



## CHRONOGRAPHY OF INFLAMMATORY BOWEL DISEASE

### Year 1955: The first clinical trial into inflammatory diseases: Corticosteroids reduce mortality<sup>☆</sup>



### Año 1955: primer ensayo clínico en enfermedad inflamatoria: los corticoides reducen la mortalidad

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Although Avicena had already, almost perfectly described how to conduct a good clinical trial, and some prior isolated examples exist, it was not until the 1940s and 1950s that the group formed by Archie Cochrane and other enthusiasts, in their passion to transform medicine into not only an empirical observational science, but also an experimental science, laid the foundations of the modern clinical trial. A few years before, Philip Hench, a rheumatologist at the Mayo Clinic, had started to use adrenal hormone extracts in the treatment of rheumatoid arthritis; in 1950 he won the Nobel Prize, together with Edward Kendall and Tadeus

Reichstein. The lack of effective treatments for practically all chronic diseases rapidly led to corticosteroids being tested for several diseases. Lloyd Witts and Sidney Truelove designed an elegant study, inventing an activity index and assessing mucosal healing by sigmoidoscopy, randomising patients to receive hydrocortisone or placebo. Hydrocortisone reduced mortality, although prolonged treatment gave rise to serious adverse effects. This study, which was published in three papers, remains the model to be followed in the design of clinical trials on inflammatory bowel disease.

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## Cortisone in ulcerative colitis; final report on a therapeutic trial

Truelove SC, Witts LJ. Br Med J. 1955 Oct 29;2(4947):1041-8

### 1955: First clinical trial on inflammatory disease: corticosteroids reduce mortality



#### Therapeutic trial

- ✓ Cortisone in chronic ulcerative colitis.
- ✗ Cases of regional colitis, ileitis or proctitis were not included.
- 🕒 6 weeks of hospital treatment.

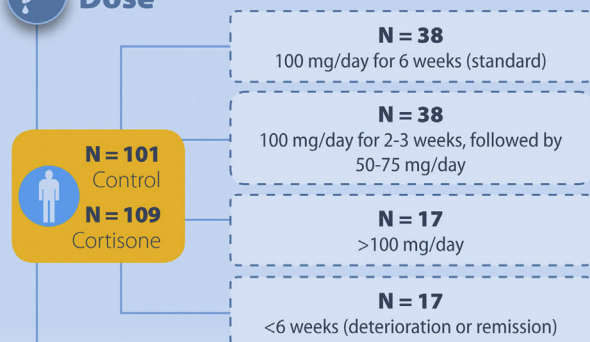


#### Patients

- 👤 213 initial patients
- ✗ 3 excluded. ✓ 210 treated.



#### Dose



#### Complications

- ✓ The combination of cortisone with penicillin and sulfonamides seems to minimise the risk of pyogenic complications.



#### Treatment

- ➔ High-protein, low-roughage diet with vitamin supplements.
- ➔ Maintenance of water and electrolyte balance, by intravenous infusion if necessary.
- ➔ Blood transfusions to maintain haemoglobin level above 70%.
- ➔ At the discretion of the treating physician: sulfonamides and antibiotics, rectal instillations and other forms of treatment.



#### Classification

- First episode.
- Relapse.

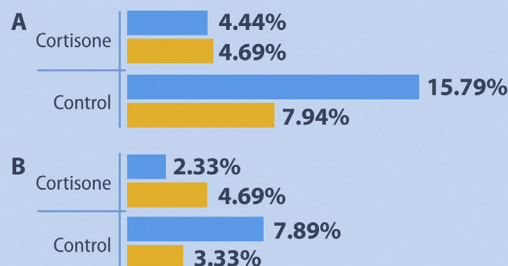
**Better results with cortisone, particularly in first episodes**



#### Results

- ➔ **9 months:** cortisone shows an advantage over the control in the first episode, but no advantage in relapses.
- ➔ **18 months:** slight deterioration in general symptoms.
- ➔ Without symptoms = 61.
- ➔ With symptoms = 119.
- ➔ Ileostomy = 44 (14% died).
- ➔ Deaths: 25 (fewer with cortisone).

**Analysis of early (A) and late (B) deaths comparing first episode (blue) and relapse (orange).**



#### Conclusions

- 1** Cortisone is very useful in the treatment of ulcerative colitis: it reduces mortality in severe episodes.
- 2** Probably better short-term outcomes with higher doses when necessary.
- 3** The effect is NOT permanent and prolonging the treatment gives rise to adverse effects.