INFLAMMATORY BOWEL DISEASE
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Inflammatory bowel disease (IBD) is a chronic inflammatory disorder affecting the small intestine and colon, and characterized by relapses and remissions. It afflicts an estimated 500,000-2,000,000 people in the United States. The incidence of IBD is approximately equal in men and women. Most research has found the greatest onset in adolescence and the young adult years, although there is a second peak incidence between the ages of 50 and 60. Idiopathic IBD is classified as two major disease entities:

- **Ulcerative colitis (UC)** is a mucosal inflammation that affects only the colon; it may involve the entire colon or only the rectum or distal colon. Its characteristic feature is diffuse, symmetric ulceration of the colonic mucosa, extended proximally from the rectum. The severity of the inflammation can vary, and is reflected in the degree of granularity, friability, bleeding and exudation. Bloody diarrhea associated with mucosal inflammation is a classic symptom: Other symptoms include urgency, tenesmus, weight loss, fatigue, fever and night sweats.
- **Crohn's disease (CD)**, in contrast to UC, can affect any segment of the gastrointestinal tract. It most often presents in the ileum (ileitis), the ileum and the colon (ileocolitis) or colon alone (Crohn's colitis). Patients with CD typically have diarrhea, abdominal pain and weight loss; bleeding also often occurs. The clinical course of CD varies from one patient to another, and is dependent on factors such as the portion of the alimentary tract that is effected and the intensity of the inflammatory processes. Although exacerbations and remissions are difficult to predict, nearly all patients experience a recurrence within 10 years of the first episode.

Management Strategies:
There are numerous treatment approaches to inducing and maintaining remission in patients with IBD. These treatments may be divided into several classes:

1. **Corticosteroids**: Although useful in inducing remission, they have not been shown to maintain remission. The side-effects of prolonged use of corticosteroids are quite daunting. These include not merely weight gain and water retention, but susceptibility to infection, adrenal gland suppression, aseptic vascular necrosis of the joints, cataracts and osteoporosis. Moreover, while high dose intravenous steroids can induce remission, their efficacy is decreased if the patient has been treated with oral steroids. Lastly, patients may develop not only steroid-induced IBD (inability to taper off steroids without inducing an exacerbation), but steroid dependent IBD (no response to re-administered or increased doses of steroids) as well.

2. **Five Amino Salicylic Acid (5-ASA) Product**: The original 5-ASA product was sulfasalazine. Sulfasalazine is a drug with an active part bonded to an inactive part. When ingested orally, sulfasalazine is largely unabsorbed from the small intestine and delivered in tact to the colon, where the bond is split by bacteria to release the 5-ASA, which acts topically on inflamed colonic mucosa. It may act by one of the following mechanisms: Inhibiting leukotriene synthesis, inhibiting granulocyte activation or scavenging reactive oxygen metabolites. Newer preparations (i.e. Asacol, Pentasa and Dipentum) have different areas of distribution and activity and less side-effects. Moreover, enema & suppository forms for distal proctitis exists. Recurrence rates may drop by 40-60% in IBD patients using these products.

3. **Antibiotics**: Metronidazole remains a useful drug in the treatment of colonic and perineal Crohn's disease and pouchitis. Dramatic healing may be seen in perianal disease, rectovaginal fistulas and complex perineal abscesses. Toxicity is common and long-term efficacy is debated.

4. **Immunomodulatory Agents**: Some patients with IBD do not respond to steroids and 5-ASAs. In refractory cases, azathioprine and 6-mercaptopurine are used. These agents may be used to decrease and eliminate steroids and to maintain remission. These medications take 3-6 months to achieve optimal therapeutic benefit. Exacerbations in patients taking these medications tend to be milder. A recent study revealed that post resection patients stay in remission longest when treated with 6-mercaptopurine as opposed to those treated with a 5-ASA product or a placebo. The study did not compare those treated with both 6-mercaptopurine and a 5-ASA product versus treatment with a single agent. The duration of treatment is debated. Nevertheless, one ongoing study seems to point to continuous treatment as opposed to stopping the drug after 5 years.

5. **Cyclosporine** is a potent immunosuppressive agent often used in organ transplant recipients. Intravenous cyclosporine has been used in severe refractory ulcerative colitis to prevent or delay colostomy. Although the onset of action is quick (within 14 days), the long-term efficacy in an oral form is disheartening. It can be used as a bridge while awaiting the onset of action of 6-Mercaptopurine. It may also be of use in patients with fistulous Crohn's disease.

6. **Methotrexate** may induce remission. However, the duration is limited in contrast to that of 6-mercaptopurine.

7. **Anti-tumor necrosis factor (anti-TNF, Remicade, Infliximab)** is an intravenous infusion of a monoclonal antibody which is approved for use in severe steroid-resistant Crohn's disease patients, as well as patients with fistulous Crohn's disease. Trials to date reveal a significant improvement in these patient populations after having been given one to three administrations of these 2-hour infusions. Studies to date compare patients at 12 weeks after treatment. Although 81% of the patients displayed significant, if not complete, remission at the end-point of the study, long-term efficacy is unknown. However, the initial reports and my own experience are quite heartening. In conjunction with previous medications, anti-tumor necrosis factor infusion is a formidable, yet underutilized weapon.

The Borland Groover Clinic is involved in active clinical research with respect to new drugs and approaches to the management of inflammatory bowel disease.

In summary, IBD is a spectrum of illnesses that is characterized not merely by abdominal pain and diarrhea, but loss of quality of life and hope. These are not patient cases, these are unrelenting, heartbreaking stories of people who are faced with years of seemingly futile battles against their own bodies. These are our neighbors who, after a while, do not even dream of a life without pain. Thankfully, these people, who previously had no recourse other than resection after resection, are now offered not just hopeful platitudes, but drugs that work. With newer medications and aggressive application of older ones, we can help in their nightmare.