Health Supervision in Children and Adolescents with IBD

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Disclosures

- TechLab
  - Sponsored Research
- Shire Pharmaceuticals
  - Consulting
- I am not Scott Snapper! He gave his talk on Friday…

Goals

- Better understand the importance of forging a new collaboration between PCP and GI subspecialty providers
- Outline relevant issues that should be addressed
- Continue to think about a standardized approach to the management of children and adolescents with IBD

Redefining the GI-PCP Collaboration

- Primary care providers are ideally positioned to address many/most GI health supervision issues
- Local care
  - More convenient
  - More cost-effective to patients (co-pays, ….).
  - May enhance compliance
- The growing prevalence of IBD limits the opportunity for expedient GI referral/follow-up
- Geography can place considerable distance between patients and subspecialty providers
- Reimbursement may favor increasing primary care responsibility for subspecialty issues

Improved PCP Education Should Improve Early Recognition of IBD Symptoms IBD in Children

- Impact on linear growth (10-35%)
- Impact on weight gain
  - Anorexia
  - Micronutrient deficiency
- Impact on pubertal development
- Psychosocial adjustment
  - Athletic
  - Scholastic
  - Academic
  - Interpersonal
- Familial stability

PCP and Pediatric GI Providers Must be "on the same page"

- Children will have IBD for a long time
- Be prepared to work together to discuss:
  - Impact of the disease over time
  - Impact of the medications used to treat disease over time
  - Impact of diagnostic modalities (CT and Fluoroscopy.
- Health Supervision relates to both medical and psychosocial health

The Office Visit

- Frequency
  - UC or CD on ASA (Q 4-6 months)
  - Well IBD on immunosuppressive/biologic therapy (Q 4 months)
  - Sick (as needed)
- Anthropomorphic
  - height, weight, BMI
  - BP
- History and physical examination
  - Consider GI and extraintestinal manifestations
  - Consider standard metrics (PUCAI and aPCDAI)
  - Assess lymphadenopathy & changes in skin (lesions or psoriasis)
  - Tanner staging
- Laboratory studies
  - CBC
  - Inflammatory markers
  - Renal and hepatic markers
  - Fecal markers (lactoferrin and calprotectin)

Common Disease Activity Indices

PUCAI	PCDAI	sPCDAI	aPCDAI
Abdominal Pain	Abdominal Pain	Abdominal Pain	Abdominal Pain
Rectal Bleeding	Stool Frequency	Well Being	Well Being
Stool Frequency	Level of Function	Changes in Weight	Stool Frequency
Stool Consistency	Laboratory Studies	Stool Frequency	Abdominal Exam
Nocturnal Stools	Physical Exam	Abdominal Exam	Perirectal disease
Level of Activity		Extraintestinal Disease	Changes in Weight
			Extraintestinal Disease
Range (0-85)	**Range (0-95)**	**(Range 0-90)**	**Range (0-70)**

Nutritional Assessment for Micronutrient Deficiency

- Iron
  - Blood loss or decreased absorption
  - CBC, ferritin, and reticulocyte count
- Vitamin B12
  - Especially in CD with ileal resection
- Folate
  - Especially in UC patients on sulfasalazine
- Zinc
  - Especially in IBD patients with low Alk Phos
- Bone Health (BMD z-score < -2)
  - Serum 25 hydroxy-vitamin D (25-OH D
  - Ca, Phos, Mag, BUN, Cr
  - PTH, ionized calcium,
  - Bone age (in those with short stature)

Bone Health

- Significant deficits in bone mass observed in 10% to 40% of children presenting with IBD
- Patient with CD at increased risk
- Peak bone mineral content
  - 90% by the end of adolescence.
  - The most important long-term predictor of skeletal health
- Consider impact of
  - Nutritional deficiencies
  - Physical inactivity
  - Inflammatory cytokines
  - Skeletal muscle mass deficits
  - Glucocorticoids

How to Use DEXA?

- Particulars
  - About 1/20 the radiation of a chest film
  - Adjust for skeletal age
  - Cost under $150*
- When to order
  - At Diagnosis
  - Growth failure
    - Height Z score <-2.0 SD
    - BMI <2.0 SD
  - Significant Fractures
  - > 6 mos steroid therapy
  - 1 ° or 2° amenorrhea
  - Severe Disease
- What to Order
  - Under 14 years: Total body and spine
  - Hip and spine: Hip and Spine

*healthcarebluebook.com

Intervening for Low BMD

- Vitamin D
  - Measuring 25-OH Vitamin D Levels
    - Check once a year, in the spring (annual nadir)
    - > 12.5 necessary to prevent rickets
    - > 32 necessary to inhibit PTH
    - > 35-40 likely necessary to see immune benefit
  - Treat if low:
    - 50,000 units once a week for 10 weeks
    - Maintain with 1-2,000 units per day
- Calcium
  - 1-3 years: 700 mg/day
  - 4-8 years: 1,000 mg/day
  - 9-18 years: 1,300 mg/day
  - 19-30 years: 1,000 mg/day
- Load bearing Exercises

Adolescent Depression and Anxiety

- Depression and anxiety are common disorders in both healthy adolescents and in adolescents with IBD
  - Risk factors include family history, more severe disease activity, and corticosteroid use
- Symptoms may be unappreciated by the patient, patient's family and providers
  - Compliance
  - School performance
- Effective therapy
  - Cognitive Behavioral Therapy
  - Medications
  - Family Centered Therapy

Screening for Depression

- General Questions
  - Changes in weight and eating habits
  - Manifestation of social isolationism
  - Drop in School performance
- Children's Depression Inventory
  - Useful for children in the 6-17 age group
  - Takes 5 minutes to complete
  - Scored from 0-54, > 10 should prompt referral

CDI – Sample items

Item 1:
- ☐ I am sad once in a while.
- ☐ I am sad many times.
- ☐ I am sad all the time.

Item 2:
- ☐ Nothing will ever work out for me.
- ☐ I am not sure if things will work out for me.
- ☐ Things will work out for me O.K.

Item 3:
- ☐ I do most things O.K.
- ☐ I do many things wrong.
- ☐ I do everything wrong.

Item 4:
- ☐ I have fun in many things.
- ☐ I have fun in some things.
- ☐ Nothing is fun at all.

Infectious Assessment

- TB
  - Assess for latent TB with anergy panel, PPD, Chest film when starting immunosuppressives
  - For patients on 6MP/MTX/anti-TNF therapy, need to use T-Spot for follow-up evaluation
- Hepatitis B
  - Latent Hep B can be activated by anti-TNF therapy
- EBV Infection
  - Risk of lymphoma higher in patients developing primary EBV infection while receiving immunomodulator (6MP or azathioprine) therapy
  - Good to check at baseline before starting therapy

Immunizations in children with IBD

- Good evidence that children with IBD respond to inactivated vaccines, even if they are receiving immunosuppressives
- Patients with IBD are often underimmunized
  - Patients think vaccine may not work
  - Patients forget
  - Patients afraid vaccines may cause flare of IBD
  - Patients afraid of vaccine associated adverse events

Immunizations

- All Patients with IBD not on immuno-suppressives should receive all non-live vaccines including:
  - Diphtheria, Pertussis, Acellular Tetanus
  - Hepatitis A
  - Hepatitis B
  - Haemophilus influenza
  - Inactivated polio vaccine,
  - Influenza
  - Pneumococcus,
  - HPV
  - Meningococcal
- All Patients with IBD on immunosuppressives should receive not receive live vaccines including:
  - Varicella
  - Shingles
  - MMR
  - Rotaviral
  - Intranasal Flu
  - Yellow Fever

What About Varicella?

- If parents cannot recall a history of natural infection, Varicella vaccine should be administered
- If the patient and/or parents are unsure, Varicella antibody titers should be checked
- If the patient does not have a history of Varicella infection/immunization, they should be vaccinated before starting immunosuppressive therapy
  - High-dose systemic corticosteroids (≥2 mg/kg/day of
  - ≥20 mg/day of steroid for 14 days or more)
  - Cyclosporine or tacrolimus
  - Immunomodulatory agents, or biologic therapy.
- It is recommended that patients wait at least 1 month after discontinuing corticosteroids before immunization with Varicella vaccine

Screening for Cancer

- Colon Cancer*
- Skin Cancer
- Lymphoma

* Something we do, but of which the PCP should be aware

The Cumulative Risk of CRC in Children with UC is Higher than Adults

	Adult Studies (26)	Pediatric Studies (5)
Cumulative Cancer Risk At	Cumulative Cancer Risk (%)	Cumulative Cancer Risk (%)
10 Years	4.4	5.5
20 Years	8.6	10.8
30 Years	12.7	15.7

Eaden, JA. *Gut* 2001;**48**:526–535

Surveillance for Colon Cancer

Highest Risk
- Pancolitis
- Active Disease
- PSC
  - PSC increases RR to 9.13
- Age a diagnosis
  - 43.8 if Dx'd < age 20 ; 2.65
  - age 20-39; Background > 60-79
- Length of time
- Family history
  - RR increased 2- fold if there is a 1st degree relative with CRC
  - Increases to 9-fold if the family member was < 50 years

Recommendations
- No evidence based guidelines
- Colonoscopy at baseline
- Repeat as clinically indicated
- Every 4-6 years in first 10 years
- Annually to biannually for patients with PSC

Counseling about Skin Cancer

- Study Design
  - 108K IBD patients matched with 434K non-IBD
  - Followed for 1-138 months
- Melanoma:
  - Risk increased from 44.1 to 57.1/100,000 person-years (RR 1.28) and greater for CD than UC (1.45, 1.13, respectively)
  - Melanoma risk related to anti-TNF and not thiopurines
  - RR increased over time (1.1 to 1.5) from 1997-2000 to 2005-2009
- Nonmelanoma:
  - Risk increased from 623 to 912/100,000 (RR 1.46) , and for both CD (1.64) and UC (1.34)
  - Associated with thiopurine (1.98), but not anti-TNF (1.1)

Long, MD. *Gastro*. 2012. 143:390-399

Counseling about Skin Cancer

- Sun Exposure
  - Geography/Sun Exposure

Bangkok (10.5)	Los Angeles (6.3)	Capetown (6.2)
New York (5.2)	Vancouver (3.6)	Paris (3.5)

  - Racial (light skinned >> darker skinned)
  - Red Hair: Defect in MCR1 causes decreased PTEN signaling
- Medications
  - Thiopurines
    - Incorporated into DNA
    - Photosensitize to effects of UVA
    - Thiopurines are photosensitive and generate ROS
    - Thiopurine use impairs DNA repair mechanisms
  - Anti TNF
    - May be releasing previously checked melanoma
    - Cancer develops with decreased immune surveillance

Setshedi, M. *J. Gastro. Hep.* 2011. 27:385-389
Cao, J. *Molecular Cell*. 2013. 51:409-422

Counseling about Lymphoma Risk in Children with IBD

- Demographics
  - 1374 patients; 6624 patient years
  - Mean follow-up approx 5 years
- 2 lymphoma patients identified
  - One UC and one Crohn disease
  - 1 Hodgkin, 1 Large Cell Anaplastic
  - Both males, both receiving thiopurines
  - Both within 3 years of diagnosis
  - Both alive 3+ years post-diagnosis
- SIR 7.51
  - (4.5 vs. 0.58 expected per 10,000 patient-years, NS)

Ashworth, LA. *Inflamm Bowel Dis.* 2012. 18(5):838-843

Hepatosplenic T-Cell Lymphoma

36 Patients Through 2011

20 Treated with INFLX and Thiopurine
- Median time was 5.5 years (1-13.5 years)
- Median # doses was 3 (1-24)

16 Treat with Thiopurine Alone
- Median time was 6 years (3-17)

4 also Treated with Adalimumab

1 Treated with:
- Infliximab
- Adalimumab
- Natalizumab

32/36 since 2006

31 Patients with Known Gender
- **29 Male; 2 Female**

30 Patients with Know Age
- 30 less than 35 years
- 10 less than 20 years
- 3 were ≤ 15 years

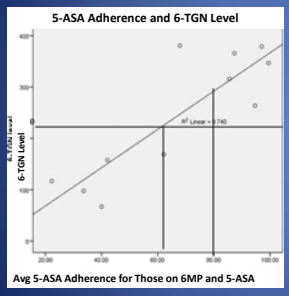
Kotlyar, DS. *Clin. Gastro Hep.* 2011 9:36-41

Hepatosplenic T-Cell Lymphoma

Condition	Relative Risk
All patients on Thiopurine > 2 years	
All patients	1:45,000
All male patients < 35 years	1:7400
Patients on concomitant therapy	1:22,000
Patient < 35 years	1:3534

Kotlyar, DS. *Clin. Gastro Hep.* 2011 9:36-41

Discussing Compliance



- Trackcap adherence for 5-ASA and 6-MP were significantly positively correlated
- 60% ASA adherence associated with a therapeutic 6-TGN level. 80% adherence suggests a therapeutic 6-TGN level near 300 pmol.
- Only 48% of children and 38% of parents reported being always adherent to IBD medications
- **Compliance as (or more) important than dose and dosing.**

IBD Journal 2013 . 19(12): 2652-2658
IBD Journal 2005 . 11(11):1006-12

Talking About Transitions To Adult Providers

- Ensuring a smooth transition is the responsibility of pediatric GI providers
- Successful transitions begin in school-aged and continue through adolescence
- Patients are ready for transition when they:
  - Understand fully their disease
  - Are confident in their ability to comply with treatment recommendations
  - Are able to advocate for themselves and engage fully and independently the health care system
- Pediatric providers must review expectations and discuss potential differences in pediatric and adult practices
  - Access to the provider by phone and email
  - Patient populations
  - The function of ancillary and support staff

Transitions (Part 2)

- Whenever possible, there is an attempt made to match patient expectations and predilections with provider attributes. This may involve
  - Provider gender
  - Provider affiliation
  - Insurance parameters
- Location and geographic proximity may be more important for young adults
- Efforts should be made to ensure that the patient's medical information is transferred to the new provider prior to the first appointment
- "Bounce Back" patients should be debriefed and redirected – It may take a few iterations

Summary

- Health supervision and anticipatory guidance will become increasingly important components of primary and subspecialty care
- Primary care providers are ideally positioned to participate in the delivery of subspecialty medicine
- Increasing cooperation between primary and subspecialty providers will improve the quality of care, save health care dollars, and improve patient quality of life

Acknowledgements

What About Counseling our Patients About Parenting?

- Fertility Issues
  - IBD patients generally similar to general population
  - Except for IPAA (26% vs. 12% with no history of IPAA)
- Genetics
  - Risk to offspring about 5-10 fold the general population (5% vs. 0.5%).