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NEUROLOGICAL COMPLICATIONS FOLLOWING DIPHTHERIA.

UNIVERSITY of NEBRASKA

COLLEGE of MEDICINE.

(Alfred)
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SENIOR THESIS.

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The purpose of this thesis is to deal with diphtheria from a neurological standpoint. In this paper I will discuss the principal neurological complications following diphtheria; as to their onset, symptoms, course and pathology in connection with the nervous system and their treatment.

As a rule the primary disease has passed two or three weeks before paralysis is apparent. H. Unterberg, in his treatise on diphtheria from a neurological standpoint, believes that paralysis rarely comes on during the active infection.

Diphtheritic paralysis may be of central or peripheral origin, but most generally it is due to a toxic neuritis, that is, the paralysis is of peripheral origin. Although the neuritis may and does involve almost any nerve in the organism, with consequent paralysis of any part of the body, still we find some parts more frequently affected than others. One of the earliest and most frequent disturbances is a paralysis of the soft palate. The patient becomes aware of this trouble by regurgitation of fluids through the nose on attempting to swallow, and by a nasal twang in his speech.

The next most frequent paralysis is a paralysis of the muscles of accomodation; this is noticed by a disturbance of vision for near objects. Frequently there is found a divergent or convergent strabismus depending on the involvement of the third or sixth nerve.

The above stated conditions are the most common of the diphtheritic palsies, and often go entirely unrecognized, or are attributed to some other cause.

The limbs, both upper and lower, are also frequently involved. Numbness and tingling and sensory disturbances are first noticed, then increasing diminution of motor power. The deep reflexes of the part affected are absent, and sometimes this is the most prominent sign of involvement of that particular part.

The sphincters are involved in some cases. Sphincteric weakness of the bladder and rectum causing involuntary escape of urine and feces, has been reported.

Unterberg is of the opinion that often times the cause of death in diphtheria is due to paralysis of the inervation of the heart muscles. It is, however, a difficult thing to prove, and if so, it must be due to a paralytic development early in the disease.

The onset of diphtheritic paralysis is slow, accompanied by restlessness and irritability, and the manner in which these paralyses follow each other in different and distant parts is almost diagnostic. The affection may be very severe and persist for a long time; in most cases, however, the paralysis clears up and recovery is complete. The age of the person affected, his previous or present health, or the severity of the diphtheritic infection, seems to have no influence on the onset or severity of the paralysis.

Sir William R. Gowers[2] reports that it is probable that one-fourth of those who do not die from the primal disease, subsequently suffer from paralysis.

Various estimates of good authorities show that paralysis occurs following diphtheria in from eight to sixty-eight percent of all cases. Many occurrences of palsy seem to follow apparently trivial infections, and many cases diagnosed as simple sore throat, which are followed by paralysis are really diphtheritic.

Post diphtheritic paralysis has been known to exist for at least one hundred and fifty years; yet the etiology

remained a problem to be solved by modern investigators . Perhaps in no field of medicine do bacteriology, medical chemistry and refined methods play so important and practical a part in the management of disease as in a case of diphtheria.

J.D.Rolleston[3] has kept and recorded two thousand three hundred completed cases of diphtheria. He has not allowed any of his patients to be dismissed before six weeks and this has made his opportunity for observing the onset of paralysis a very favorable and accurate one. It is accurate because it is exceptional for paralysis to develop after six weeks time.

Of the two thousand three hundred cases, four hundred seventy seven or twenty percent showed some forms of paralysis. Of these cases one hundred eighty four were severe and eighty five were fatal. With the clearing of the membrane from the throat, Rolleston has classified his cases and listed them in one of six classes. The purpose of this was to determine the relation of the initial angina to the frequency and severity of the subsequent paralysis. The cases were divided into very severe, severe, moderately severe, moderate,mild and very mild. In the severe attacks the percentage of post diphtheritic paralysis

was much higher than in the milder forms. The percentage of mortality was also much higher. Paralysis was also found to be more frequent and severe in cases in which the nostrils were involved as well as the throat, than in those in which the fauces alone were affected. Thus,Rolleston found that among five hundred seventy faucial and nasal cases there were two hundred forty paralysis cases or forty two and one tenth percent. In comparison he found twenty laryngeal cases in which no paralysis followed.

Children, between the ages of two and six years, are more subject to post diphtheritic paralysis than adults. During the first year of life diphtheria is very uncommon, but between the second and thirteenth years we have our greatest percent of paralysis. In eighty cases of cardiac paralysis the oldest patient was found to be thirteen years of age. Of sixteen cases of paralysis of the diaphragm the oldest patient was eight years of age. Of seventy three cases of post diphtheritic hemiplegia the oldest patient was seventeen.

Rolleston has also shown that Babinski's sign may be found in a considerable percentage of all cases of diphtheria, during the acute stage; being probably due to a transitory irritation of the pyramidal system by the circulating toxins. Among one thousand five hundred, fifty

cases of diphtheria in which the knee and ankle jerks were examined, the knee jerks were lost in two hundred, sixty seven and the ankle jerks in one hundred ninty six, but only four of these cases occurred in patients over fourteen years of age, although one hundred forty nine of the one thousand five hundred fifty were above that age. The above mentioned reflexes therefore, in relation to diphtheritic paralysis show a marked decrease frequency and duration after two to fourteen years of age.

The only palsies which occur during the first two weeks of the disease are cardiac and palatal paralysis. The term cardiac paralysis though convenient is by no means a suitable term, for in several of the so called cases of cardiac paralysis there has been an absence of nerve lesions. Much experimental work on animals nave shown that vaso-motor paralysis is a more accurate designation, the heart failure being secondary to the vaso-motor affection.

The term cardiac paralysis from a neurological point of view is applied to a syndrome arising after the throat has become clean. The symptoms are alteration of the normal heart sounds, low blood pressure, enlargement of the liver and sometimes anuria and vomiting. Death is preceded by a stuporous state, sometimes lasting many days,

in which no radial pulse can be felt. The term cardiac paralysis is usually applied only to the fatal cases, although with the above symptoms, recovery may take place and the heart may resume its normal condition.

Disturbance of the heart's action may occur at any period of convalesence. However in the actual cardiac paralysis the case which doesn't show paralysis symptoms before the end of the second week does not very often end fatally. Sudden, unexpected death is seldom met with in convalesence from diphtheria.

Closely analogous to the early cardiac paralysis is the so called precocious paralysis of the palate, which is revealed by a nasal voice and regurgition of fluids through the nose. This paralysis usually always appears in the first two weeks of the disease. It is also associated with the malignant forms of diphtheria.

According to Rolleston,[4] ocular palsies never occurred before the third week and exceptionally before the fourth week. Cycloplegia usually precedes squint and in most cases paralysis of accomodation exists alone without coincident paralysis of the sphincter pupillae. Later cases cited will bear out this statement. Squint which in most cases is an internal strabismus usually occurs later and is much less

frequent than paralysis of accomodation.

Between the second and fifth weeks there need be no fear of palsy. But in the fifth, sixth and seventh weeks a possible generalized form of paralysis may develop, including paralysis of the pharynx and diaphragm. Vasomotor changes, such as diffuse and transient erythema, urticaria, and dermographism are frequently associated with the generalized paralysis.

Palsies of facial or lip muscles and of the bladder or rectum may occur at this time but are quite rare in occurrence.

EYE PARALYSIS IN DIPHTHERIA.

Ocular complications following diphtheria are of especial interest because they usually are the precursor of complications still more serious to the patient.

Ocular complications are likely to arise as the result of distinct cause, first, those lesions produced by the circulating toxin and its effects and, second, those lesions produced by bacillus finding a nidus directly in the tissues of the eye. The first group is the one we are most interested in as the toxin causes direct neurological sequelae and causes a pathological state of the visual apparatus as induced by a diphtheritic cause.

The intensity of the disease is an important factor in determining the degree of the completeness of the resultant paresis. Besides the intensity of the disease another factor determining the degree of ocular palsies is the degree of individual susceptibility. The constitutional factor to which the term "diathesis" is applied was clearly defined by Robertson, who when writing on this subject more than a hundred years ago, expressed the opinion that there are particular individuals whose constitutions are from the commencement of their existence much more subject to one kind of morbid affection than another, at least to one particular class of disease.

The above statement is of great interest because it has been proven that some individuals are more liable to paralytic sequelae than others.

This has been substantiated by M. Shaw[5] who writes that his clinical investigations have shown that, first, palsies may occur even after the early administration of large doses of diphtheria antitoxins. They have ensued upon the injection intramuscularly of seventy-two thousand units of antitoxin although the patients had been seen early in the disease. Second, the light constitutional signs and symptoms which the patient may present at the onset of the disease do not signify that paralysis will follow. Third, particularly interesting and illustrative have been the cases of group infection. When members of the same community are attacked by diphtheria it may be safely presumed that in each case the infecting organism is of the same virulence. A clinical classification of these patients into groups presenting comparable signs and symptoms has shown that, although they may be comparable clinically, nevertheless, whilst some may make an uneventful recovery, others will fall victims to the paralytic complications of diphtheria.

Ocular palsies are often overlooked due often times to the slightness of the symptoms. If watched for carefully the ocular palsies are almost as frequent as palatal palsies. These paralyses may occur no matter where the site of the initial infection. Gayton records a case of diphtheria of the genitalia, which was succeeded three weeks later by palatal paralysis and marked strabismus. Pope has published a case of diphtheritic vulvo-vaginitis with subsequent paralysis of accommodation, in a child twelve years of age, which disappeared after three weeks. He is of the opinion that the oculist will, perhaps, find in rare instances an etiologically unexplained case of paralysis of accommodation cleared up when thinking of the etiology in this case.Paralysis of accommodation has also been recorded following diphtheritic lesions of the skin. In an analysis of sixty such cases there was found cyclopegia in approximately thirty-three percent.

It would seem that these palsies would likely be the result of severe cases of this disease. However they do follow mild attacks also. Lombardo, states that paralysis of accommodation may result from a light infection, whilst, paralysis of the external muscles are apt to follow the severe cases. In the absence of what may be termed the

" paralytic diathesis of diphtheria", ocular palsies are only the consequence of an attack of especial virulence and that paralyses of the external muscles only accrue from the very severe infections.

The side of the palate to become attacked initially in the onset of palatal palsy subsequent upon faucial diphtheria is that in closest proximity to the area of the pharynx most severely affected by the exudate. It is the opinion of most writers that the eye first to show signs of paresis, following faucial diphtheria, often corresponds with that side of the pharynx upon which there has been the larger area of membrane. To account for this, I think that probably the spread of toxin may be effected through communications between the lymphatic chain draining the pharynx and the lymphatics in the orbitol cavity through the spheno-maxillary fissure. Guy[7] is of the opinion that this lymphogenous conduction of the toxin would affect the ocular nerves by entering through their peri-neural sheaths and the time relationship between faucial infection and the appearance of ocular palsy might therefore depend on the rapidity of lymphatic spread.

Another manner in which the toxin may cause pathology in the nervous system, even in the absence of faucial infection and still cause paralysis of accommodation, might be due to hematogenous and selective absorption of the diphtheria toxin on nerve cells. Gonzalez writes of a most interesting case in which a boy of twelve years was suffering from a diphtheritic sore of the leg with slight constitutional symptoms. This patient developed paralysis of accommodation. A swab of the throat disclosed the presence of Clebs-Loefflers bacilli. This would indicate the necessity of taking swabs and culturing all cases ill of diphtheria even though they do seem to be extra-faucial clinically. It would also indicate there is some closer connection between ocular palsies and faucial diphtheria than lymphogenous spread.

Eye paralysis usually occurs during the third and fourth week of the disease, seldom as early as the second week. In most cases the throat symptoms will have by this time disappeared. The onset is sudden and there are few premonitory symptoms. A prognostic factor is the severity of the initial attack. Later the patient is apathetic and listless, and the pulse rate is slow, while its volume is probably diminished. Usually marked anorexia is a prominent

symptom. Cases giving rise to greatest anxiety are those exhibiting marked restlessness.

Paralysis of accommodation (Cyclopegia) is the lesion most frequently met with. It is usually a bilateral affection although the eyes may not be equally affected.

Flieringa has recorded a case of unilateral paralysis of accommodation , and Faith, [8] records that it occurs in from five to six percent of all diphtheria cases; while Rolleston kept a series of diphtheria cases and found that cyclopegia complicates twenty-seven percent of his entire series . He also found that cyclopegia affects myopic subjects least and often passes unnoticed as they have no need to accommodate for near objects as do those patients whose vision was previously normal. In a few of his cases he found an accompanying external ophthalmoplegia and found that paralysis of the external muscles is less common than cyclopegia. A most important symptom with external muscle paralysis is diplopia. The character of the diplopia depends upon the muscle involved. The external rectus oculi is the muscle most commonly found to lose its function. There is probably a co-existent internal ophthalmoplegia and the other ocular muscles may suffer too. Children are apt to lose their fusion faculty during the period of paralytic deviation, and the squint persists after recovery and changes from a paralytic to a con-

comitant one.

A case of total oculo-motor paralysis has been reported by Parkinson.[9] In this case he found that ptosis results and there is a proptosis consequent upon loss of muscle tone. As a result the eye is deviated downward and outward, due to the pull of the two muscles which retain their function, namely the external rectus and the inferior oblique. The pupil is dilated and immobile and there is a co-existant cyclopegia. Paralysis of associated movements is never a consequence of diphtheria.

Although the following cases are very uncommon and fortunately so, Oliver[10] has observed a case of bilateral chorio-retinitis and optic atrophy following diphtheria. Jessop[11] has published a case of concentric contraction of the visual fields with defective color vision. Lacquer observed, although lesions of sensation are very infrequent, a case of paralysis of the sensory division of the right trigeminal nerve and neuroparalytic keratitis ensued. As stated above these last three cases cited are very infrequent.

As a result of all possible ocular complications following diphtheria and taking the above in consideration, I would draw the following conclusions; First, paralysis of the eye muscles can occur whether or not diphtheria anti-toxin has been given, Second, these complications are an

indication of the patients sensitiveness to the diphtheria toxin and measures should be taken to watch and avoid any cardiac embarrassment. Third, individual susceptibility to paralytic sequelea of diphtheria is an important etiological factor. Fourth, there is nearly always full return of function of the eye muscles. Fifth, drugs used for their action on the nervous system have no influence on these paralyses and are practically valueless.

POST DIPHTHERITIC PARALYSIS OF ACCOMMODATION.

An interesting case of paralysis of accommodation is reported by A. Brav.[12] In this case a girl, age nine, was brought to the hospital complaining of dimness of vision. Her voice had a nasal intonation and her speech was rather low. Examination disclosed nothing abnormal in the outer aspect of the eyes. Both cornea were clear from any opacities and were senstive. Pupils were round and normal in size but reacted sluggishly to light. No change of any organic nature could be noted. From the history it was found that the child had been in bed five weeks with diphtheria and was now in her third week of convalescence.

Further examination proved far vision to be normal but near vision was almost impossible. These were all evidences of a post diphtheritic paresis of accommodation and account for the dimness of vision and inability of the child to read. This paralysis of accommodation was accompanied by paralysis of the soft palate; the uvula was relaxed and insensitive to touch; there was complete pharyngeal anesthesia and the reflexes were absent. This case would therefore be diagnosed as a post diphtheritic paresis of accommodation accompanied by pharyngeal paralysis.

In cases of this type anxious parents are often under the impression that the child's eyes should be refracted at once. Whereas the child does not need a refraction but should be ordered not to exert her eyes or do any close work. The more rest the eyes get the better for the patient. Other treatment should be given, such as is prescribed under general treatment found under the topic of that heading.

Paresis of accommodation is a common sequelae of diphtheria and occurs in about ten percent of all cases. It usually sets in during the stage of convalescence, from three to six weeks after all symptoms characteristic of the disease have subsided. This paresis is the most common of all ocular palsies due to this disease and is next in frequency to paralysis of thepharyngeal vault and soft palate.

Patients suffering from paralysis of accommodation find it to be a very insidious affair. The patient feels first that near vision becomes difficult, next somewhat blurred and finally impossible. Especially is this true in cases where the sphincter pupillae is not affected and there is no dilatation of the pupil. In cases where the sphincters are paralyzed and the pupils consequently dilated, indistinct vision for near objects is more sudden, as the diffusion circle is greater, the base of the cone of light being much greater.

POLYNEURITIC DIPHTHERIA.

J. Woroshilsky[13] has reported a case in which a large amount of anti-diphtheritic serum, divided in small doses, gave very satisfactory results. Woroshilsky cites the case of a four year old child, ill of diphtheria of the tonsils and soft palate. The patient had a high temperature and serious nervous manifestations. An injection of six thousand units of the anti-diphtheritic serum cleansed the tonsils and soft palate of the membrane and the temperature fell to normal. But after three weeks, paralysis of the soft palate and the arms and legs appeared. At the same time constipation , anorexia, sleeplessness, emaciation and general malaise appeared in consequence of the paralytic lesion of the corresponding nerves.

Then an injection was given of thirty-six thousand units of anti-diphtheritic serum, in divided doses over a period of eleven days. Woroshilsky states that the soft palate, the arms and legs began to move more regularly, the constipation disappeared, appetite was restored, normal sleep restored, and the child began to recover. He further states that, at the same time he observed that the exudative diathesis which had existed from the first year of the child's

birth, wholly disappeared and the child recovered, well in every particular.

This case is very interesting and instructive. It has proven, in this case, that great quantities of the serum, thirty to forty thousand units, may be given in divided doses to little children with great success. It also would prove that even after three weeks from the beginning of the disease the neurological complications of diphtheria can be cured very satisfactorily by the injection of anti-diphtheritic serum.

HEAD DROP FOLLOWING DIPHTHERIA.

Post diphtheritic paralysis has a far reaching effect as illustrated by head drop following the disease. Joseph Beard M. D. has cited a very interesting case of paresis of the retro-cervical muscles following diphtheria.[14]

A patient, age six, was admitted to the hospital. The case required immediate attention as the child's face was turning black and she was gasping for air. A tracheotomy was done and the color soon became normal again. Six thousand units of antitoxin were injected.

The patient improved a great deal and at the end of three days no longer needed the tube.

On the fifth night in the hospital the child jumped up in bed, and, after gasping for breath and tugging at her throat, had dropped back pulseless and breathless. " I found the child with a very feeble and rapid pulse, and very shallow slow respiration. I gave her an injection of five minims of liquor strychnine and she improved. However twenty minutes later I found her twitching very badly about the face and arms. The pulse and respiration were improved. A few whiffs of chloroform caused the twitching spasm to subside and following this the child passed a very good night."

The child improved steadily for three weeks but she developed a nasal tone to her voice and a little fluid returned through her nose, when she was drinking.At this time the patient had trouble in raising her head and keeping it raised. The drooping of the head got worse until the patient had no control over it and when raised and let go it fell upon the chest and towards the left shoulder.

The patient went home after forty-six days in the hospital. Eighteen days later the child came in again with small pox. But at this time she could do practically any movement with her head and showed no signs of head drop. Although close examination revealed weakness of the neck muscles.

This type of paralysis, if slight, may escape notice in older children. It also may escape notice in infants where the head is not yet under stable control from birth.

POST DIPHTHERITIC HEMIPLEGIA, PROBABLY, OF NEUROL ORIGIN.

This is a case reported by J. Collins, [15] in which the author presents a boy nine years old with paralysis and contracture of the left hand and foot. The reason for seeing this patient was due to the request of a surgeon, who suspected a tumor of the cortical motor area. The history disclosed that two and one half years ago the patient had a severe attack of diphtheria, for which antitoxin was administered on the fourth day. A week later the child was very weak and his hands, feet and face were swollen. Three weeks after the onset of the disease, the patient began to walk and it was noticed that he dragged his left foot. Next, the left hand became weak and then the left angle of the mouth was seen to draw up. At this time fluids regurgitated through the nose. During the next year his left foot and left hand became greatly flexed. It was very difficult for the patient to get a shoe on and he had to slip the shoe on quickly, while the flexors were partially relaxed. He never complained of pain. His ability to run and jump was limited only, by the flexed position of the foot. The fingers, hand and forearm were in a state of flexion, and the fingers and hand inclined to extreme flexion. This contracture could be overcome by

pressure. Knee jerks were present on both sides and were equal. There were no sensory disturbances and no atrophy. There was nothing present of the stigmata of hysteria, unless the contracture might be considered such. The case was therefore diagnosed as post diphtheritic neuritis resulting in contracture and faulty attitude simulating hemiplegia.

Athetoid movements of a pronounced character were present. If, with eyes closed, the patient was asked to grasp one's hand firmly with the well hand, the affected hand would at once go into the athetoid position. Dr. Collins states that he has never seen nor could he recall ever having seen this condition in hysteria or neuritis. He suggests the probability of a post diphtheritic encephalitis as the original cause.

The history of the case does not point very distinctly to a post diphtheritic paresis and such a distinctly hemiplegic character would be unusual for a neuritis. Therefore the weight of the evidence seemed to point to a post diphtheritic cerebral hemiplegia.

POST DIPHTHERITIC DISSEMINATED MYELITIS.

Since peripheral nerve involvement in diphtheria is so frequent, it is probable that post diphtheritic lesions of the central nervous system are not so rare as their infrequent mention in the literature would indicate. Until 1922, I have been able to find disseminated myelitis or sclerosis following diphtheria reported only seven times.

Hale Powers,[16] cites a case of this form of myelitis. He finds that some authors use the terms disseminated myelitis and multiple sclerosis synonymously and interchangeably. He is of the opinion that the former term applies to those cases in which the condition has been of gradual development. Therefore it seems better to regard disseminated myelitis as an acute or chronic condition that may or may not terminate in disseminated sclerosis, and also to assume that all conditions of disseminated sclerosis are the result of disseminated myelitis, either acute or chronic. This provides a rule for the use of the two terms, the former being the most inclusive. The outcome of the case therefore really determines whether it be called myelitis or sclerosis, for myelitis may terminate either in recovery or sclerosis.

Powers' case was of a boy, aged ten, who entered the hospital on January, 15, 1921. The family and past history were negative. One month before, the patient had a sore throat, and his physician, although not making a culture or giving a diagnosis, gave him one thousand units of diphtheria antitoxin as a precaution. His present condition had developed during his illness. He was unable to walk without a great deal of assistance. His speech was indistinct. He had no lethargy nor headache but slept poorly. For some time, fluids escaped from the nose when drinking but he had recovered form this symptom. The sphincters were not paralyzed.

Examination disclosed negative heart findings, tonsils diseased, fundi normal, pupils equal, regular and reacting to light and accommodation. Nystagnus-lateral with quick phases to the right, on looking to either side. No diploplia. Slight double ptosis. Ataxia present. A large error in the finger to nose test. Rhomberg ataxic. Gait-ataxic with feet far apart. Some incoordination of upper extremities. Slight intention tremor. Adiadokokinesia. Knee jerks and ankle jerks absent. No lateral curvature of spine. Keeps head flexed. Tactile sense normal. Vibratory sense normal. Mental state good. Culture from throat does not contain diphtheritic organism. Diagnosis:- disseminated myelitis and polyneuritis.

By January 28th the general condition and gait improved. Nystagnus and ataxia were still present. Accommodation weak. Speech still very indistinct. Says"mall" for ball. The patient cannot walk without assistance.

By February 4th he is much improved. He can walk for a short distance without assistance. Diplopia on looking to either side.

February 14th:-Left knee jerk has returned. Intention tremor better, patient can hold a glass of water without spilling it.

April 22nd:-Some nystagmus still present. Both knee jerks present and normal. Much less ataxia. Tonsillectomy advised.

October 14th:- Only a suggestion of nystagnus. Other neurological findings negative.

Since the diagnosis here may be questioned the following points should be emphasized. Frequently a polyneuritis will produce motor disturbances resembling the ataxia produced by lesions of the cord or the cerebellum, these latter conditions are known to occur in diphtheria. It should be possible for an experienced observer to distinguish between those disturbances of motor function resulting from the muscular weakness of peripheral neuritis and a true ataxia.

Nystagnus of the type observed in this case cannot be accounted for by peripheral neuritis. That there has been complete functional recovery is not evidence that myelitis did not exist.

As to the pathology in such cases as the one mentioned above, Powers found that Enriquez and Hallion and J. Crocq. Jr. did some interesting work. Enriquez and Hallion injected diphtheria toxin into dogs and produced hemorrhagic lesions of nerve roots and in the white substance of the cord. J.Crocq Jr. produced disseminated sclerosis in dogs in two ways:- first, by inoculating them with diphtheria bacilli, and second, by injecting the toxin alone. Other workers have produced disseminated myelitis in animals by the injections of cerebro-spinal fluid and blood from human cases intraventricularly, intraperitoneally, and subcutaneously.

In the above case cited by Hale Powers the picture of disseminated myelitis was complete, but apparently , in this case, myelitis was not terminated in sclerosis.

POST DIPHTHERITIC ATAXIA.

Wilson[17] reports, in his treatise on the resemblance of the sensory symptoms of post diphtheritic ataxia to those seen in the cord changes of severe anemia, that we must differentiate carefully our findings. He reports three cases in which the sensory loss shown is exactly similar to that seen in the combined sclerosis of pernicious or severe secondary anemia. The subjective symptoms of the three cases about to be cited are of the same character that is so common in anemia.

Case 1. A man, age 22, had diphtheria two months before the onset of symptoms which were, paresthesia in hands and feet, fatigue on exertion and difficulty in walking. Examination revealed a Rhomberg sign; loss of all deep reflexes; loss of the sense of position and vibration in feet and legs; marked impairment in recognizing the points of a compass . All other forms of sensation were in tact.

Case 11. A soldier, age 24, contracted diphtheria in France, early in January 1918. Shortly after his throat cleared up he had difficulty in reading; regurgitation of fluid from the nose; six weeks later paresthesias in the feet, soon involving the legs and hands; marked ataxia in all extremities; Rhomberg sign present; all deep reflexes

lost; sense of position , vibratory sense, and the compass test markedly disturbed in the feet, legs and hands; all other forms of sensation in tact.

Case 111. A woman, age 37, had diphtheria in November 1917; at Christmas, paresthesias in feet which in time involved legs and hands; difficulty in walking and in performing fine movements with hands; gait and station markedly ataxic; sense of position and vibration impaired in toes and feet; touch sense slightly impaired over dorsum of feet; all other forms of sensation normal.

From an analysis of the sensory symptoms in these three cases it is seen that all three had paresthesias in the hands and feet. They all also show a marked loss or impairment of the sense of position and of vibration, and in two of the cases where there was absolute preservation of touch sense there was an impairment of the ability to recognize the two points of a compass. The ability to discriminate two points on a compass depends on the integrity of the touch sense. If touch sense is impaired the compass test is of little use. The power of determining two points of a compass is impaired on the side of the motor weakness and is associated with loss of the sense of position and passive movement. In the peripheral nervous system there is

a close relationship between sensibility to deep pressure and the pain produced by it, and the ability to recognize passive movement and position. All three are present or absent after lesions of the peripheral nerves and all three depend on the integrity of those fibers which run with the muscular nerves. This is true because in the spinal cord the fibers carrying the sense of position and passive movement are separated from those carrying deep pressure and the pain of deep pressure and ascend with the vibratory or osseus sense in the posterior columns.

Therefore in the above cases described, I would place the lesions accounting for sensory loss in the posterior columns of the cord and not in the peripheral nerves. The reason for this deduction is that the osseus sense, sense of position and ability to recognize points of the compass are grouped together. Also in these three cases the motor loss is insignificant and the ataxia was the predominating factor. If lesions of the peripheral nerves were responsible for the above mentioned sensory loss you would expect to find in addition a loss of deep pressure sense and a marked impairment of motor power.

To further support this I have already mentioned under the heading "Pathology" that the posterior columns of the

cord are most usually attacked and most seriously damaged when the cord is involved during or following an attack of diphtheria.

A SECOND ATTACK OF GENERAL POST DIPHTHERITIC PARALYSIS OCCURING AFTER AN INTERVAL OF TWO YEARS.

The literature cites several cases of a second attack of general post diphtheritic paralysis. A particularly interesting case is the one cited by F. E.Coulter[18], Omaha Neb. neurologist, who tells of a case in which there was a second attack of general post diphtheritic paralysis occuring after an interval of two years. This condition, although it rarely occurs, is entirely possible as one attack of diphtheria provides immunity for only a limited period of time. Second attacks of diphtheria have been known to appear in as short a time as six months .

The case Dr. Coulter cites had a second attack of paralysis. The patient,S.McH; was first seen February 15,1904 by a doctor in Pender, Nebraska. Patient was 24 years old, single, occupation-farmer, but had been a soldier with service in the Philippines. Family history was inconsequential. Past history inconsequential.

P.I.; On November 8th, 1903 patient became ill with a sore throat and membrane appeared. A competent Pender physician diagnosed the case as diphtheria but no antitoxin was given nor were any cultures taken. Patient was in bed about two weeks. At the end of two weeks his throat cleared,

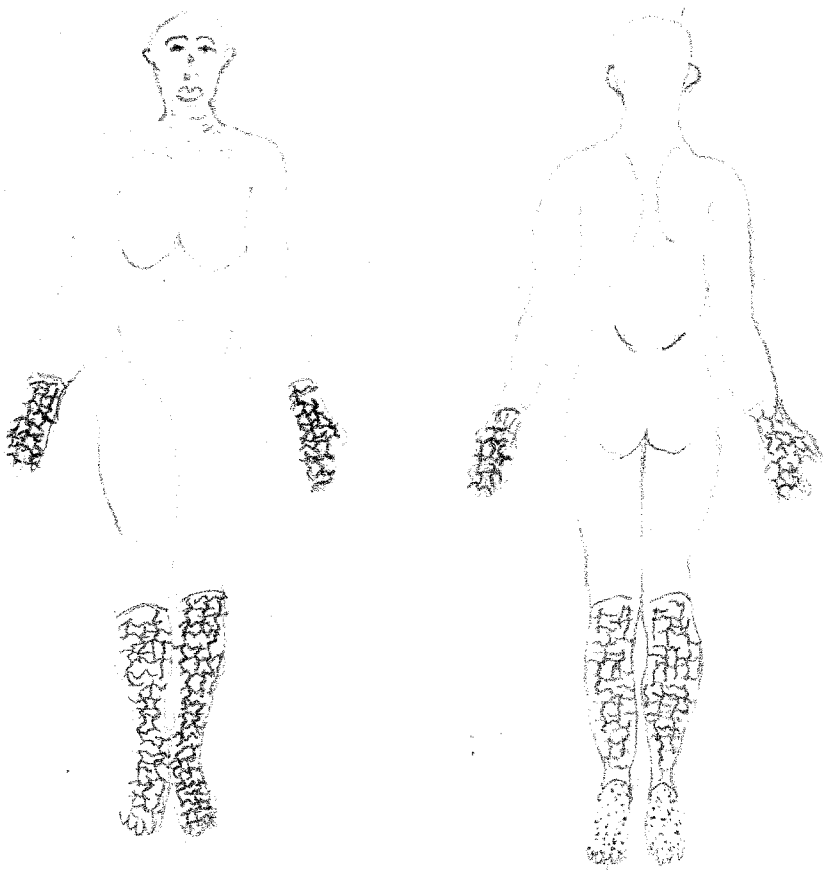
fever subsided and he seemed to be well except for a generalized weakness. A week later he began to have difficulty in swallowing liquids which would regurgitate through the nasal cavities. He also had a dimming of vision at this time. Six weeks after the original onset of the illness the weakness became so pronounced in his limbs that he was unable to go up steps and had fallen down several times while trying to walk in the house. The right side was markedly weaker in proportion than the left. There was no pain noticed up to this time. This weakness increased up until the latter part of January 1904 , when the patient noted a numbness in his feet and legs. This numbness increased until his legs felt cold. His upper extremities were also weakened at this time. No trouble developed with the sphincters at any stage. Sensory examination at this time showed a blunting to pain and touch, of a glove and stocking type . The blunting extending slightly above the wrists and on the legs up to a short way above the knees. The muscles were rather tender to pressure and the median and ulner nerves were very tender to pressure.

Motor examination showed a greater weakness on the right than on the left. Right hand grasp was weak. The gait was feeble and unsteady. Support was required.

Reflexes- the superficial reflexes were normal but the deep reflexes, namely; the supinator, biceps, triceps knee jerks, ankle jerks, ankle clonus were all absent.

The patient was admitted to the hospital where he was treated with strychnine, massage and faradism. Three weeks later on March 9,1904 patient was improved and could now walk without assistance. Patient returned home and continued to improve steadily. Three months after leaving the hospital, in June 1904, he considered himself entirely well and returned to his work as a laborer on a farm.

First Attack.



Represents Anesthesia.

Represents Analgesia.

Represents Hyperesthesia.

SECOND ATTACK.

January 8th,1906, about two years after the first attack, the patient was again contacted. He had remained well up until February 1905, when he had a recurrence of sore throat but did not call a doctor at the time. He recovered from his sore throat in about a week but noticed a weakness which lasted about two weeks. He then continued hard labor until December 1905, and,then while in New Mexico. he suffered again from sore throat which lasted about ten days. During this time he had a headache, backache, sore throat and fever and was confined to his bed. He used a gargle and some medicine internally which was prescribed by a physician. After taking this medicine his throat improved. About two weeks later he began to notice a weakness in his legs and arms. This weakness gradually grew worse so that he could hardly walk and on December 31 he fell and could not rise without assistance. With the increasing weakness he also noticed numbness in the hands and feet, which extended, in the former, up to the elbows and in the latter up to the knees . In January 1906 he was using crutches to get around. With this anesthesia and analgesia he again had the symptoms of difficulty in swallowing, nasal regurgitation, and for one week he could not

read at all. With this second attack he also complained of a tight feeling around his chest, especially in the region of his heart.

Examination at this time disclosed the following:-

Cranial Nerves:-all seem normal and equal excepting the pupils, which react fairly well to light but are sluggish to accommodation. The palate reflex upon voluntary effort gave a weakened response and upon touch was found to be anesthetic.

Sensory Findings:- Nerves and muscles in extremities slightly tender on pressure. The area of anesthesia and analgesia was found in the arms to extend above the elbows half way to shoulders, and in the legs midway between knee and trunk. These areas were increased over those found in the first attack.

Motor System:- Marked weakness in all extremities. Unable to raise knees and arms if any pressure put upon them. Marked incoordination in use of feet. Trunk and abdominal muscles fairly good. Distal segments of all extremities weakened.

Reflexes:- Superficial, epigastric and abdominal present. Plantars not obtained and cremasteric weak both right and left.

Remarks:- The throat was clear of membrane but mucosa was of a liver red color. Cultures showed definite bacteriological evidence of the presence of Klebs-Loeffler bacillus. No antitoxin was given as it was deemed he had passed the stage when it would do him any good.

Patient was hospitalized January 10,1906 and given the same treatment as he was given following the first attack.

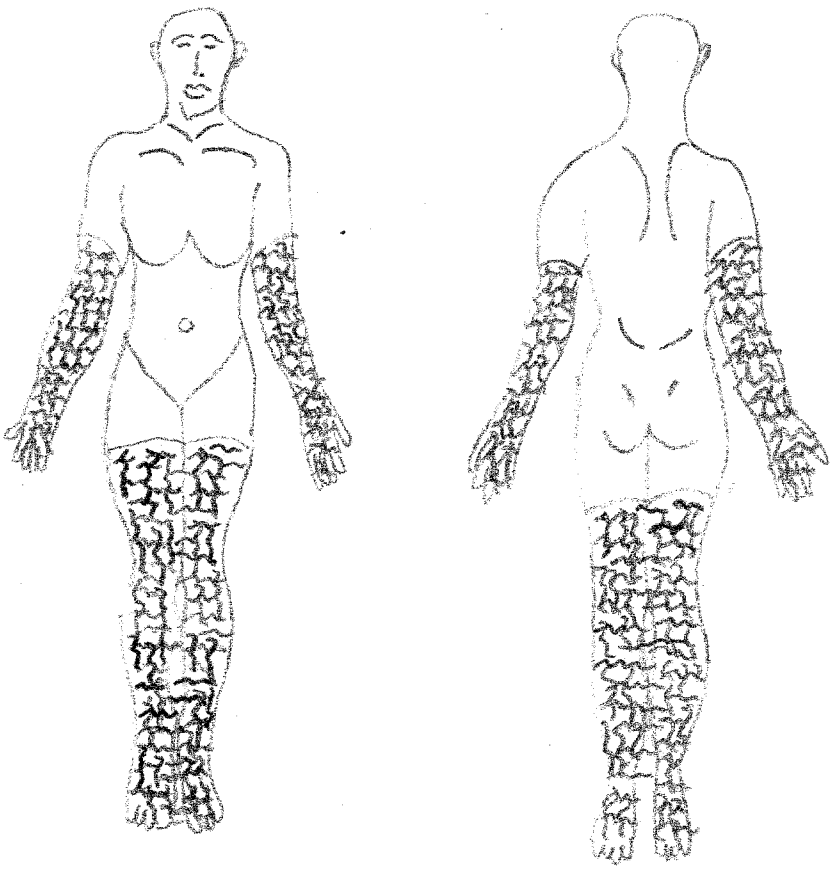
By January 27th patient could take a few steps unaided. By February 5th anesthesia and analgesia was confined only to fingers and toes. By March 2nd, crutches were discarded and patient could do a little light work. By May 10th 1906 patient was back at hard labor. He had taken a job as locomotive fireman and was working from ten to eighteen hours daily.

From the above clinical observations it would seem apparent that the amount of residual antitoxin in this particular individual two years after the first attack of diphtheria was practically nil. It would have been very interesting to see the results of more bacteriological observations in this case, especially the results which might have been found during the interval between the attacks as well as the time the case first came under observation.

However the case does prove that immunity in diphtheria is limited according to the individual's physical condition and resistance and that a second attack of post diphtheritic neuritis may follow after an interval of two years.

Second Attack.

Condition on June, 9, '06



Represents Anesthesia

Represents Analgesia.

Represents Hyperesthesia

A CASE OF PARALYSIS OF THE DIAPHRAGM, PROBABLY POST DIPHTHERITIC.

The occurrence of paralysis of the diaphragm is sufficiently rare to justify the publication of a severe case of it.

The following case has been reported by Dr. Downie, Glasgow aural and laryngeal surgeon.[19] The case concerns a woman who was admitted to the medical ward. Her chief complaint was of a difficulty she had in swallowing.

When the case was examined it was found that the difficulty was not obstructive in character but was due to paralysis of the soft palate and constrictor muscles. Her speech had a nasal intonation and when she attempted to swallow fluids, considerable portions returned through her nose.

In her history she told the interne she had a sore throat five weeks previously but had not considered it serious enough to call in medical aid. At the present time she was seeking advice in regard to her huskiness and difficulty in swallowing.

The doctors passed a bougie and after withdrawing it decided there was no obstruction present.

After being in the hospital for several days the woman

suddenly experienced great difficulty in breathing and became cyanosed. A tracheotomy was discussed to relieve the patient's distress, but before this was done the cyanosis passed away and her pulse, though feeble, became regular again. During her paroxysm she lay on her right side with the right half of her face buried in the pillow. Both lower limbs were drawn up and her left thigh was fully flexed and firmly pressed against the abdomen. Her respirations appeared to be carried on by the voluntary upraising of her shoulders for each inspiration, and each effort was accompanied by contraction of the intercostal muscles.

The patient was conscious, and, with help she was turned on to her back in order to have her throat examined. The change in position and exertion in doing this caused a great increase in the rapidity of her pulse and the dyspnea became more urgent. Unless held, the patient tended to again take this right sided position.

Throat examination disclosed that the soft palate was paralyzed, both voluntary and reflex movements being absolutely abolished. The lower pharynx contained a considerable quantity of tenacious muco-pus and the arytenoids and upper part of the larynx were covered with a similar secretion. The glottis was open and both vocal cords remained fixed in

the cadaveric position. The walls of the trachea looked reddened and there were patches of muco-pus here and there over the surface. The patient could not cough and so was unable to clear away the accumulation of muco-pus which lay in her pharynx, larynx and trachea.

The patient died within eight hours after this second period of dyspnea. A post mortem examination was made. There was no stenosis of the larynx, trachea or esophagus, but the interior of the larynx and trachea when split open, bore evidence of acute inflammation, the mucous surfaces being injected and covered with muco-pus. The bronchi were also found to be acutely inflamed. The lungs were edematous and showed irregular patches of consolidation with localized abscess formation, a condition typical of insufflation pneumonia.

Paralysis of the diaphragm may be caused by injuries to the spinal cord, by pressure on or injury of the phrenic nerve, by lead poisoning, and by diphtheria. The last appears to be the most common cause. This patient was too weak to permit an examination of the diaphragm with X-Rays but the clinical evidence of paralysis of that structure was convincing.

In this case there was no clear cut history of diphtheria. However we know that diphtheria is not infrequently first diagnosed by the onset of paralysis, particularly of the palate, the primary faucial lesion having been so mild as to escape notice.

This patient started with a sore throat followed four or five weeks later by symptoms of paresis of the palate, followed by symptoms which pointed to an extension of the paralytic affection to the muscles of the pharynx and larynx , the routine usually followed in cases of post diphtheritic neuritis.

With the involvment of the nerve supply to the larynx and consequent loss of sensation and movement, food gained ready entrance to the air passages without exciting the reflex cough, and when the diaphragm became paralyzed, neither the insufflated food nor the secretions formed within the trachea and bronchi could be expelled. Insufflation pneumonia was bound to occur as was shown in the septic process which led to the formation of numerous abscesses in both lungs.

VASO MOTOR INTESTINAL PARALYSIS FOLLOWING DIPHTHERIA.

The complications and sequelae of diphtheria are at times more serious than the disease itself and paralysis in one form or another is the most frequent complication.

Dr. Rugh[20] reports a case which has unusual interest because of its unusual character and therapeutic peculiarity. The case concerns a girl, twelve years of age, well nourished and healthy. In the fall of 1903 she had an attack of bronchitis which lasted a month. At the end of this time she had a chill, vomiting , and developed a sore throat. A profuse typical membrane appeared in the throat. Antitoxin was given, nine thousand five hundred units in five days. Her highest temperature was 103.5 F. and pulse 108. In ten days her throat was free of membrane and she seemed on the way to recovery.

The heart showed marked weakness and the radial pulse was hardly palpable. To combat this the patient was kept in bed for another ten days. After this she was allowed to sit up in bed.

The day following a slight diarrhoea set in, which gradually grew worse. The patient continued to eat well but diarrhoea became worse. After several days she lost control of the bowels and they moved every hour or so.

The strychnine and iron tonic which she had been taking was discontinued and tablets of tannin and formaldehyde were given every two hours. These tablets had no effect. Crotan powder was given in fifteen grain doses, but this also had no effect.

By this time the intestinal discharge was almost constant. The greater part of the discharge was a brownish fluid. The patient complained of pain, so pulv. opii. grains ¼ were given. After twelve doses of this drowsiness came on but no alteration of the discharge took place. Next she was given bismuth subgallate, fifteen grains every two hours, and the opium was continued in larger doses. At this time the patient was failing rapidly. She was eating well but losing strength rapidly.

A consultant was called and he advised stopping the opium, continuing the bismuth and giving two to three minim doses of adrenalin. He was fully convinced the case was clearly one of vaso-motor paralysis of the intestinal walls.

This plan was carried out but without any results. The child was in extremus. When the pulse was scarcely perceptible strychnine sulphate, grains one sixtieth was given every three hours. Following this the child seemed

worse and to avoid pain the family allowed the doctor to give morphine sulphate in one sixth grain doses as often as necessary. After the first shot of morphine the child became quiet within thirty minutes and slept for two hours. Following subsequent shots her bowels stopped moving and she commenced to improve rapidly. The cardiac weakness subsided and the child regained her health completely.

The value of the morphia in this case is questionable. The drug may simply have been coincidental with the re-establishment of the vaso-motor control.

A CASE OF POST DIPHTHERITIC PARALYSIS FOLLOWING A CUTANEOUS WOUND INOCULATION OF DIPHTHERIA BACILLUS.

Walshe[21] records a case in which a post diphtheritic paralysis followed an infected wound on a man's thumb.

This case concerns a certain doctor who performed a tracheotomy on a patient with a fatal case of laryngeal diphtheria. He was not aware of cutting himself, but the next morning noticed a painful bleb on the dorsum of the first phalanx of the right thumb. Later this broke down, leaving a sore raw surface, which spread rapidly and became covered by a greyish yellow slough.

Five days later he felt ill and shivery, and there was a marked lymphangitis up the arm and swelling of axillary glands. After several more days the diphtheria bacillus was isolated from the wound in pure culture and he was hospitalized and given antitoxin.

While in the hospital he showed marked symptoms of toxemia and during the next ten days experienced vomiting, cardiac disturbance and showed albumin. The knee jerks were brisk.

He left the hospital in three weeks and felt quite well. He resumed work exactly eight weeks after the accident to his thumb.

A few days after resuming work he noticed a numbness of his thumb around the wound area. A numbness to touch and pressure. This impairment of sensation increased slowly and spread over the whole arm. Writing became difficult and his grasp was weak and clumsy. At this same time he began to find going upstairs difficult, his knees felt as if they were going to collapse under him and the legs ached on exertion. Tingling and " pins and needles" sensation then appeared in both feet and also in the left hand. He was then readmitted to the hospital; ten weeks after the wound inflicted on himself while performing the tracheotomy.

On examination at this time there was no defect of vision, deglutition or speech. The cranial nerves were perfectly normal. The arms were weak and showed wild ataxic movements. This ataxia was clearly sensory in type and all the phenomena of loss of position sense were present. Falling away of the extended hand, "pseudo-athetosis", and error of projection in the finger to nose test when the eyes were closed. Both legs were flabby and weak, the dorsiflexors being especially affected. Slight Rhombergism.

The sensory showed marked changes of the peripheral

type, impairment of touch, pain , temperature and deep sensibility in the distal segments of the limbs, most marked in the extremities. The whole of the right hand was insensitive to touch and pin prick. All tendon jerks were abolished. Abdominal and plantar reflexes were normal. Heart and urine were normal.

After three weeks rest in bed the sensory and motor symptoms began to recede. Recovery was slow but steady.

This case is particularly valuable since the patient himself was a medical officer and a most careful and skillful observer. It shows a definite example of an extensive diphtheritic paralysis beginning locally in the inoculated limb and then becoming generalized in the spinal nerves. The cranial nerves were never affected in the slightest degree. The association of this condition with a diphtheritic infection is also certain and illustrates that this case is an example of a true lymphogenous ascending infection of the central nervous system along a nerve, as I have described a little later under the heading "Pathology".

PATHOLOGY OF POST DIPHTHERITIC PARALYSIS.

Diphtheria may involve the nervous system in a number of ways. The involvement may be severe or very mild. Thus, at times, the only sign that the nervous structures have been attacked may be paralysis of the soft palate or of accommodation. The disease, however, often produces serious disturbances of motion and co-ordination in the extremities. There is often a diffuse weakness or paralysis of the lower or upper extremities or of all four extremities. Another manner in which diphtheria may involve the nervous system is in the production of an acute ataxia, which has been described by some writers as simulating a peripheral neurotabes.

From a pathologic point of view there is a widespread involvement of the nervous tissues in diphtheria. The diphtheritic toxin or poison acts upon the whole nervous system producing marked symptoms, first at one site and then at another, most often in the peripheral nerves. There may be toxic effects in certain areas without producing structural changes in them.

Many investigators have examined the nervous system in diphtheria. In some cases material has been studied after the death of the patient with an acute illness, while others

have studied material from patients who have died weeks or months after an attack of diphtheria. Some have approached the subject from an entirely experimental angle.

The findings of these investigators run about the same. Many found a marked degeneration of the peripheral nerves. In the cord are usually found numerous hemorrhages, chiefly in the gray matter. The white substance remains normal except in several cases which presented an advanced grade of degeneration in the posterior columns. Several men found in cases of post diphtheritic paralysis and ataxia degeneration of the posterior column and to a lesser degree of the posterior roots. Some cases examined showed extensive degeneration of all nerves examined and capillary hemorrhages in the cord.

One of these investigators by the name of Thomas, found degeneration of the peripheral nerves and in the cases where the cord was examined definite pathology was found in the posterior columns which were always most seriously affected.

Henschen[22] reported the pathology in a case of acute disseminated sclerosis following diphtheria. His examination was taken from material of a patient who died three months after the initial attack of the disease. Microscopic study of the nervous system showed, in addition to a marked poly-

neuritis, a great number of disseminated areas of sclerosis in the cord, most marked in the posterior columns and associated with intensive peri-vascular infiltration. He also found a general edema and softening in the cord, most marked in the posterior and lateral columns.

Rolleston, in his investigations was interested from a clinical standpoint. He found that various parts of the central nervous system may be involved during an attack of diphtheria. The plantar reflex was investigated in eight hundred seventy cases of diphtheria. In one hundred seventy-two of these the extensor response was obtained at some period of the illness showing that the pyramidal tracts were involved either through a toxic action or by edema and capillary hemorrhage. The mortality was found to be higher among those patients who developed the Babinski reflex and the incidence of paralysis was greater.

Several cases of Freidrichs ataxia which developed after a post diphtheritic paralysis have been reported by Taylor[23]. After close analysis of the symptomatology of the case it seems that the patient never really recovered from the diphtheritic involvement of the central nervous system.

Investigators report, although a rare occurrence, a case of chronic bulbar paralysis following diphtheria. From a pathological standpoint the occurrence of the bulbar symptoms would make it necessary to assume that the toxins traveled along the nerves and ultimately produced sclerosis of certain nuclei of the cranial nerves.

PATHOGENESIS OF DIPHTHERITIC PARALYSIS.

Walshe,[24] in a paper on pathogenesis of diphtheritic paralysis, says that paralysis in diphtheria, in the majority of cases, is related to the seat of formation of the toxin and that the nerve centers are attacked by a process of ascending toxic neuritis in tetanus and hydrophobia. Rabies and tetanus have long been recognized as toxemias ascending the nerves. The spread of tetanic spasms proves this.

Many investigations have been made on this subject and the result of these investigations establishes the existence of an ascending perineural lymph stream and the infection of the central nervous system by organisms and toxins along this path. It is important, because of this, to consider the pathogenesis of diphtheritic paralysis and to examine the possibility of the hypothesis that it is a toxemia of the nervous system ascending the nerves inervating the infective focus by their lymph channels.

Toxins and organisms reach the central nervous system by this path and spread in the lymph spaces of the pia-arachnoid and in those in the substance of the cord. Here they give rise to an inflammatory reaction in the connective tissue elements of the cord, to chromatolysis in the nerve cells, and to myelin degeneration in the spinal roots. These changes occur in those segments of the central nervous system bearing anatomical relationship to the nerve supply of the infective focus. The nerves from this focus show an ascending perineuritis spreading to the cord by the spinal ganglia and spinal roots. In some cases of diphtheritic paralysis the nerve findings are negative. Myelin degeneration when it occurs, is found almost exclusively in the intramedullary course of the nerves, that is, from the point where the neurilemma sheath is lost. Therefore it must be the presence of the neurilemma sheath, or, more probably the peripheral situation of the lymph channels which protects the myelin sheath in the peripheral course of the nerves.

Babonniex, 25 arrived at a similar conclusion to the one above. He drew his conclusion from the results of experimental work. By injections of diphtheria toxin subcutaneously into animals he was able to produce local paralysis and also acute ascending paralysis of Landry type. He also noted a

a close anatomical relationship between the primary inoculation lesion and the paralysis. Following injections into the sciatic nerve he found, associated with a local paralysis an "ascending neuritis" and pathological changes in the lumbar cord; chromatolysis and myelin degeneration in the spinal root fibers. He therefore drew the conclusion that the paralysis in diphtheria followed an ascending neuritis and secondary involvement of the central nervous system.

Regardless of the above experiments there are numerous differences and divergences of opinion among authors. The reason for this is probably due to an omission on the part of observers to discriminate between the pathology of human and experimental diphtheria. The presence of actual diphtheritic membrane, as in faucial diphtheria, is bound to present a different clinical picture than diphtheritic injections into a guinea pig. It is not wise to compare these two situations without qualification . There is, however, a comparative analysis possible. In comparing diphtheritic paralysis in man with that produced experimentally, it is necessary to correlate the seat and nature of the local lesion with the topography of the paralysis and that of the morbid changes in the nervous system. If we do this we find at once a striking parallelism between clinical and exper-

imental diphtheria of the nervous system. and in both instances strong evidence in favor of a lymphogenous infection by the peripheral nerves.

For example let us take a case of human and experimental diphtheria which shows a striking parallelism.

Human diphtheria: First, the local lesion. The infective focus in this disease in man is constantly situated on the tonsils and fauces, occasionally in the nose and larynx. The circumscribed lesion is inervated by the fifth, ninth, tenth, and eleventh cranial nerves. Second, the symptomatology. Diphtheritic paralysis in man is ushered in by extensive cranial nerve palsy, frequently followed in two or three weeks time by what is clinically a multiple neuritis. This evolution and course is characteristic of the paralysis due to diphtheria, and in no other clinical form of polyneuritis is there a cranial nerve involvement at all comparable with this type of one. With regard to the cranial nerve involvement, it has been noted that of the nerves concerned those inervating the tonsils and fauces are earliest and most severely affected. One irregularity is the fact that the third nerve, which commonly shows involvement, does not bear any anatomical relation to the local lesion. The spinal acessory nerve is affected and shown by a weakness and tender-

ness to pressure over both sterno-clido mastoids during the first stages of diphtheritic paralysis. The above statements prove there is a close anatomical relationship between the nerve supply of the infective focus and the incidence of the paralysis in its initial and most characteristic stage. Third, the pathological changes. In fatal cases of diphtheria Bolton[26] found acute degenerative changes in the medulla; marked chromatolysis in the vagal nuclei, involving the whole cell body and even associated with changes in the cell processes. The vagus nerve usually is found in tact. Whether the degenerative changes noted in the cell processes may be taken to indicate myelin degeneration in the intramedullary course of the vagus is not certain, but negative findings in the peripheral course of the nerve have, as has been shown in parallel conditions, no significance. The balance of evidence shows that in man the medullary nuclei constantly show changes.Of spinal cord changes it is difficult to make any statement on which there is much agreement.

On the whole, however, there is a correspondence between the seat of the toxin formation and the incidence of the morbid changes in the nervous system.

Experimental diphtheria. First, local lesion. A similar analysis of experimental diphtheritic paralysis affords parallel

results. The local lesion is usually a subcutaneous injection into a limb. Second, the symptomatology. Ranson,[27] inoculating the hind limbs of guinea pigs subcutaneously, records that there are no bulbar symptoms; but the paralysis begins locally in the injected limb and becomes generalized, involving the neck and abdominal muscles, but especially those of the hind limbs. Crocq, states that diphtheritic paralysis is distinctly different in man and in the rabbit. In man it generally begins with involvement of the palate and throat, in the rabbit by weakness of the hind limbs. In man diphtheria seems to produce two different kinds of paralysis, in which the one remains localized in the mouth, eyes, larynx and pharynx, while the other is generalized and may affect the whole body, beginning with the lower limbs. Also it is to be noted that in man muscular paresis in diphtheria most commonly affects the muscles supplied by the cranial nerves. It seems therefore that in the higher mammals the poison especially attacks the medullary centers and the cranial nerves, and in the lower mammals, the spinal centers and spinal nerves. Third, pathological changes. Examination of the morbid anatomy of the nervous system is quite parallel to that found in the human example. Intravenous injections of toxins to rabbits produced chromatolysis in spinal, medullary, pontine and mesencephalic cells. In the cords the diphtheria

poison produces very marked alterations of the grey matter, the cells become swollen, they stain badly, their nucleus and processes disappear; the neuroglia and ependyma proliferate but the white substance is rarely affected. In the peripheral nerves a degeneration is produced. The cranial nerves are not affected by the poison and a primary myelitis and a secondary peripheral neuritis are produced.

From the comparison of these two cases, namely a comparative analysis of human and experimental diphtheria with reference to the nervous system, the following conclusions may be drawn. First, that in both human and experimental diphtheria the involvement and position of the paralysis and the incidence of the morbid changes in the central nervous system are closely related to the innervation of the infective focus. When, in experimental investigation, intravenous injections have been used we find generalized paralysis from the outset and widespread changes in cord and brain stem.

Second, the apparent differences between the symptoms and morbid anatomy of diphtheritic paralysis, in man and in animals respectively have a simple mechanical explanation and depend on the seat of toxin formation, and do not demand for their explanation any speculations as to selective action

of the toxin on medullary centers in man on the one hand and spinal centers in animals on the other.

The majority of writers agree that the blood stream is the great carrier of the toxic substance although the selective power exercised in some instances, as when the palate alone is affected, accommodation paralyzed etc. is hard to explain, unless the proximity of the special structures involved renders them more vulnerable.

Many of the earlier writers and some writers of today contend that paralysis is due to a peripheral nerve change of a parenchymatous nature and that little or no change is found in the cord and brain. Others maintain that the cells in the anterior horns of the cord are the primary seat of lesion, the peripheral nerve change being only secondary to spinal lesions. A more conservative view and the one generally accepted now, is that the entire neuron, either motor or sensory, may be the seat of pathological changes, the peripheral neuritis usually predominating and often existing without demonstrable change in the cord.

In an article by Luther Peter[28] on a pathological study of diphtheritic paralysis we can divide these paralyses into

four groups. First, those showing purely muscular change without nerve involvement; second, polyneuritis; third, lesions of the spinal cord, which were either localized in the grey matter leading to atrophy of muscles or involved the white matter of the cord, in a similar way to that seen in locomotor ataxia or multiple sclerosis, and fourth, cerebral hemorrhage chiefly due to circulatory change. This fourth is not a true diphtheritic palsy, as a palsy of this type should be termed so only when they are caused by the direct action of the diphtheritic toxin.

The question as to which part of a neuron is diseased probably offers greater difficulty than the cause of the palsy. Lesions of the cells in the anterior horns are as a rule so small that the palsy is limited to a single group of muscles or even to a single muscle. When the peripheral nerves are affected the distrubition of the palsy is usually general and the paralyzed parts tend to recover rather rapidly and completely.

In considering the pathology present in cardiac failure there has been much discussion. The myocardial changes are now thought to be secondary to functional disturbances of the vagi and probably due to organic changes in the nerve structure. As stated before, children from the age of

two to nine are the most frequent sufferers. The onset as a rule is early in cardiac failure in diphtheria. Symptoms usually show up about the seventh day of the disease.

In pathologically accounting for sensory loss, which is a common occurrence, the most reasonable place to find the lesions would be in the posterior columns of the cord. The reason for this is cited in another part of this paper. The nature of the pathological process is not necessarily destruction of tissue, but a toxic action on the posterior columns and very likely some accompanying edema and capillary hemorrhages which usually clear up.

EYE PARALYSIS IN DIPHTHERIA .

The neuromuscular apparatus of the ciliary muscle, the pupil and of the ocular muscles is, next to that of the knee jerk, a delicate indication of the sensitiveness of the patient to the diphtheria toxin, and the occurrence of paralysis of these structures is an important observation to the clinician, for, they may precede the onset of more serious lesions, such as cardiac, diaphragmatic and pharyngeal paralyses.

Gonzalez[29] is of the opinion that the substances present in the blood exert a selective action on the neuro-muscular synapses in the iris and ciliary muscle and on the ciliary ganglion. This view is based on physiological experiments, which show that the points in the nervous chain most susceptible to the strain are the synapses and the neuro-muscular junctions. It is well recognized, however, that the ocular palsies in diphtheria may arise from direct involvement of the nerves supplying the internal and external muscles of the eye owing to a resulting neuritis.

Some workers have found changes confined to the peripheral nerves, while others state that microscopial findings show changes which are confined to the muscles, but these are probably secondary to the nerve lesions. One can not yet come to a definite conclusion as to whether the cause of the palsy is central, peripheral or both.

PALATAL PARALYSIS.

Hochhaus and DeGuy have advanced the theory that an interstitial myositis causes pathology in palatal paralysis. An extensive superficial necrosis occurs always in the malignant form of diphtheria, which ends in palatal paralysis.

Histological investigations by DeGuy and Hochhaus and others have proved the condition to be due to an interstitial myositis. The fact that the side of the palate initially attacked by the membrane is the first to show paralysis, tends to prove the merits of this theory.

SUMMARY OF PATHOLOGY.

In summing up the anatomy of post diphtheritic paralysis we can therefore state nothing as absolutely definite or specific. However there seems to be a general tendency to the belief that it is a peripheral neuritis, as there is great susceptibility of the nervous system to the diphtheritic toxin. It may perhaps, be due to a local disturbance of the circulation, and nerve force is restored as soon as the circulation readjusts itself. The facts that post diphtheritic paralysis recovers so speedily and that there is an ambulatory paralysis makes the theory of circulatory disturbances more rational than the theory of an organic peripheral neuritis.

There is also a weight of evidence which may be considered sufficient to justify us in concluding that diphtheritic paralysis, at any rate in the initial and most characteristic of its stages, that of cranial nerve involvement, is an ascend-

ing infection of the central nervous system; the toxin elaborated in the membrane passing up to the medulla in the perineural lymph channels of the cranial nerves innervating the tonsils and fauces.

It has, however, already been pointed out that of the cranial nerves involved, one at least, the oculo-motor nerve, bears no relation to the infective focus. We cannot therefore in this instance be dealing with an ascending infection of the nerve. A clinical study of the condition makes it seem highly improbable that the mechanism of production of the various cranial nerve palsies is other than a single one. Very probably it is not the passage of the toxin up in the lymph channels of the nerves that produces the lesion giving rise to the paralysis, but its action on the central nervous system, that is on the nuclei of the nerves involved, that constitutes the primary and essential lesion. The rarity with which, in both human and experimental diphtheria, the peripheral nerves along which the toxin passes show any lesion of the axis cylinder or myelin sheath, and the constancy of central cell changes make this extremely probable.

Therefore in regard to so-called "ascending neuritis" we are not dealing with a neuritis at all, but with the

passage of the toxin along the course of the nerve. This may produce some inflammatory reaction, in the lymph channels through they pass, but not an actual neuritis. The lesion which gives rise to the symptoms is central.

We have, however, still to consider the generalized paralysis which commonly appears somewhat later than the development of these cranial nerve paralyses. Clinically this resembles in every particular a multiple neuritis. It has these characteristics, namely; that its onset is delayed, it appears simultaneously in all the spinal peripheral nerves, and it is more chronic in its course than the earlier cranial nerve symptoms. The involvement of the nervous system in this instance must be a part of the general systemic toxemia, an intoxication by the blood stream. In every case of diphtheria the toxin circulates in the blood and must reach the nervous system, central and peripheral, by the lymphogenous route. Therefore there is really a two fold mechanism in the production of diphtheritic paralysis in man. There is the initial sometimes severe and relatively short lived "local paralysis" due to the action of the toxin which has ascended the nerve innervating the local lesion, on the nerve nuclei in the brain stem. Secondly, ther is the later, longer lasting "generalized paralysis",

which is part of the general systemic toxemia.

TREATMENT.

SERUM THERAPY.

Statistics show and prove that the number patients suffering from post diphtheritic paralysis has materially declined since the use of antitoxin. Statistics also prove that the best results are obtained by its early administration. After the third day of the disease the efficiency of the serum is not so great, but it should be used in every case, no matter how mild or malignant and desperate the case may seem. Serum treatment is not detrimental to intubation or tracheotomy. Therefor it is indicated both early and late in this disease. Neurologists vary in their opinions as to the influence antitoxin injection has on the onset of paralysis. Some believe it is a definite aid if given early enough. Others believe it has no effect or influence on the onset of paralysis. The correct answer to this problem depends on close clinical observation and data in the future.

The above statement is the opinion of neurologists who do not usually see the initial stage of the disease and do not have statistical data on which to prove their opinions. At the present time all clinicians are in favor of early use of antitoxin and if patient has not had it

early,administer it as soon as possible.

In addition to the use of early antitoxin the patient should have good hygienic and dietetic care.

HYGIENIC AND DIETETIC TREATMENT.

Proper care ahould be given when the membrane falls off. It is just this period which should be utilized for the reestablishment of the circulation and the building up of the general condition, to restore the vitality and strength of the patient. Proper care during this period will very probably lessen the frequency of post diphtheritic palsies.

Fresh air, good food, absolute rest, both physical and mental are needed. Push fluids and give a tonic of iron, quinine and strychnine.

Rest, as mentioned above, is a very important thing. Rest in bed in a recumbent position for a period varying with the severity of the initial angina. In mild cases the patient may be allowed to sit up by the end of the third week, and several days later to leave his bed.In severe cases it is not advisable to let the patient sit up before the end of the sixth week and then only if no paralysis has developed. If by the end of the seventh

week there is no other paralysis but that indicated by a nasal voice, defective accomodation or an irregular heart, the patient need not be kept in bed.

OCULAR TREATMENT.

Treatment in ocular complications has originated largely from the French School. They have from time to time advocated the administration of diphtheria anti-toxin in the paralytic stage of the disease in order to lessen its severity and hasten the patients recovery.

Eserine has been applied locally in cyclopegia, hoping to achieve results through its stimulant action on the nerves involved. Strychnine has been given internally for its stimulant action on the nervous system, with the same object in view as in the eserine treatment. Many regard these treatments as valueless and only are done because of excessive zeal.

In paralysis of accomodation the essential treatment is; rest to the eyes, no close work, no exertion to the eyes, tonic and absolute rest. A gradual recovery must be expected.

CARDIAC, PHARYNGEAL AND DIAPHRAGMATIC TREATMENT.

In active cardiac paralysis and paralysis of the pharynx and diaphragm active measures are required. In all severe cases the prophylactic administration of adrenalin is of service, either by mouth or subcutaneously, to forestall or combat the suprarenal insufficiency which play so large a part in cardiac paralysis. Support can also be given to the heart by hypodermics of strychnine.

If vomiting is present it should be met by the prohibition of food by mouth and the substitution of nutrient enema. The enemas should contain potassium bromide grains XXX and tincture of Belladonna minims XX in alternate feeds. The dangers of nasal feeding in pharyngeal paralysis owing to the anesthesia of the larynx and the risk of deglutition broncho-pneumonia make it advisable to substitute rectal feeding, which may be adopted all the more readily as the paralysis does not as a rule last longer than a fortnight. During this period injection of strychnine and the addition of belladonna to the nutrients is indicated.

The loss of motor power in the lower limbs, which as we have seen is most likely to be met with in cases

convalescent from pharyngeal palsy, is not usually of long duration.

The physical element which is present even in young children needs to be taken in consideration. Fear of falling tends to increase their unwillingness to move and requires vigorous counter suggestion. It will usually be found that by encouragement and support remarkable progress will soon be made. In some cases as in cases of hemiplegia- electricity and massage are required.

In severe respiratory paralysis, artificial respiration has been known to save life.

If all of the above treatment is given in its proper place and time there will be much less severity in the occurrence of paralysis.

PROGNOSIS AND CONCLUSION.

The outlook in diphtheritic paralysis may be said to depend upon the age of the patient, the date of onset, and the situation of the paralysis. The older the patient the better the prognosis. Cardiac, pharyngeal, and diaphragmatic palsies are the only forms which need cause anxiety. Previously in this paper it was shown where no fatal case was met with above the age of thirteen and that no case of paralysis of the pharynx was met with over fourteen years, or of the diaphragm over eight years.

Paralysis of the palate occurring during the first two weeks is not only likely to be more persistent than the ordinary form but also not unfrequently heralds fatal cardiac paralysis. Closely associated with the so called cardiac paralysis is a progressive enlargement of the liver partly due to congestion and partly to fatty degeneration. In Rolleston's series of cardiac paralytic cases, out of one hundred eleven who showed any signs of liver enlargement, seventy-one died, a mortality of sixty-three percent as compared with a mortality of six and seven tenths percent among one thousan nine hundred twenty cases of diphtheria which show no enlargement of the liver.However if the heart remains normal until after the third week, cardiac paralysis

may occur but is seldom fatal to the patient.

The prognosis of pharyngeal palsy depends upon the ability of the patient to support artificial feeding, the extent of involvement of the other muscles, especially the diaphragm, and the condition of the lungs. When once the power to swallow is regained progress as a rule is rapid.

Ocular palsies usually are of a transitory character and the literature mentions no cases in which permanent eye damage has resulted from diphtheritic paralysis. Therefore the prognosis of ocular palsies is usually a good one. Most writers are of the opinion that if other organs do not become involved the patient tends toward a spontaneous recovery.

P.N.K. Schwenk[30] is of the opinion that recovery from an attack of post diphtheritic paralysis of accommodation is more rapid in the young than in those more advanced in years.

The location of the membrane and symptoms shown are of considerable importance. Symptoms with unusual gravity are paralysis of heart and respiratory muscles and the muscles of the neck.

In conclusion I might state that all degrees of severity are met with in post diphtheritic paralysis. All degrees from a mild general paresis with slight emaciation to the most complete palsy of all the muscles of the body associated with cardiac and respiratory paralysis. Instead of this general widespread palsy certain nerves may become the seat of great intensity of toxemia giving rise to special distinct forms of local paralysis. Four of these local palsies are of special interest as they occur alone or are part of a general palsy. Named in order of frequency, they are palatal, ocular, cardiac, and diaphragmatic.

The ocular and palatal types rarely are a menace to life but should be closely watched in a patient.

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