



Hyperemesis Gravidarum

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I. CASE REPORTHYPEREMESIS GRAVIDARUM

Case is white female, 18 years old, admitted to University of Minnesota Hospitals 7-20-34 and expired 8-17-34 (28 days).

Pregnancy out-of-wedlock

4-11-34 - Last menstrual period.

5- -34 - Nausea and vomiting.

Emesis

6- -34 - Unable to retain food or liquids. Losing weight. No other symptoms. Being treated by intravenous therapy and nothing by mouth. Does not respond to treatment.

Hyperemesis Gravidarum

7-20-34 - Continuous vomiting. No response to treatment. Admitted. Physical examination - mumbles incoherently, has purposeless movements of hands, tremor of hands and feet. Answers questions slowly with effort. Cannot give a consistent history. Marked salivation. Eyes - yellowish tinge of sclerae. Blood pressure 124/78. Loud systolic murmur over precordium. No other chest findings. Abdomen - liver and spleen not palpable, old appendectomy scar present. Pelvic - uterus size of 3½ mo. pregnancy.

Laboratory

Urine specific gravity 1.026, no albumin, 3+ sugar, occasional leucocytes; no acetone, diacetic acid or erythrocytes. Blood - hemoglobin 72%, leucocytes 13,350, neutrophils 38%, lymphocytes 12%, non-protein nitrogen - 22.2 mgs. per 100 cc. Blood urea nitrogen - 10 mgs., uric acid 1.35, sugar 205, CO₂52, chlorides 625. Icteric index 25 (Is this blood chemistry report the result of the previous intravenous therapy?)

Progress

Pulse 120. Temperature 100.8. Given nothing by mouth. 2500 cc. saline given subcutaneously; 1000 cc. intravenously. Sodium luminal and sodium bromide by hypodermic and per rectum, respectively.

Better

7-21-34 - Temperature 103, pulse 140.

4000 cc. fluid given paraorally. Sedatives continued as before. Feels much better. Is alert. Responds to questions. No vomiting since last night. Excessive salivation absent. Urine - sugar absent. Leucocytes 12,000. Icteric index 20.

7-24-34 - Temperature has ranged in the interval from 101 to 103, pulse between 120 and 140. Urine (2 occasions) - trace of sugar. Icteric index - 16.

Good response to Treatment

7-26-34 - Very much improved. Normal temperature. Pulse 150. Now taking fluids by mouth. Icteric index - 11.6.

7-31-34 - Now on dry diet. Temperature normal. Pulse within normal limits. Paraoral fluid now given by subcutaneous route because patient dislikes punctures.

8-9-34 - Continues to vomit once or twice a day. Was found attempting to induce vomiting by inserting finger down throat. Condition appears good.

Worse

8-10-34 - Not doing well. Vomiting more frequent than before.

8-12-34 - No better. Frequent vomiting.

Operation

8-13-34 - Definitely worse. Hemoglobin 60%. Icteric index 18. Pulse 140. Temperature 101.6. Operation: because an adequate course of treatment has failed to stop the recurrence of vomiting and because the patient is rapidly appearing worse, a decision to empty the uterus is made. Vaginal hysterotomy performed.

8-14-34 - Condition no better. Restless. Restraints necessary. Picks and pulls at bedclothes. Incontinent. Pulse up to 150.

8-15-34 - Pulse up to 180. Temperature around 102. Totally irrational. Complains of numbness. Apprehensive. Marked salivation.

Neurological condition

8-16-34 - Condition same. Confused. Disoriented. No cooperation. Eye grounds show edema. Deep reflexes present. Abdominal reflexes absent. Shere

appears to be considerable strength in the extremities. Incontinence present. Difficult to make out any peripheral neuritis because of patient's condition. Numbness in hands has been complained of while patient is rational. No nerve damage can be made out clinically. Blood urea nitrogen - 14.3. Uric acid - 1.5. CO_2 - 53. Icteric index - 6 units.

Expired

8-17-34 - Temperature 105.6. Becoming weaker. Various stimulants given without effect. 9:30 A.M. - Expired.

Autopsy

Body is of poorly nourished, fairly well-developed, white female, 18 years of age, measuring about 152 cm. in length and weighing approximately 90 lbs. McBurney scar present. No definite jaundice or cyanosis. Pupils are equal.

Peritoneal Cavity contains no excess fluid or adhesions. Appendix not found.

Pleural Cavities contain no excess fluid or adhesions. Pericardial Sac contains no adhesions or excess fluid.

Heart weighs 225 grams. Valves are soft and show no vegetations. Root of Aorta is smooth. Coronaries are soft and patent.

Right Lung weighs 400 grams and shows slight posterior hypostasis. Left Lung weighs 200 grams, shows no nodules or consolidation.

Spleen weighs 150 grams. Pulp is somewhat soft.

Liver weighs 1400 grams and shows no areas of necrosis on gross section. Normal color, slight cloudy swelling present.

Gall-Bladder contains no stones.

Gastro-Intestinal Tract shows no ulcerations or other changes.

Pancreas is of normal consistence. No hemorrhages noted.

Adrenals show no hemorrhage or necrosis.

Right Kidney weighs 150 grams. Pelvis not dilated or injected. No abscesses.

Left Kidney weighs 200 grams. Pelvis

slightly dilated and infected. Ureter somewhat dilated. Slight cloudy swelling present.

Genital Organs: Hysterotomy scar present just below fundus, between cervix and fundus proper.

Head - not examined.

Microscopic: Cloudy swelling of kidneys. Slight fatty change in liver.

Diagnosis

1. Hyperemesis gravidarum (clinical).
2. Cloudy swelling of viscera.
3. Postpartum uterus with hysterotomy wound.

II. ABSTRACT

HYPEREMESIS GRAVIDARUM

Probably the best way to introduce this subject is to use the statement of one author who said that the illness is a "disease of theory".

Etiology

Throughout the literature, there is the impression that the disease, hyperemesis gravidarum, is an exaggeration of the "normal" process known as the vomiting of pregnancy. Vomiting seems to be a manifestation of some physiological adjustment to pregnancy. It is present only in humans, apparently unknown in animals. The cause of vomiting of pregnancy or that of the persistent form is entirely unknown. A large number of theories have been presented. One author suggested that individuals with gray eyes are more predisposed. None of the theories appear conclusive. The following review of some of these theories shows the marked variability.

Hyperthyroidism (Falls)

This author contends that there is a normal functional hyperplasia of the thyroid during pregnancy. He points out that most pregnant women have an elevated basal rate which sometimes is as high as 110 and frequently ranges between 50 and 60. He points out that symptoms of hyperthyroidism are referable to the gastro-intestinal tract. He gives as

patients Lugol's solution and claims that he gets excellent results. Objections to this theory are: (1) not all cases with hyperemesis gravidarum show an elevated basal metabolic rate, and (2) all pregnant women with a high basal rate do not show hyperemesis gravidarum.

Adrenal Insufficiency (Kemp)

This author points out that the adrenal cortex undergoes a hyperplasia during pregnancy and feels that the hyperplasia in some cases is not sufficient for functional demands. He points out that the symptoms of adrenalectomized animals begin with gastro-intestinal disturbances. In Addison's disease, there may be anorexia and vomiting. He claims relief of the hyperemesis by feeding adrenal cortex.

Gastro-Intestinal Reflex

Alvarez has shown that there is a reversal of the gastro-intestinal gradient in pregnant rabbits. Other authors also believe that this is true in humans and point out that the gastric content in pregnancy is uniformly low in free hydrochloric acid with a normal total chloride content. The neutralization of the free acid with transformation of the hydrochloric acid into chlorides is said to be due to excessive duodenal regurgitation indicating the reversal of intestinal gradient. One author feels that the presence of this neutralized gastric content in the stomach in the early morning hour gives rise to nausea and vomiting, and he feels that the intake of food or the giving hydrochloric acid relieves the patient because it increases the acidity of the stomach and promotes normal peristalsis.

Liver Injury

It has been repeatedly shown that in hyperemesis gravidarum there is a low blood sugar with fluctuations as low as 30 or 40 mgs. per 100 cc. In addition to this, there is retention of nitrogenous products in the blood and a high excretion of ammonia in the urine. It is therefore suggested that these features indicate some damage to the liver, probably due to absorption of toxins from the fetus.

specific theories of etiology, there are the usual general statements that the disease is due to a toxemia from absorption from the fetus, that there is a neurotic factor or that infection is a causative factor.

Pathology and Disturbed Physiology

The gross and microscopic findings at autopsy in the usual case of hyperemesis gravidarum show nothing of note. There may be cloudy swelling of the liver and kidneys but no actual demonstrable necrosis. Some autopsies have been reported as showing necrosis in the liver and kidney, but, especially in the latter organ (these changes appear to be postmortem autolysis?). In contrast to these negative autopsy findings, a large number of disturbed physiological processes have been described during life. The following is a summary of these findings:

Gastric contents: Fifty cases (Arzt)

	Early Pregnancy	Late Pregnancy
Free acid	5 to 15°	10°
Total acidity	15 to 30	20 - 25
Total chlorides	normal	normal

In 29 of these patients, there was total absence of free hydrochloric acid. The normal total chlorides in the presence of a low free acid is considered to indicate increased neutralization due to excessive regurgitation from the duodenum. This reversal of the intestinal gradient has been demonstrated experimentally by Alvarez and Hosoi (A.J. of Obst. & Gyn. 19: 35, 1930). Late in the disease, bleeding of the capillary type from the mucosa may occur giving rise to hematemesis.

Carbohydrate Metabolism:

Underhill and Rand (1910) first demonstrated low blood sugar values in hyperemesis gravidarum. From this time on, this finding is repeatedly observed. Titus and Dobbs (1928) reported a moderately large series of cases in which the blood sugars ranged as follows:

In addition to these more or less

	<u>Under</u> <u>80 mgs.</u>	<u>80 to</u> <u>100 mgs.</u>	<u>Over</u> <u>100 mgs.</u>
Moderately severe cases	18	11	3
Severe cases	<u>7</u>	<u>1</u>	<u>0</u>
Total	25	12	3

The degree of hypoglycemia in this group under 80 mgs. was as follows:

20 to 29 mg.	- 1
30 to 39 mg.	- 0
40 to 49 mg.	- 2
50 to 59 mg.	- 2
60 to 69 mg.	- 8
70 to 79 mg.	-13

These patients do not manifest the convulsions or coma found in either the hypoglycemia following excessive dosage of insulin or the spontaneous hypoglycemia. It is suggested that the gradual development of the hypoglycemia allows the patient to compensate in some way without developing convulsions. Accompanying the hypoglycemia, there is an acidosis with both diacetic and acetone in the urine. Van Slyke test is usually somewhat lowered with an average of about 50 to 55, although readings as low as 30 have been obtained. The explanation of hypoglycemia is not apparent. Some authors have suggested that it is the cause of a hyperemesis gravidarum, others have indicated that it is a result. It is suggested that the low intake of food, the vomiting and the strain upon the mother's body by the growing child all contribute to lowering the carbohydrate reserve. No reference is found suggesting that the hypoglycemia is spontaneous such as might result from some hyperplasia or hyperactivity of the pancreas. Frequent reference is made to the suggestion that the liver has been injured by some form of toxic substance and cannot store glycogen.

Chloride and Nitrogen Metabolism

The blood chloride and blood nitrogen changes resemble very much those found in intestinal obstruction. There is a drop of the chlorides to an average level of 300 to 400 mg. with occasional readings as low as 200 to 300. The drop is thought to be secondary to the loss of chlorides in the vomitus. Accompanying

this, there is an elevation in the nitrogenous products in the blood. It has been suggested that the disturbance is due to liver damage. The fact that both these changes revert back to normal after administration of sodium chloride has led to the opinion that the changes in the blood nitrogen are either a protective phenomena or are otherwise related to the drop in chlorides. The following blood study is given as illustrative of the changes before and after the administration of sodium chloride:

	<u>On</u> <u>Admission</u>	<u>After</u> <u>sodium</u> <u>chloride</u>
N.P.N.	5.4	26.0
B.U.N.	19.8	6.1
Creatinine	1.3	1.6
Uric Acid	5.3	2.9
Amino acid nitrogen	3.0	6.6
Chlorides	300.0	475.0
P.S.P.	10.0	33.0

The urine frequently showed a high excretion of ammonia nitrogen and this is used, particularly by the French, as a prognostic sign. All these blood changes have been pointed to as etiological factors. However, it is most probable that all are secondary to the vomiting rather than a cause.

Diagnosis

There usually is no question regarding the diagnosis. Occasionally, confusion may be caused by such conditions as brain tumor, cholecystitis, ulcers or meningitis.

The work of Falls suggests that severe hyperthyroidism may be confused with hyperemesis gravidarum. He states that the normal metabolic rate in pregnancy is elevated. Readings of 60 or 70 are frequent and they may be as high as 110. Apparently, hyperthyroidism is not uncommon in pregnancy and it seems possible that some forms of so-called toxemias may be on this basis.

Berkwitz and Lufkin emphasized a neurological condition associated with hyperemesis gravidarum which for the present may be spoken of as a complication. This consists of a polyneuritis

with mental changes which frequently goes on to death.

These authors were able to collect 48 cases of the condition from the literature, added 6 more, and since the article appeared several authors have confirmed the findings. Clinically, nerve involvement may occur during the course of the hyperemesis gravidarum or may follow the therapeutic abortion from a few days to several weeks. The disease is first manifested by weakness in the legs, especially of the extensor muscles, and sometimes in the arms. Rarely, the involvement is of the ascending type. Hyperesthesia of the skin is variable, sometimes being absent, other times marked. There is usually pain in the nerves when pressure or tension is applied. Tendon reflexes are absent. The weakness may be so severe that the patient cannot raise the limbs from the bed. Accompanying this, there is a variable degree of mental involvement. Delirium, psychosis, stupor or various manifestations ranging between these may be present. Less characteristically, there is involvement of the cranial nerves such as paralysis of the eye muscles, deafness and dysphagia; choreiform movements; ataxia and loss of sphincter control. Pathologically, very little change is found grossly. Microscopically, nerve degeneration may be demonstrated in the large trunks going to the involved extremities. Degenerative changes may be observed in the anterior horn motor cells. Petechial hemorrhages in the cord and brain have been observed. The prognosis is poor. In the 4 cases reported by Berkwitz and Lufkin, 3 died and only 1 recovered. In the collected series, the mortality was 25%. Plass and Mengert reported 28 cases with a mortality of 68% (collected cases). Even when the patient recovers, the paralysis or paresis may be permanent. The pathogenesis is not clear. Berkwitz and Lufkin observed that the clinical and pathological features resembled those of beriberi. Luikart emphasizes this vitamin deficiency factor. He points out that, experimentally, dehydration hastens the appearance of symptoms in vitamin "B" deficiency. He states that the capacity for storage of this vitamin is limited in the human and he believes that the

increased basal metabolic rate attending pregnancy, the dehydration and the low intake of food during the illness produces the disease. The treatment which he suggests is yeast and rice polishings and he feels that this diet is of benefit.

Treatment

The routine treatment of hyperemesis gravidarum has been fairly well standardized, withholding food by mouth, maintaining the intake of fluid by paraoral administration (either per rectum, subcutaneously or intravenously) and removing outside stimuli from the patient as much as possible. Sometimes a course of treatment which is very disagreeable to the patient is adopted, such as making her vomit in bed, giving painful subcutaneous injections, strict isolation, etc. Whenever the emesis becomes serious and is accompanied by the secondary changes as outlined above, therapeutic abortion is indicated. Various men give criteria as to when this procedure should be done, for instance elevation of pulse above 140, presence of temperature, presence of acidosis, hypoglycemia, etc. In addition to these terminal methods of treatment, some men have suggested specific forms of therapy.

Falls, in addition to the general therapy outlined above, gives the following:

Lugol's solution by proctoclysis in a solution made up as follows:

Glucose	50 gm.
Alcohol	50 cc.
Sodium bromide	4 gm.
Sodium bicarbonate	30 gm.
Lugol's solution	45 gm.
Saline	Up to 1000 cc.

As soon as the patient is able to take food by mouth, 30 minims of Lugol's is given each day. Luikart urges the addition of vitamins, particularly vitamin "B" to the diet. Kemp gives suprarenal extract (grains vi) one to 3 times a day. Arst, because of a low or absent free hydrochloric acid in the stomach, attempts to raise the acidity by the administration of acid or some substitute. He stated that if hydrochloric acid was so disagreeable to the

patient that he substituted Muriatogen. This consists of coated synthetic silicate which dissolves in the stomach, yielding an equivalent of 10 minims of hydrochloric acid. More recently, he has been giving 3 grains of caffeine citrate which seemed to stimulate the increase in acidity. He gives the gastric acidity curve in 10 cases in which there was an average rise to 35° following the use of caffeine citrate. This author believes that the greatest value of this form of treatment is in the early cases, in the vomiting of pregnancy rather than in hyperemesis gravidarum. He feels that it is a prophylaxis against the development of the viscous type. All authors emphasize the necessity for chlorides and glucose intravenous injections. The elevation of nitrogenous substance in the blood apparently recedes when the chloride level is maintained.

References

1. Brennon, A. N. and Hicks, C. F.
Pathological and chemical changes in hyperemesis of pregnancy.
J. of Obst. & Gyn., Brit. Emp. 33: 60-70, 1926.
2. Haden, R. L. and Guffey, D. T.
Case of pernicious vomiting of pregnancy with low blood chlorides and marked response to sodium chloride treatment.
Am. J. of Obst. & Gyn. 8: 486-491, 1924.
3. Kessler, R. and Abers, H.
Hypochloramie and Azotamie bei Hyperemesis gravidarum.
Zentrablatt f. Gynak. 57: 2479-2484, (Oct. 21), 1933.
4. Kretzschmar, H.
Hyperemesis and Hypochloramie.
Ibid. 2353-2358, (Oct. 7), 1933.
5. Titus, P. and Dobbs, P.
The etiological significance of lowered blood sugar values in vomiting of pregnancy.
Am. J. of Obst. 16: 90-96, 1928.
6. Labbe, M.
Le trouble du metabolisme azote au course des vomissements avec acidose de la gestation.
Presse Med. 4: 921-922, (June 10,) 1933.
7. Anderson, D. F.
Gastric acidity in emesis and hyperemesis gravidarum.
J. of Obst. & Gyn., Brit. Emp., 39: 558-565, 1932.
8. Arzt, F.
Further observations on the gastric juice in pregnancy.
Am. J. of Obst. & Gyn. 20: 382-385, 1930.
9. Berkwitz, N. J. and Lufkin, H. H.
Toxic neuronitis of pregnancy.
Clinico-pathological report.
Surg., Gyn. and Obst. 54: 746-757, 1932.
10. Plass, E. D. and Mengert, W. F.
Gestational polyneuritis.
J.A.M.A. 101: 2020-2023, 1933.
11. Luikart, R.
Avitaminosis as a likely etiological factor in polyneuritis complicating pregnancy with the report of a case.
Am. J. of Obst. & Gyn., 25: 810-815, 1933.
12. Kemp, W. N.
Hyperemesis gravidarum treated as a temporary adrenal cortex insufficiency.
Canad. Med. Assoc. J. 28: 533-591, 1933.
13. Falls, F. H.
Observations in the use of Lugol's solution in hyperemesis gravidarum.
Am. J. of Obst. & Gyn. 22: 882-890, 1931.

III. STAFF MEETING

Date: November 8, 1934

Place: Recreation Room,
Nurses' Hall

Time: 12:15 to 1:15

Attendance: 99

Program: Typhoid Fever

Discussion: Next Week.

IV. SOUND MOVIES

Title: The Work of Running
Water -- by University Film Foundation,
Harvard University. One reel.

V. SOME FACTS

There are 165 women and 1 man registered in the course of Medical Technology at the University of Minnesota. The curriculum was developed about 10 years ago and more than 175 graduates are now out in the field.....There is a sequel to Dr. Rossen's story of the woodpile. See him for details.....The pingpong tournament in the Intern's quarters goes merrily on. Dr. Ainsworth is now among the leaders.....When Clark Shaughnessy, coach of the Chicago football team, was here last summer, he asked us to reserve about 10 beds for his Chicago players to be used after the game Saturday which was just another way of paying a compliment to the Minnesota Power Trust.....The meeting on Typhoid Fever last week was one of the most interesting we have had for some time. This was due to the very remarkable interest by the group in discussing the problem. Some intimated that we served coffee royale, but we did not.....When Mighty Hunter Erickson and friends stopped in St. Paul to eat, they discovered a large crowd waiting around their car looking at the game. Much publicity

resulted.....M.H. William T. Peyton and K. W. Stenstrom are now on their annual hunting trip with results earnestly awaited.....Harold Clausen, former information clerk, is now practicing Dentistry in Marshall, Minnesota and doing very well.....The Biology class of the Carver High School paid a surprise visit on their radio teacher this week by coming to the studios of WCCO to listen to the lecture in person. They arranged themselves around the microphone and took notes as they do at home. Following the talk, they were shown about the studio and apparently were most interested in the Fels Naphtha trio which was rehearsing at the time... ..The Community Fund picture and talk by Rev. Tyner, the golfing Pastor, featured the mass meeting held on Monday.The solicitors are meeting with a very good response, and we thank you all for your generosity.....The Executive Council of the Directors of the University Hospitals is meeting at our institution Saturday. Among others, former Superintendent, Paul Hill Fesler, will attend.Dr. Thomas M. Rivers of the Rockefeller Institute will give the annual address of the Minnesota Pathological Society Tuesday, November 20, 1934, at 8 P.M. in the Institute of Anatomy. His subject will be "Filterable Viruses with particular reference to Psittacosis."Miss "pardon my southern accent" Harrington of the Record Room is a daughter of Health Commissioner Harrington, of Minneapolis....Director Halbert Dunn in addition to being a tennis addict is also an ardent disciple of the art of fencing....A group of executives from the canning industry were tasting corn not long ago, and because of its peculiar taste thought of the possibility of botulism. In the Dakota epidemic in which home brew and infected food had been taken, it was found that those who were well saturated were not so seriously affected. When our patients were brought to the hospital, they were in a hilarious mood. After the effects of the alcohol had died off, it was learned that they did not have botulism. A good time was had by all. The University Department of Bacteriology is prepared to make examinations of suspected food of this sort on a moment's notice.....

At the Woman's Exposition at the Minneapolis Auditorium the latter part of this month, many of our lady leaders will be present to explain how it is done. One of the lectures will be on "How to get a job and keep it." The University of Minnesota is the only college or university in the United States which offers a course in funeral directing and embalming. Started more than twenty years ago, it was referred to in the Americana column of the Mercury as the "higher education in Minnesota." Studies show that within a year after its establishment the autopsy percentage in Minneapolis started to rise. For many years Minneapolis has had the highest percentage of autopsies in the United States. We believe there is cause and effect.