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## Toxic neuronitis complicating pregnancy

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**"TOXIC NEURONITIS" COMPLICATING PREGNANCY**

by

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## DEFINITION AND INTRODUCTION

"Toxic Neuronitis" is a complication of pregnancy. The etiology of which is unknown (16) and is entirely theoretical as to whether it is a toxic or vitamin B deficiency or possibly both. Pathologically it is characterized by mild degenerative changes in the anterior horn cells of the spinal cord and slight if any visceral changes. Clinically it usually manifests itself by uncontrollable vomiting in the first trimester of pregnancy, which may cease abruptly or continue in a mild form with the onset of neurological symptoms and findings. If not early recognized and treated, death may occur or permanent paralysis of the affected part of the body may result.

"Toxic Neuronitis" of pregnancy is a term which was first suggested by Berkwitz and Lufkin (1) in 1932 for this complication of pregnancy which previous to this time had been referred to in the literature as a toxemia under such titles as "Peripheral Neuritis", "Polyneuritis", and "Toxic Myelitis of Pregnancy". Berkwitz and Lufkin adopted the term "Toxic Neuronitis" because they believed

that term fitted the pathological findings better than any other term suggested, for this reason I will consider this complication of pregnancy under that name.

Because of the variability of nomenclature for this complication of pregnancy there is very apt to be some question, as to whether all the literature referred to describes the same condition as this disease takes on a fairly variable group of symptoms. The one phase of this disease which is common to all pregnant women developing this complication is the neurological phase. It is upon this common phase that I have referred to case reports and literature.

In this paper a small amount of history has been included with the part dealing with the etiology. The etiology deals with the presentation of numerous theories and hypothesis relative to the possible cause of the disease. An attempt has been made to adequately cover the clinical symptoms, signs, and findings, for it is upon the clinical picture and neurological examination that a diagnosis is made. Likewise considerable attention has been given to means of treating this condition. The pathology found in this disease of pregnancy has been described and the incidence and occurrence as well as the prognosis

have been discussed. A few abstracts of case reports found in the literature have been included to stress or point out certain features of the disease.

## INCIDENCE AND OCCURRENCE

Figures relative to the incidence of "Toxic Neuronitis" are not available except that Taylor and McGoogan (37) give ninety six as the total number of cases reported in the literature.

Plass and Mengert (30) have seen twelve certain or probable cases within seven years and printed their work in 1933. They are of the opinion that the condition is not as rare as has been generally thought and as the knowledge concerning the essential clinical picture becomes more complete the more frequent will the diagnosis of these cases be made. No true estimate can be offered. Cases of so called toxic vomiting, they believe, should be placed in this category of neuritides, also those cases where there is a suspicion of "hysteria" because of the type of subjective complaints these patients give and because of the presence of almost no visceral disease.

Ford (11) compared the references in the literature of the United States with those in the literature of Britain and came to the conclusion that it appears as

though this disease of pregnancy is, as yet, much more prevalent in the United States.

"In the United States the vast majority of cases reported have been from the Mississippi valley, very few cases are seen on either seaboard area." (37)

According to Vandel (41) polyneuritic cases are frequent in pregnant women living in regions where beri-beri tends to be endemic, but he does not give any figures as to the relative frequency in these regions.

Gillespie (15), and Plass and Mengert (30) are of the opinion that this complication of pregnancy is more frequent in the first and second pregnancy. Berkwitz and Lufkin (1) note the frequency to be greatest between the ages of twenty one and thirty five years, coinciding to the time when the incidence of pregnancy is highest. Women with multiple previous gestations are not exempt from the condition however, and patients who have previously shown evidences of mental instability may be more susceptible. (30)



## HISTORY AND ETIOLOGY

Many theories and hypothesis have been formulated in regard to the etiology of this particular complication that may complicate pregnancy. As early as 1859, Churchill (4) suggested hysteria, anemia, rheumatism, and cold as possible causes of paralysis occurring during pregnancy. Later Jaccoud (18), "made the theoretical suggestion that exhaustion of the nervous system due to prolonged and continual excitement of the cord, and that impulses were transmitted by the uterine nerves, exhausting the excitability of that particular segment of the cord and closing avenues by which motor impulses pass."

In 1885 there were published reports on two cases by Jolly (19) in which he ascribed the paralysis as being of functional origin, and suggested hysteria as a possible cause for the paralysis. However, according to Berkwitz and Lufkin (1), it may be presumed that the paralysis in those two reported cases was due to a toxic condition appearing during the months of pregnancy.

Moebius (29), 1887, perceived of the idea that "a morbid condition of the blood" existed in the pregnant

woman. Thus, the theory of auto-intoxication took origin as a possible means of explaining the etiology. (1)

The French Academy of Medicine (2), in 1889, reported a case in which they attributed the paralysis to a reflex action occurring from the uterus.

Whitfield (43) was one of the first to note that paralysis associated with pregnancy; exclusive of the paralysis occurring as a result of trauma, infections, and other diseases; was found in cases which developed toxic vomiting of pregnancy. Tuillant(39), like Whitfield also noticed the relation of vomiting to the neurological findings and due to the fact that he noticed the vomiting was of a severe type before the neuritis appeared, "lack of nourishment" was advocated as a probable cause of the disease. However, it was only a few years later when Lindemann, (21) in 1892, published his experimental work on dogs which showed that no matter how severe a state of malnutrition existed in dogs there were no microscopic degenerative changes, in the nerves, a finding in direct opposition to the idea suggested by Tuillant.

In studying forty nine cases of peripheral neuritis, Reynolds (31), in 1897, noted the disease more common in multiparous women. In fifteen of these cases there was definite history of sepsis in some form or another, in

eleven of the cases there was marked evidence of severe vomiting. Four cases gave alcoholic histories, and he questions if there were not more. He states however, that by carefully studying the symptoms of puerperal neuritis that alcoholism usually never gives rise to symptoms associated with paralysis of the cranial nerves and also that alcoholism causes neuritis in the arms along with the paralysis of the legs. In many of the cases he was unable to find any cause, but he concludes that sepsis or vomiting of incessant type as the most outstanding factors in producing this complication. The neuritis following incessant vomiting is explained by him in two possible ways--first, that the vomiting may be the result of a toxin and that same toxin gives rise to the neuritis; second, he suggests as a hypothesis that because there is incessant vomiting there is set up a condition which he denotes as acetonaemia, and it is the acetone or some "allied body" present in the blood stream which produces the neuritis, and he likens this condition to the possible situation which may exist in diabetic neuritis.

Hornstein (17), in 1916, mentions a case reported by Seige in 1911, in which there was persistent vomiting for ten weeks, ceasing in the fourth month, following which the patient made a slow recovery. The neuritic

findings in this case were at that time attributed to the marked cachexia which followed the vomiting.

This complication of pregnancy has been explained as a disturbance due to the direct result of the action of some toxin which is produced by the product of conception and that this toxin has a special affinity for the nervous system, but evidence for the support of such a view according to Plass and Mengert (30) is lacking in that termination of pregnancy fails frequently to arrest the progress of the disease, and in such cases the disease is aggravated by emptying the uterus.

Due to the fact that Whitfield noticed that polyneuritis was preceded or accompanied by persistent vomiting, Strauss and McDonald (34) are of the opinion that in this complication of pregnancy there appears to be evidence favoring the view that it is a dietary disorder. The vomiting prevents the patient from ingesting and absorbing proper nourishment. Another factor which they mention, and is in keeping with a dietary deficiency disorder is one that was noted by Mettler and Minot (28), that any disturbance or abnormality in the gastro-intestinal tract plays an important role in deficiency diseases. In pregnancy, according to Strauss and Castle (33) there is a marked decrease of secretion in the stomach. A third factor that Strauss

and McDonald (34) give as a causative agent favoring a dietary deficiency disease is that the fetus in a pregnant woman removes a variety of substances from the maternal body, no matter how depleted the mother may be in these substances. They also state that clinically polyneuritis is identical to alcoholic polyneuritis and to beriberi, which is also in harmony with the view favoring a dietary disease. From the three cases which they reported in the literature they therefore conclude that it is not a toxemia but rather a dietary deficiency disorder, similar to beriberi due to a vitamin B deficiency.

Gerstle and Lucia (14) in many respects appear to be in harmony with Strauss and McDonald, clinging to a deficiency disorder, stressing avitaminosis. They state that polyneuritis from any cause is invariably associated with a reduction or even complete absence of free hydrochloric acid in the gastric secretion, and go on to say that "it is probable that the avitaminosis may be due not only to a lack of ingestion of food, but also to the inability to digest, assimilate, or metabolize it." They also state, "quite possibly the presence of the fetus in utero may, in some way disturb these processes so that

polyneuritis may occasionally be encountered in pregnancies during the course of which little vomiting occurs." Wechsler (42) found that in many cases of polyneuritis, other than those cases which are associated with pregnancy, such exogenous poisons as alcohol, arsenic, phosphorus and lead which are supposed to give neuritic symptoms that it was not unusual to find the additional factor of avitaminosis. These toxic substances seem to affect the mucosa of the stomach, liver, or both and in all probability seem to disturb the normal absorption of foods. It is in this way that Gerstle and Lucia (14) suggest that it may be possible for the fetus in susceptible women, to act analogously to an exogenous poison in the non pregnant individual, to cause a decrease in the normal vitamin metabolism. Relative to the part that vitamins play in the etiology, they state that vitamins B<sub>1</sub> and B<sub>2</sub> are anti-neuritic and are involved in connection with the diseases termed beriberi and pellagra. Which of the several vitamins concerned in the more obscure syndromes has not been proven exclusively but they state that experimental evidence points to an absence of vitamin A and also possibly vitamins C and D to cause changes which are degenerative in character in the spinal cord, the spinal roots and peripheral nerves. Possibly therefore if there

should be an absence of one or several of these vitamins the presence of some toxin may then tend to give rise to degenerative changes in the central nervous system. (14)

Luikart (24) is of the opinion that there definitely is some concomitant etiologic factor existing in addition to the pregnancy. He states that there is possibly a complication developing as a sequela of the disease or that possibly our "modern scientific therapy" of pernicious vomiting gives rise to a condition of avitaminosis. The avitaminosis occurring because fluids are forced in the treatment of pernicious vomiting and this tends to wash out the vitamin B from a body which is already depleted. Another factor which he brings up that may cause a disturbance in the vitamin B complex ( $B_1, B_2$ ) is the 20% or more elevation of the basal metabolic rate that usually occurs in the pregnant woman. He basis this idea on Cowgill's work where it was found that in animals the vitamin B complex intake in animals is significantly increased when there has been an elevation of the metabolic rate by the administration of thyroid.

Gillespie (15) makes the statement, "that there should be neurological aspects in pregnancy is not surprising when we consider the changes that take place in the blood, in the vital organs, and in the new direction

of increased metabolic activity during this period." He sums up the various views of different investigators and states that it is a disease due to an obscure toxin of autogenous origin, possibly arising from a disturbance in metabolism associated with defects in the organs of excretion during pregnancy.

Vandle (40) believes that a quick succession of pregnancies may be a contributing factor to the etiology of this disease.

Ford (11) seems to have summed up the factors of etiology in this condition when he states, "etiology is undecided, vitamin B deficiency has received such a consensus of support that it must be considered very seriously. On the other hand, post-mortem findings are consistent in revealing evidence of general toxæmia. It is, on the whole, probable that a combination of both these factors is necessary to produce this clinical entity."



## PATHOLOGY

Cases in which the disease progressed to a fatal termination and on which post-mortem examinations were performed have been fairly consistent in not showing marked pathological changes. Hoffman (16) states that this disease presents a clinical and pathological picture which is distinct from other complications which result from toxic conditions of pregnancy. Lindemann (22) reported a case in which vomiting was present. In this case the pathology was that of a well marked neuritis. Mader (25), in a case of persistent vomiting found neuritic changes in the peroneal, sciatic and tibial nerves with pigmentary atrophy of the extensor muscles of the thigh, but by the use of Marchis method no pathological changes were evident in the spinal cord.

Stuart (36) did an autopsy and a systematic and complete microscopic study of representative areas of the central nervous system and found typical changes of neuritis, and extensive degenerative findings in

the lateral and posterior tracts of the spinal cord and also of its ganglionic cells. The cells in the anterior horns in the cervical region of the cord apparently seemed to show the most marked changes. East (20) found an area in the inferior cervical part of the spinal cord showing yellowish softening and microscopically showing great swelling of the axis cylinder. While Dustin (9) found a decrease in the size of the larger nerve trunks.

Probably the most complete pathological report and with which investigators since have found to be most consistent is that given by Berkwitz and Lufkin. (1) They state that careful microscopic examinations of the central nervous system reveal definite lesions. However, they say these lesions are less marked than the severity of the clinical symptoms would cause one to expect. Almost invariably nerve degeneration is demonstrated in the anterior horn cells in the cord. But unlike Kast and Stuart they found the degenerative changes most marked in the lumbar region of the cord. The characteristic findings were; loss of Nissl substance and a swelling of the cells, eccentricity of the nuclei and occasional cell necrosis was observed. In three of their cases in which post-mortem examinations were done they found in addition evidence of petechial hemorrhages occurring in the brain

of two of the cases and in the other case these petechial hemorrhages were noted in the spinal cord. Absence of gross anatomical changes was an outstanding characteristic, only cloudy swelling and mild fatty changes in the liver and kidney were noted. Plass and Mengert (30) state that mild degenerative lesions of the heart and supra renals may also be demonstrated.

## SYMPTOMS + SIGNS - DIAGNOSIS

There has been a tendency in the past to regard early evidences of neuritis in the pregnant woman as merely recurrences of a neurosis. In many of these patients in which the disease has manifested itself, have in former pregnancies suffered from hyperemesis gravidarum which responded to simple form of treatment. They therefore have been regarded as "neurotic." Especially has this been true of the subjective complaints such as generalized weakness and hyperesthesia and the tachycardia which are frequently seen in disorders of a functional origin. (30)

The first appearance of the disease is similar to a form of nausea and vomiting (morning sickness) that occurs in 50% of the pregnancies, during the first trimester of the pregnancy; during the first month being more or less "physiologic" and in the second month progressing into the pernicious type and in a great majority of the cases lasting for several weeks before paralysis manifests itself.(1) However, Maisel and Woltman (26) report one case in which the paralysis was not preceded by vomiting. Thus, they refute the dogmatism of

those who say that this complication of pregnancy is always preceded by vomiting of the pernicious type.

The vomiting in this condition rarely responds to the usual form of treatment and it terminates abruptly as the symptoms of paralysis become apparent. (1) (15) However, McGoogan (27) states that the vomiting yields to treatment, and then recurs, accompanied by changes in the nervous system. He has noted no abrupt cessation of the vomiting, but states that it has continued as a less severe form.

Weakness is a complaint made by the patients which may very easily be confused with the weakness due to inanition resulting from hyperemesis. (1) The weakness is a general weakness, usually first appearing in the lower extremities and may be limited to them only. The extensor muscles are usually more involved than the flexor group, but the distribution is not uniform. The knees and elbows may be more affected than the ankles or wrists, or the weakness and paralysis may be of the ascending type. (30) This ascending type of paralysis according to Reynolds, (31) and Taylor and McGoogan (37) is not unlike that seen in Landry's paralysis. The paralysis usually has its onset in the third month of gestation. (27) The muscles become soft and flabby because of the progressive weakness and evident atrophy that occurs. (30)

In a great number of the cases according to Reynolds, (31) the disease starts as a sensory disturbance, especially is this so in those parts which later become paralyzed. These sensory symptoms are such as numbness, tingling, paraesthesia, or severe pains. Flass and Mengert (30) state the hyperesthesia is exceedingly variable, occasionally the skin is hypersensitive, but usually, according to them increased tenderness is illicited only on deep pressure over the muscles or over the nerves. Exquisite pain is produced by forceful manipulation of the extremity causing tension of the nerves. (30)

The absence of the tendon reflexes in affected parts points to an involvement of the lower neurons; the achilles reflex and the knee jerks are usually the first to disappear, while the triceps and biceps reflexes may be only weakened or may disappear late in the disease. (30)

A sign which is practically always uniformly present and may be one of the earliest to attract one's attention is tachycardia, "the cardiac rate is not altered by physiologic doses of atropine, a fact that suggests actual involvement of the vagus." Studies made by the use of the electrocardiograph show no evident change in heart action except for the increased rate. (30)

According to Ely (10), Von Hosslin noticed a Korsakoff syndrome in multiple neuritis following toxemia of pregnancy before Korsakoff placed this syndrome of mental disturbance found frequently in alcoholic multiple neuritis in the literature. Von Hosslin also stated that this psychosis is more frequent in neuritides following gestational toxemia than in alcoholic neuritis. McGoogan (27) states this syndrome appears at the time that the paralysis occurs. Plass and Mengert (30) are of the opinion that the Korsakoff syndrome as manifested in "Toxic Neuronitis" denotes cerebral involvement. It is characterized by a loss of recent memory, disorientation, both as to time and place and there is a tendency toward confabulation. This syndrome may appear late in the disease, or in the milder type may disappear within one or two weeks, while on the other hand, it often persists for long periods or even months, or it may become permanent. Especially is this true in regard to loss of recent memory. Dupouy and Courtis (8) are of the opinion that the Korsakoff syndrome appears more frequently in primipara.

Some of the less characteristic and more inconstant conditions found in this complication of pregnancy.

are ocular findings such as nystagmus in the vertical and lateral planes; there may be squint, usually of the divergent form, and diplopia may follow.(30)

Optic neuritis may be manifested by a blurring of vision.

(16) Berkwitz and Lufkin (1) observed optic neuritis in all four of the cases that they reported in the literature in 1932. Plass and Mengert (30) state the examination of the fundi of the eye may reveal indistinct and raised disc margins and a slight enlargement of the veins, however ophthalmoscopic examination may be negative and yet the decrease in visual power may be due to optic neuritis. Retinal hemorrhages have been reported. Exophthalmos is rare.

Occasionally central deafness is noticed. This is believed to be due to impairment of the receptivity of the cerebrum giving rise to a delay in response to hearing. In some cases the auditory nerve itself is involved. (30)

Delirium and lethargy may be present with the psychosis already mentioned or there may be mental changes independent of the Korsakoff's syndrome. Choreiform movements of the head and face have rarely been observed. (30)

Dysphagia and dysphonia may occur due to bulbar



involvement.(30) Burr (3) reports a case of bulbar symptoms where the patient suddenly lost her speech and had a slight palsy of the right side of her face occurring on two successive pregnancies in the eighth month. The aphasia was real and lasted on both occasions two to three months after normal labor. Four out of five cases reported by McGoogan (27) showed bulbar symptoms.

Paralysis of the intercostal muscles and diaphragm may occur giving rise to dyspnea, and may be associated with partial atelectasis of the lungs. (30) Four out of five cases reported by McGoogan (27) died of respiratory paralysis.

Positional sense, due to ataxia of the limbs may be lost, and occasionally pain in the affected limbs may be present without pressure on them or without motion. (30)

Ely (10) reports two cases of temporary loss of sphincter control, which suggests the possibility of spinal cord involvement. Plass and Mengert (30) state the bladder and rectal sphincter disturbances are seen frequently, but usually they are late in the disease. In other cases retention may occur and catheterization must be resorted to.

Jaundice is occasionally seen, but no marked necrosis of liver cells has been demonstrated pathologically. (30)

Relative to the laboratory findings variations may occasionally be noted. The urine is usually normal but albumin and casts may be present when dehydration is marked. The blood cells frequently show a moderate hypochromic anemia and occasional leukocytosis is noted. The blood chemistry studies are usually within normal range, although nitrogen retention may occur in a few cases. The carbon dioxide combining power may range from normal to a slight increase and the hydrogen ion concentration tends to reach the superior limit of the normal curve. (30) According to McGoogan the spinal fluid pressure is usually under normal pressure. There may be an occasional increase in the number of cells present in the spinal fluid. In some cases the spinal fluid protein content may be elevated. (37) An achlorhydria may be present as was demonstrated in the three cases reported by Vandel. (40) Blood pressure and temperature changes are uncommon, unless intercurrent infections occur resulting in elevation in temperature. (30)

That symptoms and findings may not occur until after emptying of the uterus, is shown in the four

cases reported by Ely.(10) Three of these cases showed evidence of profound toxemia before termination of pregnancy.

In regard to differential diagnosis Ford (11) states, "differential diagnosis presents great difficulties. Distinction must be made from anterior poliomyelitis and from peripheral neuritis. Furthermore, cases of more or less transient unilateral or more limited pareses occur which are almost certainly embolic in origin, and must not be confused."

## TREATMENT

The line of treatment to follow in these cases of pregnancy complicated with "Toxic Neuritis" appears to be a very controversial one. Some investigators cling to the idea that the disease is a toxic condition and advocate interruption of pregnancy, others adhere to conservatism and treat the condition entirely on a vitamin and dietary basis, and still others combine these forms of treatment, depending upon the individual case.

Cline (5) believes that therapeutic abortion is possibly too long deferred in many cases of hyperemesis gravidarum. He is of the opinion that termination of pregnancy is the best remedial measure and the most sure means of preventing multiple neuritis. Lubin (23) reports a case where vomiting was controlled by intravenous glucose, hypodermoclysis of saline with glucose, Harris drip and no food by mouth. When about four and one half months pregnant she had a sudden onset of paralysis of the arms and legs. An anterior vaginal hysterotomy was performed. She made a good post operative

recovery, but the neurologic symptoms fluctuated daily. In general there was very little improvement in the neurological manifestations. Three and one half months after onset of the disease the patient died of Bronchopneumonia. Brocklehurst (2) reports a woman 23 years of age in which pregnancy was terminated at about the seventh or eighth month and within two days her mental condition, which was of the Korsakoff syndrome type, was noticeably improved.

Gillespie (15) is of the opinion that the sooner artificial induction of labor is considered the better will the prognosis be. He states most patients show immediate improvement after the pregnancy has been terminated, while other patients seem to grow worse for a period of about two or three weeks. Hoffman (16) states the condition is amenable to early treatment. He also states, "individuals with severe vomiting of pregnancy should be carefully watched for occurrence of any neurological changes. As soon as diagnosis is established the uterus should be emptied."

According to Plass and Mengert (30) emptying of the uterus has been made the treatment of choice because it has been quite effective. There is an association of the condition with pregnancy, thus giving an apparent cause and effect relationship. They also state that the

symptoms have in some cases been increased by emptying the uterus or by the presence of a dead fetus. This seems to them to give evidence of the fact that therapeutic abortion is not a therapeutic aid. On the hypothesis that this complication of pregnancy results from a vitamin B deficiency, they suggest especially as prophylactic measures, the giving of adequate and proper food during hyperemesis gravidarum.

The treatment other than therapeutic abortion appears to be mainly on a dietary basis and an attempt to keep a vitamin balance. (24) Gerstle and Lucia (14) state that if there is excessive vomiting there should be a persistent administration of a super abundance of vitamin and for actual treatment of this complication a diet fortified with vitamins constitutes the most logical and hopeful therapy. Tashjian (38) states that vitamin deficiency is prevalent among obstetrical cases and wherever there are nutritional or deficiency disturbances of long standing the patient should be supplied with the anti-neuritic vitamin B<sub>1</sub>.

Fouts, Gustafson, Zerfas (13), report a case which was treated with daily saline and glucose injections intravenously, with frequent carbohydrate feedings and continuous Murphy drip of soda-bicarbonate and glucose.

Under this treatment the vomiting ceased. When the patient was six months pregnant she had almost complete paralysis of the left leg. At that time she was put on the following treatment:

5/5/33 to 10/20/33 Cod liver oil, drams 2 o.d.  
 5/5/33 to 7/6/33 Vegex (autolyzed yeast prep.)  
 grams 12 o. d.  
 5/6/33 to 6/5/33 Liver Ext. vials 3 per day  
 6/5/33 to 10/20/33 Liver Ext. vials 6 per day  
 5/17/33 to 6/14/33 Iron and ammonium citrate  
 grains 30t.i.d. a.c.  
 6/14/33 to 10/20/33 Reduced iron, grains 10 per  
 day  
 6/12/33 to 7/3/33 Liquid vit. B, concentrate  
 (rice polishings) 3c.c. o.d. (100-200 units vit.  
 B<sub>1</sub>)  
 7/3/33 to --- Vit. B<sub>1</sub> capsules (con. ext. of rice  
 polishings) 8 per day (1 capsule-200u. vit. B<sub>1</sub>)  
 5/25/33 to 7/7/33 Weekly intravenous injections  
 20 c.c. of liver extract derived from 100 grams  
 whole liver  
 7/7/33 to --- Weekly intramuscular injections  
 (6 c.c.) of concentrated liver extract derived  
 from 200 grams of whole liver.

When the patient was started on this regime of high  
 vit  
 vitamine diet and liver there was no progression of  
 signs or symptoms of the disease. The mental improve-  
 ment was the first noted. The pulse which had fluc-  
 tuated, reaching 130 almost daily, gradually declined  
 in rate. There was a gradual improvement in the blood  
 picture. Marked improvement was noted in the neuro-  
 logical symptoms during the administration of large  
 doses of vitamine B<sub>1</sub>. The muscles became more firm

and less flabby.

Cook (6) in addition to a liberal vitamine diet, especially of vitamine B, gave a patient generous sun-tanning in hopes that it would augment the vitamine intake.

Of those who have treated patients both on a dietary basis and by doing therapeutic abortions, Strauss and McDonald (34) report a case in which Cesarean section was performed at the end of six months to stop vomiting which had persisted for three months. In this case neurological symptoms set in after the section had been done. This patient is reported to have made a slow but steady improvement on a high protein diet and a diet rich in vitamine B and iron, the iron because of a macrocytic hypochromic anemia. To another case they gave, orange juice, 100 grams of raw liver, 6 yeast vitamine Harris tablets daily and 6 grams iron ammonium citrate daily with improvement. To still another case they gave 6 grams iron ammonium citrate daily, 12 grams autolyzed yeast ( $B_1, B_2$ ) and 12 c.c. Cod liver oil daily. Later the patient developed an intolerance to the iron, so liver extract No. 343 N.N.R. rich in vitamine  $B_2$  derived from 600 grams liver, and 12 yeast vitamine  $B_1$  (Harris) tablets were given daily



with improvement both in the nerves and blood ten days after treatment was started. These men state that rational therapy should however, avoid operative intervention and treatment should be directed to supply suitable material to <sup>the</sup> dietary deficiency that occurs. If such material can not be retained by the stomach they advocate intramuscular therapy. They recommend the use of liver and liver extract both by mouth and by injection in cases not responding to preparations of vitamins B<sub>1</sub> and B<sub>2</sub>, because they are of the opinion that there possibly exists a dual mechanism at work in this complication of pregnancy in as much as macrocytic anemia is often observed.

A case reported by Stroh (35) had on two previous pregnancies severe vomiting ending in spontaneous abortion, and in her third pregnancy she again developed severe vomiting. When three and one half months along she developed paralysis and foot drop. He started her on concentrated yeast tablets ii t.i.d., Galan B t.i.d. and adrenalin cortex tablets t.i.d. With her past history of recovery from pernicious vomiting following spontaneous abortion, pregnancy was terminated. There was a definite increase in appetite and disappearance of dysphagia and a slow and steady improvement

following this form of treatment. He advocates high vitamine B doses as a prophylactic and if the the patient develops a typical polyneuritic syndrome then therapeutic abortion should be considered and performed in selected cases.

Forman (12) reports a case where brewer's yeast one and one half ounces daily, and two weeks later five oranges daily and one hundred and thirty grams of fresh animal protein and a daily caloric intake of twenty five hundred to three thousand calories, plus nine tablets daily of Meade Johnson's brewer's yeast were given to a patient which had a therapeutic abortion because of vomiting and after which neurologic symptoms developed. Recovery was practically complete after a period of twenty months under such a dietary regime.

Falls, in a response to a paper by Plass and Mengert (30) stated that he had noticed a similarity between patients having this complication of pregnancy and thyrotoxicosis and has noticed an improvement in these patients if given a compound solution of iodine. Because the symptoms are similar to polyneuritis, Sure, in response to the same paper states that he gave 120 to 150 grains of calcium lactate with benefit to the patient.

To all toxemias of pregnancy, including polyneuritis, Ross (32) suggests as a prophylactic diet, 6 brewer's tablets, 8 ounces of tomatoe or orange juice, 1 to 2 pints of milk, 2 teaspoonsful of lactose, and 3 ampoules of plain haliver oil.

When paralysis occurs the muscles and joints should be given active and passive exercise as soon as the pain and tenderness will permit to prevent contracture.(15) Massage and electrotherapy, and orthopedic appliances are very valuable in over coming contractures that may occur.  
(30)

## PROGNOSIS

Berkwitz and Lufkin (1), in 1932, gathered from the literature forty eight cases and among that group of cases there were nine deaths, which gives a mortality rate of 18%.

In an unpublished paper by Taylor and McGoogan (37) 27 cases had been reported by, Plass and Mengert, McGoogan, Berkwitz and Lufkin, Strauss and McDonald, and Wilson and Garvey, in which there were 18 deaths, a mortality of 66%. Since these figures were compiled, Taylor and McGoogan, state fifteen additional cases have been reported in which there were four deaths, and five cases of their own series in which there were two deaths. From this group of compiled cases there were ninety five cases reported with thirty three deaths giving a mortality of 34.7%.

The reason that the incidence of deaths has been on the increase in recent years since the year 1932 when Berkwitz and Lufkin reported their work Plass and Mengert (30) state is due possibly to the fact that the condition has since that time been recognized more definitely in the patients where death ensued early in the disease.

Hornstein (17), in 1916, noted that if the paralysis of the pregnant woman occurred late in pregnancy, recovery was more probable to occur; this seemed evident to him if the causative factor was removed before sufficient time had elapsed for atrophy to take place.

In other words as Hoffman (16) states, the length of time which symptoms persist or their permanency is dependent to a large extent upon the stage of the disease in which pregnancy is terminated, also the higher level in the body that the pathological process reaches the poorer is the prognosis apt to be.

If the patient survives more than a period of two weeks after diagnosis has been made by doing a physical examination the possibility of complete recovery is good, and in fulminating cases death may ensue three or four days after the onset of the first symptom has been noted. Death may be due to intercurrent disease, but frequently it is the result of a complete paralysis of the respiratory muscles or of those muscles used in the process of deglutition.(30)

When recovery occurs it occurs slowly but is not always complete, occasionally however, nerve changes have progressed and have become too extensive, consequently in such cases full function of the extremity

is not regained (30), in such cases contractures of the extremities are very prone to occur if proper treatment is not instituted.(1)

"Patients who survive should not undertake another pregnancy for instances of recurrence are known. A few have a normal pregnancy in a subsequent gestation. If Pregnancy should occur immediate therapeutic abortion should be considered. In the event that evacuation was not performed, or a patient desired another pregnancy the patient should have adequate vitamins and associated therapy to prevent the recurrence of the neuronitis or to at least diminish its severity.(37)

## SUMMARY

"Toxic Neuronitis" is not a common complication of pregnancy. Some ninety six cases have been reported in the literature. This complication of pregnancy is more frequent in the first and second pregnancy, or between the ages of 21 and 35 years, coinciding to the time when the incidence of pregnancy is the highest.

Ever since 1859 numerous theories and hypothesis have been formulated in regard to the etiology of this complication of pregnancy, and up to the present time the etiology is undetermined. The two etiological factors to which most men adhere to and seem to be best supported are: that it is a toxemia of pregnancy due to some unidentified toxin, or that it is a deficiency disease mainly an avitaminosis with the greatest stress on a vitamin B deficiency.

The pathological findings are usually less marked than the severity of the disease would lead one to suspect. The characteristic findings are: nerve degeneration in the anterior horn cells of the cord, loss of Nissl sub-

substance and swelling of the cells, eccentricity of the nuclei, and occasional cell necrosis. Petechial hemorrhages may be noted in the brain or the cord. Internal visceral changes are slight, only cloudy swelling and mild fatty changes are noted.

The disease has its onset usually during the first trimester. It usually starts out with nausea and vomiting (morning sickness). The vomiting becomes uncontrollable or of the pernicious type, lasting for several weeks. It may or may not cease abruptly with the onset of neurological manifestations. Weakness in the lower extremities is the most frequent first noted symptom--going on to paralysis in those parts of the body. However, sensory disturbances may be the first noted symptoms. Tachycardia and an absence of tendon reflexes in the affected extremities is characteristic. A Korsakoff syndrome is a frequent cerebral manifestation. Some of the less frequent findings are optic neuritis giving blurring of vision, nystagmus, squint, diplopia, deafness, and certain bulbar manifestations such as dysphagia and dysphonia. Paralysis of the diaphragm and loss of sphincter control may occur.

Laboratory findings do not deviate, but slightly from normal. Moderate hypochromic anemia and achlorhydria are



are among the most common. The pH of the blood tends to reach the superior limits of normal.

In a few cases neurologic symptoms do not appear untill after the uterus has been emptied.

The disease must be differentiated from Anterior Poliomyelitis, Peripheral Neuritis, and Transient unilateral pareses of embolic origin.

Treatment seems to depend upon whether one believes the disease is due to a deficiency disorder or to a toxic condition. Therapeutic abortion is strongly advocated by some men, especially before the paralysis becomes a prominent part of the picture. Some advocate therapeutic abortion in every case. Others are more conservative and treat the complication with a high vitamine diet, with stress on vitamine B. Iron and Liver are given for the anemia. Some men combine the high vitamine therapy and therapeutic abortion.

Physio-therapy such as passive and active exercise, massage and electrical stimulation should be given the affected muscles and joints.

Prognosis depends upon early diagnosis and treatment. Neurological examination should be performed in all cases of hyperemesis gravidarum. Recent investigators give a mortality rate of 66%; of all the cases

reported in the literature the mortality is about 34.7%.

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