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FURTHER EXPERIENCES WITH PHENO-
BARBITAL (LUMINAL)
IN EPILEPSY *

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At the session of the American Medical Association in 1920, I had the privilege of making a summary report on personal experiences with phenobarbital (luminal) in the treatment of epilepsy¹ which was based on the observation of about 100 cases. The majority of them had been under treatment for periods varying from several months to two years, while only a small number had been under uninterrupted treatment since 1914.

This paper is based on a total of 200 cases of epilepsy under my care, exclusive of the patients sent only for consultation and of those who did not return after one or two visits.

My first patients were principally the mild type of ambulatory epileptic, who naturally brought to the office similar material. Following the publication of my paper, however, I was visited by persons with some of the most intractable cases—patients who had received various remedies with little or no benefit, and others who had already been given phenobarbital with indifferent or no results. This might explain the differences in results as compared with the first patients treated with phenobarbital.

The uncertain manner in which different patients reacted to the same remedy must have also puzzled some of my colleagues, from whose correspondence I

*Read before the Section on Nervous and Mental Diseases at the Seventy-Third Annual Session of the American Medical Association, St. Louis, May, 1922.

1. Grinker, Julius: Experiences with Luminal in Epilepsy, J. A. M. A. 75: 588 (Aug. 28) 1920.

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learned that they were gravely disturbed by the possibility that the American-made product might not be identical with that manufactured in Europe. In order to gain some certainty on this point, I ran two series of ten cases each, one group receiving the domestic article, while the other was given imported phenobarbital. From a careful comparison of results I concluded that there were no essential differences between the two products, that if there were any differences, they were those of patient and disease, not of drugs.

In order to facilitate description, I shall record my experiences under the subheadings of (1) grand mal, (2) petit mal, (3) mixed types, (4) psychic epilepsy, (5) epilepsy in the insane, and (6) epilepsy in the feeble-minded.

GRAND MAL EPILEPSY

There being very few cases of grand mal without an admixture of some petit mal attacks, I class under this caption the cases in which the attacks are principally of the major type, though occasional minor seizures are also recorded. There were under my observation sixty cases—forty for a period of three years, ten during a period of five years, and ten from a few months to seven years. Eight of the patients belonging in this group had no attacks in four years, and twenty none in two years, while the rest enjoyed immunity from seizures during periods varying from a few months to nearly two years. Three of my patients were uninfluenced by treatment; even maximum doses failed to produce the slightest effect on the attacks.

The average dose was 2 grains (0.13 gm.) of phenobarbital daily, given at night before retiring in nocturnal epilepsy, and during the day in the diurnal form. The benefits obtained from average doses of phenobarbital within a few days from the beginning of treatment were such that for some time at least I gave myself up to the belief that failure to obtain results in a given case of epilepsy meant that the dose of phenobarbital was inadequate. Like others, I soon discovered that even in this, the most responsive group to the phenobarbital treatment, there are individuals who are refractory to the largest doses of phenobarbital; fortunately, these are exceptions. In a general way the statement still holds good that the convulsive variety of epilepsy almost always yields to

phenobarbital in correct dosage, and that it is mostly the wrong dose which is responsible for unsatisfactory results and toxic symptoms.

PETIT MAL EPILEPSY

In this group I put the patients suffering principally from minor attacks, with almost complete freedom from the major ones. Minor seizures may last from a few seconds to a minute, and are accompanied by vasomotor phenomena, such as a change in color, especially blanching of the lips at the oral angle, momentary losses of consciousness, or the development of slight motor phenomena short of convulsions.

For the purposes of this report I may divide the entire group into two subgroups: (a) petit mal cases in which attacks occur at short or long intervals as isolated seizures, with perhaps an occasional major attack, and (b) cases in which the seizures occur quite frequently—from twenty to a hundred daily, with only occasional major attacks.

(a) There were seventy cases belonging to this subgroup, that is, they were patients who suffered from petit mal seizures and had a history of but few major attacks. In ten cases there was complete disappearance of both petit and grand mal attacks during a period of from one to two years, while in sixty there was marked diminution as to frequency; instead of one or two daily there were perhaps two monthly spells.

The cases were treated by the fractional method of administering phenobarbital, namely, in divided doses of from $\frac{1}{2}$ grain to $1\frac{1}{2}$ grains (0.03 to 0.1 gm.) of phenobarbital three times daily. Improvement in this class of patients was marked. All spoke of eventual cures, and none desired to return to older methods of treatment.

(b) In patients affected with numerous petit mal attacks daily, each lasting perhaps a second, phenobarbital was not nearly so effective as in those of subgroup a; nevertheless, the drug exerted a beneficial effect in that the number of seizures was considerably reduced. Of the thirty-five cases coming under my observation, I was unable by the administration of moderate-sized doses of phenobarbital to modify the course in eight, while very large doses became pro-

hibitive on account of the production of drowsiness and apathy. We were evidently confronted with the worst form of epilepsy, and the failures were less surprising than the successes.

The average dose of phenobarbital administered to these patients was $1\frac{1}{2}$ grains (0.1 gm.) three times daily, but I usually begin with three-fourths grain (0.05 gm.) and then increase to 1 grain (0.065 gm.), $1\frac{1}{4}$ grain (0.08 gm.), $1\frac{1}{2}$ grains (0.1 gm.), 2 grains (0.13 gm.), $2\frac{1}{4}$ grains (0.15 gm.) and then to a maximum dose of $2\frac{1}{2}$ grains (0.16 gm.) of phenobarbital, three times daily. Each of the doses mentioned is tried for only three days in order to discover its efficacy for a particular case. The rule is to give as little as possible, but sufficient to make an impression on the number of attacks. In some cases that are slow to respond to medium-sized doses, occasionally results are obtained by overpowering the system with large doses, thus breaking the epileptic habit, and then gradually returning to average doses.

MIXED TYPES

As the majority of patients with epilepsy suffer from both grand mal and petit mal attacks, all of the cases may be considered mixed. But, having already divided epileptics into the predominantly grand mal and the predominantly petit mal cases, I speak of those patients as belonging to the mixed types in whom the two kinds of attacks occur in about equal proportions. Of this group I treated thirty-five cases during periods varying from a few months to several years. There was improvement in all of them. In ten of the cases there had been no attacks of either variety during periods of from several months to one year; then perhaps one or two attacks would occur with another interval between, lasting weeks or months. In the remaining twenty-five cases of this group, major attacks did not return, while minor seizures were reduced to occasional ones—possibly once or twice monthly. In two cases only the major attacks were favorably influenced, having become less frequent, while minor attacks continued as before.

The usual dose of phenobarbital administered in these cases was from 2 to 3 grains (0.13 to 0.195 gm.) daily, divided into two or three doses.

PSYCHIC EPILEPSY

Four cases of psychic epilepsy came under my observation, all responding favorably to treatment with phenobarbital. One patient with postparoxysmal excitement and homicidal tendencies following the major attacks ceased to develop furors since the remedy caused the disappearance of the convulsions. Another patient, the victim of epileptic somnambulism occurring monthly or bimonthly, has been free from sleep walking during an entire year while under treatment with 2 grain (0.13 gm.) doses of phenobarbital nightly. Similarly, a case of postparoxysmal ambulatory automatism lasting sometimes hours after an attack reacted favorably to treatment with phenobarbital. The fourth case was one of postparoxysmal delirium with destructive tendencies. There were no outbreaks of furor during eight months while under treatment with phenobarbital.

EPILEPSY IN THE INSANE

My personal experience with epilepsy in the insane was limited to one patient who presented symptoms of dementia praecox with advanced mental deterioration. After a short course of phenobarbital the seizures became few, but the psychotic manifestations were as numerous as before treatment.

On account of the dearth of cases in my own practice, I may be pardoned for briefly referring to the work of others:

Foley² relates his clinical experiences with phenobarbital in the insane and arrives at the following conclusions:

Notwithstanding the reduction in the number of convulsions, the severity of each convulsive attack of those having convulsions was greatly increased; there was a marked increase of irritability and in some this increased to deep furor. Attacks were so severe in some that removal to the hydrotherapeutic department became necessary. A few developed status with fatal results. The attendants in charge experienced greater difficulty in controlling the patients while under the luminal treatment than under the bromide medication. Injuries were more numerous, and at the end of the three months' period the luminal treatment was discontinued.

2. Foley, E. A.: Institution Quarterly, Springfield, Ill., June 30, 1921.

From our observation of these two groups we have decided that so far as luminal in the treatment of the epileptic with psychosis is concerned, it is of no special benefit. We are getting better results with the old-time bromide mixture and careful regulation in diet. Our patients are quieter and injuries are less than during the months when they were under the luminal treatment.

Sands,³ an equally reliable observer, and one working with similar material, had more favorable results: He studied eighty-six cases of epilepsy, covering a period of eight months and limited to female psychotic epileptic patients. He employed the dose of three-fourths grain (0.05 gm.) three times daily, and speaks of striking results. There was a decided decrease in the number of seizures (from 502 recorded seizures in May, 1919, to only eight seizures in May, 1920), and the convulsions were milder and of shorter duration. There was a definite decrease and change in the unpleasant after-effects of the seizures. He was enabled to parole patients whom he otherwise would not have considered fit to leave the institution. Patients became quieter, and the general morale of the ward showed a decided improvement. There was a decided decrease in the number of injuries received during seizures, and in the number of altercations with other patients. Fewer demands were made on the overworked staff. The after-effects of the drug have been practically nil.

Kirk,⁴ of the Arkansas Hospital for Nervous Diseases, with a clinical material of more than 200 cases of epilepsy, speaks thus of his experiences with phenobarbital:

On December 8, 1919, the most severe cases were selected for treatment. The results were so remarkable that all cases of idiopathic epilepsy were given treatment. The method consisted of 1½ grains of luminal at bedtime. There were sixty-one patients who had no convulsions since treatment was begun. One hundred and six patients had less than five convulsions while under treatment; forty-five had more than five. There was immediate decrease in the severity of the seizures, many of them changing from grand mal to petit mal; decrease in the severity of furor and a shortening of

3. Sands, I. J.: Luminal Therapy in the Control of Epileptic Seizures, *Arch. Neurol. & Psychiat.* 5:305 (March) 1921.

4. Kirk, C. C.: Analysis of More Than Two Hundred Cases of Epilepsy Treated with Luminal, *J. Arkansas M. Soc.* 17:128 (Nov.) 1920.

the time of confused states; a general improvement of the moral tone of the wards, and a complete cessation of seizures in a large number of cases. No deleterious effects were observed on kidneys or stomach; circulation, temperature and respiration were uninfluenced. It is not a habit-forming drug and is not attended by any pleasurable or disagreeable sensation. In certain cases the drug is effective in twenty-four to forty-eight hours; in others not until a week or more has passed.

EPILEPSY IN THE FEEBLEMINDED

There were eleven patients belonging to the feeble-minded group, in all of whom except one there was noted decided mental improvement after lessening or cessation of convulsions. This exception was the case of an idiotic boy, aged 3 years, suffering from numerous petit mal seizures daily. At first the attacks became considerably reduced in number, but drowsiness and a state of bewilderment regularly followed the taking of moderate doses of phenobarbital; later even large doses failed to reduce the number of attacks. This was an extremely unfavorable case for treatment, bromid having failed before phenobarbital. Contrary to the experiences of some observers of the frankly insane, the feeble-minded epileptic seemed to receive a new impetus to higher mental growth. As is well known, numerous epileptic seizures favor mental deterioration even in otherwise normal persons. As soon as the cause, the epileptic attacks, had been removed, greater possibilities were created for stimulating what little mentality there was in these mentally underdeveloped patients.

Thus, an epileptic girl, aged 3 years, the subject of numerous petit mal seizures, before the administration of phenobarbital paid not the slightest attention to her environment and failed to express joy in the satisfaction of her wants. Her eyes did not follow the light, and noise left her unmoved; she did not appear to recognize persons, even her mother. Never having learned to walk or move about, she was practically a breathing automaton. After the exhibition of phenobarbital for a period of six months, during all of which time there was no recurrence of seizures, the patient began to recognize her mother; followed the light, and manifested considerable excitement at the jingling of keys; in addition, she learned to crawl and to stand up

against a chair. Though the patient is still an idiot and will probably always remain one, this glimmer of intelligence makes her less of a charge than before treatment.

Another case worth special mention is that of an imbecile woman, aged 35. She suffered from mixed epileptic seizures all her life, and finally had deteriorated physically and mentally, so that she rarely left her bed and never her room. Before treatment she enjoyed the pleasures of a 3 year old child. After a short course of treatment with phenobarbital in $1\frac{1}{2}$ grain (0.1 gm.) doses night and morning, she regularly joined her family at meals, engaged in general conversation, and cleared up to a degree never anticipated by her people.

BY-EFFECTS OF PHENOBARBITAL (TOXIC SYMPTOMS)

During the administration of phenobarbital, whether given to produce sleep or as an antiepileptic remedy, certain unpleasant after-effects have been observed. These followed mostly the administration of large doses, though in a few instances average doses had the same effect. Chief of these were: (a) certain forms of dermatitis resembling the exanthem of measles and scarlet fever, appearing either early or late in the course of treatment with phenobarbital; (b) states of apathy; drowsiness and sluggish mentality, bordering on idiocy; ataxia, and slow speech—conditions often observed after large doses of bromid in the days before phenobarbital—especially after large doses of phenobarbital; (c) conditions of asthenia, or extreme muscular weakness, characterized by an inability to dress or attend to nature's calls; (d) extreme irritability and an irascible temper, leading sometimes to violent acts, and (e) states of intoxication allied to that of alcohol and often mistaken for it.

(a) In my series of 200 cases I found six patients with hypersensitive skins who developed rashes resembling measles: two of this number regularly when the dose of phenobarbital exceeded 3 grains (0.195 gm.) daily; of the others two became somewhat feverish with the rash; the remainder could not take the smallest dose of phenobarbital without suffering

from an itching eruption. After the administration of liquor potassii arsenitis (Fowler's solution) in 5 drop (0.3 c.c.) doses three times daily, three of the patients could continue with moderate doses of phenobarbital so as partially to control the epileptic seizures.

(b) As an example of apathy may be cited the case of a man, aged 25, who had suffered during a period of ten years from numerous petit mal attacks, with occasional grand mal attacks. Small doses of phenobarbital failed to effect a decrease in the frequency of seizures; it became, therefore, necessary to push the dose to 3 grains (0.195 gm.) three times daily. The effect was a subsidence of attacks; but the patient talked and acted like a dribbling idiot, became ataxic in gait, and his speech was unintelligible. With these after-effects following the larger doses, it became necessary to reduce the dose of phenobarbital, but the effect on the attacks remained minimal.

(c) The patient with asthenia was a boy, aged 17, who had suffered from attacks of petit mal to the number of from twenty-five to fifty daily; bromids exerted little or no effect. The patient was referred to me for the exhibition of phenobarbital in effective doses, the usual dose having been tried by the family physician without the slightest benefit. After doses of 8 grains (0.5 gm.) daily, the patient became practically a vegetating automaton; he became weak and could not move about; the weakness was more muscular than mental. Smaller doses are now being given by the family physician, who reports that the attacks are not quite as frequent, but the patient manages to get about and is otherwise fairly comfortable.

(d) After taking phenobarbital, several of the patients changed from a state of more or less constant depression before taking the remedy to one of exaltation, irritability, quarrelsomeness and general fault finding. Not having previously noticed this phenomenon in my patients, I attempted to explain to myself the irritable attacks as epileptic equivalents. Soon, however, I discovered similar phenomena in others, and I concluded that they were the result of treatment with phenobarbital. In most of the cases these manifestations were lessened in frequency when the dose was slightly reduced, or disappeared after the same dose was continued. One patient not only displayed an

irascible temper, but also became violent and assaulted his family. In that case I was obliged to give very small doses of phenobarbital, combined with moderate doses of bromids, and thus I lost the beneficial effects on the epileptic seizures, while gaining peace for the family.

(e) An example of phenobarbital producing a state of intoxication like that of alcohol is the case of a man, aged 54, who was a sufferer from numerous attacks of minor epilepsy which had a tendency to throw him to the floor suddenly. Average doses of $1\frac{1}{2}$ or 2 grains (0.1 or 0.13 gm.) of phenobarbital did not have the desired effect on his attacks; the larger doses, up to 4 and 5 grains (0.26 and 0.32 gm.) daily, had a marked beneficial effect on the seizures, but the patient after taking the medicine acted and felt as though under the influence of alcohol. So much did this state resemble ordinary drunkenness that his friends and neighbors repeatedly accused him of drinking "moonshine." During these phenobarbital "sprees" his speech became thick and indistinct, he slurred his words and syllables, and he developed a reeling gait. Mentally he was alert, and conversed on topics of the day, but was rather euphoric and always in an exalted mood. It became necessary to reduce the dose and allow the patient to have occasional attacks.

Almost from the day that the drug had become known as a hypnotic, the continental journals contained references as to the toxicity of phenobarbital. The doses administered were naturally larger than those given in epilepsy, and toxic effects were observed often. Thus, Emanuel⁵ reported on the exanthems of phenobarbital in 1912, and Patschke⁶ in the same year reported a case of phenobarbital intoxication in which the patient became loquacious, excited, exalted, manifested a flippant behavior and altogether acted like an alcoholic. Another of his patients, after 5 grain (0.324 gm.) doses of phenobarbital regularly, had the feeling as though she had imbibed a glass of whisky. A praecox patient, after receiving the equivalent of 6 grains (0.4 gm.) of phenobarbital for sleeplessness, became excited, got out of bed, threw about his clothes, and behaved as a drunken man. The same author observed

5. Emanuel, Gustav: *Neurol. Centralbl.* **31**: 563, 1912.
6. Patschke, F.: *Neurol. Centralbl.* **31**: 899, 1912.

a measles-like rash in four cases, which disappeared in from six to eight days after the administration of the remedy had ceased. He also observed vertigo of an alarming type in one case.

Deist,⁷ von Klebelsberg⁸ and Fuchs,⁹ in 1914, all warned against the indiscriminate use of phenobarbital because of the toxic effects produced by large doses. Ungar,¹⁰ in 1914, reported a most interesting case of phenobarbital poisoning after the administration of 45 grains (2.9 gm.). In that case there was complete loss of consciousness, areflexia, Cheyne-Stokes' respiration, absent pulse, limp paralysis of the extremities, blindness, contracted pupils with sluggish light reaction, vertigo, vomiting, rash, paralysis of the bladder and rectum, aphasia and convulsions. The patient recovered in twenty-five days. In 1914, Christinger,¹¹ as did Foley, in 1921, stated that in her opinion the suppression of the motor manifestations in insane epileptics has an unfavorable effect on the psychic outbreaks of the patients. Many are worse, and attacks occur more frequently. Curschmann¹² and Strauss¹³ each reported on several cases of phenobarbital exanthems, which they describe as resembling measles more than scarlatina. There was desquamation in one of Strauss' cases; of the other cases, two were of cardiac or renal type, and in his remaining two cases there was an elevation of temperature. Phillips¹⁴ reported a case of his own under the title of phenobarbital poisoning, and cited some of the newer literature on phenobarbital poisoning to which the reader is referred. In his case the course was similar to that of measles, with high temperature, sore throat, severe gastro-intestinal disturbances, rash, desquamation, etc., but there was also nephritis. This author in his conclusions states that the drug should be administered with great care—a statement which everybody will accept; also that patients should report to their physician on the first appear-

7. Deist, H.: *Sommer's Klinik f. Psych. u. Nervenkrankh.* **8**: 1, 1913.
8. Von Klebelsberg, Ernst: *Psych. neurol. Wchnschr.*, 1912, p. 415; *Neurol. Centralbl.* **32**: 193, 1913.
9. Fuchs: *Neurol. Centralbl.* **33**: 128, 1914.
10. Ungar: *Wien. klin. Wchnschr.* **27**: 847, 1914; *Neurol. Centralbl.* **34**: 68, 1915.
11. Christinger, Minna: *Neurol. Centralbl.* **33**: 760, 1914.
12. Curschmann: *Therap. Halbmonatsh.* **31**: 148, 1917.
13. Strauss: *Therap. Halbmonatsh.* **31**: 338, 1917.
14. Phillips, John: *Phenobarbital (Luminal) Poisoning*, J. A. M. A. **78**: 1199 (April 22) 1922.

ance of a skin rash or of any untoward symptom, and should immediately stop taking the drug. However, experience prompts me to take exception both to premise and conclusion of the following paragraph:

Since there is little difference between the therapeutic and fatal dose, phenobarbital should not be prescribed in single doses of more than $1\frac{1}{2}$ grains (0.1 gm.), and not more than 3 grains (0.2 gm.) should be taken in twenty-four hours.

There is a vast difference between the therapeutic and the fatal dose. In treating the insane it has often been necessary to give for short periods of time 3 to 5 grain (0.195 to 0.324 gm.) doses of phenobarbital daily, either to subdue maniacal attacks or to produce sleep—and I have encountered no ill effects from its use. In the treatment of epilepsy I have occasionally given 3 and $3\frac{1}{2}$ grains (0.195 and 0.23 gm.) of phenobarbital three times daily without the slightest ill effects, toxic symptoms or fatalities. As for the same author's admonition to examine the urine of patients taking phenobarbital once or twice weekly, I regard this as a luxury, not a necessity. My ambulatory patients are seen only once a month, and urinary examinations are made occasionally. Thus far I have not seen a case of nephritis following the administration of phenobarbital.

SUMMARY

The best results from phenobarbital were obtained in cases of grand mal, and in petit mal when there was a motor element in the attacks. Less benefit was observed in the cases characterized by isolated petit mal attacks, and least of all in those with numerous petit mal attacks. When the sensory and psychic components predominated in the seizures, reduction of attacks was the rule, while complete cessation for long periods was the exception. The feeble-minded epileptic was greatly benefited by treatment with phenobarbital, provided the drug caused a cessation of convulsions. Psychic epilepsy is favorably influenced by phenobarbital if the psychic outbreak is the consequence of complete or incomplete convulsions. The efficacy of phenobarbital in the epileptic insane has not been proved, as of the four equally competent authorities, two are extremely optimistic, while the other two have assumed a forbidding attitude toward phenobarbital.

Perhaps further proof will be forthcoming from our large colonies for epileptics to decide this question for us.

Regarding the so-called toxic effects from phenobarbital, the number occurring in my series was small compared with the total number (200) under observation, namely, a dozen cases, and these were rather mild compared with those reported in the literature. There were no fatalities from phenobarbital in my practice, and I believe that the danger, though a real one, has been greatly exaggerated.

The bromids have been entirely displaced by phenobarbital in my management of epilepsy, although the former drug still finds a place when phenobarbital is not well tolerated.

In a general way I have adhered to the dietary rule of not permitting red meats, but I do not insist on a restricted or salt-free diet, as I formerly did when using bromids.

The doses of phenobarbital varied from $1\frac{1}{2}$ grains (0.1 gm.) daily to from 9 to 10 grains (0.6 to 0.65 gm.) daily. The last doses were administered in few cases and then only for short periods of time, while in the majority of cases from 2 to 3 grains (0.13 to 0.195 gm.) of phenobarbital constituted the average daily dose.

I can report no cures. Knowing that phenobarbital is only a symptomatic remedy, I am loath to withdraw it altogether even from patients who have remained free from attacks for from five to seven years.

Parentetically, I may state that my confidence in the efficacy of phenobarbital as an antiepileptic remedy has caused me to utilize it as a therapeutic test in two of my cases. One was a case of true somnambulism occurring monthly or bimonthly, without a history of epileptiform attacks. Phenobarbital in 2 grain (0.13 gm.) nightly doses at once caused the cessation of sleep walking, which has not recurred during the entire period of its administration (one year). Another case in which phenobarbital acted in the double rôle of therapeutics and diagnosis is the following: A school-girl, aged 13, developed peculiar motor spasms during which there was tetanoid contraction of the upper and lower extremities. Soon after the administration of average doses of phenobarbital there were no more

attacks, and the patient believed herself cured. Then followed another attack, phenobarbital was resumed, and there have been no attacks since (fourteen months).

COMMENT

It will be observed that the best results from phenobarbital were obtained in those forms of epilepsy which are accompanied by convulsions, namely, the grand mal variety, while less brilliant results were seen in the so-called petit mal attacks and in the psychotic outbreaks. I believe that the explanation will be found in an analysis of the epileptic attack itself. Each convulsion, either major or minor, reveals two components in different proportions: (*a*) the motor element, and (*b*) the sensory element in a broad sense, which includes the psychic. The efficacy of phenobarbital—an anticonvulsive remedy—increases in proportion to the predominance or not of the motor element in a given attack; hence the splendid effects in grand mal and in those cases of petit mal with motor manifestations. And for the same reason phenobarbital is less effective in the sensory losses or so-called “absences” of petit mal epilepsy. In other words, the greater the motor upset, the more effective is the remedy, while sensory and psychic upheavals are benefited only secondarily. With this in mind we can also understand why the mentality of epileptics taking phenobarbital is improved. It appears that mental deterioration in the epileptic largely depends on the disturbances of the cerebral circulation by repeated attacks acting mechanically or through the vasomotor mechanism. The prevention of frequent mechanical insults is an indirect means of mental improvement; and epileptic dementia, in many cases really bromid depression, rapidly disappears under phenobarbital medication. The effect may even be greater than anticipated, for many patients, especially early in the treatment, appear somewhat exalted. Epileptic dementia consists for the most part of apathy, lack of concentration and general mental inertia with memory losses. After inhibiting attacks, the patient becomes more animated in his conversation and more active physically, the characteristic facies and gait of the epileptic disappear, and he again appears as a normal individual.

Whether the explanation given is correct or there is some other, the fact remains that the patient's mentality is often improved after the successful administration of phenobarbital, as was shown not only in the normal epileptics, but also in the defectives under my observation.

CONCLUSIONS

1. Phenobarbital is the most effective symptomatic remedy in the management of epilepsy.
2. The best results are obtained in the convulsive types of the disease—both grand mal and petit mal, with effects that are almost specific. The sensory and psychic forms of epilepsy are greatly benefited, if not by cessation then by reduction of seizures.
3. There has been no mental deterioration from the administration of phenobarbital; on the contrary, patients have become more alert and keen, have lost their unnatural reticence and the fatuous, acne-marked facial expression previously the sign of an epileptic.
4. Phenobarbital, when taken over many years, neither causes damage to the viscera nor results in habit formation.
5. Large doses are mainly responsible for the so-called toxic and by-effects.
6. The art of administering phenobarbital consists in finding a dose suitable to each case without the production of unpleasant by-effects. One should begin with average doses of from $1\frac{1}{2}$ to 2 grains (0.1 to 0.13 gm.) of phenobarbital daily, and “feel” his way up or down the scale until results are obtained. Large doses should not be resorted to unless the smaller ones prove ineffective; and even then there should be a gradual return to smaller doses.
7. An indiscriminate use of phenobarbital is fraught with danger and is certain to bring discredit on the most valuable antiepileptic remedy in our therapeutic armamentarium.

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