

# **Epidermal Growth Factor – An Alternative Therapy in UC**

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# Epidermal Growth Factor

- 53 aminoacid peptide
- Potent stimulator → proliferation  
restitution
- Strong ligand for EGF-receptor (Basolateral  
surface *Playford RJ Gut 1996; 39(2):262-6*)
- Exposed to luminal EGF when epithelial  
damage.
- Stem Cell hypothesis

# Laboratory experiments

# Animal colitis model

- Colitis induced chemically

- Reduction in microscopic erosion
- Reduction in degree of inflammation

*Procaccino et al. Gastroenterology 1994; 107(1):12-7*

- After induction of colitis → Increase in EGF and TGF- $\alpha$  mRNA expression

*Hoffmann P et al. Scand J Gastroenterol 2000; 35(11):1174-80*

- Incubated in EGF buffer solution

- Enterocyte migration
- Epithelial restitution
- Reduction in damage

*Riegler M et al. Gastroenterology 1996; 111(1):28-36*

**Clinical Application...**

## A multi-centre, randomised, double-blind clinical trial examining the effect of oral human recombinant EGF on the healing of duodenal ulcer.

*Palomino et al. Scand J Gastroenterol 2000; 35(10):1016-22*

- The ulcers were healed
  - 70.6% in group C
  - 40.0% in group B (lower dose)
  - 35.3% in group A (placebo) ( $P = 0.007$ )

## Epidermal Growth Factor Enemas with Oral Mesalamine for Mild to Moderate Left-Sided Ulcerative Colitis / Proctitis

Sinha et al.

- Remission Rates

### **2 weeks**

EGF	10/12 (83%)	Placebo	1/12 (8%)
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### **4 weeks**

EGF	10/12 (83%)	Placebo	3/12 (25%)
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**Questions need answering....**

# Hypothesis

- Inadequate amount of EGF reaching the colon or insufficient response by colonic mucosa during mucosal injury.

## Questions to be answered:

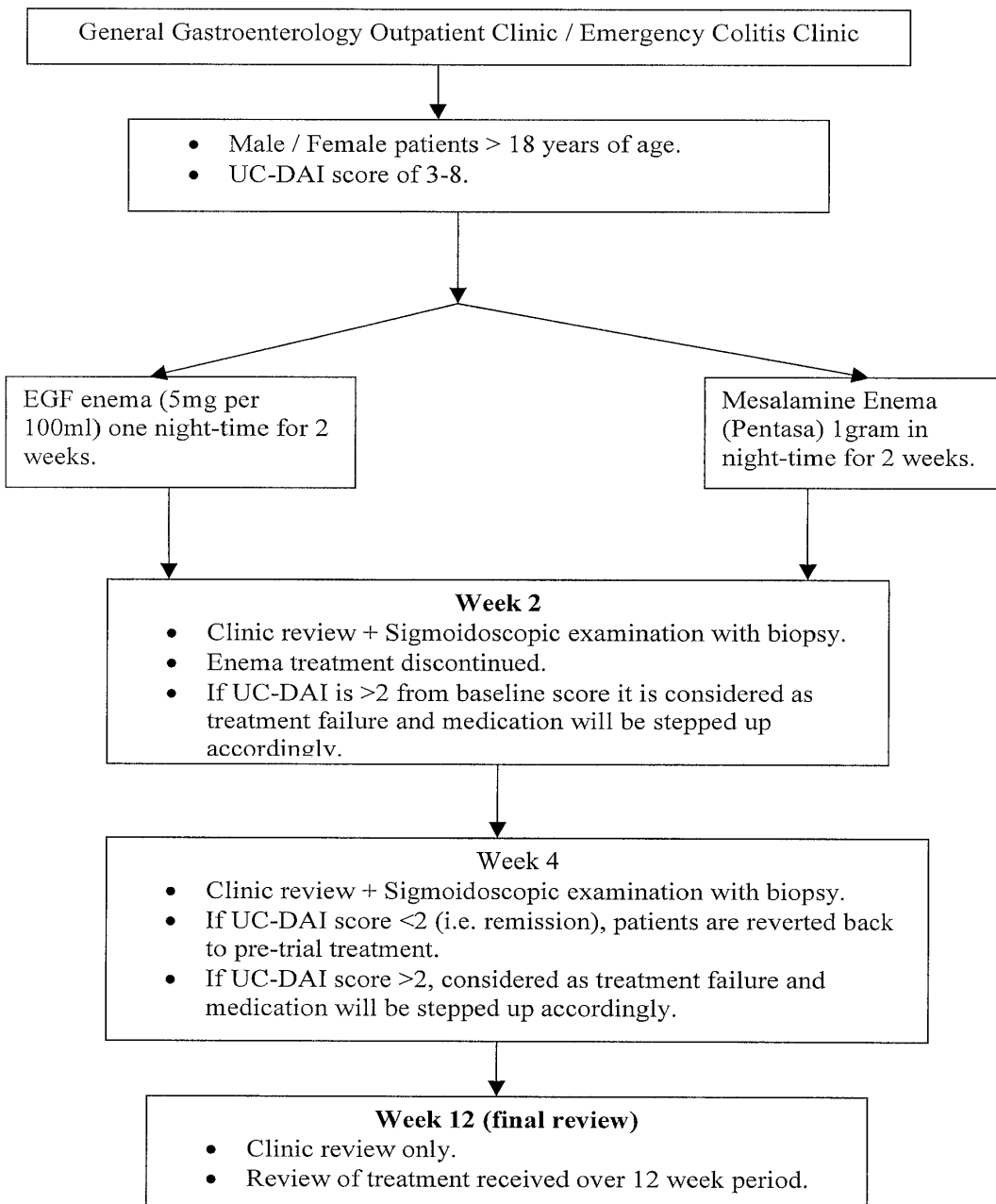
- (i) Is EGF enema more effective than mesalamine enema?
- (ii) Is there a sub-optimal response to EGF in the colon?
- (iii) Is there a failure of EGF produced from the upper gut to reach the colon?
- (iv) Is there reduced production of EGF in patients with UC?

**Further studies.....**

# EGF Vs Mesalamine enema in Rx Left sided UC

- Randomised, double blind, single centre study.
- Emergency colitis clinic / Outpatients
- Inclusion: UCDAI 3-8
- Exclusion: Immunosuppressants  
Steroids  
NSAIDs  
>3g oral mesalamine

- Randomised to receive:
  - 5mcg EGF enema/night for 2 weeks
  - or
  - 1g Pentasa/night for 2 weeks
- Reviewed week 2, 4 and 12.
- Sample size → 25 patients each arm  
(based on EGF remission rate 80%;  
mesalamine remission rate 45%)



\*The endoscopists and pathologist are blinded from the treatment patients receive and the timing of the sigmoidoscopic examination during the follow-up period.

## Primary Endpoint

- Remission at week 2 (UCDAI  $\leq 2$ )

## Secondary Endpoint

- Remission at week 4 (UCDAI  $\leq 2$ )
- Improvement of UCDAI  $\geq 2$  from baseline wk 2 or 4
- Improvement histological score  $\geq 2$  from baseline wk 2 or 4

# Investigate the effect of EGF on the mucosa in UC

- Biopsies taken during the clinical trial.
- Microdissection technique
- Cell proliferation and crypt fission

**Major hurdle.....**

- **Clinics are setup; ethical approval.**
- **Sourcing of EGF**
- **New Research Directive in UK / MHRA!**

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