Etiology and Pathogenesis.—Although the causes of *true* neuritis, including the "neuralgias," are very numerous, the pathogenesis is the same in every instance, *i.e.*, some primary physical interference with the normal functions of the nerve.* We may thus have neuritis due to mechanical injury of the nerve, as from blows, contusions, wounds, stretching (as in dislocations, fractures, etc.) and pressure, the latter including compression by aneurysms, tumors, crutches, sleeping upon the arm, etc., and excessive use of an extremity. The lesion is essentially local and what degree of neuritis occurs is associated with an attempt at repair.* This applies likewise to the extension of localized disease, carcinomatous, syphilitic, tuberculous or other foci, or tumors, caries of bone, etc. In any of these, destruction of the nerve may lead to trophic disorders, paralysis, etc., differing in no way from those observed in trigeminal and other severe neuralgias.

In 30 cases of Morton's disease, *i.e.*, metatarsal neuralgia, Robert Jones[103] traced 10 clearly to injury. Neuralgia of various nerves of the arm, due to excessive professional use of this member, was observed in 30 cases by Bernhardt;[104] leeching over the nerves was found to give marked relief in some cases—evidence that hyperæmia and neuritis, therefore, were the cause of pain.

The lesion is primarily local also in the most frequent cause of neuritis: exposure of a part of the body, one side of the head and face, the neck, the gluteal region, etc., to a draught of cold air, especially while the area exposed is warm, flushed and perspiring. The arterioles of the cutaneous tissues being suddenly chilled while dilated, the temperature of the auto-antitoxin is reduced, thus inhibiting the action of its trypsin, and two sets of morbid phenomena occur: (1) temporary paresis of the local arterioles; (2) temporary inhibition of the proteolytic process through which the local waste-products of metabolism are reduced to eliminable end-products.* We are dealing here with a neuritis, since the morbid dilation of the neural arterioles necessarily entails hyperæmia of the perineurium and engorgement of the endoneurium, and pressure, therefore, upon the *nervi nervorum*. In addition to this passive hyperæmia, the region becomes the seat of the active hyperæmia incident upon

* *Author's conclusion.*
[103] Robert Jones: Liverpool Med.-Chir. Jour., vol. xvii, p. 1, 1897.
[104] Bernhardt: Semaine médicale, vol. xvi, p. 13, 1896.

the reparative process, including the destruction of detritus.* Hence the severity of the pain in neuralgia.

As in migraine, neuralgia may be due to reflex action owing to some ocular, aural, nasal, cutaneous or other lesions.

The pathological anatomy of the local lesions we have seen is invariably connected with local congestion. This controverts a prevailing misconception of the manner in which neuralgic pain is provoked, viz., that it can be caused by a deficiency of blood in painful areas, or by "poisons" circulating in the nerve. Even in joints, the accumulation of endogenous poisons does not provoke pain directly; were it otherwise, it would be impossible to account for the disappearance of pain under the influence of hot, dry air, and other measures which do not destroy chemically the poison directly. But the action of hot, dry air is readily explained—as well as the beneficial effect of heat in neuralgia—when we recall that the activity of the blood constituents—the ferment in particular—which destroy the toxics is enhanced by heat.* The need of the antitoxic inflammation being reduced, the local hyperæmia is correspondingly diminished, and pain is reduced in proportion. In other words, it is not the poison which causes the pain, but the reparative process which the presence of the poison engenders, and particularly the congestion it entails.

Neuralgia frequently occurs irrespective of any apparent exciting cause, such as a cold, a traumatism, etc. The causative neuritis appears almost invariably after puberty, in subjects debilitated by physical or mental overwork, infectious diseases, malaria, prolonged lactation, or by the prolonged ingestion or absorption of certain poisons, alcohol, lead, arsenic, etc. Here, the neuritis is secondary, in the sense that it is evoked as a complication of another, but general, disorder.*

The debilitating influences mentioned react on the general organism, we have seen, by reducing the functional efficiency of the anterior pituitary body.* In a large proportion of cases the inefficiency of this organ is inherited, "neuralgia" being often observed in families in which epilepsy, hysteria and other nervous diseases have prevailed. Entailing as it does, a reduction, more or less marked, of the blood's properties, poisons of autogenetic origin such as those that occur in the blood in gout, rheumatism, uræmia and kindred conditions, are allowed to accumulate in the blood-stream. Hence the frequent association of both neuritis and "neuralgia" noted by clinicians.* When this accumulation of physiological poisons has reached a certain degree, the phenomenon witnessed in epilepsy, migraine, etc., occurs, viz., a violent reaction of general centers of both

* *Author's conclusion.*

lobes of the pituitary, including those of the sympathetic and vasomotor systems.*

Important in this connection is the fact that the intestinal canal takes an active part in the morbid process, the inadequate evacuation of excrementitious materials causing it to act as a source of autoinfection. There is usually constipation and the stools are exceedingly foul. The underlying cause of this is an imperfect disinfection of the intestinal contents by the succus entericus, *i.e.*, by the auto-antitoxin it contains,* the result, we have seen, of insufficiency of the adrenal system.*

The kinship between neuralgia, migraine and epilepsy extends even to the characteristic symptoms of the latter disease. Gowers, for instance,[105] refers to two cases of neuralgia attended with vomiting; to another in which opisthotonos was "so severe that the patient rested on the head and the heels." Anton[106] also observed two cases in which attacks of trigeminal neuralgia lapsed into typical epileptic seizures. Grinker,[107] on the other hand, reported a case in which right trigeminal neuralgia coincided with neuritis of the left sciatic, etc. Féré[108] and others have emphasized the analogy between certain forms of neuralgia, the *tic douloureux*, for instance, and epilepsy. In Putnam's[109] opinion, that difference between neuralgia and migraine is one of degree rather than of kind. Lange[110] has called attention to the frequency of the alternation of migraine with neuralgia.

The pain is limited to a given area, and recurs in that area because its vessels have, some time in the course of the patient's life, been exposed to one or more of the many exciting causes capable of bringing on an attack, cold, traumatism, pressure, etc. These exciting causes evoking, as stated above, an inflammatory process in the walls of the neural vessels, this process forms the starting-point of the endarteritis and arteriosclerosis found, we have seen, in advanced cases.* When, therefore, the accumulated blood-poisons provoke, by irritating the sympathetic and vasomotor centers, a rise of the blood-pressure of the entire body, the neural blood-vessels of the "neuralgic" area yield more readily than those throughout the rest of the body, and the nerve becoming hyperæmic, pain is provoked.

We have seen that in epilepsy and migraine there is primarily a general constriction of the arterioles, because the sympathetic center is the first stimulated; and that this is succeeded by general vaso-

* *Author's conclusion.*

[105] Gowers: *Loc. cit.*, vol. ii, p. 800, 1893.
[106] Anton: Wien. klin. Woch., Bd. ii, S. 231, 1889.
[107] Grinker: Jour. Amer. Med. Assoc., July 15, 1905.
[108] Féré: Revue de médecine, vol. xii, p. 497, 1892.
[109] Putnam: *Loc. cit.*
[110] Lange: Hospitalstidende, p. 581, 1891; Satellite of the Annual of the Univ. Med. Sci., Mar., 1892.

motor constriction when the vasomotor center yields to the irritation. The case is the same in neuralgia. The great influx from the ventral vessels to the periphery which attends general vasoconstriction soon overcomes the resistance of the weakened arterioles of the affected area and enforces their dilation. Although it has so far remained unexplained, this sequence of events has been actually witnessed. Thus, Gowers states that the first effect is usually "a constriction of the vessels of the part" and that "this is often followed by their relaxation."*

Treatment.—Neuralgia, especially the trigeminal and sciatic forms, involves so much suffering that the first indication is to control the pain. In the light of the pathogenesis of neuritis described in the foregoing pages, this reduces itself to the use of measures calculated to diminish the congestion of the neural blood-vessels, and thus to reduce the pressure upon the nervi nervorum. The next indication is to remove, if possible, the cause of the disorder itself.

Measures which Reduce the Congestion of the Painful Area.—The majority of cases observed in general practice occur in subjects predisposed to frequent recurrences. Even the worst form of neuralgia, tic douloureux, is characteristically prone to remissions, of days', weeks', and even months' duration. The pain, therefore, cannot be ascribed to the permanent lesions in the nerve itself; it must be due to some *fluctuating* agency:* the local hyperæmia, we have seen. It is not only therefore in mild cases that reduction of the local congestion is indicated, but also in the worst cases. To accomplish this, we have at our disposal four groups of remedies:—

(1) Drugs which cause general vasodilation by depressing directly the general vasomotor center.*

The *bromides* are useful agents of this class in mild cases. In the average case, however, they are unreliable, unless large doses are used, when gastric disorders, bromism and accumulation of toxic wastes in the blood are likely to follow. By giving small doses—10 grains (0.6 gm.)—and using the sodium salt, these drawbacks are reduced to a minimum, while its analgesic properties may be increased by means of *chloral hydrate*, 10 grains (0.6 gm.), the central action of which is similar to that of the bromides. The combined use of these two salts, every two hours, aided by one of the local remedies enumerated below, usually masters the mild forms commonly

* *Author's conclusion.*

observed. When the pulse is tense and hard, especially in plethoric subjects, a third vasomotor depressant, *veratrum viride,* may be added, 2 drops (or four times this amount: 1905 U. S. P.) of the tincture being given every two hours. When no heart lesion is present, the pain may be relieved by the inhalation of three drops of *amyl nitrite,* in the physician's presence. Five or six drops poured on absorbent cotton in an emery-stoppered bottle, affords the patient a convenient and safe means, through which he can obtain relief by taking an occasional "whiff." The preliminary use of amyl nitrite—which also lowers arterial tension—followed by the bromide-chloral mixture, generally proves more satisfactory, however. *Nitroglycerin* advantageously replaces the latter agents in many cases, especially when large nerves, those of the brachial plexus and the sciatic, for instance, are inflamed. It depresses both the vasomotor and sympathetic centers,* and by thus reducing the vascular tension in all vessels, counteracts the pressure in the hyperæmic nerves, and bleeds them, as it were, into the great central trunks. In trifacial neuralgia, the pain may be increased at first through the dilation of the arterioles; but this does not occur after a few doses of the bromide-chloral mixture.* The dose, one minim of the 1-per-cent. solution gradually increased to four minims, three times daily. While nitroglycerin is often curative, the bromides, chloral and amyl nitrite are only temporary expedients which should be withdrawn after cessation of the pain.

The influence of general vasodilation is well illustrated by Pommerol's case,[111] in which a sciatica of five years' standing was cured by the bite of a viper. The value of nitroglycerin has been recognized by Herter,[112] Mikhalkine,[113] Lawrence, Krauss[114] and others.

(2) Drugs which cause general constriction of the arterioles by stimulating the general sympathetic center.*

Of this group, the coal-tar products are the most effective, especially *acetanild* in 5-grain (0.3 gm.) doses every hour three times, then every three hours, until the pain ceases. By causing powerful constriction of the peripheral arterioles, they reduce greatly the proportion of blood supplied to the inflamed nerves;* the latter being simultaneously depleted in the veins, the pressure upon the nervi nervorum ceases and the pain likewise. *Phenacetin,* in 10 to 15 grain (0.6 to 1 gm.) doses, is also useful. *Antipyrine* is more apt to provoke untoward effects than acetanild, but it has proved valuable especially in sciatica, when injected, with an equal quantity (10 grains—0.6 gm.) of sterilized water, in the tissues immediately overlying the nerve. The coal-tar products should be used only temporarily as analgesics. *Morphine* relieves pain in the same way, whether administered orally or subcutaneously close to the diseased nerve. Deep injections, practically down to the nerve, of $^1/_6$ grain (0.01) morphine and $^1/_{120}$ grain (0.0005 gm.) *atropine* are very effective, even in sciatica. This should be repeated daily. When there is reason to believe that a drug-habit may be initiated by using the foregoing drugs internally, the same physiological effects may be obtained with *aconitine,* $^1/_{400}$ grain (0.00015 gm.) every four hours, gradually increased until the first "physiological" effect, *i.e.,* tingling, appears, when the dose should be somewhat decreased. The tincture of *aconite* root (1905 U. S. P.) 4 minims (0.25 gm.) may be used instead if preferred; it is especially effective when given with the tincture of *gelsemium,* 10 minims (0.6 gm.), given every hour, until the labial and digital tingling of aconite is felt. These two remedies sometimes prove curative. *Cocaine* also relieves pain by causing constriction of the arterioles. It has given good results when injected in doses of $^1/_4$ to $^1/_2$ grain (0.016 to 0.03 gm.) in solution, over the seat of the pain. In neuralgia of the face it may be injected into the arm, carefully avoiding a vein. *Osmic acid,* which acts similarly, is sometimes very effective in severe cases, when 10 to 20 minims (0.6 to 1.2 c.c.) of a 1-per-cent. solution are injected near the nerve, or better into its substance after exposing it surgically.

Cocaine has also been used in sciatica in the form of intrarachidian injections, but the ordinary methods are as effectual. The danger of penetrating a vein was suggested by Bergmann,[115] who, having obtained immediate relief in a case of sciatica by injecting 15 minims (0.90 c.c.) of a 5-per-cent. solution of cocaine, without observing the least untoward effect, caused violent symptoms of intoxication the next

* *Author's conclusion.*

[111] Pommerol: Gaz. des hôpitaux, Aug. 2, 1900.

[112] Herter: *Loc. cit.*

[113] Mikhalkine: Med. Obozrenie; Revue de thérap. médico-chir., vol. lxii, p. 122, 1895.

[114] Krauss: N. Y. Med. Jour., Feb. 29, 1896; Buffalo Med. Jour., Oct., 1897.

* *Author's conclusion.*

[115] Bergmann: Münch. med. Woch., Bd. xlvii, S. 392, 1900.

day in the same patient by an injection of only 5 minims (0.3 c.c.) of the same solution. As recommended by Cagney,[116] cocaine should be used with prudence. Osmic acid has been recommended by many observers since Billroth suggested its use over twenty years ago. J. B. Murphy,[117] G. A. Wright,[118] and others, now expose the nerve in rebellious trifacial neuralgia under anæsthesia, and inject from 5 to 10 minims (0.3 to 0.6 c.c.) of a 1.5-per-cent. solution into the nerve-substance and between the nerve and its sheath. This is thought to cause degeneration, the pain ceasing permanently in most cases.

(3) Local remedies which produce reflex constriction of the peripheral arterioles, including those of the painful nerves, by irritating directly the cutaneous sensory terminals.*

Aconitine acts in the same way, applied locally, in the form of an ointment composed of 4 grains (0.25 gm.) of the alkaloid, 2 drachms (8 gms.) of glycerin, and 6 drachms (24 gms.) of cerate; *veratrine,* 10 grains (0.6 gm.), may be added for severe cases. Care should be taken to avoid rubbing this ointment over an abrasion, since it is violently poisonous. *Ethyl chloride* sprayed over the painful region daily sometimes proves curative. The skin should be protected by a thin layer of grease. In mild cases *menthol* rubbed freely on the skin is quite effective. Its efficiency is greatly increased by the addition of guaiacol; 15 grains (1 gm.) of each may be dissolved in 5 drachms (20 gms.) of absolute alcohol, and rubbed gently over the congested nerve. Again, *cocaine,* 15 grains (1 gm.), may be combined with menthol, 10 grains (0.6 gm.), in one drachm of vaselin, and rubbed into the skin with a wad of cotton. *Chloral hydrate,* with equal parts of *camphor,* forms a thick liquid which, painted freely over the affected region, serves often to prevent the pain until internal treatment has controlled the cause. *Galvanism,* the anode well moistened with salt water, being placed over the painful spot, also relieves pain by causing constriction of the vessels that supply the nerves.

(4) Measures which provoke direct or indirect depletion of perineural arterioles, and, therefore, of the endoneural capillaries.*

Guaiacol is so active in this connection that 15 drops applied to the skin have caused a marked decline of the peripheral temperature, and even prostration. Equal parts of guaiacol and glycerin painted over the diseased nerves promptly relieves pain.

* *Author's conclusion.*
[116] Cagney: Provincial Med. Jour., Apr. 1, 1895.
[117] J. B. Murphy: Jour. Amer. Med. Assoc., Aug. 22, 1903.
[118] G. A. Wright: Med. Chronicle, Feb., 1904.

Leeches afford a ready means for direct depletion; but in brachial neuritis *bleeding* may be resorted to with advantage, the abstraction of a few ounces of blood sufficing. *Cupping* is still recommended by some eminent neurologists. *Hydrochloric acid* painted over the nerve, three or four times at 48 hours' interval, affords effective counterirritation in neuralgia of the extremities. *Superheated dry air* is very effective, not only because it draws blood to the skin, which becomes quite red, but because the activity of the auto-antitoxin of the blood is greatly enhanced.* *Warm pack* about the abdomen or even the ordinary hot water applied over this region markedly facilitates the action of any drug administered internally calculated to deplete the congested area. *Heat* applied to the latter in the form of the hot-water bag, a hot brick, a hot hop or bran bag are familiar derivatives which assist the curative process also by increasing catabolic activity of the trypsin in the auto-antitoxin.*

Measures which Tend to Eliminate the Cause of the Neural Congestion.—Of the many exciting causes of neuritis enumerated, those that belong to the domain of the physician are closely allied, we have seen, (1) to disorders, such as migraine, gout, epilepsy, etc., which are attended by an accumulation of toxic wastes in the blood, and (2) with intestinal torpor due to the same central cause, and entailing auto-intoxication. Since the pain occurs in most cases as intermittent paroxysms caused by the accumulation of toxic materials in the blood, measures which prevent the latter should prevent the return of the pain.

In some cases purgatives now and then suffice to prevent the accesses. *Castor oil,* of all remedies of this class, has given the best results in 1 to 2 ounce (28 to 56 gm.) doses each morning. Mixed with two or three tablespoonfuls of ale (preferably Bass's, owing to the large quantity of gas it contains) it forms an emulsion and cannot be tasted. After the first few days it causes but one evacuation daily. The oil causes both catharsis and disinfection by increasing reflexly the relative proportion of auto-antitoxin in the intestinal juice.* *Citrate of magnesia* and other saline purgatives taken occasionally, only prevent the attacks in mild cases, and require the aid of rem-

* *Author's conclusion.*

edies that stimulate the adrenal system. The *dietetic* measures recommended for migraine[119] are also indicated in cases of neuralgia when at all severe. This applies likewise to the use of *saline solution* when the general symptoms point to a considerable accumulation of toxic wastes in the blood, especially in sciatica. In all such cases the free use of *pure water* as a beverage is very beneficial, while the use of alcohol, coffee, and tea is harmful.

Castor oil has given excellent results in the various forms of neuralgia. Ochsner reported 13 cases all materially improved. Moyer[120] treated 15 cases in the manner outlined in above text. Of seven reported but one failed to be benefited, four being cured. Aldrich,[121] Waxham[122] and others, have also recommended this treatment. Debove and Bruhl[123] found a saline solution composed of 5 per millie each of sodium chloride and sodium sulphate, effective in sciatica.

Of the drugs which have been used to controvert the "gouty" state—by stimulating the adrenal system—*sodium salicylate,* or *salicin,* 5 to 15 grains (0.3 to 1 gm.) in cachets, followed by a glassful of water, has given good results, but both agents sometimes cause gastric disorders. A more satisfactory remedy is *strychnine* in full doses, $^1/_{40}$ grain (0.0016 gm.), gradually increased to $^1/_{20}$ grain (0.0032 gm.) three times daily. It powerfully stimulates the anterior pituitary body, thus enhancing the oxidizing power of the blood, and is especially active in early cases, and when anæmia is present. In sthenic cases *sodium iodide* in 10 grain (0.6 gm.) doses in a large glassful of water after each meal is more effective. It may be gradually increased, but as soon as any sign of iodism appears the doses should be reduced as needed to avoid this phenomenon, the smaller dose being continued. When gout or rheumatism is present *colchicum,* 10 minims (0.6 gm.) of the tincture, increases greatly the efficiency of the iodide; *colchicine,* $^1/_{120}$ grain (0.00054 gm.), may be used instead of the tincture. *Quinine* is often recommended, but it is really beneficial when malaria underlies neuritis and when anæmia is present. In sthenic cases, it causes hypertonicity and increases the pain. The *benzoate of sodium.* 5 grains (0.3 gm.) every three hours the first two days, then

[119] *Cf.* this vol., p. 1526.
[120] Moyer: Jour. Amer. Med. Assoc., Apr. 21, 1900.
[121] Aldrich: Cleveland Med. Gaz., Nov., 1900.
[122] Waxham: Colo. Med. Jour., Dec., 1901.
[123] Debove and Bruhl: Gaz. des hôpitaux, vol. lxviii, p. 365, 1895.

after each meal, is often efficacious in children or young adolescents.

In neuralgia as well as migraine, the case should be carefully examined lest the pain be reflex. Any causal disorder of this kind should, of course, be eliminated. This being done and the measures recommended failing to remove the suffering, surgical measures should be resorted to, especially in *tic douloureux.* In this acutely painful form of neuralgia, the best operation so far devised is that of division of the sensory root of the fifth nerve, a safer and more efficacious operation than removal of the Gasserian ganglion.

Strychnine in heroic doses was found effective by Dana[124] in cases of one or two years' duration. It arrested the disease almost invariably. In cases of six or seven years' duration and in those in which inflammatory changes—especially scleroses—were present, no benefit resulted. It is usually given hypodermically, but as more than one injection can hardly be administered daily, a large dose has to be given. I have found it more advantageous to give it internally as stated, *i.e.,* in divided doses, since a larger aggregate of the drug can thus be used.

Division of the sensory root of the fifth pair for *tic douloureux* has recently been perfected by Frazier and Spiller, who introduced this operation. In the four cases reported[125] there had been no recurrence of the pain, the longest time elapsed being two years and eight months, and the shortest fourteen months. It entails much less hæmorrhage than removal of the Gasserian ganglion, is less dangerous, avoids ocular distufbances and particularly ulceration of the cornea.

[124] Dana: Jour. Amer. Med. Assoc., May 5, 1900.
[125] Frazier and Spiller: *Ibid.,* Oct. 1, 1904.