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Syphilitic meningitis

Porter S. Cannon
University of Nebraska Medical Center

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Porter S. Cannon

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INTRODUCTION

Of all diseases of the nervous system syphilis is undoubtedly the most wide-spread and the most disseminated. It affects every part of the cerebrospinal axis; the nerves, the blood-vessels the meninges, and the parenchyma of the brain and spinal cord. (23)

Etiology of Syphilitic Meningitis will not be covered in this paper as the discovery of the Spirocheta pallida, the perfection of the serologic tests, and the demonstration of the spirochete in practically all the specific lesions of the nervous system have settled all doubts as to the ultimate causation of neurosyphilis. There is some evidence to show that there is a special neurotropic strain of spirochetes with selective affinity for the nervous system. (18) But admitting that the spirochete or its toxin is the cause of neurosyphilis, it is still not known why a small percentage of infected persons ultimately develop the various affections of the nervous system and others do not. (18)

SYPHILITIC MENINGITIS

HISTORY

Syphilis appeared in Europe in the years immediately following the return of Columbus from his first voyage to America. It spread from Italy with the dispersal of the Army of Charles VIII of France in the spring of 1495. Spanish mercenaries were in Charles' army who were regarded at the time as the source of the epidemic that attacked it. This source of the disease has been definitely mentioned in contemporary Spanish documents. It was recognized as a new disease and no name existed for it.

Its spread and recognition as a new disease can be traced through contemporary documents that have to do with the control of the epidemic. These documents are all subsequent to the return of Columbus. Attempts to show that some of these documents are of earlier origin and that there were descriptions of diseases identical with syphilis in the Middle Ages and earlier in the fifteenth century have failed. On the contrary the number of documents concerned with syphilis immediately after the return of Charles' army is innumerable. This circumstantial historical evidence is emphasized by the direct evidence, which was first unearthed by Montejo, of many Spanish documents of the period, specifically reporting the occurrence of syphilis in the West Indies, and its transmission to Europe by men in Columbus' fleet. All ancient literature has been examined for syphilis, but no convincing

description of it has been found.

Evidence from ancient bones points only to America, the number of even suspicious bones found in the Eastern Hemisphere is relatively few. No convincing specimans have been found. In contrast, in America the number of ancient bones that are probably syphilitic is large. Such bones have been found in many collections. Bones have been found from widely distributed areas which meet the exacting criteria of syphilis.

The preponderance of evidence for the American origin of syphilis is overwhelming. (1)

The spread of syphilis from Italy can be traced in the local chronicles of the time, step by step with the dispersal of Charles's army. It appeared in France and Germany and Switzerland early in 1495, in Holland and Greece in 1496. It spread to England and Scotland in 1497; to Hungary and Russia in 1499.

Studies of syphilis began to be recorded immediately. Albert Durer illustrated syphilis in a pamphlet published in 1496, and as early as 1497 or 1498 Bartholomew Steber's "Treatise on Syphilis" was published. The literature of syphilis in the sixteenth century and the knowledge of the disease which it shows is of surprising extent. Syphilis, with its constitutional symptoms, was distinguished from the long known venereal diseases at the

beginning of this period. The chancre was recognized as a lesion of syphilis, and gonorrhea and soft chancre were separated from it by their lack of constitutional symptoms. Unfortunately Paracelsus began the confusion of all of them by calling syphilis "French gonorrhea" in 1530, and by the middle of the century it was current. This confusion was gradually cleared up by the end of the eighteenth century. The infectious character of the chancre and of other genital lesions was recognized. Extragenital infections were known to be of common occurrence, such as infection of children from sleeping with syphilitic persons.

As early as 1497, Leoniceno in his treatise on syphilis pointed out that the internal organs were often involved in this disease and that paralysis sometimes followed. Other writers who succeded him expressed similar views. Nicolas Mans described a case of mania due to syphilis in which there were intense pains in the head, which completely recovered under the use of mild purgatives "Indian pills". (2) Astruc also in many places in his treatise mentioned syphilis of the nervous system and pointed out many types of nervous disorders due to this disease. Nevertheless John Hunter combated the theory of syphilis of the internal organs including the brain, and in this way as well as by his theory of the unity of syphilis and gonorrhea set back the knowledge of syphilis many decades. However in 1834 Lallemond showed

conclusively that the brain and meninges were sometimes affected with syphilis. While numerous contributions concerning syphilis of the nervous system followed the work of Lallemond, it was left for Virchow to describe accurately the patholcgical anatomy of gummata of the tissues, including the meninges. (2)

By the latter half of the eighteenth century there had been accumulated the great fund of knowledge of syphilis. To enumerate only some of the important items: The symptoms had been fully described, the distinction between gonorrhea and chancroid and syphilis had been made. The enormously important subject of syphilis of internal structures had been well worked out by many investigators. Hereditary syphilis was well known and its most important facts described. The dangers and importance were recognized of extragenital infections, and of mediate transmission of the disease; of infection by kissing and by innocent contact with infected individuals, as of children sleeping with syphilitic parents or of physicians and midwives from syphilitic patients; of infections from surgical instruments and from contaminated utensils.

Mercury in the treatment of syphilis comes into view almost as early as the disease itself. Paracelsus is given credit for having introduced it, but it had long been used by the Arabs in scabies, psoriasis, leprosy and other skin diseases, and was doubtless tried in syphilis. The usual method of administration was by inunction, but it was also given by

mouth, by fumigation and by the application of mercurial plasters. Arsenic was probably used by Paracelsus as early as 1530. The use of guaiacum by the Indians is mentioned in the earliest Spanish chronicles, and it was highly prized. Various other vegetable infusions, sulphur baths and hydrotherapeutic measures were used.

In 1835, Wallace established the contagiousness of secondary lesions of syphilis, and in 1834, he introduced the use of patassium iodide in the treatment of syphilis. During the last quarter of the nineteenth century the clinical distinctions between the venereal diseases were confirmed in the laboratory. In 1879 Neisser discovered the specific organism of gonorrhea. In 1889 Ducrey demonstrated in the pus of chancroid and in 1892 Unna demonstrated in the tissue the specific organism of chancroid. And, to anticipate, Schaudinn and Hoffmann in 1905, discovered the organism of syphilis. Fournier at the St. Louis Hospital Paris, demonstrated the causal relationship of syphilis to paresis and tabes. Metchnikoff failed in determining the causative organism, but he demonstrated that it could be transmitted to apes. Schaudinn reported the discovery of Spirochaeta pallida, May 2, 1905. It was not until 1909 when Ehrlich introduced arsphenamine.

Probably the first investigator to treat syphilis of the nervous system by intraspinal injections was Schachmann who in 1901 treated four cases by the injection of 1 cc. of a 1 percent solution of mercury benzoate. One case of syphilitic

myelitis is reported in detail. This patient received twenty-three injections in twenty-five days, showing marked improvement. The first injection caused restlessness, slight rise in temperature and insomnia, but by the fifth injection no untoward symptoms were observed. (3)

Horsley, in 1910 reported favorably on the use of intraspinal irrigations with solution of mercuric chloride; however the work of Swift and Ellis on the intraspinal injection of arsphenaminized serum was the first to arouse any considerable attention, and since the publication of their investigations numerous workers have applied their method and similar procedures, so that today intraspinal therapy has taken a permanant place in the therapy of syphilis of the central nervous system.

Vidal (De Cassus) 71 years ago reported and discussed a case of syphilitic meningitis which recovered. From that time on cases were reported by different observers, and in 1903 Ravaut, in a careful study of 83 cases found the spinal fluids definitely pathological in 65 percent of the series. Tobler studied normal children to obtain criteria for his subsequent study of 14 syphilitic children of whom 12 possessed abnormal spinal fluids. The year 1906 saw Ravaut and Ponselle demonstrate the presence of the treponema pallida in the brain. (4) Bonnet and Gonjut in 1855, differentiated syphilitic meningitis from the other disorders of the Central Nervous System, and established it as a distinct clinical entity. (6, 17)

OCCURRENCE

The prevalence of syphilis among peoples and among classes is a matter of sexual habits. Sexual promiscuity is the source of syphilis in any class, and the relative incidence of syphilis in any class is an index of sexual habits. The occurrence of syphilis in an individual is not necessarily a stigma, for much of it, particularly in women, is contracted innocently, but a high incidence of syphilis in any class is a mark of low sexual morality. Because of factors which are obvious, the prevalence of syphilis varies widely in different statistics; from less than 1 percent to 20 percent or more of the population are examined for syphilis. A large number of the more conservative statistics of Great Britain and the United States indicate that the incidence of syphilis is from 6 to 10 percent. But these statistics chiefly concern men, and, as it is probably at least two or three times as frequent in men as in women, they indicate an incidence of syphilis for the entire population of about 5 percent.

European statistics indicate that it is more frequent in European cities than American. Many statistics indicate that it is much more frequent in urban than in strictly rural districts. Parran, on the basis of a very wide survey of syphilis finds that "five cases exist in cities for every one in rural districts." In these same statistics Parran finds it twice as frequent in men as in women.

That is a much higher proportion in women than many other statistics show.

In certain Middle West rural areas and among certain university groups syphilis is a comparatively rare disease. (0.5 to 1 percent, Parran). The most extensive survey which has been made of the incidence of syphilis is one by the United States Public Health Service in cooperation with the American Social Hygiene Association. This survey has been made in such a way as to approximate accurately the incidence of syphilis among 26,000,000 people of the United States. It was a survey of the number of cases of syphilis under treatment by physicians on a given date--not of all syphilis. It shows that in this enormous population, 4.26 persons per thousand of population were under treatment for syphilis at a given date. This of course does not show the prevalence of syphilis at the time. It takes account of patients who sought treatment. According to these statistics, assuming a population of 130,000,000 there are under treatment in the United States at any given time over 500,000 cases of syphilis. Parran concludes that there is actually an annual crop of new cases in the United States of 871,000. (1)

OCCURRENCE OF SYPHILITIC MENINGITIS

During the course of syphilis there often develop symptoms suggesting an acute meningitic reaction which is accompanied by fairly definite changes in the spinal fluid. This constitutes what will be considered as acute syphilitic meningitis.

Meningitis of leutic origin, occurring in the very young is sufficiently rare to warrent the recording of all cases. Still points out that syphilitic meningitis and juvenile paresis of the insane resemble each other very closely.(6) The relative infrequency of the disease may be assumed from statistics quoted by Nonne,(13) in which 2 cases were reported between the ages of 1- 10. In Still's series of 100 fatal cases of meningitis, other than tuberculous, there were but 6 due to syphilis. It is entirely possible that these figures do not represent its occurence in urban communities, for there are not any figures available to determine its frequency in the fetus. If it were not for the appalling mortality in antematal and neonatal life, meningitis of syphilitic origin would undoubtedly be an every day clinical problem.

Carr (7) studied 12 cases from 1921 to 1928 at the Barnes Hospital in St. Louis. During this period 22,650 patients were admitted on the Medical service of Barnes Hospital. Of this number 2.3 percent had syphilis of the nervous system of the meningovascular type. The incidence of

acute syphilitic meningitis (12 cases) is 0.0053 or 0.05 of 1 percent in this series. The majority of the patients were in the late twenties or early thirties. Eight of the 12 cases were males.

The earliest date following infection at which involvement of the central nervous system has been noted is the case reported by Read (2) in which marked symptoms were present two weeks after the appearance of the chancre. Several other investigators have reported cases of syphilis in which the chancre was present, but no cutaneous manifestations had appeared, in which either clinical symptoms or spinal puncture or both revealed involvement of the central nervous system. Numerous investigators have reported the involvement of the nervous system slightly later in the course of the disease, that is, during the early active cutaneous manifestations. Wile and Stokes (8) go so far as to state "that in all probability every case of syphilis which reaches the secondary stage has more or less involvement of the cerebro-spinal axis."

Mazzeo (9) reported four cases in children between 5 and 24 months of age. Strom-Olsen (10) described a case occurring in juvenile dementia paralytica.

SYMPTOMATOLOGY

ONSET.

Acute syphilitic meningitis may begin abruptly or gradually. (5) The onset is generally within two to eight months following the initial lesion. Im most of the cases the patients had received early and intensive treatment, especially with the arsenicals. This is not suprising because in early syphilis it is the custom to give intensive treatment. For in the first place it is essential to abort, as rapidly as possible the spread of the syphilis and secondly to rapidly render the patient noninfectious.(7) The earliest date following infection at which involvement of the central nervous system has been noted is the case reported by Read (2) in which marked symptoms were present two weeks after the appearance of the chancre. Syphilitic meningitis may also occur late in the course of the disease; in fact, Ricord classified syphilis of the nervous system with his so-called tertiary manifestations. Carr states that the longest time elapsing between the date of the chancre and onset of symptoms of acute syphilitic meningitis was five years.(7) Wilson (14) says that the majority of syphilitic nervous affections are generally conceived of as running a semi-chronic if not actually chronic course may have thrown some what into the background the idea of a syphilitic infection of the meninges as acute, as abrupt, and as serious as that of any other toxic-infective condition.

Fever.

Karpas stated that acute syphilitic meningitis is afebrile in course unless complicated by some other infecting organism. (11) Turner (22) states that fever is ordinarily, but not invariably absent. Drake supports this by saying that fever is present in less than one half of the cases. (5) He reports fifty cases in which there were only 18 with any fever. Carr (7) finds that the temperature shows irregular rises up to 38' Centigrade, but rarely higher.

Cervical Rigidity

Cervical rigidity is almost always present and varies in degree of severity according to Drake. (5) While Karpas (11) states that rigidity of the neck, Kernig's sign and photophonia are rarely manifest. In Carr's report of 12 cases, eight of the patients had some degree of stiff neck during the course of the acute illness, but Kernig's sign was infrequent and transitory. (7) Sezary divided the clinical manifestations of syphilitic meningitis into three groups. (15) Type three under his classification (that of the acute meningo-encephalitic type) has the condition of high fever and marked rigidity of the neck. Drake's series of fifty patients with acute syphilitic meningitis show 35 with cervical rigidity. (5)

Headache

Acute syphilitic meningitis is almost always ushered in by headache, which is constant and severe, and tends to show acute exacerbations. It is not always worse at night. (5) Carr states (7) that the acute symptoms are violent with intractable headaches, nausea, vomiting and dimming of vision. Glass and Garvey (16) say that in all these conditions are found headaches, vomiting, dizziness, convulsive seizures, disturbances of consciousness, cranial nerve palsies, and other signs of general or focal brain disease. Karpas finds that headache is the most predominate symptom. (11) Thompson (2) says that headache is the most frequent symptom of specific meningitis of the base of the brain. It is present in practically all cases and may be severe pain deep in the orbits of the eyes and sometimes the headache is localized upon the forehead or over the eyes. Headache is also the most constant symptom with meningitis ofthe convexity. However, in this condition, while the headache may be severe and diffuse, although it may be dull, there is usually also a definite sever pain localized in some particular spot. Most authors state that the pain is worse at night, although this is not always the case. There is usually localized tenderness on pressure and percussion and a difference in the percussion note may be observed.

THE SYMPTOMS AND THEIR INCIDENCE IN FIFTY CASES (DRAKE)

HEADACHE	46
NAUSEA AND VOMITING	19
MENTAL DISTURBANCES	5
DISTURBANCES OF CONSCIOUSNESS	13
FEVER	18
CRANIAL NERVE PARALYSES	24
CONVULSIONS	4
VISUAL DISTURBANCES	8
CERVICAL RIGIDITY	35
KERNIG'S SIGN	10
BABINSKI SIGN	6
APHASIA	3
HEMIPARESIS	2

Nausea and Vomiting.

Vertigo and reeling and staggering are often noted. (2) Vomiting, which often occurs without anything in the stomach, is a very frequent symptom, although not a constant one, and may precede all other symptoms. Six of Carr's (7) series of 12 complained of nausea or vomiting. Glass and Garvey (16) also Drake (5) find that vomiting is present in most of their cases.

Mental Disturbances.

Delirium or coma may be the first sign of this disease.(5) Some mental disturbance is almost always present at some time during the course. It may vary from a mild depression to an acute mania. Mental irritability and confusional states are common. Loss of memory is a prominent symptom. Amesse (6) states that the child fails to hold up its head at the usual time, it is anemic, its appetite fails, and the usual spontaneous alertness of the growing child is lost. Thompson (2) says the psychic symptoms vary greatly. The most frequent condition is one of stupor, from which the patient may be aroused temporarily. There may be a purposeless motor delirium. More or less complex acts may be performed on command, although the urine and feces may be passed in bed. There is usually loss of memory, especially for recent events, and a disorientation for time and place. There may be more or less periods of excitement or there may be marked depression with suicidal tendency.

Consciousness may last for a long time followed by sudden appearance of coma and death. Turner (22) states that at times the patient can be roused to answer in monosyllables, but promptly subsides into the lethargic state and may become unconscious and comatose for a few moments, for an hour or for several days. When he talks it is in an uncertain and unreliable way.

General convulsions of an epileptiform type are often observed or there may be partial or unilateral convulsions.

Cranial Nerve Palsies.

The cranial nerves are usually more or less affected, the resulting conditions and symptoms depending upon the nerves involved. (2) Involvement of the olfactory nerve and consequent anosmia is not very rare. Neuralgia of the trigeminal, resulting in pain, hyperthesia, anesthesia, and neuroparalytic keratitis, may occur. Unilateral or bilateral facial paralysis is not at all rare; and involvement of the eight nerve, with deafness, is rather common, particularly as a neurorecidive reaction after insufficient salvarsan therapy. As the process extends further back, the rest of the cranial nerves, either peripherally or intramedullary, may become involved; so that paralyses of the palate, larynx, sternomastoid and trapezeus muscles, and the tongue become manifest. Polyuria and polydipsia

occasionally result from involvement of the floor of the third ventricle and tuber cinereum. (18) Carr (7) states that the diplopia may be due to direct involvement of the cranial nerves by the luetic process, but may also be a part of the pressure syndrome. Three of his patients had some weakness of the seventh nerve. In but two cases were there multiple cranial nerve defects. Jakob (5) finds that the cranial nerves, especially the optic and auditory are often markedly infiltrated with lymphocytes and plasma cells. This infiltration accumulates not only in the sheaths, but also in the nerve tissue itself. The third, fourth, and sixth cranial nerves are, most frequent of all the nerves, involved in the luetic basilar meningitis. In fact, over half of all ocular muscle palsies are luetic in origin. (23) They frequently are all involved together, or there may be bizarre combinations of portions of each nerve involved.

In the meningitis which involves the anterior fossa, the olfactory, optic and part of the trigeminal nerves are affected; in the middle fossa, the chiasm, oculomotor nerves and trigeminal; while posterior fossa meningitis implicates the fifth to twelfth nerves. An isolated third nerve palsy is most common. A total third nerve palsy is probably nuclear, because a perineuritis would affect only a few fibers. When all the oculomotor nerves and the first branch of the trigeminal are affected, the process is probably in the orbital fissure and is associated with amaurosis, exophthalmus and orbital edema.(23)

FINDINGS

Papilledema

The occurrence of choked discs in cases of acute luetic meningitis or meningo-encephalitis is of considerable clinical importance, more particularly so from the standpoint of differential diagnosis. (16) The disclosure of a choked disc upon initial examination is more likely to suggest some disease of the brain other than syphilis, usually tumor. Glass and Garvey state that three of their cases were admitted to the hospital for operation, presumably for cerebral neoplasm. In Carr's series of 12, nine of the patients had bilateral choked discs. This was the most constant and striking physical finding. Amesse (6) states that choked disc is practically a constant feature. While Wechsler (18) states that choked disc is very rare, but that optic atrophy secondary to the neuritis is not uncommon. The majority of the investigators seem to maintain that papilledema is frequently met with in this condition.

Grinker (23) says that the ophthalmological picture is that of a neuritis or choked disc and secondary optic atrophy eventually ensues. The retrobulbar portion of the nerve may be involved, and central scotoma produced by implication of the maculopapillar bundle. The usual story is, however, an involvement of the peripheral fibers producing a concentric decrease in the visual fields, a peripheral interstitial neuritis. Any possible defect may be produced by combinations of tract and chiasmal lesions.

Spinal Fluid

In acute luetic meningitis the spinal fluid Wassermann is always positive. (20, 7, 5,) Polleri (21) has reported a case in which both the blood and the cerebrospinal fluid were negative, and the patient recovered following anti-syphilitic therapy. Also Marinesco and Minea demonstrated in five of eight cases that the presence of Treponema pallidum was positive, while in three of these five the spinal fluid was negative in all other respects. (19) Grinker (23) states that the blood and spinal fluid Wassermann reactions are usually strongly positive.

The globulin reaction is usually strongly positive. (20, 7, 25 5, 18, 15) Allen (20) finds that the spinal fluid pressure is seldom found below 30 mm. of mercury. He also states that the spinal fluid pressure decreases after each treatment (Sulpharsphemamine followed by spinal drainage) until the average for such cases is reached. The pressure is found to be more fluctuating than in any other known disease. Within five days it may vary 18 mm. of mercury, probably to reach the mean level at the following treatment. However, after the initial fall in pressure there seems to be no correlation of a sudden rise with more marked or severe symptoms. In fact, it is most unusual for the acute manifestations to recur after intensive treatment has been instituted. But on the other hand the spinal fluid pressure never subsides to the normal level. The fluid is from clear to turbid and faintly yellow, and it usually contains a

fibrin clot. (5) Grinker (23) finds that spinal puncture reveals fluid under markedly increased pressure. There is turbidity due to the large number of cells, ranging from hundreds to thousands. These cells are mostly lymphocytes. (26)

The majority of the cell counts are between 200 and 400 lymphocytes per cubic centimeter. (27) The counts may go higher, and much lower, varying from 10 to 1500 cells per cubic centimeter. (5)

The Lange colloidal gold curve, may vary from the paretic-like curve to the low meningitic type of curve. (7, 18) Allen (20) states that the colloidal gold reaction is not always conclusive. The chlorides and sugar content may be normal or slightly decreased. (5)

PATHOLOGY

That the meninges may be the seat of syphilitic involvement early in the course of the disease has been deduced both by clinical evidence and by lumbar puncture. No one, however, has described the pathological anatomy in early syphilitic involvement of the meninges. Later in the course of the disease, meningitis may occur as a diffuse inflamatory process, or as a gummatous condition. It may involve all three of the enveloping coats of the brain and spinal cord. It may originate in the bones or periosteum and later affect the meninges or the meninges may primarily be involved. (2)

According to Jakob, (5) this form of meningitis presents its most characteristic form in the early secondary stage. It is characterized by a diffuse, small cell infiltration of the pia-arachnoid in which lymphocytes predominate. Plasma cells are few in number or are entirely missing. In severe cases polymorphonuclear cells are present, but are soon replaced by lymphocytes. The intensity of the infiltrative process varies greatly. For the most part it occurs around the blood vessels, producing infiltration, intimal proliferation and inflammatory changes, but without degeneration. The diffuse inflammatory meningitis is characterized by an exudation of endothelial cells and polymorphonuclear leukocytes and formation of fibrin. (2) There is generally a marked infiltration of lymphocytes, and giant cells are usually observed, while the spirochaetes are more or less abundant. It is probable that this is the type of meningitis which exists when the meninges are involved early

in the course of the disease, although it is undoubtedly less extensive than when the process occurs later. After a certain period hyperplastic connective tissue invades the meninges. (5) The meningeal involvement is commonly present over the cerebrum, especially in the region of the chiasm and sylvian fissures. It also involves the brain stem and circumference of the spinal cord. Not uncommonly the cerebral and cerebellar convexities, as well as the ventricles are involved. The infiltration follows along the path of the larger vessels into the brain tissue. There is frequently a penetration of the exudative process into the marginal zones of nerve tissue with the formation of encephalitic areas. The cranial nerves, especially the optic and auditory, are often markedly infiltrated with lymphocytes and plasma cells. This infiltration accumulates not only in the sheaths, but also in the nerve tissue itself. The spirochetes are not always found. They may be seen in the meninges, in the lumens of the blood vessels and the marginal zones.

The vessel walls, aside from adventitial infiltration, may be quite normal, but usually show severe changes, espedially in long-standing cases. The adventitia and media are involved, the elastic lamina splits, and the intima proliferates. In those cases in which the process develops in latent forms there are, of course chronic changes in the vessels. The end-results of this process may be the regression and disappearance of the inflammatory elements corresponding to a clinical cure, or chronic changes may result if death

does not occur. (5)

Gummatous meningitis, which usually complicates the inflammatory type may either be a diffuse process or consist of circumscribed nodules of varying size. Any one of the membranes may be affected alone, but it is usual for all to be involved. The gummatous meningitis usually is associated with a fibrous hyperplastic condition in which the dura may be several times thicker than normal. The leptomeninges usually are adherent, thickened and contain gummatous deposits either diffuse or circumscribed. (2) Circumscribed gummata of the meninges vary in size from one millimeter to several centimeters and may be found in any location. They usually appear in the fresh state as grayish-red nodules, but may be of a yellowish tint. The piarachnoid is thickened, opaque and frequently adherent to the cortex. (6) The sulci are wide and convolutions sunken. On section the ventricles are found to be dilated and there may be a separation between the upper and lower planes of the cortex. There is an excess of mononuclears in the cerebrospinal fluid.

The most frequent seat of both the circumscribed and diffuse type of gummatous meningitis is the base of the brain and from here it may involve the cranial nerves, extend down the meninges of the cord and affect the spinal nerves.

On the base, the region of the chiasm and interpeduncular space are most often affected. The convexity of the brain is also usually involved and rarely may be the sole seat of the pathology. (2)

The meninges of the cord alone may be invaded by the syphilitic process. The most frequent location seems to be the cervical region, while it is most often observed on the posterior surface of the cord. However the condition may completely surround the cord like a collar. The lumbar region is very rarely affected alone. This condition is usually associated with vascular lesions as well.

The microscope reveals that the vascular lesions are similar to those seen in other parts of the body. (12) They consist primarily of a swelling of the endothelium of the vessels with the production in the adventitia, the media and the intimal layers of the vessels of the new tissue, composed of spindle cells and loose interstitial connective tissue. In this interstitial tissue there are frequently found large numbers of lymphocytes. In other words we have in the early period of this disease an endarteritis, an inflammatory process involving the blood supply to the brain and the symptoms resultant there from are due to interference with the blood supply to the nervous system or secondary to pressure produced by the edema of the inflammatory process. At this stage there has been little or no destruction of the parenchyma of the nerve tissue. However, as the process continues the newly

formed tissue gradually alters into a dense sclerotic fibrous tissue, which ultimately destroys the muscular and elastic lamina of the vessels. The lumen of all the vessels are reduced in every case and may be totally obliterated in some. The changes in the vessels result in degenerative processes within the nerve tissue itself due to lack of nutrition to the brain substance. (12)

The Treponema pallidum has been demonstrated in the spinal fluid from cases in the post-secondary period, showing acute form of neurosyphilis, by the following investigators; Nichols and Hough, Gaucher, Reasoner, Graves, and Wile. In late neurosyphilis the spinal fluid has been examined and reported negative for treponema by: Nonne, Ravaunt, Graetz, Siebert, Neisser, Thiberge, and Graves and others. However, positive findings in the some type of cases have been reported by other writers. (19)

The supporters of the theory of an increased susceptibility of the nervous system due to salvarsan have advanced several hypotheses, none of which seems very acceptable. Finger considers that salvarsan injures the walls of the small cerebral vessels, leading to a "locus minoris resistentiae" for syphilitic arteritis. This subsequently spreads and involves the nervous tissue. Other authors consider that salvarsan changes the reaction of the body to the syphilitic virus and use as simile the occurrence of the so-called Thallmann's chancre on the skin. Others again consider that there is " an aboli tion of inhibiting substances" or "an increased supply of the

food material necessary for growth." Ehrlich has suggested that the sterilization of the rest of the body leads to the increased development of the few spirochetes remaining in the central nervous system, inacessable to salvarsan. (24)

Syphilitic secondary meningitis, therefore, may occur early in the disease. It may be latent, causing no obtrusive symptoms, over long periods. It is a more frequent complication than we have commonly considered. The so-called nerve recurrences after salvarsan are examples of such a meningitis. In most cases the infection of the nervous system has probably already occured before the institution of treatment. They represent the development of the disease in a region notoriously difficult to reach with curative agents. The contention that salvarsan predisposes in any way to the development of disease of the nervous system has not yet been established. (24)

DIAGNOSIS

The diagnosis of syphilis of the meninges, as with all syphilis of the nervous system, can in many cases be made with considerable certainty upon clinical evidence alone, but such a diagnosis is rarely justifiable without the examination of the spinal fluid. (2) The diagnosis is often based on the history of syphilis, the positive Wassermann reaction, and the large number of lymphocytes in the spinal fluid. (23) (5) The differentiation from purulent meningitis may be based on the absence of a source of infection, the milder systemic symptoms, longer chronicity and the cerebrospinal fluid findings. Differentiation from tuberculous meningitis is not so easy, for the variability of symptoms, the character of the spinal fluid cells and the chronicity are similar. The only sure diagnostic sign is a positive Wassermann. (23)

TREATMENT

Syphilis of the meninges as well as all other syphilis of the nervous system is caused by the same organism that causes syphilis of other portions of the body, nevertheless the treatment of syphilis of the nervous system presents problems which differ in many respects from the treatment of other syphilitic involvement. The ideal which it is desirable to attain in the treatment of any case of syphilis is completely to rid the body of the invading organisms and to restore to normal the portions of the body involved. In the case of syphilis of the meninges this may be undertaken by the administration of specific remedies by the ordinary methods as in in any case of syphilis with the hope that these remedies will be carried to and destroy the organisms, and by the direct administration of specifics to the parts involved. All cases of syphilis of the meninges should be most vigorously treated with specifics in the same manner as syphilis of any other portion of the body. Added to this, in refractory cases intraspinal therapy should be undertaken. (5)

Amesse recomends Jean's method in treatment of infants and children. This consists of innunctions of mercury daily, preferably with an abdominal binder. When the skin is intolerant bichloride of mercury baths (5 to 15 grains per 5 gallons of water) may be substituted. The period of immersion not to exceed fifteen minutes and the temp-

erature running from 100 to 105' F. With either of these, mercury with chalk, grains 1, three times a day for an infant of one year may be added. In addition arsphenamine should be administered intravenously, three injections being given every two months, the doses one week apart and 0.01 grains per kilo. (6)

To avoid Herxheimer reactions, treatment should be begun carefully, and pursued vigorously later on. Mercury or Bismuth and salvarsan are still the two best drugs. It may be well to begin with mercury, either intramuscularly or by inunction. and follow or alternate with small, but gradually increasing, doses of salvarsan, neosalvarsan, or silver salvarsan intravenously, (0.1 to 0.6 gram). Silver salvarsan (0.1 to 0.2 gram) is superion to both the salvarsan or neo-arsphenamin. (18) When salvarsan cannot be given intravenously, sulpharsphenamin may be injected intramuscularly. Salvarsan may be given every three or four days up to once a week, and so may mercury injections. Inunctions ($\frac{1}{2}$ dram to 2 gram) throughly rubbed in, are given daily on different parts of the body. They are sometimes more efficient than intramuscular injections; they are also less painful, but considerably more unpleasant and more time consuming. In urgent cases mercury may be injected intravenously. In all cases treated either with mercury or

salvarsan alone, or the two combined, the kidney function should be carefully watched, and if signs of nephritis appear the treatment must be interrupted for a time. Stomatitis and gingivitis must be guarded against or treated with a mouth-wash of chlorate of potash. Potassium iodide, in 10 to 30 or 40 grain doses, three or four times a day, may also be given, and is especially recommended in gummatous syphilis. It is gradually losing what little reputation it has left. For Salvarsan dermatitis, sodium thiosulphate intravenously (10 to 15 grains, 0.6 to 1 gm., in a few cubic centimeters of sterile water) may be given every forty-eight hours until the skin lesions clear up.

The intraspinous method of treatment used to be recommended by some neurologists and many syphilologists. It is at the present time practically discarded, though spinal drainage is still employed by some therapists. Repeated spinal puncture is especially indicated where the meningeal reaction is marked and the pleocytosis high. Spinal drainage, that is allowing all the fluid to come out, is performed about half an hour after an intravenous injection of salvarsan is given. For intraspinous treatment the Swift-Ellis method was generally used. After salvarsan is given intravenously a sufficient quantity (50 to 75 cc.) is withdrawn, allowed to stand for a time, and the serum is drawn off and inactivated. Spinal fluid equal in quantity to the serum about to be injected is withdrawn and the latter introduced into the subarachnoid space by the gravity method.

The Ogilvie modification of adding about one milligram of salvarsan to the serum is not used at all because of the severe meningeal reaction which sometimes follows.(18)

Treatment is generally kept up until the serology becomes negative. Ordinarily, salvarsan and mercury are given in courses of eight or ten alternate injections, followed by a period of rest of about six to ten weeks, and again by another course, and so on. As a rule, meningo-vascular syphilis yields up to certain point, beyond which no amount of treatment is capable of restoring destroyed nervous tissue. It is useless, therefore, to persist in treating, for example, a residual paralysis which can no longer be restored. After one is satisfied that there are no more active signs of neurosyphilis, and the serology is negative (sometimes the spinal fluid Wassermann remains positive despite all therapy), treatment should be discontinued, but the patient should be seen from time to time to anticipate or prevent a return of symptoms. (18)

PROGNOSIS

The prognosis of complete recovery from the syphilitic meningitis seen early in the course of the disease probably is better than that of any other syphilitic condition of the nervous system. With the institution of vigorous antisyphilitic treatment most cases become normal both clinically and from a laboratory standpoint, in a surprisingly short time.

Syphilitic meningitis occurring later in the course of the disease during the second or third year, is more serious, although even this meningitis may be completely cured by proper therapy. Meningitis of the convexity is more refractory to treatment than basilar meningitis. This is especially true if the basilar meningitis is limited to one side of the brain. Syphilitic meningitis of the spinal cord is also quite amenable to treatment. (5)

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NOTE: Articles 1to 27 cited in paper, Articles 1 to 33 read.