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Inflammatory Bowel Disease: medical vs surgical vs "sociological" treatments

The human gut continuously hosts an excess of white blood cells in its wall thickness, this lingering inflammation serving to protect us from the outer world that uses the gut as an invading pathway. Unchecked gut inflammation delineates the picture of Inflammatory Bowel Disease (IBD); IBD localizing preferentially to the colon mucosa is named Ulcerative Colitis (UC), the leading topic of this summary.

Clinics and Epidemiology
UC typically presents with bloody diarrhea *hitting civilized societies.* Of the 1.6 million Americans affected by IBD, some 900,000 are reported with UC, which therefore seems to be more common than Crohn's Disease, the other IBD presentation.

Classical treatment of UC
For decades after its description in 1859, UC has remained an ominous acute disorder because of unchecked gut bleeding. In the 1940's, adrenal corticosteroids (cortisone) were made available for injection and were used for treatment of a group of patients with severe UC. The results of this trial, first published in the UK, claimed a 60% response rate, with a number of responders being maintained in a state of chronic acceptable disease.

Aiming to the pharmacologic suppression of acute UC: Beyond cortisone
At the end of the 1980's, Simon Lichtiger and Daniel Present, gastroenterologists at the New York Mount Sinai Hospital, were reckoning that initial enthusiasm over the impressive results achieved in the UK could have obscured the very fact that still some 40% of all the acute UC patients failed to respond, needing life-saving colectomy, with the dangerous complications of such an emergency procedure. Contemporary progress indicating that UC was likely to be sustained by activated killer lymphocytes of the "T" subset, combined with the evidence that such cells did mediate rejection of transplanted organs, made Lichtiger and Present guess: transplant surgeons are now controlling rejection of solid organs using this anti-T new drug, why this drug could not be also our drug for the 40% UC patients who fail steroids?

Cyclosporine
Cyclosporine (CsA) is a small protein from a Scandinavian fungus. Studies in the 1980's proved that cyclosporine was the most potent anti-T lymphocyte drug ever disclosed for that time, and data on solid organ transplant survival were confirmatory.

CsA for refractory UC patients at Mt Sinai Hospital
In July 1990, Lichtiger and Present proved that 11 of 15 UC patients facing colectomy for cortisone-refractory UC responded to a 14-day course of continuously injected CsA through a syringe device. These results, duplicated many times in the following years contributed to establish intravenous CsA as the main treatment for unresponsive UC: 80% of the treated patients respond initially, and 60% of the whole group do maintain a stable disease on proper immune suppression based on the immune suppressive drug "azathioprine".

The competitors of CsA: 1) Anti-cytokine molecules; 2) Colectomy

1. An alternative strategy to CsA, developed in the late 1990's, aimed at using manipulated antibodies (monoclonals) to block a number of soluble small proteins (cytokines) that lymphocytes use to communicate. Initial trials using a blocker of the cytokine Tumor Necrosis Factor (TNF), proved that IBD patients treated with this blocker (Infliximab) could achieve remission avoiding colectomy. Head-to-head trials have now suggested that CsA and Infliximab are equally effective; the heterogeneous toxicity of the two drugs makes it impossible to conclusively compare the profiles of the two competitors.
2. When medical treatment of severe UC fails (whether CsA or Infliximab) emergency colectomy is mandatory to save patients' lives. Modern reconstructive techniques are now highly competitive.

Conclusion

TheIBDs are likely to be the result of factors hidden in our society, chiefly life-style and diet. Failure to address these variables explains failure to cure IBD so far.

Acknowledgment: Dr Actis wishes to cherish the memory of Dr Daniel Present, deceased in 2016.

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Publication

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