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REVIEW

Preventative Care in the Patient with Inflammatory Bowel Disease: What Is New?

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Abstract Patients with inflammatory bowel disease (IBD) do not receive routine preventative care at the same rate as general medical patients. This patient population is at increased risk of vaccine preventable illness such as influenza and pneumococcal pneumonia. This review will discuss health maintenance needs and preventative care issues in patients with IBD.

Keywords IBD patient · Immunization · Vaccination · Health maintenance · Immunosuppressed

Introduction

Patients with inflammatory bowel disease (IBD) do not receive routine preventative care at the same rate as general medical patients [1]. A survey of general practitioners revealed that only 37 % of family medicine physicians were comfortable providing primary care to patients with IBD [2]. It is imperative that gastroenterologists are familiar with the general health maintenance needs of this patient population.

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Vaccination

Patients with IBD are at increased risk of vaccine preventable illnesses [3]. This risk is further exacerbated by use of corticosteroids, immunomodulators (azathioprine, 6-mercaptopurine and methotrexate) and biologic therapy (infliximab, adalimumab, certolizumab, golimumab, natalizumab, and vedolizumab). Fatal cases of hepatitis B reactivation have been reported in patients treated with biologic therapy [4, 5]. Low uptake of vaccines further increases the risk of infection. Underutilization of vaccines for patients with IBD has been frequently reported in the literature. In a survey of 169 patients with IBD, only 28 % reported regularly receiving an influenza vaccine and only 9 % reported receiving a pneumococcal vaccine [6]. Low vaccination rates are exacerbated by a lack of awareness toward vaccinating the IBD patient. This places a substantial risk on this patient population. Numerous barriers exist that limit increasing vaccination rates; such barriers include general public apathy, fears, and concerns about the side effects of vaccination, and costs associated with storage and administration of vaccines. There are also several logistical barriers such as location of providers and wait time to see a physician [7, 8].

Uncertainty exists among providers regarding whose role it is to vaccinate the patient with IBD. In a survey of 108 gastroenterologists, 64 % of physicians believed that the primary care physician should be responsible for determining which vaccinations to give patients. Roughly 20–30 % of gastroenterologists recommended live vaccinations which are generally contraindicated for patients with IBD, illustrating deficiencies in knowledge regarding vaccination of the IBD patient [9].

Immune Response

Several studies have demonstrated that patients with IBD can mount an appropriate immune response to vaccines [10]. However, the immune response is often diminished when compared to healthy controls. Patients' immune response is further diminished by combined immunosuppressive therapy. In a study of 64 patients with IBD, immune response to the 23-valent pneumococcal polysaccharide vaccine (PPSV23) was significantly diminished with combination (TNF blocker and immunomodulator) therapy compared to non-immunosuppressed patients with IBD [11].

Goals of Vaccination

A thorough vaccination history should be obtained promptly after a diagnosis of IBD is established. If the vaccination history is unclear appropriate, titers should be obtained. Inactivated vaccines can be safely administered in all patients with IBD regardless of the degree of immunosuppression.

The relative degree of immunosuppression in patients with IBD is related to the duration of immunosuppressive therapy and disease activity. Based on expert opinion, patients are considered immunosuppressed based on any of the following parameters:

1. Treatment with glucocorticoids (>prednisone 20 mg day equivalent or 2 mg/kg/day if <10 kg, for 2 weeks or more, and within 3 months of stopping).
2. Ongoing treatment with effective doses of 6-MP/azathioprine or recent discontinuation within the previous 3 months.
3. Treatment with methotrexate or recent discontinuation within the previous 3 months.
4. Treatment with infliximab, vedolizumab, adalimumab, certolizumab, natalizumab, or recent discontinuation within the previous 3 months.
5. Significant protein–calorie malnutrition.

Live vaccines are generally contraindicated in immunosuppressed patients, and therefore, these patients should be vaccinated 4–6 weeks prior to the initiation of immunosuppressive therapy or 3 months after discontinuation of therapy [12].

There has been concern that vaccinating patients with IBD may increase their disease activity. Vaccinations are generally well tolerated with few adverse reactions. A study evaluating the safety and efficacy of influenza vaccinations in patients with IBD reported a flare rate of less than 5 % up to 1 month after vaccination [13]. A similar study evaluating the safety and efficacy of the pneumococcal vaccination in patients with IBD on immunomodulator therapy reported no flares after vaccination [14]. Vaccinations are thus safe for patients with IBD and unlikely to precipitate disease activity.

Live Vaccines

As noted previously, live vaccines are generally contraindicated in patients that are immunosuppressed. The live vaccinations that are recommended are MMR, varicella, and herpes zoster (Table 1).

MMR

MMR should be administered to all children starting around 1 year of age and is administered as two doses given 1 month apart. If adult vaccination status is unknown titers should be checked. If the titers are positive, the patient is considered immune and vaccination is not necessary. If the

Table 1 Live vaccine recommendations

Vaccine	Check titers prior to administration?	Prior to immunosuppressive therapy	If patient already on immunosuppressive therapy	Household contacts
MMR	If vaccine history unknown	Administer two doses, 28 days apart, contraindicated if starting therapy within 6 weeks	Contraindicated	Safe to vaccinate
Varicella	If vaccine history unknown, or no history of varicella infection	Administer two doses, 4–6 weeks apart days apart, contraindicated if starting therapy within 1–3 months	Contraindicated	Safe to vaccinate, if patient develops rash IBD patient on immunosuppressive therapy should avoid contact
Herpes zoster (for age >60)	No	Administer one dose, contraindicated if starting therapy within 1–3 months	Contraindicated if on a biologic, can administer if on low doses of immunosuppressive therapy (see text)	Safe to vaccinate, if patient develops rash IBD patient on immunosuppressive therapy should avoid contact

MMR measles, mumps, rubella

titers are not positive for any of the three viruses, then the patient should be vaccinated with the MMR vaccine as long as there is no plan to begin immunosuppressive therapy within the next 6 weeks. MMR may be administered safely to household contacts regardless of the immunosuppressive state of the patient [15].

Varicella

Patients with IBD are at increased risk of varicella infection [16]. Fatal cases of varicella in IBD have been reported [17]. The varicella vaccine is recommended for immunocompetent children and adults with no known history of varicella. If a patient's history is unknown, titers should be checked. If the titers are negative, then the patient should be vaccinated with the varicella vaccine. Current recommendations are to wait at least 1–3 months between vaccination and the initiation of immunosuppressive therapy. Vaccination is not contraindicated in household contacts. However, if a family member that is vaccinated develops a vaccine-related rash, the IBD patient should avoid contact with that family member for the duration of the rash [18, 19] (Table 2).

Herpes Zoster

The estimated risk of developing herpes zoster infection in the general population is 30 %. This risk is significantly increased after the age of 60. A wide array of complications (post-herpetic neuralgia, conjunctivitis, keratitis, and uveitis) are associated with herpes zoster [20]. 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. In addition, herpes zoster also occurs at a younger age in IBD patients [21]. The zoster vaccine is recommended for individuals over the age of 60 to prevent herpes zoster and to reduce the severity and risk of developing complications. No clear consensus exists on when to vaccinate for zoster in IBD patients, but the typical recommendation is to vaccinate 1–3 months prior to the initiation of immunosuppressive therapy. The CDC recommends that the administration of the zoster vaccine is safe in patients with low doses of immunosuppression (6-MP, azathioprine and methotrexate) [22]. A recent large administrative database study in 633 patients with several immune disorders including IBD on biologic therapy who received the herpes zoster vaccine reported no cases of herpes zoster infection 42 days post-vaccination [23]. A recent study demonstrated a blunted immune response to the herpes zoster vaccine in IBD patients on low dose immunosuppressive compared to non-immunosuppressed subjects [24]. Despite this difference, there were no serious adverse effects in either group at 1 year. Future studies will be needed to validate the safety of administering the zoster vaccination to patients on biologic therapy. Checking titers prior to vaccination is not recommended. Household contacts may be vaccinated. However, as in the case with varicella, if a household contact develops a rash after vaccination, the IBD patient should avoid contact with the household member [18, 23–25].

Table 2 Vaccination checklist for first office visit

Titers to check at first visit
MMR—if vaccination history is unknown
Varicella—if vaccination history unknown, or no history of the previous infection
Hepatitis A—except those with evidence of protective titer within 5 years of vaccine administration
Hepatitis B—except those with evidence of protective titer within 5 years of vaccine administration
Vaccinations to administer to specific patient groups, regardless of immunosuppression
Influenza (yearly)
Pneumococcal (PCV13 and PPSV 23)
Tdap
HPV
Hepatitis A (if not immune)
Hepatitis B (if not immune)
Meningococcal
Vaccinations to consider if NO plans to begin immunosuppressive therapy
MMR (if not immune)
Varicella (if not immune)
Herpes zoster (age 60 and older)

Inactivated Vaccines

Inactivated vaccines are well tolerated in patients with IBD regardless of their state of immunosuppression. The recommended inactivated vaccines include; influenza, pneumococcal, tetanus and diphtheria, HPV, hepatitis B, and meningococcal (Table 3).

Influenza

Patients with IBD are at increased risk of influenza [3]. The influenza vaccine is available in a live intranasal form, an inactivated intramuscular form, and an inactivated intradermal form. Studies have found that patients with IBD who are being treated with immunomodulators or biologics can mount adequate immune responses to the inactivated flu vaccine. The live intranasal vaccine should be avoided in immunosuppressed IBD patients. IBD patients should be

Table 3 Inactivated vaccine recommendations

Vaccine	Check titers prior to administration?	Prior to immunosuppressive therapy	If patient already on immunosuppressive therapy	Household contacts
Influenza	No	Administer intramuscular inactivated vaccine annually, avoid live vaccine	Safe to vaccinate per ACIP recommendations	Safe to vaccinate, avoid live vaccine
Pneumococcal pneumonia	No	If no vaccine history, administer PCV13 then PPSV23 8 weeks later. Administer second dose of PPSV23 5 years after first, then another dose after 65. If history of PPSV23 vaccine, administer PCV13 1 year later	Safe to vaccinate per ACIP recommendations	Safe to vaccinate
Td/Tdap	No	Td booster every 10 years, if no vaccine history Tdap may be given as one booster	Safe to vaccinate per ACIP recommendations	Safe to vaccinate
HPV (for males and females 11–26)	No	Administer three doses at 0, 2, 6 months	Safe to vaccinate per ACIP recommendations	Safe to vaccinate
Hepatitis A	Yes	Administer three doses, 6 months apart	Safe to vaccinate per ACIP recommendations	Safe to vaccinate
Hepatitis B	Yes	Administer three doses at 0, 1–2, and 4–6 months, then recheck titer after 1 month and revaccinate if inadequate response with double dose	Safe to vaccinate per ACIP recommendations	Safe to vaccinate
Meningococcal	no	Administer one dose to high-risk patients can administer booster after 5 years	Safe to vaccinate per ACIP recommendations	Safe to vaccinate

PCV13, pneumococcal conjugate; PPSV23, pneumococcal polysaccharide; Td/Tdap, tetanus, diphtheria, pertussis; HPV, human papillomavirus

vaccinated seasonally for influenza with the inactivated intramuscular vaccine [26–28].

Pneumococcal Pneumonia

New ACIP guidelines recommend that patients on immunosuppressive medications be vaccinated once with pneumococcal conjugate vaccine (PCV13) followed by pneumococcal polysaccharide (PPSV23) at least 8 weeks later, and a second dose of PPSV23 5 years after the first dose, and then again after the age of 65 [29]. A recent study assessing the immune response of PPSV23 in patients on biologic therapy found that approximately half of patients on anti-TNF therapy were not protected against PPSV23 as evidenced by low titers [30]. The ideal time to vaccinate with PPSV23 would be prior to beginning immunosuppressive therapy, though there is no contraindication to vaccinating anytime during therapy.

Tetanus and Diphtheria

One study has shown that patients with IBD have impaired immune response to the tetanus toxoid booster, [31] while another study demonstrated normal anti-tetanus antibody response [32]. Despite these conflicting data, the tetanus and diphtheria vaccine should be administered to patients with IBD once every 10 years. The DTap (tetanus, diphtheria, acellular pertussis) vaccine should be given once during this period. Patients with unknown Td history should be given the Td series (three doses of Td) [33].

HPV

Female patients with IBD are at increased risk of developing neoplastic cervical lesions. This risk is slightly elevated in patients with CD and patients on immunosuppressive therapy [34]. The HPV vaccination is recommended for all females between the ages of 11 and 26, and women with a history of genital warts, abnormal pap smears, or a positive HPV test [35]. Males between the ages of 11–26 should be also be vaccinated for HPV [36].

Hepatitis B

Patients with IBD are at risk of HBV infection. Risk factors include unprotected sex with multiple partners and travel to regions where HBV is endemic. Case reports of patients with fatal viral hepatitis have been reported after beginning anti-TNF therapy [4, 37]. A recent Canadian study found that vaccine uptake in patients with IBD was 61 % [8]. The response rate to the HBV vaccine is lower in patients with IBD, but is substantially improved with booster revaccination [38]. Titers should be checked 4–6 weeks after the last vaccination when seen in the office for routine care. If

titers are inadequate (<10 mIU/ml), vaccination with a double dose should be given at 0, 1–2, and 4–6 months [39, 40]. If titers do not show an adequate response, one may revaccinate or use the combined hepatitis A, hepatitis b vaccination (twinrix). Patients should be vaccinated for hepatitis A who are not previously immune [39].

Meningococcal

Patients with IBD should be vaccinated for meningococcal as per recommendations from the ACIP for the general population. The vaccine should be administered to college students living in dormitories, military recruits, individuals traveling to endemic areas, and adults who are asplenic or have complement deficiencies [41].

Traveler with IBD

Patients with IBD often feel that their disease restricts their ability to travel. Unfortunately, few patients seek pre-travel advice from their clinician [42]. It remains debated whether travel can induce flares in patients with IBD; nevertheless, studies have shown travelers with IBD may be at greater risk of having a flare compared to healthy individuals. Risk factors for flares during travel include prior hospitalizations, number of previous flares, and remission status within the past 3 months [43]. While the exact etiology of increased flares within the IBD traveler is unknown, many possible explanations exist such as medication non-adherence during travel and exposure to infectious diseases such as traveler's diarrhea [44]. A recent study detailed an association between high-altitude travel (>2000 ft) and increased risk of IBD flares. The authors postulated that at high altitudes hypoxia can lead to gastrointestinal inflammation.

Prior to travel, gastroenterologists should encourage their patients to visit the CDC http://wwwnc.cdc.gov/travel/destinations/list.aspx and WHO http://apps.who.int/tools/geoserver/www/ith/index.html websites to learn about the various infectious diseases endemic to their destination. Vaccination is an important issue to consider in the traveler with IBD. Yellow fever vaccination is strongly encouraged for patients traveling to endemic areas and is actually required for 16 specific countries [45]. The yellow fever vaccine is a live attenuated vaccination. Patients on immunosuppressive therapy therefore must be off immunosuppressive medications for at least 4 months prior to vaccination. Patients should be discouraged from traveling to areas endemic to yellow fever if they cannot stop their immunosuppressive therapy in order to be vaccinated. Patients traveling to areas where hepatitis B is endemic (Southeast Asia, China, Africa) should have titers checked prior to travel. If patients are immunosuppressed a booster vaccination should be administered when HBs antibodies are below 10 mIU/mL [46]. Other vaccines that should be considered for the IBD traveler include the typhoid vaccine (patients traveling to India, Southern Africa), the cholera vaccine (endemic areas where access to clean water and sanitation is limited), and the Japanese Encephalitis vaccine (travel to parts of Asia and patients on anti-TNF therapy) [47, 48].

National societies recommend that travelers with IBD bring antibiotic prophylaxis on trips in case they develop gastroenteritis although this remains controversial [44, 49]. Patient should also have immunity to vaccinations confirmed prior to travel and should not travel to areas endemic to yellow fever, if live vaccines are contraindicated in the patient.

Patients with IBD who are planning travel in the near future should see their gastroenterologist prior to travel. The gastroenterologist can consider a referral to a traveler's clinic. Travel should be discouraged if patients have not been in remission over the past 3 months.

Smoking

Smoking cessation should be encouraged in all patients with IBD. Smoking has been shown to increase the risk of extraintestinal manifestations in Crohn's disease patients [50, 51]. Smoking also increases disease activity in Crohn's disease and is associated with increased risk of more frequent steroid use [52, 53]. Particular attention should be paid to smokers who report short time to first cigarette in the morning, as they have been shown to have more difficulty quitting [54]. Smoking cessation should be discussed at every visit (Table 4).

Hypertension

Patients with IBD often use medications that increase their blood pressure such as corticosteroids. In most instances, elevated blood pressure resolves after cessation of steroid therapy. In 2014, JNC 8 (the Eighth Joint National Committee) established new guidelines for treating hypertension. Patients over the age of 60 should be treated to a blood pressure goal of <150/90. Patients less than the age of 60 should be treated to a blood pressure goal of <140/90. The lower goal also applies to patients with diabetes and renal disease [55]. Blood pressure should be checked at every visit. If patients require long-term steroid therapy, or blood pressure remains elevated after cessation of therapy, their primary care provider should be informed to consider antihypertensive therapy [56].

Table 4 Other general health maintenance concerns

Smoking	Assess at each visit, encourage smoking cessation
Hypertension	Over age of 60, BP goal <150/90, otherwise goal <140/90
Bone health	Check vitamin D 25-OH in all patients
	Assess bone health with DEXA scan if:
	Patient is on steroid therapy
	Cumulative use of steroid therapy >3 months
	Patient appears frail
	Maternal history of osteoporosis
	Age over 60
	Postmenopausal state
	History of low-trauma fracture
	Prescribe vitamin D and calcium with use of steroids and if patient has low vitamin D
Depression	Assess at each visit, refer to PCP or mental health if moderate–severe depression
Sexual health	Assess at initial visit with BISF-W and BSFI questionnaires, and periodically follow-up
Ophthalmologic health	Refer to ophthalmologist if eye pain or changes in vision, yearly ophthalmologic examinations
Cancer prevention	Colon cancer
	Surveillance every 1–3 years, 8 years after initial of UC (extending beyond rectum) or CD (disease involving 1/3 of colon);
	If diagnosed with Primary Sclerosing Cholangitis, survey at time of PSC diagnosis and yearly thereafter
	Chromoendoscopy is an alternative to white-light endoscopy
	Cervical cancer
	Annual pap smears for females who are immunosuppressed
	Skin cancer
	Consider annual skin examination by dermatologist in patients on thiopurines or anti-TNFs, counsel on preventative measures to decrease sun exposure

Nutrition and Diet

Patients with IBD are at risk of malnutrition and micronutrient deficiencies. Particular vitamin and mineral deficiencies include but are not limited to iron, vitamin B12, vitamin D, folate, zinc, calcium, and magnesium [57]. Patients with CD are more likely to develop nutritional deficiencies compared to patients with UC given involvement within the small bowel. Such deficiencies can lead to significant weight loss, growth failure, and hypoalbuminemia. Unfortunately, malnutrition is often underdiagnosed in patients with IBD; thus, it is important to screen for nutrient deficiencies and assess dietary patterns in all patients with IBD regardless of disease activity [58].

Patients with IBD frequently ask their gastroenterologist what foods they should be consuming to control symptoms such as abdominal pain. A recent survey found that 66 % of patients with IBD restricted various foods from their diet to avoid foods they believe may act as triggers for flares [59]. Therefore, referral to a nutritionist and or dietitian should be considered in patients at risk of malnourishment and to ascertain a patient's baseline nutritional status early in the course of their disease.

Several studies have examined the role of dietary modifications in the management and prevention of IBD [60]. Most diets focus on the concept of exclusion whereby specific food components thought to contribute to mucosal inflammation are eliminated from the diet. For instance, exclusive enteral nutrition has been shown to induce remission in pediatric patients with Crohn's disease compared to steroid therapy. Enteral nutrition consists of an exclusive liquid formula that is given to patients for 6–8 weeks. Enteral nutrition should be a preferred choice in the pediatric population as to avoid delayed growth in pubertal development associated with corticosteroid therapy. In adults, corticosteroids are preferred to enteral nutrition given patient preference and poor compliance with the exclusive nature of enteral nutrition [61]. The European Crohn's and Colitis Organization guidelines currently recommend that patients whose disease is well controlled consume a diet high in fiber while patients with moderate to poorly controlled disease should avoid fiber in their diet given their increased risk of intestinal obstruction [62]. More work is certainly needed to determine whether dietary interventions can have a role in treating and even preventing the development of IBD.

Bone Health

Osteoporosis is the most common metabolic bone disease in the USA. Osteoporosis is defined as reduced bone density on dual X-ray absorptiometry (DEXA). Osteopenia is defined as a *T*-score of −1 to −2.5 on DEXA, and osteoporosis is a *T*-score below −2.5 [63]. Patients with IBD are increased risk of developing metabolic bone disease. Patients with Crohn's disease are at greater risk compared to patients with ulcerative colitis, likely secondary to ileal involvement [64–66]. Corticosteroids have an inhibitor effect on osteoclastogenesis while promoting apoptosis of osteoblasts and osteocytes which leads to decreased bone formation [67]. As noted previously, patients with IBD also have diminished vitamin D and calcium absorption, putting them at further risk of developing metabolic bone disease. A low percentage of patients with IBD are screened for metabolic bone disease [68]. A recent study suggests that patients treated with vitamin D are more likely to remain in clinical remission [69]. The American Gastroenterology Association (AGA) and the American College of Gastroenterology (ACG) published guidelines detailing the management and prevention of osteoporosis in patients with IBD. Patients on steroid therapy or patients who have had a cumulative use of steroid therapy for greater than 3 months should be screened for osteoporosis. In addition, patients over the age of 60, patients in a postmenopausal state, and patients with a history of low-trauma fractures should be screened for osteoporosis [70–72]. Patients with a T-score <−1 should take supplemental vitamin D and calcium, and have these levels checked at regular intervals. Bisphosphates are the primary treatment in patients diagnosed with osteoporosis. If osteoporosis is diagnosed, referral to an endocrinologist should be considered.

Depression

Rates of depression are higher in patients with IBD compared to the general population [73–75]. A recent study assessing body image dissatisfaction found that levels of body image dissatisfaction were associated with increased disease activity and steroid treatment. A negative body image correlates with psychosocial dysfunction, high levels of anxiety, and depression [76]. It is important for the gastroenterologist be aware of the psychosocial well-being of patients with IBD. Effective screening for depression can be accomplished with a two question questionnaire.

> Over the past month, have you felt down, depressed, or hopeless?
> Over the past month, have you felt little interest or pleasure in doing things? [77]

If positive, a more detailed history should be taken. Mild depression can be followed and assessed at each visit. Moderate to severe depression should prompt a discussion with the patient's primary care physician or a referral to a mental health specialist.

Sexual Health

Women with IBD are more likely to experience sexual dysfunction and thus have decreased sexual activity. In a survey of 50 women, the most common reason cited for decreased sexual activity was dyspareunia. Other reasons included abdominal pain, fear of diarrhea, and fecal incontinence during sexual activity [78, 79]. In a recent survey, less than 20 % of gastroenterologists asked women about their sexual health [80]. Many questionnaires exist to assess sexual dysfunction in both males and females. The Brief Index of Sexual Functioning for Women (BISF-W) is a validated 22-item questionnaire designed for the assessment of female sexual functioning and satisfaction. Domains assessed include desire, arousal, frequency of sexual activity, receptivity/initiation, pleasure/orgasm, relationship satisfaction, and problems affecting sexual functioning [81]. For males, the Brief Male Sexual Function Inventory (BSFI) is validated questionnaire that can be used to assess male sexual function. Domains assessed include, sexual drive, erection, ejaculation, perception of problems with sexual function, and overall satisfaction [82]. Providers should assess sexual health in all patients with IBD.

It is important to remember that the patient with IBD is at increased risk of thrombosis [83]. There has been concern regarding the use of oral contraceptives in patients with IBD and risk of thrombosis. To date, there are no prospective studies looking at increased risk of thrombosis in patients with IBD who are taking oral contraceptives. Women with IBD should be offered the same options for contraceptives as women without IBD. These include combine oral contraceptives, progestin only pills, and progestin only injectables such as depot medroxyprogesterone acetate and copper intrauterine devices [84]. Patients with primary sclerosing cholangitis should not be offered combined oral contraceptives [85].

Ophthalmologic Health

Episcleritis and uveitis are the most common ophthalmologic manifestations of IBD. Prompt diagnosis of uveitis is crucial, as this condition can lead to glaucoma and rarely blindness [86, 87]. Glaucoma is also known adverse side

effect of steroid therapy [88]. Any patient that complains of eye pain or changes in vision should be referred urgently to an ophthalmologist. Patients with IBD should have yearly ophthalmologic examinations [56].

Colon Cancer

Patients with IBD are at increased risk of developing colorectal cancer. Cancer is the second most common cause of death in patients with IBD, though rates of colorectal cancer have been decreasing [89]. The risk is further increased in patients who have had primary sclerosing cholangitis. A cohort study evaluating surveillance colonoscopy in patients with IBD found a 100 % 5-year survival related to colon cancer in patients in a surveillance group compared to a 74 % 5-year survival related to colon cancer in patients in a non-surveillance group ($p = .042$) [90]. ACG and ASGE guidelines recommend that patients with IBD (UC with disease proximal to the sigmoid colon and CD with more than one-third of colon involvement) undergo surveillance colonoscopy 8–10 years after diagnosis. Surveillance colonoscopies should occur at 1- to 3-year intervals and ideally when patients are in remission. Surveillance should be yearly in patients with active disease, anatomic abnormalities, history of dysplasia, family history of colon cancer in a first-degree relative or primary sclerosing cholangitis. If a patient has been diagnosed with primary sclerosing cholangitis, they should undergo colonoscopy at the time of diagnosis. With the use of high-definition colonoscopies, we now know that most dysplasia in IBD is visible. Recent guidelines have recommended chromoendoscopy as an alternative to taking random colonic biopsies for the detection of dysplasia. Chromoendoscopy is the process whereby the colonic mucosa is stained with methylene blue or indigo carmine. These dyes allow better visualization of dysplastic tissue. A meta-analysis of prospective studies comparing chromoendoscopy to white-light endoscopy for detection of dysplasia revealed 7 % incremental yield in patients screened with chromoendoscopy with targeted biopsies compared to patients screened with white-light endoscopy and random biopsies [91]. When performing colonoscopy with high-definition colonoscopes, chromoendoscopy is suggested [92, 93]. It is important to note that patients with ulcerative proctitis and proctosigmoiditis are not at increased risk of developing colorectal cancer and thus should be screened according to average risk guidelines [94–96]. Smoking is a risk factor for developing colorectal cancer. As noted previously, tobacco use should be assessed at every office visit and smoking cessation should strongly be encouraged [56].

Cervical Cancer

Female patients with IBD are at increased risk of developing cervical dysplasia [97]. As noted previously, this risk is slightly greater in Crohn's disease compared to ulcerative colitis. In a sample of 134 women with IBD, the incidence of abnormal pap smears was 36 % greater compared to controls. Females exposed to immunosuppressive therapy were more likely to have an abnormal pap [98]. Females should undergo pap testing annually as per American Congress of Obstetricians and Gynecologists (ACOG) recommendations [99]. As mentioned previously, it is important to vaccinate young females for HPV.

Anal Cancer

Anal dysplasia shares much is common with cervical dysplasia and is caused by HPV. Females with cervical dysplasia are at increased risk of developing anal dysplasia. Other risk factors include HIV, men who have sex with men and history of HPV infection. Data are sparse regarding the incidence of anal dysplasia in patients with IBD [100–102]. High-risk patients are often screened with an anal pap smear. However, no guidelines exist at this time regarding use of anal pap smears. Some state agencies have developed guidelines for screening the HIV population [103]. Further research is needed to understand the risk of developing anal dysplasia in IBD and the utility of anal pap smears.

Skin Cancer

Non-melanoma skin cancers (NMSC) are the most common form of cancer in the USA. Fortunately, these cancers are usually curable. Previous data support the notion that patients with IBD are at increased risk of developing NMSC. It is thought that this increased risk may be associated with the use of thiopurine medications. Less is known about the risk of developing melanoma [66]. A nested case–control study sought to evaluate the risk of developing NMSC and melanoma in IBD patients. In patients with IBD not on immunosuppressive therapy (biologics or thiopurines), there was no increased risk of developing NMSC (OR .99 CI .92–1.08). However, the risk of NMSC was increased in immunosuppressed patients [thiopurine use (OR 4.27 CI 3.08–5.92), anti-TNF use (OR 2.18, CI 1.07–4.66), combined thiopurine and anti-TNF agent (OR 6.75, CI 2.74–16.55)]. A decrease in NSMC was seen in patients who had discontinued thiopurines [104].

Melanoma is much less common than non-melanoma skin cancer with an estimated 76,000 cases in 2014, but compared to non-melanoma skin cancer melanoma has more serious consequences. IBD has been associated with an increased risk of melanoma, independent of treatment. Use of anti-TNF for 1 year conferred a nearly twofold (OR 1.88 CI 1.08–3.29) increased risk of melanoma. Interestingly, use of biologic therapy with concomitant steroid therapy was not associated with an increased risk of skin cancer [105, 106]. Further research is needed to assess the impact of steroid therapy on risk of skin malignancy.

These data illustrate that patients with IBD who are exposed to immunosuppressive medications have an increased risk of developing NMSC. Patients with IBD regardless of medication use have an increased risk of developing melanoma. All patients should be counseled on ways that they can minimize their risk of developing skin cancer. Preventative measures include wearing protective clothing, use of sunscreen SPF-30, decreasing exposure to UV light, and avoidance of tanning beds. Patients on immunosuppressive therapy should be referred to a dermatologist for annual skin checks [104].

Therapy-Related Testing

Medications used to treat IBD have various adverse effects, and thus, it is important to obtain appropriate testing prior to undergoing specific therapies. Therapy-related testing is listed below in table format.

Aminosalicylates—yearly renal function.

Corticosteroids—monitor bone health (25-OH vitamin D), monitor eye health, and monitor blood sugar

Azathioprine/6MP—prior to initiation of therapy check thiopurine methyltransferase (TMTP), CBC, and liver function; during therapy monitor CBC with differential and liver function after 2, 4 weeks, and then if stable every 12 weeks [56].

Methotrexate—prior to initiation of therapy check CBC, liver function, and renal function; during therapy monitor CBC, liver function, and renal function after 2 weeks, then after 4 weeks, and if stable then every 8 weeks [66, 107].

Biologic therapy—prior to initiation of therapy, screen for TB with PPD or QuantiFERON gold and CXR. High-risk patients, patients on immunosuppression, patients with history of TB or history of BCG vaccination can be screened with interferon-gamma release assay (IGRA) (QuantiFERON) [108]. Providers should be aware that IGRA results may be indeterminate in patients on immunomodulator therapy [109]. Thus, providers should use IGRA testing prior to initiation of immunomodulator therapy in patients with IBD. Patients on anti-TNFs should have CBC, renal function, and liver function checked prior to initiation of therapy, and periodically monitored while on therapy.

Patients on natalizumab should have a JCV antibody checked prior to initiation of therapy and rechecked every 6 months after beginning therapy.

CBC and liver function should be checked prior to initiation of therapy and monitored while on therapy. Patients on vedolizumab should have CBC, renal function, and liver function checked prior to initiation of therapy, and periodically monitored while on therapy [110–113].

Conclusion

Health maintenance care in patients with IBD is often complex. Adequate preventative care of the patient with IBD requires a multi-disciplinary team approach, involving the gastroenterologist, nurses, primary care physicians, and various other specialists. Patients with IBD often see their gastroenterologist as their sole provider. Thus, it is important for gastroenterologists to have a firm understanding of vaccinations, smoking cessation, hypertension, bone health, mental health, sexual health, eye health, cancer prevention, and various therapy-related testing. Gastroenterologists must take a proactive role in providing routine preventative services for their patients.

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Compliance with ethical standards

Conflict of interest The authors listed above declare that there are no relevant conflict of interest.

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