THERAPY UPDATE

Antibiotics in Crohn's disease

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There have been several reviews recently on the efficacy of antibiotics in Crohn's disease, and no text on inflammatory bowel disease is complete without a chapter that addresses this issue. This is perhaps an unanticipated sequel to the *Mycobacterium paratuberculosis* story of the 1980s, because prior to that putative viruses held our attention and antibiotics were seldom considered. The *M paratuberculosis* initiative prompted renewed use of antituberculosis regimens—some of which succeeded some of the time—and there followed a notion that if combinations of antituberculosis antibiotics were beneficial, maybe other broad spectrum antibiotics would be as well. Those who wish to make judgements about drug dose, duration, etc, for the various forms of Crohn's disease may consult recent reviews and their summary tables,[1 2] but the difficulties encountered will become apparent. No two Crohn's disease patients are the same, and no two clinics group them the same for therapy trials. Various parameters are used to measure efficacy in small, mostly open, trials, and there are variations in what authors choose to call success.

Current medical management is often successful in the treatment of superficial and short term manifestations of Crohn's disease, and even fistulas. The evidence appears to show that anaerobes play an important role in perianal disease and fistulas and that therefore metronidazole should be effective—and it is in the majority of patients.[3] There is also evidence that acute flare ups have some bacterial components. These are responsive to ciprofloxacin or metronidazole, alone or in combination.[4 5]

A different problem, and one for which we all seek a solution, is the new onset or recurrence of intestinal disease. For the patient, that process we call Crohn's disease has been long in incubation and latency, perhaps months or years, and it is unrealistic to expect that its resolution can occur in any less time, under the best of medical circumstances. Similar to what happens in Whipple's disease, intestinal malakoplakia, or intestinal tuberculosis, once effective antibacterial therapy has been initiated, time is required for the ulcers to heal, for lymphocytes and plasma cells to decrease in number, for macrophages and giant cells to die, and for lymphatics to clear or otherwise re-establish patency. If long term therapy is to be tested, the antibiotics chosen must be selected wisely to ensure freedom from side effects, activity against extracellular and intracellular bacteria,[6] and broad spectrum efficacy against, for now, the organisms we know to be participants—*Escherichia coli*, enterococci, *Bacteroides*, and the fistula forming anaerobes.[7 8] Lesions will undoubtedly improve over time if inflammation is reduced, if oedema is resolved, and if antibiotics eliminate intramural bacteria and prevent the influx of new ones. A synergistic combination of immunosuppressors and antibacterial drugs is thus compelling although it has never been formally tested.

The pathology of Crohn's disease, the likely primary and known secondary pathogens in this disease, and the successful responses in animal models all plead for trials of antibiotics in Crohn's disease.[9] This is a call to select patients more carefully, and to continue antibiotics for longer than is customary. Patients should be stratified according to pathological type,[10] and perhaps genetic and bacteriological markers.

Key points

- Evidence of bacterial participation calls for the use of antibiotics in Crohn's disease.
- The chronicity of the intestinal lesions calls for long term treatment.
- Antibiotics should be broad spectrum, free of side effects, and active intracellularly.
- Anti-inflammatory drugs and immunosuppressors can be synergistic with antibiotics.
- Patients need to be stratified to evaluate efficacy correctly.

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