

Perianal Crohn's Disease: Current Treatment Approach

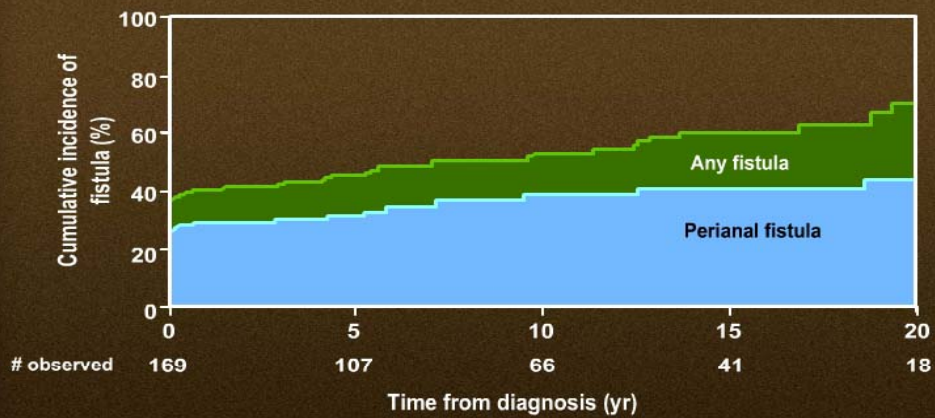
David A Schwartz, MD

Director, Inflammatory Bowel Disease Center

Vanderbilt University Medical Center

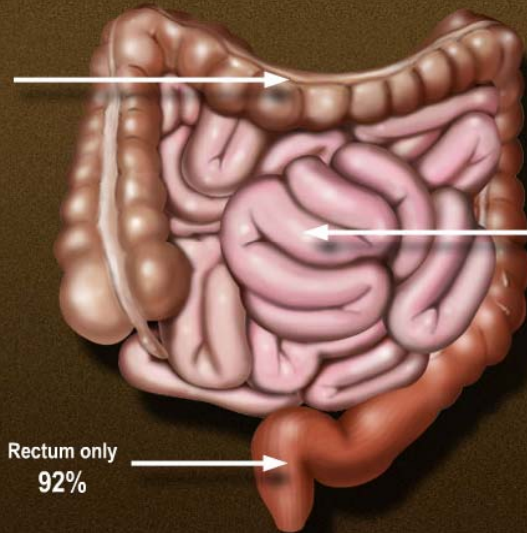
Epidemiology / Morbidity

Cumulative Incidence of Crohn's Fistulas



Frequency of Perianal Fistulas According to the Anatomic Location of Bowel Involvement

Colon only
(without rectal
involvement)
41%



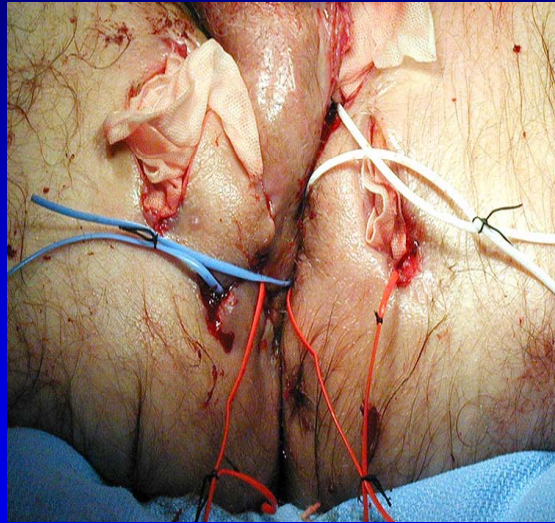
Small intestine only
12%

Combined ileocolic
involvement
15%

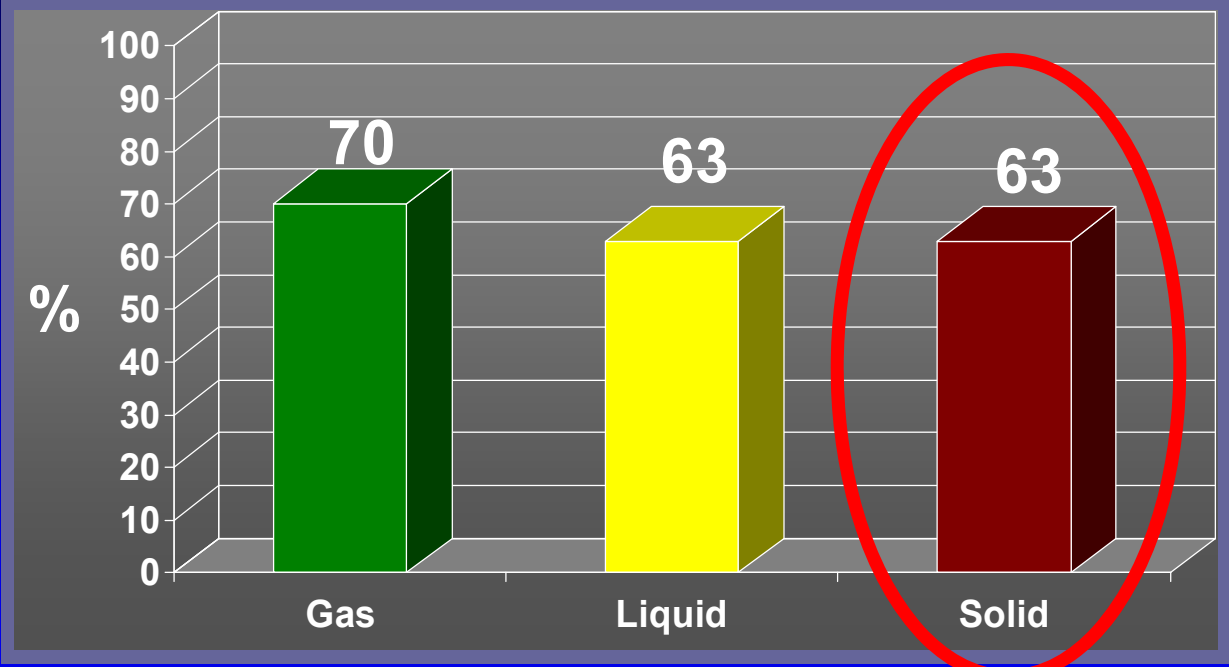
Rectum only
92%

Hellers et al, Gut 1980

Just What are We Talking About?

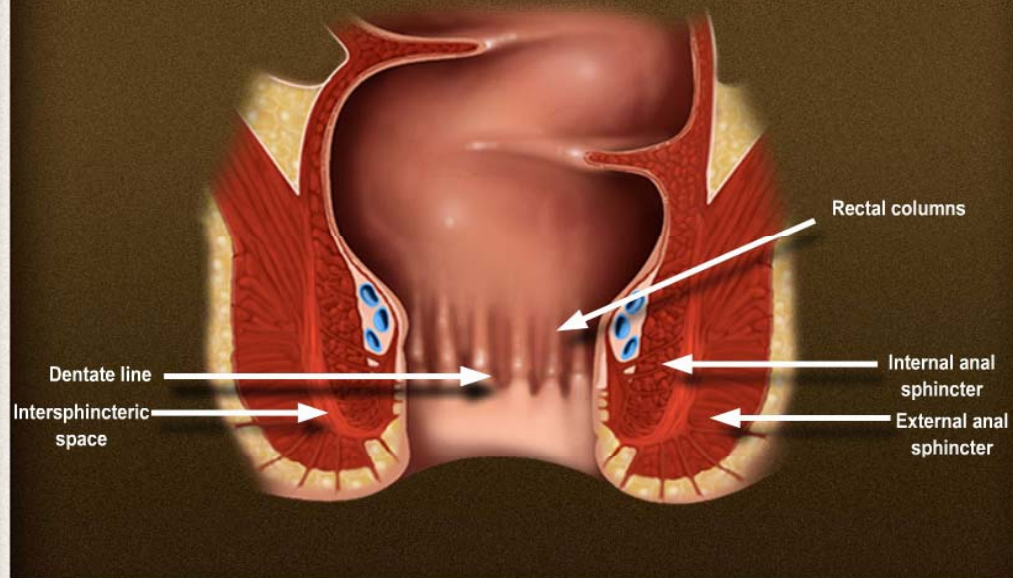


Patients with Frequent Episodes of Fecal Incontinence (≥ 1 / week)



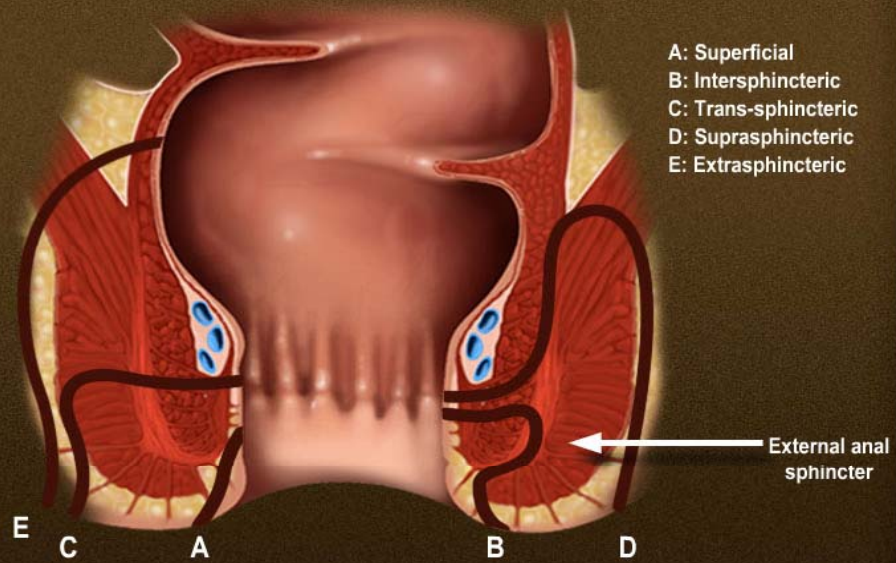
Anatomy

Anatomic Relationships in the Pelvis

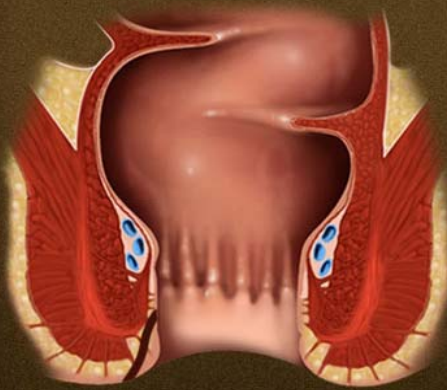


Classification Systems

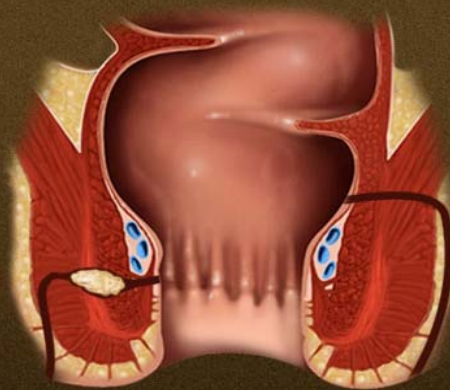
Park's Classification of Perianal Fistulas



Simple vs. Complex Fistula



SIMPLE



COMPLEX

Diagnosis

Why is a precise evaluation important?

The key to successful management is to establish adequate drainage of all abscesses and to control fistula healing. An imaging modality should provide a virtual road map for this purpose.

Diagnostic Options Used in the Classification of Perianal Crohn's Disease

- **History**
- **Physical Exam**
- **Imaging**
 - **Fistulography**
 - **CT**
 - **MRI**
 - **Endorectal ultrasound**

Study Results

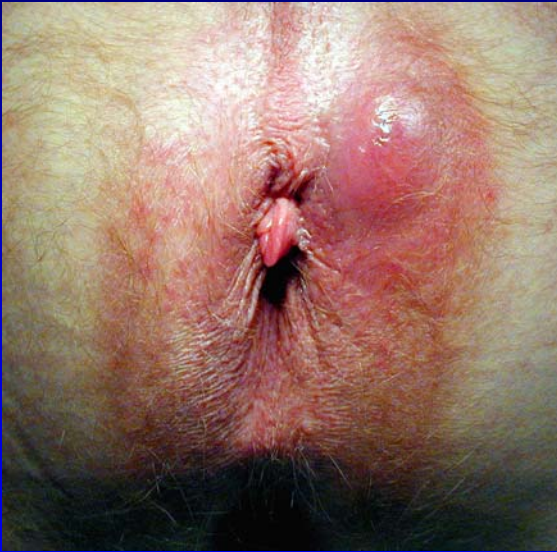
- A prospective triple blinded study compared EUS, MRI and EUA in 32 patients with suspect perianal Crohn's disease.¹
- All three methods showed excellent accuracy in assessing these patients
 - EUS – 91% (95% CI 75% - 98%)
 - EUA – 91% (95% CI 75% - 98%)
 - MRI – 87% (95% CI 69% - 96%)
- Combining either of the imaging modalities with EUA increased the accuracy to 100%

Therapy

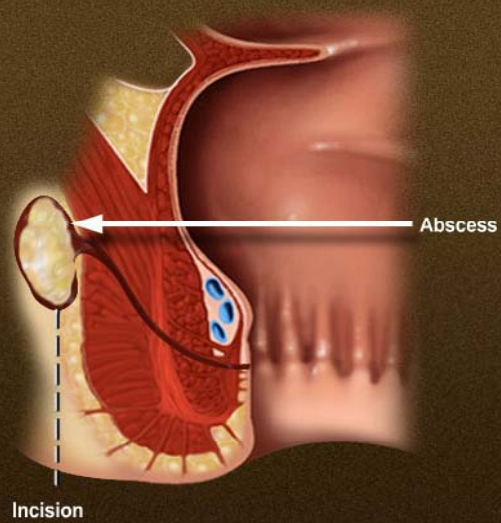
Surgical Treatment

Abscess

Abscesses



Incision and Drainage

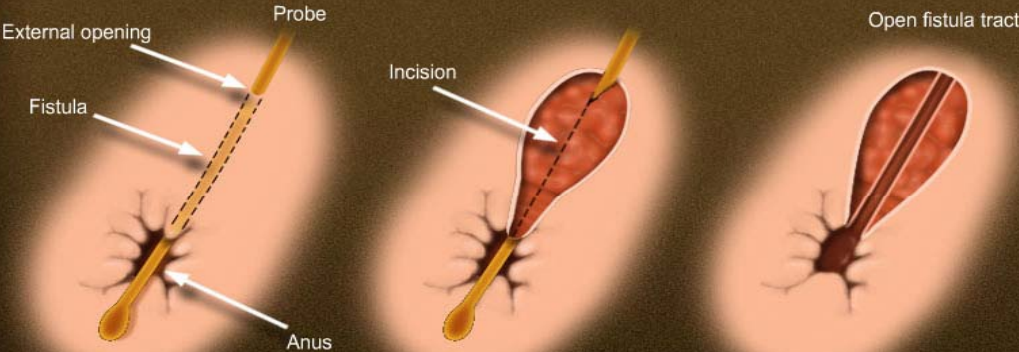


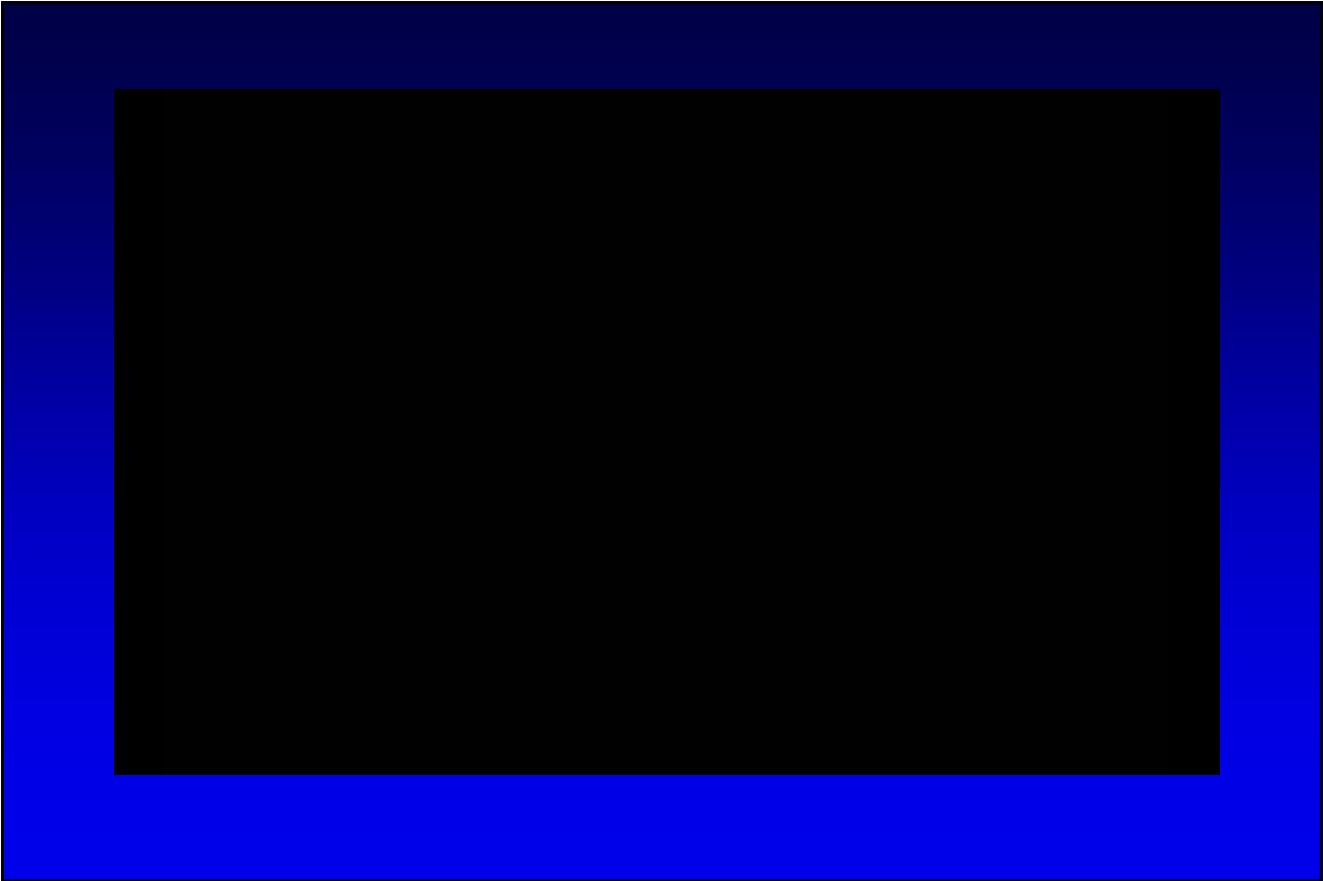
Fistulas

Perianal Crohn's Disease – Surgical Treatment Options

- **Fistulotomy**
- **Setons**
- **Advancement Flap**
- **Fibrin Glue / Fistula Plug**
- **Diversion / Proctectomy**

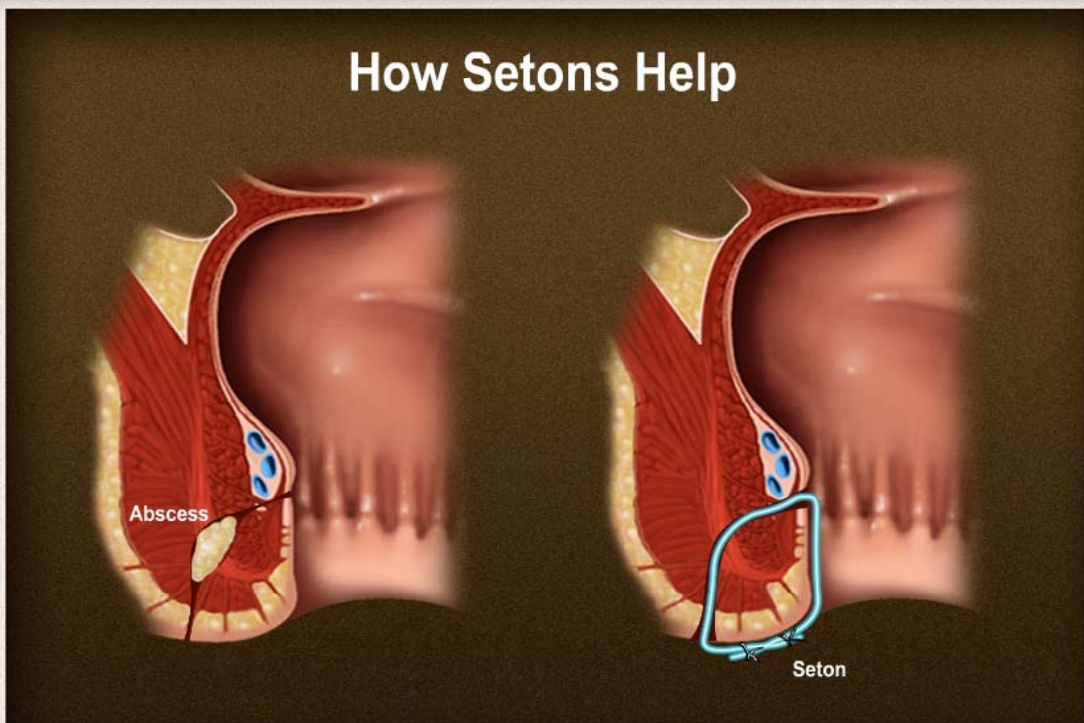
Fistulotomy



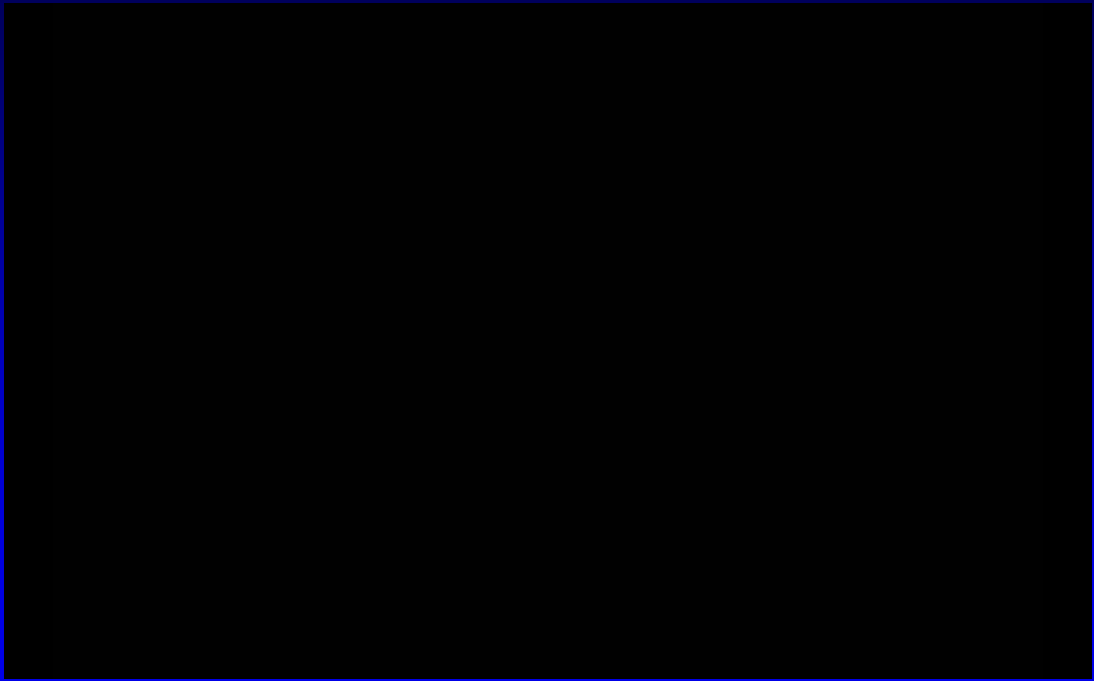


Setons

How Setons Help



Seton Placement



Other Surgical Options for Fistulas

- Cutting Seton
- Diverting Ileostomy
 - Does not alter course of disease
 - Only a small percentage get restoration of the intestinal continuity
 - 6 / 29 (21%)¹
 - 2 / 21 (9.5%)²

1- Harper, British J Surg 1982

2- Zelas, Annals Surg 1980

Proctocolectomy

- **Despite intensive therapy around 10 -15% of patients with perianal Crohn's disease will come to proctectomy.**
- **Rate of proctectomy at Mayo was 8.4% at 10 yrs and 17.5% at 20 years¹**

1- Wolff, Diseases Colon Rectum 1985

Medical Therapy

MEDICAL THERAPIES

Probable Efficacy	Proven Efficacy
Antibiotics	Infliximab
Azathioprine / 6-Mercaptopurine	Tacrolimus
Cyclosporine	? Adalimumab

Agents with Probable Efficacy

Antibiotics

Antibiotics

- **Metronidazole: Typical dose is 250 - 500mg po tid /qid, improvement seen after 6-8 weeks.**
 - All studies are open label.
 - Largest study conducted by Bernstein et al ¹
 - 21 patients studied, healing seen in 83%
 - Three other studies found healing rate of between 34 -50% ²⁻⁵

1-Bernstein et al. *Gastro* 1980

2-Schneider et al. *Deutsche Med W* 1981

3-Jakobovits et al. *American J Gastro* 1984

4-Schneider *Deutsche M W* 1985

5.Brandt et al *Gastro* 1982

Antibiotics (Metronidazole)

- Fistulas re-occur once medicine is stopped**
- Adverse events include metallic taste, glossitis, nausea and a distal peripheral sensory neuropathy**

Azathioprine / 6 - MP

Azathioprine / 6 - MP

- **The 5 Controlled trials were summarized in a meta-analysis¹**
 - **22 / 41 (54%) of patients who received AZA /6-MP responded vs. 6 / 29 (21%) who received placebo.**
 - **Pooled odds ratio was 4.44 in favor of fistula healing**

1-Pearson et al. *Ann Intern Med.* 1995

Cyclosporine

Cyclosporine

- **10 studies published using CYA to treat fistulas (a total of 64 patients) ¹⁻¹⁰**
 - **Overall initial response rate is 83%, improvement seen by 2 weeks.**
 - **Response is not durable**

1-Fukushima, Gastro Jpn 1989

2-Lichtiger, Mt Sinai J of Med 1990

3-Hanauer, Am J Gastro 1993

4- Present, Dig Dis Sci 1994

5- Markowitz, Gastro 1990

6-Abreu-Martin, Gastro 1996

7-O'Neill, Gastro 1997

8-Hinterleitner, Zeit fur Gastro 1997

9-Egan, Am J Gastro 1998

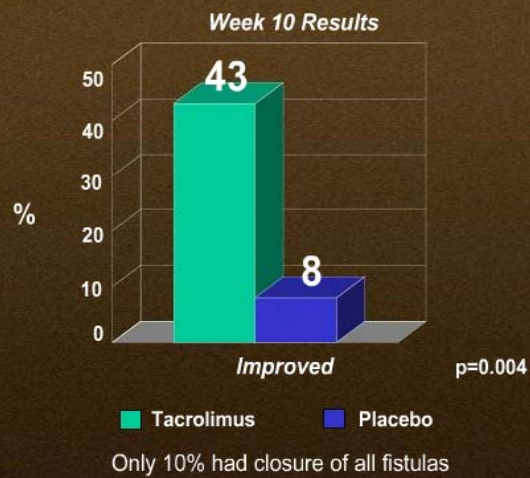
10-Gurudu J Clin Gastro 1999

Agents with Proven Efficacy

Tacrolimus (FK-506)

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The double blinded placebo study of 48 patients randomized to receive 0.20mg/kg/day for 10 weeks. Primary endpoint was improvement defined as closure of $\geq 50\%$ fistulas and maintenance of closure for ≥ 4 weeks.



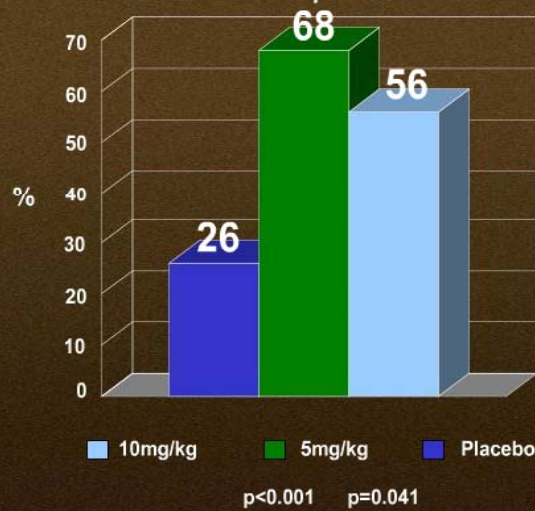
Sandborn et al. , Gastro 2003

Anti-TNF α Antibody

Infliximab for Crohn's Perianal Fistulas

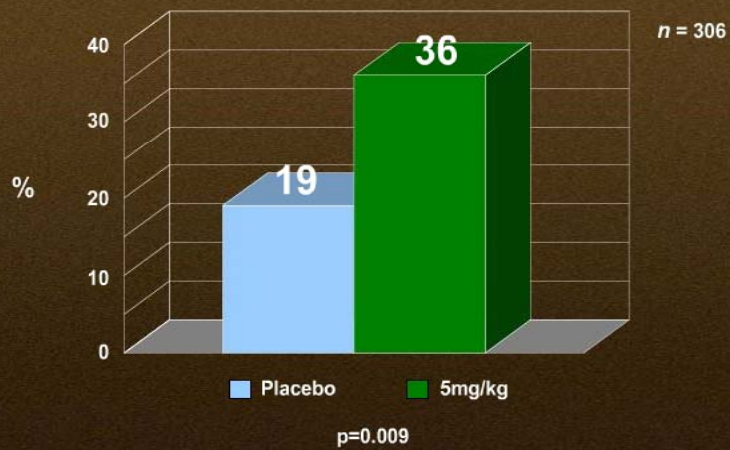
Primary endpoint; $\geq 50\%$ reduction in open fistulas

Initial Fistula Response to Infliximab $n = 94$

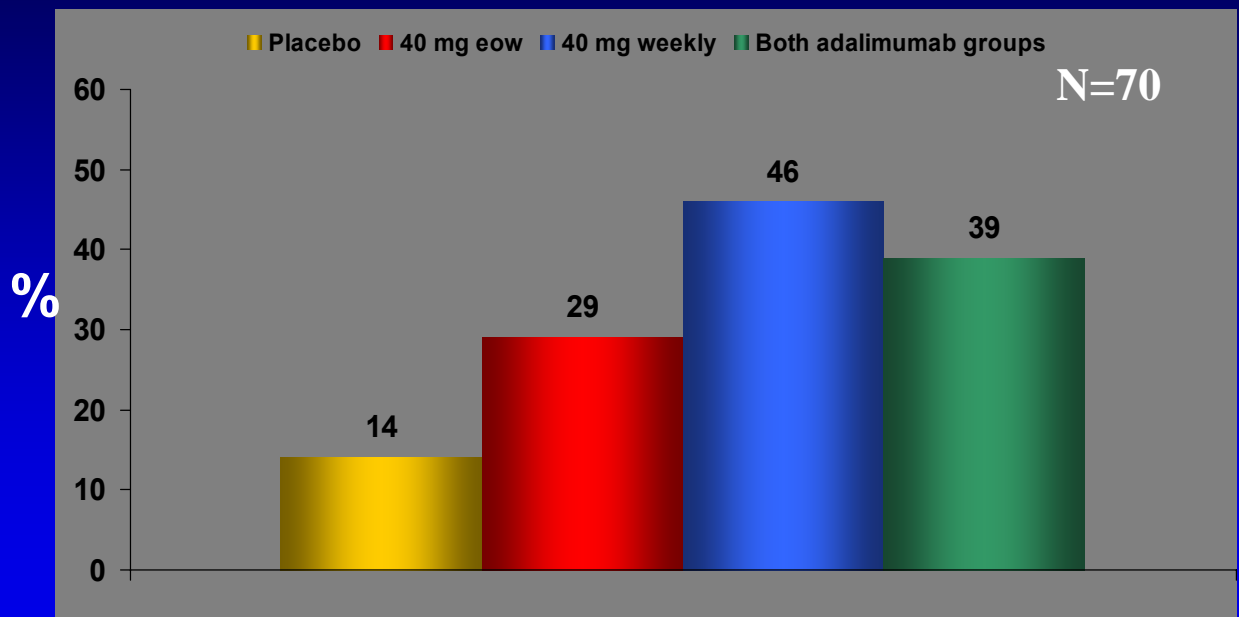


Accent II: Infliximab for Maintaining Fistula Closure (54 weeks)

Percent of Patients Maintaining Complete Fistula Closure



Adalimumab: Complete Healing of Draining Fistulas at Both Wks 26 and 56: Randomized Responders



Colombel, Gastro 2007

**How Can We Improve Outcomes
for Patients with Crohn's Perianal
Fistulas?**

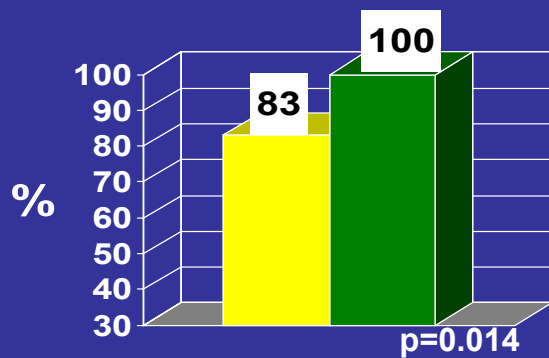
Does Controlling Fistula Healing Make a Difference?

N = 32

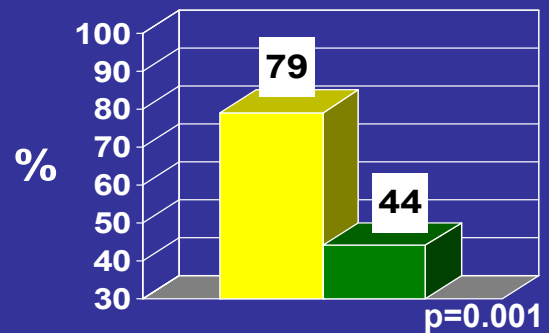
■ Infiximab only

■ EUA before Infiximab

Response to Treatment



Fistula Recurrence



Requeiro et al, IBD 2003

The Use of Imaging to Guide Therapy

21 pts with Perianal Crohn's Disease



Rectal EUS / Colonoscopy



EUA with I&D and Seton Placement



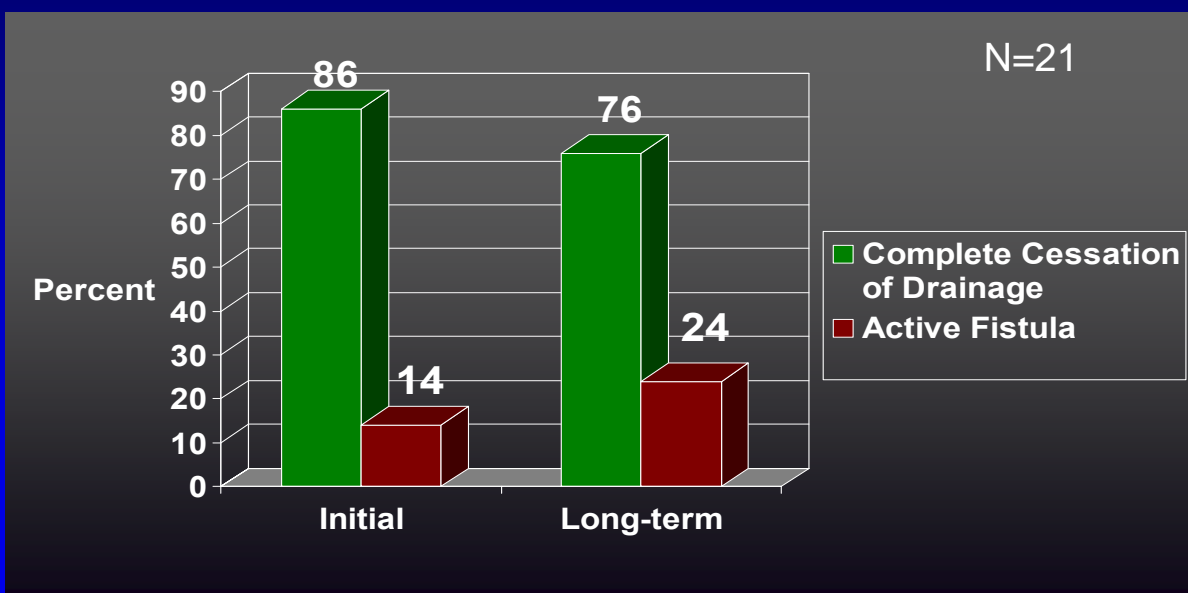
AZA/6-MP, Cipro and Remicade



Serial rectal EUS Exam

**Setons were not removed unless EUS
proved the Fistulas were inactive**

Utilizing EUS to Improve Fistula Healing

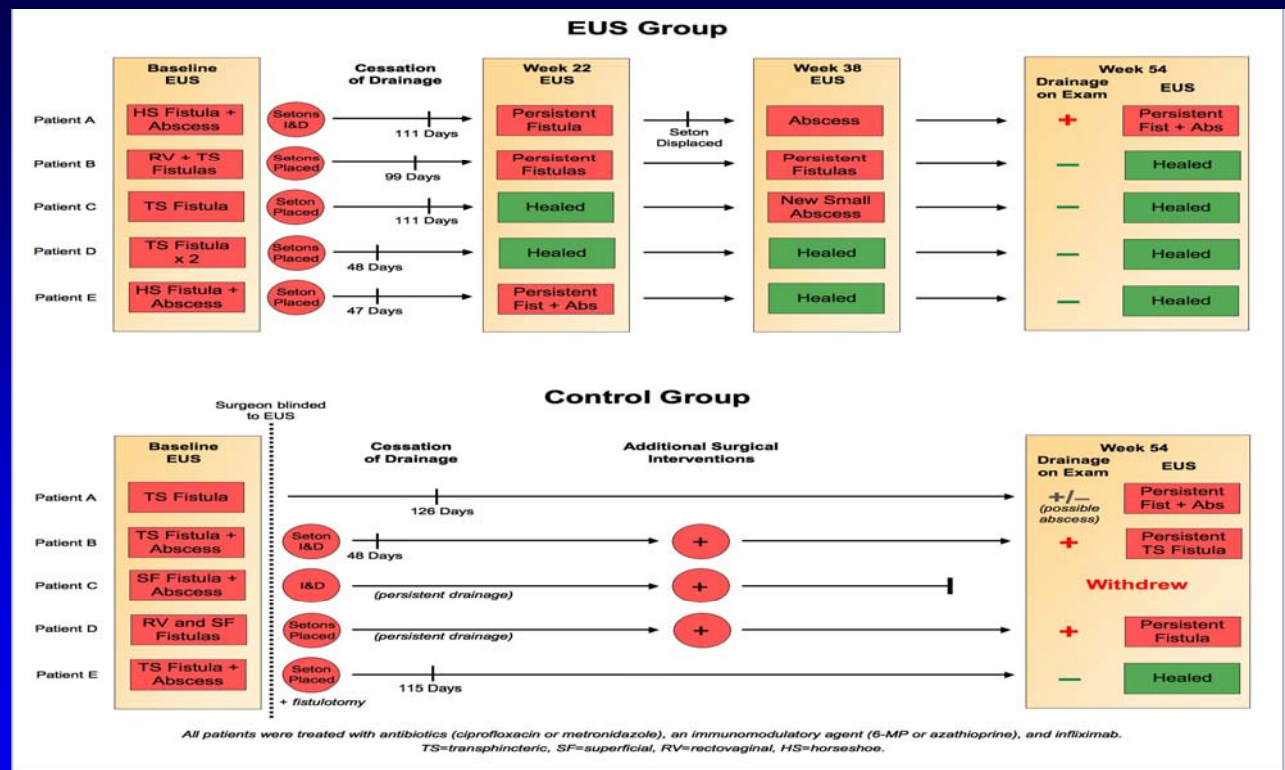


Schwartz et al, IBD 2005

Results

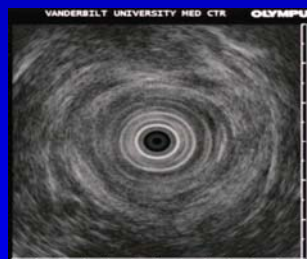
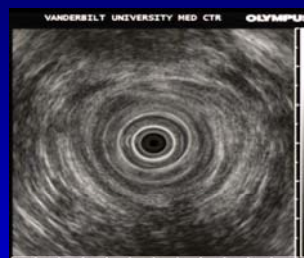
- Median time to cessation of drainage was 10.6 wks (4-32).
- Median time to EUS evidence of fistula inactivity was 21 weeks (12-37 weeks).

Results- Prospective Trial of EUS Guidance

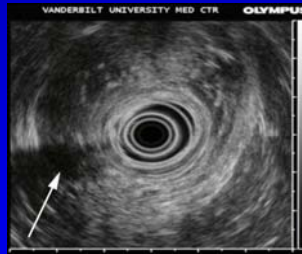
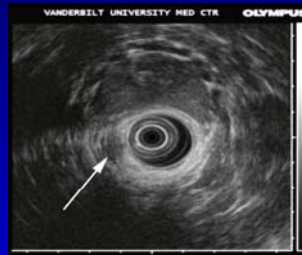


Spradlin, Schwartz Am J Gastro 2008

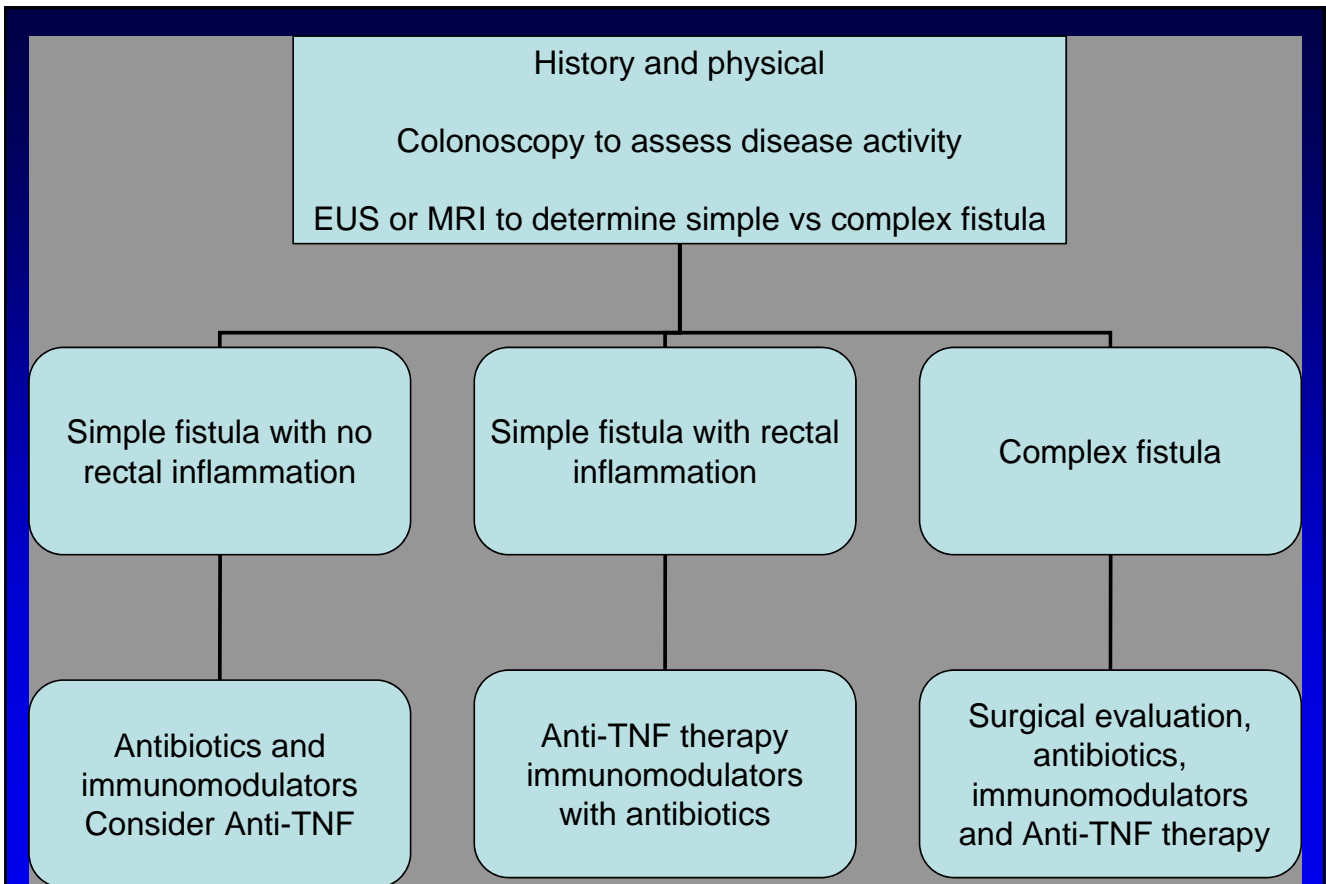
EUS Patient C



EUS Patient A



Conclusion



Thank You for Your Time

