



“Queasy not Cwazy” – Chronic Nausea - Not all in your Head

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*Relationships
Eh...What's
Up Doc?*

I have the following financial relationships to disclose:

Abbott Labs – Professional Advisory Board
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* Janssen - Professional Advisory Board

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Drugs Lacking Specific US Indication

- ◆ Domperidone

Objectives

- Review the pathophysiology of chronic nausea in children and adolescents
- Review the evidence for remediation of chronic nausea
- Outline an approach to the patient with refractory symptoms



Case Presentation

- 10 year male transferred for ongoing management of recurrence of hematochezia
- Previously diagnosed pan-ulcerative colitis confirmed on repeat colonoscopy/biopsy
- Responds to weaning course of prednisone 2mg/kg over 8 weeks

Three month visit

- Father:
 - ◆ Parents “spending all night on internet”
 - ◆ Patient is unwell and being homeschooled
- Principle complaint is chronic nausea
- Patient looks well – P/E normal
- Meds: 5'ASA 500 mg tid, 5'ASA 0.5 gm enema nightly
- Labs : Hgb 136 WBC 8 Eos 0.7 ESR 1

Next steps?

- ◆ Family requests letter supporting homeschooling
- ◆ Watch + wait or investigate?
- ◆ Investigations?
 - ◆ Labs
 - ◆ Diagnostic Investigations
 - ◆ Endoscopy

Strategy

- Parental Anxiety identified as a distinct problem
- Parents and patient interviewed separately

Strategy

- Parental Anxiety
 - ◆ Patients symptoms improve on “sleepovers”
- Patient Re-Interview
 - ◆ 3 stools per day - intermittent urgency
 - ◆ Only occasional blood per rectum
 - ◆ Nausea is the Debilitating Symptom accounting for school absence

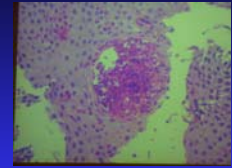


Investigation

- Colonoscopy
 - ◆ *Minimal Rectal Inflammation*
- Upper Endoscopy
 - ◆ *Esophageal Furrowing*
 - ◆ *White Plaques*

Investigation

- Colonoscopy
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 - ◆ *White Plaques*
 - ◆ *Pathology – Eosinophilic Esophagitis*



Outcome

- On further inquiry parents report:
 - ◆ Black mould in basement extending to bathroom wall adjacent to patient's bedroom
 - ◆ Symptoms resolve with mould remediation



Chronic Nausea - 6 months of cases

- *10 y/o male – Eosinophilic esophagitis
- 17 y/o male – Gastroparesis
- 10 y/o male – Dysautonomia
- 16 y/o female – Post Infectious Dyspepsia
- 16 y/o male – Functional Dyspepsia
- 16 y/o male – Post Concussive Syndrome
- 15 y/o female – Gastroparesis/GB Dyskinesia

Chronic Nausea - 6 months of cases

- *10 y/o male – Eosinophilic esophagitis
- * 17 y/o male – Gastroparesis (Family dysfunction)
- *10 y/o male – Dysautonomia (Family dysfunction)
- 16 y/o female – Post Infectious dyspepsia
- 16 y/o male – Functional Dyspepsia
- 16 y/o male – Post Concussive Syndrome
- *15 y/o female – Gastroparesis/GB Dyskinesia (Had been kicked out of home for marijuana use)

Chronic Nausea – Differential Dx.

- Stress – Physical, Psychological
- Infection – Hepatitis, Mononucleosis, Sepsis, Helicobacter
- CNS – Infection/ Space Occupying Lesion, Meunier's
- GI Disease – Gastritis/enteritis, Gall Bladder, Pancreas + Liver
- Endocrine – Adrenal Insufficiency
- Metabolic – Hyper-Hypoglycemia, Uremia, Fatty Acid Defects
- Drug, Intoxicants and Poisons
- Physical Stress – Motion Sickness, Heat Stroke, Overexertion
- Emotional Stress - Anxiety

Less Obvious Causes of Chronic Nausea

1. Gastroesophageal Reflux/Eosinophilic Esophagitis
2. Hiatus Hernia/Prolapse Gastropathy
3. Chronic Sinusitis, Urinary Tract Infection
4. Pregnancy
5. Anxiety – *The Queasy Teen*
6. Autonomic Dysfunction
7. Post Viral Gastroparesis
8. Vertebral Compression
9. Drugs – i.e. Chemotherapy, **Cannabis*

Common Denominator - Stress

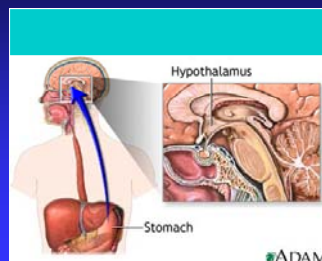
- Afferent Inputs
 - ◆ Auditory-Ophthalmologic Discord
 - ◆ Chemoreceptors
 - ◆ Pain –Trauma/fracture
 - ◆ Psychic Stress

Neuroendocrine Response to Stress

- Sympathetic discharge
- ACTH
- Cortisol Releasing Factor CRF
- Antidiuretic Hormone ADH

The Vomiting Centre

- Paraventricular reticular formation in the lateral medulla (Meadows 1995)
- Vomiting may be produced by stimulation of the region
- Vomiting centre receives input from vagal and sympathetic afferent nerves
- The emetic signal travels by either system from the stimulating organ



The Endocrinology of Vomiting

Y Tache 1998

- ADH markedly elevated in cyclic vomiting - G Robertson
- Nausea is a potent stimulus to huge ADH secretion
- ➡ ADH ↓ blood flow to stomach and intestine
- ➡ Gastroparesis
- "Stress" releases corticotrophin-release factor (CRF)
- CRF acts in the CNS and periphery to inhibit gastric emptying and empty the lower bowel

Anticipatory Nausea – Easily Conditioned

- Chemical
 - ◆ alcohol
 - ◆ cannabinoids
- Chemotherapy – 55%
- Psychosocial Stress 8-10%



Epidemiology of Stress - Jackiewicz 2006

- Cumulative prevalence: 8-10%
- Separation Anxiety: 3-5%
- Simple Phobias: 2-9%
- Social Phobias: 1%
- Generalized Anxiety Disorders: 3-4%
- Panic Disorders: 0.6% (adolescents)
- OCD: 2%

PETER WAS A BORN WORRIER ...



Distinguish from Cyclic Vomiting Pattern

CVS Guidelines – NASPGHAN 2007

- At least 5 attacks or a minimum of 3 attacks occurring over a 6-month period (100%)
- Episodic attacks of intense nausea and vomiting lasting from 1 hour to 10 days and occurring at least 1 week apart (100%)
- Stereotypical in the individual patient (99%)
- Vomiting during attacks occurs at least 4 times/hour for at least 1 hour (77%)
- A return to baseline health between episodes (94%)
- Not attributed to another disorder (97%)



EE- Eosinophilic Esophagitis

Liacouras et al JPGN 1998

- Symptoms by age:
 - ◆ Childhood – Vomiting – 82%
 - ◆ Latency and teens
 - ◆ 69% Nausea
 - ◆ Abdominal pain and “dysphagia” -26%

TEENS - Cannabinoid Hyperemesis

Nicholson SE Psychosomatics 2012

- Cyclical vomiting
- Chronic cannabis use
- Compulsive bathing behaviours



Cannabinoids and GI motility

Sharkey K 2009

- Cannabinoid agonists inhibit excitatory cholinergic contractions of guinea pig ileum, without altering the response to Acetylcholine.
- Cannabinoids inhibit esophageal, gastric and intestinal motility in isolated preparations of the gut and *in vivo*.

Differentiate from Rumination Syndrome

- Effortless repetitive regurgitation, reswallowing and/or spitting within minutes of starting a meal
- Lasts for about an hour, rarely occurs at night
- Appears to serve purpose of self-stimulation in intellectually handicapped children
- Depression-anxiety cluster disorders are reported in up to one-third of affected individuals

Rumination Syndrome Manometry and Gastric Emptying

- Characteristic manometric abnormality is synchronous increase in pressure across multiple recording sites in the upper gut
- These features found in 40-67% of adolescents with rumination, and mildly delayed gastric emptying found in 46%

Post-Prandial Distress PPD Syndrome

Geeraerts and Tack - J of Gastroenterology 2008;43:251-5

- Post-Prandial Distress Syndrome - PPD
- Differentiates PPD as a Sub-category of Rome III Dyspepsia Criteria – absence of underlying disease
 - Epigastric Pain/Burning
 - Post Prandial Fullness Bloating
 - Early Satiety
 - Mannometry – impaired gastric accommodation

Post-Prandial Distress PPD Syndrome

Geeraerts and Tack - J of Gastroenterology 2008

- Post-Prandial Distress Syndrome - PPD
- Differentiates PPD as a Sub-category of Rome III Dyspepsia Criteria
 - ◆ Dyspepsia responds to acid suppression
 - ◆ * PPD responds to pro-kinetics

What's been tried

- Prokinetics
 - Metaclopramide, domperidone, cisapride, erythromycin
- Antiemetics
 - Phenothiazines
 - Ondansetron
- Sedatives
 - Lorazepam
- Antidepressants
 - Amitriptylene
- SSRP's

Non-Medicinal Approaches

- Acupressure – results equivocal/not sustained
- Acupuncture – small studies in chemotherapy
 - ◆ > 0.05 improvement in sham or auricular stim.
- Gastric Pacing – small studies
 - ◆ Adult study of 30 pts w 5 year F/U
 - ◆ 27% improved quality of life
 - ◆ Nausea improved in 67%

Chronic Nausea and Anxiety Framing the Discussion

- Teens with chronic nausea often very defensive
- They feel accused of fabricating symptoms

Chronic Nausea and Anxiety Framing the Discussion

- Teens with chronic nausea often very defensive
- They feel accused of fabricating symptoms
- Strategy
 - ◆ Identify and validate the concern
 - ◆ *"It's not all in your head ..it's lower than that"*
 - ◆ Translation – Stress related nausea is
 - ◆ a physical "fight/flight" brain stem reaction
 - ◆ not an intentional frontal lobe decision

Behavioral Approaches – any combination

- *Family and Child Counseling
- *Imaging
- *Relaxation Therapy
- *Biofeedback
- *Exercise Medicine
- * More effective than placebo in chronic abdominal pain

Evidence Informed Approach

- Consider starting a PPI and Prokinetic
- Frame recovery as rehabilitation
- Normalize patient's routine
 - ◆ Meals
 - ◆ School
 - ◆ Sleep
 - ◆ Exercise
- Family assessment in support of above

Summary

- Chronic nausea is a cardinal manifestation of physical, psychic and emotional stress
- Physical and psychic/emotional stress express through identical physiology with considerable overlap
- Entertain a broad differential
- If it doesn't make sense, use a "CSI" approach,
Go back and pick through the dirt at the scene of the crime
Figure out "who you're seeing" not "what you're seeing"



Information and Family Supports

Cyclic Vomiting Syndrome Assoc (CVSA)
2819 W. Highland Blvd Milwaukee WI 53208
414-342-7880 Fax 414-342-8980
cvsa@cvsaonline.org www.cvsaonline.org

International Foundation for Functional GI Disorders (IFFGD)
PO Box 170864, Milwaukee WI 53217
414-964-1799
www.aboutkidsggi.org www.iffgd.org

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