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Causalgia

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CAUSALGIA

Historical

During the latter part of the Civil War, S.Weir Mitchell, W.W.Keen, and G.R.Morehouse were commissioned by the Surgeon General to conduct an investigation of nerve injuries received by soldiers. In the course of this investigation they noted a peculiar, complicating syndrome arising from some of these injuries in a relatively small number of cases.

This condition was characterized by a burning sensation in, and trophic changes of, the affected part, which was usually the palmar surface of the hand or the dorsal surface of the foot, and was most often due to an injury to the median nerve or to the tibial nerve. To this condition he first applied the term 'Causalgia,' meaning burning pain.

The following description by Mitchell, quoted by Pollock and Davis (26) is so comprehensive that little has been added to it by writers since that time: "The seat of the burning pain is very various, but it never attacks the trunk, rarely the arm or thigh, and not often the forearm or leg. Its favorite site is the foot or hand. In these parts it is to be found most often where the nutritive skin changes are met with; that is to say, on the palm of the hand, or palmar part of the fingers, and on the dorsum of the foot; scarcely ever on the sole of the foot or the back of the hand. Where it first existed in the whole foot or hand, it always remained last in the parts above referred to, as its favorite seats.

The great mass of sufferers described this pain as superficial, but others said it was also in the joints, and deep in the palm. If it lasted long it was referred to the skin alone.

Its intensity varies from the most trivial burning to a state of torture, which can hardly be credited, but which reacts on the whole economy until the general health is seriously impaired.

The part itself is not alone subject to an intense burning sensation, but becomes exquisitely hyperesthetic, so that a touch or a tap of the finger increases the pain. Exposure to the air is avoided by the patient with a care which seems absurd, and most of the bad cases keep the hand constantly wet, finding relief in the moisture rather than in the coolness of the application. Two of these sufferers carried a bottle of water and a sponge and never permitted the part to become dry for a moment.

As the pain increases, the general sympathy becomes more marked. The temper changes and grows irritable, the face becomes anxious and has a look of weariness and suffering. The sleep is restless and the constitutional condition reacting on the wounded limb exasperates the hyperesthetic state, so that the rustling of a newspaper, a breath of air, another's step across the room, the vibrations caused by a military band, or the shock of the feet in walking give rise to increase of pain. At last the patient grows hysterical, carries the limb tenderly with the sound hand, is tremulous, nervous, and has all kinds of expedients for lessening his pain. In two cases, at least, the skin of the body became hyperesthetic when dry, and the men found some ease from pouring water into their boots. They said, when questioned, that it made walking hurt less, but how or why, unless by diminishing vibration, we cannot explain.

One of the men went so far as to wet the sound hand when obliged to touch the other, and insisted that the observer should also wet his

hand before touching him, complaining that dry touch always exasperated his pain. The skin affected in these cases was deep red and mottled, or red and pale in patches. The epithelium appeared to have been partially lost, so that the cutis was exposed in places. The subcutaneous tissues were nearly always shrunken, and when the palm was attacked, the part so diseased seemed to be a little depressed and firmer, and less elastic than common. In the fingers there were often cracks in the altered skin, and the integuments presented the appearance of being tightly drawn over the subjacent tissues. The surface of all the affected part was glossy, and shiny as though it had been skillfully varnished. Nothing more curious than to see red and shining tissues can be conceived of. In most of them the part was devoid of wrinkles and perfectly free from hair."

Mitchell however was not the first to describe the condition as there is a case recorded as early as 1815 by Denmark, quoted by Harris,(11) in which the patient was a soldier wounded in the battle of Talavera. In this patient Denmark states that the pain was of a burning nature and so violent as to cause a continual perspiration from his face. The original injury was a bullet wound of the upper arm. (11)

Other earlier cases, as quoted by Leriche (20) are, one by Langstaff in 1832, another by Hamilton in 1838, and another by Paget in the same year as those of Mitchell, 1864.

Since there are relatively few nerve injuries during peace time, and also since the incidence of causalgia following such injuries being only about 1 in 730, according to Carter, (7) it is only natural that the condition should be relegated to a rather inconspicuous position in medical literature.

These wounds preceding the injury are usually located near the elbow and the popliteal space. In such cases there is generally found to be an extravasation of blood through the cellular tissues and muscles. That there are other factors entering into the production of causalgia must be admitted. If no other circumstance other than a wounded artery or nerve was necessary to produce it in a given patient, then it would be as common as are such injuries. Certainly an incidence of 1 in 750 injuries to nerves is ample evidence of the need of something more than a torn nerve or artery.

One might speculate as to a bacterial, virus or parisitical origin, but nowhere is there related any evidence of an organism that might be incriminated, sepsis is not present except as a complication of the injury and the wound may be well healed--in fact usually is--before the onset of the painful burning sensation.

Attempts have been made to call this a "hysteria," and Harris (11) being at a loss to explain the continuation of the pain in some cases even after nerve blocking with alcohol above the injury, considered the above possibility, and also, as he says, "That there might be a central functional effect upon the pain centers in the optic thalmus, set up by the injury, resulting in persistent pain." Such an explanation of the origin of pain such as that apparently suffered by the causalgia patient must be an attempt to rationalize it into a psychosis or psychoneurosis; indeed, he further states that "Such pain may be compared to the acute mental distress of some anxiety neuroses and melancholias, where there is no question of organic injury."

Leriche, early in the World War, after observing some few cases, was struck with the resemblance of the condition to certain of the sympathetic disorders. He states "The cyanosis, the sweating, the paroxysmal nature of the pains, the effect on the general mental state, and the reference of painful phenomena to a distance--all pointed in that direction."

These observations seem to be the first hint of the possibility that the disease might actually be a dysfunction of the autonomic nervous system. Leriche now believes that the neuroma which is frequently found at the site of the injury weeks later, causes an irritation and produces afferent impulses to the central nervous system, which is mediated to the sympathetic, and through the various components of that system bring about the vaso-motor disturbances in the affected part; this in turn resulting in the pain and trophic changes. He attempts to explain the relative infrequency of the condition by the differences in the vaso-motor equilibrium of the individual, there being only a small number of persons having exactly the right set-up. He states "That every body injury implies an injury to the vaso-motor mechanism, the functional disturbance of which usually develops according to a well recognized plan--to return again in a few days to normal, but in some individuals the disturbance is more prolonged and gives rise to spreading pains, disturbances of tone or skeletal rarefaction." He began early in the World War to attempt treatment of causalgia with one or another type of sympathectomy. Others have followed his lead and the resulting failures and successes have lead to a tremendous amount of further research into the vagaries of the autonomic nervous system. This, in turn, has brought about a

far better understanding of other vascular disorders such as Raynaud's disease, Thromboangiitis-obliterans and Angina pectoris, and has given a rational basis for surgery in many of these cases. Results have varied but, according to Smithwick (30), in the case of Thromboangiitis-obliterans, sympathetic ganglionectomy has resulted in a decrease in the incidence of major amputations from 75% of cases to 6% of cases (31).

Causalgia then may, and rightfully so, be considered a pathological condition of relative unimportance because of its rarity, but the stimulation for investigation that its peculiarities have brought has given physiologists new concepts, has given surgical science new knowledge, has given anatomists added interest for further research, and has given great relief to victims of other similar yet more common sympathetic disorders, even though surgeons have not as yet conquered this original disease.

Anatomy and Physiology of the Autonomic System.

In the discussion of this division of the nervous system we will use the terminology of Gaskell and Langley in which the autonomic nervous system is divided into two component parts--the sympathetic and the parasympathetic divisions. Each division has two distinct sets of neurons, the pre-ganglionic and the post-ganglionic (3) (27). All neurons of these systems are embryologically derived from the neural tube along with other elements of the nervous system. (35). The sympathetic division has its pre-ganglionic cells of origin in the anterior horn of the spinal cord, the axons of which emerge from the cord through the anterior roots from the first thoracic through the second lumbar, and then are immediately diverted to the sym-

pathetic ganglia by way of the white ramus communicans. In this ganglion they may either synapse with the post-ganglionic neuron or continue either ventrally or dorsally through the sympathetic nerve trunk to synapse with a post-ganglionic cell in another of the ganglion chain. (3) (27). Other pre-ganglionic fibers do not synapse at any point in the chain but simply pass on through it to ganglia located in the great plexuses such as the coeliac and cardiac (35). The post-ganglionic neurons of this division have then their cells of origin in either the sympathetic chain or the ganglia of the great plexuses.

The following is a table denoting the various segments of the cord and the distribution of the visceral and somatic efferent sympathetic impulses:

	HEAD & NECK	ARMS	HEART LUNGS	G.I.	ADRN.	KIDNEY	BLAD. GEN.	SIGMOID RECTUM	LEGS
THORACIC									
1	X								
2	X		X						
3	X		X						
4	X	X	X						
5	X	X	X	X					
6		X	X	X					
7		X	X	X					
8		X		X					
9				X					
10				X					
11				X	X				X
12					X	X			X
LUMBAR									
1						X	X		X
2							X		X

The vasoconstrictor and the sudomotor fibers to the blood vessels and sweat glands of the upper extremities have their post-ganglionic cells of origin located in the stellate ganglion (inferior cervical and first thoracic) and in the middle cervical ganglion. The pre-ganglionic fibers coming to these above ganglia from the fourth, fifth, sixth, seventh and eighth thoracic segments. (3) (10) (35). Excision then of the stellate ganglion will therefore interrupt the sympathetic impulses to the upper extremity as well as those to the head, neck and heart. (3) The treatment of Causalgia as practiced originally by Leriche is based upon this interruption of vaso-motor impulses to the extremity. This operation has not always been successful and one explanation accoridng to Best and Taylor (3) is that there is frequently a gray ramus (Kuntz nerve) passing from the second thoracic ganglion by way of the first thoracic nerve to join the brachial plexus. The post-ganglionic neurons to the lower extremities have their origin in the first and second lumbar ganglia, and derive their pre-ganglionic fibers from the eleventh and twelfth thoracic and the first and second lumbar segments. Post-ganglionic fibers leave the superior cervical ganglion for sympathetic innervation of the eyes, the salivary glands, and the smooth muscle of the head and neck.

The parasympathetic division has pre-ganglionic fibers arising from nuclei located in the mesencephalon and the medulla, namely the Edinger-Westphal neucleus of the third cranial nerve, the salivary neucleus with fibers entering the seventh and ninth cranial nerve and the dorsal motor neucleus of the tenth nerve. (38) Post-ganglionic fibers to the eye arise in the ciliary ganglion where they synapse

with the pre-ganglionic. Post-ganglionic salivary fibers arise in ganglia near or in the innervated structures. Pre-ganglionic vagus fibers from the dorsal motor nucleus synapse in the ganglia of the cardiac, pulmonary, esophageal and coeliac plexuses. In the sacral portion of the cord there are also pre-ganglionic fibers arising in the lateral portions of the anterior horns, whose axons emerge through the second and third and occasionally through the fourth sacral anterior roots. The post-ganglionic neurons which synapse with these arise in the intrinsic plexuses of the bladder, genitalia and rectum. (3) (35) There is another important group of fibers which enter the spinal nerves through the posterior root and which are probably parasympathetic in character and most likely are the vaso-dilators for the peripheral vessels. According to Kahr and Sheehan (16) (1933) vasodilation was shown to occur on mechanical and electrical stimulation of the peripheral stumps of posterior spinal roots by Stricker as early as 1877, and has since been confirmed by many investigators, including Gartner (1889), Hasterlik and Biedl (1893), Bayliss (2) (1900) and Langley (1923).

Kure' et al (17) (1928) demonstrated that the posterior roots contain many finely medullated efferent fibers with cells of origin within the cord. These findings have been well substantiated by his additional work in 1931 and by that of Kahr and Sheehan (16) (1933). That there are also vaso-dilator fibers re reaching the periphery through the sympathetics has been pointed out by Lewis and Pickering (22) as sympathetic ganglionectomy destroys the power of the arteries to dilate as well as constrict.

The presence of vaso-dilator fibers in the posterior roots and in the spinal nerves, as will be brought out later, offers a logical explanation of many of the puzzling features of causalgia. Physiologically and pharmocologically the sympathetic and the para-sympathetic divisions of the autonomic system differ. The mechanical actions which their stimulation produce and the chemical means of their mediation at the neuro-muscular and neuro-glandular junctions, are entirely different, and in cases where both divisions enter the same organ or structure, their actions are definitely antagonistic. In the eye, for example, the para-sympathetics cause pupillary constriction while the sympathetics produce dilation; in the regulation of cardiac rythm the para-sympathetics are the inhibitors, while the sympathetics are the accelerators; but in the gastro-intestinal tract peristalsis is inhibited by the sympathetics and stimulated by the para-sympathetics. (3) (28) (36) The regulation of the vaso-motor system and also of the sudomotor system by the two divisions is apparently of prime importance in the syndrome of causalgia. Leriche was the first to recognize this fact and direct surgical intervention to the correction of its dysfunction. (20)

The sympathetics are primarily concerned with vaso-constriction, and although, according to Lewis and Pickering (22), section of the sympathetic nerves abolishes partially both vaso-dilation and vaso-constriction, there are the other vaso-dilator fibers found in the spinal nerves. The presence of these latter fibers gives us the reasonable assumption that they are the active vaso-dilators and are a part of the para-sympathetic system.

At this point it will be well to bring in the chemistry of the two systems. Stimulation of all preganglionic fibers results in the release of acetyl-choline which mediates the stimulus to the post-ganglionic neurons, this release taking place within the ganglia. Following this impulse the parasympathetic post-ganglionic fibers release at their neuro-muscular or neuro-glandular junction, additional acetyl-choline, this release being followed by muscular action or glandular secretion. (5) On the other hand the sympathetic post-ganglionic neurons, although receiving their stimulus from the acetyl-choline released by their pre-ganglionic connections, release at their neuro-muscular and neuro-glandular endings, the substance adrenaline, or at least, according to Cannon (5), an adrenaline-like substance, sympathin.

These secretions, according to White (35), are important in diffusing the impulse in the region of the nerve ending, since all smooth muscle cells do not contain such endings. A mild stimulus will then probably produce only a minimal reaction in the muscle cells as only a minute quantity of one or another of these secretions is released, while a stronger stimulus will release a larger quantity, its diffusion will be wider, more muscle cells will be affected, and the reaction will be correspondingly greater.

Grant, Bland and Camp (9) (1932) have shown that degenerated post-ganglionic fibers apparently cause the smooth muscle cells to become more sensitive to the action of adrenaline. This fact, according to Smithwick (30) (31) (32), readily explains some of the failures of sympathectomy in the treatment of

Raynauds disease; that is, if in the operation a number of post-ganglionic fibers are destroyed or removed then there will develop in a few days to weeks a hypersensitization of the smooth muscle cells to circulating adrenaline with consequent vaso-constriction, equal in many cases to that which existed before operation. He believes that an operation which removes the pre-ganglionic portion and leaves the post-ganglionic portion intact would give better results in the operative treatment of the condition, and has devised operations with this fact in mind.

The fibers to the sweat glands, which course through the sympathetic division differ from the remainder of the sympathetic fibers in that they produce acetyl-choline upon stimulation, instead of adrenaline. (3) (36) All nerves, which upon stimulation produce acetyl-choline are designated as cholinergic, in contradistinction to those which produce adrenaline or sympathin, which are adrenergic. Therefore the parasympathetic nerves are cholinergic as are also the sudomotor fibers of the sympathetic system, while the remainder of the sympathetic fibers, except the pre-ganglionic, are adrenergic. (36)

At this point it is well to bring in two or three important features of the causalgia syndrome in order to correlate some of the previously mentioned findings with its behaviour. In the first place, according to Leriche, causalgia is primarily a vaso-dilation phenomena, and since it has been found that sympathectomy not only releases the vaso-constrictor impulses of the arteries but also the vaso-dilator to a certain extent, he performs this operation to relieve the symptons. If causalgia is due to dys-

function of the vaso-dilator mechanism which presumably is, for the most part, a para-sympathetic function, and since these fibers are cholinergic motor fibers of the sympathetics may also play a part in producing the picture. Further substantiation of this possibility lies in the fact that the parts most frequently affected by the burning pain and trophic disturbances are the parts which are most abundantly supplied with sweat glands. The palms of the hands, according to Gray, contain about six times as many sweat glands as the trunk and thigh. The latter rarely, if ever, enter into the condition. Again, it has not, to my knowledge, been explained why injuries to other parts where no damage to the sympathetics has been suffered, may produce the syndrome. An explanation of this may rest in that in such injuries as those of the median nerve it may be that there is damage to the para-sympathetic fibers, which are probably cholinergic, and which course through the nerve, having reached it from the posterior root of the spinal cord.

With the above conceptions of autonomic function in mind, I believe that we may find most, if not all, of the answers to the puzzling pictures that are presented by causalgia, and its response to treatment. I wish then, to consider it as a dysfunction of the cholinergic portion of the autonomic nervous system, due primarily to injury suffered by one or another of the cholinergic groups of fibers, whether such injured group is a part of the anatomically distributed sympathetic division or a part of the parasympathetic efferents which are presumably distributed over the spinal nerves.

In the following sections I will attempt to further harmonize such postulation with the symptoms and treatment of the condition.

Symptoms

Weir Mitchell's classical description of the syndrome of causalgia, as previously quoted, gives in detail all of the important symptoms and objective manifestations of the disease. I will repeat only briefly these findings.

There is always the history of an antecedent injury, the most frequent type of which are injuries to either the median or the sciatic or tibial nerve, or injuries to such arteries as the axillary, brachial and femoral. (20) (23) The onset of the burning pain and hyperesthesia of the affected part is most often from a few days to several weeks following the injury, rarely at the time of injury. (20) The hand or other affected portion becomes splotchy reddened from vaso-dilation taking place in the sub-cutaneous tissues. If this state continues for a variable period of time then the part takes on the 'glossy skin' appearance so characteristic of advanced stages of the condition. (23) The pain is most often superficial, but at times it is also in the joints or deep tissues. Long continuation, however, always produces final reference of the pain to the skin alone. (23) The intensity of the burning varies, and in the worst cases the patient seems to instinctively seek to keep the hand continually moist, so that finally the skin becomes macerated in addition to the remaining findings. In such long-

standing cases the pain seems to produce marked mental changes so that the least possible physical or emotional disturbance will bring an acute exacerbation of an already intolerable pain. (7) (18) (20) (23)

The most frequent type of nerve injury preceding causalgia is an injury in which there is laceration but not complete severance of the nerve; there is seldom enough damage to the nerve to result in much more than a partial paralysis or paresis. (20) In such an injury as this it is easy to see how it would be possible to damage the finely myelinated efferent parasympathetic fibers of the spinal nerve, without producing very grave injury to the remaining sensory and motor fibers. At the site of the injury there may develop a neuroma which may initiate centrally referred reflex stimuli, resulting in stimulation of the cholinergic fibers which remain intact in the damaged nerve and cause a consequent vaso-dilation in the area. On the other hand, there may be an analogous phenomenon to that which takes place after degeneration of the adrenergic fibers producing adrenaline sensitivity in the arteries; that is, after degeneration of the cholinergic fibers, a period of time elapses during which degeneration takes place and the smooth muscle cells then become sensitive to minute amounts of acetyl-choline. This sensitivity of the affected smooth muscle cells would then produce vaso-dilatory response to minimal concentrations of the substance. Since acetyl-choline is destroyed by choline-esterase there may then be an additional factor entering into this part of the picture. Although I have nothing on which to base the premise other than the known fact of

ionic changes in inflammatory fluids and ischemic tissues there is the possibility that in the area of constant vaso-dilation there may be a change in the chemistry which prevents the proper formation of choline-esterase to nullify the effects of the acetyl-choline present. In either case, whether there is increased sensitivity to acetyl-choline due to degeneration of the cholinergic fibers, or lack of destruction of the acetyl-choline present, the result would be the same, the arteries would be in a constant state of vaso-dilation.

In cases where there has been an immediate onset of the burning pain at the time of the injury, there is a possible explanation in that there may have been such an injury as to cause an immediate stimulation of the cholinergic fibers of the nerve, bringing about the extreme vaso-dilatory response without the necessity of neuroma formation or fiber degeneration. Such irritation could conceivably be caused by edema of the adjacent tissues or by hematoma formation, or even by the presence of a foreign body such as a bullet or piece of shell in the proper position.

The other type of injury which results in causalgia, and, according to Leriche more frequently than nerve injuries, is the type in which an artery is damaged. In such an injury there is of necessity damage to the cholinergic fibers belonging to the sudomotor group coursing through the periarterial sympathetics and to the other previously mentioned vaso-dilator nerves which are apparently present in this system. These nerves, however, according to White, have not been iso-

lated. It is [illegible] possibility that [illegible] vaso-dilation as occurs from sympathetic stimulation may be due to acetyl-choline production and diffusion [illegible] vaso-motor fibers, but in the [illegible] vaso-dilatory fibers [illegible] the sympathetic.

The [illegible] peripheral sympathetic [illegible] the clinical picture of causalgia. Now injuries to this group of cholinergic fibers, that is direct or reflex stimulation of acetyl-choline in excess, absence or diminition of choline-esterase in the involved area, or hypersensitivity of the smooth muscle cells to acetyl-choline due to regeneration of the cholinergic fibers. The frequent occurence of excess sweating over the region also, as before stated, supports the conception of causalgia as primarily a dysfunction of the cholinergic nerves.

Treatment

Weir Mitchell originally treated the condition with the use of wet dressings, blistering applications , or with morphine injected directly into the affected tissues. Success with this type of treatment, as it has been since with all other forms of treatment, both medical and surgical, has been variable. Some cases cleared up then, as they do now, with or without treatment, sometimes in the course of a few weeks and sometimes after a period of months. Explanation of this spontaneous relief, according to White (35), probably lies in the regeneration of affected fibers and the restoration of normal function. When viewed in the light of

cholinergic nerve dysfunction, this relief would come with regeneration, or with the restoration of a normal balance between the acetyl-choline and choline-esterase present, or with the reduction of sensitivity of the smooth muscle cells to acetyl-choline. It is probable that the few successes obtained by Mitchell and others by the use of empirical means were due to one or another of these mechanisms.

The first real advance in the treatment and the first with a sound physiological basis came with Leriche's sympathectomy; this operation or the operation of blocking the injured nerve trunk with alcohol has been successful in many cases, according to White. Neither have been completely successful. Harris (11) (1926) states that in slight cases light massage may be bearable, and if persisted in may result in a cure; however the lightest touch, not to mention massage is rarely tolerated. In some patients, he states that anodyne liniments such as opium and belladonna may give relief but that the more resistant cases should have the site of the injury explored, the scar tissue excised and the nerve decompressed. If no improvement results in a fortnight he reopens the wound and injects the nerve at this point with 90% alcohol. This will, in some cases, but by no means in all, block the pain impulses. It will in addition result in paralysis of the innervated portion, at least until regeneration takes place.

White (35) (1935) states that all cases should be studies by novocaine block for purposes of localizing the route of the pain. If clear-cut relief is obtained by blocking the sympathetic ganglia,

he advises that a ganglionectomy be done or that the ganglia be destroyed by alcohol injection. This procedure, he states, has given lasting relief in cases reported by Pierre (1930), Spurling (1930) and Flothow (1930). In cases where diagnostic novocaine block has shown that ganglionectomy will be ineffectual, intraneural injection of alcohol is advised. Lewis and Gatewood (21) (1920) report three successful cases so treated. The nerve is freed up several centimeters above the injury and one cc. of 60% alcohol injected at this point. White advises the use of ligatures applied temporarily to insure localized destruction of the nerve. With this method he states that regeneration can ordinarily be counted upon within three or four months, and that frequently no recurrence of the pain follows. If all of the above fail he believes that the only recourse is one of the following radical spinal cord operations: Subarachnoid alcohol injection or cordotomy with section of the spino-thalamic tract.

Leriche has been the foremost exponent of sympathectomy on the basis of his belief that the disorder is primarily a dysfunction of that system. This operation again has not always been successful. According to the postulation advanced in this paper the only cases in which this operation would be successful are those in which the primary injury has resulted in damage to the sudomotor, cholinergic nerves of the periarterial sympathetics. Damage to the arteries is, according to Leriche, the most frequently injury leading to causalgia. Kwan (18) (1935) reports a case occuring in China due to a war wound, in which he found the axillary artery to be only a fibrous cord, weeks after the in-

jury. All operations, of which there were three done in this case, were totally unsuccessful until thoracic ganglionectomy was done. This bears out the above contention that in damage to the periarterial sympathetics with cholinergic dysfunction, it is necessary to relieve by sympathectic ganglionectomy and that this is the only type of causalgia which can be so relieved except where there is damage to the same group before it leaves the spinal nerve.

As before mentioned White states that where diagnostic blocking of the sympathetic ganglia show that sympathectomy will not bring relief, that alcohol injection of the spinal nerve should be resorted to.

From the success of both these operations but the lack of infallibility in either it is apparent that either or both the cholinergic group of fibers of the sympathetic and of the spinal nerves may be at fault. Naturally an operation directed at the sympathetic ganglia would fail if the difficulty lay in a spinal nerve parasympathetics, and vice versa. In the rare cases of failure of either operation we may explain such failure on the same basis as Smithwick's explanation of failures of sympathectomy in Raynaud's disease--that is [illegible] hypersensitization of smooth muscle [illegible] to acetyl-choline [illegible] failure of production of choline-esterase to inhibit its action.

Conclusion and Summary

1.
Causalgia is a condition following nerve, artery and occasionally other injury, which is characterized by burning pain of varying degree, and at times by trophic changes of glossy skin over the

affected part.

2. It is essentially an excess vaso-dilation of the small blood vessels of the painful area which may be due to

(a) Reflex stimulation of parasympathetic cholinergic fibers which are probably present in spinal nerves, reaching them by way of the posterior roots but with ~~ganglia~~ cell bodies located within the cord.

(b) Irritation of these same fibers causing an excess production of acetyl-choline in the affected part.

(c) Changes in the area involved which prevent the formation of adequate choline-esterase to properly inhibit the action of the acetyl-choline produced.

(d) Both (b) and (c) above existing simultaneously.

(e) Degeneration of the above fibers and a sensitization of the smooth muscle cells to circulating acetyl-choline, with again the possibility of insufficient choline-esterase.

(f) Degeneration of the cholinergic sudomotor fibers of the sympathetic system with sensitization as in (e).

(g) Irritation of these fibers causing excess acetyl-choline production affecting both the vaso-dilator fibers and the sweat glands.

(h) Central reflex irritation of the entire group of cholinergic fibers to the part from either of the two groups of fibers.

3. Treatment has included many empirical procedures and limited success has followed all methods probably due to spontaneous regeneration of the aforementioned fibers.

4. Best results have been obtained by sympathetic ganglionectomy and alcoholization of the nerve trunk.

5. Neither of these has been entirely successful, it is believed because:

(a) Sympathectomy should be successful only if the sudomotor cholinergic fibers are at fault. This can be determined by novocaine infiltration of sympathetic ganglia.

(b) Alcoholization of the trunk should be successful only in cases where the parasympathetics of the trunk are involved.

(c) In some cases both groups may be injured.

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