Nutritional consequences of cancer therapy

Nutritional support and monitoring in radiation enteritis

Bernard MESSING (France)
Nutritional Support and Monitoring in Radiation Enteritis

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Radiation Enteritis: Acute (ARE) & Chronic (CRE)

- Objectives to learn:
  - Prevalence:
    • Some recent prospective data for CRE
  - Mechanisms:
    • Some experimental tracks emerge very recently
  - Diagnosis & clinical aspects:
    • Need grading
    • No anatomical boundaries
  - Management:
    • Few data about nutritional support & monitoring
What is the starting point?

- Patients expect their symptoms to be given legitimacy, even if they cannot be cured but amended.

- Malfunctions of gastrointestinal physiology, depending on the affected site, which if correctly diagnosed may enable a patient with difficult symptoms to be helped.

- Grading of symptoms is needed for multicentre trials.

- Prediction of combination of treatments needed is difficult.

- Many patients will also need some long-term support.

- The lack of randomised trials reflects multifaceted aspect of this poorly recognised disease - and the medical community’s lack of interest in this area.

- They are few chronic disorders where the effect on patients, is so little recognised and for which there is such an absence of support.

J Andreyev. Lancet Oncol 2007; 8:1007-17
Acute & chronic Radiation Enteritis

- **Acute RE**
  - Symptom-free phase: 3 to $n$ months
  - Severity (Grading) of ARE to be available in records

- **Chronic RE**
  - 3 mo to 30 years
  - Epi(endo)thelial lesions to / and Endo(epi)thelial lesions
Radiation therapy, alone or combined with other types of treatment, is given to 70% of all cancer patients. Cancer specific survival is improved with higher radiation dose, and technical improvements limit exposure of normal tissues like the bowel.

Nevertheless, delayed radiation enteropathy continues to be a dose-limiting factor for long-term uncomplicated cancer cure.

Prevalence estimates of moderate and severe late bowel effects varies from 5%-30%.

Larsen A, Reitan JB, Aase ST, Hauer-Jensen M
The risk of CRE is significantly increased with:

- Surgery before RT: for example, after RT for prostate cancer

- Preexisting cardiovascular disease:
  3500 patients irradiated for advanced uterine cervical carcinomas: smoking status: yes
  hypertensive disease and diabetes mellitus: yes

- Severe acute GI symptoms during RT:
  553 patients receiving RT for prostate cancer

Preventing acute symptoms could be a strategy to help reduce the risk of delayed radiation effects.

Microvascular dysfunction in ARE

Ossama OA et al
Arterio Scler Thromb Vasc Biol
2006; 26: 287-94
Acquired microvascular dysfunction in CRE

Case report: 2 year post Rx; Ileal webs & stricture formation

*Ileal 20 cm resection, submucosal arterioles*

Endothelial dysfunction in the pathogenesis of Radiation Enteropathy


Table 1 Potential pharmacological strategies for modulating post-radiation endothelial dysfunction to ameliorate development of radiation enteropathy and some of their respective limitations

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Major limitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet aggregation inhibitors</td>
<td>Narrow therapeutic window (bleeding)</td>
</tr>
<tr>
<td>Direct thrombin inhibitors</td>
<td>Narrow therapeutic window (bleeding)</td>
</tr>
<tr>
<td>Thrombin receptor blockers</td>
<td>Blocks only cellular thrombin effects</td>
</tr>
<tr>
<td>Recombinant thrombomodulin</td>
<td>Does not restore endothelial thrombomodulin</td>
</tr>
<tr>
<td>Activated protein C</td>
<td>Only partly blocks the effects of preformed thrombin</td>
</tr>
<tr>
<td>Statins</td>
<td>Non-specificity</td>
</tr>
<tr>
<td>Pentoxifylline</td>
<td>Non-specificity</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Non-specificity and variable efficacy</td>
</tr>
</tbody>
</table>

Proteinase Activated Rp1 inhibitors...
Inhibition of Rho Kinase decrease fibrogenic expression by decreasing Connective Tissue Growth Factor

6 CRE vs 6 Controls in vitro SMC  Bourgier C et al Gut; 2005; 34 : 336-43
Acute & chronic Radiation Enteritis

**ARE**
- Epithelial obvious
- From Cell Necrosis to inflammation

**Main Lesions**
- Villous atrophy

**CRE**
- Endothelial obvious
- Fibroblastic deposits
- Submucosal & serosal Hyalinosis
- Vasoocclusive

**Ischemic bowel**
Serosal adhesions → strictures: Ileal resection
strictures: Ileum > sigmoid

Serosal adhesions

Vaso-occlusive lesions

Submucosal fibrosis

Villous atrophy

Erosions, telangiectasia
Chronic symptoms

- Damage to blood vessels
- Ischaemia
- Fibrosis
- Changes affecting specific gastrointestinal physiological function depending on the affected site
- Factors unrelated to radiotherapy
- Symptoms
- Radiotherapy

No anatomical boundaries

J Andreyev
Lancet Oncol 2007; 8:1007-17
Chronic Radiation Entéritis (CRE)

- Anamnesis of previous radiotherapy to be sort out (blue tag on the skin...)
- Symptoms and clinical presentation:
  - Malnutrition and mineral - micronutrient deficits:
    - Reduction of intake: Pain, Occlusion, Vomitus,
    - Dehydration
    - Hypokaliemia, hypomagnesemia, anemia
    - Diarrhea: - hydroelectrolytic and frequently fatty
      - Malabsorptive: Bacterial overgrowth (BO) due to stenoses, or Iléopathy,
  - Occult or overt blood losses: telangiectasia, ulcers, BO
  - Atypical and rare features:
    - Early: necrosis of a bowel segment
    - Late: protein loosing enteropathy (lymphatics)
    - Late: Pancreatic insufficiency
    - Very late: Thrombo-stenosis of big arteries
- Diagnosis & prognosis require complete morphological & functional intestinal and nutritional work up:
  - Ongoing cancer - initial staging/date: 5-15%; 20-25% if fistulae
  - Other radiation complications: uronephro, myelo-plexo-pathy...
### Table 1 Causes of diarrhoea after radiotherapy: the published data

<table>
<thead>
<tr>
<th></th>
<th>Ludgate&lt;sup&gt;34&lt;/sup&gt; (n = 26)</th>
<th>Danielsson&lt;sup&gt;35&lt;/sup&gt; (n = 20)</th>
<th>Andreyev&lt;sup&gt;25&lt;/sup&gt; (n = 78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bile salt diarrhoea</td>
<td>50%</td>
<td>65%</td>
<td>1%</td>
</tr>
<tr>
<td>Large bowel strictures</td>
<td>15%</td>
<td>–</td>
<td>3%</td>
</tr>
<tr>
<td>Vitamin B12 deficiency</td>
<td>11%</td>
<td>30%</td>
<td>14%</td>
</tr>
<tr>
<td>Bacterial overgrowth</td>
<td>8%</td>
<td>45%</td>
<td>12%</td>
</tr>
<tr>
<td>Diverticular disease</td>
<td>8%</td>
<td>–</td>
<td>22%</td>
</tr>
<tr>
<td>Relapse of primary cancer</td>
<td>4%</td>
<td>–</td>
<td>10%</td>
</tr>
<tr>
<td>Pelvic sepsis</td>
<td>4%</td>
<td>–</td>
<td>3%</td>
</tr>
<tr>
<td>New Gl neoplasia</td>
<td>–</td>
<td>–</td>
<td>8%</td>
</tr>
<tr>
<td>Drug related</td>
<td>–</td>
<td>–</td>
<td>5%</td>
</tr>
<tr>
<td>IBD</td>
<td>–</td>
<td>–</td>
<td>4%</td>
</tr>
<tr>
<td>Proctitis</td>
<td>–</td>
<td>–</td>
<td>33%</td>
</tr>
<tr>
<td>Other</td>
<td>–</td>
<td>–</td>
<td>5%</td>
</tr>
</tbody>
</table>

Vitamin B12 deficiency is not a cause of diarrhoea but is included because it is reported prominently in the two previous studies, is important in its own right, and may indicate ileal or gastric disease or the presence of bacterial overgrowth.
**Chronic Radiation Entéritis (CRE)**

### Grading:

1. **Asymptomatic**

2. **Alterad GI function**

3. **Severely altered GI function**

4. **Life threatening consequences**

5. **Death**

### Glossary:

- Enteritis (clinical & endoscopy)
- Fistula
- Ileus
- Malabsorption
- Obstruction
- Stricture/stenosis
- Vomiting
- Necrosis
- Perforation
- Anal incontinence

**EORTC & ERTOG**:

- Cox JD 1995 & Trotti A 2000
- Int J Radiol Oncol Biol Phys.
- CTCAE v3.0 (2003, published 9.08.2006, p 19-28)

- 1 year (median time) post surgery:
  QoLQ-C30 in 220 patients (86% response rate (rr))
  Anorectal-sexual function questionnaire 118 (86% rr)
• 65% of patients had anorectal function impairment
• 20% of patients stated that this impaired their QoL

(B) Long-term effect of preoperative radiation therapy on anorectal function.

- 14 year (median time) post surgery
  Irradiated patients (n=21) vs non Irradiated (n=43) had:
• fecal incontinence: 57 vs. 26 %, P = 0.01
• soiling: 38 vs. 16 %, P = 0.04
• more bowel movements /wk: 20 vs. 10, P = 0.02

Ano rectal function was similarly impaired in both modalities of Radiotherapy for rectal cancer.
Compared with patients treated by surgery alone (n=454), Irradiated patients (5 x 5 Gy the week before surgery) (n=454) had an increased relative risk (RR) of

Late small bowel obstruction: 14 yr follow-up: 13.9% vs 5.5%
  RR 2.49 (95 %CI: 1.48 to 4.19)
  The risk of late small bowel obstruction requiring surgery was greatly increased: RR 7.42 (95 %CI: 2.23 to 24.66).

Abdominal pain: RR 2.09 (95 %CI 1.03 to 4.24)

Irradiated patients with postoperative anastomotic leakage were at increased risk for late small bowel obstruction
  RR 2.99 (95 %CI: 1.07 to 8.31).

Submucosal fibrosis

Villous atrophy
Treatment(s) proposal(s)
**Acute & chronic Radiation Enteritis**

**To decrease fibrosis:**
- Anti TGFβ...
- Anti inflammatory drugs
- NSAIs & SAI
- Pentoxifylline
- Other...

**To increase perfusion:**
- GLP2
- Pentoxifylline
- Statins

**To increase the repair**
- To avoid malnutrition
- To feed the intestines:
  - Gln
  - Enteral supplements
  - SCFAs
- Antioxidants:
  - Vitamins E, A, C
  - Hyper Baric O₂ (HBO)
- Trophic hormones
  - GLP2

**To protect mucosa:**
- Sucralfate
- Prostaglandins analogues
- Probiotics

- Enteral supplements
- SCFAs
- Antioxidants:
  - Vitamins E, A, C
  - Hyper Baric O₂ (HBO)
  - Trophic hormones
  - GLP2

- Sucralfate
- Prostaglandins analogues
- Probiotics
<table>
<thead>
<tr>
<th>Author</th>
<th>yr</th>
<th>Nb</th>
<th>treatments</th>
<th>duration wk</th>
<th>Scoring</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cavcié 2000</td>
<td></td>
<td>60</td>
<td>Mesalazine 3g, Bethametazone 5mg ± Metronidazole 1200mg</td>
<td>4</td>
<td>Bleeding</td>
<td>p &lt;0.04 + I &amp; L (1yr)</td>
</tr>
<tr>
<td>Kochhar 91</td>
<td></td>
<td>37</td>
<td>Placebo or oral Sucralfate 2g + Sulfasalazine 2g, Prednisone 20mg</td>
<td>4</td>
<td>Overall</td>
<td>p&lt;.05 50% vs 66%</td>
</tr>
<tr>
<td>Kneebone 04</td>
<td></td>
<td>298</td>
<td>Oral Sucralfate 3g vs Placebo during Rx</td>
<td>yes</td>
<td></td>
<td>1yr : NS</td>
</tr>
<tr>
<td>Rougier 92</td>
<td></td>
<td>32</td>
<td>Hydrocortisone 90mg &gt; Betamet</td>
<td>4</td>
<td>Clinical</td>
<td>33% vs 80%</td>
</tr>
<tr>
<td>Talley 97</td>
<td></td>
<td>15</td>
<td>SCFA (60ml) vs Placebo (cross over)</td>
<td>2</td>
<td>Overall</td>
<td>NS</td>
</tr>
<tr>
<td>Pinto 99</td>
<td></td>
<td>19</td>
<td>SCFA (60ml) vs Placebo</td>
<td>5</td>
<td>scoring</td>
<td>NS at 6mo</td>
</tr>
<tr>
<td>Khan 2000</td>
<td></td>
<td>16</td>
<td>Misoprostol (Cytotec) suppo vs P</td>
<td>5</td>
<td>yes</td>
<td>p&lt;.05 at 9mo</td>
</tr>
<tr>
<td>Ehrenpreis 05</td>
<td></td>
<td>20</td>
<td>Retinol palmitate (10000UI/d) vs p</td>
<td>12</td>
<td>Clinical</td>
<td>+ up to 3mo</td>
</tr>
<tr>
<td>Kennedy 01</td>
<td></td>
<td>20</td>
<td>Vitamins E (800mg) &amp; C (1g)</td>
<td>1yr</td>
<td>before/after</td>
<td>+trend</td>
</tr>
<tr>
<td>Jensen 97</td>
<td></td>
<td>21</td>
<td>Heater probe (4 to6/wk) vs bipolar electrocoag. Probe</td>
<td>1...</td>
<td>Bleeding</td>
<td>+ stop transfusions</td>
</tr>
<tr>
<td>Clarke 2004</td>
<td></td>
<td>68</td>
<td>Hyper (2)Baric O₂ (30 to 40)</td>
<td>up to 8</td>
<td>Healing</td>
<td>+ at 3mo</td>
</tr>
</tbody>
</table>


*Considered inconclusive because non multifactorial study +++
Chronic Radiation Proctitis (n=14) or Enteritis (n=7) Comparison with 9 controls (7 P, 2E). Retrospective.

Time to the occurrence of CRE: 12(3-48) mo, Grading I & II (EORTC/ERTOG) Previous failure: NSAID & SAID (topic), Sucralfate...

Duration of treatment: 10 (2-30) mo dosing: P = 2x400mg, Vitamin E = 2x500 mg

Hille A et al Strahlender Onkol 2005; 181: 606-14
Overall therapy of CRE

• Medical treatment:
  - Gastroenterological: of bacterial overgrowth
  - Nutritional support: of nutrient deficits
  - Systemic: treat comorbidities that reduce blood flow delivery (HBP, tobacco…)

• Home Parenteral Nutrition:
  - 5% - 25% of patients requiring long term HPN

• Surgical treatment if complications:
  - Therapeutic window: “not to early, not to late”
  - Resection preferable to by-pass
  - With peri-operative nutrition & antibio-prophylaxy
  - Post-op complications & repeated surgery worsen CRE
24 CRE with (sub)occlusion or malabsorptive diarrhea

4 groups: NPT or NEE ± Methyl Prednisolone 80 mg/j IV
Several weeks
No obvious response in Enteral Nutrition (exclusive)
Better evolution in TPN (exclusive):
Clinical ++, biological ++ in TPN group
with Radiological improvement in MePred group

Frequent clinical recurrence in the 2 yr follow-up

Loiudice & Lang  *Am J Gastroenterol* 1983; 78: 481-7
**Role of HPN in CRE**


**Criteria:** Occlusion only

- S vs. HPN first
- Symptoms after Rx: 14 vs 17 mo, NS
- Duration: 8 vs 2 mo, .01
- BMI: 20 vs 17.5, .01

Suggest that **bowel rest (2 mo)** & HPN alone could solve the obstruction in 50% of patients.


---

**Table 2. Surgery Data and Clinical Outcomes**

<table>
<thead>
<tr>
<th>Variable</th>
<th>S Group (N = 17)</th>
<th>HNP Group (N = 13)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N of subsequent surgeries (after first treatment)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>10 (58.8)</td>
<td>7 (53.8)</td>
<td>1.00</td>
</tr>
<tr>
<td>1 Surgery</td>
<td>5 (29.4)</td>
<td>6 (46.2)</td>
<td></td>
</tr>
<tr>
<td>≥2 Surgeries</td>
<td>2 (11.8)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Postoperative fistula*</td>
<td>4 (15.4)</td>
<td>0 (0.0)</td>
<td>0.57</td>
</tr>
<tr>
<td>Total length (months) of HPN, mean (SD)</td>
<td>55.2 (47.1)</td>
<td>19.3 (18.0)</td>
<td>0.03</td>
</tr>
<tr>
<td>Persistence of obstructive symptoms</td>
<td>7 (41.2)</td>
<td>4 (30.8)</td>
<td>0.71</td>
</tr>
<tr>
<td>Nutritional autonomy</td>
<td>10 (58.8)</td>
<td>13 (100.0)</td>
<td>0.01</td>
</tr>
<tr>
<td>Mortality related to chronic enteritis</td>
<td>3 (17.6)</td>
<td>0 (0.0)</td>
<td>0.24</td>
</tr>
</tbody>
</table>

Data presented are numbers of patients (%), when not otherwise specified.

*Percentages are calculated over the total number of surgeries (26 in the S group and 36 in the HNP group).
## ETIOLOGY OF ADULT SHORT BOWEL

<table>
<thead>
<tr>
<th>Condition</th>
<th>UK (n = 84)</th>
<th>France (n = 124)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemia</td>
<td>10%</td>
<td>40%</td>
</tr>
<tr>
<td>Crohn's</td>
<td>55%</td>
<td>9%</td>
</tr>
<tr>
<td><strong>Radiation Enteritis</strong></td>
<td><strong>10%</strong></td>
<td><strong>23%</strong></td>
</tr>
<tr>
<td>Volvulus</td>
<td>6%</td>
<td>7%</td>
</tr>
<tr>
<td>Post-op/adhesions</td>
<td>8%</td>
<td>11%</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>11%</td>
<td>10%</td>
</tr>
</tbody>
</table>

Survival rate of 124 adult patients with nonmalignant short bowel according to main types of primary disease.

Radiation enteritis

Death due to recurrent cancer: 18/54

Scolapio J et al, Am J Gastro 2002

Messing B et al Gastroenterology 1999
Hysterectomy in 09. 2000 + 2 previous abdominal surgery 03.2005: Rxtherapy 45Gy for recurrent uterine carcinoma End 2005: Subocclusion and diarrhea January 2008: (Photograph) Severe CRE (Occlusion: Grade 4) in a 74 yr-old lady Treatment was pre and post surgery HPN Requiring large ileal resection with a Transient stoma 120 cm J- 84% Colon. Actually 3 HPN/wk; + 15 kg & BMI 21
Treatment of Radiation Enteritis is multifactorial

- **Monitoring:**
  - ARE & CRE: Use Recognized Grading for scoring
  - CRE: Improve recognition by implementing database

- **Symptomatic & Supportive:**
  - ARE: Loperamide, Octreotide ++ Reduce diarrhea
  - ARE: diet and supplement(s) + May reduce CRE
  - Severe CRE perioperative, HPN +++ Life saving period(s) of bowel rest

- **Pathophysiological:**
  - ARE & CRE: dont forget comorbidities +++ Vascularisation
  - ARE: Topical for proctitis + Antiinflammatory
  - CRE: bleeding ++ Heat probe/HBO
  - CRE: trend in antioxydants + Pentoxy + E (A,C)
Thanks for your attention
Therapeutics proposals in CRE

• Correct malnutrition and specific deficits

• Bowel rest : Exlusive HPN during 1-2 month

• Antioxydants : Vitamin E IV then oral (1g) + Se (100ug)/d

• Antiinflammatory & provascular : Pentoxyphilline : 800 mg/d

• Provascular : Statine, i.e., Tahor 20 mg/J

• Other main points : Stop tobacco impérative

Strict Control of blood pressure & diabète

• When to treat :
  • Randomisation possible with 2 groups
    - immediate if grading ARE : ≥ 2
    - As soon as detected in ERC : all grades

BM.08.2008
Acute & chronic Radiation Enteritis

- **Principles and Strategy of medical treatment:**

- **Acute RE**
  - 30 seconds to 3 mo
  - Epi(endo) thelial lesions to / and Endo(epi)thelial lesions

- **Chronic RE**
  - 3 mo to 30 years

- **Symptom-free phase**
  - 3 to n month

To reduce the *conversion rate* between acute & chronic

- To correct / prevent malnutrition (overt & micronutrients)
- To enhance anti-apoptotic power & decrease permeability
- To enhance repair through anti-inflammatory treatments
- To protect from scaring with anti-fibrotic treatments

Severity (Grading) of ARE to be available in records
Consolidation radiotherapy for 106 Stage III Ovarian adenocarcinoma

• Residual disease < 1 cm: all patients after second look surgery
• Rx: whole abdomen for all 22.5 Gy
  + pelvic (22 Gy In 71) + Lombo-aortic (12 Gy in 33 patients)
• Patients recruited between 1983 & 1993
• Median Follow up: 14 yr
• Severe ARE: Rx stopped in 11 patients = 10%
• Severe CRE: 21 patients = 20%
  9 of whom require surgery = 8%
• Overall survival: 53% et 36% at 5 & 10 yr

Conclusion: Rx effective in selected patients but high intestinal toxicity incidence

Petit T et al Gynecol Oncol 2007 : 104; 104-08
Maintenance of Rx-induced Fibrosis

Figure 3 A: Bright field photomicrograph of fibrosis-derived intestinal smooth muscle cells (RE SMC) and normal cells (N SMC) observed after crystal violet staining; B: Fibronectin secretion level in RE SMC and N SMC assessed by ELISA (Chemicon).
Abdominal, pelvic, ano-rectal:
- ≥ 2/3 (up to 95%) of patients
- Classical significant variables for ARE:
  - Dosing, fractionation and volume:
  - Sensitivity: Small bowel > stomach > colon > oesophagus
  - Size of tumor
  - Associated Chemotherapy

Underlying Conditions facilitating CRE:
- Severe ARE.
- Previous surgery. *Malnutrition.*
- Vascular compromise: blood pressure, diabetes, tobacco.
CRE: late small bowel obstruction after Rx for Rectal Cancer
RR 2.49 (95% CI: 1.48 to 4.19)

Birgisson H et al.
Acute Radiation Enteritis (ARE)

• After an irradiation of 1.5 to 3.0 Gy:
  - necrosis of crypt cells in 12 – 24 hours
  - cystic dilation of crypts
  - Epithelial partial/subtotal transient (villous) atrophy,
    • Resolution in 2 to 6 weeks (to see Citrulline curve/decline)
    • severity of - lesions and of - previous malnutrition...

• Medical Treatment:
  - The Goal is to complete Radiotherapy but:
    • When symptoms are severe radiotherapy should be modified...
  - To avoid the adverse event(s) of radiotherapy:
    • Symtomatic treatment: pain, diarrhea, mucositis (topical…)
    • Physiopathological treatment:
      - “Acute” epithelial & “chronic” endothelial intestinal lesions...
Acute Radiation Enteritis (ARE) - symptoms -

- Enteritis
  - Nausea vomitus
  - Abdominal pain
  - Diarrhea:
    - Secretory
    - Decreased absorptive lining
    - Inflammatory
    - Increased permeability
    - Motor
    - Accelerated transit
    - Malabsorptive
    - Of lactose
    - Of Biliary salts

- Proctitis
  - Rectal pain

Grading the severity of diarrhea:

1. < 4/d (over pre treatment). No cramping
2. 4-6 /d or nocturnal. Moderate cramping
3. ≥ 7/d. Severe cramping. Incontinence
4. > 10/d. Grossly bloody or dehydration

- Of Biliary salts
Figure 4  Time course of the plasma citrulline concentration between hematopoietic stem cell transplantation (HSCT day -6 to +21). [Reproduced from reference [82] with permission of Cancer, 2005, Wiley Interscience]. Lines represent mean citrulline concentration and 95% confidence intervals.

No correlation
With symptoms
Or permability tests

Lutgens LC et al
Cancer 2005 :
103, 191-99
<table>
<thead>
<tr>
<th>Marker (n = paired samples obtained)</th>
<th>Time-point</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
</tr>
<tr>
<td></td>
<td>28.1 (8.3)</td>
</tr>
<tr>
<td>Citrulline [µM; mean (s.d.) (n = 50)]</td>
<td></td>
</tr>
<tr>
<td>CRP [mg/L; mean (s.d.) (n = 51)]</td>
<td>7.5 (20.9)</td>
</tr>
<tr>
<td>ECP [µg/L; mean (s.d.) (n = 20)]</td>
<td>32.3 (15.9)</td>
</tr>
<tr>
<td>Calprotectin [µg/g; mean (s.d.) (n = 49)]</td>
<td>35.7 (103)</td>
</tr>
</tbody>
</table>

* P = 0.02 paired samples t-test.
** P = 0.01 t-test on ln per cent change.

Acute Radiation Enteritis (ARE)

- **Symptomatic treatment:**
  - **Pain:** 1st line: antispasmodic, 2nd line, ± narcotics
  - **Diarrhea:** to be graded (National Cancer Institute)
    - To decrease osmotic diarrhea: Lactose free diet
    - To decrease accelerated transit time: Loperamide: 6 mg/d
    - To decrease Bile salts malabsorption: Loperamide: 6 mg/d
    - If resistant to standard treatment°: Octreotide: 300-450\(\mu\)g/d 5d
  - **Mucositis especially Proctitis** (topical treatment):
    - To protect mucosa: Sucralfate, Prostaglandine analogues...
    - And to reduce inflammation: Salycilates, steroids….: no consensus
  - **Of weight loss**:
    - Supplement elemental seep feeding (50% to 75% compliance)

Topkan E et al / Oncology 2006; 71: 354-360 : ° Resistant to Loperamide
# Treatment of Acute Radiation Proctitis

<table>
<thead>
<tr>
<th>Author</th>
<th>yr</th>
<th>Nb</th>
<th>treatments/d</th>
<th>duration wk</th>
<th>Scoring</th>
<th>Results</th>
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<tbody>
<tr>
<td>Kilic 2001</td>
<td></td>
<td>31</td>
<td>Sulfasalazine 2g versus placebo</td>
<td>5</td>
<td>yes*</td>
<td>grade≥2: &lt;02 20% vs 63%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Pelvic (Recto &amp; Histo : NS)</td>
<td></td>
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<tr>
<td>Resbeut 97</td>
<td></td>
<td>153</td>
<td>Mesalazine (5-ASA) vs placebo</td>
<td>5</td>
<td></td>
<td>Diarrhea NS 69% vs 66%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Pelvic : prostate &amp; uterus</td>
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<tr>
<td>Jahraus 05</td>
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<td>27</td>
<td>Balsalazide 4.5g (5-ASA) vs placebo</td>
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<td></td>
<td>Clinical (sum) p = .04</td>
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<tr>
<td>Kneebone 2001</td>
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<td>335</td>
<td>oral Sucralfate 3g vs Placebo</td>
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<td>yes</td>
<td>NS 87% vs 85%</td>
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<td>prostate carcinoma</td>
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<td>Sanguineti 2003</td>
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<td>134</td>
<td>Hydrocortisone foam 100mg vs Sucralfate 3g vs mesalazine 4g oenema</td>
<td>5</td>
<td>yes</td>
<td>62% vs 52%</td>
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<tr>
<td>O'Brien 97</td>
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<td>86</td>
<td>Sucralfate 3g vs placebo oenema</td>
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<td>yes</td>
<td>NS 88% harmful</td>
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<tr>
<td>Pinto 99</td>
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<td>19</td>
<td>SCFA (60ml) vs Placebo</td>
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<td>Bleeding p &lt;.02</td>
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<tr>
<td>Khan 2000</td>
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<td>Misoprostol (Cytotec) suppo vs P</td>
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<td>yes</td>
<td>p&lt;.05</td>
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<tr>
<td>Kozelsky 03</td>
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<td>Gln (8g) vs placebo</td>
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<td>yes</td>
<td>NS, at 1&amp;2yr</td>
</tr>
</tbody>
</table>

Updated July 2008 Medical treatments (RCT). LENT-SOMA*