



What The PCP Needs to Know about IBD

Anne Tuskey M.D.
Assistant Professor of Medicine
University of Virginia Digestive Health
Center

Disclosure

- No potential conflicts of interest

Part I: Treatment Options



Treatment Options for IBD: An Overview

Crohn's Disease

- Antibiotics
- Corticosteroids
- 5-ASA
- Azathioprine/6-MP
- Methotrexate
- Biologics
 - Infliximab
 - Adalimumab
 - Certolizumab pegol
 - Natalizumab

Ulcerative Colitis

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 - Infliximab
 - Adalimumab



Case #1

- 32 year old male with ulcerative colitis in remission for last 7 years on 2.4 gm Asacol (mesalamine) presents for routine physical exam
- What laboratory tests should you order?
 1. CBC
 2. BMP
 3. Vitamin B12
 4. None are necessary



Corticosteroid Safety

- Conventional corticosteroids: higher rates of serious infection/mortality compared with all other therapies
 - Short-term efficacy, but major downsides
- Budesonide: good safety profile
 - First choice for ileal or right sided Crohn's disease



Aminosalicylate (5-ASA) Safety

- Generally well tolerated
- Possible increased rate of interstitial nephritis
 - Check renal function within 6 months of starting therapy and yearly thereafter



Azathioprine/6-MP Safety

- Overall toxicity/intolerance ~15%
 - Serious infection (5%)
 - Malignancy
 - Lymphoma
 - Non-melanoma skin cancer
 - Pancreatitis (3%)
 - Hepatotoxicity
 - Leukopenia



Anti-TNF Safety

- Infection
- Malignancy
- Immunogenicity

Bongarz JAMA 2006;295:2275
Lichtenstein et al. Am J Gastroenterol 2008;103:S436
Toruner et al. Gastroenterology 2008;134:929
Keane N Eng J Med 2001;245:1098
Theis Alimen Pharm Ther 2008;27:19



Managing risk: Bottom line

- Most serious adverse events (e.g. lymphoma, TB) are extremely rare

Event	Estimated frequency (annual, in patient-years)
NHL (baseline)	2/10,000
NHL (IMM)	4/10,000
NHL (anti-TNF)	6/10,000
Death from sepsis	4/10,000
Death from tuberculosis	5/10,000

Siegel CA. CCF A 2008



Part II: IBD and Pregnancy



Case #2

- 28 year old female with ileal Crohn's disease in remission on Cimzia (certolizumab pegol) wants to discuss pregnancy planning. What should you advise?
 1. She will have a more difficult time becoming pregnant than a female without Crohn's disease
 2. She should stop Cimzia as it can lead to birth defects
 3. She should be followed by a high risk OB even if her Crohn's remains in remission during pregnancy



Pregnancy outcomes in IBD

- Even in remission, women with IBD have higher rates of adverse pregnancy outcomes compared to the general population
 - Higher rates of spontaneous abortion, premature birth, low birth weight and complications of labor and delivery
- All women with IBD should be followed as high risk obstetric patients

Mahadevan U, Kane S. Gastro 2006;131:278-82



Medications and Pregnancy

- Mesalamine
 - Category B
 - Low risk in pregnancy and breast feeding
- Prednisone
 - Category C
 - Risk of gestational diabetes. Use in 1st trimester associated with small risk cleft palate
 - Low risk in pregnancy – used for flares



Medications and Pregnancy

- Azathioprine and 6-MP
 - Category D
 - Controversial – majority of data suggests they are low risk in pregnancy
- Anti-TNF agents
 - Category B
 - IFX and ADA cross the placenta in the 3rd trimester – time last dose around 30-32 weeks
 - CP has very minimal placental transfer



Medications and Pregnancy

- Methotrexate is absolutely contraindicated
- Metronidazole and ciprofloxacin are relative contraindications
 - Brief courses of metronidazole for 7-10 days may be used in the 2nd and 3rd trimesters
 - Breast feeding is not recommended



Part III: Preventive Care



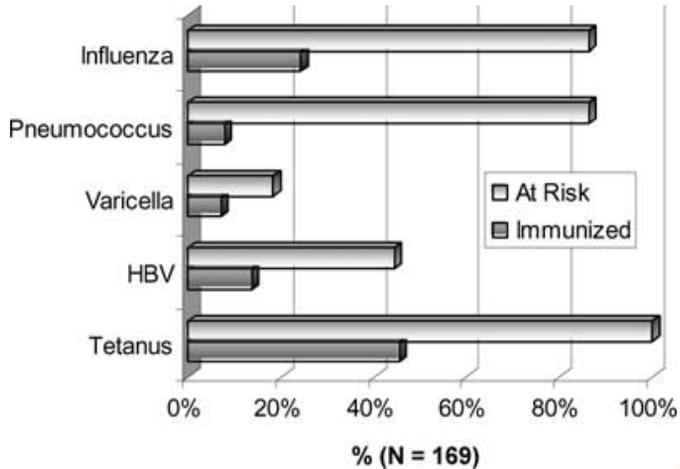
Case #3

- 20 year old female with new diagnosis of pan-ulcerative colitis presents to your office for routine health exam. Her primary GI physician started her on 6-MP.
- What vaccinations should be considered?



Minority of 'At Risk' Patients are Immunized

Over 80% of patients had a PCP visit within previous 12 months



Melmed et al. Am J Gastro 2006;101:1834-40



Influenza

- All patients on immunosuppressive therapy should receive annual inactivated influenza vaccine.
- Live influenza vaccine is not recommended



Streptococcus pneumoniae

- IBD patients, especially those on immunomodulators are at increased risk of pneumococcal infections
- Vaccinate with 23-valent vaccine and revaccinate every 3-5 years if still on immunosuppressive therapy



Hepatitis B

- Reports of fulminate/fatal HBV in patients on anti-TNF agents, including reactivation of latent HBV in exposed individuals.
- All IBD patients should be tested for HBV infection and vaccinated if seronegative
- HBV vaccination while on immunosuppressive therapy may not be efficacious so serologic response to vaccination should be documented after 3 doses



Human Papilloma Virus (HPV)

- HPV linked with cervical and anal cancers
- Women with IBD are at increased risk for abnormal Pap smear
 - Increased risk with > 6 months of IMM use
- HPV vaccine is available and safe in immunosuppressed patients but no specific guidelines for IBD

Kane et al. Am J Gastroenterol 2008;103:631 008
Bhatia et al. World J Gastro 2006
www.cdc.gov



Varicella

- Patients should be questioned about VZV status
- If they have not had VZV infection or vaccination then should be immunized with VZV vaccine prior to institution of immunosuppression



Live Vaccinations

- Avoid in immunosuppressed patients
- Inhaled influenza
- Measels, Mumps, Rubella
- Typhoid (oral)
- Varicella
- Anthrax
- Yellow Fever
- Zoster



Take Home Point: Vaccination Strategy

- All IBD patients, regardless of immunosuppression status should be considered for the following vaccines:
 - Influenza (annually)
 - Pneumococcal polyvalent
 - HBV in those that are seronegative
 - HPV
 - VZV if there is no history of VZV infection or vaccination and VZV serology is negative
 - Tdap (tetanus, diphtheria, acellular pertussis)



Clostridium difficile

- In the IBD population C. difficile is most often community acquired
- IBD patients with C. difficile are more likely to be hospitalized, more likely to have a longer hospital stay, and are at increased risk of death
- Test for c. difficile with onset of each flare
- Some advocate for first line use of oral vancomycin



Case #4

- 21 year old male with ulcerative colitis on 6-MP wants to travel with the Peace Corps to Cameroon, an endemic area for yellow fever. What do you advise?
 1. Get the vaccine before you go
 2. The vaccine is contraindicated so go with out it
 3. Don't go to Cameroon



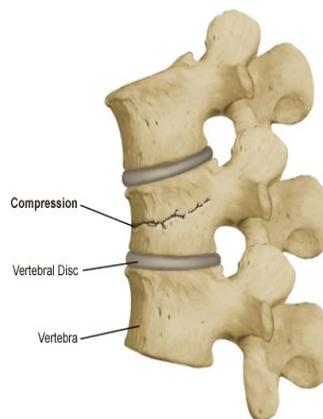
Preventive Care: Travel Guidelines

- Patients considering travel to developing countries should see a travel medicine specialist prior to travel
- Vaccination with inactivated virus vaccines (ideally prior to immunosuppression) as indicated for the particular geographic region
- Live virus vaccines such as Yellow Fever or oral typhoid vaccine should not be administered in the setting of immunosuppression



Preventive Care: Osteoporosis

- Screening in patients with prolonged corticosteroid use (>3 months)
- Patients with Crohn's disease with symptoms > 6 months prior to diagnosis should have baseline DEXA



Bernstein et al. Gastroenterology 2003;124:795
Sakellariou et al. Joint Bone Spine 2006;73:725-8



Osteopenia and Osteoporosis

- Osteopenia: Increased vitamin D and calcium intake
- Osteoporosis: Bisphosphonate in addition to the above
- Avoidance of corticosteroids
 - Budesonide



Preventive care: Malignancy Cervical Cancer

- Higher prevalence of cervical neoplasia in Crohn's and immunosuppressant therapy
- ACOG Guidelines: annual screening if immunocompromised.
- Consider HPV vaccine

Kane et al. Am J Gastroenterol 2008;103:631
Saslow D, et al. CA Cancer J Clin. 2002;52:342



Preventive care: Malignancy Colorectal Cancer

- Patients with UC or CD are at 2-3 fold greater risk of developing CRC than the general population
 - Surveillance every 1-2 years beginning
 - 8-10 years for extensive colitis
 - 15 years for limited colitis
 - No surveillance required for small bowel disease



Itzkowitz SH et al. Inflamm Bowel Dis 2005;11:314



Preventive care: Minimizing Flares

- Tobacco cessation in Crohn's disease
 - In Crohn's, smoking associated with a
 - Reduced response to medical therapy
 - Increased risk of postoperative recurrence
 - Shorter duration of remission

Moscandrew et al. Inflamm Bowel Dis 2009;15:1399



Preventive care: Minimizing Flares

- Nonselective NSAIDs
 - Increase gut permeability
 - Cause intestinal injury in healthy colon and small intestine (enteropathy, strictures)
 - May trigger flares in up to a third of patients
- Use acetaminophen, tramadol, and celecoxib as alternatives

Sigthorsson G et al. Gut 1998; 43:506
Kaufmann HJ et al. Ann Intern Med 1987;107:513



Preventative Care Take Home Points

- Preventive care remains important
 - Vaccination
 - Cancer surveillance
 - Metabolic bone disease
 - Smoking cessation
 - Avoid NSAIDs

