Antibiotic Use in Crohn’s Disease
Why and How?

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Contents

Summary .................................................................................................................. 293
1. Rationale for the Use of Antibiotics in Crohn’s Disease ........................................ 294
2. Bacteria as a Primary Cause of Crohn’s disease ...................................................... 295
   2.1 Evidence ........................................................................................................ 295
   2.2 Effect of Antimycobacterial Therapies .............................................................. 295
3. Bacteria as a Cause of Relapse in Crohn’s Disease .................................................. 297
4. Role of Intestinal Flora ......................................................................................... 298
5. Antibiotic Treatment in Crohn’s Disease ............................................................... 298
   5.1 Broad Spectrum Antibiotics ........................................................................... 299
   5.2 Metronidazole ............................................................................................... 299
   5.3 Ciprofloxacin ............................................................................................... 301
6. Conclusion ........................................................................................................... 303

Summary

On the assumption that bacteria in the gut may be a cause of symptoms and/or complications of Crohn’s disease, various antibiotics are efficaciously employed in some affected patients. However, we do not know exactly why and how they are helpful. A possible explanation is that one or several bacterial species may have a primary role in the aetiology of Crohn’s disease, but this is not supported by the data in our possession. Another hypothesis is that intestinal bacteria may cause flare-up of the disorder, either by inducing intestinal lesions or by an interaction with the immune system, but we know today that specific pathogens can cause flares only in a minority of cases. On the contrary, there is considerable evidence that the intestinal microflora and its products may amplify and perpetuate inflammation in Crohn’s disease.

Despite the fact that few controlled trials have been conducted, and have shown inconclusive results, antibiotics are widely employed for improving symptoms and for inducing remission of active phases. At present, a combination of metronidazole and ciprofloxacin, active against many enteric bacteria, has proved to be effective in the treatment of Crohn’s disease complications. This therapy also seems to be effective in acute flares as an alternative to, or in combination with, corticosteroids.

Crohn’s disease is a chronic intestinal inflammatory disease of unknown origin. In human pathology, chronic non-neoplastic diseases of the intestine are generally considered to be of immunological origin. Consequently, and similarly to chronic inflammatory diseases of other organs,
they are mainly treated with corticosteroids and/or other immunosuppressive drugs. Many experienced clinicians, however, despite scant supporting data for the efficacy of antibiotics in Crohn’s disease, employ different types of antibiotics in their clinical practice, and consider their use helpful for improving symptoms and inducing remission of active phases. The rationale for this empirical use is based on the clinical picture which Crohn’s disease patients often present – abscesses, pus in the stools, fever and toxic signs – all of which suggest a bacterial participation in the process. There are, however, other less empirical justifications for the use of antibiotics.

1. Rationale for the Use of Antibiotics in Crohn’s Disease

Other chronic intestinal diseases characterised by diarrhoea, such as Whipple’s disease and tropical sprue, are successfully treated with antibiotics. Minocycline and other antibiotics have been shown to be effective in the treatment of rheumatoid arthritis, a chronic inflammatory disease of the joints that shares other treatments with Crohn’s disease. Metronidazole prevented chemically induced arthritis in rats being reactivated by bacterial overgrowth. The usual improvement of acute phase reactants, and especially of C-reactive protein (CRP), during the antibiotic treatment of active phases of Crohn’s disease is similar to that seen with treatment of chronic bacterial infection such as bacterial endocarditis or chronic osteomyelitis.

Moreover, Crohn’s disease lesions are usually located in upstream valves, and it is well known that bacteria overgrow in areas where the flow of bowel content slows down. The diversion of faecal stream heals Crohn’s disease lesions; this has recently been shown in a study in which patients in whom a terminal ileostomy was constructed proximally to ileo-colo anastomosis did not experience recurrent disease until the ileostomy was closed.

Fistulisation, a pathological characteristic of Crohn’s disease, is less frequent when the disease is localised in the jejunum than in the terminal ileum and the colon, where the bacteria concentration is higher. In fact, antibiotics are successfully employed in the treatment of perianal fistulae and seem to be helpful in the management of entero-enteric and enterocutaneous fistulae. Moreover, some mycobacterial diseases such as intestinal tuberculosis and Johne’s disease, a chronic, wasting enteritis of ruminants caused by Mycobacterium paratuberculosis, show pathological characteristics similar to those of Crohn’s disease. M. avium intracellulare has been identified as the cause of intestinal lesions identical to Crohn’s disease in patients with AIDS. Other infective agents cause ileal and colonic lesions in various animals similar to lesions of Crohn’s disease.

| Table I. Results of trials of antimycobacterial therapy in Crohn’s disease |
|-----------------------------|-----|------------------|-------------------|-------------------|-------------------|
| **Drugs**                  | n   | **Duration of treatment (mo)** | **Control**       | **Remission (%)** | **Reference** |
| Sulphadoxine + pyrimethamine | 51  | 12               | Placebo           | 33                | 41.6            | 60               |
| Rifampicin + ethambutol     | 27  | 12               | Placebo           | 48                | 25             | 66               |
| Rifampicin + isoniazid + pyrazinamide or clofazimine | 20  | 9                | Placebo           | 50                | 63             |                  |
| Rifabutin                   | 24  | 6                | Placebo           | 41.7              | 50             | 71               |
| Clofazimine                 | 49  | 12               | Placebo           | 48                | 25             | 66               |
| Rifabutin + ethambutol      | 16  | 12               | Placebo           | 50                | 22.2           | 67               |
| Rifampicin + ethambutol + isoniazid | 126 | 24              | Placebo           | 71.4              | 12.5           | 69               |
| Ethambutol + clofazimine + dapsone + rifampicin | 40  | 9                | Placebo           | 50                | 22.2           | 67               |

**Abbreviations:** n = number of patients; NS = not significant.