NEW CONCEPTS IN CROHN’S DISEASE

GLENDON BURRESS, MD
PEDIATRIC GASTROENTEROLOGY
ROCKFORD, IL
CROHN’S DISEASE

- Chronic disease of uncertain etiology
- Etiology- genetic, environmental, and infectious
- Transmural (not just superficial) inflammation of GI tract
  - 80% have small bowel disease
  - 50% have ileocolitis
  - 33% with perianal disease
- Present with prolonged symptoms
  - Diarrhea +/- bleeding, abd pain, weight loss, fatigue
  - Skin, mouth, eye, and joint disease
  - Small bowel strictures, fistulas to bowel, bladder, skin, vagina, retroperitoneum
CROHN’S DISEASE
Presentation
CROHN’S DISEASE
APHTHOUS ULCER
CROHN’S DISEASE
PYODERMA GANGRENOSUM
CROHN’S DISEASE

- Laboratory features
  - Elevated ESR, CRP, platelets
  - Decreased albumin and hemoglobin (anemia)
  - Blood in stool, elevated fecal calprotectin, and WBC
"Wow, this prep is so delicious, I think I'll drink another!"

... said no one ever
YOU WILL GO TO SLEEP

OR I WILL PUT YOU TO SLEEP
CROHN’S DISEASE
Endoscopic Appearance
CROHN’S DISEASE
Endoscopic Appearance

http://www.gastrolab.fi/videos/vid1702.jpg
CROHN’S DISEASE

Treatment

- **Corticosteroids** - prednisone, methylprednisolone, Budesonide
- **5-aminosalicylates** - Pentasa, Delzicol, Lialda, Apriso, Rowasa
- **Immunosuppressants**
  - Thiopurines - azathioprine (Imuran and 6-MP)
  - Methotrexate
- **Biologics**
  - Infliximab (Remicade)
  - Adalimumab (Humira)
NEW CONCEPTS

- Pre-diagnosis-
  - Fecal Calprotectin assessment
  - Viral titers (Varicella, EBV, other viruses)
  - TPMT levels

- Confirmation of diagnosis-
  - Magnetic Resonance Enterography (MRE)
  - Video Capsule Endoscopy (Pillcam)

- Treatment-
  - Therapeutic drug levels (Anser IFX)
  - Combination therapy
  - Fecal transplant
Fecal Calprotectin

- Calcium binding protein
- Released by activated neutrophils during inflammation
- Amount in the stool proportionate to the number of neutrophils
- Helps distinguish IBD from IBS (<50 unlikely to be IBD)
- Good for monitoring disease activity and response to treatment
Fecal Calprotectin

Tarbet A, 2016. Pros and Cons of De-escalating IBD Therapies
Fecal Calprotectin

- Can be elevated in infections, food allergies, Celiac disease, and colorectal cancer
- Abnormal is > 120 mcg/g
- Slow turnaround (stool WBC quicker, less sensitive or specific)
VARICELLA

- Varicella-zoster virus (Herpesvirus family)
- 2 weeks after exposure: fever, malaise and rash
- Worse in infants, elderly, immunocompromised
  - Varicella zoster immunoglobulin
  - IV Acyclovir for severe infections and immunocompromised pts
- Immunity: positive varicella IgG
  - Vaccine is a LIVE virus vaccine
  - If negative, then vaccinate and wait 4 weeks for Crohn’s treatment

cdc.gov/chickenpox/hcp/persons-risk.html
EPSTEIN BARR VIRUS (EBV)

Human Herpesvirus 4
90% of US population infected by age 25
Acute mono with sore throat, fever, and lymphadenopathy
Latent infection
  Immortalized- lives and reproduced in lymphocytes and epithelial cells forever
Associated with many tumors

Bennett NJ, Domachowske J. Pediatric Mononucleosis and Epstein-Barr Virus Infection, Medscape, Nov 2016
EPSTEIN BARR VIRUS (EBV)

Diseases Associated with EBV

EBV in B Cell
- Infectious mononucleosis
- X-Linked Lymphoproliferative Disease
- Chronic active EBV
- Hodgkin Disease
- Burkitt Lymphoma
- Lymphoproliferative disease

EBV in Other Cells
- Nasopharyngeal carcinoma
- Gastric carcinoma
- Nasal T/NK cell lymphomas
- Peripheral T cell lymphomas
- Oral hairy leukoplakia
- Smooth muscle tumors in transplant patients

Mononucleosis causes:
- Fever
- Fatigue
- Sore throat
- Swollen lymph glands

DR. T.S. ADAM
OTHER VIRUSES

- Hepatitis B
  - Check Hep B surface antibody
  - Higher vaccine dose recommended
- Influenza vaccine recommended (not the LIVE nasal vaccine)
- Pneumococcal vaccine
- Meningococcal vaccine
TPMT Genotype Testing Prior to Initiating Thiopurine Treatment

- Thiopurine methyltransferase
- Enzyme for metabolizing thiopurines (Imuran and 6-MP)
- Homozygous nonfunctional (nonfunctional alleles)
  - Low or absent (0.3% of population)
  - Life-threatening bone marrow suppression with usual dosing
  - Thiopurine therapy not recommended
- Heterozygous (1 nonfunctional, 1 functional)
  - Intermediate (10%)
  - Increased risk of myelosuppression with usual dosing
  - Reduce usual dosage by 50 to 70%
- CBC w/platelet count
  - Weeks: 0, 2, 4, and 8, then every 3 months
MAGNETIC RESONANCE ENTEROGRAPHY (MRE)

- MRI of the abdomen and intestines
  - Imaging of the small bowel
  - Imaging of extraintestinal findings
    - Fistulas
    - Abscess
- Avoids radiation
- More expensive than CT
## MRE vs CT

<table>
<thead>
<tr>
<th>Feature</th>
<th>CTE</th>
<th>MRE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Examination time</td>
<td>Short</td>
<td>Long</td>
</tr>
<tr>
<td>Spatial resolution</td>
<td>High</td>
<td>Lower</td>
</tr>
<tr>
<td>Contrast resolution</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Radiation exposure</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Functional imaging (DWI, cine imaging)</td>
<td>Not possible</td>
<td>Possible</td>
</tr>
<tr>
<td>Artifacts (peristaltic, bowel gas)</td>
<td>Less</td>
<td>More</td>
</tr>
<tr>
<td>Cost</td>
<td>Cheaper</td>
<td>Expensive</td>
</tr>
</tbody>
</table>

CTE: CT enterography, MRE: MR enterography, DWI: Diffusion weighted imaging
VIDEO CAPSULE ENDOSCOPY

- Noninvasive imaging of the small intestine unable to be reached by an endoscope
- Resolution is higher than an endoscope
- 2 images per second transmitted by radio frequency to a recorder
- 11 x 26 mm in size (can be placed into the bowel endoscopically)
VIDEO CAPSULE ENDOSCOPY

- Indications- unexplained bleeding, assessing indeterminant colitis, localization of Crohn’s Disease, assess NSAID damage, screen for polyps
- Contraindications- suspected stricture (Patency capsule can be used)
- Requires careful examination of the images
- Disadvantages- can’t obtain a biopsy
- Detection rate= 60%
- Change in management= 74%

VIDEO CAPSULE ENDOSCOPY
THERAPEUTIC DRUG MONITORING

- Biologic agents - Infliximab (Remicade) and Adalimumab (Humira)
- Previously - checked drug and antibody levels when patients were having problems
  - If low levels of the med, then increase dose.
  - If antibodies present against the med, then change meds
- Currently - monitor therapeutic levels
  - adequate levels prevent complications
  - adequate levels prevent antibody formation
  - if antibodies present, then can add an immunosuppressant and follow for loss of antibodies
- Insurance coverage issues
COMBINATION THERAPY

- Increased lymphoma risk with thiopurines alone or when combined with an anti-TNF (such as Imuran with Remicade)
- Hepatosplenic T-cell Lymphoma
- Many occur with primary EBV infection
- Young males with at least 2 years thiopurine exposure
- Avoid combination of Imuran/6-MP with anti-TNF (Remicade, Humira) in boys
- Consider Remicade with methotrexate in boys
- Still using Remicade with Imuran/6-MP in girls
Fecal Transplantation of feces from healthy donor to pt with GI disease. Modulates dysbiosis and colon inflammation. Microbes thought to play a role in many diseases.

Delivered by enema, colonoscopy, NG tube, or capsules.

Proven effective for C difficile treatment.

Promising studies with Crohn’s Disease.
Dose size, number of doses, donor and recipient bacteria, duration of response, remission vs maintenance, side effects.

Many new concepts

Viral testing
  Balance long-term protection vs treating Crohn’s

Pharmacogenetic testing to help in dosing thiopurines (Imuran or 6-MP)

Diagnostic testing
  Balance disease information vs costs

Treatment
  Balance costs of drug levels vs more flare-ups
  Balance costs of drug levels vs antibody formation
  Balance combination therapy vs complications
Let's call it a day, I'm pooped.