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.

- **Gastroenterologists need to explicitly inform the primary care provider of the unique needs of the IBD patient, especially those on immuno-modulators 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**
- **identification of depression and anxiety and**
- **smoking cessation.**

- **As part of this guideline preparation, a literature search was conducted using Ovid MEDLINE from 1946 to 2015, EMBASE 1988 to 2015, and SCOPUS from 1980 to 2015. The major terms were the controlled subject headings in MeSH: IBDs, colitis, ulcerative, and Crohn's disease.**

Preventive health maintenance recommendations

- **Statement 1a: All adult patients with IBD should undergo annual vaccination against influenza.**

Conditional recommendation, with very low level of evidence.

- **Statement 1b: Those on immunosuppressive therapies and their household contacts should receive the non-live trivalent inactivated influenza vaccine, but not the live inhaled influenza vaccine.**

Conditional recommendation, with very low level of evidence

- **Statement 2: Adult patients with IBD receiving immunosuppressive therapy should receive pneumococcal vaccination with both the PCV13 and PPSV23, in accordance with national guidelines.**

  Conditional recommendation, with very low level of evidence.

- **Statement 3: Adults with IBD over the age of 50 should consider vaccination against herpes zoster, including certain subgroups of immunosuppressed patients.**

  Strong recommendation, with low level of evidence.

- **Statement 4: Adults with IBD should be assessed for prior exposure to varicella and vaccinated if naive before initiation of immunosuppressive therapy when possible.**

  Conditional recommendation, with very low level of evidence.

- **Statement 5: Patients with IBD who are immunosuppressed and traveling to endemic areas for yellow fever should consult with a travel medicine or infectious disease specialist prior to travel.**

  Conditional recommendation, with very low level of evidence

- **Statement 6: Adolescents with IBD should receive meningococcal vaccination in accordance with routine vaccination recommendations.**

  Conditional recommendation, with very low level of evidence.

- **Statement 7: Household members of immunosuppressed patients can receive live vaccines with certain precautions.**

  Conditional recommendation, with very low level of evidence.

- **Statement 8: Adults with IBD should receive age-appropriate vaccinations before initiation of immune suppression when possible.**

  Conditional recommendation, with very low level of evidence.

- **Statement 9: Vaccination against Tdap, HAV, HBV, and HPV should be administered as per Advisory Committee on Immunization Practice guidelines.**

  Conditional recommendation, with very low level of evidence.

- **Statement 10: Women with IBD on immunosuppressive therapy should undergo annual cervical cancer screening.**

  Conditional recommendation, very low level of evidence.

- **Statement 11: Screening for depression and anxiety is recommended in patients with IBD.**

  Conditional recommendation, low level evidence

- **Statement 12a: Patients with IBD (both ulcerative colitis and CD) should undergo screening for melanoma independent of the use of biologic therapy.**

  Strong recommendation with low level of evidence.

- **Statement 12b: IBD patients on immunomodulators (6-mercaptopurine or azathioprine) should undergo screening for NMSC while using these agents, particularly over the age of 50.**

  Strong recommendation with low level of evidence.

- **Statement 13: Patients with conventional risk factors for abnormal bone mineral density with ulcerative colitis and CD should undergo screening for osteo-porosis with bone mineral density testing at the time of diagnosis and periodically after diagnosis.**

  Conditional recommendation with very low level evidence

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- **Statement 14: Patients with CD who smoke should be counseled to quit.**

  Strong recommendation with low level evidence.

- **Members of the gastroenterology team are often the only clinicians that a patient with IBD will see.**

- **It is crucial to clarify with the patient the limits of the specialist's responsibilities and delegate routine health care issues to the primary care clinician.**

VACCINATIONS

- **Patients with IBD are often treated with long-term immune-suppressive therapies and may thus be at increased risk for infections, many of which are preventable with vaccinations**

- **In general, adherence to age-appropriate vaccination schedules is recommended, although special considerations exist for patients receiving or initiating immunosuppressive therapies**

- **For patients in whom treatment is needed, however, delaying some vaccinations may be necessary to facilitate timely administration of immunosuppressive therapy**

- **All adult patients with IBD, regardless of immunosuppression status, should receive non-live vaccines**

Table 2. Inactivated vaccine recommendations[a]

Infectious agent	Target population	Check titer before immunization	Dosing regimen
Corynebacterium diphtheria, Clostridium tetani, Bordetella pertussis	All patients	No	A single dose of Tdap recommended at age 11 through 64 years; Td booster every 10 years
Hepatitis A	All patients	Yes	2 doses at 0 and 6 months
Hepatitis B	All patients	Yes	3 doses at 1, 1–2 and 4–6 months; check titers 1 month after the last dose; if no response, 3 options: revaccinate, double dose HBV vaccination or combined HAV/HBV vaccine
HPV	Female and male; 11 to 26 years of age	No	3 Doses at 0, 2, and 6 months
Influenza	All patients	No	Annual immunization with trivalent inactivated influenza vaccine; "high dose" vaccine for patients 65 and older; live attenuated intranasal influenza vaccine is contraindicated in immunosuppressed patients
Neisseria meningitidis	High risk adults	No	Two or three doses depending on vaccine
Streptococcus pneumonia	All patients	No	If no previous vaccination, PCV13 followed by a dose of PPSV23 after 2–12 months; if received 1 or more doses of PPSV23 should receive PCV13 one or more years after PPSV23; another dose of PPSV23 should be administered 5 years after the initial PPSV23 dose and at age 65 years or older if at least 5 years have elapsed since their previous PPSV23 dose

HAV, hepatitis A; HBV, hepatitis B; PCV, pneumococcal conjugate vaccine; PPSV, pneumococcal polysaccharide vaccine.

[a]See text for details.

- **Although all non-live vaccines can be administered to patients regardless of immunosuppression status, certain live vaccines (i.e., herpes zoster vaccine) are recommended for patients on "low-level" but not "high-level" immunosuppression.**

- **Patients with low-level immunosuppression include individuals receiving a daily dose of systemic corticosteroids for ≥14 days (prednisone 20 mg/day equivalent and within 3 months of stopping) or receiving alternate-day corticosteroid therapy, and those receiving methotrexate ≤0.4 mg/kg/week and within 3 months of stopping, azathioprine ≤3.0 mg/kg/day, or 6-mercaptopurine ≤1.5 mg/kg/day and within 3 months of stopping. Significant protein calorie malnutrition is also associated with immunosuppression.**

- **The IDSA considers patients on anti-tumor necrosis factors (TNFs) to have high-level immunosuppression**

- **The package insert for vedolizumab states that patients on this biologic agent may receive non-live vaccines (e.g., influenza vaccine injection, etc) and may receive live vaccines if the benefits outweigh the risks**

Table 3. Live vaccine recommendations[a]

Infectious agent	Target population	Check titer before immunization	Dosing Regimen	In patient already on immunosuppressive treatment	Vaccination for family contacts
Measles Mumps Rubella	If unknown vaccination history	Yes	Two doses (>28 days apart) at least 6 weeks before starting immunosuppressive therapy	Contraindicated	Yes
Varicella	If unknown vaccination history or exposure	Yes	2 doses (4–6 weeks apart) at least 1 month before starting Immunosuppressive therapy	Depends on the type of immunosuppressive medications	Yes, if vaccine related rash occurs, immunosuppressed IBD patient should avoid contact
Herpes zoster	For patients aged 50 or older	No	1 dose at least 1 month before starting immunosuppressive therapy	Depends on the type of immunosuppressive medications	Yes, if vaccine related rash occurs, immunosuppressed IBD patient should avoid contact

IBD, inflammatory bowel disease.

[a]See text for details.

- **One concern raised by clinicians and patients is that vaccination may exacerbate IBD disease activity.**
- **Several studies of patients with rheumatologic disorders failed to demonstrate that vaccination was associated with an increase in disease activity.**
- **There is no convincing evidence that IBD activity will be exacerbated by vaccination.**

INFLUENZA VACCINATION

Recommendations

- **1a . All adult patients with IBD should undergo annual vaccination against influenza.**
- Conditional recommendation, with very low level of evidence

- **1 b . Those on immunosuppressive therapies and their household contacts should receive the non-live trivalent inactivated influenza vaccine, but not the live inhaled influenza vaccine.**
- Conditional recommendation, with very low level of evidence

- **Patients with IBD are at increased risk for acquiring influenza infection relative to age-matched patients without IBD. This risk is particularly increased when patients are treated with immunosuppressive therapies**

- **Furthermore, some patients with IBD who acquire influenza infection are more likely to experience hospitalization and co-infection with pneumonia**

- **Several studies have evaluated the safety and efficacy of influenza vaccination among children and adults with IBD and found the vaccines to generally induce appropriate immune responses**

- **However, when patients are receiving immunosuppressive therapies with combined thiopurines and anti-TNF agents, serologic responses to vaccines are impaired**

- **Since 2009, universal recommendations for influenza vaccination recommend that all those over the age of 6 months should generally receive influenza vaccination**

- **However, because of the theoretical risk of live virus transmission, it is recommended that household contacts of immunosuppressed individuals should receive the trivalent inactivated vaccine and not the the live attenuated influenza vaccine Flumist**

PNEUMOCOCCAL VACCINATION

Recommendation

- **2 . Adult patients with IBD receiving immunosuppressive therapy should receive pneumococcal vaccination with both the PCV-13 and PPSV23, in accordance with national guidelines.**
- Conditional recommendation, with very low level of evidence

- **Patients with IBD are at increased risk for pneumonia relative to age-matched patients without IBD (adjusted Cox proportional HR 1.54, 95% confidence interval (CI) 1.49–1.60) (61);**
- **this risk is apparent among both CD and UC.**

- **This risk appears increased in patients who are being treated with narcotics, corticosteroids, biologic medications, thiopurines, and proton-pump inhibitors relative to patients not receiving these medications**

- **. Furthermore, patients with IBD hospitalized with pneumonia may be at increased risk of death during hospitalization**

- **Vaccination with both PPSV23 and PCV13 is recommended for those receiving immunosuppressive treatment, to maximize the breadth of serotypes covered (i.e., with PPSV23) and ensure optimal protection against the most common and virulent strains (i.e., with PCV13)**

HERPES ZOSTER VACCINATION

Recommendation

- **3 . Adults with IBD over the age of 50 should consider vaccination against herpes zoster, including certain subgroups of immunosuppressed patients.**

Strong recommendation, with low level of evidence

- **Patients with IBD are at increased risk of developing herpes-zoster infections.**

- **The risk of herpes-zoster is higher in patients with IBD regardless of duration of disease.**

VARICELLA VACCINATION

Recommendation

- **4 . Adults with IBD should be assessed for prior exposure to varicella and vaccinated if naive prior to initiation of immunosuppressive therapy when possible.**

Conditional recommendation, with very low level of evidence.

- **Data suggest that IBD patients be tested for varicella exposure and be vaccinated if nonimmune**

YELLOW FEVER VACCINATION

Recommendation

- **5 . Patients with IBD who are immunosuppressed and traveling to endemic areas for yellow fever should consult with a travel medicine or infectious disease specialist before travel.**

Conditional recommendation, with very low level of evidence.

MENINGOCOCCAL VACCINATION

Recommendation

- **6 . Adolescents with IBD should receive meningococcal vaccination in accordance with routine vaccination recommendations.**

Conditional recommendation, with very low level of evidence.

LIVE VACCINATIONS IN HOUSEHOLD MEMBERS OF IMMUNOSUPPRESSED IBD PATIENTS

Recommendation

- **7 . Household members of immunosuppressed patients can receive live vaccines with certain precautions.**

Conditional recommendation, with very low level of evidence.

- **Individuals who live in a household with immunocompromised patients age ≥6 months should receive influenza vaccine annually (strong, high).**

- **Immunocompromised patients should avoid contact with persons who develop skin lesions after receipt of varicella or zoster vaccine until the lesions clear**

VACCINATE PRIOR TO IMMUNOSUPPRESSION

Recommendation

- **8 . Adults with IBD should receive age-appropriate vaccinations before initiation of immune suppression when possible.**
- Conditional recommendation, with very low level of evidence.

- **In general, patients on monotherapy with an immunomodulator have a normal immune response compared with controls or patients on 5ASAs.**

- **In patients on monotherapy with anti-TNF, some but not all studies demonstrate a diminished immune response compared with controls or patients on 5ASAs.**

- **Finally, in patients receiving both an immunomodulator and anti-TNF agent, there is a diminished immune response to vaccines compared with those on mono therapy with an immunomodulatory, anti-TNF, or 5ASAs.**

TDAP, HEPATITIS A, HEPATITIS B AND HUMAN PAPILLOMA VIRUS VACCINATIONS

Recommendation

- **9 . Vaccination against Tdap, HAV, HBV, and HPV should be administered as per ACIP guidelines.**

  Conditional recommendation, with very low level of evidence.

- **Given the importance of HBV infection in IBD patients, specific attention should be given to assessing HBV status. Reactivation of hepatitis B infection has been reported in immunosuppressed IBD patients with serious consequences**

- **Testing for HBV infection (HBsAg, HBcAb, and HBsAb) and vaccination of the non-immune patient is recommended before starting anti-TNF's**

- **. In healthy individuals, protective antibody concentrations after the primary three dose HBV vaccine series is >95%.**

- **In contrast, studies on HBV vaccination in IBD patients have reported efficacy rates from 33–76%**

- **Some experts advise that immunocompromised patients have titers checked every 12–24 months to confirm immunity**

- **In those patients with waning protective titers, it is reasonable to give a single booster shot, and if titers do not rise appropriately, consider administration of another 3 vaccination series at the regular dose.**

OTHER HEALTH MAINTENANCE ISSUES

- **In addition to vaccination issues, it is important to identify the subgroups of patients with IBD that have an increased risk of developing cervical cancer, non melanoma skin cancer and melanoma.**

- **Additionally assessing bone health, screening for depression and recommending smoking cessation in patients with CD are important measures to address when caring for IBD patients**

SCREENING FOR CERVICAL CANCER

Recommendation

- **10 . Women with IBD on immunosuppressive therapy should undergo annual cervical cancer screening.**

Conditional recommendation, very low level of evidence.

- **Known factors associated with an increased risk of cancer include cigarette smoking and a compromised immune system, both of which can be seen in patients with CD.**

- **A recently published meta-analysis found sufficient evidence to suggest an increased risk of cervical high-grade dysplasia and cancer in patients with IBD on immunosuppressive medications with an adjusted odds ratio of 1.34**

SCREENING FOR DEPRESSION AND ANXIETY

Recommendation

- **11 . Screening for depression and anxiety is recommended in patients with IBD.**
- Conditional recommendation, low level evidence.

- **The etiology of IBD and disease activity following periods of remission is complex, and likely involves an interaction between multiple factors. Psychological stress has been reported by both care givers and patients to exacerbate disease but the published literature is conflicting**

- **In a review of 12 studies, antidepressants were found to be effective for treating both psychological and somatic symptoms in patients with IBD**

SCREENING FOR MELANOMA AND NON-MELANOMA SKIN CANCER

Recommendations

- **12a. Patients with IBD (both UC and CD) should undergo screening for melanoma independent of the use of biologic therapy.**

  Strong recommendation with low level of evidence.

- **12b. IBD patients on immunomodulators (6-mercaptopurine or azathioprine) should undergo screening for non-melanoma squamous cell cancer (NMSC) while using these agents, particularly over the age of 50.**

  Strong recommendation with low level of evidence.

- **Widespread use of anti TNF therapy and immunomodulatory therapy has led to the recognition of two malignant complications associated with the use of thiopurines and anti-tumor necrosis factor therapy: NMSC associated with the past or current use of thiopurines and the potential for melanoma in patients with IBD or those exposed to anti-TNF therapy.**

- **It is suggested that all individuals who are initiating immunosuppression therapy for the treatment of IBD should use sunscreen that is protective against UVA and UVB light as well use sun protective clothing.**

- **It is recommended that all patients starting or who are already on immunosuppressive medications should be evaluated by a dermatologist, so that risk assessment according to the individual risk factors and a tailored and case-by-case surveillance strategy is defined for each patient.**

SCREENING FOR OSTEOPOROSIS

Recommendation

13 . Patients with conventional risk factors for abnormal bone mineral density with UC and CD should undergo screening for osteoporosis with bone mineral density testing at the time of diagnosis and periodically after diagnosis

Conditional recommendation with very low level evidence.

- **It has been recognized that reduced bone mineral density (BMD) and bony fractures are more common in persons with IBD, however, the actual disease burden is not well characterized.**

- **BMD measurement (with a DEXA scan) is recommended in all patients starting oral corticosteroid therapy specifically in those who have used oral corticosteroid therapy for longer than 3 consecutive months in a dose ≥7.5 mg/day of prednisone-equivalent in the absence of base-line BMD measurement.**

SMOKING CESSATION IN PATIENTS WITH CROHN'S DISEASE

Recommendation

- **14 . Patients with CD who smoke should be counseled to quit.**

  Strong recommendation with low level evidence.

- **For CD, there are data to suggest that smoking is associated with (i) development of disease, (ii) disease progression and (iii) poorer medical and surgical outcomes.**

- **Smoking also appears to adversely affect response to therapy.**

- **Early reports of anti-TNF therapy found that 22% of smokers vs. 74% of nonsmokers responded to episodic use of infliximab, and a prospective study of 74 patients given a single dose of infliximab found that at 4 weeks smokers were less likely to have a response (OR 0.22; 95% CI, 0.08–0.41) and a shorter duration of response than non-smokers**

CONCLUSIONS

- **Patients with IBD often consider their gastroenterologist to be the primary provider of care. Health maintenance issues need to be co-managed by both the gastroenterologist and primary care team.**

- **In addition to vaccinations, referral to dermatology, gynecology, psychiatry, and endocrinology may be necessary on a case by case basis.**

Thanks for your patience and attention