GASTROENTEROLOGY IN FANCONI ANEMIA

JOSE M GARZA MS, MD
• Patients with Fanconi anemia experience many gastrointestinal, hepatic, and nutritional consequences of the disease and its treatment

• Judicious use of diagnostic tests specially those that involve radiation
• Approximately 7% of patients with FA have gastro-intestinal tract anatomic abnormalities

• The most common anomalies are esophageal atresia (EA) with or without tracheoesophageal fistula (TEF), duodenal atresia, and ano-rectal malformations

• Most anomalies are diagnosed and treated in early infancy, often long before the diagnosis of FA
POOR GROWTH

• Many patients and families complain of poor growth in children with FA

• Each clinical visit must include an assessment of growth.
  • Weight and height, measured appropriately for age, are plotted on appropriate growth curves

• Weight-for-height (<2 years) or body mass index (BMI) for age (>2 years)
FAILURE TO THRIVE...

Lutter Emmet Holt

• In 1897 Described an infant who “CEASED TO THRIVE”

• The term FTT might have not been used in print until 1933
WHAT IS FAILURE TO THRIVE?

• 1933 – 2013 Still no consensus on definition and criteria

• It is a descriptive term or symptom

• NOT A DIAGNOSIS
DEFINITION 1

Drop in weight below the 3rd percentile

- Easy to implement
- Widely accepted and understood
- Inevitably includes a number of normal children
- Can miss those who weight drops from higher percentiles
DEFINITION 2

Weight falls across two percentile lines after having achieved a previously stable pattern.
DOES IT MATTER WHICH GROWTH CHART?

CDC

WHO
- GI
- Systemic illness
- Endocrine defects
- Genetic defect of FA.
PICKY EATING VS POOR GROWTH

One, both or neither
• Approximately 60% of children with FA have short stature as part of the genetic background of this disease

• These children will also have proportionately lower weights
• Parents should have a chance to discuss their child’s growth curves

• Particularly the weight for height curve (up to age 2 years) and the BMI curve (after 2 years)

• Aggressive methods of trying to increase the child’s intake will not increase their height or overall health, and may create disordered eating or family problems with meals
Drop growth velocity

Gastro-intestinal “disorders” should be ruled out when the weight is affected first or predominantly (Wt/Ht or BMI)
PICKY EATERS

• Children who are “picky eaters” and their families may benefit from behavioral therapies to increase the variation in food selection

• These therapies have not been studied in FA, but have been effective in other patient populations with poor oral intake, for example, cystic fibrosis.
Genetic + Environment → Actual Growth
Absorb and utilize?

Get enough?

Normal Requirement?

GROW
Normal Requirement ?
• **Chronic inflammation and/or infection**
  - Laboratory studies, including urine culture and measurement of serum C-reactive protein or erythrocyte sedimentation rate, may point to infection or systemic inflammation

• **Other systemic disease**
Absorb and utilize ?
DIARRHEA

May also result from:

• Complications of anatomic abnormalities
  • small bowel overgrowth

• Opportunistic infection of the gastrointestinal tract
  • stool examination for ova and parasites, giardia antigen, cryptosporidium, and other opportunistic agents

• Medications

• Enzyme deficiencies

• Constipation with fecal soiling is common, and families may mistake it for diarrhea
SMALL BOWEL OVERGROWTH
SMALL BOWEL OVERGROWTH

Associated with small bowel stasis

- Impaired peristalsis
- Abnormal Anatomy

Symptoms:

- Excessive bowel gas
- Diarrhea
- Bloating
- Abdominal Pain
- Anemia
- B12 deficiency
- Malabsorption
- Weight loss / failure to gain weight

Diagnose with Hydrogen breath test or can try empiric trial of metronidazole
Get enough ?
IN FA CAUSES OF POOR ORAL INTAKE MAY INCLUDE:

- Complications of anatomic gastrointestinal abnormalities ( strictures or complications of repair)
- Medication side effects
- GI symptoms
- Neuro-logic/behavioral problems
- If the patient has non-specific poor oral intake, with or without nausea and abdominal pain, evaluation for evidence of occult infection may be useful
ESOPHAGEAL ATRESIA AND TRACHEOESOPHAGEAL FISTULA
ESOPHAGEAL ATRESIA AND TRACHEOESOPHAGEAL FISTULA

• Only the minority of cases is diagnosed prenatally, so any neonate noted to have excessive oral secretions, feeding intolerance or respiratory difficulties at birth should raise concern for EA.

• Long-term complications related to the severity of the primary lesion and the quality of the repair.

• After EA repair:
  • gastroesophageal reflux (GER), esophageal dysmotility and respiratory problems are very common.
Duodenal atresia is less frequent than EA.

Postoperative patients are usually asymptomatic and show normal growth but late complications do occur in 12-15% of patients and include:

- abdominal pain, delayed gastric emptying, peptic ulcer, megaduodenum, duodenogastric reflux.

There is frequently poor duodenal motility above the anastomosis.
NAUSEA

Nausea can be multifactorial

• In FA patients most frequently resulting from:
  • infections
    • (particularly urinary tract infections or sinusitis)
  • post-infectious gastroparesis
  • medications
• This usually is a transient problem, resolving with resolution of the infection or stopping the medication

Psychological stress, anxiety, and depression can also present with nausea, abdominal pain or exacerbating existing gastrointestinal complaints
REFLUX

• Gastroesophageal reflux disease can be empirically treated if children are old enough to reliably explain symptoms or can be tested using manometric placed pH/impedence probe studies.

• Gastritis and other peptic disease should be diagnosed by endoscopic biopsy without the need for imaging.

• Peptic disorders should be treated with proton pump inhibitors (omeprazole, lansoprazole, etc.) rather than H2-blockers (ranitidine, etc.) because of the risk of marrow suppression.
GASTROPARESIS

- Gastroparesis is a motility disorder of the stomach that is characterized by slowed emptying of gastric contents in the absence of mechanical obstruction.
GASTROPARESIS

• Can be suspected clinically nausea, early satiety and vomiting of food eaten several hours earlier.

• The most common study used is the nuclear medicine gastric emptying study, which involves radiation.

• Omitting a gastric emptying study and initiating a trial of medical therapy is acceptable to avoid radiation exposure if a patient has classic symptoms, normal physical exam and obstruction has been ruled out.
GASTROPARESIS

• If the patient has delayed gastric emptying dietary counseling with a dietitian is warranted to adjust meal content and frequency
  • favoring small and frequent meals with restriction of fats and nondigestible fibers, while maintaining adequate caloric intake

• A trial of prokinetic agents may be given, like erythromycin (5 mg/kg/dose) three times per day
  • Careful with interaction with other medications

• The use of metoclopramide (reglan) is not recommended because of the potential dangerous side effects including irreversible tardive dyskinesia.
  • FDA BLACK BOX WARNING
GASTROPARESIS

• Other alternative to refractory gastroparesis are surgical and include:
  • endoscopic therapy with pyloric dilatation and botulinum toxin injection
  • jejunostomy or gastrojejunostomy

• Before submitting a patient to surgical complications physicians must keep in mind that most cases of idiopathic gastroparesis in children resolve over time
GASTROPARESIS VS ACCOMODATION DEFECT
In cases of severe, intractable nausea without a detectable cause, a trial of ondansetron may be warranted if there is no improvement with cyproheptadine.
TREATMENT OF POOR GROWTH

• Analysis of a prospective three-day dietary record may indicate deficits in protein and calorie intake

• Dietary counseling, with or without evaluation by a feeding specialist, may be enough to improve oral intake in some patients

• If oral intake does not increase counseling should be aimed at maximizing calories by addition of high calorie foods and liquid or powder supplements
APPETITE STIMULANTS

• None has been tested in FA populations
• Prior to using such medications: diagnosable causes of failure to thrive and poor appetite must be first investigated and appropriately managed
• Appetite stimulants will not treat gastroparesis, depression, chronic infection or other treatable causes of failure to thrive.
• Maintenance of weight gain after medication has been stopped has not been demonstrated
WHO SHOULD WE TREAT MORE AGGRESSIVELY

• Children who are persistently
  • less than expected weight for height
    • for children < 2 years of age
  • have a BMI percentile for age persistently below 3rd percentile
  • who have failed to gain weight over a 3-6 month period

• Supplemental feeds are formula feeds delivered directly into the stomach or small intestine, bypassing appetite and food interest
• Enteral supplementation is preferable to parenteral (intravenous) supplementation in all practical cases

• Supplemental parenteral feeds require placement of a central line, with increased risk of infection and metabolic disorders, including hepatic injury

• Parenteral feedings should be limited to those patients unable to meet their needs with enteral nutrition
To reduce the impact on the daytime appetite, supplemental feedings can be given at night.

Once appropriate weight-for-height is attained, it may be possible to reduce the number of days of the week supplementation is given.

Some patients experience heartburn after starting enteral feeding supplementation, particularly with nocturnal feeds. Vomiting may occur, particularly in the morning. Diarrhea at night also can be a problem.
ENTERAL ALIMENTATION

• Nasogastric tube
• Naso-jejunal tube
• Gastrostomy
  • Gastric or gastrojejunalostomy tube
NASAL TUBES

- Most patients tolerate nasal tubes well
- Some risk of sinusitis
- There is less risk of dislodgment with the nasojejunal tube but when dislodged, the tube must be replaced by a radiologist with fluoroscopy

- Ideal for patients anticipating supplemental feedings for less than three months

- Many children can be taught to place the tube at bedtime and remove it on awakening before going to school
GASTROSTOMY TUBES

• Provide more permanent access to the gastrointestinal tract for administration of enteral feedings

• In general, it is recommended that patients have a nasogastric or nasojejunal feeding trial before

• Placement requires a surgical procedure Percutaneous endoscopic vs. surgical gastrostomy

• If platelets are very low at placement, bleeding is a risk

• Unfortunately, once FA patients become neutropenic, the risk of significant local infection at the gastrostomy tube site is increased and may prevent placement of the tube
PERCUTANEOUS ENDOSCOPIC GASTROSTOMY TUBE

- Esophagus
- Trachea
- Lungs
- Stomach
- Intestines
GastroJejunal (GJ) Tube
SKIN CARE

Some drainage is normal

Skin immediately adjacent to tube will likely be slightly red, but redness should not extend very far out from site
COMPLICATIONS

Skin Irritation
Granulation Tissue
Leaking
Pain
Gastric Prolapse
OVERWEIGHT AND OBESITY IN FA

- As in the general population, overweight is being seen in patients with FA

- Overweight is defined as BMI >85th percentile and <95th percentile for age

- Obesity is defined as having a BMI >95th percentile for age
Significant complications may result from overweight and obesity, including:

- hyperlipidemia
- diabetes
- obstructive sleep disorder
- metabolic syndrome

The impact of non-alcoholic steatohepatitis or liver disease during HSCT is unknown. It may surprise some families to face this issue after previous concerns with underweight, but modification of lifestyle is essential.
VITAMINS

- Patients with FA may also have deficiencies or increased need for specific vitamins and minerals, including folate and zinc. “Need to talk with primary care physician before starting any supplements or vitamins”

- All patients should be screened for vitamin D deficiency at least once a year (preferably during the winter) by checking blood levels of 25-OH vitamin D
  - If level is less than 30 supplementation with PO vitamin D once a week is indicated
  - Levels should be checked after 8 weeks and supplementation should be continued for as long as 25OH vitamin D level is below 30
ALTERNATIVE THERAPIES
Alternative Therapies

• Alternative therapies are those not supported by evidence-based clinical studies, used in place of standard medical care.

• Many families view food and, by extension, dietary supplements, vitamins, and micronutrients, as “natural” and thus safe.

• The industry that produces complementary/alternative nutritional regimes and supplements is a multibillion dollar industry without regulation, but with a clear incentive to promote their product regardless of the degree of evidence for effectiveness.

• Many complementary/alternative nutritional regimes and supplements are directly harmful or, by displacing standard medical therapy, indirectly harmful.
“This is no ordinary lemonade. It’s a tart blend of fruit and green tea that is not only refreshing but sufficiently high in antioxidants. Plus it grows hair.”
ANTIOXIDANTS

• Patients with FA may consider megavitamin therapy and antioxidant or trace element supplementation

• Patients may be aware that there is research on oxidant stress in FA, but be unaware that this research does not prove that oral anti-oxidants change the course of FA

• It is not clear that oral anti-oxidants even reach the intracellular site of oxidant stress in FA

• Concerns about these therapies include the potential toxicities of some supplements and whether some supplements may promote tumor development.

• In particular, vitamins A, D, C, and niacin may be toxic in excess
ANTIOXIDANTS

No therapy using antioxidants, megavitamins, or micronutrients has been shown to be effective in treatment of FA using evidence based criteria.

Particular risk is associated with products containing

- supplements of iron
- vitamins A, C, and E
- omega-3 fatty acids
  - Can increase risk of bleeding due to platelet inactivation

Products containing iron must be avoided to reduce risk of exacerbating iron accumulation in liver and other tissues. Vitamin C potentiates iron absorption.
PROBIOTICS AND MICROBIOME

Sherrill's
Eat Here
And
Get Gas
Tipton, Indiana
Probiotic:

• An oral supplement or a food product that contains a sufficient number of viable microorganisms to alter the microflora of the host and has the potential for health benefits

Prebiotic:

• Nondigestible food ingredient that benefits the host by selectively stimulating the favorable growth and/or activity of 1 or more indigenous probiotic bacteria

Synbiotic:

• A product that contains both probiotics and prebiotics
Clinical Report—Probiotics and Prebiotics in Pediatrics

- There is a paucity of RCTs examining prebiotics in children
- Confirmatory well-designed clinical research studies are necessary
- Questionable safety in immunocompromised children, ill preterm neonates, children with intravenous catheters and indwelling medical devices
• Hematopoietic stem cell transplant (HSCT) patients can present a number of nutrition challenges despite recent advancements in medical care.

• Several areas of controversy exist, including whether probiotics can be safely used; the use of probiotics continues to expand but efficacy and safety is a concern in immunocompromised patients, including HSCT recipients.
TAKE HOME POINTS...

• Evaluate weight-for-height or BMI when addressing growth… 60% of children with FA will have short stature and therefore proportionately lower weights

• Sequential and judicious approach to diagnosis
  • Always start with less invasive approach

• There is no “wonder drug”

• Natural is NOT ALWAYS better or safe

• Make decisions about supplements WITH your physician
QUESTIONS...