

THE FREQUENCY OF NEURITIS IN LEPROSY.
ITS SYMPTOMATIC TREATMENT WITH INTRAVENOUS
CALCIUM GLUCONATE*

By

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Neuritis is one of the most distressing complications of leprosy which the writer treats at the National Leprosarium. During the month of January 1944, 203 unselected ambulatory patients were examined. It was found that at some time in the course of the disease 56 per cent had suffered from neuritis. From a consideration of the pathology of the disease — a lymphocytic infiltration of the nerve with subsequent proliferative change involving the entire nerve trunk — it would appear that pressure, which may destroy function at times, results in painful irritation of the nerves.

In most cases, untreated leprosy neuritis runs a relatively prolonged course. In our series of 203 unselected ambulatory cases, there were 60 patients who had received no special treatment for the nerve pains. The peripheral nerves most often attacked were the ulnar, peroneal, radial, median, and superficial cervicals. In 19 of these cases, it was possible to determine the duration of the last attack. In the remainder, the attack was either still in progress or the patient could not remember with reasonable accuracy the duration. In these 19 untreated cases, the shortest attack lasted two weeks, the longest seven years, with only short intervals of subsidence of pain during which periods the nerve trunks remained enlarged, painful, and tender to the touch. There were frequent acute attacks with dull aching pains during this time. In 26.3 per cent of cases the last attack had ended spontaneously in less than one year. In 73.7 per cent the attack persisted one year or longer. From these percentages it appears that in a study of treatment of leprosy neuritis over a period of 12 months, such as this, substantially more than 26.3 per cent of the cases should improve on the treatment under question, in order to establish that treatment as being of any value.

The first type of treatment to be discussed is that of leprosy itself. Obviously, the best treatment of a symptom of a disease is that of the disease itself. It is well known that there is no generally accepted specific treatment for leprosy. During the 12 months of 1943, which are being considered in this study, a considerable number of patients received the time-honored chaulmoogra oil treatment in its various forms, while another group received

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the more recently advocated promin treatment (1). Other experimental studies in treatment did not include enough cases of neuritis for statistical significance, although in passing it might be mentioned that patients receiving I.A. No. 307 of Parke, Davis & Co. (sodium salt of p-p-diamino-diphenyl-sulfoneo-acetyl-sulfonamide) suffered less from nerve pain than patients receiving promin or chaulmoogra oil and its derivatives.

Of 203 cases, there were 115 who received chaulmoogra oil or its derivatives. In 55 per cent nerve pains were present. In 1.7 per cent nerve pains became less on treatment, while in 1.7 per cent they seemed worse. Of 41 cases who received promin during most of the year, results were substantially the same. With 56 per cent having nerve pains, 14.5 per cent thought the nerve pain was improved, and as in the case of chaulmoogra oil treatment, the same number (14.5 per cent) thought the nerve pain was worse. There were 34 cases in which treatment was very irregular or absent, of which 61 percent reported nerve pains, while none reported changes, good or bad.

From this it appears that while the treatment of leprosy itself may be theoretically the ideal treatment of the neuritis which is present so often, nevertheless, the routine treatment given during 1943 in the National Leprosarium did not have any demonstrable effect within 12 months on the course of nerve pains.

Let us now consider the routine symptomatic treatment of the leprous neuritis, as carried out at the National Leprosarium. Because of the chronic nature of the ailment, habit-forming narcotics are contra-indicated. During 1943 demerol was not available for study in this institution, but a more recent preliminary study indicates that temporary relief is given to a large number of patients by 100 mg. of demerol administered by mouth or intramuscularly. Simple analgesics, such as aspirin, aspirin with acetophenetidin, and aminopyrin are used rather freely. Codeine is sometimes added, orally or hypodermically, but usually only for patients in the infirmary. Many times these simple measures do not bring relief, or bring relief that is too transient. One of our routine therapeutic agents is heat, which is given by the inductotherm, diathermy, or infra-red lamp. In mild cases analgesic balm or imadyl unction is of value as the source of heat or counter-irritation. In the cases tabulated below, a "severe case" of nerve pains is one in which codeine is of no value in helping pains. A "moderate case" is one which would require codeine almost constantly to control pain. A "mild case" is one which is helped considerably by aspirin and acetophenetidin given together..

Because of the encouraging results reported by Badger and Patrick (2) with thiamine in the treatment of the neuritis of leprosy in Hawaii, vitamin B₁ has been used rather freely at the National Leprosarium, although in somewhat larger dosage than suggested in the earlier literature. The vitamin B₁ cases are divided into orally and parenterally treated cases. The oral cases were given three to fifteen mg. daily by mouth for considerable

periods of time; the parenteral cases received 150 mg. intramuscularly, usually in divided doses over a period of three days. Results were as follows:

Results following routine treatment of nerve pain

Type of treatment	Severe neuritis		Moderate neuritis		Mild neuritis	
	Number of cases	Per cent improved	Number of cases	Per cent improved	Number of cases	Per cent improved
Heat	2	*	5	40	10	90
Vitamin B ₁ orally	2	0	7	57	15	86
Vitamin B ₁ parenterally	4	50	13	62	3	100

* Both patients definitely worse.

Conclusion: Most of the mild cases improve on vitamin B₁ or heat. About half or more moderate cases improve on vitamin B₁; slightly less on physiotherapy. For severe cases, parenteral vitamin B₁ is needed, and is effective about half the time.

Intravenous Calcium Gluconate Treatment

In an attempt to give relief that will persist for months at a time, soluble calcium was tried on a series of 35 cases during 1943. It is believed that the pharmacological action of calcium includes decreasing the irritability of nerves (3), as well as decreasing permeability of cells, favoring dehydration, dilating blood vessels, stimulating of the vagus nerve, contributing to coagulation of blood, and activation of digestive enzymes. Absorption of calcium given orally is variable, depending somewhat on formation of insoluble carbonate and phosphate in the intestine. In the writer's series he chose intravenous administration of calcium gluconate. In general, the most satisfactory technique was to inject 1.0 Gm. in 10 cc. of distilled water rather slowly, intravenously, daily, for one week, after which time the injections were usually reduced to one to three injections per week until the patient was free, or relatively free, of nerve pain for several weeks. Because of danger of ventricular fibrillation, calcium was not given intravenously to any patients who were receiving digitalis (4).

During 1943, the writer gave 914 Gm. of calcium gluconate to 35 patients with neuritis, with results to be outlined in detail below. He also gave 47 Gm.

to 4 patients with erythema nodosum, with poor results; and 1 Gm. to 1 patient with acute upper respiratory infection, with good result.

The selection of cases should be explained at this point. There were 11 cases of truly severe neuritis not helped by other measures. There were also 15 cases which were given calcium later in the year without necessarily trying all other medications first. These 15 cases are grouped separately, as it is not known that heat or vitamin B₁ might have helped them. Because of the momentary flush and sensation of generalized warmth that comes with the vasodilation during the intravenous administration of calcium, the writer has tried to avoid use of this drug in cases which can be helped by vitamin B₁ or physiotherapy. Below the writer presents case abstracts of 35 patients, classified according to severity of nerve pains and reactions to other medications:

CALCIUM GLUCONATE — CASE HISTORIES

Cases of severe nerve pains not controlled by other measures:

CASE 1468: Severe nerve pains were present for 8 months, accompanied by painful swelling of the right ulnar nerve. Vitamin B₁ and heat were of no value. Over a period of 12 months a total of 108 Gm. of calcium gluconate, average 1 Gm. every 3.3 days, was given intravenously. When less than 2 injections a week were given, pains were so severe that daily injections were needed for several weeks before they could be reduced to two to three injections per week. After intensive treatment for 2 weeks, patient did very well on 2 to 3 Gm. per week.

CASE 1325: Severe nerve pains of legs and arms were not helped by vitamin B₁. Over a period of 10 months, 34 Gm. of calcium gluconate were given intravenously. At times a single dose would stop the pain for several months. At other times it would have to be given 2-3 times a week for several weeks.

CASE 1374: Nerve pains were severe in the right foot and were not helped by vitamin B₁. During a period of 10 months, 16 Gm. of calcium gluconate were given intravenously with complete relief from nerve pains.

CASE 1512: Severe nerve pains were not helped by vitamin B₁, heat, or intravenous calcium gluconate in spite of 48 Gm. being given over a period of 8 months. This case is a failure of calcium treatment.

CASE 1407: Severe nerve pain was present with swelling of right ulnar nerve. There was no help from vitamin B₁ or heat. Over a period of 10 months, 92 Gm. of calcium gluconate were given intravenously with moderate improvement in symptoms. Nerve pains were not completely relieved but now easily respond to simple analgesic agents.

CASE 1435: Nerve pains improved over a period of 9 months, during which time 22 Gm. of calcium gluconate were given intravenously. The drug was stopped because of nausea. There had been no help from vitamin B₁ or heat.

CASE 1269: Severe nerve pains were not helped by vitamin B₁ or heat. Over a period of 6 months, a total of 25 Gm. of calcium gluconate was given intravenously. Nerve pains were improved after 6 to 8 injections and are now absent.

CASE 1482: Severe nerve pains were not helped by vitamin B₁. Pains vanished after 31 Gm. of calcium gluconate were given intravenously over a period of 3 months, and are still absent 7 months later.

CASE 818. Severe nerve pains were not helped by vitamin B₁ or heat, but stopped completely after a few weeks on calcium gluconate. Over a period of 5 months 37 Gm. have been administered intravenously. Injections are continued for paresthesia (abnormal sensations of coldness) which is benefited by calcium.

CASE 1232: There was no help from vitamin B₁ or heat. Nerve pains are relieved at present since 18 Gm. of calcium gluconate were injected intravenously over a period of 10 months with several months relief after each 5 to 6 Gm. course.

CASE 651: After failure of alcohol injection and vitamin B₁, intravenous calcium gluconate gave complete relief from sphenopalatine neuralgia and nerve pains of the extremities, 18 Gm. being given in one month.

Cases of moderate nerve pains not controlled by other measures:

CASE 1332: Moderate nerve pains were not helped by vitamin B₁. They were relieved after 4 Gm. of intravenous calcium gluconate.

CASE 1314: Nerve pains were severe enough to interfere with sleep. There was no help from vitamin B₁. Over a period of 6 months, 32 Gm. of calcium gluconate were given intravenously, with nerve pains absent while taking 1 to 2 Gm. a week but present whenever a week was missed.

CASE 1491: There has been moderate improvement in nerve pains in 4 months after 28 Gm. of intravenous calcium gluconate in patient not helped by vitamin B₁ or heat.

CASE 1480: There was no help from vitamin B₁. Nerve pains were quite severe, but have been relieved completely by 15 Gm. of calcium gluconate intravenously given during 4 months.

CASE 1377: There had been no help from vitamin B₁. Nerve pain was relieved after 4 Gm. of intravenous calcium gluconate, which is being continued in hope of preventing contracture of little finger which is starting to develop.

CASE 1498: There had been no help for moderate nerve pain from vitamin B₁ or heat, or intravenous calcium gluconate, total 9 Gm. given over a 2 months' period. It is felt that dosage was inadequate, but patient is classed as a failure.

CASE 706: There had been no help from vitamin B₁. Nerve pains vanished after 8 Gm. of calcium gluconate given intravenously during 1 month, and have not returned over several months.

CASE 1058: Severe paraesthesias (abnormal sensations of warmth) were not helped by vitamin B₁; vanished after 6 Gm. of intravenous calcium gluconate given over a period of 2 months.

CASE 1445: There had been no help from vitamin B₁. Nerve pains markedly diminished on intravenous calcium gluconate therapy; 13 Gm. given in 1 month.

Cases of mild neuritis also helped by other measures:

CASE 1388: Nerve pains moderately better on vitamin B₁ or intravenous calcium gluconate; 6 Gm. were given over 2 months.

CASE 1019: Calcium was given intravenously to decrease erythema of the face (secondary to promin) with good results. Nerve pain also cleared up after 34 Gm. were given over a 10 months' period.

CASE 1399: Nerve pain was not helped by 3 Gm. of calcium gluconate given intravenously during 1 month. Treatment is deemed inadequate but classified as a failure. Patient prefers vitamin B₁ treatment.

CASE 1412: Nerve pain was completely stopped after 3 Gm. of intravenous calcium gluconate given in 1 month.

CASE 1208: Calcium was used with marked success in relieving itching and erythema due to promin therapy. Nerve pain was also relieved; 49 Gm. of calcium gluconate were injected intravenously during an 8 months' period.

CASE 1555: Nerve pain is much improved after 31 Gm. of calcium gluconate given intravenously over a period of 6 months.

CASE 1090: Nerve pain was relieved by calcium gluconate (6 Gm. intravenously in 1 month) and also by vitamin B₁.

CASE 1391: Nerve pain was relieved by 1 Gm. of calcium gluconate intravenously. Patient also gets over nerve pain on oral calcium lactate gr. X t.i.d.

CASE 1514: Calcium gluconate was administered intravenously for eczematoid dermatitis with good results at the rate of 30 Gm. in 4 months. Nerve pains also cleared up.

CASE 1542: Nerve pains were stopped by intravenous calcium gluconate used prophylactically after cessation of initial pains; 31 Gm. were given in 3 months. No other medication was tried.

CASE 576: Pain in eye after iridocyclitis was stopped by 4 Gm. of intravenous calcium gluconate, from which it is presumed that the pain was possibly neuritis of the ophthalmic branch of the fifth cranial nerve.

CASE 1574: Nerve pains were relieved by 8 Gm. of calcium gluconate intravenously in 1 month. Calcium lactate and vitamin B₁ are now given by mouth with good results.

CASE 1432: Nerve pains were relieved by 8 Gm. of calcium gluconate intravenously in 1 month. They were also helped by vitamin B₁.

CASE 1235: There has been questionable response to other types of medication. Nerve pains stopped for several months after each intravenous injection of 2 to 4 Gm. of calcium gluconate. A total of 14 Gm. were given during 6 months.

CASE 890: Nerve pains were relieved by vitamin B₁ or by intravenous calcium gluconate (21 Gm.) given over a period of 6 months.

Effect of intravenous calcium gluconate on neuritis

Classification according to response to previous treatment and severity	Number of cases	Per cent improved
Not helped by other measures		
Severe	11	91
Moderate	9	89
Total	20	90
Helped by other measures		
Mild	15	93
Total	35	92

In summary it was found that 90 per cent of the patients whose neuritis was not helped by vitamin B₁ or local heat were either completely relieved of nerve pains, or helped so that simple analgesics gave complete relief within a week or two of starting treatment utilizing intravenous calcium gluconate. When all cases are considered, the average is higher than 90 per cent.

The writer repeats that the best treatment for leprous neuritis should be the cure of leprosy. Failing in this, calcium gluconate given intravenously proves to be one of the most valuable drugs for the symptomatic relief of leprous neuritis.

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The intravenous calcium gluconate treatment outlined above was started at the suggestion of G. H. Faget, Senior Surgeon, U.S.P.H.S. who recommended trial of the drug for patient no. 1468 who was suffering from severe right ulnar neuritis which stoutly resisted all other attempts at treatment. Because of the remarkable success of calcium therapy in this instance, the remainder of the study was carried out under the direction of Dr. Faget.

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