EXPERIENCES WITH LUMINAL IN EPILEPSY

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Luminal is comparatively unknown in the treatment of epilepsy. Introduced in this country shortly before the war, its importation was stopped before the medical profession became thoroughly acquainted with its properties. Thus it happened that the claims made for it by German writers in the medical journals of 1912 and 1913 have not been verified until quite recently.

My attention was directed to the value of luminal in epilepsy by the casual reading of an article by A. Hauptmann, published in 1912 in the *Münchener medizinische Wochenschrift*, and confirmed by others, whose bibliography is herewith appended.

Hauptmann selected for his tests cases of epilepsy which had been previously under supervision for several years, or in which an exact history was obtainable. Most of these had received large doses of bromids for long periods. In reviewing his experience he says:

Luminal tends to exert a favorable influence on epilepsy by reducing the number and severity of the attacks. Its field of applicability will be chiefly in those very severe cases of epilepsy which can no longer be controlled by the largest doses of bromids. In cases of medium intensity the attacks failed to occur under doses of 0.15 to 0.2 gm. (2 to 3 grains) daily, while in the more intense 0.3 gm. (5 grains) need not be exceeded. No injurious by-effects of any kind have been observed after months of daily administration, and especially no cumulative action has developed. Therefore, luminal can advantageously replace the bromids even in the milder cases where these appear contraindicated on account of by-effects.
My clinical experience with luminal began toward the end of 1913 in the case of a clergyman’s son, whose history is as follows:

Case 1.—A boy, 13 years old, was first seen, June 4, 1913. The family history is negative: Father, a well-balanced clergyman, mother, brothers and sisters are well and there is no epilepsy in the collateral branches of that family. Born in normal labor, patient developed as other children, with diseases usual in childhood, but no serious illnesses. Teething was unaccompanied by convulsions; but there were peculiar spells described by the mother as so-called “inward” convulsion, and certain attacks which were undoubtedly those of “minor” epilepsy. About thirteen months before coming under my observation a severe nocturnal convulsion occurred—the first major attack—and one month before my examination a similar attack occurred. Meanwhile the minor attacks have become quite frequent—five to six daily. In these the patient never falls, but remains standing and appears dazed for a few seconds only. Any slight indisposition such as a cold or indigestion, seems to cause an increase in the number of spells. The examination revealed no sign or symptom of organic disease.

An acne-like eruption covered the patient’s face, due largely to the bromids administered for the attacks. My treatment at first consisted in giving the well-known Bechterew mixture—sodium bromid, 15 grains; Fowler’s solution, 4 drops, in an infusion of adonis vernalis, three times daily. Though there was improvement, the severe and the light attacks did not entirely disappear, and I decided to try luminal in daily doses of 1½ grains. The effect was marvelous and almost instantaneous. No more attacks were reported and the acne rapidly disappeared. The boy progressed in his school studies. There were no attacks of any kind during the following two years. However, after some indiscretion in diet two slight attacks were noted, but none after that.

Shortly after observing the effects of luminal in this case, I cautiously administered the drug in other cases, with similar results.

In the discussion following Dercum’s paper on Epilepsy with Special Reference to Treatment, read before the Section on Nervous and Mental Diseases of the American Medical Association in 1916, I was the first in this country to express an opinion on the use of luminal in epilepsy. Dr. Ball, who participated in the same discussion, also emphasized the value of

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1 Dercum, F. X.: Epilepsy with Special Reference to Treatment, J. A. M. A. 67: 247 (July 22) 1916
luminal in the treatment of the epileptic attack. At that time my experiences was limited to few cases, but since then I had the opportunity of studying over 100 cases of "essential" epilepsy, which constitute the basis for this report.

In order to avoid misunderstandings as to what may be expected from the use of luminal, we must be reminded that in spite of the numerous attempts at a rational, or causal, therapy of epilepsy, most of the methods hitherto proposed have proved fallacious, as has been so well shown by Russell G. MacRoberts. Our therapy is still limited to the prevention of the convulsion or, failing in this, we endeavor to render the attacks less frequent and less severe. The convulsion being only a symptom, though the most conspicuous one, we are far from deluding ourselves into a belief that in causing the arrest of convulsions we have succeeded in curing the disease. But the convulsion, or its equivalent, being nevertheless the one symptom which stigmatizes the individual suffering from it as an epileptic, it is necessary to concentrate our efforts in the direction of ameliorating the epileptic's lot. Though we cannot cure his disease, we endeavor to influence the attacks which make his life so burdensome.

It would be wasting time were one to enumerate all the drugs which have been recommended for the treatment of epilepsy. It will suffice to state that the bromids have held undisputed sway since their introduction by Laycock in 1857. After a short trial with chloral, borax, nitroglycerin, belladonna, adonis vernalis, and the opium-bromid treatment, the medical profession has accepted bromids as the anticonvulsive remedy of undisputed merit.

Let us briefly examine some of the effects, pleasant or unpleasant, which bromids exercise on the human economy.

In medium-sized doses, bromids reduce the number of attacks, but they also act as motor depressants and lessen the activity of the intellectual centers. In moderately large doses there is produced apathy, listlessness, lack of interest in one's surroundings, and a peculiar dull expression. After the long-continued administration of the remedy in large doses there occasionally develops a state resembling dementia.
The circulation is often affected by lowering of the blood pressure, cold hands and feet, anemia, and an irritable heart. In toxic doses, arrest of the heart’s action in diastole may occur.

The gastro-intestinal functions may become affected by the drug, causing a diminution of the normal secretions of stomach and intestine, thus producing indigestion and constipation.

In those taking bromids in large doses and for a considerable period of time we may note depression, loss of mental and physical strength, forgetfulness, slow speech and retardation of the thought processes. The skin often shows the well-known acne-rash, and even pustules in some cases.

The late Dr. Spratling, certainly an authority on epilepsy, makes the following statement in his well-known book:

Bromids should be given as a last resort. Cures by the bromid treatment are not to be expected. I know of no drugs, save those which produce habits, such as opium and cocaine, that are so universally abused as bromids. The effects of these drugs on the heart, respiration, gastro-intestinal canal, skin and nutrition, are five points against their use in epilepsy compared to one in their favor, namely, their power of lessening overexcitability of nervous tissue.

While one may not accept in its entirety this author’s disparaging remarks on the effects of bromids, it is nevertheless a fact that bromids act unfavorably on many individuals, thus becoming contraindicated in the treatment of epilepsy. Besides, most authors agree that bromids exercise but little influence on the petit mal attacks, and that they are practically useless in the psychic forms of the disease and in the so-called psychic equivalents.

Gowers, an ardent advocate of the bromid treatment, regrets that the amount of bromids administered to epileptics at the National Hospital for Paralyzed and Epileptics had to be steadily increased, and that for thirty years the physicians have been constantly endeavoring to discover an efficient substitute for it without success.

There is no doubt of the fact that those having much experience with epilepsy have become disappointed with the bromid treatment and, while still prescribing bromids, are constantly searching for efficient substitutes.
In my opinion a good substitute has been found in luminal, a drug first prepared in 1911 and given to the medical profession in 1912.

Physical Properties of Luminal.—Luminal, whose chemical name is phenobarbital or phenyl-ethyl-barbituric acid, occurs in tablets of 1½ grains and in the form of a white, odorless and slightly bitter powder. It is almost insoluble in cold water, slightly soluble in hot water, soluble in alcohol, ether and chloroform, and in alkaline solution.

There is also a soluble preparation of luminal, luminal sodium, which is phenobarbital sodium. This preparation is principally used for hypodermic injection in the form of a 20 per cent. solution, prepared by dissolving the salt in boiled and cooled distilled water. The dose of luminal sodium is 10 per cent. greater than that of luminal.

Actions and Uses.—The drug was first recommended as a hypnotic and substitute for barbital (veronal), whose formula differs from the latter in the fact that one phenyl group displaces one ethyl group, and it is claimed that this change increases the hypnotic power of luminal (phenobarbital) over that of barbital. The dose of luminal as a hypnotic is from 3 to 5 grains, increased if necessary to 12 grains.

Method of Administration of Luminal in Epilepsy.—I usually prescribe luminal in doses of 1½ grains, either in tablet or capsule, to be given at night before retiring. The patient is instructed to report within a few days. If the dose administered suffices to reduce the attacks or cause them to subside, it is given regularly in the same manner. If this dose is found to be insufficient to cause a cessation of attacks, it must be increased to 2 grains, given at night. Should this dose also prove too small, then another daily dose of luminal is added to the preceding one. In that event my rule is to prescribe a small dose, say 1 grain, to be given in the morning, while the larger dose is administered before retiring. Only rarely have I been compelled to give three daily doses of luminal, but one need not hesitate when it becomes necessary to increase the dose in order to get results. For instance, in one case of severe epilepsy of many years, the patient suffered from six to twelve convulsions daily, and nothing less
than 3 grains three times daily caused any change in the patient's condition. After several days or weeks, it will usually be possible to return to the smaller doses, when the effects will be as favorable as with the initial larger doses. When drowsiness and apathy appear, it is always time to reduce the dose. My invariable rule is to give as little as is necessary to keep the patient free from attacks, and no more. In cases that have been treated with bromids continuously for long periods of time it is advisable to begin the luminal treatment with somewhat larger doses at first, to be reduced later. The treatment is continued for years systematically; any interruption is apt to be followed by a number of severe attacks—the same as with the bromid treatment.

The effect of the change from bromid to luminal is especially marked on the mentality of the patient—the manner of speech and general reaction to environmental conditions—who appears to become a different individual.

A point worthy of mention is the experience that even moderate doses of luminal seem to exert a favorable effect on the minor attacks, while the bromids are comparatively ineffective in these conditions.

Contraindications.—I know of no definite reasons why luminal should not replace the bromids in most cases of epilepsy requiring drug treatment.

Regarding skin eruptions, I can report that among my number of treated cases (100) I have only seen two patients with rashes that necessitated a discontinuance of the luminal treatment.

Urinary disturbances from luminal I have never seen, though continental writers speak of their occurrence and advise as a preventive measure to omit one day's treatment out of the seven.

On the whole, I believe that there are not contraindications to the administration of luminal in kidney or cardiovascular conditions.

To demonstrate more clearly the results of treatment with luminal on the attacks and general condition of epileptics, I have made the following abstracts from the records of several representative case histories.

Case 2.—Miss M.G., aged 23, with negative family and personal history, came under my observation, March 2, 1918. Though her health and development during infancy were of
the average kind, peculiar "crying" spells without apparent cause are reported by the mother, and also the circumstance that even slight illnesses were accompanied by physical upset and high temperatures. Menstruation was regular and painless.

At 18, while at college, the first "fainting spell" occurred; the second came one year later. Then followed several similar attacks in periods varying from six months to one year apart. The last attack, one month before consulting me, was attributed by the patient to "shock from dental work."

The first few attacks were accompanied by loss of consciousness, biting of tongue, frothing at mouth and the striking of head against objects encountered in falling. Duration of attack, five minutes; it is usually followed by severe headache and sometimes by sleep. The earlier attacks were more severe than any of the later ones, during the last of which she experienced premonitory warnings in the nature of a "receding" feeling, lasting long enough to enable her to lie down before the attack actually appeared. In addition to the attacks described, there are present smaller ones, consisting of peculiar sensations accompanied by dizziness and lasting only a second—evidently "petit mal" attacks.

I prescribed luminal in doses of 1½ grains, to be taken at night. The results were satisfactory. Though the patient has visited me monthly, there has been no record of a single attack since beginning the new treatment. This means that not only have convulsions disappeared, but also the minor attacks.

CASE 3.—I. C., aged 13, schoolgirl, with good family and personal history, was seen, May 6, 1918. Was born in normal labor and developed normally, but suffered from teething convulsions at the age of 1½ years. Six months after the last of these, attacks returned at monthly intervals, then at shorter intervals. The convulsion consists of a short tonic, followed by a longer clonic stage, with foaming at the mouth and the other phenomena of an epileptic attack. There were both diurnal and nocturnal attacks occurring about once in six months when patient was 8 years old. Somewhat later, and up to the time of her first visit to my office, an aura developed before each attack, consisting in a peculiar drowsy feeling. In addition, the serial form of epilepsy made its appearance—there occurred a number of diurnal convulsions following each other rapidly.

Luminal in 1½ grain doses, taken at night, caused a complete cessation of attacks since the first dose was administered.

CASE 4.—W. X., aged 24, with negative family and personal history, was first examined, Sept. 13, 1914. The beginning of his trouble was while a cadet at a military academy; then after a strenuous march he suffered from a so-called "fainting spell." Within a half year five similar attacks appeared in rapid succession. In all of these he became unconscious and
keeled over, but consciousness quickly returned. These were undoubtedly minor attacks of epilepsy. His first major attack occurred two years before consulting me; the second one about a year after the first. While the severe convulsions have been coming on an average once yearly, many minor attacks have been noticed in the interval.

The administration of luminal in the usual doses (1½ grains nightly) was followed by happy results: not one attack has appeared in two years, in spite of additional duties imposed on the patient by the necessities of the war. Only once or twice has patient suffered mild attacks while taking luminal—always, however, after disregarding essential hygienic rules.

CASE 5.—O. H., aged 45, came under observation, April 23, 1915. Epileptic attacks appeared since his eighteenth year, which were mild and infrequent at first, but became more frequent and intense later. In the last few years his nocturnal attacks occurred on an average once in six weeks; during these there was complete loss of consciousness, frothing at the mouth, and biting of the tongue, with occasional involuntaries. There is no mental impairment, but casual spells of ill temper are mentioned by his spouse. The case was seen by Erb and other European neurologists, who diagnosed "essential" epilepsy.

Owing to the presence of high blood pressure (170 systolic) I thought it best to try the combination of bromids and nitroglycerin. Though improvement was marked, attacks continued to come every few weeks. After the systematic administration of luminal in doses of 1¼ grains, mornings and evenings, there have been no attacks in two years and eight months.

CASE 6.—J. G., aged 5½ years, was examined, Jan. 27, 1912. First convulsion at 4 years; in the beginning attacks were rather infrequent, but became more frequent later and occurred up to five or six times in twenty-four hours. Though well-developed physically, the boy had always been backward in his school studies.

Bromids were administered in 15 to 20 grain doses three times daily, and long intervals of freedom from attacks were the result. But while still taking massive doses of bromids, the attacks recurred with greater frequency and severity.

January, 1920, I placed the patient on 2-grain doses of luminal daily. There have been no attacks since.

CASE 7.—Mrs. J. D., first seen, Feb. 20, 1916, is 54 years old, has been married thirty-five years, and gave birth to three healthy children. The first convulsion occurred only six months before consulting me; three months after the first came a series of convulsions. The examination in this case pointed clearly toward a vascular cause for the epileptiform attacks.
The administration of luminal in 1½ grain doses nightly failed to exert any appreciable effect on the attacks. The dose was consequently increased to 2 grains. There have been no attacks in two years.

CASE 8.—A Sister of Charity, 22 years old, was seen June 28, 1918. The first convulsion occurred when she was 4 years old. Following this there was a long period of freedom from attacks until puberty. Then "fainting spells" appeared, and a little later attacks of momentary "abstraction." The last kind of attack occurred very frequently. Still later, regular convulsive attacks came to dominate the scene; at first only once or twice yearly, but recently every seven to ten days.

Luminal in doses of 1½ grains, increased later to 2 grains, nightly, caused a disappearance of attacks during the past one and one-half years.

CASE 9.—C. R., aged 5 years, suffered from attacks of epilepsy for six months prior to April 7, 1912, when I saw him for the first time.

Treatment was begun with bromids, and the results were favorable, though there were still occasional attacks. Not until I began the administration of luminal did attacks cease entirely for a long period of time. After indiscretions in diet and after illness a convulsion is still recorded, but the average of freedom from one was lengthened from one a month to one yearly.

CASE 10.—H. B., a factory girl, aged 23, under observation since Aug. 27, 1918, had suffered from teething convulsions at 1½ years and subsequently was backward in school. Two and a half years before visiting me she had her first nocturnal epileptic convulsion. There also developed petit mal attacks, consisting of peculiar automatic movements of the fingers, blanching of the face, and momentary losses of consciousness.

After the administration of luminal there were no attacks during a period of three weeks. Patient considered herself cured and omitted taking the medicine for four days. Then a series of attacks occurred, worse than any she had had before.

This case seems to support the statement frequently made, that with cessation of treatment, the attacks recur even in greater severity than before taking luminal.

In this connection it must be stated that several of my patients returned after having taken luminal for a short time believing themselves cured. I always explain to such patients that there is great danger in discontinuing treatment abruptly and that I expect worse attacks than they ever had before, if they omit the remedy. Such a statement often has the desired effect.
In other instances, patients fail to put in appearance and act as though they were cured, neglecting every sort of rule and leading a riotous life. A series of convulsions usually brings them to their senses. Then they visit the physician and promise to be good. For a time rules are adhered to, the medicine is regularly taken, and the patient is again in fine spirits. They often fall from grace more than once, before they finally learn their lesson.

CASE 11.—A housewife, aged 34, first seen, July 13, 1917, gave the following history: After a case of pleurisy she developed peculiar attacks described by her as staring spells, during which the face turns white, then flushes, a jerking of hands and feet occurs, and a feeling as though the body was leaving her is experienced. Patient appears to speak to her dead grandmother, wrings her hands continually and asks, "Oh! grandma, what is it?" For all of this the patient herself has no recollection. These minor attacks repeat themselves several times daily. The first epileptic convulsion, a major attack, occurred, Oct. 26, 1916, at night. Subsequent attacks of this type have occurred once monthly and always in the morning. During these she utters a shrill cry, bites her tongue and froths at the mouth; then follows deep sleep. The next day patient is weak and depressed.

The administration of sodium luminal in 2½ grain doses nightly caused a remarkable improvement.

CASE 12.—Mr. H. F. B., aged 34, was first seen, Aug. 30, 1918. At 16 years his first convulsion occurred, since which time convulsions appeared at irregular intervals. There are both major and minor attacks. The patient's general health and habits are good, and there is no evidence of syphilis. A relationship has been noticed between his habitual constipation and the frequency of epileptic attacks.

The treatment consisted in regulating the bowels and the administration of luminal tablets in 1½ grain doses. Up to the present time there has been no recurrence of attacks excepting one minor attack. For this reason the dose was increased to 1¾ grains of luminal nightly. There have been no attacks since and the patient is able to attend to the business of a large banking house.

CASE 13.—G. M., aged 22, fireman, with good family history, was first seen, Dec. 31, 1919. Suffered from meningitis at 5 years. Shortly thereafter a severe convulsion occurred; similar convulsions returned at irregular intervals, always at night. During these the patient cries, turns his head, stiffens, and bites his tongue. Fatigue and muscular soreness are present for twenty-four hours succeeding the attacks. There were intervals of freedom from spells of varying duration, the longest interval being one year.
Patient was given luminal in 1¼ grain doses at night. He reported at my office, Jan. 9, 1920, stating that no attack had occurred since the middle of November. March 10, 1920, the patient reported no attacks since taking the medicine (1½ grains of luminal).

Case 14.—E. L., aged 11, schoolgirl, came under observation, July 9, 1919. Father, mother, one brother and one sister well. The patient was born in normal labor, talked and walked at 14 months; teething at the usual time. As an infant was somewhat undernourished and during childhood suffered from tonsillitis, measles, jaundice, pertussis, scarlet fever, and diphtheria. After a second attack of diphtheria four years ago patient developed a peculiar “stupor.” Last autumn suffered from “grip,” and her first convolution occurred in October, 1918. After passing through a case of influenza, a second attack occurred, December 25 of the same year. Another convolution occurred, May 30, 1919, and the last attack was observed, July 9, 1919, the day of my examination.

The patient appears active, nervous and tired, and there is seen a more or less constant jerking of facial muscles and of the eyebrows. Mother describes certain peculiar attacks which began four years ago, and which came on while patient was at school. They consist of a momentary confusion when she raises her hand in order to answer teacher’s questions. Of late these “absences” have become more frequent. A premonitory symptom noted by mother prior to the development of grand mal attacks is a peculiar stupor when patient first awakens in the morning and a tendency to frequent urination at the same time. Invariably an attack follows the stupor. The attack itself is described as regular tonic, followed by clonic convulsions, lasting from two to three minutes.

Luminal in doses of 1½ grains nightly has caused a diminution of attacks and patient is able to follow her school work regularly. The dose of luminal had to be increased to 1¾ grains before the attacks were entirely controlled.

Case 15.—That in some instances it is necessary to begin with very large doses of luminal in order to prevent attacks and that subsequently smaller doses may suffice to keep the convulsion under control is shown by the case of a feebleminded epileptic, hemiplegic girl of 10 years of age, who had serial epilepsy consisting of dozens of attacks daily. She was given bromids in large quantities without the slightest benefit. On the administration of ordinary doses of luminal, there was no change. Returning to the bromids, the attacks were as frequent and as violent as before. I then decided to give 3 grain doses three times daily, with the result that attacks ceased at once. After several days I reduced the dose to 2 grains twice daily, and the patient has been free from attacks for an entire year.
CASE 16.—That even symptomatic epilepsy responds well to the luminal treatment was demonstrated by the following case: The patient, 52 years old, suffered from generalized attacks of epilepsy during a period of five years, as the sole manifestation of a brain tumor. The administration of even 10 grain doses of bromids caused gastric derangement, extreme weakness, and apathy. I decided to try luminal in doses of 1½ to 2 grains. This and nothing else kept the patient comfortable for many years. In the course of time, however, the patient succumbed from the effects of an inoperable tumor.

Some of my cases have been free from attacks for a period of three to four years, others from one to two years, and still others, and these constitute the large majority of cases, for a number of months. Owing to the scarcity of luminal during the war, I was often obliged to use sodium luminal, of which there was still a quantity left. However, the dose is much larger and the effects do not equal those of luminal. Fortunately, both products are now being manufactured in America.

SUMMARY

Luminal in small doses, from 1½ to 2 grains, once or twice daily, has been found capable of causing an arrest of convulsions in epilepsy.

Larger doses than those mentioned are seldom required, but may be safely given.

Large doses may be administered when beginning treatment, especially after sudden withdrawal of the bromid treatment; even in such cases the dose may be gradually reduced to what constitutes an average dose, namely, 1½ to 2 grains.

No harmful effects have thus far been observed from the long-continued administration of luminal.

It does not appear to be a habit-forming drug.

The effect on the mentality of patients taking luminal for epilepsy was surprising. Patients receiving average doses of luminal do not show the peculiar mental torpor of those taking bromids.

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