Health Care Maintenance in the Patient with IBD

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• Discuss the gap between recommendations for health care maintenance and receipt of services by the average patient with IBD

• Identify the key elements of basic health care maintenance for patients with ulcerative colitis and Crohn’s disease beyond treatment of IBD

• Ensure that patients with IBD receive appropriate vaccinations, cancer screening, osteoporosis screening, and general health screening
Lack of Primary Care

- Many patients with IBD are young and do not have comorbid illnesses
- The gastroenterologist will often serve as their only physician
- Patients with IBD receive less preventive health services than general primary care patients

Selby L et al. *Inflamm Bowel Dis.* 2008;14:253-258.
General Categories

• Vaccines
• Laboratory examinations
• Cancer screening
  – Colon, anal, skin, breast, prostate
• Smoking cessation
• Osteoporosis
• General health
  – Blood pressure, glucose, depression
For most IBD patients, immunization should not deviate from general population

Goal: Prevent infections in a population that is often immunosuppressed

- Influenza and pneumococcal pneumonia are the most common vaccine preventable illnesses in adults

Exceptions:

- Early dosing
  - Pneumovax
  - Zoster
- Live virus vaccines:
  - Contraindicated with immunosuppression

Patients with IBD are Undervaccinated

- 169 patients surveyed
- 146 (86%) reported current or past immunosuppressive agent use
- 76 (45%) tetanus vaccine in past 10 years
- 41 (28%) received regular influenza shots
- 13 (9%) had pneumococcal vaccine
- 47 (28%) hepatitis B vaccination

Most common reason for nonimmunization
- Lack of awareness (49%)

**Recommended Immunization Schedule for Persons Aged 0 Through 6 Years – United States * 2011**

For those who fall behind or start late, see the catch-up schedule.

<table>
<thead>
<tr>
<th>Vaccine ▼</th>
<th>Age ▼</th>
<th>Birth</th>
<th>1 month</th>
<th>2 months</th>
<th>4 months</th>
<th>6 months</th>
<th>12 months</th>
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<th>19-23 months</th>
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**Range of recommended ages for all children**

**Range of recommended ages for certain high-risk groups**

Rotavirus (Live Virus)

- Rotarix at ages 2 and 4 months or RotaTeq at ages 2, 4, and 6 months
  - For infants who have not received rotavirus vaccine by age 2 months, give first dose at the earliest opportunity but no later than age 14 weeks 6 days
  - Do not administer any rotavirus vaccine beyond the age of 8 months 0 days

- Contraindications:
  - Diagnosis of severe combined immunodeficiency (SCID)

- Precautions:
  - Altered immunocompetence
  - Chronic gastrointestinal disease
  - History of intussusception
  - Moderate or severe acute illness with or without fever

- If levels of biologic drug are detectable, rotavirus is relatively contraindicated in the newborn

# 2011 Adolescent Immunization

Recommended Immunization Schedule for Persons Aged 7 Through 18 Years – United States * 2011

For those who fall behind or start late, see the schedule below and the catch-up schedule

<table>
<thead>
<tr>
<th>Vaccine ▼ Age ▶</th>
<th>7-10 years</th>
<th>11-12 years</th>
<th>13-18 years</th>
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<td>Influenza (Yearly)</td>
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<tr>
<td>Pneumococcal⁵</td>
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<td>Hepatitis B⁷</td>
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<tr>
<td>Inactivated Poliovirus⁸</td>
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<td>IPV Series</td>
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<td>Measles, Mumps, Rubella⁹</td>
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<tr>
<td>Varicella¹⁰</td>
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</tbody>
</table>

Range of recommended ages for all children

Range of recommended ages for catch-up immunization

Range of recommended ages for certain high-risk groups

Human Papilloma Virus

• Higher incidence of abnormal Pap smears in women with IBD
  – 4 tertiary care center studies
    • Kane: 40 patients with 134 paps vs. 120 controls: on immunomodulators: OR = 4.5 (1.5-12.3)
    • Bhatia: 116 IBD: 18% vs. 5% controls abnormal pap (p=0.004)
    • Venkatesan: 518 IBD: INF ↑ risk of abnormal pap (OR 5.0, 2.11-11.85)
    • Lees (Scotland) 362 IBD women;1644 controls: no difference
  – 2 population-based studies
    • Singh: >10 OCP, CS + AZA increased risk OR 1.41, CI 1.09-1.81
    • Hutfless: no increased risk cervical cancer (OR 1.45 CI 0.74-2.84)

• All women <age 26 with IBD should get HPV vaccination
  – HPV: 0, 2, 6 months for females 9-26 yrs.
  – Recommended age at 11-12 years

• Should men be vaccinated as well?
  – The 3-dose series of HPV4 may be administered to males 9 through 26 years of age to reduce their likelihood of acquiring genital warts
  – Increased anal dysplasia with perianal CD
  – High-risk behavior

2011 Adult Immunization Schedule

- HPV: 0, 2, 6 mos for females 9-26 yrs.
- Td/Tdap (Combined Tetanus, Diphtheria and Pertussis):
  - 1 dose up to age 64 years; Then Td booster every 10 years
- Hep A, B: high risk, all who wish, all IBD
- Influenza: annually > 50 years
  - In IBD, annually for all patients
  - Intranasal LAIV is live virus: avoid if immunosuppressed
- Herpes zoster (live):
  - 1 dose > 60 yrs.
  - ? Earlier in IBD patients
- Pneumococcal:
  - 1 dose age 19-64 with revaccination after 5 years if immunocompromised; 1 dose >65
- Measles, Mumps, Rubella (MMR) (live)
  - Students in educational institutions

Immunization and Response in IBD

• 5-ASA medications and Reye’s syndrome
  – Acute encephalopathy, hepatic dysfunction and microvesicular steatosis
    • Avoid use of aspirin in children with viral illness
  – Given low serum concentrations, theoretical concern of Reye’s with 5-ASA and live viral vaccination, consider holding 5-ASA for a brief time before and after live virus vaccination
  – No cases reported. Theoretical risk.

Vaccine Response in IBD

- **Tetanus**
  - No difference between inactive CD and healthy controls

- **Influenza**
  - TNF blocker + immunomodulators had lower response

- **Pneumococcal (PPV23)**
  - 6MP/AZA does not impair response

Immune Response to Influenza Vaccine in Children with IBD

- 146 children with IBD, immunosuppressed (IS) and nonimmunosuppressed (NIS)
- The proportion of seroprotected and geometric mean titers at post-vaccination were similar between NIS and IS groups
  - Patients on anti-TNF were less likely to be seroprotected against strain B (14%) compared to NIS (39%, $P=.025$)
  - Vaccine was well tolerated
- No true evidence of IBD exacerbation with vaccination

Response to Pneumococcal Vaccination by Treatment Exposure

- Response = both >2-fold titer and >1 mcg/mL in ≥3 antibodies
- Patients on anti-TNF plus immunomodulator (IMM) therapy have significantly lower response to pneumococcal vaccination compared with IBD and healthy controls

Live Virus Vaccines

- Bacille Calmette-Guérin
- Influenza inhaled (LAIV) – parenteral attenuated
- Measles, Mumps, Rubella
- Typhoid (oral) – parenteral attenuated
- Vaccinia (smallpox)
- Varicella
- Yellow Fever
- Zoster

Definition: A "live virus" vaccine is a vaccine that contains a "living" virus that is able to give and produce immunity, usually without causing illness

Anti-TNF Therapy and Live Virus Vaccination

• Theoretical concerns:
  – Reactivation of underlying disease
  – Disseminated disease caused by live vaccine

• Live virus vaccines are contraindicated in patients on anti-TNF therapy
  – Debate on whether they can be used in azathioprine/6-MP/methotrexate
    • CDC: safety not known
Zoster Vaccination

• **Contraindication:** High-dose corticosteroids (\(\geq 20\) mg/day of prednisone or equivalent) lasting two or more weeks. Zoster vaccination should be deferred for at least 1 month after discontinuation of such therapy.

• Short-term CS therapy (<14 days); low-to-moderate dose (<20 mg/day of prednisone or equivalent); topical; intra-articular, bursal, or tendon injections; or long-term alternate-day treatment with low to moderate doses of short-acting CS are not considered sufficiently immunosuppressive to cause concerns for vaccine safety.

• Therapy with **low-doses of methotrexate** (\(\leq 0.4\) mg/Kg/week), **azathioprine** (\(\leq 3.0\) mg/Kg/day), or **6-mercaptopurine** (\(\leq 1.5\) mg/Kg/day) for treatment of RA, psoriasis, polymyositis, sarcoidosis, IBD, and other conditions are also **not considered sufficiently immunosuppressive** and are not contraindications for zoster vaccine.

• Persons receiving recombinant human immune mediators and immune modulators, especially the **antitumor necrosis factor agents adalimumab, infliximab, and etanercept**. The safety and efficacy of zoster vaccine administered concurrently with these agents is unknown. If it is not possible to administer zoster vaccine to patients before initiation of therapy, physicians should **assess the immune status of the recipient on a case-by-case basis to determine the relevant risks and benefits**. Otherwise, vaccination with zoster vaccine should be **deferred for at least 1 month after discontinuation of such therapy**.

Summary

- Patients with IBD should generally follow the same vaccination guidelines as the general public, **except**
  - Patients on anti-TNF should not get live virus vaccines
  - Newborns with detectable levels of anti-TNF should not get rotavirus vaccine or other live virus vaccine
  - Early dosing for influenza, pneumococcus, zoster

- At the time of diagnosis of IBD, vaccinations should be checked and updated prior to starting any immunosuppressant (if possible)
Laboratory Exams

• Annually
  – CBC, LFTs, creatinine, B12, folate, iron, 25-OH vitamin D, lipids, glucose

• Medication-based
  – Azathioprine/6MP/Methotrexate
    • TPMT
      • Initially weekly, monthly
      • Maintenance every 2-3 months
  – Anti-TNF agents
    • Every 3 months
    • Check HAV, HBsag, HBsAb, HCV

Tuberculosis Screening

• Exposure history
  – PPD/Quantiferon +/- Chest X-ray

• Tuberculin skin testing (PPD)
  – >5 mm induration is positive (American Thoracic Society (ATS))
  – BCG vaccine older than 10 years doesn’t affect it
  – 71% may be anergic (83% if on steroids, immunosuppressive agents)

• Quantiferon and T-Spot:
  – Expensive, logistically challenging
  – Benefit in BCG treated
  – Can be false negative in the setting of immunosuppression

• No data on efficacy of repeat annual testing

Serial TB Skin Test (TST) to Diagnose Subclinical TB in IBD Patients Receiving Infliximab Therapy

- Prospective study of 62 IBD patients with negative 2-step TST and CXR before starting infliximab therapy who underwent annual TST while on anti-TNF therapy
  - 43/62 on steroids and 14/62 on concomitant immunomodulators at baseline
- 8/62 subjects converted TST within 3 years
  - None of these were taking steroids
  - Only 1 of 8 had known exposure to TB
  - All converted patients received 9 months of isoniazid and continued infliximab
  - None had evidence of active TB at median 16 months follow-up
- **Annual TST among high-risk populations may identify additional patients with subclinical TB, facilitating prophylactic treatment**

Taxonera C et al. DDW 2011; abstract no. 991
Cancer Screening

- Colon cancer
  - Every 1-2 years after 8 years of disease
- Start immediately for primary sclerosing cholangitis (PSC)
- Cervical dysplasia
  - Annual pap smears
  - Increased rate among women on immunosuppressants
- Anal dysplasia
  - May be increased with perianal disease
  - Behavioral risk

Cancer Screening (cont’d)

• **Skin cancer**
  - Increased with immunosuppression.
  - Possible increase in CD

• **Breast cancer**
  - Same as baseline population: CBE q3 years: Mammograms annually after age 40
  - CD patients may be treated less aggressively and survival is worse

• **Prostate cancer**
  - Prostate-specific antigen starting at age 40 (controversy over benefit); 1/6 men in US with prostate cancer

Sogaard KK et al. *Inflamm Bowel Dis.* 2008;14:519-525.
Tobacco Cessation

• Cardiac, pulmonary and oncologic risk

• Active smoking is a risk factor for CD
  – Reduce response to medications
  – Increase rate of post-operative recurrence
  – Shorten duration of remission

• Active smoking may benefit UC

• Medical therapy for smoking cessation

Osteoporosis

• IBD patients are at increased risk for osteoporosis
• Dual energy x-ray absorptiometry scanning (DXA)
  – IBD men and women aged ≥50
  – Prolonged (>3 months) steroid use
  – History of low trauma fracture
  – Hypogonadism
• Calcium 1200 mg daily
• Vitamin D 400-800 IU daily

General Health

• Blood pressure screening
  – <140/90 or <130/80 for diabetes, CRI
  – SBP 120-139, DBP 80-89 (prehypertensive)
    • Lifestyle modification
  – IBD patients increased risk for secondary hypertension: medications (CS, CSA)

• Blood glucose screening
  – IBD patients increased risk due to corticosteroid use

• Ophthalmologic exam
  – Annual exam
  – Risk of glaucoma on steroids
  – Risk of iritis, optic neuritis, scleritis with IBD

CRI = chronic renal insufficiency
CS = corticosteroids
CSA = cyclosporine

Depression

- Rates of depression in IBD are 15% to 35%\(^1\)
- A comparison of lifetime prevalence suggests higher rates of panic, generalized anxiety, and obsessive-compulsive disorders and major depression and lower rates of social anxiety and bipolar disorders in the IBD sample than in national samples in the United States\(^1\)
  - Twice the rate of depression as in controls
- Depression reduces health-related quality of life and increases self-perceived functional disability irrespective of symptom severity

Summary

• Patients with IBD have important general health care needs

• The gastroenterologist should perform:
  – Appropriate laboratory and TB testing
  – Colon cancer surveillance

• The gastroenterologist should advise patient and primary care provider:
  – Make sure vaccines are up to date
  – Tobacco cessation
  – Osteoporosis, hypertension, glucose, ophthalmologic screening
  – Cancer: Cervical, anal, skin, breast, prostate
  – Ask about depression and make appropriate referral