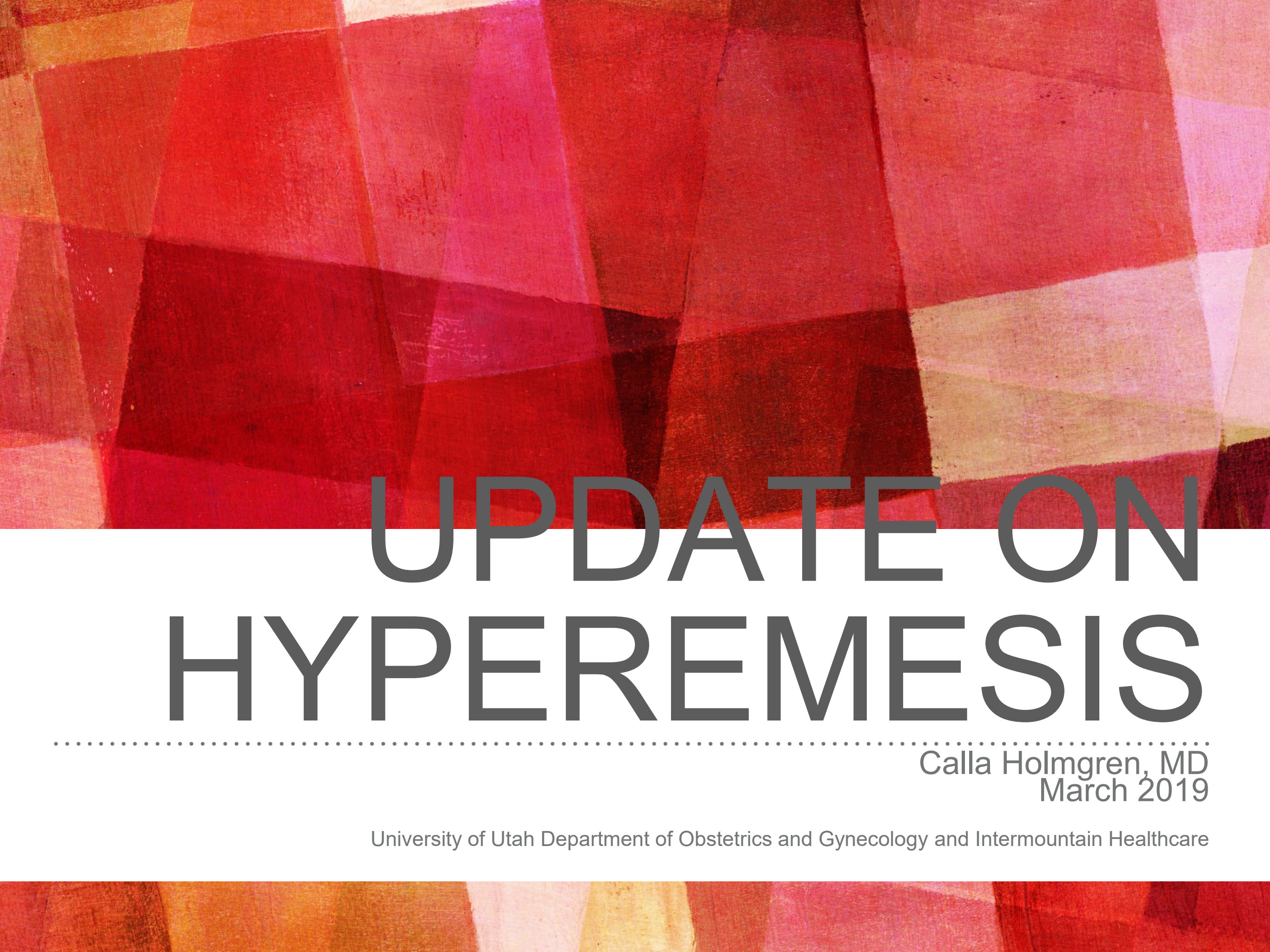




UPDATE ON HYPEREMESIS

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SPECIFIC AIMS

- **Identify** Hyperemesis Gravidarum (HEG)
- **Differentiate** between normal nausea and vomiting of pregnancy and Hyperemesis Gravidarum
- **Describe** the complications of Hyperemesis Gravidarum
- **Explain** management of Hyperemesis Gravidarum

INTRODUCTION

Nausea/vomiting is a common complaint during pregnancy

None	25%
Nausea alone	25%
Nausea and vomiting	50%

IT IS A NORMAL PHENOMENON!!!

NORMAL NAUSEA AND VOMITING

- Primigravidae
- Multiple pregnancy
- History of previous pregnancy with nausea and vomiting or motion sickness
- Molar pregnancy
- Younger women
- Obese women
- Women who are sero-positive for *Helicobacter pylori*

NORMAL NAUSEA AND VOMITING

- Rising levels of B HCG hormone
- Theories for normal nausea and vomiting
 - Feto-protective
 - Genetic
 - Placenta and appetite genes GDF15 and IGFBP7
 - Immunological
 - Biosocial

Weeks from LMP)	Percent of Patients
<3	6.9%
3-4	6.5%
4-5	21.3%
5-6	27.1%
6-7	23.7%
7-8	8.2%
>8	6.2%

NORMAL NAUSEA AND VOMITING.....

- Onset is in the first trimester
- If the initial onset is after 11 weeks, other causes need to be considered

IMPROVEMENT IN SYMPTOMS

Weeks	% of Patients
<8	8.2
8-9	9.2
9-10	9.9
10-11	15.1
11-12	17.5
12-13	8.6
13-14	11.0
14-15	7.2
15-16	4.1
>16	9.2

NORMAL NAUSEA AND VOMITING

- Although normal, can cause significant disability
 - Psychosocial difficulties
 - Time off work
 - Restriction of domestic and leisure activities
- THE MORE IT IS IGNORED, THE WORSE IT GETS
 - Fiaschi et al., Clinical management of nausea and vomiting in pregnancy and hyperemesis gravidarum across primary and secondary care: a population based study. BJOG 2019

HYPEREMESIS

- Hyperemesis is a severe form of nausea/vomiting of pregnancy
 - Incidence
 - 3-5/1000
 - 0.3-3.6%
 - Persistent vomiting
 - Large ketouria/ketonemia
 - Electrolyte imbalance
 - Dehydration
 - Longterm sequelae
 - Hepatic
 - Central nervous system
 - Renal damage

HYPEREMESIS

- Pathogenesis
 - Largely unknown
 - Tends to be a disorder of Western countries
 - Psychological factors
 - Conversion/Somatization disorder
 - Response to stress
 - Hormonal Changes
 - Elevated HCG
 - Abnormal GI motility

HYPEREMESIS

- Obstetric Conditions
 - Multiple gestation
 - Fetal anomalies
 - Triploidy
 - Down syndrome
 - Hydrops fetalis-late
 - Gestational trophoblastic disease

HYPEREMESIS

- Lab abnormalities
 - Hyponatraemia
 - Hypokalemia
 - Low serum urea
 - Raised hematocrit
- Liver function tests are abnormal in up to 40% of women with HG
 - Most likely a rise in transaminases
 - Bilirubin levels can be slightly raised but without jaundice
 - Amylase levels can be mildly raised too.
- Ketonuria with a metabolic hypochloraemic alkalosis.
- If severe, a metabolic acidemia may develop

HYPEREMESIS

- Abnormal thyroid function tests
 - 2/3 of patients
 - This is based on a structural similarity between thyroid-stimulating hormone [TSH] and hCG
 - Biochemical thyrotoxicosis and raised free thyroxine levels with or without a suppressed thyroid stimulating hormone level
 - These patients rarely have thyroid antibodies and are euthyroid clinically
 - The biochemical thyrotoxicosis resolves as the HG improves and treatment with antithyroid drugs is inappropriate

HYPEREMESIS

- Non Obstetric Conditions
 - Gastrointestinal
 - Gastroenteritis, biliary tract disease, hepatitis, intestinal obstruction, PUD, pancreatitis, appendicitis
 - Genitourinary
 - Pyelonephritis, uremia, torsion, renal stones, degenerating fibroid
 - Metabolic/Endocrine
 - DKA, porphyria, Addison's, hyperthyroidism

HYPEREMESIS

- Recurrence
 - 15.2% recurrence in a Norwegian hospital registry study
 - Trogstad et al, BJOG, 2005
 - 81% if using self-reported diagnosis
 - Fez et al, Reproductive Sciences, 2010
- Incidence in second pregnancy changes!
 - Change in paternity (10.9%)
 - No change in paternity (16%)
 - AOR 0.6 95% CI 0.39-0.92

HYPEREMESIS

- Fetal Effects

- Dobbs et al. 2006 Obstetrics and Gynecology

- Population based retrospective cohort

- Examined 1,270 patients admitted with HG

- Pregnancy weight gain of 15.4 lbs or more

- Fetal outcomes similar to women without HG

- Low pregnancy weight gain (<15.4 lbs)

- Low birth weight

- Small for gestational age

- Preterm delivery

- 5 minute Apgar score <7

HYPEREMESIS

- Maternal Effects
 - Wernicke's encephalopathy
 - Central pontine myelinolysis
 - Mallory Weiss tear/Esophageal Rupture
 - Splenic avulsion
 - Rhabdomyolysis
 - Pneumothorax
 - Peripheral neuropathy
 - B6 and B12 deficiency

NAUSEA AND VOMITING EXAMINATION

➤ HISTORY

- Previous history of NVP/HG
- Quantify severity using PUQE score: nausea, vomiting, hypersalivation, spitting, loss of weight, inability to tolerate food and fluids, effect on quality of life
- History to exclude other causes:
 - abdominal pain
 - urinary symptoms
 - infection
 - drug history
 - chronic *Helicobacter pylori* infection

NAUSEA AND VOMITING EXAMINATION

➤ EXAMINATION

- Temperature
- Pulse
- Blood pressure
- Oxygen saturations
- Respiratory rate
- Abdominal examination
- **Weight**
- Signs of dehydration
- Signs of muscle wasting
- Other examination as guided by history

NAUSEA AND VOMITING EXAMINATION

➤ INVESTIGATION

- Urine dipstick (quantify ketonuria as 1+ ketones or more)
- Complete Blood Count (anemia, infection)
- Urea and electrolytes
 - Hypokalaemia/hyperkalaemia
 - Hyponatraemia
 - Dehydration
 - Renal disease
 - Glucose
- Ultrasound scan
 - confirm viable intrauterine pregnancy
 - Exclude multiple pregnancy or gestational trophoblastic disease

NAUSEA AND VOMITING

- General dietary guidelines
 - Advise the patient to rest; eat small, frequent meals that are high in carbohydrate and low in fat
 - Avoid any foods or smells that trigger symptoms
 - The use of ginger products may be helpful
 - Evidence is limited and lacks consistency but there is some evidence of benefit over placebo.
 - Try eating a dry biscuit first thing on waking in the morning before getting up

NAUSEA AND VOMITING

- Alternative therapies
 - Acupuncture
 - Cochrane reviews have found no evidence for benefit
 - Acupressure
 - Wrist acupressure is recommended as a potential option by 2008 National Institute for Health and Care Excellence (NICE) guidelines
 - Subsequent Cochrane reviews have found there to be limited evidence of benefit
- Vitamin B6 supplements have also been recommended

NAUSEA AND VOMITING

- Initial management outside the hospital (other than alternative therapies) involves the use of antiemetics
- Care providers should prescribe medications they are familiar with and often combinations are required
- Consideration for different medications should include the following:
 - Safety
 - Efficacy
 - Need for combination of medications
 - Adverse reactions

NAUSEA AND VOMITING

- Medications

- First Line

- Antihistamines (H1 receptor antagonists)

- promethazine, cyclizine, cinnarizine, doxylamine

- Phenothiazines

- prochlorperazine, chlorpromazine and perphenazine

- Second Line

- Metaclopramide

- Ondasteron

NAUSEA AND VOMITING

- Metoclopramide
 - Risk of short-term extrapyramidal disorders and tardive dyskinesia
 - Particularly in young people
 - Only prescribed for short term use
 - Max of 30 mg in 24 hours or 0.5 mg/kg in 24 hours
 - Max duration of 5 days
 - If infusion is ordered, needs to be given over 3 mins

NAUSEA AND VOMITING

- Ondasteron
 - Safety studies are mixed
 - Danish birth registry of 608,385 patients found no increased risk for major birth defect, stillbirth, preterm labor or small for gestational age
 - Case-control study comparing about 5000 cases to 5000 controls found a two fold increased risk of cleft palate (aOR 2.37, 95% CI 1.18-4.76)
 - Data from Swedish Medical and Birth register demonstrated a small increased risk of cardiac septal defects (OR 1.62, 95% CI 1.04-2.14), but no major malformations

OTHER MEDICATIONS

- Corticosteroids
 - Have resulted in dramatic and rapid improvement in case series
 - The results of randomized studies are conflicting
 - There are some questions of safety if given less than 10 weeks
 - A prospective double-blind study of 40 women admitted to intensive care with severe HG demonstrated that daily intravenous hydrocortisone 300 mg was superior to intravenous metoclopramide in reducing vomiting and recurrence
 - Corticosteroids should not be used until conventional treatment with intravenous fluid replacement and regular antiemetics has failed
 - Suggested dose is intravenous hydrocortisone 100 mg twice daily, and once clinical improvement occurs convert to oral prednisolone 40–50 mg daily, with the dose gradually tapered until the lowest maintenance dose that controls the symptoms is reached

OTHER MEDICATIONS

- Benzodiazepines
 - A randomized trial investigated 50 women with HG
 - Treatment included infusions of saline, glucose, vitamins and randomly allocated diazepam
 - While the addition of diazepam to the treatment regimen reduced nausea, there was no difference in vomiting between those treated with or without diazepam
 - Currently not recommended

OTHER MEDICATIONS

➤ Marijuana

- In 2012, approximately 38.1% of American women aged 12 and over reported ever using marijuana and 9.2% reported using it in the past year
- The most common illicit drug used by women in the United States
- In one study from Hawaii, women who reported severe nausea during pregnancy were significantly more likely to report marijuana use during pregnancy (3.7% vs 2.3%; PR=1.63, 95% CI: 1.08–2.44)

OTHER MEDICATIONS

- Marijuana
 - Recent publication in Green Journal (Conner et al. 2016) did not find link to marijuana use and adverse neonatal outcomes
 - After adjusting for confounding factors (specifically tobacco use)
 - Primary outcomes were low birth weight (less than 2,500 g) and preterm delivery at less than 37 weeks of gestation
 - Risks associated with fetal development are unclear

NAUSEA AND VOMITING

- If women are unable to tolerate oral antiemetics or oral fluids, consider ambulatory care
- McCarthy et al., Obstetrics and Gynecology, 2014
 - Randomized controlled trial of 98 women evaluated ambulatory IV fluids and stepwise increments in antiemetic therapy vs. inpatient care
 - Found reduction in inpatient stay
 - More acceptable to patients
 - Need to have resources available

WHAT TO DO ABOUT HYPEREMESIS

- Patient should be in the hospital
- Multidisciplinary approach
- There are no defined criteria for parenteral or enteral feeding
 - Can be successful
 - Are often employed as a last resort when all other medical therapy has failed and the only other practical option is termination of the pregnancy
- Enteral feeding options to consider include nasogastric, nasoduodenal or nasojejunal tubes, or percutaneous endoscopic gastrostomy or jejunostomy feeding
- Parenteral feeding with a peripherally inserted central catheter (PICC line) is often better tolerated than enteral feeding; however, it carries a higher risk of infection, thrombosis and vascular perforation

PICC LINES

- Infection
 - Local
 - Catheter colonization
 - Exit or insertion site infection
 - Phlebitis
 - Tunnel infection
 - Systemic
 - Bloodstream infection
 - Suppurative thrombophlebitis
 - Distant complications
- Thrombosis

PICC LINES

- Holmgren et al. AJOG, 2006
 - Complication rate from PICC line in HEG patients was about 70%
 - Complications included infection, thrombosis or both
- Allen et al. JVIR, 2000
 - Thrombosis rate of 38% in 344 PICC lines placed in 119 patients
- Cheong et al. Int Med Jo, 2004
 - PICC line complication rate of 40.7% in patients with solid tumors
- Ogura et al. AJOG, 2003
 - 52 pregnant patients
 - 26 of the patients (50%) had a complication (thrombosis, mechanical failure or infection)

WHAT TO DO ABOUT HYPEREMESIS

- Total parenteral nutrition (TPN) is complex and high-risk
 - It should only be used as a last resort when all other treatments have failed
 - It is inconvenient, expensive and can be associated with serious complications such as thrombosis, metabolic disturbances and infection
 - A strict protocol with careful monitoring is essential when undertaking total parenteral nutrition
- Folk JJ et al., J Reprod Med, 2004
 - TPN group had a marked and significant increase in serious complications directly related to TPN use

ALTERNATIVE NUTRITION

- May need nutrition
- Get nutrition consult/Use nasoduodenal tube
 - Hsu JJ et al., Obstet Gynecol, 1996
 - Review of hyperemesis patients revealed good outcomes after Dobhoff tube placement
 - Stokke G et al., Acta Obstet Gynecol Scand, 2015
 - Treated 558 women for HEG over 10 years
 - 107 received NJ tubes
 - NJ tubes associated with adequate maternal weight gain and favorable outcomes

OTHER ISSUES

- Thromboembolism
 - A retrospective study found that the odds ratio for venous thromboembolism with HG was 2.5 (95% CI 2–3.2)
 - A Canadian study using hospital discharge data found an adjusted odds ratio for deep vein thrombosis of 4.4 (95% CI 2.4–8.4) in women with HG
- Preterm delivery/Fetal growth
 - One observational study demonstrated that women with HG and less than 7 kg weight gain were at an increased risk of preterm delivery (adjusted relative risk 3.0, 95% CI 1.9–4.3) and low birthweight (less than 2500 g; adjusted relative risk 2.8, 95% CI 1.7–4.3)
 - Argument for serial US for growth

OTHER ISSUES

- Increased risk for depression
 - Depression and poor psychological health were found to be associated with NVP and HG in numerous studies
 - Researchers found that this resulted from the disease and were not the cause of HG or NVP
 - A cohort study of 648 women found that symptoms of major depression are associated with moderate and severe NVP, but prior history of depression is not a determinant

TO SUM UP....

- Nausea and vomiting of pregnancy is a normal physiological phenomenon in most patients
- However, NVP can be very debilitating
- Women with mild NVP seen and treated as outpatients
 - First line medications include antihistamines
 - Metoclopramide should not be used as a first-line antiemetic
- Evidence to suggest that outpatient IV meds and fluids can be beneficial and prevent admission
- DON'T USE PICC LINES

TO SUM UP....

- Admission may be required for those very refractory to outpatient therapy
- Thiamine supplementation should be given to all women admitted with prolonged vomiting
- Women with HG who are admitted to hospital should be evaluated to receive thromboprophylaxis with low-molecular-weight heparin, unless there are contraindications
- Consider alternative feeding options/multidisciplinary approach
- Women with severe NVP or HG who have symptoms extending into the late second trimester or beyond should have ultrasound scans to assess fetal growth