



A conference that is for us and by us

Hyperemesis Gravidarum in the ED

April 4th, 2025

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Owner/Consultant, HG Pharmacist®
Las Vegas, NV

Disclosure

- Medical Science Liaison at Pharmacosmos Therapeutics Inc. (PTI)– no conflict
- This presentation is based solely on my education and experience and not related to any of the companies or organizations for which I work or volunteer

Danielle Plummer, PharmD

- Certified Doula (CD)
- Certified in Pharmacogenetics
- HER Foundation Board Member 2019–2021
- 3x Hyperemesis Gravidarum survivor

Learning Objectives

Upon completion of this activity, participants will be able to:

1. Identify:

- key clinical features
- risk factors
- diagnostic criteria

associated with hyperemesis gravidarum patients presenting to the emergency department.

2. Apply evidence-based pharmacologic and supportive care strategies to effectively manage hyperemesis gravidarum, optimizing both maternal and fetal outcomes in the ED setting.

Definition

Hyperemesis gravidarum (HG) is a **potentially life-threatening pregnancy disease** characterized by:

- Severe nausea and/or vomiting, leading to
- Significant weight loss, dehydration, and malnutrition
- Electrolyte disturbances and possible organ dysfunction
- Risk of long-term health issues for both mother and baby

HER Foundation & Clinical Research:

The HER Foundation defines HG as more severe than typical morning sickness, often requiring hospitalization, medical intervention, and nutritional support.

HER Foundation. "About Hyperemesis Gravidarum." HER Foundation, <https://www.hyperemesis.org/about-hyperemesis-gravidarum/>. Accessed 24 Mar. 2025.

Windsor Definition: *HG is defined as a condition that starts early in pregnancy (before 16 weeks gestation) and is characterized by severe nausea and/or vomiting, inability to eat and/or drink normally, and strong limitations in daily activities.*

Jansen, L. A. W., et al. "The Windsor Definition for Hyperemesis Gravidarum: A Multistakeholder International Consensus Definition." *European Journal of Obstetrics & Gynecology and Reproductive Biology*, vol. 266, 2021, pp. 15–22.

What HG is NOT / Does Not

- Morning Sickness
- Resolve at 12 weeks (or 15 or 20...)
- Because mom does not want to be pregnant
- A woman seeking attention
- A mental health condition

HG Fast Facts

- No cure (yet!), no FDA approved medications, no standardized, effective guidelines for prevention, treatment or recovery
- Up to 10.5% of all pregnancies¹
- Up to 34% terminate or miscarry²
- ~375,000 ED visits / \$2.5 billion annually³
- Job loss (pay, 401K + matches, bonuses, career advancements)
- Cause of maternal mortality⁴

1.Liu C, Zhao G, Qiao D, Wang L, He Y, Zhao M, Fan Y and Jiang E (2022) Emerging Progress in Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum: Challenges and Opportunities. *Front. Med.* 8:809270. doi: 10.3389/fmed.2021.809270

2.Poursharif B, Korst LM, Macgibbon KW, Fejzo MS, Romero R, Goodwin TM. Elective pregnancy termination in a large cohort of women with hyperemesis gravidarum. *Contraception.* 2007 Dec;76(6):451-5. doi: 10.1016/j.contraception.2007.08.009. Epub 2007 Nov 9. PMID: 18061703.

3. HER Foundation. *About Hyperemesis Gravidarum.* <https://www.hyperemesis.org/about-hyperemesis-gravidarum/>. Accessed March 24, 2025

4.Munira Z. Gunja, Evan D. Gumas, and Reginald D. Williams II, "The U.S. Maternal Mortality Crisis Continues to Worsen: An International Comparison," *To the Point* (blog), Commonwealth Fund, Dec. 1, 2022. <https://doi.org/10.26099/8vem-fc65>

HG is a disease of malnutrition. Early intervention and treatment of women with mild to moderate symptoms may prevent progression to severe disease - ACOG

Potential Complications

Mom

Neurologic, end organ failure, coagulopathy, muscle wasting, sepsis, metabolic dysfunction, Postural Tachycardia Syndrome (PoTS), mitochondrial dysfunction, Osmotic Demyelination Syndrome (ODS), refeeding syndrome, cardiovascular complications, depression, Mallory Weiss Tears, PTSD, job loss, financial and social devastation...²

Early delivery, congenital heart disease, integumentary abnormalities, low birth weight, shorter length, undescended testicles, hip dysplasia, neurodevelopmental sequelae, skeletal malformations, perinatal death, behavioral/emotional disorders, Sensory Processing Disorder...²

Baby

Etiology

Genes:

- GDF15
- GFRAL

HCG
Progesterone
estrogen
Cortisol
Thyroid
H. Pylori
Gastrointestinal dysfunction
Inflammation
Autoimmune disorders
Twins +
Seminal Plasma Allergy

Fejzo, M. S., MacGibbon, K. W., First, O., Quan, C., & Mullin, Patrick M. (2022). Whole-exome sequencing uncovers new variants in GDF15 associated with hyperemesis gravidarum. *BJOG: An International Journal of Obstetrics & Gynaecology*, 129(11), 1845–1852. <https://doi.org/10.1111/1471-0528.17129>

Genome-wide association study meta-analysis of HG Confirms GDF15 and identifies additional risk loci

Conclusion and Clinical Implications

Genetic loci in hCG and its receptor, were not associated with HG in any of the analyses, providing no support for the historical hypothesis that the pregnancy hormone is the cause. GDF15, IGFBP7, PGR, and TRPC6 are all highly expressed in the developing placenta. Overall, this study contributes to our understanding of the biology of nausea and vomiting in pregnancy and may lead to future research evaluating new treatment avenues.

CLINICAL IMPLICATIONS:

Of note, drugs targeting the nausea and vomiting hormone GDF15 have shown great promise in mitigating weight loss, loss of appetite, and vomiting in animal models and are currently in clinical trials in cancer cachexia, a disease with similar symptoms to HG. The strong link to this pathway in HG suggests these drugs, if safe, may hold great promise for treating HG in the future.



References, COI, Contact

Fejzo et al., Nature Communications (2018)

Nana et al., AJOG (2021)

Munk-Olsen et al., Translational Psych (2022)

Hromatka et al., Human Molecular Genetics (2015)

Eilassen et al., Pharmacogenetics and Genomics (2021)

Mishra et al., Cell Metabolism (2022)

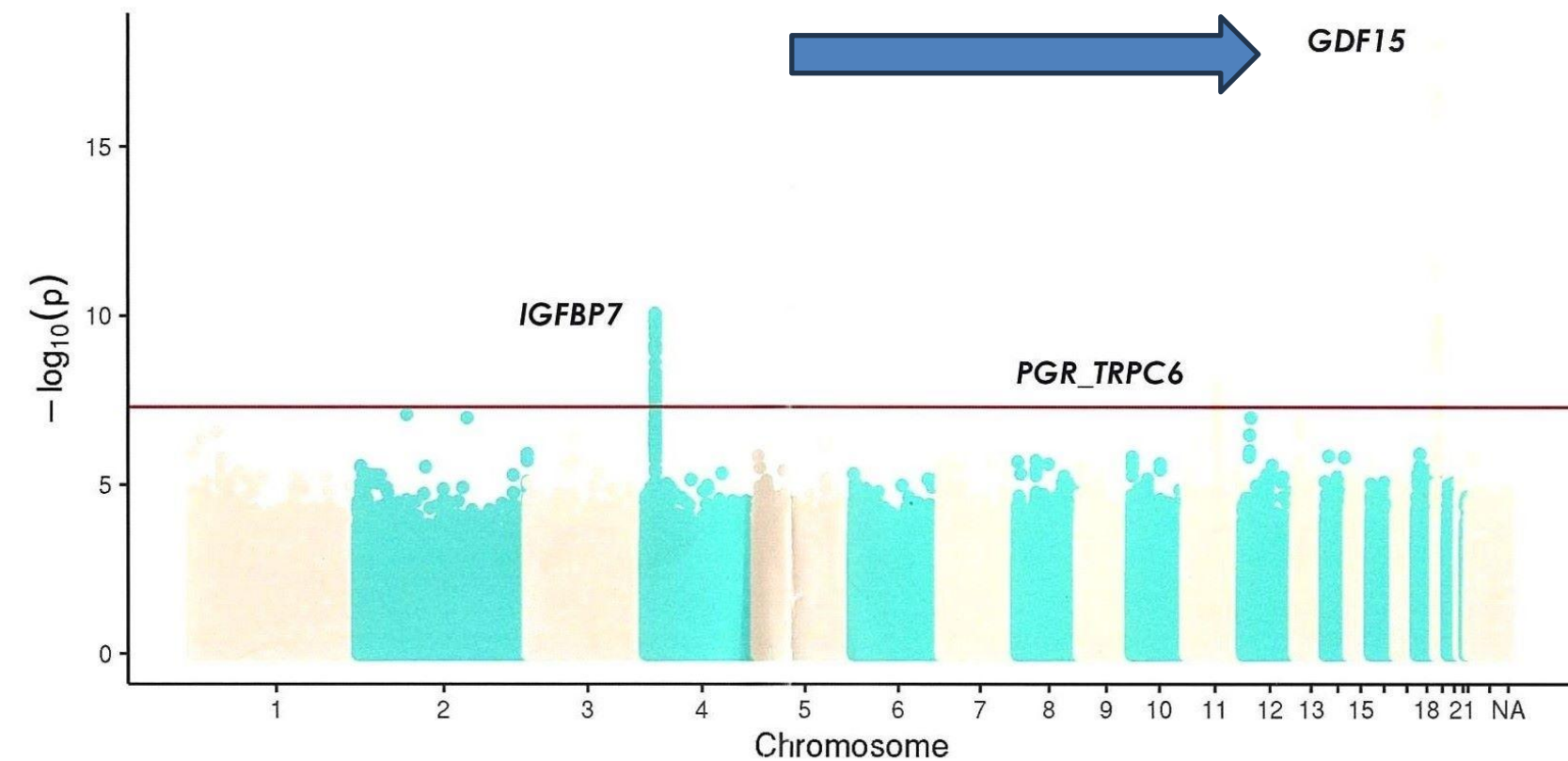
Hasna et al., Cell Physiol Biochem (2019)

[https://www.pfizer.com/sites/default/files/investors/financial_reports/annual_reports/2021/story/new-pathways-to-treat-unintentional-weight-loss/\(2021\)](https://www.pfizer.com/sites/default/files/investors/financial_reports/annual_reports/2021/story/new-pathways-to-treat-unintentional-weight-loss/(2021))

COI: Dr. Fejzo is a paid consultant for Materna Biosciences

CONTACT: Marlena Fejzo mfejzo20@gmail.com

Results

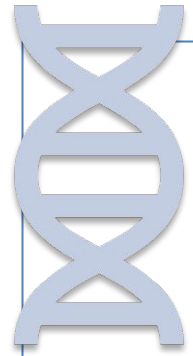


We identified genome-wide significant ($P < 5 \times 10^{-8}$) variants at GDF15 (rs1058587, $P = 8.93 \times 10^{-19}$), IGFBP7 (rs9312688, $P = 8.45 \times 10^{-11}$), and PGR_TRPC6 (rs4754754, $P = 1.13 \times 10^{-8}$), replicating our previous studies of HG. These genes are activated during placentation, consistent with a putative role in HG risk.

Using a relaxed P-value threshold of 5×10^{-6} , other potential associations include SDK1, linked to motion sickness, chemotherapy nausea, and mutated in a family with HG, PTPRD, an orexigenic receptor linked to postoperative nausea, as well as the GDF15 co-receptor gene RET unique to the Estonian GWAS, and the thyroid stimulating hormone receptor gene TSHR unique to the Finnish GWAS.

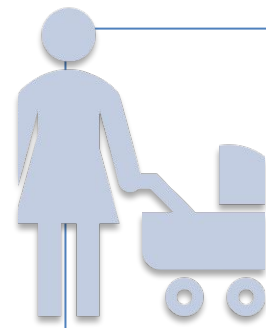
Risk Factors

Anyone can be at risk for HG!



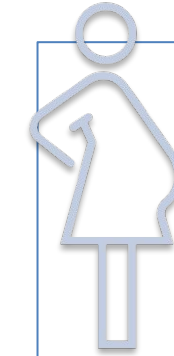
Genes

- GDF15
- GFRAL

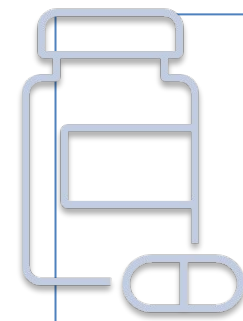


Family history

- 1st degree relative



Multiple gestations



History of:

- Migraines
- Motion sickness
- Thyroid Dysfunction
- Gastrointestinal disorders



Other:

- Obesity
- Under 30
- High stress

Risk factors predicting ER visits

- Person of color
- not having children
- being too sick to work, and
- having extreme weight loss

Utilization of medication and nutritional therapies is inconsistent and inadequate in this population, which may increase visit frequency

de Vera, Miranda. *Risk Factors for Infusions, Emergency Room Visits, and Hospitalization: Ondansetron Use in Hyperemesis Gravidarum*. HER Foundation, Dec. 2024, <https://www.hyperemesis.org/wp-content/uploads/2024/12/2024-de-Vera-Risk-factors-for-infusions-emergency-room-visits-and-hospitalization-ondansetron.pdf>.

Diagnosis

Never decide Dx or Tx based off 1 lab result!

***HG is a
disease of
rule – out***

www.hyperemesis.org/differential-diagnosis/

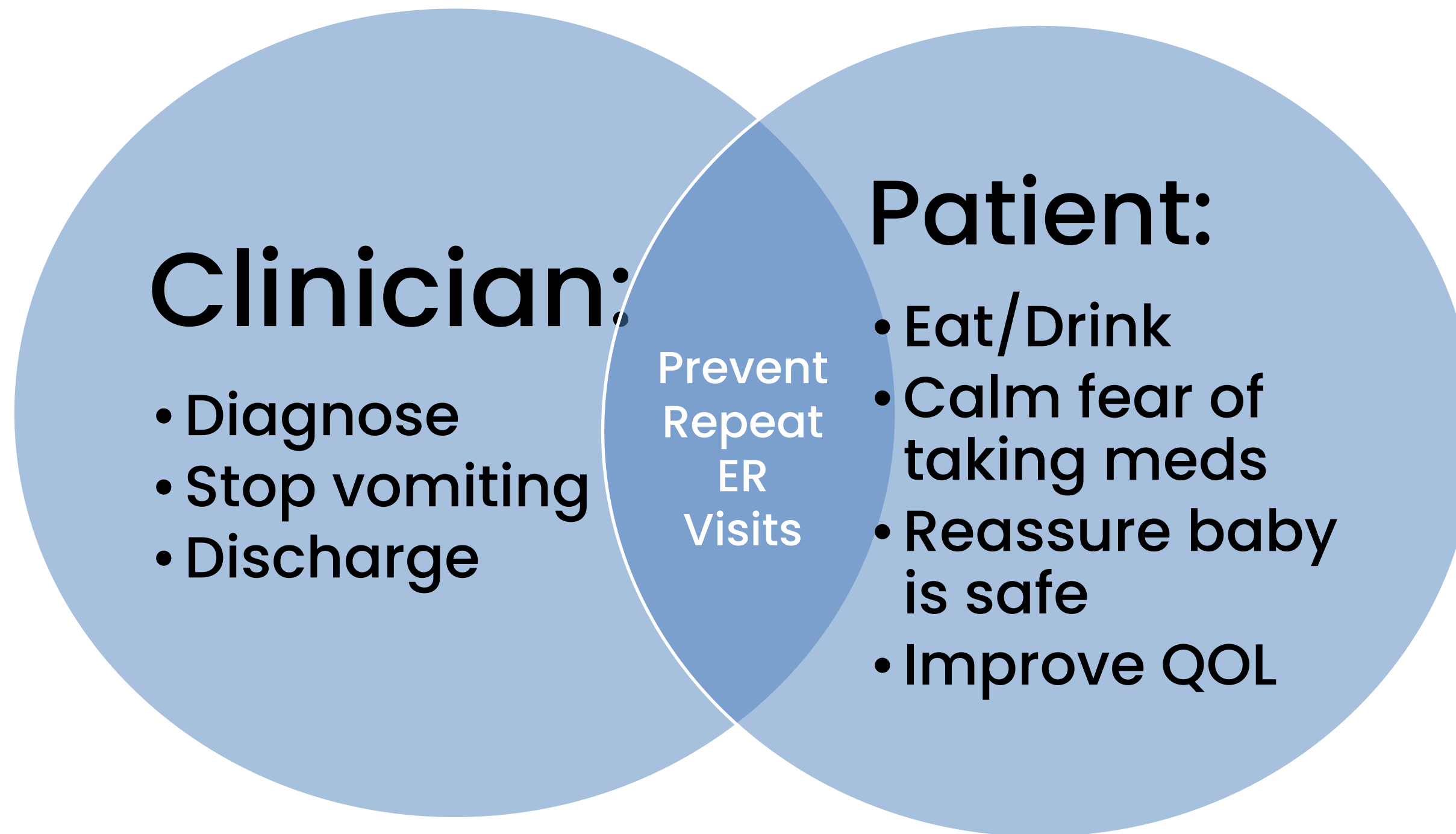
Subjective

- Vomiting
- Weight Loss
- Activities of Daily living (ADL)
- Missed Work
- Failed Treatments
- Dizzy/tachycardic
- Starving/thirsty
- Malnourished
- Prolonged fatigue, brain fog, depression

Objective

- Labs:
 - Electrolytes, Vitamins, Acid/base imbalances
 - Glucose
 - Iron panel
 - Ketones, urine specific gravity
 - Thyroid Antibodies
 - LFTs, BUN, SCr
- Weight Loss
 - 1-2 lbs / week
 - 5-20 lbs
 - > 5% pre-pregnancy weight
- Loss of muscle mass
- Vital signs: Hypovolemia, BP, HR,
- Physical signs: skin turgor, dry mucous membranes, clammy skin, reduced urine output, altered mental status,

Align Goals



Assessment

- Determine severity of disease:
 - Nausea alone
 - Vomiting without hypovolemia, OR
 - Vomiting with hypovolemia
- Correct hypovolemia, ketonuria and electrolytes
- Prevent serious complications of persistent vomiting and hypovolemia
- Minimize adverse effects of pharmacological treatment

To improve physical, mental and financial health of patient

Not a Treatment Plan

NSN 7540-00-634-4176

MEDICAL RECORD **CHRONOLOGICAL RECORD OF MEDICAL CARE**

DATE	SYMPTOMS, DIAGNOSIS, TREATMENT, TREATING ORGANIZATION (Sign each entry)
H SEP 00	BP 110/64 T 98.8 R 20 P 79 8 WEEKS ROB
WT 121	2: c/o constant nausea. Vomited 5-6
HT 5'4"	times yesterday - today & vomiting
AGE 29	but still @ nausea & diarrhea & fevers
MEDS &	(+) HCG
ALLERGIES:	0: Alert W/W/D N/A/D
PCN	HEENT Ears TMS fairly good
SULFA DRUGS	Nose clear throat d/c clear
TO	Neck supple & LA
A@	lung c/o @ W/M 5 @
	ABN soft, generalized tenderness
	@ BS @ masses
LMP	A: 1 Hyperemesis gravid @ pregnant
17 July 00	
8:4	
	P: Phenergan 25mg Supp
	2 Encourage fluids
	3 RTC if sx persist
	J. S. [Signature]

History obtained: 21 wks preg

PNV Tylenol @ 1430

28 y/o F 21 wk G2P1

Sore throat/nasal congestion yesterday. Vomiting (yellowish) x 10 times. HA across frontal area (BL) 6/10 intensity continuous @ Neck pain @ Stiffly @ numbness/pressure in character

drinking @ vaginal bleeding @ cramp. @ baby baby

Green NAD. HEENT PERRL/THUS clear throat reddish @ exudate Neck supple @ lymph node

CV: RRR @ (SEM 2/6) @ MMM

Lug: CTA @

abd: @ TTP soft.

Foal Heat beat 150-160 bpm

Vomiting -> dehydration possible viral infection at foils much myeloid VSS. Tol po.

(PHH) - viral infection hospitalized x1

(fled) - PNV styeal

(Allergy) - PC - rash - sulfa - vomiting

(PSH) - ankle ggt remove

(STE) @ cig @ ETOH

(Ob/Gyn) - h+ hyper-emesis.

u/a SG-1.03 @ Nitroce ketone 3+ @ Leukocyte Est Epi 3-5/Hpt WBC 0-3 RBC 0-3 2+ Bacteria

W. [Signature]

Kosh to JAP LT Sauckel, M, US NR

1 Drink lots of fluids

2 Return to 1 previous

3 call Pim in a gpt

Not a Treatment Plan



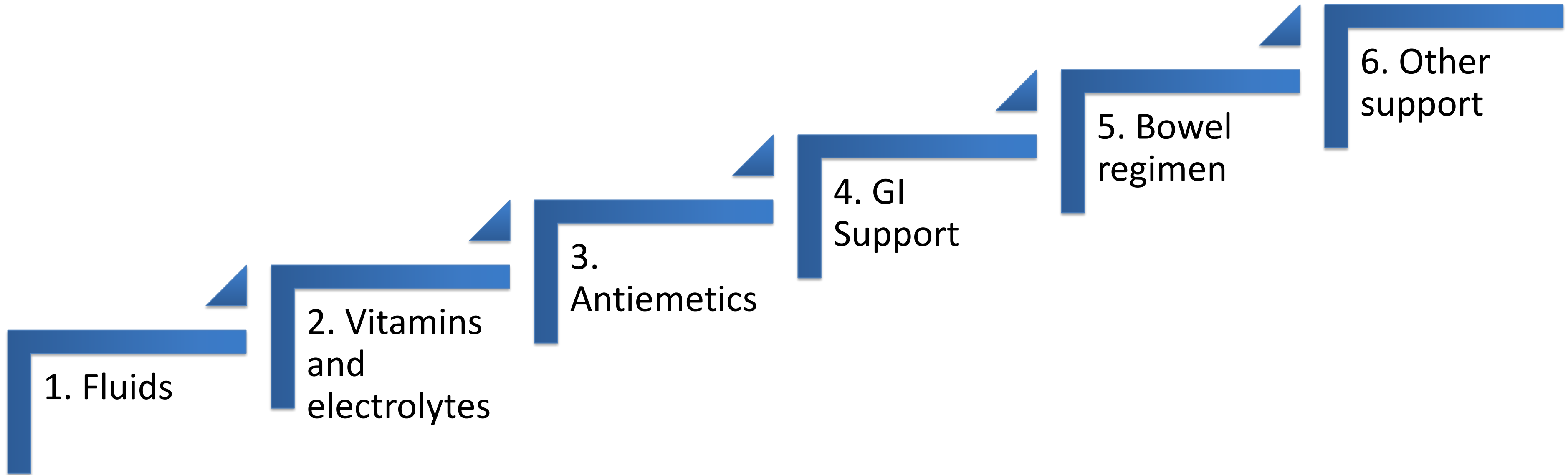
Photo from HG Clinical Solutions, used with permission

You're welcome! I was diagnosed after 6 different hospitals but only because I brought it up . I had thrown up so much it caused a hemotoma in my uterus and I bleed so much

We've visited the ER 7 or 8 times in the last 3 weeks. Each time we've been to the ER it's been mostly the same. Bags of fluids, some benadryl, and a different prescription for another nausea med. We went to her OBGYN this morning (WHASN) and they gave her an ice cream bar (which she couldn't eat due to being lactose intolerant) a diet coke (which she couldn't drink because even before being pregnant, she never touches caffeine) and a trash bag to throw up in and said she'll be fine and it's not serious.

I was wondering, is anyone currently experiencing health problems that link back directly to having HG? My teeth are a wreck (and I'm thin, so convincing a dentist I'm not on meth...)and now I'm starting to have kidney issues, as the docs warned me of at the time. I spent 27 months of my life vomiting 20+ times a day (even after zofran first came out with my 2nd), keytones in my urine, dehydrated, malnourished...my body is apparently still being put through challenges as result. Anyone else?

Treatment Plan- 6 Steps



Step 1: Fluids

Lactated Ringers (LR)

- 2 liters over 3–5 hours

½ NS

- Less shift, renal damage, osmotic demyelination syndrome

D5W

- Infuse thiamine 1 hour prior

Step 2: Vitamins, Electrolytes...

Vitamins:

- Thiamine (B1): 100 mg
- Pyridoxine (B6): 10 mg
- Folic acid (B9): 1 mg
- Cyanocobalamin (B12): 500 mg
- Multivitamin: 10 mL
- Optional: vitamins C, D, K...

Electrolytes / Other:

- Sodium
- Potassium
- Magnesium
- Calcium
- Glucose
- Iron

Step 3: Antiemetics

Signaling the chemoreceptor trigger zone (CTZ)



Choose a combination of medications reaching different targets

Serotonin antagonists (Choose 1)

Ondansetron
IV or ODT, 4-8mg q 4-6h

Granisetron

Mirtazapine

H1 antagonists (Choose 1)

Promethazine - rectal

Diphenhydramine (12.5 - 50mg)

Meclizine

Doxylamine

Doxylamine/B6 combinations

Dimenhydrinate (12.5-50mg)

Hydroxyzine pamoate

Hydroxyzine hcl

Dopamine antagonists (Choose 1)

Metoclopramide

Prochlorperazine

Chlorpromazine

Olanzapine

Haloperidol

Droperidol

Steroids After 9 weeks (Choose 1)

Prednisone

Methylpred-nisolo
ne

Hydrocortisone

Other

Lorazepam
Diazepam
Clonazepam

Gabapentin

Scopolamine

Cannabis

Step 3: Ondansetron Safety

“One out of every four pregnant women receive a prescription for ondansetron”
– UT Southwestern Medical Center

Potential Adverse Effects on Mom:

- QT Prolongation
- Constipation
- Serotonin Syndrome

Original Investigation | Obstetrics and Gynecology



April 23, 2021

Comparison of Pregnancy Outcomes of Patients Treated With Ondansetron vs Alternative Antiemetic Medications in a Multinational, Population-Based Cohort

Conclusions and Relevance:

In this large, multicenter cohort study, there was no association between ondansetron exposure during pregnancy and increased risk of fetal death, spontaneous abortion, stillbirth, or major congenital malformations compared with exposure to other antiemetic drugs.

Step 4: GI Support

H2RA

- Famotidine

PPIs

- Pantoprazole
- Omeprazole
- Esomeprazole
- Lansoprazole
- Dexlansoprazole

Other Digestive Support

- Probiotics
- Digestive enzymes
- Sucralfate
- Simethicone

Watch for drug-drug interactions!

Step 5: Bowel Regimen

Assess if necessary

Stool softeners:

- docusate

Laxatives:

- senna
- bisacodyl

Osmotic laxatives – Oral

- polyethylene glycol 3350
- lactulose

Magnesium

Glycerin
suppository

Enema

- saline
- mineral oil
- warm water
- lactulose

Step 6: Other

“HG destroys mental health, not the other way around” – DP

“Enteral support during early pregnancy can reduce perinatal morbidity – ACOG

□ **Mental Health:**

- Antipsychotic for antiemetic properties / EPS
- Abnormal involuntary movement scale (AIMS) evaluation
- Do not refer to mental health hospital or support for eating disorders
- Train staff to have empathy & never compare to another pregnancy

□ **Cannabis:**

- Know your laws / Fear of child protective services
- Be clear about drug testing
- HG or Cannabis Hyperemesis?

□ **Dietary:** evaluate for PN or TPN

Clinical Pearls

- **Referrals:** MFM, case mgm't, GI, cardiology, nephrology, home health, physical therapy, maternal fetal medicine (MFM)
- Do NOT mention crackers, ginger or BRAT diet
- Name their diagnosis and code insurance as HG
- Educate on dental care / ptyalism
- If muscle wasting, no IM
- Watch for: refeeding syndrome, HELLP, Postural Tachycardia Syndrome (PoTS)– 60% experience HG, Wernicke's Encephalopathy, Osmotic Demyelination Syndrome, Neuroleptic Malignant Syndrome, Esophageal Tears, Mast Cell Activation Syndrome

Discharge

Education on disease state

- Include family
- When to return



Medication reconciliation / discharge medications



Referrals

Create an ER Protocol / Policy

Treatment Plan

- Ex: Banana bag

Differential Diagnosis

Drug testing

Discharge versus admission

Option to direct admit / bypass ER – to which unit?

Which patients warrant referrals

On the Horizon - 2025

□ Precision Medicine

Clinical trial for targeted treatment to GDF15,

- NGM Bio's EMERALD Phase 2
- In UK and Australia

□ Pharmacogenetics

Vitamins:			
Folic Acid	⊗ CONSIDER ALTERNATIVES (e.g., supplements containing methylfolate) due to significantly reduced folic acid conversion	MTHFR C677T/C677T	C677T Homozygous Mutation

Plummer, D. (2019, February). [Pharmacogenetic Test Results]. Personal collection.

Antiemetics (Selective 5-HT3 Receptor Antagonist):			
Dolasetron (Anzemet®) Granisetron (Sancuso®)	⚠ USE CAUTION due to increased risk for QTc interval prolongation	NOS1AP c.106-38510G>T/c.106-38510G>T/c.178-20044C>T/c.178-13122C>T	rs10494366 TT genotype/rs10800397 T Allele Carrier/rs10919035 T Allele Carrier
Antiemetics (Selective 5-HT3 Receptor Antagonist):			
Ondansetron (Zofran®)	⚠ USE CAUTION due to increased likelihood of nausea and vomiting	ABCB1 c.3435T>C/c.3435T>C/c.2677T>A/c.2677T>G	rs2032582 TC genotype/rs1045642 GG genotype
Antiemetics (Selective 5-HT3 Receptor Antagonist):			
Palonosetron (Aloxi®)	✔ NORMAL RESPONSE EXPECTED	CYP2D6 *10/*41	Normal Metabolizer

Sample Case

Patient: 28-year-old G2P1 at 9 weeks gestation

Chief Complaint: Intractable N/V x 5 days

Vitals:	HR 112 bpm, BP 94/60 mmHg, afebrile
Symptoms:	Reports inability to tolerate any oral intake; vomiting ~8–10 times/day
Physical Exam:	Dry mucous membranes, mild orthostatic hypotension
Labs:	K ⁺ : 3.1 mmol/L Na ⁺ : 132 mmol/L Glucose: 58 mg/dL Mg = 1.3 mg/dL Hgb: 9.1 Ketones in urine

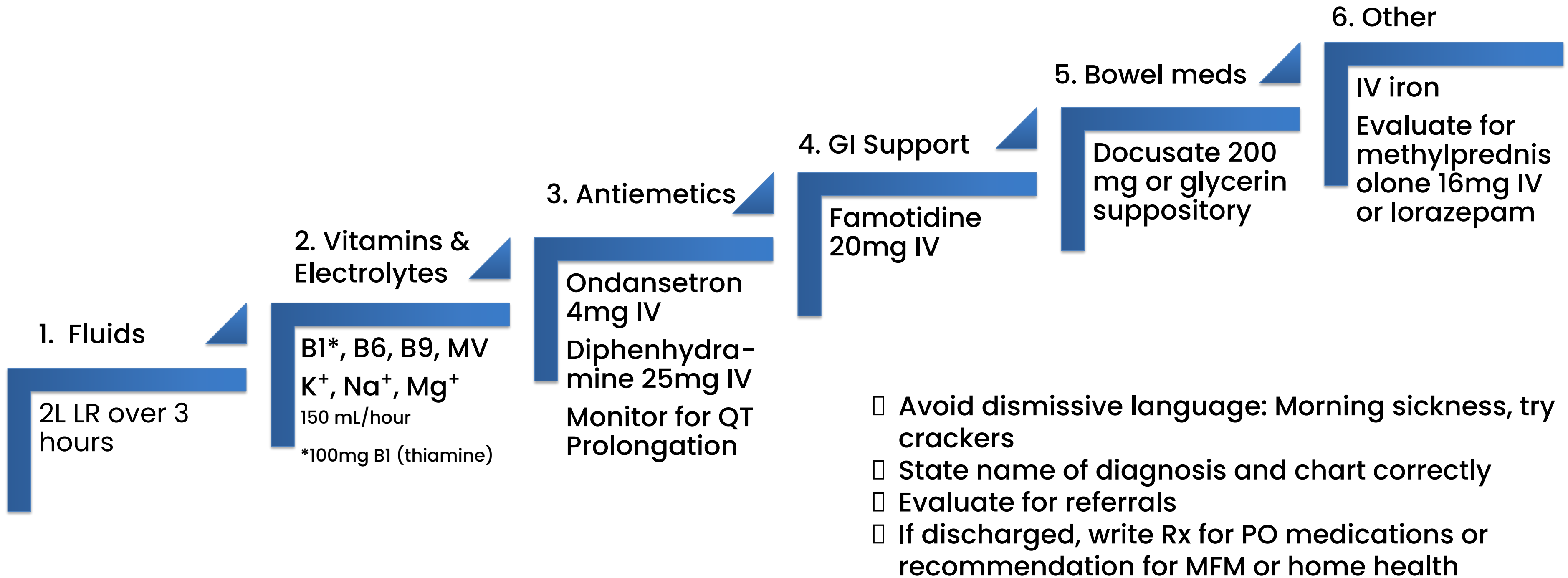


Assessment:

- Meets Windsor Definition of HG: Early pregnancy, severe nausea/vomiting, inability to eat/drink, major impact on daily functioning
- Rule out other causes: No abdominal pain, fever, or signs of infection

Treatment Plan

28-year-old 9 weeks gestation
Intractable N/V x 5 days



Test Your Knowledge

Which of the following is NOT a diagnostic criterion for hyperemesis gravidarum?

- A) Severe nausea and vomiting leading to dehydration
- B) Electrolyte imbalance and weight loss
- C) Presence of fetal heart tones
- D) Need for hospitalization due to inability to tolerate oral intake

Test Your Knowledge

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Test Your Knowledge

Which treatment strategy is MOST appropriate for hyperemesis gravidarum patient presenting to the emergency department?

- A) Oral antiemetics and reassurance
- B) IV fluids, thiamine, and antiemetics
- C) Immediate total parenteral nutrition (TPN)
- D) Restricting all oral intake for 48 hours outpatient

Test Your Knowledge

Which treatment strategy is MOST appropriate for hyperemesis gravidarum patient presenting to the emergency department?

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- D) Restricting all oral intake for 48 hours outpatient

Test Your Knowledge

Which of the following is the primary factor believed to contribute to the extreme vomiting seen in hyperemesis gravidarum?

- A) Increased progesterone levels slowing gastric motility
- B) Elevated levels of human chorionic gonadotropin (hCG)
- C) Genetic variations in the GDF-15 gene
- D) Low estrogen levels affecting the gastrointestinal tract

Test Your Knowledge

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A conference that is for us and by us

Thank you!

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