UPDATE:
ACG PREVENTIVE HEALTH GUIDELINES IN IBD

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ACG Clinical Guideline: Preventive Care in Inflammatory Bowel Disease

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Recent data suggest that inflammatory bowel disease (IBD) patients do not receive preventive services at the same rate as general medical patients. Patients with IBD often consider their gastroenterologist to be the primary provider of care. To improve the care delivered to IBD patients, health maintenance issues need to be co-managed by both the gastroenterologist and primary care team. Gastroenterologists need to explicitly inform the primary care provider of the unique needs of the IBD patient, especially those on immunomodulators and biologics or being considered for such therapy. In particular, documentation of up to date vaccinations are crucial as IBD patients are often treated with long-term immune-suppressive therapies and may be at increased risk for infections, many of which are preventable with vaccinations. Health maintenance issues addressed in this guideline include identification, safety and appropriate timing of vaccinations, screening for osteoporosis, cervical cancer, melanoma and non-melanoma skin cancer as well as identification of depression and anxiety and smoking cessation. To accomplish these health maintenance goals, coordination between the primary care provider, gastroenterology team and other specialists is necessary.

SUPPLEMENTARY MATERIAL is linked to the online version of the paper at http://www.nature.com/ajg

Am J Gastroenterol advance online publication, 10 January 2017; doi:10.1038/ajg.2016.537
Why are we talking about this?

“Specialists who care for immunocompromised patients...

...share responsibility with the primary care provider for ensuring that appropriate vaccinations are administered to immunocompromised patients.”

...share responsibility with the primary care provider for recommending appropriate vaccinations for members of immunocompromised patients' household.”

A Minority of ‘At Risk’ Patients are Immunized

Over 80% had PCP visit within Previous 12 months

Melmed et al. Am J Gastro 2006
Vaccinations

- Annual vaccination against influenza
- Pneumococcal vaccination with both PCV13 and PPSV23 in immunosuppressed
- Over 50 years vaccinate against herpes zoster
  - Anyone starting Tofacitinib?
- Varicella negative (VZV Ab -) adults should be vaccinated before starting immunosuppressive therapy
- Human Papillomavirus Vaccine (age 18 to 26, up to 45!)
  - Women with IBD on immunosuppressive therapy should undergo annual cervical cancer screening
  - Men
Influenza Is More Common in IBD

Tinsley A, et al. Increased risk of influenza… among patients with IBD. *IBD* 2018
Influenza Complications are Greater Among IBD vs Controls

Tinsley A, et al. Increased risk of influenza… among patients with IBD. IBD 2018
Influenza Vaccination in IBD: The Data

• Multiple studies
• IBD generally does not impact response
• Immunosuppression
  – Generally impaired response for 1-2 antigens, especially if on combo therapy
  – Those more heavily immunosuppressed had lower levels of protective titers
  – No significant increase in adverse events

DeBruyn JC et al. Inflamm Bowel Dis 2011 Apr
Influenza: Who Should Get Vaccinated?

- (2010) – *Everyone* over 6 months
- High risk groups
  - immunosuppression
  - “Potential Transmitters” of the flu
    - (Healthcare workers)
  - Household contacts of high risk individuals
Pneumonia risk is increased in IBD

<table>
<thead>
<tr>
<th>Medication*</th>
<th>IBD overall (n=23,784)</th>
<th>Crohn’s disease (n=12,025)</th>
<th>Ulcerative colitis (n=11,645)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjusted OR** (95% CI)</td>
<td>Adjusted OR (95% CI)</td>
<td>Adjusted OR (95% CI)</td>
</tr>
<tr>
<td>5-ASA</td>
<td>1.07 (0.98-1.16)</td>
<td>1.08 (0.96-1.23)</td>
<td>1.05 (0.93-1.53)</td>
</tr>
<tr>
<td>Biologic</td>
<td>1.32 (1.11-1.57)</td>
<td>1.30 (1.07-1.58)</td>
<td>1.44 (1.00-2.08)</td>
</tr>
<tr>
<td>Thiopurine</td>
<td>1.13 (1.00-1.27)</td>
<td>1.06 (0.92-1.23)</td>
<td>1.26 (1.03-1.53)</td>
</tr>
<tr>
<td><strong>Corticosteroid</strong></td>
<td>1.91 (1.72-2.12)</td>
<td>1.80 (1.55-2.08)</td>
<td>2.05 (1.75-2.39)</td>
</tr>
<tr>
<td>PPI</td>
<td>1.15 (1.04-1.26)</td>
<td>1.17 (1.03-1.04)</td>
<td>1.12 (0.97-1.29)</td>
</tr>
<tr>
<td>Narcotic use</td>
<td>2.28 (2.09-2.48)</td>
<td>2.17 (1.93-2.45)</td>
<td>2.42 (2.13-2.75)</td>
</tr>
</tbody>
</table>

*any use in prior 120 days  
**Conditional logistic regression models adjusted for health-care utilization, comorbidities, 5-ASA, biologic, thiopurine, corticosteroid, PPI, narcotic medication use as appropriate.

Combination therapy impairs response to PPV23

* *p<0.05, **p<0.01

Melmed GY et al. Am J Gastro 2010
PCV13 Prevents Invasive Pneumococcal Disease in IBD while PPSV23 Alone Does NOT

Cohort study of 74,500 veterans with IBD; 1,798 IPD cases identified according to ICD codes. Vaccination with PCV13 or PPSV23 vaccines and any use of IM or anti-TNF therapies were extracted from medical records.

### Pneumococcal Vaccinations Status

<table>
<thead>
<tr>
<th>Status</th>
<th>HR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No vaccination</td>
<td></td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>PPSV23 only</td>
<td>1.05</td>
<td>0.95-1.16</td>
<td>0.315</td>
</tr>
<tr>
<td>PCV13 only</td>
<td>0.25</td>
<td>0.15-0.30</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PCV13 &amp; PPSV23</td>
<td>0.16</td>
<td>0.13-0.20</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### Immunosuppressants & TNF-antagonist

<table>
<thead>
<tr>
<th>Status</th>
<th>HR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No use</td>
<td></td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Immunosuppressant</td>
<td>1.13</td>
<td>0.93-1.37</td>
<td>0.21</td>
</tr>
<tr>
<td>TNF-antagonist</td>
<td>1.39</td>
<td>1.00-1.93</td>
<td>0.05</td>
</tr>
<tr>
<td>Both</td>
<td>1.39</td>
<td>1.08-1.78</td>
<td>0.01</td>
</tr>
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</table>

Kaplan-Meier Survival Until Invasive Pneumococcal Disease

Log-rank P-value: <0.001

Adjusted for demographics, medications, vaccination status, and comorbidities

Guidelines Recommend both PCV-13 and PPSV23

1. **Pneumococcal vaccine – naïve immunocompromised* adult patients age ≥ 19 years**
   - PCV-13
   - 2-12 months later
   - PPSV23
   - 5 years later
   - PPSV23

2. **Previous vaccination with PPSV23 in immunocompromised* adults ≥ 19 years**
   - ≥ 1 year after last PPSV23
   - PCV-13
   - 5 years later
   - PPSV23

3. **Pneumococcal vaccine – naïve adults age ≥ 65 years**
   - PCV-13
   - 6-12 months later**
   - PPSV23

4. **Adults with previous vaccination with PPSV23 before age 65 years, who are now aged ≥ 65 years**
   - ≥ 1 year after last PPSV23
   - PCV-13
   - 6-12 months later**
   - PPSV23

5. **Adults with previous vaccination with PPSV23 at age ≥ 65 years**
   - ≥ 1 year after last PPSV23
   - PCV-13
Human Papilloma Virus (HPV)

- HPV linked with cervical and anal cancers
- Women with IBD have an increased risk for abnormal Pap smear
  - Increased risk with >6m IM use
  - Higher risk for HPV serotypes 16, 18
- HPV/Pap guidelines q3y or q5y
  - Do NOT apply to women who are immunocompromised
- HPV vaccines available and safe in IS

Kane et al. Am J Gastro April 2008
Bhatia et al. World J Gastro 2006
Van Assen et al. Ann Rheum Dis 2011
www.cdc.gov
Zoster in IBD increases with Age

Long et al. Alim Pharm Ther 2013
## Zoster: Medication Risk Factors

<table>
<thead>
<tr>
<th>Medication*</th>
<th>Crohn’s disease (OR)</th>
<th>Ulcerative colitis (OR)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude</td>
<td>Adjusted</td>
</tr>
<tr>
<td>5-ASA</td>
<td>1.27 (1.10-1.46)</td>
<td>1.09 (0.94-1.27)</td>
</tr>
<tr>
<td>Biologic</td>
<td>2.37 (1.92-2.92)</td>
<td>1.72 (1.92-2.15)</td>
</tr>
<tr>
<td>Thiopurine</td>
<td>2.31 (1.98-2.70)</td>
<td>1.93 (1.63-2.28)</td>
</tr>
<tr>
<td>Corticosteroid</td>
<td>2.28 (1.91-2.72)</td>
<td>1.54 (1.27-1.86)</td>
</tr>
</tbody>
</table>

*Any use in prior 120 days
Adjusted for health care utilization, comorbidities, 5-ASA, biologic, thiopurine, corticosteroid use as appropriate

HZ: Medication Risk Factors, Tofacitinib

- OCTAVE Sustain trial of tofacitinib for UC
  - 1.5% HZ in 5 mg tofacitinib group
  - 5.1% HZ in 10 mg tofacitinib group
  - 0.5% HZ in placebo
- No HZ was a serious adverse event
- No discontinuation due to this
- Most affected one dermatome or 2 adjacent
1. Recombinant zoster vaccine (RZV) is recommended for immunocompetent adults ≥50 years.

2. RZV is recommended even if previously received zoster vaccine live

3. RZV is preferred over ZVL

Give RZV even if prior shingles

Not recommended to check VZV status

Bone Health

- Patients with IBD are at increased risk of both osteoporosis and osteoporotic fracture.
- Check vitamin D25-OH at least once in all patients; supplement as necessary
- Baseline recommendations include calcium 1200 mg/day and vitamin D 400–800 IU/day, tobacco cessation, weight-bearing exercise, and minimizing alcohol/caffeine intake.

DEXA
- Postmenopausal women/men >50 years of age
- Prior history of fracture
- Corticosteroids >3 consecutive months or past chronic use of 1 year within prior 2 years
- Hypogonadism
- Maternal history of osteoporosis
- Malnourished/very thin; amenorrheic
- Chronic inflammation, smoking

Skin Cancer Screening

• Approximately one in five Americans will develop skin cancer by age 70\(^1\)

• Nonmelanoma skin cancer (NMSC): basal and squamous cell carcinoma\(^1\)
  • Estimated 3.3 million people diagnosed with NMSC in 2012.*\(^1\)
  • No documented increased risk of NMSC at baseline for IBD patients

• Melanoma skin cancer
  • Less common than NMSC; 91,270 new cases expected in 2018\(^1\)
  • More serious than NMSC, accounting for vast majority of skin-cancer deaths\(^1\)
  • IBD is associated with increased risk of melanoma, independent of treatment (IRR 1.29; 95% CI 1.09 –1.53)\(^2\)

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Thiopurines Are Associated With NMSC

Abbreviation: NMSC, nonmelanoma skin cancer.

Anxiety/Depression Screening

- Affects 15%-35% of IBD patients
  - Relapsing nature of disease
  - Chronic pain
  - Steroids
- Recommendation: Screen patients for anxiety / depression

SCREENING QUESTIONS

1. Over the past month, have you felt down, depressed, or hopeless?
2. Over the past month, have you felt little interest or pleasure in doing things?
Cigarette Smoking and IBD

Ulcerative Colitis
- 13 studies, >11,000 patients for UC
- Current smoking is protective of development of UC
  - OR, 0.58 (95% CI, 0.45-0.75)
- Quitting smoking is associated with UC
  - OR, 1.79 (1.37-2.34)

Crohn’s Disease
- 9 studies, >10,000 patients for CD
- Current smoking associated with CD
  - OR, 1.76 (95% CI, 1.40-2.22)
- Former smoking is weakly associated with CD
  - OR, 1.30 (0.97-1.76)

Effects of cessation: 65% lower risk of flare up vs continuing. Lower needs for steroids + medications.


Abbreviations: OR, odds ratio; CI, confidence interval.
Summary: ACG Preventive Care Recommendations

In general, adherence to age-appropriate vaccination schedules is recommended. Adults with IBD should receive vaccinations prior to receiving immunosuppressive therapies when possible.¹

- Everyone: annual vaccination against influenza¹
- Adult patients on immunosuppressive rx should receive both pneumococcal vaccines
- Adults with IBD over 50 years of age should receive vaccination against herpes zoster¹
  - Adults with IBD should be vaccinated against varicella if naïve before initiation of immunosuppressive therapy¹
- Vaccination against Tdap, HAV, HBV, and HPV should be administered per the Advisory Committee on Immunization Practice (ACIP) guidelines¹
- Bone health – risk factors
- Pap smears annually if immunosuppressed
- Skin cancer screening
- Smoking cessation

PCV, pneumococcal conjugate vaccine; PPSV, pneumococcal polysaccharide vaccine; HAV, hepatitis A virus; HBV, hepatitis B virus; HPV, human papilloma virus

Questions?