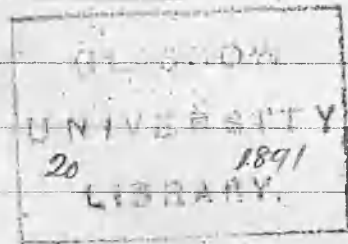


Thesis for the Degree of Doctor of Medicine.



Some Notes

on the Use of
Sulphonal.

By

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Some Notes on the Use of Sulphonal.

In giving the results of his experience of the use of Sulphonal, the writer has thought it best not to encumber his pages with a statement of the experience of other observers, of which there is now much published in the British & Continental journals, nor to inflate his paper with general remarks upon hypnotic drugs & upon the necessity, which every physician feels, of a safe & certain sleep-bringer. Nowhere is this necessity felt to be more pressing than in the treatment of the insane. It is in this branch of medicine that the present writer's practice lies, & it is to cases of insanity that all the following remarks apply. Like other physicians, the writer has made trial of many "hypnotics", both of the old fashion & of the new, & with results gratifying, discouraging, & discouraging. In Sulphonal he has found a drug productive of much good, & in the hands of the injudicious, productive of not a little harm. The results of his experiments with it are stated briefly & without prejudice in the following pages. Not theory has been favoured or disfavoured; simply, what happened & was observed has been set down. The first fifty cases in which he made use of Sulphonal have been selected for analysis. The drug has since been freely used by him in many other cases, which are here excluded from consideration; the results in these cases, it may, however, be stated, have been very similar to those afforded by the earlier ones.

In prescribing Sulphonal the object, in the first
(instances,

instance, was to procure sleep. It was soon discovered that, in addition to its hypnotic property, the drug had a strong sedative action, & as a sedative it was accordingly given a large trial. No particular class of cases was selected for treatment. The sleepless, the excited, & the miserable, all such as required rest or sleep & could not attain it, but by drugs, — to these, as they came, Sulfonal was administered. What sleep & rest they got, & what other changes they experienced are here told.

It was found that among the most characteristic properties of Sulfonal are the duration of its action, the prolonged duration of its effects, & the tendency for the phenomena accompanying its use to become increasingly more profound & more prolonged under the continued administration of the drug. It has, accordingly, been thought advisable to change the results in three divisions, namely (1) The effects produced by single doses, or doses separated by long intervals, (2) those produced by doses repeated at intervals of forty-eight hours, & (3) those produced by doses repeated at intervals of twenty-four hours or more frequently. For the sake of convenience, these doses will be referred to in the statement under the names of (1) Single doses, (2) Interrupted doses, & (3) Continuous doses.

A. Effects produced by Single doses.

Fifty cases were treated; 13 males & 37 females. The ages of the males ranged from 24 to 67, & of the females from 22 to 74. The general health of the patients was considered to be good or average in 21 cases (4 males & 17 females), poor in 23 (5 males & 18 females), & distinctly bad in 6 (4 males & 2 females).

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The following bodily diseases or other complications were present, namely: Phthisis Pulmonalis in 3 cases (1 male + 2 females), Heart Disease in 5 (4 males + 1 female), Isianthraex with Fever in 4 (1 male + 3 females), Epilepsy in 2 (1 male + 1 female), Acute Alcoholism in 2 (1 male + 1 female), Chronic Alcoholism in 1 (female), Blindness in 1 (female), Chorea in 1 (female), Hemiplegia in 1 (male), Epithel in 1 (female), Internal Haemorrhoids in 1 (female), Inguinal Herma in 1 (female), Amenorrhoea in 1, Pregnancy in 2, Uterine Displacement in 1, Fracture in 3 (femur 1 male, clavicle 1 female, & humerus 1 female), Incised Wounds of Neck + Anus in 1 (female), & Simplex Ulcer in 1 (male).

The mental condition of the patients was as follows: Seven suffered from acute or recent Mania (1 male + 6 females), 14 from acute or recent Melancholia (4 males + 10 females), 13 from chronic Mania (3 males + 10 females), 4 from recurrent Mania (2 males + 2 females), 4 from chronic Melancholia (1 male + 3 females), 3 from Idiosy or Imbecility (all females), 2 from Secondary dementia (both females), 1 from organic dementia (male), & 2 from general Paralysis of the Insane (1 male + 1 female).

Dose & mode of administration.

Sulphonal was given in doses of 10, 15, 20, 25, 30, & 40 grains. It was administered in fine powder, or dissolved in water, tea, milk, soups, &c., or mixed with porridge, bread + butter, or other article of food, or suspended in mucilage. As it is almost devoid of taste & has no smell, there was no difficulty in getting the patient to take it in his food without his being aware of its presence. The method of administration did not influence the results or the rapidity of action to any appreciable extent.

It was, as a rule, given at the evening meal about two hours before the usual bed-time, but, in order that the rapidity of action might be fairly tested, the patient was put to bed immediately after administration.

I. Hypnotic Effect, or Effect upon Mental Condition

(a) General Results.

Very considerable differences in the individual reaction to the drug was experienced, 10 or 15 grains acting as an efficient hypnotic in some cases, & 30 or 40 grains being required in others. Between 30 & 40 grains was found to be the most suitable average dose. In no case did Sufonal fail to produce sleep, & the right dose for each case having been ascertained, the action of the drug was fairly constant. The hypnotic effect was highly satisfactory in 40 cases (80 per cent.) & moderately satisfactory in 10 (20 per cent.). Women appeared to require much the same doses as men; but strong, robust cases generally required larger doses than feeble, debilitated cases.

In stating the results of single doses, the average is given where the patient had more than one dose.

(b) Rapidity of Action.

The duration of the interval between the administration of the drug & the occurrence of sleep varied from half-an-hour to seven hours & three-quarters, the average being a little under three hours & a-half. This average represents very fairly the length of the interval in the great majority of the cases. [With reference to the statement of results in this paper, it does not carefully come in mind that the cases dealt with were, for the most part, of a much more intractable class than those which are met with in ordinary

(General

general practice, & moreover, that comparatively few of the patients were capable of making intelligent or trustworthy statements in regard to their symptoms].

(c). Personal Condition.

No excitement or other disagreeable symptoms occurred in any case during the interval before sleep. What usually happened was that excitement & distress slowly & gradually subsided until the patient was found to have fallen quietly asleep.

(d). Duration of Sleep.

The sleep which followed lasted from two hours to eleven hours, the average being nearly seven hours.

(e). Nature of Sleep.

In the great majority of cases the sleep was tranquil & natural, & light rather than sound; it was rarely profound; it was often easily broken by any noise or other disturbance, & it was never (as far as the evidence went), accompanied by disagreeable dreams.

(f). The awakening & the day following.

As a rule, the patient awoke feeling refreshed & free from any uncomfortable sensations; but in about a fourth of the cases slight drowsiness or somnolence occurred during the course of the succeeding day, the patient, if undisturbed, being found nodding or slumbering lightly. Occasionally, but rarely, a feeling of confusion was complained of. In several instances indifference or disinclination for exertion was noticed. In one case (chronic melancholia) isolated doses were occasionally followed by some slight exacerbation of the mental disorder, in the shape of increased bewilderment, watchfulness, & irritability. Otherwise, no unpleasant (cerebral

cerebral symptoms were ever noticed. Almost invariably there was an appreciable improvement, slight in some instances & marked in others, in the mental phenomena, the drug appearing to exercise a soothing & composing effect on the vitable brain & nervous system. This improvement occasionally persisted for two or three days.

(9). The second night & succeeding nights.

In 80 per cent. of the cases the hypnotic influence of the drug appeared to be continued on the second night after its administration, the patient sleeping or resting better on this night than he was used to do. In 20 per cent. the effects appeared to have passed off before the second night. Occasionally the patient slept better on the second night than on the first. On four occasions a distinct deferred action was noticed, little or no effect being produced on the first night, & more or less prolonged sleep occurring on the second; but the cases in which this occurred reacted in the ordinary manner on other occasions. In a few cases the patient slept better for several nights after a single dose.

II. Other Cerebral & Nervous Effects.

In one case (Female; age 28; acute mania; hallucinations of hearing; mild chorea; advanced pregnancy) the patient fell asleep in about two hours after receiving 30 grains; she slept straight on for 10 hours, & slumbered nearly the whole of the following day; the next night she slept 8 hours, & the next day she slumbered with short intervals till the evening; when awakened she complained of having lost her hearing; the deafness passed away rapidly; the choreic spasms were slightly modified while she was under the influence of the drug.

In two cases of fractured bones doses of 30 grains
(assisted

assisted in procuring rest, or, possibly, exercised a mild analgesic effect, or controlled to a certain extent the muscular spasms.

With the above exceptions, Sulphonol in Single doses had no distinct effect on the motor or sensory functions, on reflex action, or on coordination, beyond the condition of indifference or mild fatigue already referred to.

III. Circulation.

Beyond a slight slowing & softening of the pulse, such as would accompany natural sleep, the circulatory system was affected in no way by Single doses.

IV. Respiration.

The results were entirely negative.

V. Digestion.

In one or two cases in which there was marked droopiness during the day following the use of the drug, the patient, as might have been expected, did not take his meals as heartily as usual. Otherwise, no impairment of appetite occurred in any case, & there was never any disturbance of digestion or other disorder of the gastro-intestinal tract.

VI. The Skin.

No change in the condition or function of the skin occurred.

VII. The Kidneys.

The urine was not examined in a systematic way. It can only be said that no ^{renal} urinary troubles followed the use of Single doses, & that, in the cases in which an examination of the urine was made, the ordinary tests revealed no change in its quantity or constituents.

VIII. Sexual Organs & Functions.

The results were entirely negative. In two cases

of advanced pregnancy, doses of 20 & 30 grains produced no uterine disturbance.

IX. Temperature.

Single doses did not appear to influence the temperature in any way.

B. Effects of Doses repeated at Intervals of Forty-eight Hours. (Intermittent Doses).

In the great majority of the fifty cases, which have been referred to under the previous head of Single doses, were treated at one time or another, & at longer or shorter intervals, with repeated doses of Preparation. It was usual, in the first instances, in each case, to allow an interval of at least forty-eight hours to elapse between each two doses. It was found that, as a rule, the full benefit of the hyps. nark & sedative action of the drug could be obtained & kept up by giving it on alternate days. Repeated in this way, it was prescribed for periods ranging from a few days up to six or seven weeks. The maximum & minimum individual doses were 40 grains & 10 grains respectively, & the mode of administration was the same as described on page 3. The following may be cited as examples of the amount & number of doses given on alternate days.

Examples of Cases treated with Interrupted Doses

Name	Sex	Age	Mental Disorder	Dose	No. of Doses	Frequency of Administration
I.M.B.	F.	44	Acute Melancholia	15 grains	5	Alternate Evenings
A.D.	F.	54	Acute Mania	20 grains	4	Do.
J.M.W.	F.	30	Imbecility	30 grains	4	Do.
M.E.	F.	39	Acute Melancholia	30 grains	4	Do.
H.G.S.	F.	31	Acute Melancholia	30 grains	4	Do.
M.J.F.	F.	39	Acute Melancholia	30 grains	12	Do.
H.T.S.	F.	64	Chronic Mania	30 grains	13	Do.
H.M.P.	F.	35	Chronic Mania	30 grains	13	Do.
R.R.	M.	24	Chronic Mania	30 grains	14	Do.
J.K.D.	F.	49	Chronic Melancholia	30 grains	26	Do.
Do.	-	-	-	40 grains	13	Do.
J.S.	F.	54	Acute Mania	40 grains	7	Do.
M.B.H.	F.	53	Chronic Mania	40 grains	15	Do.

I. Effect upon Sleep, Mental Condition, & Nervous System.

The first few repeated doses were followed by the same results as regards the rapidity & duration of the hypnotic action & the other after effects as those produced by single doses. After a few days' treatment, the period varying considerably, according to the dose, the peculiarities of the case, & individual idiosyncrasy, the action of the drug almost invariably tended to become more prolonged; so that the effects of one dose had not entirely passed off when the next dose was given. At the same time the hypnotic action became gradually more pronounced & went on slowly increasing as long as the drug was continued, the improvement in sleep being shown not only on the nights when Sulphonal was given, but also on the nights when it was withheld. When the patient was brought well under the influence of the drug, the difference in the amount of sleep between the Sulphonal nights & the non-Sulphonal nights was generally slight.

It was never necessary to increase the dose owing to habituation; on the other hand, after a few days' treatment sleep could occasionally be secured by gradually diminished doses. On stopping the drug, the improvement in sleep almost invariably continued for periods varying from a few days to a few weeks, according, as a rule, to the quantity & number of doses administered. In several instances a few doses were sufficient to induce & establish the sleep function, & in other instances, where sleeplessness again returned, a few more doses would again secure sleep for a considerable period.

After several doses had been given, drowsiness during the day became increasingly more frequent, & it was always present to a greater or less extent after prolonged treatment. Along with this symptom, a sort of dreamy confusion became noticeable, & following it, an idiotic condition, which passed with further treatment into slight weariness & fatigue, followed in extreme cases by slight unfeelingness & shakiness of locomotion. These phenomena were distinct in some cases & very slight in others, the individual reaction to Sulphonal showing great variation; but the symptoms were never (with interrupted doses) such as were considered alarming, & they speedily passed off when the drug was stopped, seldom, even after several weeks' treatment, persisting more than a few days.

With the exception of the phenomena referred to, Sulphonal, in the doses & at the intervals stated, gave rise to no disagreeable cerebral symptoms or appreciable disturbances of the motor, sensory, or reflex functions.

With repeated interrupted doses, a gradual, generally prolonged, & frequently permanent improvement

in the mental condition occurred, characterized by a marked diminution of the excitement, the irritability, the motor restlessness, & the restlessness. In no case did Sulphonal fail to effect at one time or another some beneficial influence on the mental state; this benefit was not accompanied by any serious drawbacks; the improvement, moreover, occurred in the feelings as well as in the conduct, the patients frequently exhibiting in their demeanour an expression of increased comfort & ease; & in only one case (that already referred to under Single Doses) was there an occasional exacerbation of the mental disorder which appeared to be due to the use of the drug.

II. Circulation.

After Interrupted Doses the pulse generally assumed a softer character than before. Otherwise the effect on the circulation was negative. No cyanosis, fainting, flushing, or pallor ever occurred, & in five cases of cardiac disease (valvular & degenerative) the circulation was not disturbed in any way.

III. Respiration.

Interrupted Doses gave quite negative results. In three cases of phthisis pulmonalis no unpleasant symptoms were caused.

IV. Digestion.

What has been said of Single Doses applies also to Interrupted Doses. Frequently the appetite seemed to improve under the use of the drug, & patients who had previously required to be fed would sometimes take their meals voluntarily after a few doses. There was no evidence of any vomiting, diarrhoea, constipation, abdominal pain or tenderness, thirst, or other gastrointestinal trouble, which could fairly be attributed to the use of Sulphonal.

phronal. It must here be stated, however, that in the cases of three patients, who were having 30 grains on alternate nights, diarrhoea did occur after a few days' treatment; but there was no reason to suppose that this was due to the Sulphonal. The Institution was at the time suffering from an epidemic of diarrhoea with fever, due to unsanitary causes, & among the victims of the epidemic there were three patients who had been treated to be receiving Sulphonal at the time. From other patients, it may be added, who were suffering from the same disorder, were, with the view of obtaining rest & sleep, treated with Sulphonal with good effect, the intestinal symptoms being in no way aggravated, but rather being somewhat ameliorated (probably owing to the quietude which was obtained).

V. The Skin.

No change in the condition or function of the skin occurred. There were no eruptions, or no unusual dryness or moisture.

VI. The Kidneys.

What has been said under the head of Single doses applies equally to the results of Interrupted doses.

VII. The Sexual Organs & Functions.

The results were entirely negative. Sulphonal was given in two cases of advanced pregnancy without the slightest evil result. One woman received two doses, one of 30 grains & one of 20 grains, separated by an interval of several days. The other received three doses of 20 grains on consecutive days, followed on alternate nights by four doses of 30 grains.

VIII. Temperature.

owing to the various physical & mental disorders present in the different cases treated, the temperature charts rarely gave a normal reading; but a careful consideration of all the factors of each case pointed to the conclusion that Sulfonal in Interrupted doses, even after several weeks' use, exerted little, if any, influence on the temperature, the only modification which could ever be shown to result consisting in a very slight fall in the scale.

C. Effects of doses Repeated at Intervals of Twenty-Four Hours or more frequently (Continuous doses).

In twenty cases Sulfonal was given in doses repeated on consecutive days or two or three times a day. The individual doses were 10, 15, 20, & 30 grains, the largest quantity given in one day being 60 grains, & the smallest 10 grains. The total quantity given in this way ranged from 40 grains spread over two days to several ounces extending over a period of two or three months. Among the larger quantities & longer periods of administration were the following:

Examples of cases treated with continuous doses.

Examples of cases treated with continuous doses.

Name	Sex	Age	Mental Disorder	Amount & Frequency of Dose	Total Quantity given	Period covered by Administration
J. H.	M.	63	General Paralysis	20 grs. every p.m. x 8 followed by 15 grs. every p.m. x 4	265 grs.	15 days.
A. L.	M.	40	Recurrent Mania	15 grs. every p.m. x 19	285 grs.	19 days.
A. G.	F.	40	Acute Melancholia	30 grs. every p.m. x 6 20 grs. every p.m. x 3 15 grs. every p.m. x 4	300 grs.	13 days.
M. R.	F.	40	Imbecility	30 grs. every a.m. & p.m. x 4 followed by 30 grs. every p.m. x 4	360 grs.	8 days.
A. V.	F.	38	Secondary Demen- tia	30 grs. every p.m. x 14	420 grs.	14 days.
M. Y.	F.	45	Chronic Mania	30 grs. every a.m. & p.m. x 10	600 grs.	10 days.
J. S.	M.	32	Acute Melancholia	30 grs. every a.m. & p.m. x 3 one day's interval. 30 grs. every a.m. & p.m. x 8	660 grs.	12 days.
J. K. D.	F.	49	Chronic Melancholia	10 grs. every a.m. & p.m. x 12 followed by 15 grs. every a.m. & p.m. x 8	480 grs.	30 days.
A. W. L.	F.	43	Chronic Mania	30 grs. every a.m. & p.m. x 14	840 grs.	14 days.
H. M. P.	F.	35	Chronic Mania	15 grs. tidie x 8, 5, 3, 1, 5, 3 with intervals of 4, 4, 4, 8, & 4 days.	1125 grs.	54 days.
R. R.	M.	24	Chronic Mania	30 grs. every a.m. & p.m. x 22	1320 grs.	22 days.
S. M. C.	F.	39	Recurrent Mania	30 grs. every p.m. x 28 30 grs. every a.m. x 41 15 grs. tidie x 4, 2 with hrs in intervals of 1 day each.	2655 grs.	84 days.
A. T.	M.	64	Recurrent Mania	30 grs. every p.m. x 3 followed by 30 grs. every a.m. & p.m. x 3	2640 grs.	4 days.

The daily or more frequent repetition of the drug had, as a rule, the effect of "supernormalizing" the patient much more rapidly & more profoundly than was the case when the doses were separated by intervals of fortnight hours. But here, again, great differences in the individual reactions was met with. Generally speaking, the phenomena which followed the use of continuous doses were the same in kind, but more pronounced in degree, than those which have been described under the head of interrupted doses.

I. Effect upon Sleep, Mental Condition, & Nervous System.

After a few days' continuous treatment, the patient invariably began to sleep better, sleep came on sooner & lasted longer & tended to become heavier in character, the awaking began to be accompanied by a feeling of mild confusion, & drowsiness during the day. This set in & became more pronounced. It was not unusual for a bad case of insomnia, where well under the influence of the drug, to sleep for ten hours regularly every night for several weeks. On pushing the drug further, the condition became one of almost continuous somnolence, the whole night being spent in unbroken sleep & the day in fitful slumber. (The patients, it should be stated, were not confined to bed during the day-time, but were encouraged to occupy themselves in the usual ways). The potency of the hypnotic action, as has been said, varied greatly in different cases, & it was found impossible to tell beforehand how much Sulfonal should be given, or how long it should be continued, to produce the desired effect. In no case did the prolonged use of the drug appear to diminish its potency. The rule was for the hypnotic action to become gradually more pronounced as long as the drug was continued, & the effect could generally be kept up by smaller doses than were at first required. The action almost invariably persisted after the discontinuance of the drug for several days, weeks, or months, according to the dose, duration of treatment, & idiosyncrasy, etc. Little doses given in the daytime the hypnotic effect at night was less pronounced than when similar doses were given in the evening, while the day-drowsiness was, naturally, more marked.

(Continuous

Continuous doses almost invariably pro-
 duced a distinct sedative & soothing action. Some-
 or later, but generally within a few days, & often after
 two or three doses, the patient was noticed to be
 much quieter than before, restlessness was replaced
 by indifference, excitement gave way to tranquillity,
 & melancholy became assuaged. With further
 doses the indifference became exaggerated into stolidity,
 which was shown, not only by the disinclination
 for exertion, but also by the hebetude & sluggish-
 ness of the mental operations, along with which
 there was always more or less bewilderment or
 dreamy confusion; the quietude assumed the
 character of torpidity; all interest in outward
 concerns seemed to be lost, & the patient's only de-
 sire was to be allowed to succumb to the sleep
 which was overwhelming his whole being, & from
 which it ultimately became somewhat difficult
 to arouse him. No disagreeable dreams ^{or} unpleas-
 ant feelings were complained of, except an occasion-
 :al "swimming in the head." The rule was for the
 mental effects to become gradually more pronoun-
 ced during the continuance of the drug & to persist
 for some time after its withdrawal, the sedative
 effects continuing for a satisfactorily long period,
 & the hebetude & confusion passing off within a
 few days. Occasionally the stupifying action
 superseded with unexpected suddenness during
 the course of treatment, & it was accordingly
 found necessary to watch very carefully the
 cases under continuous doses.

In every case where continuous doses
 were given for periods of more than a few days'
 duration certain motor symptoms became ap-
 parent. These ranged from mild feelings of
 languor

languor & fatigue up to a condition of complete
 muscular collapse, in which the patient could
 neither walk, nor stand erect, nor help himself
 in any way. Great variation in the individual
 reaction was experienced, & in this particular,
 women appeared to be more susceptible to the
 influence of the drug than men. Thus, one
 man, after having 30 grains three times daily for
 twenty-two days, merely suffered from slight
 lassitude & fatigue; while another man, after
 sixteen days' treatment with 15 grains once
 a day, displayed distinct unsteadiness of gait;
 & a woman, after a few days' treatment with
 15 grains three times a day, suffered from great
 muscular debility with staggering gait & great-
 ly impaired powers of locomotion. The
 first symptom noticed was the intolerance &
 disinclination for exertion already referred to;
 this became more pronounced & passed into
 distinct weariness & fatigue, followed by un-
 steadiness of gait, which developed into distinct
 staggering, accompanied by enfeeblement & un-
 certainty of the movements generally, the lower
 extremities being always the most affected, &
 the patient lurching about insecurely on his
 legs like a "bad sailor" at sea. On pushing the
 drug further, the patient became reduced to an
 utterly helpless condition; he could neither walk,
 nor stand erect, nor sit up; his arm & hand
 movements were feeble & clumsy; his articulation
 resembled that of alcoholic intoxication, & his
 whole appearance was that of a very drunk
 man. With this "drunkenness of the muscles"
 there was not associated any of the excitement
 or hilarity or other characteristic signs of alcoholic
 (intoxication)

intoxication, the mental state, as has been said, being one of comparatively mild stupor, the patient when aroused being able to converse with very considerable clearness & sobriety. The symptoms were occasionally accompanied by a feeling of giddiness; but the essence of the condition apprehended to be extreme motor fatigue with impairment of muscular control & coordination. The progress of the symptoms was, as a rule, slow & gradual; but occasionally there was a sudden increase in their intensity during the course of treatment. They disappeared, for the most part, within a few days after stopping the drug; but the feeling of languor often persisted for a considerable time.

In no case was there any appreciable modification of general sensation or of the special senses of sight, hearing, taste, smell, or pain. In extreme cases the "muscular sense" appeared to be much impaired & the fine touch sense was probably considerably modified, the hand & finger movements being very clumsy & fumbling, & the gait being strongly suggestive of peculiar feelings in the feet & legs.

The skin & tendon reflexes were not affected to any extent.

Continuous doses were employed for the most part, in those cases in which the acuteness of the symptoms was such as would not yield to less frequent doses. In cases of ordinary severity the fine hypnotic action could nearly always be obtained with interrupted doses, & a sufficient sedative effect could at the same time be secured, which was free from any unpleasant or alarming symptoms. In those intractable cases, how-

(over,

ever, although some sleep might be procured, but little abatement of excitement occurred until the drug was given in daily doses, & in extreme cases, violent & protracted excitement was only modified by doses repeated twice or three times daily. Such doses were always followed sooner or later by quietude; but, the more rapidly the drug was repeated, the more apt was the quietude to be accompanied by the somewhat grave cerebral & motor symptoms which sooner or later invariably supervened. The results of the experiments pointed to the conclusion that, where these unpleasant symptoms were at all pronounced, it was very doubtful whether any real benefit had been conferred on the patient; for, although no distinct permanent injury could ever be clearly shown to result, it was evident in several cases that no permanent good had been effected; & the writer was inclined to think that in some instances a certain blunting of the mental faculties, & possibly a certain loss of physical vigour might with some plausibility be attributed to the prolonged use of Sulfonal in continuous doses. In those cases, however, in which it was possible to secure a maximum of the beneficial influences of the drug with a minimum of its injurious effects, the improvement in the mental condition was not only gratifying at the time, but was generally lasting, several patients owing their recovery (in the writer's opinion) in part at least to the judicious continuous use of Sulfonal.

The impression made on the writer's mind by the results of the experiments recorded in this paper may be gathered from his present practice

in prescribing Sulphonal, which is always to be given with single doses administered in the evening, & when it is necessary to repeat these, to do so at intervals of forty-eight hours. If this is found insufficient to procure sleep & quiet, the interval is next reduced to twenty-four hours. In this way a satisfactory hypnotic effect has always been obtained; but, where the excitement is intractable & the drug is employed primarily for its sedative action, it is not infrequently found necessary to further reduce the intervals by giving it three a day, namely in the morning & evening. By prescribing it more frequently than three a day no distinct advantage has ever been gained.

II. Circulation.

Beyond the fact that the pulse was ^{as} a rule soft in character, continuous tests gave quite negative results as far as the circulation was concerned.

III. Respiration.

The only case in which any modification of the respiration occurred was that of a male General Paralytic, aged 63, who received 20 grains every evening for eight days followed by 15 grains every evening for seven days. In this case there was a distinct slowing of the rate towards the end of the period.

IV. Digestion.

In four cases (one man & three women) the appetite occasionally failed after large doses or prolonged treatment. Two of the women suffered from vomiting, one very slightly after a month's continuous treatment, the other more severely on several occasions after a few doses. (This woman

(was

was in other respects very susceptible to the action of the drug). Otherwise, no gastrointestinal trouble occurred & as in the case of Interrupted losses, it was not unusual to witness an improvement in the appetite & general health during the continuance of the drug. When the patient was thoroughly under its influence, he, as a rule, showed no inclination for food or any thing else; but, even at this stage, he swallowed his food readily when it was presented to him, & the digestive function was apparently not injuriously affected in any way. No constipation, diarrhoea, or thirst, or abdominal pain or tenderness was ever complained of.

V. The Skin, Kidneys, & Sexual Organs & Functions.

Continuous losses gave the same negative results as Single & Interrupted losses.

VI. Temperature.

After a careful consideration of the records, allowing for all sources of interference with the heat-state, the conclusion come to was that, even after several weeks' continuous losses, Sulphonal produced very little, if any, effect upon the temperature. In a few cases a very slight fall occurred, & this was followed in one or two cases after prolonged treatment by a very slight rise in the scale.

D. General Effect of Sulphonal upon the different Forms of Mental Disorder.

Acute or Recent Mania.

Seven cases were treated (1 male & 6 females). In all the results were highly satisfactory. Given in sufficient quantity & for a sufficient length of time the drug invariably acted as an efficient

(sedative

sedative & hypnotic; the general condition of the patients, both mental & physical, improved steadily under its use; & no evil effects of any importance or permanence followed. Four of the patients have recovered, & in the remaining three cases recovery is anticipated.

Acute or Recent Melancholia.

Fourteen cases were treated (4 males & 10 females). In three cases the drug exerted little beneficial effect on the mental condition, & the hypnotic action was not pronounced; the drug, however, was not given a sufficiently long trial, & one of the patients was in a dying condition when it was prescribed. In the remaining eleven cases the results were distinctly satisfactory, both the hypnotic action & the soothing effect upon the mental disorder or excitement being very gratifying. Two of the patients were suffering from acute alcoholism, & in their cases single doses of 30 grains were given with distinct benefit. Eight of the patients have recovered, & recovery will, in all probability, take place in a majority of the remaining cases. None have suffered in any way from the use of the drug.

Chronic Mania.

Thirteen cases were treated (3 males & 10 females). In seven cases only a few doses were given. Six cases were under more or less prolonged treatment. In every case the hypnotic & sedative effects were distinctly satisfactory. With repeated doses given for prolonged periods there was always an abatement of the excitement; restlessness, noisiness, or intractability gradually diminished, & the patient became quiet, docile, & inoffensive. There was thus effected in each case a marked temporary improvement, (which

which always persisted for some time after stopping the drug. This beneficial effect was, however, apt to be attended by disagreeable conditions of drowsiness, stupor, & fatigue, which, on pushing the treatment further, assumed the somewhat grave characters already described. None of the chronic cases could be said to have been permanently benefited by the use of Euphrasia; but they were all previously looked upon as hopelessly incurable, & none suffered any appreciable damage. While under the influence of the drug the patient was for the time kept in a quiet & not uncomfortable state & was saved from the risks & the wear & tear of system to which his excitement would, otherwise, have exposed him; while, as regards his neighbours, he ceased to be a nuisance.

Recurrent Mania.

Four cases were treated (2 males & 2 females). One female had only a few doses (with good sedative & hypnotic effect). Three cases were under continuous treatment for prolonged periods & on different occasions. The results were not constant, but on the whole they were gratifying. All three were subject to periodical attacks of noisy, dangerous, & destructive excitement, & one suffered from occasional epileptic seizures. The duration of the attack was sometimes shortened by Euphrasia & sometimes not; its intensity was always modified to a greater or less extent. Repeated doses gave the patients sleep & reduced them to a quiet, inoffensive & moderately rational condition. The drug was pushed in each case, & the cerebral & motor phenomena were marked, but no permanent evil effects resulted. All the cases

(were

were of old-standing & quite incurable. Five being treated with Euphronal, it is right to add, one of the patients has died, partly from the effects of an accident & partly from old heart disease, & the two others are dying of phthisis pulmonalis. No connection can be traced between the causation of the disease & the treatment.

Chronic Melancholia.

Four cases were treated (1 male & 3 females). In three cases only a few doses were given (with good sedative & hypnotic effect). The fourth patient was on several occasions kept under the prolonged influence of Euphronal. The results in her case were not, on the whole, satisfactory. She suffered from sleeplessness, & both by day & night she was restless, loquacious, excited, & miserable. In sufficient doses Euphronal seldom failed to give her sleep; but it was sometimes followed on the next day by disagreeable drowsiness, confusion, & increased irritable excitement; & though, when pushed, it ultimately quelled her excitement, it produced at the same time a stupifying or bewildering effect accompanied by a feeling of great fatigue, & no permanent improvement followed its use.

Idiocy or Imbecility & Secondary Hysteria.

Three cases of Idiocy or Imbecility & two of Secondary hysteria (all females) were treated for sleeplessness or attacks of excitement. In all the hypnotic & sedative effect was satisfactory.

Organic Hysteria.

One man was treated. He suffered from heart disease, with softening of the brain, hemiplegia, & occasional epileptic seizures. In his case 30 grains acted as a powerful & harmless hypnotic.

General

General Paralysis of the Insane.

One man & one woman were treated. In the case of the woman the results were mild & somewhat negative; but the drug was not given a sufficient trial. In the man's case, one of obstinate sleeplessness & continued restlessness, the hypnotic & sedative effect was most pronounced, quietude & sound sleep of prolonged duration being produced by single & repeated doses.

E. General Conclusions.

Based on one's conclusions on the foregoing statement of results, the advantages & disadvantages of Sulphonal may be briefly summed up as follows.

In properly regulated doses, it is an efficient & safe hypnotic, & compared with other hypnotics, its action is fairly certain & constant. Although it is bulky & very insoluble, it has no smell & is almost free from taste & can be readily given either in the form of powder or dissolved or mixed in food. The sleep produced by it is natural & tranquil & undisturbed by dreams. It has no injurious effect on the circulation, respiration, appetite, digestion, or temperature, or on the general health. After a time it may be discontinued, or the dose reduced, while the improvement in sleep continues.

It has a distinct sedative action in mental excitement or distress & may be employed with great benefit in cases of insanity, especially in such as are of a recent or acute character.

Its chief disadvantages are the slowness of its action & the tendency of the action to be prolonged

longed into the succeeding day & to be followed by drowsiness, confusion, giddiness, or fatigue; & the sensorial cerebral & motor symptoms which are apt to follow the use of repeated doses.

While the writer is unable to claim for Sulfonal that it is a perfect hypnotic, he is convinced that it is a very valuable one; & while he cannot extol without reserve its undoubted sedative properties, he feels satisfied that in this respect Sulfonal is a most useful addition to the medicine-chest.

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14 September 1891.