While those ages 6-17 demonstrated a statistically significant increase in small bowel involvement, predominantly ileocolonic in nature. Furthermore, older children had a more complicated disease course with increased risk for the development of an abscess, fistula, or stricture. While medical management of IBD is preferred, children with extensive disease are at risk for surgical interventions such as intestinal resection. In a retrospective study using data from six IBD centers, Gupta et al. observed surgical rates of 5.7% at one year, 17% at five years and 28.4% at ten years in pediatric CD. Prospective data from the Pediatric IBD Registry showed a 5% rate of Crohn's related surgery at 1 year and 13% at 4 years. Thus, although treatment of CD primarily is medical, many patients will require surgery at some point.

Communication with the child's school can be as important an intervention as providing medication.

**Clinical Presentation**

The clinical presentation of IBD typically involves chronic abdominal pain accompanied by some combination of weight loss, diarrhea, or hematochezia. (Table 1) Additionally, some patients may present with (or later develop) extra-intestinal manifestations. (Table 2) In the pediatric population, malnutrition, growth failure, and pubertal delay can be a significant component of disease presentation and morbidity. Between 25-80% of children newly diagnosed with CD will present with some degree of linear growth impairment. This may be attributed to sub-optimal oral intake, chronic inflammation and protein-losing enteropathy. The effects of corticosteroid treatment and chronically elevated inflammatory cytokines may further impair growth. Population trends towards normal laboratory values (hemoglobin, platelet count, albumin, and ESR) were present in 21% of patients with mild CD and 54% with mild UC. This suggests that the diagnosis of IBD should still be pursued in the patient with a clinical presentation consistent with IBD but with normal laboratory values.

**Laboratory Assessment**

Laboratory evaluation of a patient with suspected IBD tends to focus on signs of chronic disease; e.g., microcytic anemia or hypoalbuminemia, as well as acute phase reactants such as ESR, C-reactive protein (CRP), and thrombocytosis. These tests can establish the presence of an inflammatory illness. Recent IBD consortium data show that among children presenting with mild (more diagnostically challenging) disease, normal laboratory values (hemoglobin, platelet count, albumin, and ESR) were present in 21% of patients with mild CD and 54% with mild UC. This suggests that the diagnosis of IBD should still be pursued in the patient with a clinical presentation consistent with IBD but with normal laboratory values.

**Measurement of Disease Activity**

Pediatric gastroenterologists have used the subjective Physicians Global Assessment (PGA) for many years. For both clinical application and research purposes, objective quantitative tools to measure disease activity are crucial. Objective assessment of disease activity in children with CD now includes evaluation of pubertal status and the Pediatric Crohn's Disease Activity Index (PCDAI). Assessment of pubertal status is performed clinically by assessing the appearance of secondary sex characteristics. The standard measurement used by pediatricians is the Tanner Stage, based on physical examination findings that focus on gender-specific changes that occur during breast, gonadal, and pubic hair development. A consensus of pediatric IBD experts developed the PCDAI in 1990; it was subsequently validated at 12 North American institutions. In comparison to the (adult) CDAI, the PCDAI decreases the importance given to subjective historical items adding instead height velocity, and adds ESR and albumin to the laboratory measurements. The PCDAI score range from 0-100: a score
The importance of successful induction and maintenance of remission is stressed by the data. The challenge is finding the balance between aggressive disease management and acceptable risk to the patient.

IBD Management in the Pediatric Patient

While generally the goals of managing IBD in children and adults are similar, there are important differences, based on the developmental stages of the patient. Therapeutic goals focus on achieving symptomatic control and mucosal healing; however, the social implications of chronic steroid exposure (i.e., cushingoid features and facial acne) are significant in the pediatric patient. A diagnosis of IBD in the pediatric patient has the potential to have devastating effects on quality of life.

In evaluating health-related quality of life (HRQOL) in the first year after diagnosis, the pediatric IBD registry administered a validated questionnaire (IM-PACT II) to 218 patients over the age of nine. Initial assessment demonstrated expected significant differences between those presenting with mild, moderate, and severe disease phenotypes. However, re-evaluation at 6 months and again at 1 year demonstrated statistically significant improvements in HRQOL overall. These data stressed the importance of successful induction and maintenance of remission. The challenge is finding the balance between aggressive disease management and acceptable risk to the patient.

Psychosocial Aspects of Disease

Symptomatic disease can result in frequent, sometimes prolonged hospitalizations requiring school absence. Some children face frequency and urgency to move their bowels, an embarrassing situation if they are unable to access a private restroom at school. Communication with the child’s school can be as important an intervention as providing medication.

Furthermore, recent data suggest that adolescents may have less than 50% adherence to IBD drug regimens. While the younger child may focus on symptomatic complaints, teenagers often struggle with regimented medication schedules and the social implications of chronic steroid exposure (i.e., cushingoid features and facial acne). A diagnosis of IBD in the pediatric patient has the potential to have devastating effects on quality of life.

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Table 2 Extraintestinal Manifestations of Inflammatory Bowel Disease

<table>
<thead>
<tr>
<th>Site</th>
<th>Manifestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>Erythema nodosum, pyoderma gangrenosum, metastatic Crohn’s disease (especially around mucous membranes)</td>
</tr>
<tr>
<td>Liver</td>
<td>Steatosis, non-specific transaminitis, chronic hepatitis, sclerosing cholangitis, cholestasis, acauleus cholecytitis, Budd-Chiari syndrome</td>
</tr>
<tr>
<td>Bone</td>
<td>Osteopenia, aseptic necrosis</td>
</tr>
<tr>
<td>Joint</td>
<td>Arthroalgia, arthritis, ankylosing spondylitis, sacroilitis</td>
</tr>
<tr>
<td>Eye</td>
<td>Uveitis, episcleritis, keratitis, glaucoma (2° to steroids)</td>
</tr>
<tr>
<td>Urinary-gynecologic</td>
<td>Nephrolithiasis, obstructive hydronephrosis, enterovesical fistula, recto-vaginal fistula, nephritis, amyloidosis</td>
</tr>
<tr>
<td>Hematologic</td>
<td>Anemia (iron, folate, B12, autoimmune hemolytic), thrombocytosis, thrombocytopenia</td>
</tr>
<tr>
<td>Vascular</td>
<td>Hypercoagulability (thrombosis, trombophileitis, portal vein thrombosis, sinus vein thrombosis)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Other</td>
<td>Growth delay/failure, pubertal delay, menstrual irregularities, increased risk of colonic malignancy with chronic inflammation (sympotoma 2° to meds)</td>
</tr>
</tbody>
</table>
Table 3 Commonly used Pharmacologic Therapy of Inflammatory Bowel Disease in Children (note: * denotes not an approved use for children)

<table>
<thead>
<tr>
<th>Medications</th>
<th>Indications</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminosalicylates (*mesalamine, *mesalamin)</td>
<td>Mild-to-moderate UC, mild Crohn’s colitis, or mild distal small bowel disease</td>
<td>Rash, headache, vomiting, dyspepsia, bloody stools, pancreatitis, alopecia</td>
</tr>
<tr>
<td>Corticosteroids (*prednisone, *budesonide)</td>
<td>Budesonide: Mild-to-moderate distal small bowel and proximal colon (CD); Prednisone: moderate-to-severe UC or CD</td>
<td>Crusting of skin, growth suppression, osteoporosis, hypertension, acne, potential adrenal crisis if not appropriately weaned</td>
</tr>
<tr>
<td>Antibiotics (*metronidazole, *ciprofloxacin, *ceftazidime)</td>
<td>Perirectal fistula, abscess, pseudomembranes (CD), bacterial overgrowth</td>
<td>Diarrhea, c. difficile, development of resistant organisms</td>
</tr>
<tr>
<td>Immunomodulators (*6-mercaptopterine, *azathioprine, *methotrexate)</td>
<td>Severe small or large bowel disease, steroid-dependent or refractory disease, severe fistula, growth failure (CD or UC)</td>
<td>Bone marrow suppression, pancreatitis, hepatitis, infection</td>
</tr>
<tr>
<td>Biologic therapy (*infliximab, *adalimumab, *certolizumab pegol)</td>
<td>Steroid-dependent or refractory CD, perirectal fistula, maintenance of remission</td>
<td>Hypersensitivity reactions, infection, autoimmune disease</td>
</tr>
</tbody>
</table>

The “biological” therapies represent the next level of medical management of IBD. The principle biological agents are monoclonal antibodies against the inflammatory cytokine tumor necrosis factor alpha (TNF-alpha). These medications offer much potential benefit to the steroid-dependent or refractory patient. The major concern is immunosuppression and risk of secondary infections. The appropriate role of biological agents (infliximab, adalimumab as well as newer agents) is the subject of active and ongoing study. Of concern, however, are reports of lymphoproliferative disease such as the highly fatal hepatosplenic T-cell lymphoma associated with infliximab exposure. The majority of the reported cases involved patients who were receiving concomitant therapy with immunomodulators such as 6-MP or systemic steroids. Thus, the true long-term risks of lymphoma and other malignancies in children receiving TNF inhibitors are unknown (but are generally estimated at about 1:1000 medication recipients).

With no definitive way to manage the child with IBD, there is marked variability among centers. Kappelman et al. demonstrated statistically significant inter-center variation in utilization of the five classes of medications most commonly used to manage pediatric CD (immunomodulators, steroids, antibiotics, 5-ASA compounds, and biologics such as infliximab). An underlying theme in these management strategies is minimizing exposure to corticosteroids. While treatment must be individualized, so far differences in outcome have not been associated with the different approaches.

Ongoing Research

Today, optimal care for children with IBD requires a multi-disciplinary team of physicians, nurses, clinical nutritionists, social workers, and child psychologists. Current research efforts are trying to address the lack of understanding of the natural history of IBD in the child as well as the role of the newest therapies (as well as many of the old standby therapies). This can be especially challenging since most therapies have never been specifically approved for use in the pediatric age group. The pediatric IBD registry follows over 1000 children with IBD. In the first 5 years since its inception in 2002, this consortium has been responsible for several major research papers describing aspects of the natural history of IBD. The division of Pediatric Gastroenterology at Hasbro Children’s Hospital has enrolled over 90 patients and is the second largest contributor to the registry. Most recently the Ocean State Crohn's
and Colitis Area Registry study has been launched in Rhode Island (OSCCAR). OSCCAR is a prospective study of an inception cohort of newly diagnosed adult and pediatric patients in Rhode Island (see previous issue, “introduction to OSCCAR”). OSCCAR promises to provide a wealth of new and exciting information into the natural history of IBD. Taken together, OSCCAR and the Pediatric Collaborative Research Consortium will provide new insights into IBD epidemiology, genomics, metabolomics, microbiology, pathophysiology and environmental determinants of disease susceptibility.

**FUTURE DIRECTIONS**

A consortium of pediatric IBD centers, including members of the IBD registry, recently reported that the rate of complicated CD increases in children as the number and magnitude of immune reactivity assays increase. Disease progression is significantly faster in children expressing immune reactivity. Whether these results will have practical consequences remains to be seen. However, this could be a powerful indicator of one’s future clinical course. As can be appreciated from this review, much of the newest data emphasize the role of studies such as the Pediatric IBD registry and OSCCAR. While both these studies are based on the biological determinants of disease, they lack focus on the equally important psychological components. Establishment of a prospective behavioral health registry that will provide knowledge from an integrated biopsychosocial model perspective is anticipated in the near future. Thus, the ongoing analysis of prospectively acquired data promises to provide much insight into the natural history of IBD and inform us about the most effective therapeutic strategies.

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**Disclosure of Financial Interests**

The authors have no financial interests to disclose.

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