GHAPP

Gastroenterology & Hepatology Advanced Practice Providers

2020 Third Annual National Conference

November 19-21, 2020

Red Rock Hotel – Las Vegas, NV

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Updates in Crohn's Disease

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Disclosures

Bridget Howard, NP

- No financial relationships to disclose

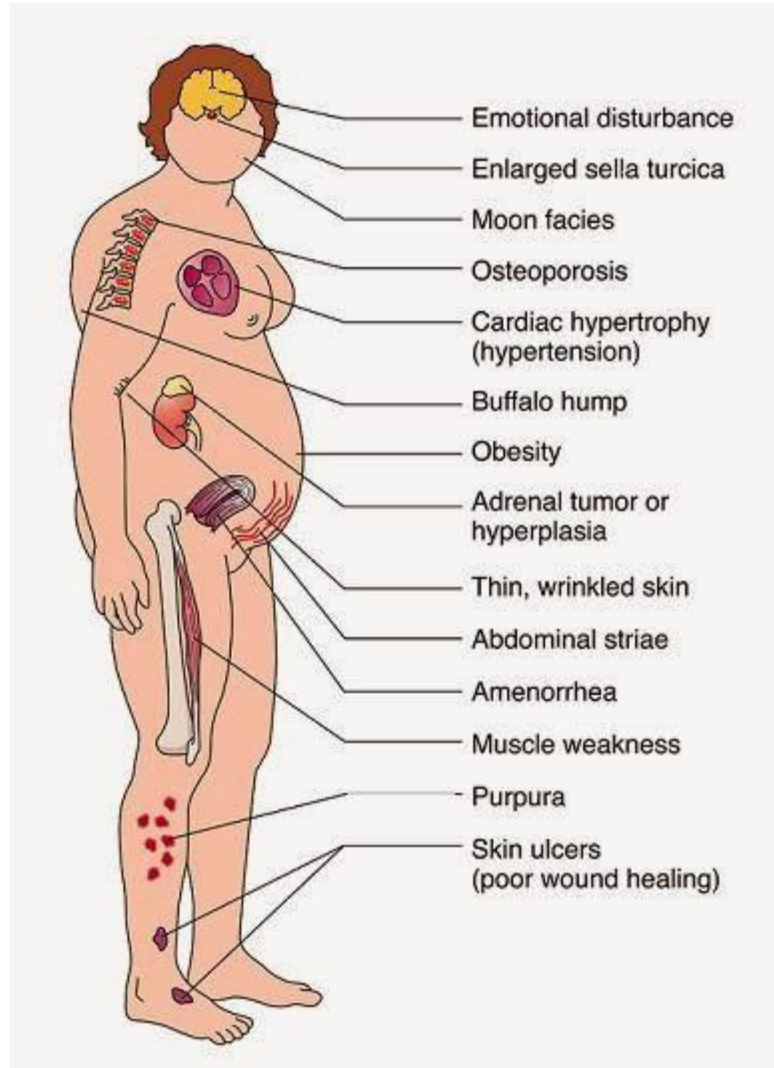
Objectives

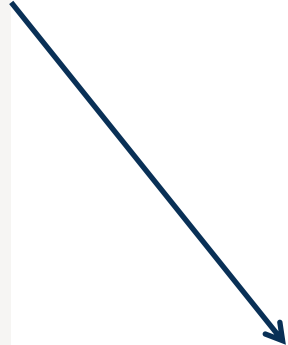
- Discuss current treatment for Crohn’s disease
- Discuss treatment for complications of Crohn’s disease
- Discuss future therapies for Crohn’s disease

Q and A

Goals of Treatment

- Individualize therapy
- Change progression of disease
- Increase quality of life
- Decrease hospitalization and morbidity
- Avoid Steroids





AVOID
Side Effects
Of Steroids

Treat to Target – Individualize Therapy

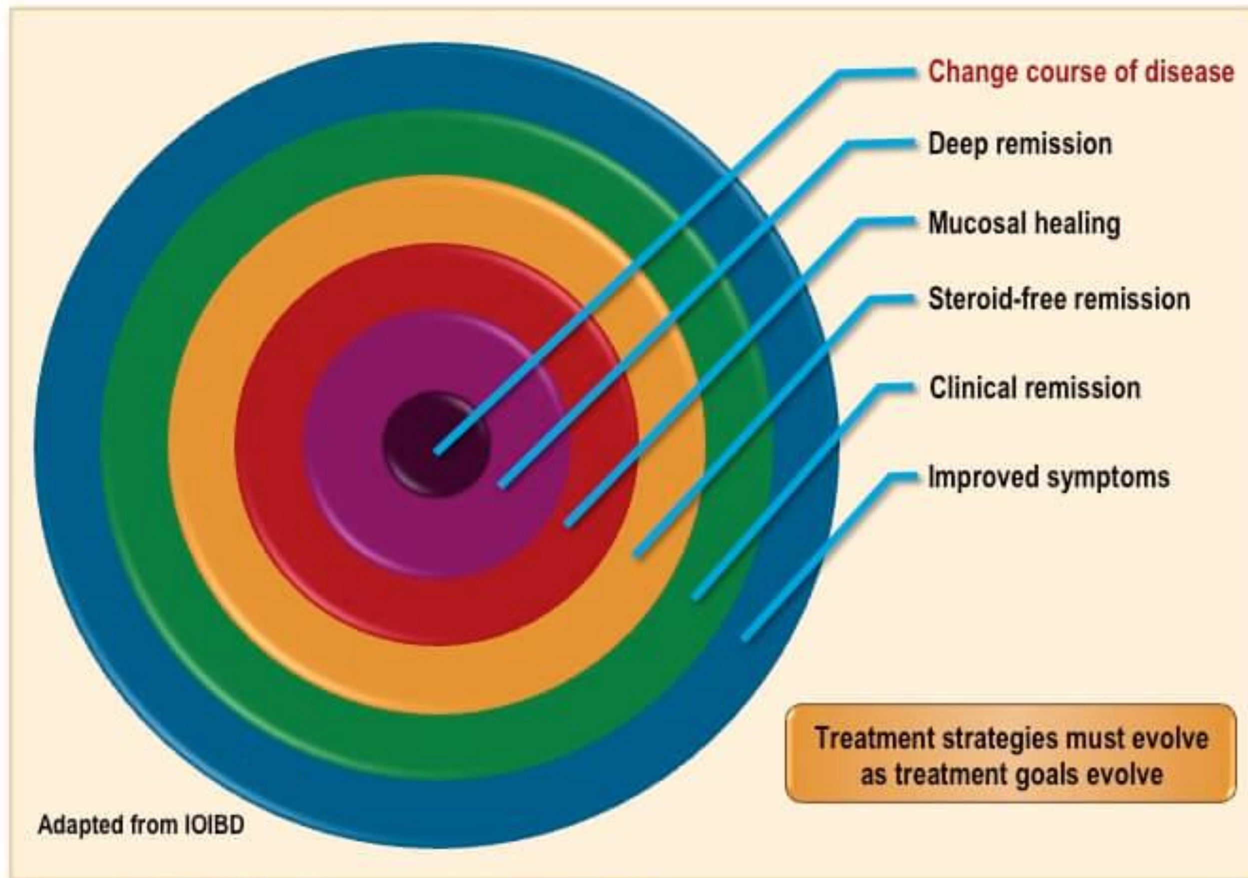


Figure 1. Evolution of treatment goals in IBD.

Low RISK Crohn’s – Treatment

Medical Therapy for Low Risk Crohn's Disease

- Mesalamine?
- Steroids, budesonide, prednisone
- Reevaluate after above with inflammatory markers, or ileocolonoscopy after 3-6 months

Medical Therapy for Moderate to Severe Active Luminal Crohn's Disease (High Risk)

- Oral and IV corticosteroids are effective for short-term induction of remission (flares) but do not consistently achieve mucosal healing
- Biologic therapy is effective for induction and maintenance of remission and early use is recommended in patients with severe or complicated disease
- Individualize old/current therapies with new therapies
- Combo therapy with immunomodulatory medications and duo biologics

Biologic Therapy for Crohn's Disease

Anti-TNF Therapy

- Infliximab
- Adalimumab
- Certolizumab

Anti-Adhesion Therapy

- Natalizumab
- Vedolizumab

Anti-IL12/23

- Ustekinumab

Combination Therapy

Duotherapy

- Biologic combos
- Antibiotics and immune suppressants
- Diet plus medications

With immunomodulator

- AZA or MTX, or 6-MP

Pre-biologic Evaluation

- Tuberculosis screening prior to therapy
  - PPD vs Quantiferon – TB Gold assay
  - Chest X-Ray (especially if high risk)
  - Consider annual TB screening
- Hepatitis B screening
- Hepatitis C screening
- Arizona: baseline cocci serology

Risks of Anti-TNF's

- Infection
  - Reactivation TB, HBV
  - Sepsis
  - OIs
- Lymphoma
- Demyelinating d/o (rare)
- Hepatotoxicity (rare)
- Drug-induced lupus (<1%)

Risks of Ustekinumab

- Increased risk of infections
- Lung inflammation
- Skin cancer
- Reversible Posterior Leukoencephalopathy Syndrome (RPLS) rare
- Allergic reactions

Risks of Vedolizumab

- Hepatotoxicity
- Headache
- Joint pain
- Fatigue
- Increased infections, primarily in gut
- Not PML

Which Drug to Choose? Shared Decision Making Individualize Therapy With "Old Drugs"

- Route: IV vs injection
- Safety: Consider vedolizumab or ustekinumab
- Extraintestinal manifestations: Anti-TNF therapy
- Lymphoma: Avoid thiopurines
- Arthritis: Use methotrexate
- High Risk: Strongly consider combination therapy

Therapeutic Drug Monitoring (TDM)

Benefits

- Enhance effectiveness
- Outcomes better
- Save therapies
- Dose escalation/ De-escalation
- Lower costs in proactive groups

Proactive/Reactive

- Both camps have points

SARS 2 Corona Virus and IBD

- COVIDIBD.ORG
- Interactive Map for cases
- US 837 (6 deaths) as of Sept 1, 2020

COVID Discussion

- Risk increases – Strong number of comorbidities
- Older age
- Use of systemic corticosteroids
- 43% exposed to Anti-TNFs (525 pts)
- Those on 5-ASA fared worse?

Gastroentrology. 2020;159.481-491

Crohn's and + SARS 2

- Stop anti TNF, biologics, immunosuppression, until 14-20 days post initial symptoms
- Taper high-dose steroids
- Discussion on updates

Steps When Medication Not Working

Switch Therapy

- Loss of response?
- Confirm adherence
- Rule out infection
- Confirm inflammation
- Assess drug and antibody levels

Can You Use the Same Medication Again?

YES

- Was disease too advanced when started and that was reason for lack of response?
- If inflammatory pathway reactivated

NO

- Due to anti-drug antibodies
- If disease progressed right through prior therapy

Remission, Now What?

De-Escalate Plan

- Confirm deep remission for greater than 1 year
- Why is it reasonable?
- Deescalate dosing or one drug first
- Have a monitoring plan
- Have a plan for flare, rescue-prior therapy or new therapy

Fistulas

- Affect 40% of patients with Crohn’s
- Predictive or poor long-term outcomes
- Difficult to treat
- Surgery is option
- Stem cells potential better approach
- Dr. Faubion Study 10/12 Success-ongoing

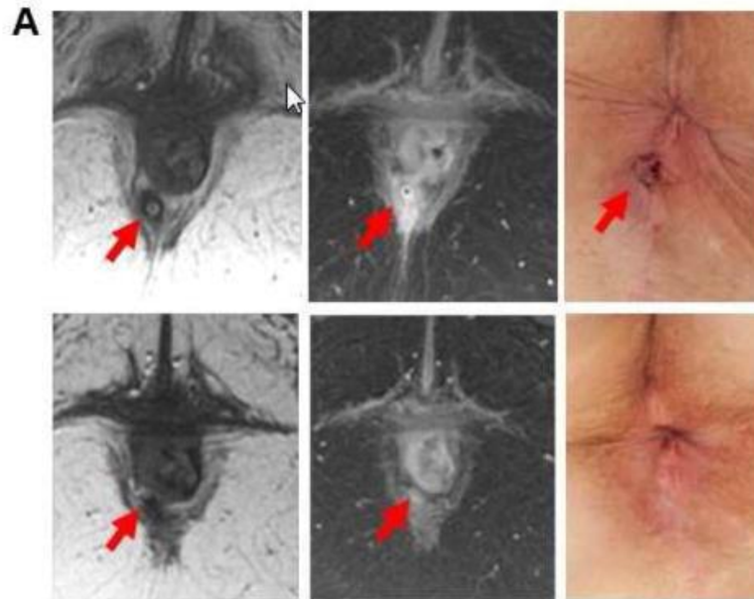
Treatment of Fistulas

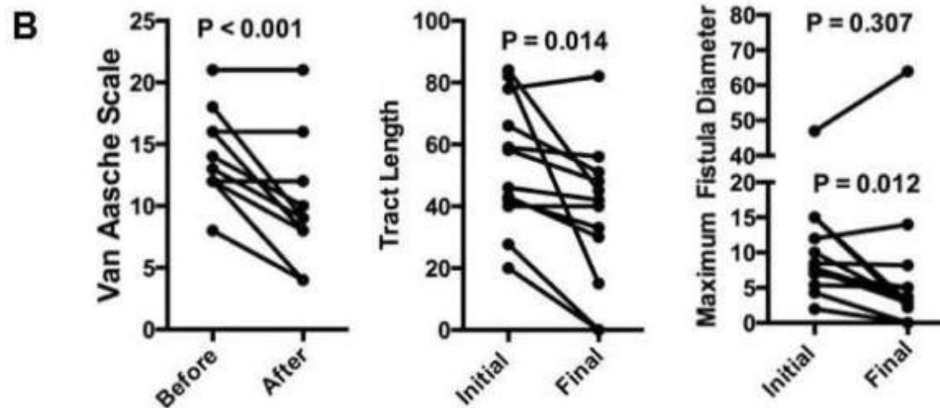
- Important to differentiate simple vs complex
- Simple perianal fistulas should be treated with Seton placement in combination with medical therapy
- Complex fistulas usually require surgery in combination with medical therapy
- High-output fistulas – Surgery usually

Medical Therapy for Simple Perianal Fistulizing Crohn's Disease

- Perianal fistulas
  - Anti-TNF therapy (IFX best studied)
  - ? Certolizumab/vedolizumab/ustekinumab
  - Azathioprine and 6-MP
  - Tacrolimus
  - Ciprofloxacin and/or metronidazole
- Antibiotics and anti-TNF therapy increases efficacy
- Always exclude pyogenic complications prior to biologic therapy

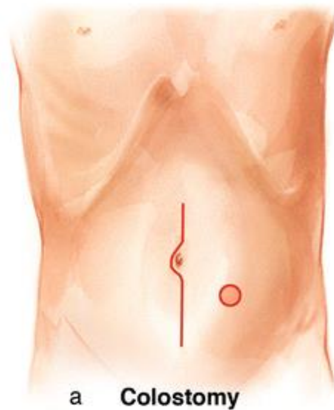
Stem Cell for Fistula Disease

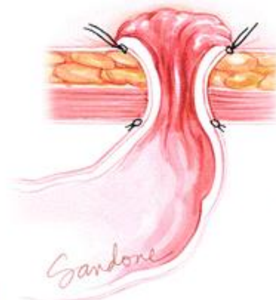


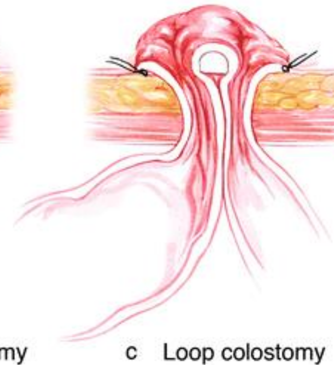


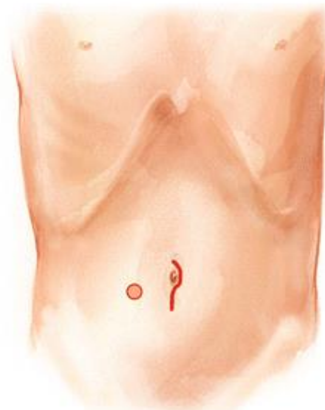
Refractory Disease – Surgery May Be Needed

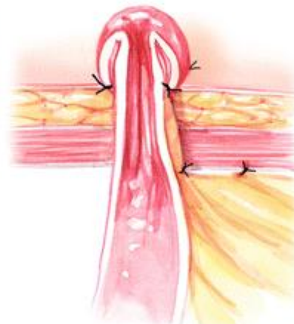
Refractory disease may require

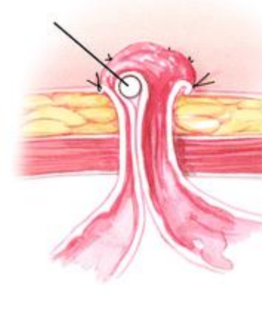






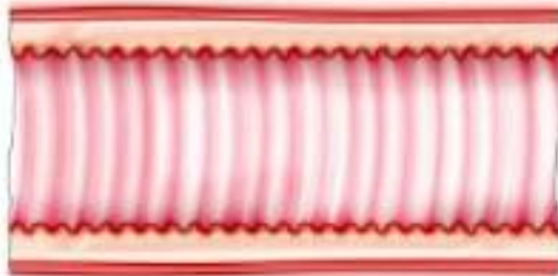




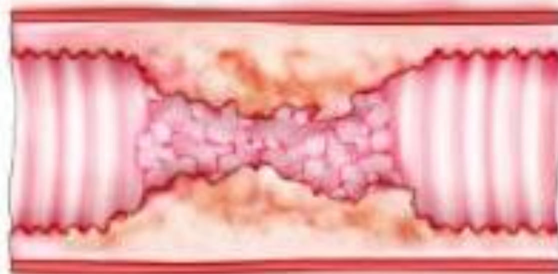


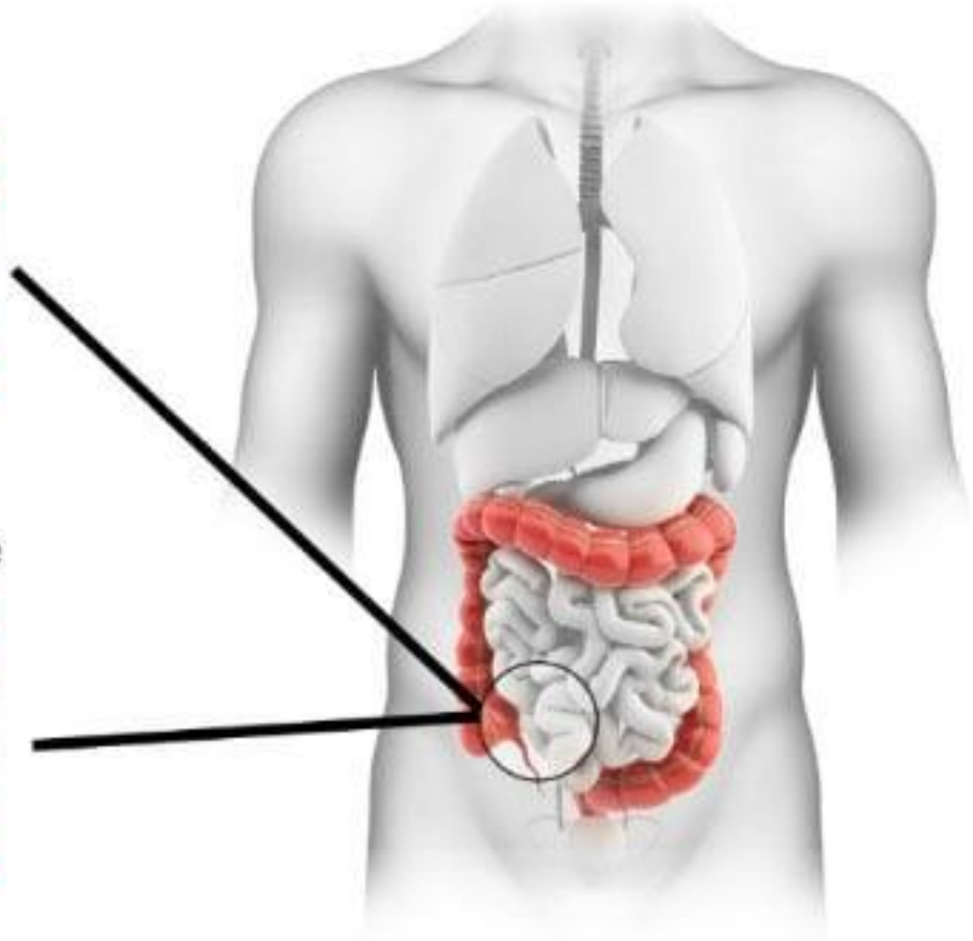
Strictures and Crohn’s

Normal Intestine



Intestine with Stricture





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Strictures in Crohn's

Small Bowel

- % of patients
- Fixed strictures
- Medical therapy
- Bowel resection or stricturoplasty

Colon

- 10% of patients
- Fixed strictures
- Medical therapy
- Bowel resection

Treat Strictures in Crohn's Disease

- Balloon assisted enteroscopy 94.9% success
- Standard ileocolonoscopy 82.3% success
- Short Clinical success with balloon dilations and re-dilation in 38.8%
- Surgical Intervention may be necessary
- (Meta Analysis published in *APT*)

Indications for Surgery in CD

- Stricture and obstruction: most common indication
  - Common site-ileum
- Intraabdominal abscess and fistulae-penetrating disease
- Perforation
- Failure of medical therapy
- GI bleeding
- Neoplasia or dysplasia

Post-Operative Prophylaxis of Crohn's Disease

- Risks – cigarettes, multiple resections, penetrating disease, short duration prior to surgery
- All patients should stop smoking
- Azathioprine and 6-MP are more effective than mesalamine or placebo
- Anti-TNF therapy for high-risk patients

Post-Operative Prophylaxis of Crohn's Disease

- Risks – cigarettes, multiple resections, penetrating disease, short duration prior to surgery
- All patients should stop smoking
- Mesalamine is of limited benefit in low-risk patients
- Azathioprine and 6-MP are more effective than mesalamine or placebo
- Anti-TNF therapy for high-risk patients

Future Therapies

- Anti-Adhesion
  - AJM300 oral, interleukin
- Anti-Chemotaxis Therapies
  - RPC1063
  - Oral-ozanimod (MS)
- JAK Inhibitors
  - Filgotinib oral
- Immune Cell Modulation
- Microbiome-Targeted and Antimicrobial Therapies

Microbiota Manipulation

- Dietary therapies (exclusion diets)
- Antibiotics
- Probiotics/Prebiotics
- Microbiota transfers
- Bacterial-derived proteins

Is Diet Effective in Treatment?

Low FODMAP

- 4 studies 2016-2019
- Relief of functional symptoms
- No effect on fecal cal
- Improved quality of life

Data

- No foods shown to increase inflammation
- Exacerbate GI symptoms
- Gut Microbiome and intestinal barrier – IBD Risk
- Efficacy scarce – ET for Peds

Health Maintenance

- Inactivated Vaccines: Influenza, Pneumococcal
- Special Considerations, HPV, Zoster
- Cervical Dysplasia Screening
- Dermatology Exams
- Screen for nutritional deficiency
- Bone Dexa Scans
- Check list: Cornerstonehealth.org

Future of Individualized Management

- Smart apps and devices
- Ongoing monitoring
- Immune panels and ongoing search for inflammatory markers
- New dominant pathways identified to treat
- REMISSION!

Final Take-Aways

- Crohn's disease is usually associated with progressive disease
- Classify patients into high- vs low-risk
- Combination therapy is more efficacious for induction of remission in high-risk patients
- The goal is mucosal healing and altering the natural history of the disease
- Therapeutic drug monitoring is important
- Decisions are complicated and must be individualized
- THANK YOU!!!

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Q&A