Unique Treatment Goals For Pediatric IBD

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Objectives

• Provide an overview of IBD in children
• Discuss how IBD impacts children physically, psychologically, and socially
• Outline various therapies for IBD, and discuss special considerations for children & teens
• Describe proper nutrition in pediatric IBD and the role of enteral nutrition
• Discuss the importance of getting the pediatric patient involved in care
• Highlight several resources for children with IBD
What is Inflammatory Bowel Disease (IBD)?

Future will be more specific classification based on cause and predicted disease course.

Images courtesy of Monroe Carrell Jr. Children’s Hospital at Vanderbilt Pediatric IBD Program.
The Burden of Pediatric IBD?

- Estimated 1.6 million people in the United States have IBD
- 25% of IBD diagnosed in pediatric age group
- Incidence: 7-10 children out of 100,000 develop IBD each year
- Prevalence: Approximately 80,000 children in the US have IBD
- 50% increase in children with IBD over past decade
- Overall cost of IBD greater in children vs. adults

Symptoms of IBD

- IBD varies, but common symptoms include:
  - Frequent and/or urgent bowel movements
  - Diarrhea (or constipation)
  - Bloody stool
  - Abdominal cramping
- Presentation more severe in children
  - UC: Higher incidence of pancolitis (>80%)
  - CD: ~20% risk of surgery or complicated disease within 3 years of diagnosis
  - More likely to have upper GI tract involvement
  - In adolescents, ratio of CD to UC is 2-3:1 (vs. 1:1 in adults)
- Delay in growth and puberty
- Unique psychological and social concerns
Potential Causes of IBD

- Child of an adult with IBD has increased risk of having IBD
  - 2-10 times
- 15%-20% of patients have close relatives with IBD
  - Higher for children
- Identical twins: 50% in Crohn’s disease, 15% in ulcerative colitis

Role of Microbiota

- Trillions of bacteria in intestine
- Bacteria change with genes, food, antibiotics
- Bacteria are different in IBD patients, and are main activator of immune system

1. Farrell M. *IBD Family Day* 2009.
2. Lewis J. *Breakthroughs in IBD Research* webcast 2012.
Effect Of IBD On Growth

- Growth often affected in children with IBD, may appear before other symptoms
- Decreased rate of growth and height percentiles
  - Adult height compromised
  - Crohn’s disease: 32-88%
  - UC: 9%-34%
- Causes
  - Inflammation
  - Steroids
  - Poor nutrition
- Growth is good marker for disease activity

Bone Health in Children & Teens

- Decreased bone mineral density common in children and adolescents with IBD
  - Poor calcium absorption/intake; vitamin D deficiency
  - Decreased physical activity
  - Steroid use
  - Inflammation

- Maximum accumulation of calcium in your bones occurs in mid-teen years

- Steroid use increases short- and long-term risk

- Important to ensure adequate calcium and vitamin D intake, as well as weight-bearing exercises
Impact on Puberty

• Medical and psychological impact

• Similar factors affect growth and onset of puberty
  – Poor nutrition
  – Pro-inflammatory cytokines
  – May or may not be made up later in life

• Delayed age of peak height velocity (mid-puberty)
  – ~25% children with Crohn’s
  – Delay usually 6-12 months

Psychological and Social Effects

• Specific issues facing children and teens with IBD
  – Defining what it means to have a chronic illness
  – Coping with procedures, clinic visits, hospitalizations
  – Adhering to complicated medical and dietary regimens
  – Quality of life and social interactions impacted
  – Body image and disordered eating patterns
  – Need for support systems at home and at school
Psychological and Social Effects

• Children and teens with chronic disease are at greater risk of psychological stressors
  – Low self-esteem
  – Poor social functioning
  – Depression

• Quality of life and support resources are key
Treatment Goals in Children

- Maximize response to treatment
- Minimize toxicity of treatment
- Maximize adherence to the treatment
- Improve quality of life
- Promote physical growth and pubertal development
- Promote psychological growth
- Prevent disease complications
IBD Therapy Mantras

Ride the wave as long as you can
Don’t burn any bridges
Difficulty with Pediatric Treatments

• Limited data in pediatric IBD therapy
  – Treatment extrapolated from adult studies
  – Not “one size fits all”

• Adverse Events
  – Infections
  – Cancer
  – Impact of lifetime therapy duration

• Outcomes for clinical trials needs to consider pediatric-specific outcomes
Types of Medication

<table>
<thead>
<tr>
<th>Crohn’s Disease</th>
<th>Ulcerative Colitis</th>
</tr>
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<tbody>
<tr>
<td>• Antibiotics</td>
<td>• 5-ASAs</td>
</tr>
<tr>
<td>• Immunomodulators</td>
<td>• Immunomodulators</td>
</tr>
<tr>
<td>• Steroids</td>
<td>• Steroids</td>
</tr>
<tr>
<td>• Biologics</td>
<td>• Biologics</td>
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Induction vs. Maintenance Therapy

**Induction Therapies**
- Prednisone
- Cyclosporine/Tacrolimus
- Exclusive Enteral Nutrition (EEN)

**Induction or Maintenance Medications**
- Biologics (infliximab, adalimumab)
- 5-aminosalicylates

**Maintenance Medications**
- 6-MP
- Methotrexate
# Steroids

Examples: prednisone, budesonide (Entocort®, UCERIS®), hydrocortisone (Cortenema®, Cortifoam®)

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very effective at inducing remission</td>
<td>Side effects</td>
</tr>
<tr>
<td></td>
<td>• Infection, acne, weight gain, mood/psychological disturbances, muscle wasting, osteoporosis, bone loss, hypertension, diabetes</td>
</tr>
<tr>
<td></td>
<td>• Concerns of dependency</td>
</tr>
</tbody>
</table>

**Take home points**
- Use for induction only
- If multiple courses needed per year, re-evaluate treatment plan
Corticosteroid therapy.....tenets

- Steroids are **not** maintenance drugs
- Steroids should be used in conjunction with an effective maintenance therapy
- Your doctor should **always** have a time frame for use and an exit strategy
Immunomodulators

Examples: 6-MP (Purinethol®), azathioprine (Imuran®, Azasan®), methotrexate (Rheumatrex®, Mexate®)

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Used effectively as steroid-sparing agents</td>
<td>Risk of serious infection</td>
</tr>
<tr>
<td>Mainstay of maintenance treatment in children</td>
<td>Teratogenicity (fetal abnormalities)</td>
</tr>
<tr>
<td>Effective at maintaining remission with or without biologics</td>
<td>with methotrexate</td>
</tr>
<tr>
<td></td>
<td>Need to monitor white blood count</td>
</tr>
<tr>
<td></td>
<td>and liver function</td>
</tr>
<tr>
<td></td>
<td>Low risk of lymphoma</td>
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</tbody>
</table>
Biologics

Examples: Adalimumab (Humira®), Infliximab (Remicade®)

**Benefits**
- Very effective induction and maintenance medications
- Support growth
- Treat fistulas and perianal disease

**Risks**
- Risk of serious infection
- Injection site issues (pain, swelling, etc.)
- Psoriasis
- Low risk of lymphoma
Biosimilars

Products that are “highly similar” to—but not exact copies of—biologic medicines

Inflectra™ is the first FDA approved biosimilar

- Has biosimilarity to Infliximab (Remicade®)
- Anti-TNF for treatment of Crohn’s disease (in adults and children) and ulcerative colitis (in adults)

Source:
http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm494227.htm - accessed 4/13/16
## Putting Risks In Perspective

<table>
<thead>
<tr>
<th>Event</th>
<th>Risk</th>
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<tbody>
<tr>
<td>Lymphoma from 6-MP or infliximab</td>
<td>4-6 in 10,000</td>
</tr>
<tr>
<td>Death from an automobile accident</td>
<td>38 in 10,000</td>
</tr>
<tr>
<td>Major surgery from Crohn’s disease in 5 years</td>
<td>1,780 in 10,000</td>
</tr>
</tbody>
</table>

**Take home points**
- Risk of lymphoma very small compared to potential benefit from medications
- If young male, evaluate risk vs. benefit of combination therapy (increased risk of hepatosplenic T-cell lymphoma)

Probiotics in UC?

Evidence supports weak (but probably real) role in:
- Induction of remission
- Maintenance of remission
- Prevention of pouchitis

Not all probiotics are created equal

Patients do not handle bacteria equivalently

Future role for “personalized medicine”

Evidence in Crohn’s is disappointing so far
“Off label” does not necessarily mean “experimental” – FDA statement

The FD&C Act does not, however, limit the manner in which a physician may use an approved drug. Once a product has been approved for marketing, a physician may prescribe it for uses or in treatment regimens or patient populations that are not included in approved labeling. Such “unapproved” or, more precisely, “unlabeled” uses may be appropriate and rational in certain circumstances, and may, in fact, reflect approaches to drug therapy that have been extensively reported in medical literature.
Questions to Ask the Health Care Team

• What are the risks of the current treatment plan?
• What are the risks of not treating the disease?
• How do we manage side effects of treatment?
• What is the plan if the current regimen stops working?
• Which vaccines are allowed?
  – If taking immunomodulators or biologics, certain vaccines may need to be given before starting treatment
Direction of Future Therapies

• Comparative effectiveness
  – Head-to-head comparison of management strategies

• Predicting disease course
  – Children with deep ulcers 2.7x more likely to have active disease at the end of 1 year than those without
  – If treated with anti-TNF therapy within 3 months of diagnosis, more than 10x less likely to have active disease at one year

• Predicting risk of therapy

• Renewed interest in diet
  – How does diet influence microbiota?

• New targets for treatment
  – Anti-α4 therapy
  – Anti-IL-12 and IL-23
  – Oral inhibitor of Janus kinases 1, 2, and 3

The Future of IBD Treatment

“IBD Panel”

Serology | Genetics | Microbial

IBD Subtype

Disease Prognosis

Patient-Specific Treatment Plan

Targeted-Specific Therapy
Indications for Crohn’s surgery

- Failure of medical therapy
- Recurrent obstruction
- Tearing of the bowel (perforation)
- Fistula or abscess
- Excessive bleeding
- Growth retardation/failure
Indications for Ulcerative Colitis Surgery

**Absolute need**
- Excessive bleeding
- Tear in the bowel (perforation)
- Cancer or pre-cancerous lesion

**Possible need**
- Not responding to medications
- Steroid dependency
- Growth retardation
- Complications from medication
## Types of Surgery

<table>
<thead>
<tr>
<th>Crohn’s Disease</th>
<th>Ulcerative Colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Strictureplasty</td>
<td>• Proctocolectomy (removal of the colon and rectum)</td>
</tr>
<tr>
<td>• Resection of small intestinal segment</td>
<td>– With ileostomy</td>
</tr>
<tr>
<td>• Colectomy (partial or complete)</td>
<td>– Restorative</td>
</tr>
<tr>
<td>• Proctocolectomy</td>
<td>(ileoanal or J pouch)</td>
</tr>
<tr>
<td>• Unlike UC, CD cannot be cured with surgery</td>
<td>– Disease is “cured” once the colon is removed</td>
</tr>
</tbody>
</table>
The Critical Role of Nutrition

Including good nutrition in your diet is essential to quality of life and improved long-term outcomes

- “Diet” = the food you eat on a daily basis
- “Nutrition” = how your body uses nutrients from your diet
- Careful food choices may
  - Lessen symptoms
  - Prevent disease exacerbation

IBD patients are prone to becoming malnourished

- Loss of appetite (caused by nausea, pain)
- Increased caloric needs caused by chronic disease
- Poor digestion and absorption of nutrients
Principles of Good Nutrition

Good nutrition is key to

• Medications being more effective
• Healing, immunity, and energy levels
• Preventing or minimizing GI symptoms
• Normal bowel function
• Preventing growth delays
Popular Diets: Fact vs. Fiction

- Enteral nutrition and Specific Carbohydrate diet have proven efficacy.
- Many options exist and are promoted on the internet but...
  - Few well-controlled published studies.
  - Can be difficult and complicated to follow.
  - Potentially risky – restrictions may lead to poor growth, poor healing, and/or nutrient deficiencies.
  - May actually worsen symptoms.
- Talk to your doctor and a registered dietitian before considering an “IBD diet.”
- Do not abandon conventional treatment!
Enteral nutrition for induction

- Efficacy 50-82% in children
- First line therapy in most of Europe (vs steroidal drugs)
- Controversy regarding its effectiveness for colon disease
- Type of formula used not very important for efficacy
Specific Carbohydrate Diet (SCD)

- **Removes**
  - All grains
  - Milk products except for yogurt fermented greater than 24 hours
  - Sugars except honey

- **Sidney Haas MD**
  - Early 1930s used to treat celiac disease

- **Popularized by Elaine Gottschall**
  - Breaking the Vicious Cycle

Courtesy of David Suskind, MD

Haas, S, Haas M, Am J Gastroenterol 1955 Apr;23(4):344-60
Eating During a Flare

- Limit insoluble fiber
  - Leafy vegetables, wheat bran, etc.
  - Don’t exclude fiber altogether
- Decrease concentrated sweets
- Smaller, more frequent meals
- Avoid nuts, seeds, and kernels, especially if the child has strictures
- Lactose-free diet
- Low-fat diet if experiencing fat malabsorption (stool test)
# Why Transition to Adult Providers?

<table>
<thead>
<tr>
<th>Social</th>
<th>Medical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age-appropriate care</td>
<td>Comorbidities</td>
</tr>
<tr>
<td>• Privacy</td>
<td>• Hypertension</td>
</tr>
<tr>
<td>• Autonomy</td>
<td>• Thyroid</td>
</tr>
<tr>
<td>Environment</td>
<td>Screening/Complications</td>
</tr>
<tr>
<td>• Work (not school)</td>
<td>• Colon cancer</td>
</tr>
<tr>
<td>Resources/Insurance</td>
<td>• Thrombosis</td>
</tr>
<tr>
<td>Relationships</td>
<td>Interactions</td>
</tr>
<tr>
<td>• Marriage</td>
<td>• Smoking</td>
</tr>
<tr>
<td>• Children</td>
<td>• Alcohol</td>
</tr>
<tr>
<td></td>
<td>• Drugs</td>
</tr>
</tbody>
</table>
Transition Should Occur in Several Phases

**Phase 1**
- Pediatric provider is the caregiver outlining patient responsibilities

**Phase 2**
- Overlap occurs between pediatric and adult spheres; begin to practice independence

**Phase 3**
- Adult provider assumes responsibility for care; patient should begin to take charge

Initiate Transition Process Around Stage of Development

Age 12-14
- Ability to name illness, medications, adherence, trade/school

Age 15-18
- Nutrition, self-management, insurance, issues of reproductive health
- Ongoing support, new health providers

Age 18-21
- Checklists available at www.naspghan.org

The 504 Plan

- Section 504 of the federal Rehabilitation Act ensures accommodations for children with disabilities
- Template available at www.ccfa.org

<table>
<thead>
<tr>
<th>Initial Diagnosis Contact List</th>
<th>Student File Letter</th>
</tr>
</thead>
<tbody>
<tr>
<td>School nurse</td>
<td>Definition of IBD</td>
</tr>
<tr>
<td>Guidance counselor</td>
<td>Symptoms, cyclical nature of disease</td>
</tr>
<tr>
<td>School social worker</td>
<td>Home tutoring option</td>
</tr>
<tr>
<td>Teachers</td>
<td>Gym considerations</td>
</tr>
<tr>
<td>Administrators</td>
<td>Mind-gut connections</td>
</tr>
</tbody>
</table>
Requesting a 504 Plan

- Make the request in writing
- Include supporting medical documentation
- Parents, patient (if age-appropriate), school nurse, administrator, and guidance counselor should meet to develop a workable plan

Sample 504 Plan Accommodations

- Bathroom pass
- Nurse’s office pass
- Nurse’s training for med administration
- Food/drink in class
- Stop-the-clock testing
- Postponement of cumulative term grades
- Revised seating chart

- Extra set of books
- Increased time between classes
- Copies of syllabi, lesson plans
- Permission to copy class notes
- In-home/after school tutoring prior to prolonged absence
- Field trip/extracurricular transportation
Requesting Support in College

All public, government-funded colleges and universities expected to comply with Section 504

- Most colleges have disability services office

- Accommodations may include
  - Providing a dorm with close bathroom access or a private bathroom
  - Mid-morning or late classes if you have bathroom activity in the early morning
  - Test accommodations

- Speak to the disability services office before heading to school

- Visit www.ccfa.org/campus-connection to learn more tips!
Involving Children in their IBD Care

• Screening
  – Is there a support network of family members/friends?
  – Is a counselor or psychologist needed?
  – Are school accommodations needed and/or in place?
  – Does child/adolescent need help with stress reduction?

• Self-management
  – Disease education and knowledge
    - Encourage use of resources available on the web
    - Review educational materials together
  – Learn necessary skills
  – Prepare for independence
IBD Therapies: Conclusions

Lots of information

• Use your physician to understand these drugs the way YOU learn and integrate information

• We are trained to help you digest this information

• Don’t burn bridges

• Ride the wave

• In our current way of practice you will still need to take a leap of faith with treatment options

• Personalized medicine will continue to refine our way of practice
CCFA Resources

- **CCFA website:** [www.ccfa.org](http://www.ccfa.org)
  - Pediatric-focused publications (teacher’s guide, parent’s guide, comic book, activity book)

- **Camp Oasis:** [www.ccfa.org/camps](http://www.ccfa.org/camps)
  - Safe and supportive summer camp for children ages 7-18
  - 12 camps throughout the US

- **Campus Connection:** [www.ccfa.org/campus-connection](http://www.ccfa.org/campus-connection)
  - Connect with other college students and learn tips for campus life

- **Support Groups and Power of Two**
  - Connect with other parents or children with IBD
  - Looking for mentors! Contact your chapter at [www.ccfa.org/chapters](http://www.ccfa.org/chapters)
NASPGHAN

- North American Society for Gastroenterology, Hepatology and Nutrition
- Several resources for families with IBD
  - Locate a pediatric GI
  - Learn about pediatric IBD research
  - [www.gikids.org](http://www.gikids.org)
    - IBD publications and podcasts
    - Transitions checklists
    - College site: [www.ibdu.org](http://www.ibdu.org)
Other Resources

• ImproveCareNow
  – A collaborative Learning Health Care system of 53 pediatric centers developing standardized care with collaboration between caregivers, patients, and researchers
  – http://improvecarenow.org

• Collaborative Collaborative Care Network (C3N)
  – Open source learning healthcare system
  – Set up to design, pilot test, and implement new ideas that improve the quality of care of children with IBD
  – Patients, clinicians, and researchers work together as co-designers to transform the system of chronic IBD care
  – http://c3nproject.org or email info@c3nproject.org