

Crohn's Disease: Immunosuppression and Surgery: Unholy Alliance?

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Klinik für Gastroenterologie
und Hepatologie

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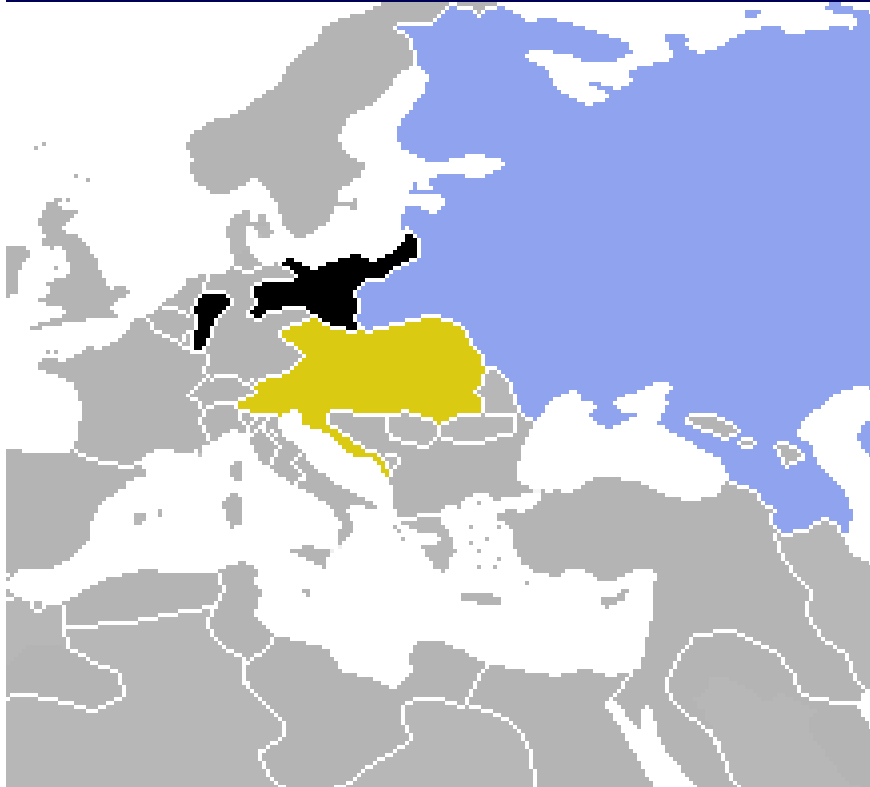
Crohn's Disease: Immunosuppression and Surgery: **What is a Holy Alliance?**

Stephan Brand

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Heilige Allianz (Holy Alliance)



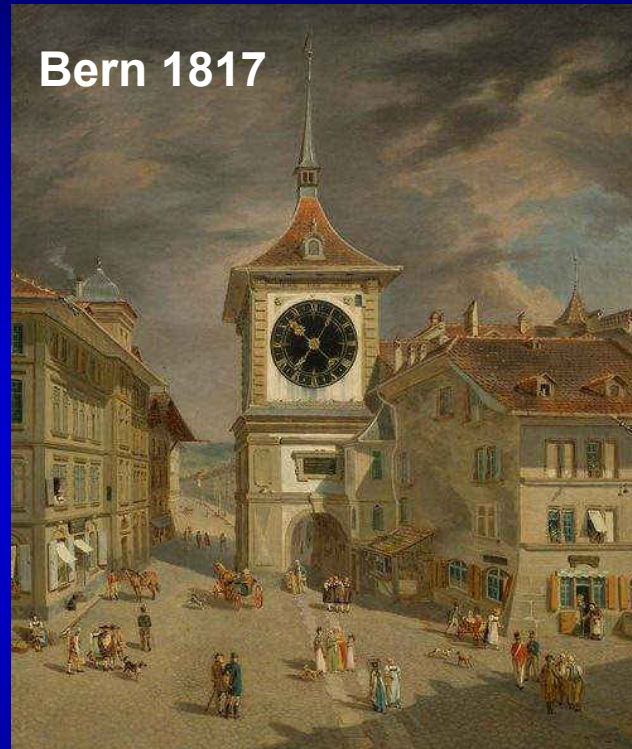
Kaiser Alexander I. von Russland

Kaiser Franz I. von Österreich

König Friedrich Wilhelm III. von Preußen

**Alliance of Prussia, Austria and Russia after
defeating Napoléon Bonaparte, signed in 1815**

Switzerland joined the Holy Alliance in Bern in January 1817, 200 years ago



Switzerland joined the
Holy Alliance
in Bern
on January 27, 1817

Erklärung über die Zustimmung der Schweizerischen Eidgenossenschaft zu den Grundsätzen des brüderlichen und christlichen Bundes, vom 27. Jenner 1817.

Die Schweizerische Eidgenossenschaft, welche von Sr. Maj. dem Kaiser aller Reußen eingeladen worden ist, dem zu Paris am 26./14. Herbstmonath 1815, zwischen Sr. Maj. dem Kaiser von Rußland und S. M. M. de, Kaiser von Oesterreich und dem König von Preußen abgeschlossenen brüderlichen und christlichen Bündnisse beizutreten, huldigt dem religiösen und moralischen Geist dieses Vertrages, dessen erhabener Zweck dahin geht, den Frieden und das Glück der Völker zu sichern. Die Schweizer, den Grundsätzen Ihrer Väter getreu, tragen eben so viel Achtung für die Rechte anderer Staaten, und lassen sich eben so angelegen seyn, mit allen das beste Einverständnis zu unterhalten, als Sie selbst auf den ruhigen Genuß der Freiheit, der Unabhängigkeit und der Ihnen so wichtigen Neutralität, welche die letzten europäischen Staatsverhandlungen Ihnen neuerdings zusicherten, den größten Wert legen. Die Eidgenossenschaft, welche in dem Bundes-Vertrag der Allerhöchsten Höfe, wovon Sr. Maj. der Kaiser von Rußland sie in Kenntniz setzen ließ, eine neue Gewährleistung dieser für Sie unschätzbar großen Güter findet, stellt die Erklärung aus: daß auch Sie die Grundsätze dieses Bündnisses als vorzüglich heilsam und unentbehrlich für das Glück der Nationen anerkennt, und daß Sie dieselben Ihrerseits nach dem wahren Geiste der christlichen Religion, die den Regierungen sowohl als den einzelnen Menschen Gerechtigkeit, Eintracht und gegenseitige Liebe zur Pflicht macht, getreu beobachten wird.

Zu dessen Urkunde haben Wir Schultheiß und Rätthe der Stadt und Republik Bern, als Eidgenössischer Vorort, gegründet auf die verfassungsmäßige Zustimmung der Stände der Eidgenossenschaft, Gegenwärtiges unterzeichnen und besiegeln lassen, in Bern den 27. Jenner im Jahr ein Tausend acht Hundert und siebenzehn.

Schultheiß und Rätthe der Stadt und Republik Bern,
als Eidgenössischer Vorort und in deren Namen:

Der Amtsschultheiß.

H. von Wattenwyl.

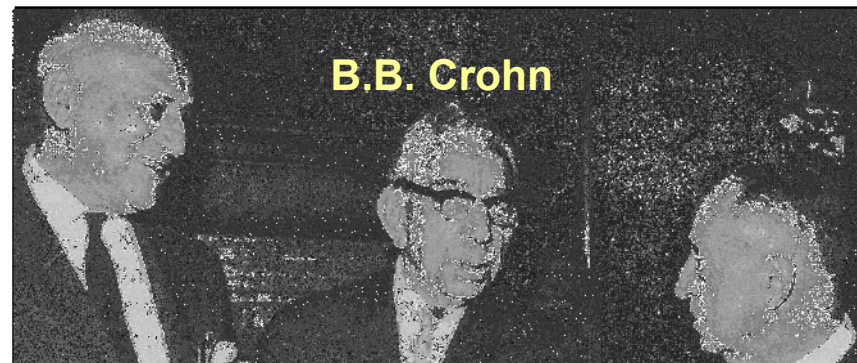
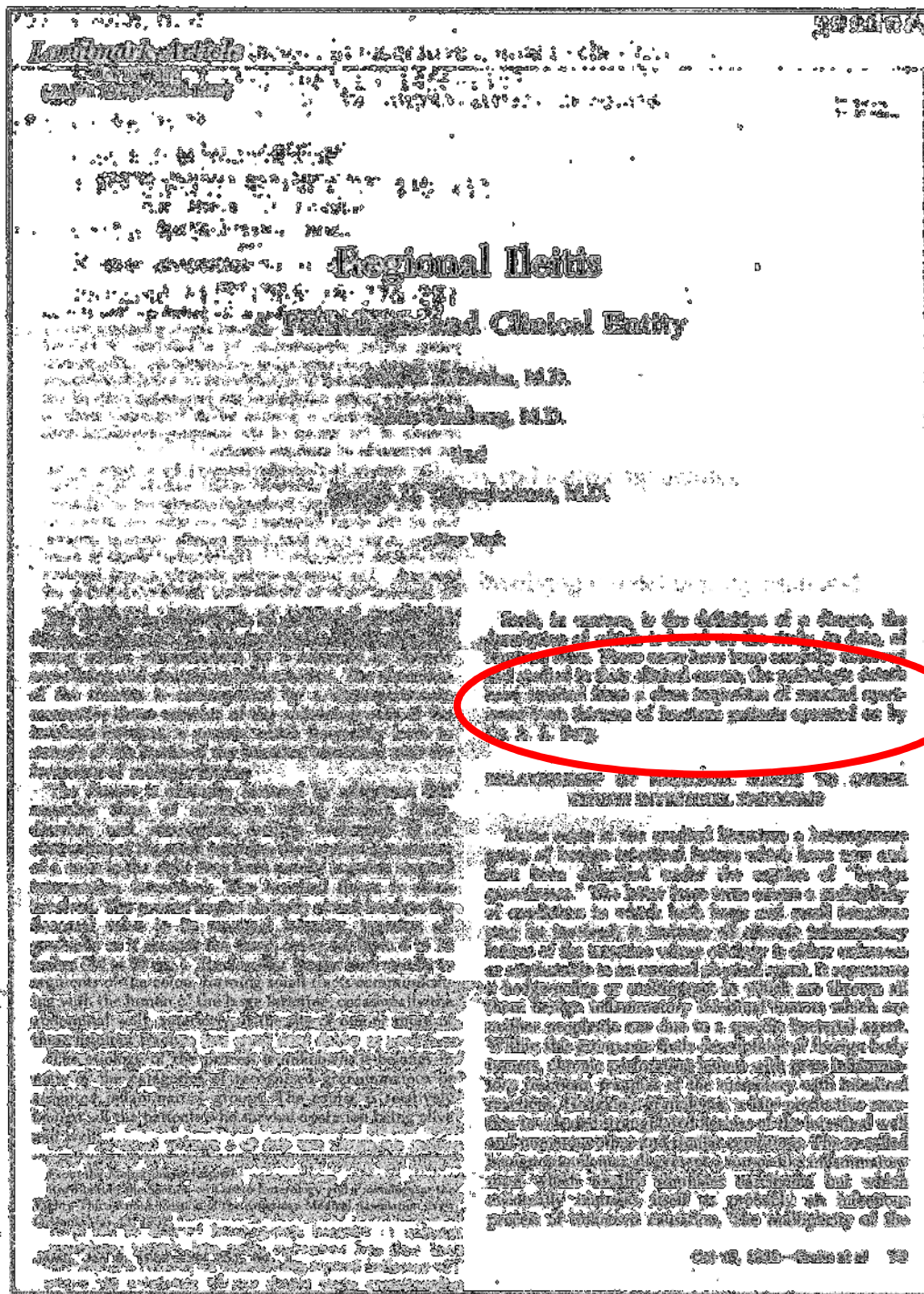
Der Kanzler der Eidgenossenschaft,
Mousson.

Immunosuppression and Surgery in Crohn's Disease

- **Surgery in Crohn's disease**
- **Safety of peri-operative immunosuppression**
- **Efficacy of immunosuppression preventing postsurgical recurrence of Crohn's disease**
- **Role of biomarkers predicting the postsurgical recurrence of Crohn's disease**

Immunosuppression and Surgery in Crohn's Disease

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B.B. Crohn

G. Oppenheimer

L. Ginzburg

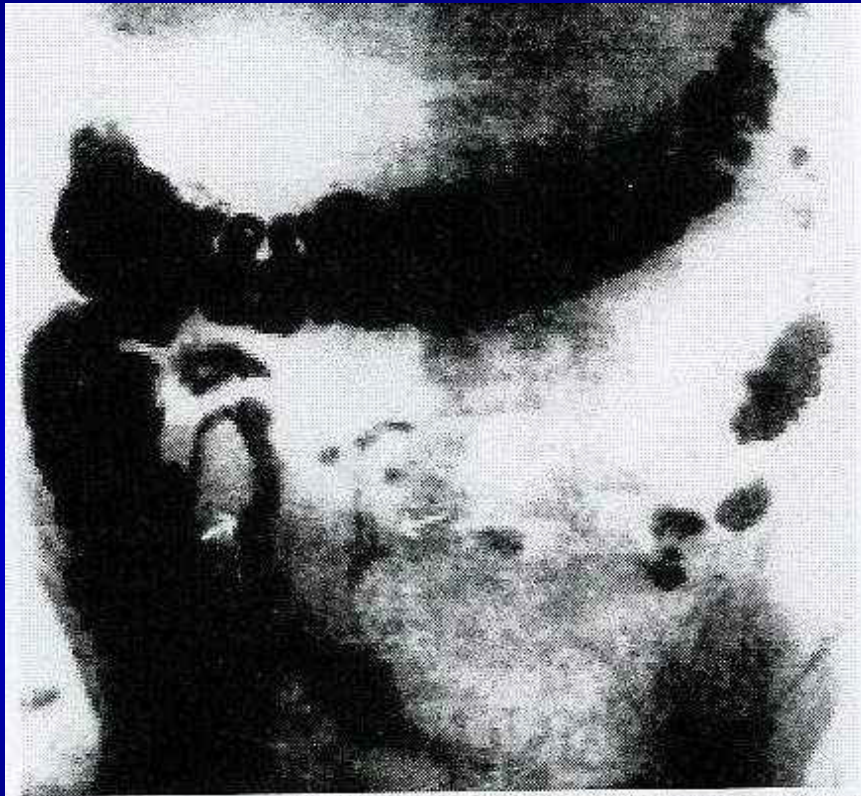
Ginzburg, until his death in the 1990s, referred to ileitis as Ginzburg's disease !

New York 1932



2018-376

Therapy of Crohn's disease in 1932



Roentgenogram of the barium meal given by mouth, showing regional ileitis. Note the extent of the strictured area.

JAMA 1932; 99:1323-1329.

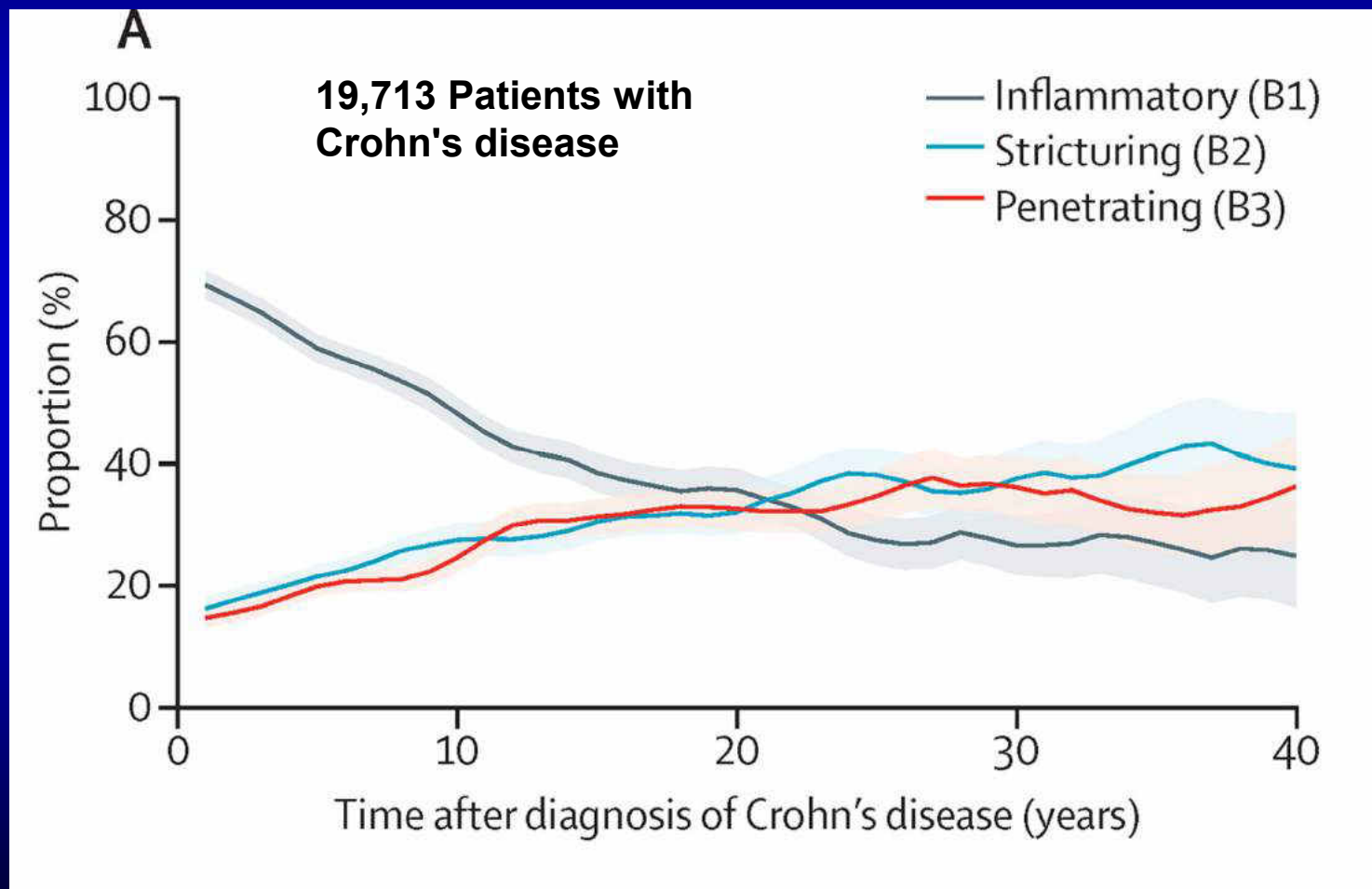
“Medical treatment is purely palliative and supportive...”

...the proper approach to a complete cure is by surgical resection of the diseased segment...”

B. Crohn:

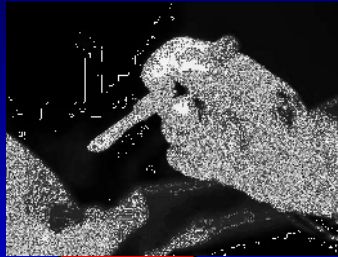
83th Annual Session of the
American Medical Association
New Orleans, May 13, 1932.

Largest study ever undertaken regarding the CD phenotype: At least two thirds of patients will develop a stricturing or penetrating phenotype



Cleynen I ... Brand S et al. *Lancet* 2016;387:156-67.

When surgery in IBD?



**Bio-
logicals**

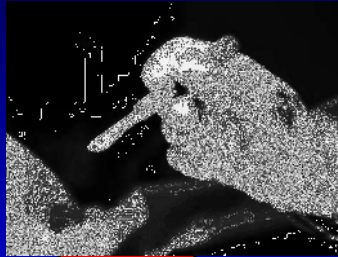
**Immun-
suppressives**

Corticosteroids

5-ASA

- Fibrostenotic strictures
- Very severe perianal fistulizing CD (protective ileostomy)
- Colorectal carcinoma, high-grade dysplasia
- Toxic megacolon
- Refractory ulcerative colitis
- Abscess

Are there alternatives to surgery?



**Bio-
logicals**

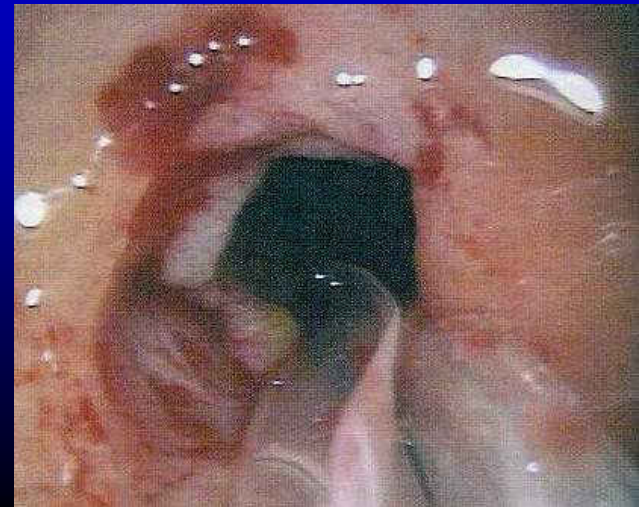
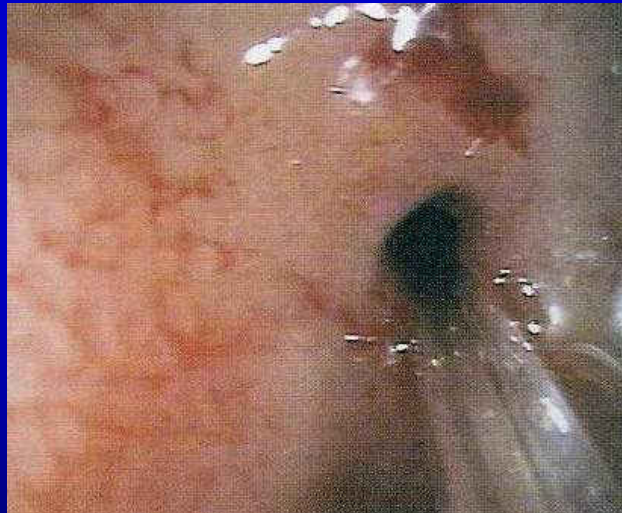
**Immun-
suppressives**

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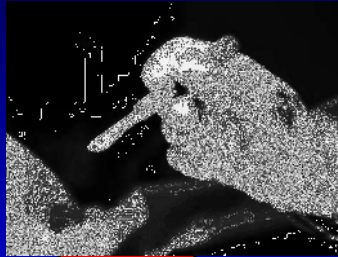
5-ASA

- **Fibrostenotic strictures**
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- **Abscess**

Ballon dilatation for stenotic Crohn's disease



Are there alternatives to surgery?



**Bio-
logicals**

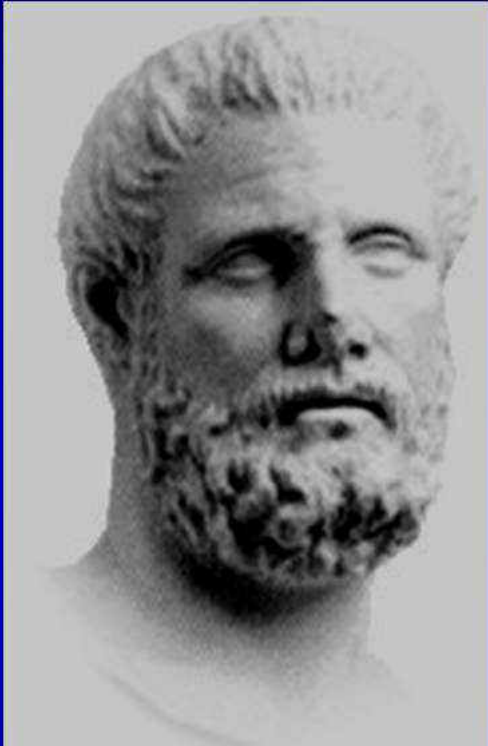
**Immun-
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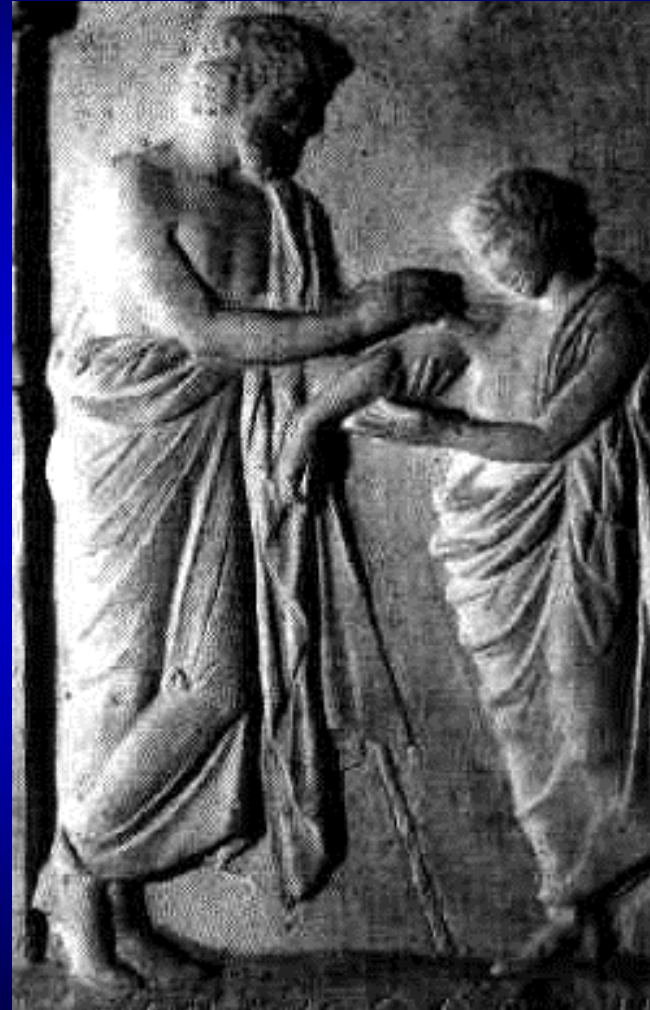
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- Fibrostenotic strictures
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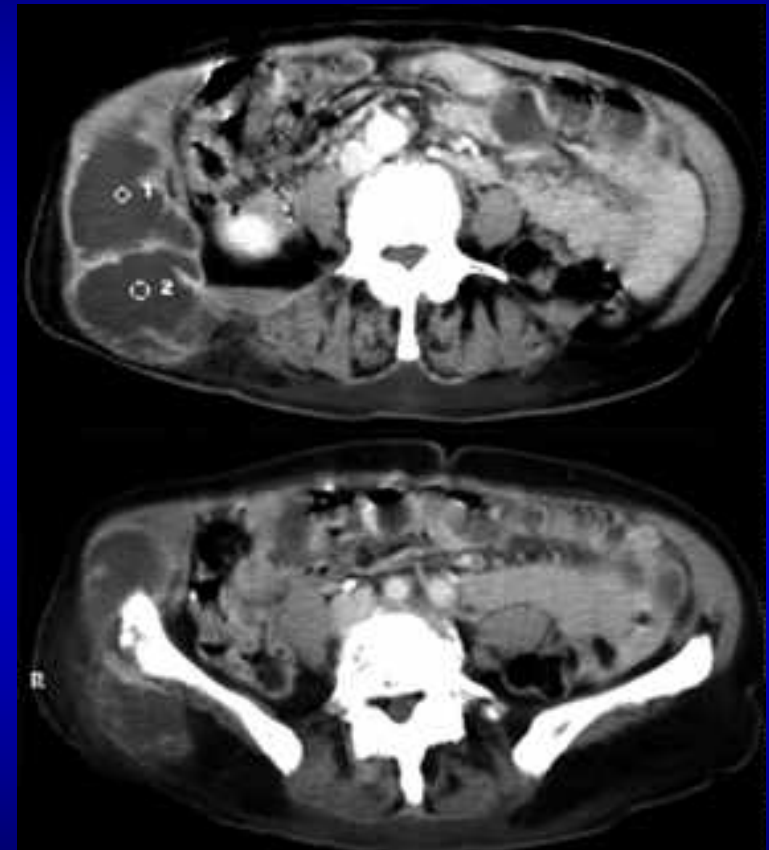
“Ubi pus ibi incisio et evacuatio”



Hippocrates
(460-377 BC)



CT-guided abscess drainage



CT-guided abscess drainage



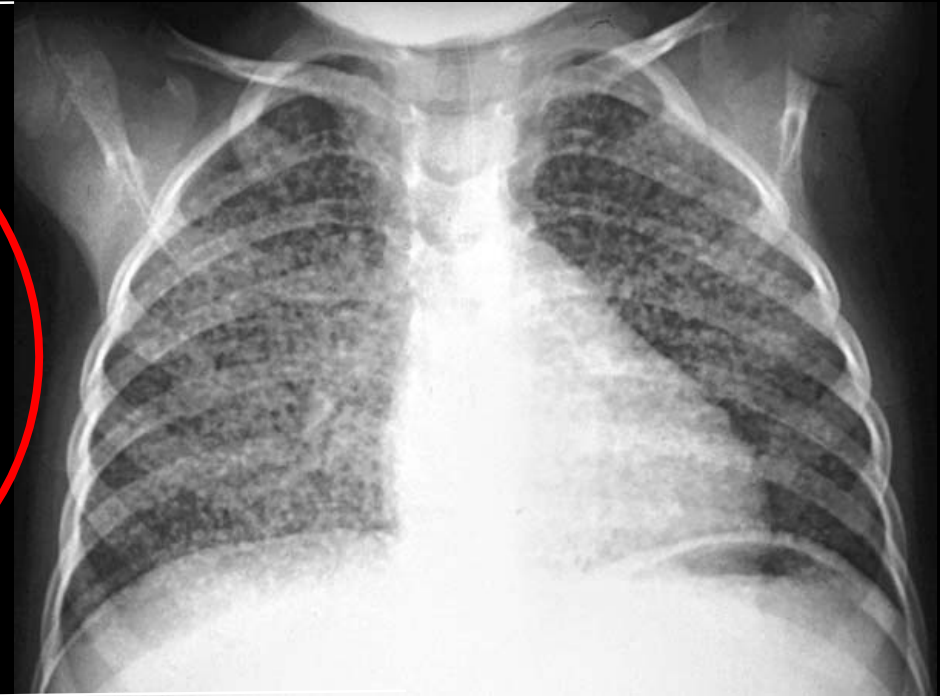
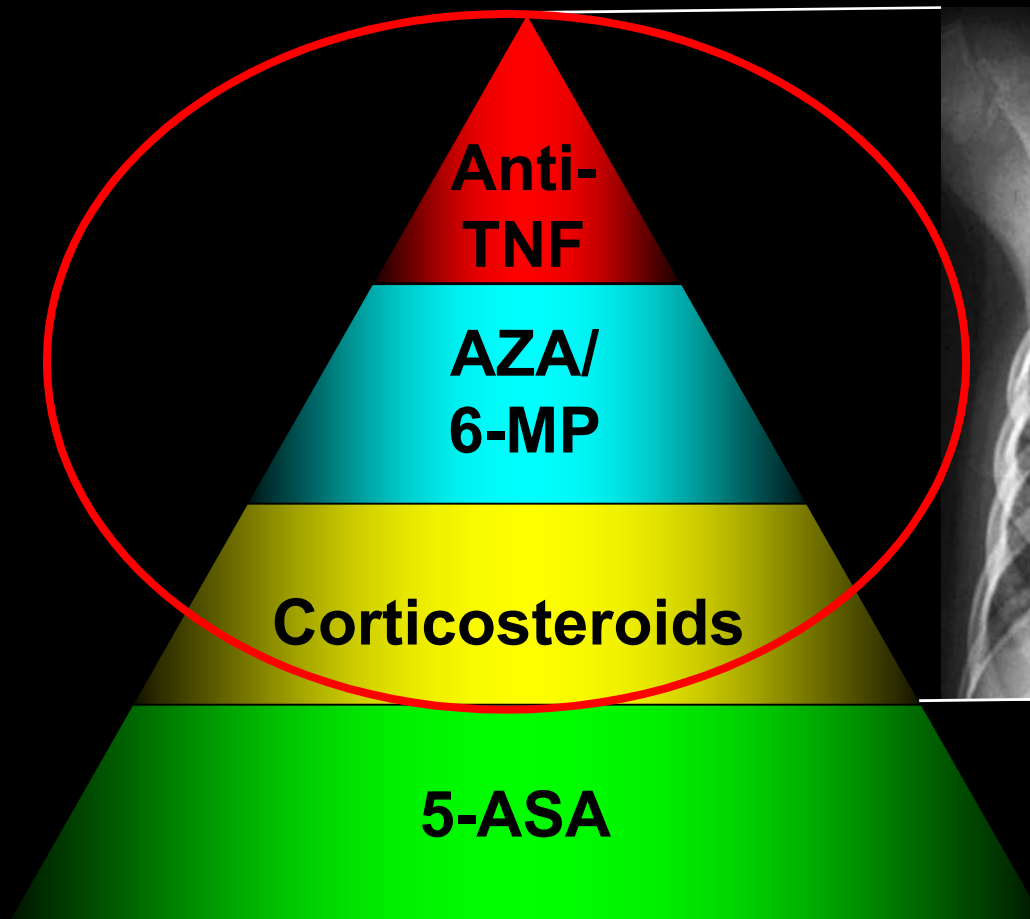
Summary (1): Surgery in Crohn's Disease

- **Approximately 50% of CD patient still require surgery (mainly ileocecal resection)**
- **Postoperatively, there is a high recurrence rate of CD**

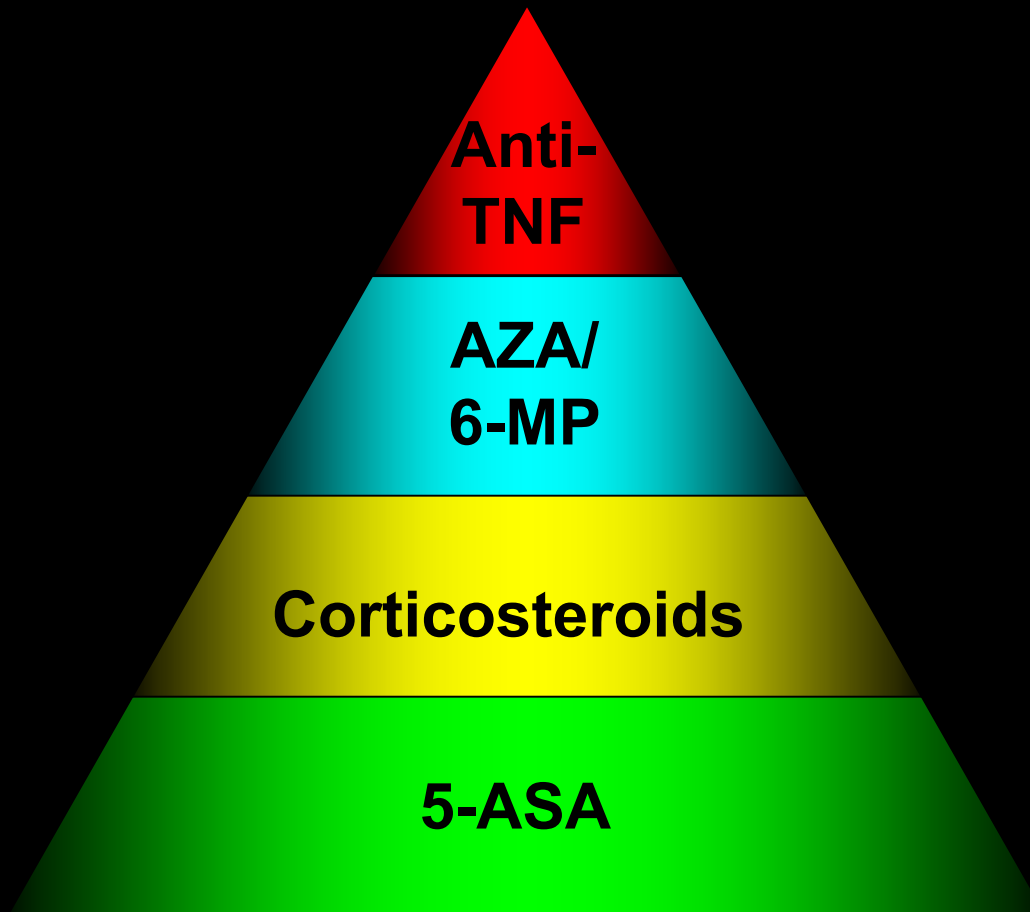
Immunosuppression and Surgery in Crohn's Disease

- Surgery in Crohn's disease
- **Safety of peri-operative immunosuppression**
- Efficacy of immunosuppression after surgery in Crohn's disease
- Role of biomarkers regarding the prediction of postsurgical recurrence of Crohn's disease

Problem of current immunosuppressive therapy: unspecific, resulting in increased rate of opportunistic infections



Preoperative corticosteroids and postoperative complications



Corticosteroids

Meta-analysis of postoperative complications with preoperative corticosteroids: Increased risk

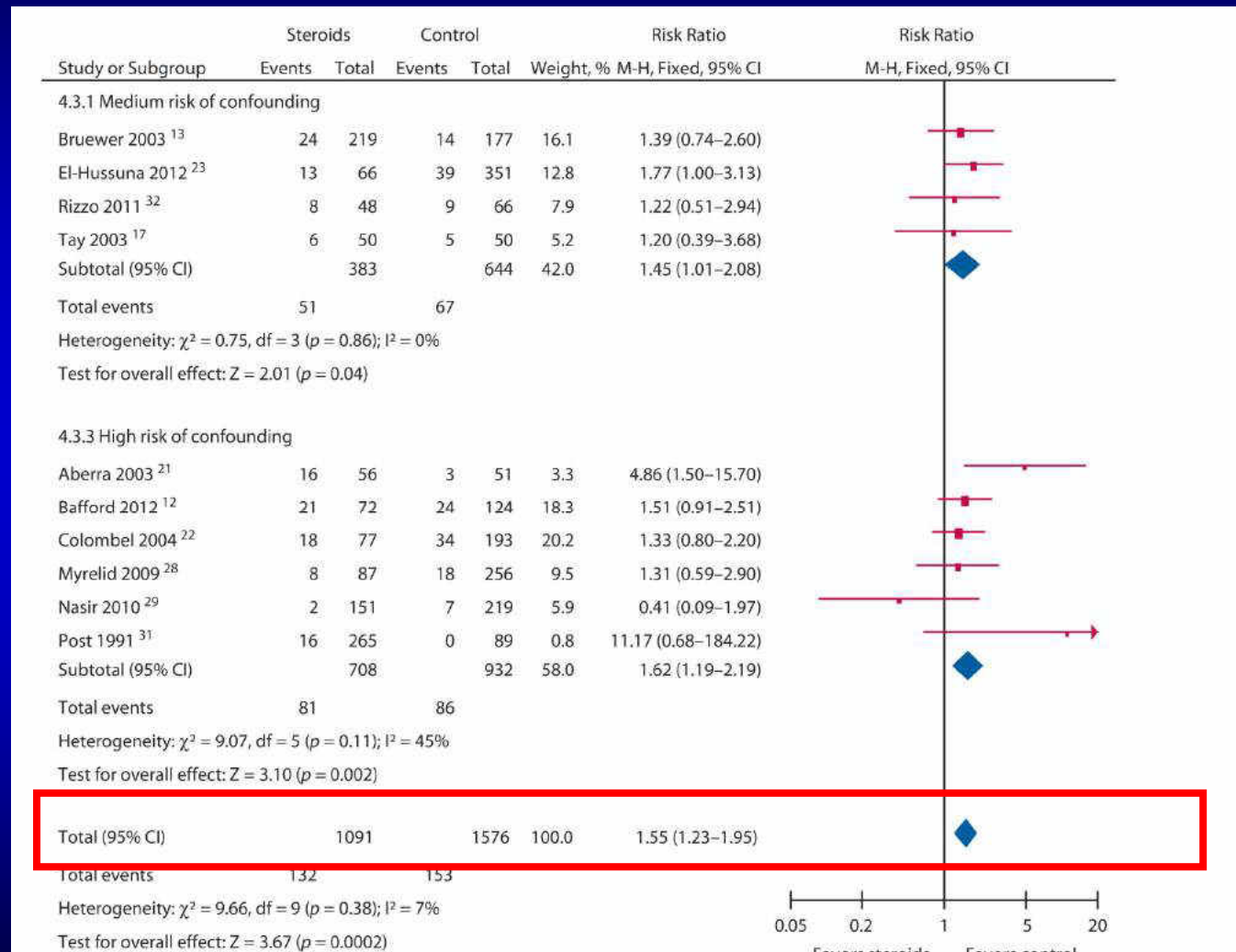
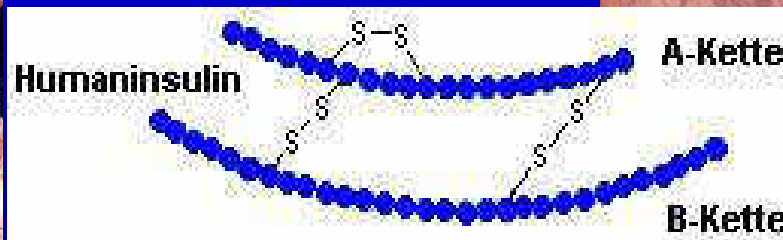
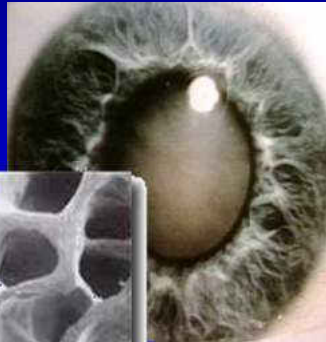


FIGURE 3. Meta-analysis of postoperative infectious complication with and without preoperative corticosteroid. M-H = Mantel-Haenszel.

Ahmed Ali U et al. *Dis Colon Rectum* 2014;57:663-74.

No maintenance therapy with steroids!

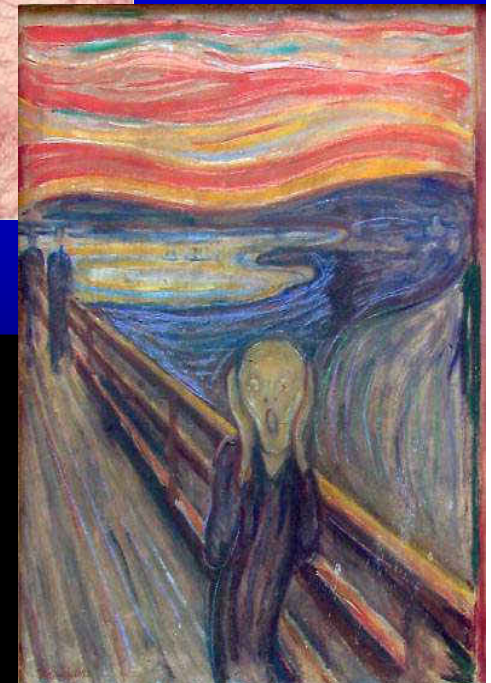
Side effects of steroids



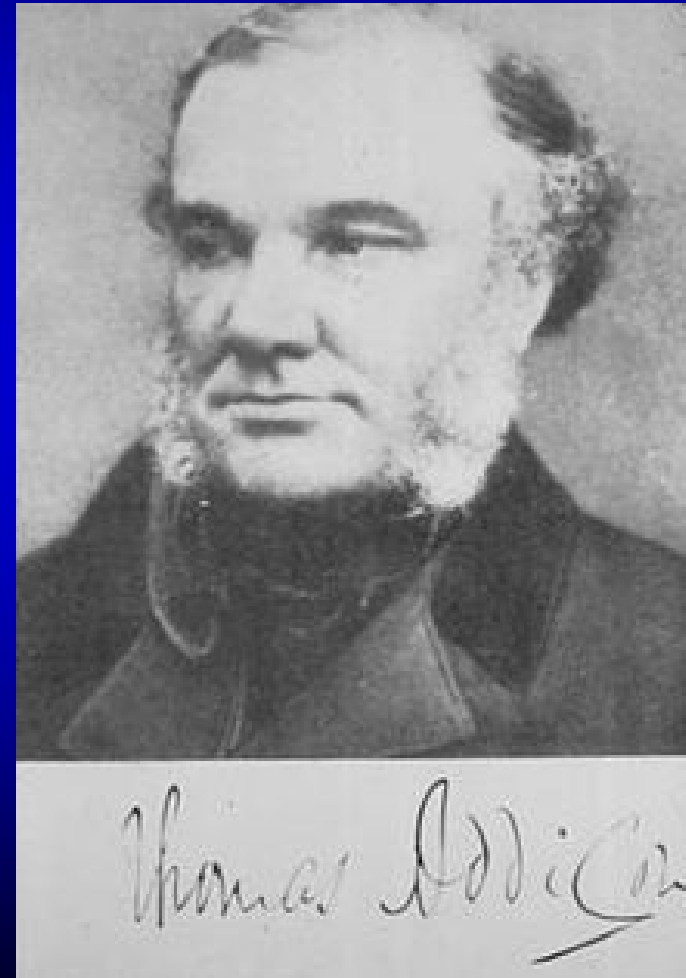
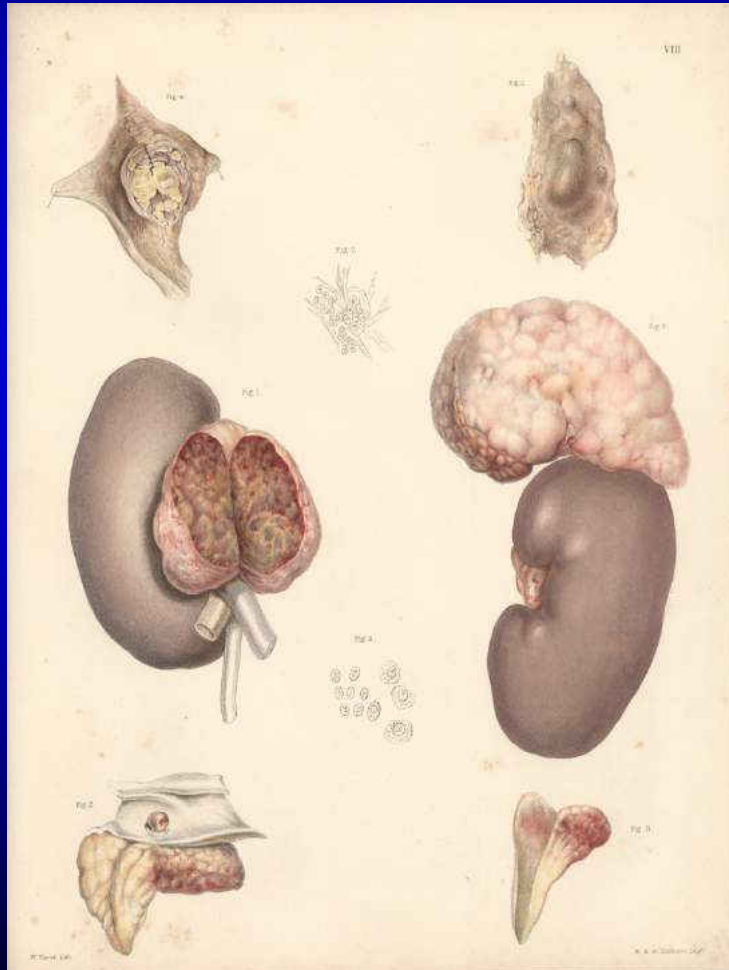
Meta-analysis:

Steroids do not prevent flare of Crohn's disease

Steinhart AH et al. *Cochrane Review* 2001



Thomas Addison (1855)
***On the constitutional and local effects of
disease of the supra-renal capsules***



Long-term treatment with steroids results in adrenal insufficiency: Stress dose during surgery

- First report of iatrogenic adrenal insufficiency (1952)
- High-dose or „stress-dose“ glucocorticoids in the perioperative period (1953)
- Management of adrenal insufficiency during surgery (1955)



A. M. A. ARCHIVES OF SURGERY

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Management of Adrenocortical Insufficiency During Surgery

JAMES A. NICHOLAS, M.D.

CHARLES L. BURSTEIN, M.D.

CHARLES J. UMBERGER, Ph.D.

and

PHILIP D. WILSON, M.D., New York

The data on three of these patients are being presented in this paper to illustrate the methods whereby we managed the problems.

One patient had been receiving intensive hydrocortisone therapy for rheumatoid arthritis when he developed acute appendicitis. A second patient had suppressed adrenocortical function produced by cortisone therapy for nephrosis and he required an elective

CASE 3.—Example of a Patient with Adrenal Insufficiency Due to Addison's Disease Requiring Elective Surgery †

A man 37 years of age had Addison's disease for seven years. He had been managed fairly successfully for several years on a program of desoxycorticosterone acetate pellets of 150 mg. implanted every three months and cortisone in doses of 25 mg. daily orally. Owing to a back injury, he had a great deal of pain which interfered with his daily routine. Orthopedic consultation suggested that he might be helped by a lumbosacral fusion together with a sacroiliac fusion. Because of the severe degree of trauma involved in these operations and because of the patient's adrenocortical insufficiency due to Addison's disease, it was deemed dangerous to proceed with these operations. However, since this young man would become incapacitated without surgical intervention, it was decided, reluctantly, to perform the operations by doing the two different procedures at different times if necessary and by having a team versed in endocrinology and surgical physiology help in the management of this patient before, during, and after the operation.



U.S. American presidents: susceptible to IBD



Dwight D. Eisenhower
34th U.S. President
Crohn's disease, ileal stenosis:
1956 Ileotransversotomy



John F. Kennedy
35th U.S. President
1934 chronic colitis (DDx:
UC) diagnosed at Mayo Clinic
Addison disease 1947

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March 20, 1953

Re: Senator John Kennedy
16789

Dr. William P. Herbst Jr.
1801 Eye Street N.W.,
Washington 6, D. C.

Dear Dr. Herbst:

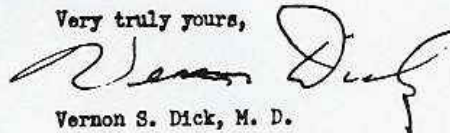
I have recently suggested to Senator John Kennedy of Boston, Mass., that he consult you sometime in the near future and wanted to give you a little of the background.

Senator Kennedy has been a patient of the Lahey Clinic at intervals since 1936, and has had quite a variety of conditions. The most serious of these has been Addison's disease which was first discovered and treatment instituted in October of 1947. He has been doing well in regard to this condition. He also has had recurrent back pain. A herniated intervertebral disc, L-5, was removed in 1944, by Dr. James Poppen.

When he was in Boston last week, his medical condition was checked by Dr. Elmer Bartels who has been following his Addison's disease since it was first discovered. He felt that he was getting along satisfactorily and plans to implant further pellets of Doca on April 10th. He is taking cortisone daily.

With best wishes, I remain

Very truly yours,


Vernon S. Dick, M. D.

March 20, 1953

Addison's disease which
was first discovered and
treatment instituted in
October of 1947...

..his Addison's disease..
He is taking cortisone
daily...

New York Times, November 10, 1960, p. 37.

