>
<td>10</td>
<td></td>
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<tr>
<td>19</td>
<td>11-12</td>
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<tr>
<td>20</td>
<td>12-13</td>
<td>2</td>
<td>George W.</td>
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<td>21</td>
<td>12-13</td>
<td>2</td>
<td>Ann M.</td>
<td>6:20 p.m.</td>
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<td>6</td>
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<td>22</td>
<td>13-14</td>
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<td>George W.</td>
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<td>11:15 p.m.</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>17-18</td>
<td>2</td>
<td>Alexander K.</td>
<td>6:45 p.m.</td>
<td>9:10 p.m.</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>
Allonal.

Synonym - Allyl-isopropyl-barbituric acid with phenyl-dimethyl-dimethylamino-pyrazolon.

Allonal is a preparation manufactured at the Hoffmann-La Roche chemical works and sold in tablet form. Each tablet contains one grain allyl-isopropyl barbituric acid and one and two-thirds grains phenyl-dimethyl-dimethylamino-pyrazolon. The recommended dose is from one to two tablets for hypnotic effect. If analgesia is desired two to four tablets are to be administered.

Patients Treated with Allonal.

George W. aet 19 years.

Admitted 4.1.28.

On admission excited. Foolish in talk and behaviour. Rambling and incoherent in speech. Disoriented in all dimensions. Attention fleeting. Auditory and visual hallucinations present. Continued to be restless and very foolish.

Sometimes very noisy at night and did not sleep.

Treatment of this excitement and insomnia is as follows:

29.1.28. One tablet Allonal 1½ hours' sleep.
30.1.28. Two " " 8 " "
31.1.28. Two " " 8 " "
2.2.28. Two " " 1 " "
6.2.28. Two tablets Allonal 7 hours' sleep.
11.2.28. Two " " 6 " "
12.2.28. Two " " 8 " "
13.2.28. Two " " 3 " "

Ann McD. or M. aet 35 years.
Admitted 29.1.28.
On admission was dull, retarded and depressed. A few days afterwards she became restless and talkative, accusing different persons of poisoning her. Resistive, excited and at times very noisy.
She was given on
8.2.28. Two tablets Allonal and slept 7 hours.
9.2.28. " " " " 8 hours.
12.2.28. " " " " 6 hours.

Mary M. aet 38 years.
Admitted 6.10.21.
This patient suffers from dementia praecox and at times becomes impulsive, violent and very noisy.
On
29.1.28. she had two tablets Allonal 8 hours' sleep.
7.2.28. " " " " 7 " "
8.2.28. " " " " 4 " "
<table>
<thead>
<tr>
<th>Date</th>
<th>Patient</th>
<th>Dose</th>
<th>Time of Administration</th>
<th>When Asleep</th>
<th>Number of Hours of Sleep</th>
<th>Remarks</th>
</tr>
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<tr>
<td>9-10 Feb.</td>
<td>James M.</td>
<td>1 cc</td>
<td>6:40 p.m.</td>
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<td>7</td>
<td></td>
</tr>
<tr>
<td>2 12-13</td>
<td>James M.</td>
<td>&quot;</td>
<td>6:30 p.m.</td>
<td>9:10 p.m.</td>
<td>7</td>
<td></td>
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<tr>
<td>3 13-14</td>
<td>Lotisa J. R.</td>
<td>&quot;</td>
<td>7 p.m.</td>
<td>7:45 p.m.</td>
<td>10½</td>
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<tr>
<td>4 13-14</td>
<td>James M.</td>
<td>&quot;</td>
<td>6:50 p.m.</td>
<td>9:15 p.m.</td>
<td>6</td>
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<tr>
<td>5 14-15</td>
<td>Duncan A.</td>
<td>&quot;</td>
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<td>6 15-16</td>
<td>Louise J. R.</td>
<td>&quot;</td>
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<tr>
<td>7 15-16</td>
<td>Jessie M.</td>
<td>&quot;</td>
<td>12:35 a.m.</td>
<td>2:30 a.m.</td>
<td>3</td>
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<tr>
<td>8 15-16</td>
<td>George W.</td>
<td>&quot;</td>
<td>11:20 p.m.</td>
<td>9:30 p.m.</td>
<td>6½</td>
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<td>9 15-16</td>
<td>Thomas M.</td>
<td>&quot;</td>
<td>6:45 p.m.</td>
<td>8:40 p.m.</td>
<td>7</td>
<td>Violent and resistive</td>
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<tr>
<td>10 16-17</td>
<td>Christina B. or M.</td>
<td>&quot;</td>
<td>12:15 a.m.</td>
<td>1:25 a.m.</td>
<td>1</td>
<td>Very violent</td>
</tr>
<tr>
<td>11 16-17</td>
<td>Helen R. or S.</td>
<td>&quot;</td>
<td>6:45 p.m.</td>
<td>8:30 a.m.</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>12 17-18</td>
<td>Roderick J.</td>
<td>&quot;</td>
<td>12:40 a.m.</td>
<td>2:30 a.m.</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>
Luminal Sodium.

Synonym - Phenobarbital-sodium

Phenylethylmalonylurea and its sodium salt.

Orally I have used luminal sodium in cases of epilepsy only. For insomnia and excitement I have always given the drug hypodermically. For use as a hypodermic injection luminal sodium is made up in a 20 per cent solution. Luminal itself is very insoluble, and therefore its sodium salt is preferable for hypodermic administration. Only freshly prepared solutions should be used, as luminal sodium in solution is unstable and tends to deteriorate, more especially if not kept in dark coloured bottles.

A 20 per cent solution is prepared by dissolving 33 grains of luminal sodium in ten cc. of distilled water. Care should be taken in making such a solution, distilled water is used, and it should be boiled for half an hour, filtered, and cooled to at least 30°C. Luminal sodium should not be dissolved in hot water as thereby its action is destroyed. Even warm water is not necessary as luminal sodium is freely soluble in cold water. If the solution is put into vaccine bottles (20 cc.) fitted with rubber caps which have previously been thoroughly sterilised, the administration of the solution at the bedside can /
can be very easily carried out with a minimum risk of contamination, for the rubber caps can be cleansed with spirit, pierced by the hypodermic needle and the required amount of the solution drawn up into the syringe and transferred to the patient.

Moreover, the dark tinted vaccine bottles prevent any deterioration of the solution which is likely to occur.

I have found the above method most convenient and highly satisfactory.

The dose of luminal sodium recommended for insomnia is from one and a half grains to five grains.

I have always given 1 cc. of this 20 per cent luminal sodium solution which makes the dose of luminal sodium given each time 3.3 grains. I have used this dose in acute excitement, and from the luminal sodium chart it will be seen that it has given good results. As all the patients noted in the chart were at the time of administration in a state of excitement, and therefore more or less alike, and as the histories of most of them have been already set down in previous portion of this thesis, I do not repeat their cases here.

In two cases my results were unsatisfactory, namely Thomas M. and Christina B.
Thomas M.  middle-aged man.
Admitted 15.2.28.

The patient is an epileptic.

On admission he was dull, confused and disoriented. Towards evening on day of admission he became restless, wanting to get out of bed, and struggling when prevented from doing so. He became more and more excited and at 6.45 p.m. he had a hypodermic injection of 1 c.c. 20 per cent luminal sodium solution, after which he became considerably quieter, went to sleep at 9.30 p.m., and slept for six and a half hours.

The following day he was excited, which state persisted all day until in the evening he was impulsive and very violent. He was again given 1 c.c. luminal sodium solution hypodermically, after which he became much more settled and less violent, but obtained no sleep. On the second occasion on which luminal sodium was given in this case excitement was very much more marked than at time of previous injection.

Christina B.  aet 40 years.
Admitted 5.2.28.

On admission patient was wildly excited, very talkative. Rambling and incoherent in speech. Disoriented for time, place and person. Attention fleeting. Restless at all times. Occasionally violently resistive.

On /
On 16.2.28. she had been restless and excited all day, but towards evening became somewhat quieter. Later on, however, she became very excited and violently resistive and at 12.15 a.m. on 17.2.28. she had 1 c.c. of luminal sodium solution, after which she was less noisy, gradually became quieter, and slept at 1.35 a.m.

She slept only for one hour but for some little time after she awoke she remained quieter, only to become restless again and had no further sleep.
Theominal is the name given to a compound preparation containing theobromine and luminal. It is one of the Bayer products and is obtained in tablet form each tablet containing five grains theobromine and one and a half grains luminal.

Theobromine is a dilator of the peripheral arteries, and thus causes dilatation of the cerebral arteries. This dilatation of the arteries is, to some extent counterbalanced by the weak stimulant action which theobromine has upon the vaso-motor centre, so that vascular tone is regulated by these opposing actions of the drug.

Luminal, owing to its anti-spasmodic action on the unstriped muscle of the vessel wall also reduces arterial hypertension, so that theobromine and luminal in the compound theominal act synergically. In cases of insomnia due to arterial hypertension then, one would expect theominal to bring about relief, and in a great number of uncomplicated cases of such origin very satisfactory results have been reported.

In slight cases of senile psychoses of arteriosclerotic origin, favourable results have also attended the exhibition of theominal. In my hands theominal has not produced such satisfactory results.
Donella M.  aet 38 years.

Admitted 31.10.27.

On admission this patient was very dull and acutely depressed. Very "theatrical" in her conduct. Weeps and moans in hysterical fashion. Oriented in all dimensions. For two days after admission she remained quiet, depressed and morbidly introspective.

She then became restless, extremely agitated and finally acutely excited, screaming that she was possessed of devils and that demons were crushing the life out of her. Visual and auditory hallucinations, which disturbed her greatly, were present.

These periods of acute agitation and distress last for about three days, during which time she is very impulsive and suicidal. She then has an interval of comparative mental stability, lasting about a week or ten days. Hallucinations persist all the time, but during quiescent periods are not so disturbing to the patient. She has remained unchanged mentally since admission and she has been sleeping very badly.

On 4.2.28. she commenced taking theominal - two tablets in the morning and two tablets at night.

On 9.2.28. the number of tablets taken daily was increased /
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**Note:**
- The chart shows a temperature chart for a patient.
- The patient's temperature varies between 36.6°C and 39.5°C.
- The patient is on *Thioninal Tablets* daily as indicated.
- The chart also includes other medical parameters such as pulse, resp., urine oz., reaction, alk. ph., and sleep.

**Additional Remarks:**
- The patient's condition is monitored daily with various tests including pulse, resp., and others.
- The chart is filled out in ink with a blue and red pen.

**Source:**
- Sutlley & Silverlock Ltd, 92 Blackfriars Road, London.
increased to six - three morning and evening.

That she did not benefit from this treatment from the point of view of lessening her sleepless hours will be seen by comparing the number of her hours of sleep before and after administration of theominal, as seen in her attached temperature chart.

**Alexander M.  aet 60 years.**

Admitted 30.3.27.

On admission was morbidly depressed. Very uncommunicative, and very unstable emotionally, weeping when asked any questions. His mental state has not improved since admission.

He remains persistently depressed.

Entertains delusions of unworthiness, and believes that he has been the cause of the death of his entire family.

Mistaken identity, believing several other patient in the ward are his sons. Has no control over his emotions. Weeps whenever anybody enters into conversation with him. His memory both for recent and remote events is very inaccurate. He is very facile. Since admission he has slept very badly and he continues to have only three or four hours of sleep each night.

Treatment with theominal, four tablets daily - two night and morning - was commenced on 29.10.27.

On /
**Name:** Alexander

**Age:** 60 yrs

**Disease:**

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<tr>
<th>Date</th>
<th>Pulse</th>
<th>Resp.</th>
<th>Urine OZ</th>
<th>Reaction</th>
<th>Albumen</th>
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**Suttley & Silverlock Ltd**

92, Blackfriars Road, London.
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**Notes:**
- Lymphatic glands are not palpable.
- Increased appetite.
- Increased activity.

**Result:**
- Thyroidal T 1 tablet daily.
- Thyroidal T 2 tablet daily.
- Thyroidal T 3 tablet daily.

**Other Observations:**
- Temperature: 101.5°F
- Pulse: 80
- Resp: 22
- Urine OZ: 20
- Reaction: 4
- Sugar: 5
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- **Pulse**
- **Resp.**
- **Urine OZ:**
- **Reaction**
- **Albumen**
- **Sugar**
- **B.O.**

*Suttley & Silverlock Ltd.*
92, Blackfriars Road, London.
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<th>Disease</th>
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|---------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| CENT.         | FAHR.|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
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| 38°           | 103°|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 37°           | 102°|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
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| 35°           | 100°|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 34°           | 99° |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 33°           | 98° |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 32°           | 97° |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 96°           |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |

- Pulse
- Resp.
- Urine Oz.
- Reaction
- Sugar
- B. O.

**Note:** The normal temperature is daily.

22.11.27
On 22.11.27. the number of theominal tablets was increased to eight tablets daily - four night and morning. He derived no benefit from theominal, and this treatment was discontinued on 25.11.27. For hours of sleep see appended temperature chart.

Charles R. aged 52 years.

Admitted 23.11.27.

This history of this patient has already been detailed under the section of this thesis dealing with "Insomnia in arteriopathic dementia" and there, from his sleep chart, it will be seen that his total amount of sleep and the number of hours of sleep each night are very small.

On 8.2.28. he commenced taking four theominal tablets - two tablets night and morning -. On 15.2.28. the number of theominal tablets was increased to six per day.

The insomnia was not relieved and consequently treatment was discontinued on 21.2.28.

In all these cases blood pressure was lowered. The temperature charts of Alexander M. and Charles R. demonstrate another interesting point - namely that during the administration of theominal the general body temperature is lowered. Compare appended temperature charts for temperature before and during treatment with theominal.
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<tr>
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- Urine Oz.
- Reaction
- Sp. Gr. Sleep.
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- B.O.
SUMMARY AND CONCLUSIONS.

General.

Hypnotics should only be employed in the treatment of insomnia and mental excitement when all other measures have failed. The treatment of these two conditions should be approached in therapeutic crescendo.

Before attempting to employ hypnotics with any patient a very careful physical examination should be carried out for two reasons.

(1) To discover if there is any physical cause at the root of the trouble.

(2) To get to know the patient's physical state, which is important as a guide as to which hypnotic may be employed.

Employment of hypnotics in asylum practice is essential and useful.

There are many indications for the administration of hypnotics in mental diseases, the principal ones being three in number.

(1) To allay acute excitement and so prevent physical exhaustion.

(2) To mitigate the impending and inevitable periods of recurrent excitement in certain patients, in the initial stages of such excitement, thus preventing its reaching /
reaching a climax.

(3) To relieve insomnia and to induce the return of the sleep habit.

In general practice the use of hypnotics is equally important. Here the main indications are:

(1) In the treatment of very mild recurrent excitement of short duration in a certain type of patient to prevent that patient being certified as insane and sent to an asylum on quite inadequate grounds.

(2) In the treatment of insane people especially cases of senile dementia in their own homes.

(3) In the treatment of insomnia in its very early stages before sleeplessness has developed into, if not a causal, at least an aggravating factor in mental breakdown.

If hypnotics are administered solely at the discrimination of the doctor, and if the patients are strictly observed during the time they are being treated with hypnotics, abuse of these drugs is not liable to occur.

The presence of insomnia and the return of the sleep habit, always taken in conjunction with other clinical signs, are important prognostic considerations.

In my experience insane people require larger doses of hypnotic and sedative drugs than do sane people to induce sleep.
Sulphonal is a drug that ought to be used with the greatest caution.

Cases in which it is to be employed ought to be carefully chosen.

It ought not to be given for acute maniacal excitement in old people.

It ought not to be employed in patients suffering from cardiac disability.

I do not now give single doses of thirty grains sulphonal as in my opinion two doses of fifteen grains each — one dose given in the morning and one in the evening — is a much more satisfactory method. In very great motor excitement fifteen grains sulphonal may not be sufficient to produce any marked diminution of restlessness in which case instead of increasing the dose to thirty grains it is preferable to give the fifteen grain dose of sulphonal combined with two and a half drachms of paraldehyde.

In old people suffering from insomnia with restlessness I have found small doses of sulphonal, never more than ten grains, given in a little hot alcohol most efficacious.

An aperient should always be given the morning following the day on which sulphonal has been administered.
tered and strict watch must be kept to see that the bowels open.

Strict vigilance for occurrence of haematoporphyrin must always be kept in the case of all patients being treated with sulphonal.

**Paraldehyde.**

In asylum practice the disadvantages of paraldehyde are far outweighed by its advantages.

I have found it an excellent hypnotic in cases of acute mania and acute melancholia. I have never known it fail to induce sleep in these cases in doses of three drachms, so I have never had to employ larger doses.

In the great majority of cases I have found two and a half drachms of paraldehyde produce the desired effect. It is a safe hypnotic.

It can be administered with confidence in cases where there is cardiac disability. Paraldehyde, in my opinion, is the most satisfactory of all hypnotics in acute mania and acute melancholia.

**Hyoscine.**

When patients are extremely excited, violent and resistive it is impossible on many occasions to administer a hypnotic by mouth.

It is useless and criminal to struggle with a patient displaying great motor excitement and tending to resistiveness /
resistiveness, therefore it is necessary to employ a hypnotic or sedative which can be given hypodermically.

In such cases hyoscine is by far the most efficient depressant to use and I have found hyoscine hydrobromide in combination with morphine sulphate and atropine sulphate as found in the hyoscine compounds "A" and "B" very excellent in the great majority of such excited patients. These compounds are easily administered, act quickly, and give on an average about six hours' sleep.

In a few extremely resistive patients with great motor excitement I have seen hyoscine compound "B" fail to allay excitement in any marked degree. In these patients I have pushed the dose of hyoscine hydrobromide—giving $\frac{1}{75}$ grain hyoscine hydrobromide with $\frac{1}{4}$ grain morphine sulphate, — which combination I have never seen fail to act quickly, producing calm in a very short time with sleep following soon after. In these cases, then, when hyoscine compound "B" proves of little use, experience has taught me to give hyoscine hydrobromide in as big doses as $\frac{1}{75}$ grain combined with $\frac{1}{4}$ grain morphine sulphate.

"15" Mixture.

Certain hypnotics give much more satisfactory results when employed in smaller doses in combination than when employed singly in large doses.

Thus /
Thus a combination of paraldehyde and sulphonal results in quick action and prolonged effect.

Similarly in "15" Mixture the combined actions of the constituents result in quick action due to chloral hydras, prolonged effect due to the potassium bromide, and analgesia from the presence of liquor opii sedativus.

I have found "15" mixture very useful in cases where sleeplessness was due to the presence of pain.

It is an excellent hypnotic when used with patients who fall asleep in the beginning of the night, shortly after they go to bed, but soon wake up and remain awake during the remainder of the night.

It is useful in restlessness in elderly people, but here care must be taken in its administration as the potassium bromide tends to produce mental confusion in such people, and should therefore be given only occasionally and with caution.

I have not found it to be of much use in acute excitement unless given in doses of six drachms.

I often use "15" mixture as a variant to other hypnotics in patients requiring a considerable amount of sedative.

On account of the presence of chloral hydras in the combination I never employ it in cardiac patients.

Orally I have never used potassium bromide alone, but in cases of persistent restlessness I have given potassium /
assium bromide per rectum in normal saline in doses of twenty grains potassium bromide to one pint of the rectal injection. I usually give one such rectal injection in the morning and repeat it late in the evening, and in many of my cases I have found this treatment very satisfactory.

**Bromural.**

In my experience bromural in doses of five grains is quite useless.

I have found ten grains of bromural an excellent hypnotic, constant in its results and producing no ill effects on the day following administration.

The action of this drug is somewhat delayed in cases where there is acute excitement or any marked degree of mental distress.

**Amylene Hydrate.**

This hypnotic is useful in cardiac patients and in cases where the circulation is poor, and therefore I have used it as a variant to paraldehyde, but in my opinion it is not nearly such a good hypnotic as the latter drug.

I have not found amylene hydrate very satisfactory in cases of acute excitement with restlessness.

As an analgesic it is useless.
**Chloralamide.**

This drug is very little use in acute excitement. It is useful in simple insomnia, but the sleep it induces is extremely light and the patient is very easily disturbed. I have found it useful in simple insomnia in aged people, and in cardiac cases, but if there was any excitement present in these cases chloralamide usually failed to have any effect. I find it useful when administered at night to a patient who, in the morning, had had fifteen grains sulphonal.

Generally speaking, it is not of much use as a hypnotic in mental diseases.

**Chloretone.**

My experience of chloretone is that it is much too uncertain and unreliable in its action for general use.

**Dial.**

I have found dial very useful in patients suffering from melancholia. In these cases it gives on an average five to six hours' sleep. I have never observed any ill effect the day following the administration of the drug. In simple insomnia I consider dial an excellent hypnotic giving sound sleep with as small a dose as one and a half grains.
Allonal.

My results from allonal have been very satisfactory. In acute mania I have found two tablets of allonal sufficient to allay excitement and induce sleep.

Luminal Sodium.

Care must be taken in the making of a twenty per cent solution of luminal sodium. I have found 1 c.c. of this solution very useful in excited patients.

In very acutely excited and violent patients my experience is that one c.c. is not a sufficiently large dose to control excitement, and in such cases 1.5 c.c. of the solution should be given.

Theominal.

In the cases in which I have employed theominal I have not met with very great success.

I have not been able to employ it in insomnia in uncomplicated cases of arterio-sclerotic origin, but its exhibition in arterio-pathic patients, in whose cases delusions and emotional instability are prominent features, is, in my experience, quite useless.

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