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THE TREATMENT OF TETANUS*

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The treatment of tetanus must be based on an understanding of the cause and a knowledge of the march of symptoms and signs in infections of different degrees of severity.

The tetanus bacillus grows under anaerobic conditions, so that the disease has the greatest chance of developing when bacilli or spores are introduced deeply into the tissues by penetrating wounds. Laceration of tissues with pyogenic infection and the presence of foreign bodies in the wound appear to favour its development. The tetanus bacillus is found in the intestines of various animals, particularly herbivora, where it exists without causing pathogenic effects; it is present in the soil, particularly in highly manured districts. It is prevalent in the intestine of the horse, and no doubt horse ploughing has helped to disseminate the organism. Owing to the resistant nature of its spores the sterilization of catgut has long presented a problem of which occasional disastrous cases of post-operative tetanus are a reminder.

The prophylactic value of tetanus antitoxin was conclusively proved during the war. It is certain that if tetanus antitoxin could be given in every case of infection within twenty-four hours very few cases of the actual disease would occur, and the few which did would be very mild. The almost universal use of prophylactic antitoxin after all deep and infected wounds has altered the type of wound which now causes tetanus in civil practice. Deep suppurating wounds of the classical type no longer give rise to the disease because they lead to the use of prophylactic antitoxin, which is successful in preventing its development. Instead, it occurs after comparatively slight and often superficial wounds which, though infected, have not been properly cleaned or dressed. Often no medical advice is asked for or, if it is, the wound appears too slight to the doctor for antitoxin to be necessary. Mild whitlows in agricultural workers and superficial abrasions in children which have been allowed to scab over without being properly cleaned are two of the commonest types of wound to cause the disease. A scab over a superficial abrasion which has not been properly cleaned will form a cavity full of pus in which anaerobic bacteria will germinate and so cause the disease. The danger of such comparatively slight wounds is not at present sufficiently recognized. If it were, and antitoxin were given in such cases, much tetanus would be prevented.

Clinical Types of the Disease

It is convenient to divide the disease into five types, although it must be remembered that these types merge into each other:

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Type 1.—That in which there is local tetanus only.

Type 2.—That in which there is generalized tonic rigidity, involving particularly the masseters, the muscles of the spine, chest, and abdomen, and, to a lesser extent, the limbs. This rigidity gradually increases, and then slowly passes off, the whole process lasting from one to four weeks. Reflex spasms and reflex excitability are slight or absent.

Type 3.—That in which the tonic rigidity described in Type 2 passes into the stage of reflex spasms, occurring at intervals, and brought on by the slightest stimulation. Such spasms persist for a few days to a fortnight and then cease, leaving the patient again in the state of tonic rigidity, which slowly passes off.

Type 4.—That in which the spasms described in Type 3 come on rapidly, becoming progressively more frequent and prolonged until they are almost continuous; death, often preceded by hyperpyrexia of 108° to 110° , takes place from cardiac or respiratory failure.

Type 5.—Cephalic tetanus, in which generalized convulsions may occur early with cranial nerve palsies and dysphagia.

How the Symptoms are Produced

Meyer and Ransom¹ and others have shown how toxin absorbed from a wound spreads to produce symptoms, and that the severity of a case depends on the amount of toxin absorbed. The mechanism is probably as follows:

Type 1.—When a very small amount of toxin is slowly absorbed it passes up the axis cylinder of the nearest motor nerve and affects the anterior horn cell or its connexions, local symptoms being originated in the muscles supplied by those cells. In producing this effect on the nerve cell the toxin is absorbed, and none is left to diffuse further into the nervous system.

Type 2.—When a slightly larger amount of toxin is absorbed it passes via the lymphatics into the general circulation and so up the motor nerves remote from the wound. The anterior horn cells are affected generally, but there is insufficient toxin to diffuse further into the nervous system. The jaw muscles are first affected because the fifth nerve is short, and the toxin has less far to travel before it reaches the anterior horn cells.

Type 3.—With still larger amounts of toxin the anterior horn cells do not absorb it all, but some diffuses into the nervous system, affecting more and more synapses. Each synapse affected absorbs a certain amount of toxin, and so the process is stopped before vital nerve centres are involved. If the patient does not die from exhaustion or respiratory spasm the toxin is gradually neutralized and its effect passes off.

Type 4.—The dose of toxin is larger and the process described in Type 3 progresses until such vital centres as the medulla or the heat-regulating mechanism are involved, and death occurs.

Type 5.—Cephalic tetanus often follows severe head wounds. Large doses of toxin pass up the relatively short cranial nerves and produce symptoms before the anterior horn cells in the

cord have had time to be involved. Severe cranial nerve symptoms therefore occur early and dominate the clinical picture.

Diagnosis

When the symptoms of tetanus have appeared it is important that a diagnosis should be made as soon as possible, because the earlier treatment is begun the greater is the chance of recovery. The most common early symptoms are stiffness of the jaw, often combined with pain in the neck, back, or abdomen. Occasionally difficulty in swallowing precedes the jaw stiffness. On examination, abdominal rigidity, sometimes as severe as that seen in acute abdominal conditions, fixed arching of the back (see figure), and increased tone of the affected

Tetanus showing arching of the back during the phase of tonic rigidity.

muscles on manipulation are the commonest signs. The facial expression is characteristic during the first twenty-four hours.

I have seen tetanus mistaken for diphtheria and tuberculous and other forms of meningitis; while tuberculous meningitis, peritonsillar abscess, and local conditions of the mouth have been mistaken for tetanus. Early diagnosis should, however, rarely present difficulty if the foregoing points are remembered, particularly the association of stiffness of the jaw and pain in the neck or back made worse by manipulation.

Prognosis when First Seen

From the point of view of treatment it is important to be able to assess the severity of a case of tetanus as soon as possible. It is well known that this tends to be inversely proportional to the length of the incubation period. This period is of great prognostic value, if it can be measured accurately, but there is always the fallacy that a wound may not have been infected with tetanus when it was incurred but that infection took place later. It is probably for this reason that cases of greater severity occur occasionally than would have been expected from the apparent length of the incubation period.

There is, however, a second measurement which is of greater value in assessing the prognosis, and this is the time from the occurrence of the first symptom to the appearance of the first generalized reflex spasms. For convenience I have termed this the "period of onset." Usually the longer the incubation period the longer the period of onset, but if there is a discrepancy and the period of onset is shorter than would have been expected from the length of the incubation period, then the period of onset gives the best indication of the severity of the disease.

For my own series of twenty-five cases,^{2 3 4} the following rule is approximately correct. In an otherwise healthy patient, if the incubation period is more than seven days, the "period of onset" is more than two days, and the combined periods are more than nine days, recovery should occur. On the other hand, if the incubation

period is less than seven days, the "period of onset" is less than two days, and the combined periods less than nine days, recovery is unlikely.

Prognosis also depends on other factors, of which the more important are: the general health, physique, and age of the patient; the severity and response of the wound to treatment; the ability to take nourishment; and the severity of the spasms. These considerations are useful in estimating how quickly the reflex spasms are likely to come on, how severe they are likely to be, and how long they will last. They are thus a useful guide to avertin treatment, which will be discussed more fully later.

Antitoxin Treatment

Treatment should be begun as soon as possible after the first symptoms have appeared, and should be directed along three lines: (1) The prevention of further absorption of toxin by the central nervous system; (2) the control of reflex spasms, which kill by exhaustion or by respiratory spasm and suffocation; and (3) the maintenance of strength by giving sufficient food and fluid and promoting sleep. Further absorption of toxin can probably be prevented in two ways: by giving antitoxin and by treating the wound.

Considerable difference of opinion has existed as to the best method of giving antitoxin. Toxin is formed locally in the wound, and reaches the motor cells of the central nervous system in the manner described. It is evident that the first symptoms appear when a certain amount of toxin has reached the nervous system, and that in most cases toxin is still at this stage passing into the nervous system from the wound and general circulation. In most patients symptoms will appear before a fatal dose has reached the nervous system, and the amount already there can be neutralized completely, as shown by cases which recover. If, therefore, further inflow of toxin from the wound and circulation can be prevented soon enough, recovery is simply a matter of time.

Consequently the aim of antitoxin treatment is to bring antitoxin in contact with toxin in large amounts as soon as possible after the first symptoms have appeared. At this stage the toxin still present in the blood and lymph can clearly most speedily be neutralized by a large intravenous dose of antitoxin.

Intrathecal and Cisternal Routes

By the time the first symptoms have appeared, however, some toxin is passing up the axis cylinders of the motor nerves, some has reached the motor nerve cells, and some is diffusing into the nervous system. It is with the hope of neutralizing this toxin that the intrathecal and cisternal routes have been advocated. Whether this object can be attained at all, and if so better by intrathecal than by intravenous injection, is still disputed. Ransom¹ states that toxin which has reached the nervous system is inaccessible to antitoxin. The problem can be studied from three angles: from a consideration of some points in the anatomy and physiology of the central nervous system, from certain animal experiments, and from clinical results.

Weed⁵ has shown that the cerebro-spinal fluid comes mainly from the choroid plexus, a small amount also passing out along the perivascular spaces to the sub-arachnoid space. From there it travels through the arachnoid villi into the venous sinuses. Fluid introduced into the theca will therefore tend to pass into the veins by the arachnoid villi, and will not come at once into close contact with the nervous tissue.

This suggests that the intrathecal route is inferior to the intravenous. All parts of the brain and spinal cord

are richly supplied with blood vessels and capillaries in close contact with the nerve cells themselves. Antitoxin, therefore, would reach these nerve cells more quickly when given directly into a vein than if it were first injected into the spinal theca and then absorbed into the venous sinuses through the arachnoid villi.

Florey and Fildes⁶ compared the two routes in rabbits. In order to be certain that the antitoxin passed out into the nervous tissue and not through the arachnoid villi into the venous sinuses they used a method of reversing the normal direction of flow of the cerebro-spinal fluid suggested by Weed. This consisted in injecting hypertonic saline intravenously so that the fluid from the arachnoid space was sucked in around the pericapillary spaces into the perineural spaces. Using this method they found that the intrathecal route had no advantage over the intravenous.

The opinions of clinicians differ. This is not surprising, because tetanus is such a variable disease that it is very difficult to compare clinically the results of two different routes, and this does not appear to have been done satisfactorily. Many observers have used more than one route in each case, or confined themselves entirely to one route in a series. The comparison of different series of cases means nothing unless a most careful comparison of each individual case is also made.

From theoretical and experimental considerations the intravenous route appears to have most in its favour, for it is clearly the most rapid way of bringing antitoxin into the general circulation, and probably also of bringing it in contact with nerve cells. Intrathecal injection, on the other hand, has several disadvantages. Lumbar puncture must to some degree irritate the nervous system, and to perform it in tetanus a general anaesthetic is necessary. In order to give sufficient antitoxin a large amount of cerebro-spinal fluid must be withdrawn. The injection of serum into the cerebro-spinal fluid is liable to cause a serous meningitis within a few days to some weeks after the injection and, if this occurs when the symptoms of tetanus are still present, it may cause a serious exacerbation. These objections also apply to the cisternal route.

Repetition of Doses

The next question is whether repeated doses of serum should be given after the large initial dose. The practice of most writers appears to be to give repeated doses of serum daily or at intervals of a few days until the disease has almost subsided. The desirability of giving repeated doses depends on the fate of the antitoxin originally injected. If this disappears rapidly it is clearly more important to give repeated doses than if it continues to circulate. Dean's⁷ evidence on this point suggests that injected antitoxin continues to circulate for a considerable period after injection, but no actual figures showing the rate of disappearance appear to be available. The fate of injected antitoxin was therefore investigated by Spooner³ in four patients, each of whom had been given a single initial dose of 200,000 units. The results of this investigation indicate that seven days after injection there are over 10 units of antitoxin per c.cm.—that is, a total of 50,000 units—still left in the circulating blood, and at the end of fourteen days between 3 and 5 units per c.cm. Since a prophylactic dose of 1,500 units is sufficient to protect in most cases, even from a severe and badly contaminated wound, the possibility of gaining any advantage from a further injection of antitoxin before the tenth day appears to be doubtful.

In my own cases I started by injecting antitoxin by all routes in repeated doses, but in view of Spooner's results I have abandoned this in favour of one large intravenous dose of antitoxin (usually 200,000 units) given

as soon as possible. The latter method has been used in the last fifteen cases, and there has been nothing in the results to suggest that anything has been lost by this. This antitoxin is given with the sole idea of preventing further absorption of toxin from the blood and lymph, and not with the hope of neutralizing toxin which is already producing its effect in the nervous system. There is no evidence to suggest that the latter is possible.

Treatment of the Wound

When the first symptoms appear it is probable that in most cases toxin is still being formed in the wound and being absorbed. It is therefore important that this should be prevented as soon as possible by thorough local treatment. Disturbance of the wound may cause further absorption of toxin, and it should therefore not be touched until the antitoxin has had ample time to reach the tissues to neutralize immediately any further toxin which is absorbed. Exacerbations of the disease have been known to follow operation on a healed wound, and the disease has been known to develop after operation on old war wounds for the removal of a foreign body, probably by stirring up and releasing infection pent up in an old scar. For this reason I am always careful to do nothing to disturb any wound for at least an hour after the intravenous injection has been given.

After this period thorough local treatment is very important. All scabs should be carefully removed, foreign bodies and septic material be evacuated, and the wound be syringed with hydrogen peroxide. In some cases excision of the edges of a wound may be desirable, and penetrating wounds should be opened up. Whitlows should be incised, and if the nail is involved it should be removed. Light porous dressings which do not exclude the air should then be applied four-hourly. Care should be taken that superficial healing does not take place.

Control of Reflex Spasms

Tetanus patients should be kept as quiet as possible in a darkened room. They should lie on a water bed and the bedclothes should be cradled. All necessary manipulation should be done as quietly as possible and at times when the patient is most deeply under the influence of drugs. In all but mild cases special day and night nurses are essential.

In mild cases in which there is tonic rigidity only without reflex spasms, and trismus is not severe enough to prevent food being given, mild sedatives such as bromide are all that are required. The reflex spasms are the dangerous symptom, and kill by exhaustion or respiratory spasm; and when, as is usually the case, they are associated with severe trismus, they make feeding difficult or impossible. Directly they appear every effort should be made to control them and keep them controlled. Avertin, the use of which in tetanus was first suggested by Momburg and Rothhaus,⁸ is undoubtedly the most valuable drug for preventing the reflex spasms and relaxing the jaw. Given rectally in doses of from 0.07 to 0.1 c.cm. per kilo of body weight, it usually stops reflex spasms and relaxes the jaw for a period of from four to six hours. As soon as the spasms begin to return a further dose should be given, the exact amount being judged by the effect of the previous one and the severity of the spasms. Very severe spasms involving the respiratory muscles and threatening suffocation are an indication for a larger dose. Doses usually have to be given at intervals of six to eight hours, and should be continued according to the severity of the spasms. As these grow less their frequency should be reduced.

The number of doses and the amount of avertin which can be safely given in this way is not at present known. Parsons⁹ showed that a dose of 0.475 gram per kilo could produce fatty degeneration of the liver in a rabbit, so that the danger of toxic effect must not be overlooked. I have given 24.4 c.cm. in twenty-three days⁴ (eighty-one basal anaesthetic doses) to a baby who started severe tetanus on the seventh day after birth, without any apparent ill effects. Of the total amount, 18 c.cm. were given in nine consecutive days, an average of over seven basal anaesthetic doses per day.

The possible dangers of the treatment have to be weighed against the severity of the disease. In my experience avertin will in most severe cases produce complete control of the reflex spasms, relaxation of the jaw, and lessening of the tonic rigidity about ten minutes after it has been given, and will maintain this relief for from three to eight hours according to the severity of the disease. The only ill effects which appear to be directly due to avertin are on the respirations. These may become more rapid and shallow about ten minutes after it has been given, and slight cyanosis may appear after about half an hour. For this reason it is advisable in some patients to inject atropine hypodermically if such respiratory symptoms appear, and warmed nasal oxygen should always be given when there is cyanosis. Slight rectal irritation occurred in one case as the result of frequent dosage. I have now used avertin in twelve cases, and I have never seen any ill effects which could be attributed to it. On the other hand, it has certainly saved several patients who would otherwise have died.

Paraldehyde is another drug which is valuable for producing sleep and relaxation, but it is not so effective as avertin. It may be given rectally in normal saline (1 drachm to 1½ oz.) in doses up to 6 drachms. I have found the combination of paraldehyde by day and avertin by night useful, but it is probably not as good as, and no safer than, repeated doses of avertin only.

For sudden severe respiratory spasm nitrous oxide and oxygen, or even chloroform or ether, may be necessary until the patient can be put under the influence of a basal anaesthetic. Chloroform or ether, however, should only be used in extreme emergency, their repeated use being very undesirable. Morphine should be used very sparingly on account of its depressing effect on the respiratory centre. It is, however, useful at times.

Curare for Control of Spasms

The idea of using curare to control the spasms of tetanus is an old one, but its administration is attended with great difficulties, and has never met with convincing success. Hartridge and West¹⁰ have used curare to control the tetany of parathyroidectomized dogs. They found considerable variation in the strength of different samples, and that only two specimens out of seven possessed the power of removing tetany in the dog without causing paralysis. West¹¹ used one of these samples in the treatment of seventeen cases of muscular rigidity resulting from diseases of the pyramidal and extra-pyramidal motor systems, and found that in doses which caused no detectable weakness or loss of power there was considerable reduction of rigidity while under the influence of the drug. The variation of strength and mode of action of different samples makes dosage a very difficult problem until some accurate method of standardization is discovered.

Florey, Harding, and Fildes¹² have used curarine to control the spasms in rabbits inoculated with tetanus toxin. They found that by injections at intervals of half an hour they were able to maintain paralysis, and so control the spasms and rigidity. They suggested that

curarine might be used to control the spasms of human tetanus, provided that a Drinker artificial respirator was used to obviate the danger of a slight overdose causing respiratory paralysis. West¹³ has recently treated three cases of very severe tetanus with curarine given by the continuous intravenous drip method. He suggests that this is the best method at present available, but emphasizes that the treatment is experimental, and should only be used for patients who will certainly die if treated by other methods. I have treated three cases with subcutaneous curare, and in one of these curare may have been the deciding factor which led to recovery.

The second case was interesting. It was the most severe case of tetanus I have ever seen. The spasms, which had been continuous, and of the most intense severity, were almost completely controlled by curare for the eight hours before death. In spite of this the general condition of the patient did not improve, and hyperpyrexia of 108° F. occurred shortly before the end. This seemed to show clearly that if sufficient toxin has been absorbed to penetrate deeply into the nervous system and reach certain centres in the brain it will kill quite regardless of whether the spasms are controlled or not. Until some method is found of neutralizing toxin in the nervous system such patients will inevitably die. In most cases, however, a sublethal dose only has been absorbed by the time the early symptoms appear, and if the further absorption of toxin is stopped by antitoxin and by treating the wound, and general exhaustion is prevented by controlling the spasms, recovery may follow.

Since using curare I have had considerable further experience with avertin. Avertin can do all that was hoped of curare or its derivatives with very much less risk to the patient, and I feel, therefore, that at present curare and curarine should not be used until more is known of their action.

Maintenance of Patient's Strength

An attack of tetanus means prolonged exertion without rest or relaxation, associated with toxæmia, severe pain, and often a high temperature. To pass successfully through such an ordeal a great deal of food is clearly of vital importance. Some idea of the amount of work which a patient with tetanus has to perform may be obtained by lying for a few minutes with the shoulders on one chair and the buttocks on another, keeping the back slightly arched. Further, a patient with a period of onset of twenty-four hours will, if he survives, probably have reflex spasms over a period of three weeks, with a period of onset of forty-eight hours reflex spasms for from one to two weeks, and with a period of onset of four days reflex spasms for one week.

In an adult patient an attempt should be made to give at least 2,000 calories daily. Every tetanus patient should have a special nurse, her main duty being to see that as much food as possible is given. Glucose lemonade and egg and milk are satisfactory foods; these should be given hourly or more often if the patient is taking well. Usually tetanus patients are very thirsty, and will take fluids well. If sweating is profuse, normal saline solution should be given by the mouth or rectally to make up for the loss of chlorides. If trismus is severe removal of teeth may be necessary. Avertin is valuable in relaxing the jaw, and so making feeding easier. Under avertin it is sometimes possible to pass a stomach tube, which is left *in situ* so that the patient can be fed. When the muscles of deglutition are early affected feeding becomes almost impossible by any other means, and the outlook is correspondingly bad. The value of the stomach tube when tetanus occurs in infants was well shown in the case of the baby who was kept under the

influence of avertin for twenty-three days. Here the tube was passed by the nasal route and left *in situ*, being removed once daily to be cleaned. By this means the average daily intake of food for the whole twenty-three days was 260 calories, the theoretical caloric requirement being 300 daily.

Rectal feeding is useful in some cases, and patients seem to retain fluids well, but it is quite impossible in a severe case to give sufficient nourishment by this means alone, and intravenous infusions are necessary. The importance of giving sufficient food can hardly be over-emphasized, and success depends largely on nursing efficiency.

Summary

The treatment of tetanus may be summarized as follows:

1. As soon as possible after the diagnosis is made give 200,000 units of antitoxin (int.) intravenously.
2. One hour after the antitoxin has been given treat the wound. After appropriate surgical treatment irrigate with hydrogen peroxide.
3. Keep the patient as quiet as possible in a darkened room. If reflex spasms have not begun give large doses of bromide and as full fluid or semi-fluid diet as possible.
4. If the period of onset is four days or longer, and the reflex spasms are not severe, treatment with avertin need not be started at once, but it should be begun if the spasms become severe or if the patient shows signs of exhaustion. In such a case one basal anaesthetic dose daily may be sufficient.
5. If the period of onset is three days or less treatment with avertin should be begun at once and continued according to the severity and duration of the spasms. With prolonged spasms causing respiratory embarrassment the dosage should be larger and more frequent.
6. When avertin treatment has begun nasal oxygen should be given as required, and atropine hypodermically if there is respiratory difficulty.
7. Arrange that any necessary manipulations such as the giving of enemas, rectal salines, hypodermic injections, or local treatment of the wound are undertaken when the patient is most deeply under the influence of avertin.
8. Continue the avertin treatment as required, and reduce the dose gradually as the spasms become less.
9. If hyperpyrexia occurs treat by tepid sponging.

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The Ministry of Health has published a list of approved treatment centres under the Public Health (Venereal Diseases) Regulations, 1916, with particulars as to the days and hours for medical examination and treatment, and for intermediate treatment by or under the supervision of nurses or male attendants. A list of the hostels and other institutions for women which accept in-patients under the approved schemes of local authorities for the treatment of venereal diseases is appended. This list, designated "7, May, 1936," supersedes its predecessor, which was issued in March, 1934.

CAVERNOUS SINUS THROMBOSIS

A STUDY OF THE CASES OF RECOVERY

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Thrombophlebitis of the cavernous sinus is generally considered a rare but fatal condition; a study of the literature published on this subject reveals but a small number of cases of recovery. It is the object of this paper to review these cases to date, not only those recorded by Eagleton in 1926 but also those which have been published subsequently, to add one case from my own experience, and to ascertain what may be learnt from this material with regard to the prognosis and treatment of this grave condition.

Historical Review

The first mention of cavernous sinus thrombosis was made in 1818 by Abercrombie, who described the condition from a post-mortem finding. Vigla, in 1839, was probably the first to make a clinical diagnosis, but it was not until 1902 that attempts were made to attack this sinus surgically, by Dwight and Germain. With regard to the first recorded case of recovery there exists some doubt as to the correct diagnosis in several of the earlier publications, but probably that of Bircher in 1893 is the most authentic, and in this case the thrombosis was probably aseptic.

Anatomical Considerations

Though from the standpoint of operative surgery the cavernous sinus is one of the more inaccessible parts of the body, from the anatomical and pathological aspect it is open to attack from many directions, and to that extent is remarkably vulnerable to any pyogenic infection of the head and neck which has overcome the bounds of tissue resistance and invaded the blood stream. Without entering into any detail of the anatomy, it may be useful to recall that the main connecting channels of the cavernous sinus anteriorly are the ophthalmic veins, communicating with the angular veins and the venous system draining the region of the face, the pterygoid plexus, connecting with the venous drainage of the buccal and pharyngeal region below, and the petrosal sinus, communicating with the jugular bulb and the internal jugular, below and behind. The fact that the veins in this region possess few valves permits not only the rapid invasion of the sinus, which may occur through afferent channels such as the ophthalmic veins, but also a slower retrograde thrombosis and spread of infection along efferent tracts such as the internal pterygoid plexus and petrosal sinuses. Herein lies, to a great extent, the explanation of the two main clinical types of thrombophlebitis of the cavernous sinus. First, the acute fulminating invasion, usually associated with septic lesions of the face, presenting at an early date the well-known classical signs of swelling of the eyelids, chemosis, and proptosis, accompanied by the symptoms of fever, with rigors, due to the general blood stream infection. The rapid onset of meningitis and a fatal termination is, almost invariably, the result in such cases, and the diagnosis is seldom, if ever, in question.

In the second type, however, the invasion is more gradual and insidious. The septic or protective thrombosis advances in a retrograde manner against the blood stream, in the pterygoid plexus or petrosal sinus, and enters the cavernous sinus in its postero-inferior region. As may be expected, this type of case is associated generally with septic lesions of the middle ear and mastoid,