

# Health Care Maintenance for the Pediatric Patient With Inflammatory Bowel Disease

Ersilia M. DeFilippis, MD, Robbyn Sockolow, MD, Elaine Barfield, MD

Nearly one-quarter of patients with inflammatory bowel disease (IBD) are younger than 20 years of age at diagnosis. Furthermore, the incidence of IBD in children continues to increase. Nevertheless, variation in management exists within the care of patients with IBD with regards to disease screening and preventive care. A multidisciplinary approach that involves the general practitioner and pediatric gastroenterologist is needed to routinely monitor growth, bone health, vitamin and mineral deficiencies, vaccination status, and endoscopic surveillance. It is also important to monitor for extraintestinal manifestations of IBD that may affect the liver, joints, skin, and eyes. The purpose of this article is to provide an updated overview of comprehensive care for pediatric patients with IBD.

Inflammatory bowel disease (IBD), which encompasses ulcerative colitis (UC) and Crohn disease (CD), results from a combination of genetic susceptibilities and environmental factors leading to a dysfunctional immune response.<sup>1</sup> Nearly one-quarter of patients with IBD are less than 20 years old at diagnosis.<sup>2</sup> The incidence of pediatric IBD continues to increase with current estimates of 7 per 100 000 annually.<sup>3</sup> The incidence of CD in the pediatric population is 4.56 new cases annually, greater than twice the incidence of UC (2.14 cases per 100 000).<sup>3,4</sup>

Caring for pediatric patients with IBD requires meticulous health care maintenance. In 2013, the Crohn's and Colitis Foundation of America (CCFA) defined process and outcome measures to reduce variation in care for patients with IBD and to improve outcomes.<sup>5</sup> To meet these best practice measures, a multidisciplinary approach should include the primary care provider, pediatric gastroenterologist, dietician,

and psychosocial support team.<sup>2</sup> This review aims to provide an updated overview of comprehensive care for pediatric patients with IBD, including monitoring growth, bone health, vitamin deficiencies, vaccinations, psychological, eye and skin health, endoscopic surveillance, tuberculosis (TB) screening, and dietary recommendations.

## GROWTH

Growth should be monitored closely in pediatric patients with IBD. Between 10% and 40% of children presenting with IBD have significant bone mass deficits.<sup>6</sup> Impaired linear growth can precede gastrointestinal symptoms and may be the only presenting sign of IBD.<sup>3</sup> Nutritional deficiencies, physical inactivity, inflammatory cytokines, and corticosteroid use negatively impact bone growth and bone formation.<sup>7</sup>

Peak bone mass is decreased in approximately half of children with IBD. Growth and restoration of bone

## abstract

**Disclaimer:** The guidelines/recommendations in this article are not American Academy of Pediatrics policy, and publication herein does not imply endorsement.

Weill Cornell Medical College, New York, New York

Dr DeFilippis drafted the initial manuscript; Dr Sockolow critically reviewed and revised the manuscript; Dr Barfield conceptualized and designed the work and drafted the initial manuscript; and all authors approved the final manuscript as submitted.

**DOI:** 10.1542/peds.2015-1971

Accepted for publication Jun 7, 2016

Address correspondence to Elaine Barfield, MD, Department of Pediatrics, 525 E 70th St, Floor 3, New York, NY 10021. E-mail: elb2020@med.cornell.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2016 by the American Academy of Pediatrics

**FINANCIAL DISCLOSURE:** Robbyn Sockolow is a speaker for Janssen, Abbvie, and Abbott and is a consultant for Peabody Law Firm for Hoffman la Roche; and Drs DeFilippis and Barfield have indicated they have no financial relationships relevant to this article to disclose.

**FUNDING:** No external funding.

**POTENTIAL CONFLICT OF INTEREST:** The authors have indicated they have no potential conflicts of interest to disclose.

**To cite:** DeFilippis EM, Sockolow R, Barfield E. Health Care Maintenance for the Pediatric Patient With Inflammatory Bowel Disease. *Pediatrics*. 2016;138(3):e20151971

density can be a marker of disease control. However, growth delays often persist after diagnosis despite improvement in inflammatory biomarkers and treatment with biologic agents.<sup>8,9</sup>

Therefore, failure to control inflammation puts this population at increased risk for fracture. The International Society for Clinical Densitometry recommends that children with IBD undergo a total body (excluding the skull) dual-energy radiograph absorptiometry (DXA) screen at diagnosis and at 6-month intervals if abnormalities are found.<sup>2</sup> Risk factors that should prompt a DXA in patients with a previously normal scan include downward crossing of height or weight percentiles, amenorrhea, glucocorticoid therapy, and clinically significant fractures.<sup>7,10</sup> There are no normal values for children younger than 5 years of age.

Z scores are preferred to T scores since DXA can underestimate bone density in children with physiologic growth delays.<sup>11</sup> DXA Z scores < -2 indicate significant deficits in bone mass and body composition requiring further evaluation including bone age, measurement of serum calcium, phosphorus, magnesium, blood urea nitrogen, creatinine, parathyroid hormone, ionized calcium, tissue transglutaminase immunoglobulin (Ig) A, and vitamin D 25-OH levels.<sup>2</sup> Patients with z score < -1 require close monitoring with repeat DXA within 6 months.<sup>2</sup> There is no data regarding follow-up for patients with normal DXA.

Although there is little consensus on the treatment of pediatric osteoporosis, first-line therapies include optimizing dietary calcium and vitamin D intake and implementing regular weight-bearing exercise.<sup>12</sup> Bisphosphonates may be appropriate in certain situations, but safety concerns remain among primary care providers.<sup>12</sup>

## VACCINATION STATUS

Pediatric patients with IBD are susceptible to vaccine-preventable diseases secondary to immunosuppressive therapies (defined below), yet, levels of vaccination coverage in this population are insufficient.<sup>13-17</sup> A study of 165 pediatric patients with IBD revealed vaccination rates of 22% for influenza, 32% for pneumococcus, 38% for hepatitis B, and 87% for diphtheria-tetanus-acellular pertussis.<sup>14</sup>

### Live Vaccines

Live vaccines should be avoided in anyone who is immunosuppressed.<sup>2</sup> Patients meeting 1 of the following criteria are considered to be immunosuppressed<sup>2</sup>:

1. Treatment with glucocorticoids: more than 20 mg/day of prednisone, equivalent of 2 mg/kg/day if less than 10 mg/day for 2 weeks or more, or within 3 months of stopping therapy
2. Treatment with thiopurines (6-mercaptopurine/azathioprine), methotrexate, or antitumor necrosis factor (TNF)  $\alpha$  agents or other biologics, or within 3 months of stopping therapy
3. Significant protein-calorie malnutrition

### Inactivated Vaccines

The CCFPA published guidelines in 2004 regarding the immunization of patients with IBD.<sup>18</sup> Inactivated vaccines are safe, even for those on immunosuppression. Administration of inactivated vaccines in pediatric patients with IBD should not deviate from Centers for Disease Control and Prevention (CDC) vaccination schedule. These include tetanus, hepatitis B, hepatitis A, inactivated (injectable) influenza, pneumococcal, human papillomavirus (HPV), and meningococcal vaccines.<sup>18</sup>

## Influenza

All pediatric patients with IBD should receive the inactivated influenza vaccine every fall. The live nasal influenza vaccine should be avoided in patients on any type of immunosuppression.

### Pneumococcal Vaccine

The Advisory Committee on Immunization Practices from the CDC released new guidelines in 2013 regarding pneumococcal vaccination in immunocompromised patients 6 to 18 years of age.<sup>19</sup> Pediatric patients with IBD who have not received the 13-valent pneumococcal conjugate vaccine (PCV13, or Prevnar; Wyeth Pharmaceuticals, Inc, Philadelphia, PA) should receive a single dose of PCV13 followed at least 8 weeks later by the 23-valent pneumococcal polysaccharide vaccine (PPSV23, or Pneumovax; Merck & Co, Kenilworth, NJ). A second PPSV23 dose should be administered 5 years later for children ages 6 to 18.

Patients who have previously been vaccinated with PPSV23 should receive a single PCV13 dose at least 8 weeks after the last PPSV23 dose. If a second PPSV23 dose is indicated, it should be given at least 5 years after the first PPSV23 dose. Pediatric patients should not receive more than 2 doses of PPSV23 before 65 years of age.<sup>19</sup>

### HPV Vaccine

Rates of cervical dysplasia and cancer are higher in immunosuppressed girls compared with healthy controls. HPV infection is associated with cervical, vulvar, and vaginal cancer in girls, penile cancer in boys, and anal and oropharyngeal cancer in both sexes.<sup>20-22</sup> Cervical and penile cancer have been reported in pediatric patients with IBD.<sup>23</sup> Given the young age of pediatric patients with IBD and the early use of immunosuppressive therapies, vaccination is crucial to reducing risk of cervical dysplasia and cancer.<sup>24</sup> The quadrivalent HPV

vaccine (Gardasil, Merck and Co, Inc, Whitehouse Station) has been shown to be efficacious in pediatric patients with IBD.<sup>24</sup>

The 2015 CDC recommendations state that the 9-valent HPV vaccine (Gardasil 9, Merck and Co) can be used for routine vaccination. Gardasil 9 was approved in 2014 and contains HPV 31, 33, 45, 52, and 58 in addition to the strains in the quadrivalent vaccine (5, 9, 11, 16). Vaccination is recommended routinely for boys and girls at age 11 or 12 years regardless of whether they are receiving immunosuppressive therapy.<sup>25,26</sup>

### Epstein-Barr Virus Infection

There is data to suggest that patients with CD with no history of previous Epstein-Barr virus exposure may be at higher risk for development of hemophagocytic lymphohistiocytosis (HLH), especially with thiopurine therapy. A few case series have demonstrated more than 100-fold greater risk in children with CD.<sup>27-29</sup> Before starting thiopurines in these patients, obtaining Epstein-Barr virus titers may have some utility although this remains to be determined.

### OPHTHALMOLOGIC HEALTH

Because IBD is a systemic disease, patients may have subclinical extraintestinal manifestations involving the eye including conjunctivitis, uveitis, and episcleritis.<sup>30-32</sup> Ophthalmologic conditions are reported in 2% to 6% of all patients with IBD.<sup>31</sup> In pediatric patients in particular, 1 complication is the development of increased intraocular pressure from corticosteroids. In some studies, this occurred in up to 20% of treated subjects.<sup>33,34</sup> Other ocular findings include uveitis and episcleritis, extraintestinal manifestations of IBD. One study revealed that 6.2% of pediatric patients with IBD had asymptomatic uveitis. Fortunately, in these cases,

the changes were mild and did not require early intervention.<sup>35</sup> Annual ophthalmologic examination including visual acuity, slit lamp examination, intraocular pressure measurements, and examination of both the anterior and posterior chambers is recommended.<sup>36</sup>

### DERMATOLOGIC HEALTH

Annual dermatology evaluation is important for skin cancer screening and monitoring for other dermatologic manifestations of IBD including erythema nodosum, pyoderma gangrenosum, and psoriasis. Erythema nodosum is characterized by deep red tender nodules typically on the anterior lower legs and is more common in CD.<sup>31</sup> Pyoderma gangrenosum is a neutrophilic dermatosis that gradually enlarges to form deep painful ulcers that frequently occurs at sites of previous trauma. Skin reactions, including psoriasis, are seen in 10% to 20% of pediatric patients on maintenance therapy with anti-TNF agents.<sup>37,38</sup> Typically, no changes are made to the treatment regimen given that psoriasis is an indication for anti-TNF agents; however, in some cases, the therapy may be discontinued due to a severe skin reaction. Further studies suggest that pediatric patients who develop psoriasis after infliximab therapy may be more likely to be homozygous for polymorphisms of the interleukin (IL)-23 receptor gene.<sup>39</sup>

In the adult literature, IBD has been associated with an increased risk of nonmelanoma skin cancer, especially in patients treated with thiopurines.<sup>40-43</sup> Some studies also suggest an increased risk of melanoma in patients with IBD independent of biologic use.<sup>44</sup> In 1 study of 698 pediatric patients with IBD, 9 patients developed skin cancer, 2 of which were basal cell carcinoma requiring local resection.<sup>23</sup> There was no significant increased

risk of basal cell carcinoma in the cohort.<sup>45</sup>

Given the risk of skin cancers associated with IBD and side effects of some of the medications used to treat IBD, all patients should use sun protection.<sup>46,47</sup> Sun protection consists of wearing sun-protective clothing, using sunscreen with SPF of 15 or higher, seeking shade, limiting activities outdoors between 10 AM and 4 PM, and avoiding indoor tanning.<sup>48,49</sup>

### JOINT INVOLVEMENT

Joint complaints have been reported in up to one-quarter of pediatric patients with IBD.<sup>50</sup> Generally, there are 3 categories of IBD-specific joint conditions: ankylosing spondylitis, peripheral arthritis, and enthesitis.<sup>50</sup> Type 1 peripheral arthritis tends to correlate with signs and symptoms of active IBD, whereas type 2 does not correlate to gastrointestinal inflammation. It is important to determine the number of joints affected, severity, frequency, and duration of symptoms. In patients with IBD, it is important to differentiate between inflammatory or mechanical pain. Inflammatory pain that improves with activity and is accompanied by morning stiffness is more concerning for a rheumatologic issue. Physical examination should involve assessing all joints for symmetry and complete range of motion. A rheumatologist evaluation should be considered when patients have poor response to therapy or have persistent joint complaints despite control of intestinal symptoms.<sup>50</sup>

### LIVER INVOLVEMENT

Transient elevation of liver enzymes occurs in 14% to 40% of pediatric patients with IBD.<sup>51</sup> Certain laboratory abnormalities warrant further workup. Studies reveal that patients with serum alanine

aminotransaminase greater than 4 times the upper limit of normal (ULN) were significantly associated with defined liver disease.<sup>52</sup> An elevated gamma-glutamyl transferase >252 suggests the presence of an underlying IBD-associated chronic liver disease such as primary sclerosing cholangitis; referral to a pediatric hepatologist is warranted.<sup>52</sup> If liver enzymes remain elevated <2 × ULN, repeat testing is recommended in 2 weeks. If the values remain elevated or >2 × ULN at any time, pediatric hepatology consultation may be warranted. If patients are on hepatotoxic medications, dose reductions or discontinuation should be considered.<sup>52</sup>

### ENDOSCOPIC SURVEILLANCE

The European Crohn's and Colitis Organization recommends upper endoscopy and colonoscopy for all pediatric patients undergoing diagnostic workup for IBD regardless of the presence of upper gastrointestinal tract symptoms.<sup>53</sup> Biopsies should be obtained from the upper gastrointestinal tract, the terminal ileum, and each colonic segment.<sup>54</sup>

Cancer screening via colonoscopy should be performed at 8 to 10 years from the time of symptoms. Patients with both UC and primary sclerosing cholangitis require annual-biannual colonoscopy with biopsies for colon cancer surveillance.<sup>11</sup> These patients are also at increased risk for the development of cholangiocarcinoma.<sup>11</sup>

### SCREENING FOR LATENT TB

Adult patients treated with anti-TNF therapy are at increased risk for reactivation of latent TB infection.<sup>55</sup> The data regarding which method of screening for latent TB is superior is controversial.<sup>56-60</sup> A positive purified protein derivative (PPD) as a marker of latent infection may

be unreliable as results are reader-dependent. Results may also be invalid in patients who received BCG immunization.<sup>56,57</sup> Therefore, both PPD and QuantiFERON TB GOLD (Cellestis, Valencia, CA) are recommended for screening before starting anti-TNF agents in children given the lack of superiority of either test.<sup>56,61</sup> Indeterminate QuantiFERON TB GOLD results may occur in patients with lower weight-for-height z scores, higher platelet counts, and lower serum albumin levels as well as higher disease activity as measured by the Pediatric Crohn's Disease Activity Index.<sup>62</sup> Furthermore, many studies reveal that children <5 years of age are more likely to have indeterminate results.<sup>61</sup> Despite this, the QuantiFERON TB Gold is generally more reliable than a reader-dependent PPD.

Indeterminate quantiferon results should be repeated. After a second indeterminate result, a chest radiograph should be obtained before initiating anti-TNF therapy. There are no guidelines regarding ongoing monitoring for TB in patients while on anti-TNF therapy; the greatest risk is at the outset of therapy.<sup>11</sup>

### VITAMIN AND MINERAL DEFICIENCIES

#### Iron Deficiency

Although several types of anemia are associated with IBD, iron deficiency anemia is the most common and may present with fatigue, lethargy, and dizziness among other symptoms.<sup>63</sup> In 1 cohort study, as many as 72% of newly diagnosed pediatric patients with IBD were anemic.<sup>64</sup> In another study of 790 pediatric patients with IBD, 30% had anemia at diagnosis. Anemia was associated with colonic involvement in patients with CD and was associated with the extent of colonic inflammation in patients with UC. Nevertheless, patients with CD with predominantly small bowel disease had higher rates of anemia compared with patients with UC

(42% vs 24%).<sup>65</sup> This anemia may represent iron deficiency anemia or anemia of chronic disease secondary to poor utilization of body iron stores especially in patients with active IBD. In the inflammatory state, hepcidin is the main regulator of iron homeostasis in IBD. Proinflammatory cytokines like interleukin-6 upregulate hepcidin gene expression leading to a reduction in iron release from macrophages.<sup>66</sup> Anemia of chronic disease can be differentiated from iron deficiency anemia with the soluble transferrin receptor as well as the serum ferritin.<sup>67</sup>

Despite a higher prevalence of anemia in pediatric patients with IBD, fewer iron deficient children receive iron supplementation compared with adults and adolescents.<sup>68</sup> The dose of elemental iron and the preferred route of administration required in patients with IBD is controversial.<sup>69</sup> Oral supplementation is inexpensive and relatively safe. However, at recommended doses (3–6 mg elemental iron/kg per 24 hours), many experience side effects including nausea, vomiting, and gastrointestinal distress.<sup>69</sup> Some believe oral iron is poorly absorbed in patients with chronic inflammation, whereas others argue that iron deficiency in IBD is predominantly due to blood loss, rather than malabsorption.<sup>69</sup> Comparative studies between intravenous and oral iron do not consistently demonstrate a significant difference.<sup>69-72</sup> In patients with an elevated C-reactive protein, intravenous iron should be the preferred route.<sup>66</sup>

#### Folate and Vitamin B<sub>12</sub>

Recent data suggest that folate and vitamin B<sub>12</sub> deficiencies are rare in children with newly diagnosed IBD.<sup>73</sup> However, if the patient is on an antifolate medication such as methotrexate or if they have significant terminal ileal disease or history of ileal resection, monitoring

of folate and vitamin B<sub>12</sub> may be warranted.<sup>74</sup> When measuring folate, serum levels are preferred over red blood cell folate levels.<sup>74</sup> Serum methylmalonic acid and homocysteine levels should be used to distinguish folate and B<sub>12</sub> deficiencies.

Controversy remains regarding the optimal method of vitamin B<sub>12</sub> supplementation. Traditionally, parenteral injections were preferred. One meta-analysis revealed high-dose oral vitamin B<sub>12</sub> to be as effective as intramuscular injections; however, this excluded patients with CD who may have had impaired absorption of oral B<sub>12</sub>.<sup>75</sup> There is also limited data to suggest that intranasal administration may lead to sustained increase in cobalamin concentrations; however, this has not been studied in the pediatric population.<sup>76</sup>

### Vitamin D

Vitamin D, a fat-soluble vitamin, is absorbed in the small intestine and promotes bone health.<sup>10,74,77,78</sup> Administration of vitamin D analogs in animal models attenuates disease scores, suppresses bleeding, and down-regulates inflammatory cytokines including IL-1, IL-6, and TNF- $\alpha$ .<sup>79,80</sup> Vitamin D, therefore, may play a role in moderating disease severity in IBD.<sup>81,82</sup> Improving vitamin D status may improve symptoms and inflammation in pediatric patients with IBD.

Serum levels of 25-OH vitamin D should be monitored at least yearly to maintain levels above 30 ng/mL.<sup>7</sup> A recent randomized controlled trial suggests that 5000 IU of oral vitamin D3/10 kg body weight weekly for 6 weeks is an efficacious dosing strategy for repletion.<sup>83</sup> Suggested maintenance doses include 1500 to 2000 IU/day.<sup>74</sup>

### Zinc

Zinc is essential for maintaining the integrity of the immune system,

protein and collagen synthesis, and wound healing.<sup>74</sup> Patients with IBD are at risk for zinc deficiency, likely due to increased losses from the gastrointestinal tract.<sup>73</sup> Zinc deficiency may reduce free radical scavenging leading to continued intestinal inflammation.<sup>74</sup> Deficiencies are more marked in CD.<sup>84</sup> In 1 study of 102 patients <18 years old, zinc deficiency was significantly more common in patients with IBD than age-matched controls (40% vs 19%).<sup>73</sup> Although serum zinc levels are a suboptimal indicator of zinc deficiency, levels should be assessed in pediatric patients with IBD at diagnosis.<sup>73,85</sup>

In children with zinc deficiency, oral replacement doses of 1 to 2 mg/kg per day of elemental zinc are recommended.<sup>86</sup>

### DIETARY RECOMMENDATIONS

Dietary interventions have been studied in pediatric IBD.

Exclusive enteral nutrition (EEN) is the use of nutritional intervention as an antiinflammatory therapy and involves the use of an elemental or polymeric formula for 6 to 8 weeks to induce remission specifically in CD.<sup>87</sup> Although dietary guidance is often provided by a dietician for symptom control during IBD flares, EEN is used specifically as an antiinflammatory agent for the purposes of inducing remission in CD. EEN is recommended as first-line therapy for CD to induce remission, preferred over corticosteroids for all children to promote mucosal healing according to consensus guidelines.<sup>87</sup> However, a Cochrane meta-analysis concluded that corticosteroid therapy was more effective than EEN in inducing remission for active CD.<sup>88</sup> In some studies, early EEN is effective in inducing clinical, biochemical, and mucosal remission and improves outcomes at 1 year.<sup>89-91</sup> Although EEN has been successfully used and proven to be highly effective,

it is often not preferred by patients due to the difficulty involved in administration. It may require tube feeding and typically consists of no food for 6 weeks. Furthermore, relapse is very common once the 6- to 8-week protocol is discontinued; most patients require concomitant use of immunosuppressive agents to achieve continued remission.

A recent study by Lee et al<sup>92</sup> compared partial enteral nutrition, EEN, and anti-TNF therapy in pediatric CD. Clinical response measured by reduction in clinical activity scores was 64% in the partial enteral nutrition group, 88% in the EEN group, and 84% in the anti-TNF group. Quality of life improvement was greatest in the EEN group.<sup>92</sup>

Dietary guidance is also a key part of the approach to pediatric patients with IBD. These patients should maintain a well-balanced diet and adequate hydration. Patients should be especially vigilant in warm weather when loss of salt and water is increased.<sup>93</sup> If tolerated, dairy products should be consumed to ensure adequate calcium intake. High fiber intake and processed fatty foods may cause increased symptoms and thus, should be avoided.<sup>94</sup> During flares, the CCFA recommends smaller more frequent meals, avoiding greasy foods, dairy, and high-fiber foods such as nuts, seeds, corn, and certain vegetables.<sup>93</sup> Increased consumption of bananas, white rice, plain cereals, pastas, electrolyte replacement sports drinks, cooked vegetables, and skinless potatoes may be better tolerated.<sup>93</sup> In addition, patients with irritable bowel syndrome-type symptoms including bloating or watery diarrhea may benefit from a low-FODMAP diet.

### PSYCHOSOCIAL HEALTH

Pediatric patients with IBD are susceptible to psychological distress that may be associated with disease flares, ongoing evaluations, and

**TABLE 1** Summary Checklist for the General Practitioners Caring for a Pediatric Patient With Inflammatory Bowel Disease

Intervention	Frequency
Measurement of height, weight, BMI, linear growth	Every visit
Bone health	
a) Bone age determination	At diagnosis if growth retardation is present At diagnosis and 6-mo intervals if abnormal.
b) DXA	Prompted by downward crossing of height or weight percentiles, amenorrhea, long-term glucocorticoid therapy, and clinically significant fractures
Minerals and vitamins	
a) Serum iron, ferritin, folic acid, vitamin D 25-OH, vitamin B12	At least yearly
b) Serum zinc level	At time of diagnosis
Vaccines	
a) Hepatitis A, hepatitis B, varicella*	Titers should be checked at time of diagnosis. If insufficient, revaccinate. (*only if not immunosuppressed)
b) Gardasil and pneumococcal vaccine	Within the first year of diagnosis, if not already given
c) Influenza	Yearly
Annual health care screening	
a) Latent TB infection	At diagnosis if starting anti-TNF
b) Ophthalmologic examination, including visual acuity, slit lamp examination, intraocular pressure measurements and examination of anterior and posterior chambers	Annually
c) Full-body skin examination	Annually

treatment. Up to 25% of adolescents with IBD expressed clinically significant symptoms of depression based on Children's Depression Index scores.<sup>11,95</sup> The Children's Depression Index is often used at the primary care level. Pediatric patients with IBD are also at increased risk of anxiety, family conflict, medical adherence issues, altered self-image, and isolation.<sup>2,95</sup> IBD is associated with poor sleep quality, which may adversely affect quality of life, especially in the adolescent population. This may negatively affect learning, memory, and school performance.<sup>96</sup> Practitioners should routinely ask about psychosocial changes and stress, screen for depression, and inquire about sleep hygiene.

Several instruments and tools are available at the subspecialist level to evaluate health-related quality of life in pediatric patients with IBD including the IMPACT III questionnaire, designed for patients with IBD 10 years or older,<sup>97</sup> and the IBD Quality of Life index (IBD-Q), in patients 18 years and older.<sup>98-100</sup> Such questionnaires help the clinician identify areas of concern and address these with appropriate psychosocial support when needed.<sup>95,101,102</sup>

### INTERNATIONAL TRAVEL

Traveling to foreign countries is associated with an increased risk of acquiring certain infectious diseases.<sup>16</sup> Primary care providers should be aware of the patient's immunization history, immunosuppressive medications, planned destination, duration of exposure, planned accommodations, food and water sources, and activities to administer appropriate vaccines and provide relevant counseling.

### Vaccinations for Foreign Travel

Inactivated vaccines such as parenteral typhoid, hepatitis A and B, Japanese encephalitis, rabies, cholera, polio, and meningococcal can be safely administered to pediatric patients with IBD and the primary care provider should follow the usual recommended schedule.<sup>25</sup> The inactivated typhoid and polio vaccines should be given to pediatric patients with IBD instead of the live vaccines. Literature is lacking regarding the efficacy of these vaccines in IBD, aside from the hepatitis A vaccine, which appears to be effective in this population.<sup>25,103</sup> Lower rates of seroconversion are

observed in patients on anti-TNF therapies.<sup>103</sup>

Yellow fever vaccination, a live vaccine, is contraindicated in patients with IBD who are immunocompromised.<sup>16,18</sup>

### Chemoprophylaxis for Travelers

Malaria is the most common cause of febrile illness in travelers.<sup>104</sup> Pediatric patients with IBD traveling to malaria-endemic areas should receive chemoprophylaxis on the basis of CDC guidelines. Primary care providers should consult with the pediatric gastroenterologist to ensure that there are no drug interactions between immunosuppressive medications.<sup>105</sup>

Another concern for the traveling pediatric patient with IBD is infectious diarrheal illness. Immunocompromised travelers are at higher risk for severe infection from bacteria and parasites.<sup>105</sup> Common microorganisms include enterotoxigenic *E coli*, *Salmonella*, *Campylobacter*, and *Shigella*. In cases of short-term travel, ciprofloxacin or rifaximin has been used for prophylaxis for gastrointestinal infections in adults.<sup>105,106</sup>

Azithromycin may be an appropriate alternative for fluoroquinolones in pediatric patients.

### Other Considerations for International Travel

Patients should be counseled about food and water safety, injury prevention, mosquito and insect avoidance, thrombosis prophylaxis, sexual precautions, high-altitude sickness, and medical emergencies.<sup>105</sup> Bottled water should be used rather than tap water when possible. When traveling, patients should carry a medication list and medical history and should identify medical centers in advance where they can seek care if needed. Patients and their families may wish to invest in medical evacuation insurance if possible.<sup>105</sup>

### CONCLUSIONS

There are many aspects to maintaining optimal health care maintenance for pediatric patients with IBD. Given the systemic nature of the disease, the related extraintestinal manifestations, and the risks associated with the various immunosuppressive therapies used to treat IBD, patients and their providers must remain vigilant about all aspects of physical and psychological health including monitoring growth, bone health, vitamin and mineral deficiencies, vaccination status, considerations for international travel, screening for depression, eye and skin health, endoscopic surveillance, TB screening and dietary recommendations (Table 1). The offices of pediatric gastroenterologists should consider having patient databases to keep track of visits, laboratory testing, and health care maintenance monitoring. A multidisciplinary team approach that is proactive is likely to ensure better outcomes for pediatric patients with IBD.

### ABBREVIATIONS

CCFA: Crohn's and Colitis Foundation of America  
CD: Crohn disease  
CDC: Centers for Disease Control and Prevention  
DXA: dual-energy radiograph absorptiometry  
EEN: exclusive enteral nutrition  
HPV: human papillomavirus  
IBD: inflammatory bowel disease  
IL: interleukin  
PCV13: 13-valent pneumococcal conjugate vaccine  
PPD: purified protein derivative  
PPSV23: 23-valent pneumococcal polysaccharide vaccine  
TB: tuberculosis  
TNF: tumor necrosis factor  
UC: ulcerative colitis  
ULN: upper limit of normal

### REFERENCES

- Griffiths AM. Specificities of inflammatory bowel disease in childhood. *Best Pract Res Clin Gastroenterol*. 2004;18(3):509–523
- Breglio KJ, Rosh JR. Health maintenance and vaccination strategies in pediatric inflammatory bowel disease. *Inflamm Bowel Dis*. 2013;19(8):1740–1744
- Rabizadeh S, Dubinsky M. Update in pediatric inflammatory bowel disease. *Rheum Dis Clin North Am*. 2013;39(4):789–799
- Dubinsky M. Special issues in pediatric inflammatory bowel disease. *World J Gastroenterol*. 2008;14(3):413–420
- Ahmed S, Siegel CA, Melmed GY. Implementing quality measures for inflammatory bowel disease. *Curr Gastroenterol Rep*. 2015;17(4):14
- Dubner SE, Shults J, Baldassano RN, et al. Longitudinal assessment of bone density and structure in an incident cohort of children with Crohn's disease. *Gastroenterology*. 2009;136(1):123–130
- Pappa H, Thayu M, Sylvester F, Leonard M, Zemel B, Gordon C. Skeletal health of children and adolescents with inflammatory bowel disease. *J Pediatr Gastroenterol Nutr*. 2011;53(1):11–25
- Malik S, Mason A, Bakhshi A, et al. Growth in children receiving contemporary disease specific therapy for Crohn's disease. *Arch Dis Child*. 2012;97(8):698–703
- Pfefferkorn M, Burke G, Griffiths A, et al. Growth abnormalities persist in newly diagnosed children with Crohn disease despite current treatment paradigms. *J Pediatr Gastroenterol Nutr*. 2009;48(2):168–174
- Pappa HM, Mitchell PD, Jiang H, et al. Maintenance of optimal vitamin D status in children and adolescents with inflammatory bowel disease: a randomized clinical trial comparing two regimens. *J Clin Endocrinol Metab*. 2014;99(9):3408–3417
- Rufo PA, Denson LA, Sylvester FA, et al. Health supervision in the management of children and adolescents with IBD: NASPGHAN recommendations. *J Pediatr Gastroenterol Nutr*. 2012;55(1):93–108
- Ma NS, Gordon CM. Pediatric osteoporosis: where are we now? *J Pediatr*. 2012;161(6):983–990
- Fleurier A, Pelatan C, Willot S, et al. Vaccination coverage of children with inflammatory bowel disease after an awareness campaign on the risk of infection. *Dig Liver Dis*. 2015;47(6):460–464
- Longuet R, Willot S, Giniès J-L, et al. Immunization status in children with inflammatory bowel disease. *Eur J Pediatr*. 2014;173(5):603–608
- Wasan SK, Calderwood AH, Long MD, Kappelman MD, Sandler RS, Farraye FA. Immunization rates and vaccine beliefs among patients with inflammatory bowel disease: an opportunity for improvement. *Inflamm Bowel Dis*. 2014;20(2):246–250
- Wilckens V, Kannengiesser K, Hoxhold K, Frenkel C, Kucharzik T, Maaser C. The immunization status of patients with IBD is alarmingly poor before the introduction of specific guidelines. *Scand J Gastroenterol*. 2011;46(7-8):855–861
- Desalermos AP, Farraye FA, Wasan SK. Vaccinating the inflammatory

- bowel disease patient. *Expert Rev Gastroenterol Hepatol*. 2015;9(1):91–102
18. Sands BE, Cuffari C, Katz J, et al. Guidelines for immunizations in patients with inflammatory bowel disease. *Inflamm Bowel Dis*. 2004;10(5):677–692
  19. Centers for Disease Control and Prevention. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among children aged 6–18 years with immunocompromising conditions: recommendations of the Advisory Committee on Immunization Practices (ACIP). Available at: [www.cdc.gov/mmwr/preview/mmwrhtml/mm6225a3.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6225a3.htm). Accessed April 1, 2015
  20. Sanchez DF, Cañete S, Fernández-Nestosa MJ, et al. HPV- and non-HPV-related subtypes of penile squamous cell carcinoma (SCC): morphological features and differential diagnosis according to the new WHO classification (2015). *Semin Diagn Pathol*. 2015;32(3):198–221
  21. Joura EA, Giuliano AR, Iversen O-E, et al; Broad Spectrum HPV Vaccine Study. A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women. *N Engl J Med*. 2015;372(8):711–723
  22. Ruel J, Ko M, Patil N, et al. Anal neoplasia in inflammatory bowel disease is associated with HPV and perianal disease. In: Abstracts of the 10th Congress of European Crohn's and Colitis Organisation; February 18–21, 2015; Barcelona, Spain. Abstract P402
  23. Peneau A, Savoye G, Turck D, et al. Mortality and cancer in pediatric-onset inflammatory bowel disease: a population-based study. *Am J Gastroenterol*. 2013;108(10):1647–1653
  24. Jacobson DL, Bousvaros A, Ashworth L, et al. Immunogenicity and tolerability to human papillomavirus-like particle vaccine in girls and young women with inflammatory bowel disease. *Inflamm Bowel Dis*. 2013;19(7):1441–1449
  25. Magro F, Abreu C. Immunisations in Crohn's disease: who? why? what? when? *Best Pract Res Clin Gastroenterol*. 2014;28(3):485–496
  26. Centers for Disease Control and Prevention. Use of 9-valent human papillomavirus (HPV) vaccine: updated HPV vaccination recommendations of the Advisory Committee on Immunization Practices. Available at: [www.cdc.gov/mmwr/preview/mmwrhtml/mm6411a3.htm?s\\_cid=mm6411a3\\_w](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6411a3.htm?s_cid=mm6411a3_w). Accessed June 20, 2016
  27. Fitzgerald MP, Armstrong L, Hague R, Russell RK. A case of EBV driven haemophagocytic lymphohistiocytosis complicating a teenage Crohn's disease patient on azathioprine, successfully treated with rituximab. *J Crohn's Colitis*. 2013;7(4):314–317
  28. Biank VF, Sheth MK, Talano J, et al. Association of Crohn's disease, thiopurines, and primary Epstein-Barr virus infection with hemophagocytic lymphohistiocytosis. *J Pediatr*. 2011;159(5):808–812
  29. Virdis F, Tacci S, Messina F, Varcada M. Hemophagocytic lymphohistiocytosis caused by primary Epstein-Barr virus in patient with Crohn's disease. *World J Gastrointest Surg*. 2013;5(11):306–308
  30. Calvo P, Pablo L. Managing IBD outside the gut: ocular manifestations. *Dig Dis*. 2013;31(2):229–232
  31. Ott C, Schölmerich J. Extraintestinal manifestations and complications in IBD. *Nat Rev Gastroenterol Hepatol*. 2013;10(10):585–595
  32. Felekis T, Katsanos K, Kitsanou M, et al. Spectrum and frequency of ophthalmologic manifestations in patients with inflammatory bowel disease: a prospective single-center study. *Inflamm Bowel Dis*. 2009;15(1):29–34
  33. Tripathi RC, Kipp MA, Tripathi BJ, et al. Ocular toxicity of prednisone in pediatric patients with inflammatory bowel disease. *Lens Eye Toxic Res*. 1992;9(3-4):469–482
  34. Tripathi RC, Kirschner BS, Kipp M, et al. Corticosteroid treatment for inflammatory bowel disease in pediatric patients increases intraocular pressure. *Gastroenterology*. 1992;102(6):1957–1961
  35. Hofley P, Roarty J, McGinnity G, et al. Asymptomatic uveitis in children with chronic inflammatory bowel diseases. *J Pediatr Gastroenterol Nutr*. 1993;17(4):397–400
  36. Mosca Andrew M, Mahadevan U, Kane S. General health maintenance in IBD. *Inflamm Bowel Dis*. 2009;15(9):1399–1409
  37. Mälkönen T, Wikström A, Heiskanen K, et al. Skin reactions during anti-TNF $\alpha$  therapy for pediatric inflammatory bowel disease: a 2-year prospective study. *Inflamm Bowel Dis*. 2014;20(8):1309–1315
  38. Perman MJ, Lovell DJ, Denson LA, Farrell MK, Lucky AW. Five cases of anti-tumor necrosis factor alpha-induced psoriasis presenting with severe scalp involvement in children. *Pediatr Dermatol*. 2012;29(4):454–459
  39. Sherlock ME, Walters T, Tabbers MM, et al. Infliximab-induced psoriasis and psoriasiform skin lesions in pediatric Crohn disease and a potential association with IL-23 receptor polymorphisms. *J Pediatr Gastroenterol Nutr*. 2013;56(5):512–518
  40. Ariyaratnam J, Subramanian V. Association between thiopurine use and nonmelanoma skin cancers in patients with inflammatory bowel disease: a meta-analysis. *Am J Gastroenterol*. 2014;109(2):163–169
  41. Borum ML, Preethi Sidhu H, Bornstein L. Physicians may inadequately counsel inflammatory bowel disease patients about immunosuppressive therapy and risk of nonmelanoma skin cancer. *Inflamm Bowel Dis*. 2011;17(5):1246
  42. Ramiscal JAB, Brewer JD. Thiopurines and risk of nonmelanoma skin cancer in inflammatory bowel disease. *JAMA Dermatol*. 2013;149(1):92–94
  43. Singh H, Nugent Z, Demers AA, Bernstein CN. Increased risk of nonmelanoma skin cancers among individuals with inflammatory bowel disease. *Gastroenterology*. 2011;141(5):1612–1620
  44. Singh S, Nagpal SJS, Murad MH, et al. Inflammatory bowel disease is associated with an increased risk of melanoma: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol*. 2014;12(2):210–218
  45. Andriole GL, Crawford ED, Grubb RL III, et al; PLCO Project Team. Mortality



- results from a randomized prostate-cancer screening trial. *N Engl J Med*. 2009;360(13):1310–1319
46. Beaugerie L, Itzkowitz SH. Cancers complicating inflammatory bowel disease. *N Engl J Med*. 2015;372(15):1441–1452
  47. Mantzaris GJ. Previous cancer and/or lymphoma in patients with refractory IBD—con: anti-TNF or conventional immunosuppressive treatment. *Dig Dis*. 2014;32(suppl 1):122–127
  48. Cohen L, Brown J, Haukness H, Walsh L, Robinson JK. Sun protection counseling by pediatricians has little effect on parent and child sun protection behavior. *J Pediatr*. 2013;162(2):381–386
  49. Lin JS, Eder M, Weinmann S. Behavioral counseling to prevent skin cancer: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2011;154(3):190–201
  50. Dotson J, Crandall W, Bout-Tabaku S. Exploring the differential diagnosis of joint complaints in pediatric patients with inflammatory bowel disease. *Curr Gastroenterol Rep*. 2011;13(3):271–278
  51. Pusateri AJ, Kim SC, Dotson JL, et al. Incidence, pattern, and etiology of elevated liver enzymes in pediatric inflammatory bowel disease. *J Pediatr Gastroenterol Nutr*. 2015;60(5):592–597
  52. Valentino PL, Feldman BM, Walters TD, et al. Abnormal Liver Biochemistry Is Common in Pediatric Inflammatory Bowel Disease: Prevalence and Associations. *Inflamm Bowel Dis*. 2015;21(12):2848–2856
  53. Shergill AK, Lightdale JR, Bruining DH, et al; American Society for Gastrointestinal Endoscopy Standards of Practice Committee. The role of endoscopy in inflammatory bowel disease. *Gastrointest Endosc*. 2015;81(5):1101–21.e1, 13
  54. Bousvaros A, Antonioli DA, Colletti RB, et al; Colitis Foundation of America. Differentiating ulcerative colitis from Crohn disease in children and young adults: report of a working group of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the Crohn's and Colitis Foundation of America. *J Pediatr Gastroenterol Nutr*. 2007;44(5):653–674
  55. Keane J, Gershon S, Wise RP, et al. Tuberculosis associated with infliximab, a tumor necrosis factor alpha-neutralizing agent. *N Engl J Med*. 2001;345(15):1098–1104
  56. Solovic I, Sester M, Gomez-Reino JJ, et al. The risk of tuberculosis related to tumour necrosis factor antagonist therapies: a TBNET consensus statement. *Eur Respir J*. 2010;36(5):1185–1206
  57. Ge L, Ma J-C, Han M, Li JL, Tian JH. Interferon- $\gamma$  release assay for the diagnosis of latent Mycobacterium tuberculosis infection in children younger than 5 years: a meta-analysis. *Clin Pediatr (Phila)*. 2014;53(13):1255–1263
  58. Hausteiner T, Ridout DA, Hartley JC, et al. The likelihood of an indeterminate test result from a whole-blood interferon-gamma release assay for the diagnosis of Mycobacterium tuberculosis infection in children correlates with age and immune status. *Pediatr Infect Dis J*. 2009;28(8):669–673
  59. Detjen AK, Keil T, Roll S, et al. Interferon-gamma release assays improve the diagnosis of tuberculosis and nontuberculous mycobacterial disease in children in a country with a low incidence of tuberculosis. *Clin Infect Dis*. 2007;45(3):322–328
  60. Sollai S, Galli L, de Martino M, Chiappini E. Systematic review and meta-analysis on the utility of Interferon-gamma release assays for the diagnosis of Mycobacterium tuberculosis infection in children: a 2013 update. *BMC Infect Dis*. 2014;14(suppl 1):S6
  61. Starke JR; Committee On Infectious Diseases. Interferon- $\gamma$  release assays for diagnosis of tuberculosis infection and disease in children. *Pediatrics*. 2014;134(6):e1763–e1773
  62. Hradsky O, Ohem J, Zarubova K, et al. Disease activity is an important factor for indeterminate interferon- $\gamma$  release assay results in children with inflammatory bowel disease. *J Pediatr Gastroenterol Nutr*. 2014;58(3):320–324
  63. Thayu M, Mamula P. Treatment of iron deficiency anemia in pediatric inflammatory bowel disease. *Curr Treat Options Gastroenterol*. 2005;8(5):411–417
  64. Gerasimidis K, Barclay A, Papangelou A, et al. The epidemiology of anemia in pediatric inflammatory bowel disease: prevalence and associated factors at diagnosis and follow-up and the impact of exclusive enteral nutrition. *Inflamm Bowel Dis*. 2013;19(11):2411–2422
  65. Sjöberg D, Holmström T, Larsson M, Nielsen AL, Holmquist L, Rönnblom A. Anemia in a population-based IBD cohort (ICURE): still high prevalence after 1 year, especially among pediatric patients. *Inflamm Bowel Dis*. 2014;20(12):2266–2270
  66. Stein J, Dignass AU. Management of iron deficiency anemia in inflammatory bowel disease - a practical approach. *Ann Gastroenterol*. 2013;26(2):104–113
  67. Skikne BS, Punnonen K, Caldron PH, et al. Improved differential diagnosis of anemia of chronic disease and iron deficiency anemia: a prospective multicenter evaluation of soluble transferrin receptor and the sTfR/log ferritin index. *Am J Hematol*. 2011;86(11):923–927
  68. Goodhand JR, Kamperidis N, Rao A, et al. Prevalence and management of anemia in children, adolescents, and adults with inflammatory bowel disease. *Inflamm Bowel Dis*. 2012;18(3):513–519
  69. Rizvi S, Schoen RE. Supplementation with oral vs. intravenous iron for anemia with IBD or gastrointestinal bleeding: is oral iron getting a bad rap? *Am J Gastroenterol*. 2011;106(11):1872–1879
  70. Erichsen K, Ulvik RJ, Nysaeter G, et al. Oral ferrous fumarate or intravenous iron sucrose for patients with inflammatory bowel disease. *Scand J Gastroenterol*. 2005;40(9):1058–1065
  71. Lindgren S, Wikman O, Befrits R, et al. Intravenous iron sucrose is superior to oral iron sulphate for correcting anaemia and restoring iron stores in IBD patients: A randomized, controlled, evaluator-blind, multicentre study. *Scand J Gastroenterol*. 2009;44(7):838–845
  72. Kulnigg S, Stoinov S, Simanenkov V, et al. A novel intravenous iron formulation for treatment of anemia

- in inflammatory bowel disease: the ferric carboxymaltose (FERINJECT) randomized controlled trial. *Am J Gastroenterol*. 2008;103(5):1182–1192
73. Alkhoury RH, Hashmi H, Baker RD, Gelfond D, Baker SS. Vitamin and mineral status in patients with inflammatory bowel disease. *J Pediatr Gastroenterol Nutr*. 2013;56(1):89–92
  74. Hwang C, Ross V, Mahadevan U. Micronutrient deficiencies in inflammatory bowel disease: from A to zinc. *Inflamm Bowel Dis*. 2012;18(10):1961–1981
  75. Vidal-Alaball J, Butler CC, Cannings-John R, et al. Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency. *Cochrane Database Syst Rev*. 2005; (3):CD004655
  76. Slot WB, Merkus FW, Van Deventer SJ, Tytgat GN. Normalization of plasma vitamin B12 concentration by intranasal hydroxocobalamin in vitamin B12-deficient patients. *Gastroenterology*. 1997;113(2):430–433
  77. Kosmowska-Miśków A. The role of vitamin D3 in inflammatory bowel diseases. *Adv Clin Exp Med*. 2014;23(4):497–504
  78. Veit LE, Maranda L, Fong J, Nwosu BU. The vitamin D status in inflammatory bowel disease. *PLoS One*. 2014;9(7):e101583
  79. Verlinden L, Leyssens C, Beullens I, et al. The vitamin D analog TX527 ameliorates disease symptoms in a chemically induced model of inflammatory bowel disease. *J Steroid Biochem Mol Biol*. 2013;136:107–111
  80. Goff JP, Koszewski NJ, Haynes JS, Horst RL. Targeted delivery of vitamin D to the colon using  $\beta$ -glucuronides of vitamin D: therapeutic effects in a murine model of inflammatory bowel disease. *Am J Physiol Gastrointest Liver Physiol*. 2012;302(4):G460–G469
  81. Cantorna MT, McDaniel K, Bora S, Chen J, James J. Vitamin D, immune regulation, the microbiota, and inflammatory bowel disease. *Exp Biol Med (Maywood)*. 2014;239(11):1524–1530
  82. Cantorna MT. Vitamin D, multiple sclerosis and inflammatory bowel disease. *Arch Biochem Biophys*. 2012;523(1):103–106
  83. Simek RZ, Prince J, Syed S, et al. Pilot Study Evaluating Efficacy of 2 Regimens for Hypovitaminosis D Repletion in Pediatric Inflammatory Bowel Disease. *J Pediatr Gastroenterol Nutr*. 2016;62(2):252–258
  84. Ojuawo A, Keith L. The serum concentrations of zinc, copper and selenium in children with inflammatory bowel disease. *Cent Afr J Med*. 2002;48(9-10):116–119
  85. Sikora SK, Spady D, Prosser C, El-Matary W. Trace elements and vitamins at diagnosis in pediatric-onset inflammatory bowel disease. *Clin Pediatr (Phila)*. 2011;50(6):488–492
  86. American Academy of Pediatrics Committee on Nutrition. Trace elements. In: Kleinman RE, Greer FR, eds. *Pediatric Nutrition*, 7th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2014:467–494
  87. Ruemmele FM, Veres G, Kolho KL, et al; European Crohn's and Colitis Organisation; European Society of Pediatric Gastroenterology, Hepatology and Nutrition. Consensus guidelines of ECCO/ESPGHAN on the medical management of pediatric Crohn's disease. *J Crohn's Colitis*. 2014;8(10):1179–1207
  88. Zachos M, Tondeur M, Griffiths AM. Enteral nutritional therapy for induction of remission in Crohn's disease. *Cochrane Database Syst Rev*. 2007; (1):CD000542
  89. Grover Z, Muir R, Lewindon P. Exclusive enteral nutrition induces early clinical, mucosal and transmural remission in paediatric Crohn's disease. *J Gastroenterol*. 2014;49(4):638–645
  90. Critch J, Day AS, Otley A, King-Moore C, Teitelbaum JE, Shashidhar H; NASPGHAN IBD Committee. Use of enteral nutrition for the control of intestinal inflammation in pediatric Crohn disease. *J Pediatr Gastroenterol Nutr*. 2012;54(2):298–305
  91. Frivolt K, Schwerdt T, Werkstetter KJ, et al. Repeated exclusive enteral nutrition in the treatment of paediatric Crohn's disease: predictors of efficacy and outcome. *Aliment Pharmacol Ther*. 2014;39(12):1398–1407
  92. Lee D, Baldassano RN, Otley AR, et al. Comparative Effectiveness of Nutritional and Biological Therapy in North American Children with Active Crohn's Disease. *Inflamm Bowel Dis*. 2015;21(8):1786–1793
  93. Crohn's and Colitis Foundation of America. Diet and nutrition. Available at: [www.cffa.org/resources/diet-and-nutrition.html](http://www.cffa.org/resources/diet-and-nutrition.html). Accessed June 20, 2016
  94. Richman E, Rhodes JM. Review article: evidence-based dietary advice for patients with inflammatory bowel disease. *Aliment Pharmacol Ther*. 2013;38(10):1156–1171
  95. Szigethy E, McLafferty L, Goyal A. Inflammatory bowel disease. *Child Adolesc Psychiatr Clin N Am*. 2010;19(2):301–318, ix [ix.]
  96. Dewald JF, Meijer AM, Oort FJ, Kerkhof GA, Bögels SM. The influence of sleep quality, sleep duration and sleepiness on school performance in children and adolescents: A meta-analytic review. *Sleep Med Rev*. 2010;14(3):179–189
  97. Otley A, Smith C, Nicholas D, et al. The IMPACT questionnaire: a valid measure of health-related quality of life in pediatric inflammatory bowel disease. *J Pediatr Gastroenterol Nutr*. 2002;35(4):557–563
  98. Ciccocioppo R, Klersy C, Russo ML, et al. Validation of the Italian translation of the Inflammatory Bowel Disease Questionnaire. *Dig Liver Dis*. 2011;43(7):535–541
  99. Surti B, Spiegel B, Ippoliti A, et al. Assessing health status in inflammatory bowel disease using a novel single-item numeric rating scale. *Dig Dis Sci*. 2013;58(5):1313–1321
  100. Irvine EJ, Feagan B, Rochon J, et al; Canadian Crohn's Relapse Prevention Trial Study Group. Quality of life: a valid and reliable measure of therapeutic efficacy in the treatment of inflammatory bowel disease. *Gastroenterology*. 1994;106(2):287–296
  101. Abdovic S, Mocić Pavić A, Milosević M, Persić M, Senecić-Gala I, Kolacek S. The IMPACT-III (HR) questionnaire: a valid measure of health-related quality of life in Croatian children with inflammatory bowel disease. *J Crohn's Colitis*. 2013;7(11):908–915

102. Werner H, Landolt MA, Buehr P, et al; Swiss IBD Cohort Study Group. Validation of the IMPACT-III quality of life questionnaire in Swiss children with inflammatory bowel disease. *J Crohn's Colitis*. 2014;8(7):641–648
103. Park SH, Yang S-K, Park S-K, et al. Efficacy of hepatitis A vaccination and factors impacting on seroconversion in patients with inflammatory bowel disease. *Inflamm Bowel Dis*. 2014;20(1):69–74
104. Freedman DO, Weld LH, Kozarsky PE, et al; GeoSentinel Surveillance Network. Spectrum of disease and relation to place of exposure among ill returned travelers. *N Engl J Med*. 2006;354(2):119–130
105. Patel RR, Liang SY, Koolwal P, Kuhlmann FM. Travel advice for the immunocompromised traveler: prophylaxis, vaccination, and other preventive measures. *Ther Clin Risk Manag*. 2015;11:217–228
106. Leder K. Advising travellers about management of travellers' diarrhoea. *Aust Fam Physician*. 2015;44(1-2):34–37

## Health Care Maintenance for the Pediatric Patient With Inflammatory Bowel Disease

Ersilia M. DeFilippis, Robbyn Sockolow and Elaine Barfield

*Pediatrics* 2016;138;

DOI: 10.1542/peds.2015-1971 originally published online August 3, 2016;

### Updated Information & Services

including high resolution figures, can be found at:  
<http://pediatrics.aappublications.org/content/138/3/e20151971>

### References

This article cites 101 articles, 3 of which you can access for free at:  
<http://pediatrics.aappublications.org/content/138/3/e20151971.full#ref-list-1>

### Subspecialty Collections

This article, along with others on similar topics, appears in the following collection(s):  
**Gastroenterology**  
[http://classic.pediatrics.aappublications.org/cgi/collection/gastroenterology\\_sub](http://classic.pediatrics.aappublications.org/cgi/collection/gastroenterology_sub)  
**Infectious Disease**  
[http://classic.pediatrics.aappublications.org/cgi/collection/infectious\\_diseases\\_sub](http://classic.pediatrics.aappublications.org/cgi/collection/infectious_diseases_sub)  
**Vaccine/Immunization**  
[http://classic.pediatrics.aappublications.org/cgi/collection/vaccine\\_immunization\\_sub](http://classic.pediatrics.aappublications.org/cgi/collection/vaccine_immunization_sub)

### Permissions & Licensing

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:  
<https://shop.aap.org/licensing-permissions/>

### Reprints

Information about ordering reprints can be found online:  
<http://classic.pediatrics.aappublications.org/content/reprints>

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since . Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2016 by the American Academy of Pediatrics. All rights reserved. Print ISSN:

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



# PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

## **Health Care Maintenance for the Pediatric Patient With Inflammatory Bowel Disease**

Ersilia M. DeFilippis, Robbyn Sockolow and Elaine Barfield  
*Pediatrics* 2016;138;

DOI: 10.1542/peds.2015-1971 originally published online August 3, 2016;

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://pediatrics.aappublications.org/content/138/3/e20151971>

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since . Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2016 by the American Academy of Pediatrics. All rights reserved. Print ISSN:

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

