Progress in managing chronic GI side effects of cancer treatments

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London, UK
"It has become appallingly obvious that our technology has exceeded our humanity."

Albert Einstein
Mr B

- 46 year old banker
- Stage IV low rectal cancer
- Neoadjuvant chemoradiation
- Low anterior resection with J pouch
- 2 years out from treatment
- 3 different clinicians involved in follow up

- 2 CT scans
- 3 MRI scans
- 1 colonoscopy
- 13 follow up appointments
- CEA checked 7 times
- No medication
Mr B

- Bowels open 10-18 times / day
- Normal - liquid stool
- Unable to attend meeting > 20 minutes
- Bowels open 3 times per night
- Tenesmus +++
- Wears nappies
The only aim of healthcare should be health gain
“All you do is treat crumble”
Professor of Oncology

Dr Andreyev is rather naïve
Professor of GI Physiology

“You don’t really do anything useful”
Senior manager

“Very provocative Dr Andreyev, come back in 10 years”
NICE

Why?

“You are not terribly mainstream, are you?”
Professor of Gastroenterology
“Pay no attention to what the critics say; no statue has ever been erected to a critic”

Jean Sibelius
A fundamental truth

Curing cancer inevitably risks damage to normal tissues
Rectal cancer

Symptoms | Surgery alone | Preoperative radiotherapy | Post operative radiotherapy
--- | --- | --- | ---
Any incontinence | 5-38% | 51-72% | 49-60%
Toilet dependency | 6% | 30% | 53%
Excellent function | 32% | 14% | N/A

Age-standardised one-year relative survival rate, rectal cancer, by sex, England and Wales, 1971-2006

A fundamental truth

Curing cancer inevitably risks damage to normal tissues - toxicity isn’t bad

What’s bad ...... is doing nothing about it.
What do symptoms mean?

- very little!
Mr. H

- 76 year old, normal bowel function pre-RT
- Prostate cancer, 1 year after conformal RT
- Normal PSA
- Bowels open x4 per day
- Urgency
- Often loose stool
- Faecal incontinence weekly
- Tenesmus
- Perianal soreness

Mr. J

- 64 year old, normal bowel function pre-RT
- Prostate cancer, 1 year after IMRT
- Bowels open 3-6 per day
- Urgency
- Often loose stool
- x2 faecal incontinence / month
- Tenesmus
- Perianal soreness

Too much fibre

Giardia
&
2cm sigmoid polyp
Why do patients develop GI symptoms?
The physiological model

Any insult

- Inflammatory changes
  - Oedema
  - Cell death
  - Atrophy / loss of stem cells

- Potentially alter specific GI physiological function(s)

- Relate to symptoms

Unrelated factors
- stress
- sepsis
- premorbid conditions

ischaemia

fibrosis

Symptoms
## Chronic loose stool after radiotherapy (1:2)

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>n=</td>
<td>26</td>
<td>11</td>
<td>20</td>
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<tr>
<td>%</td>
<td></td>
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<tr>
<td>Bile acid malabsorption</td>
<td>50</td>
<td>73</td>
<td>65</td>
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<td>Large bowel strictures</td>
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<td>9</td>
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<td>Bacterial overgrowth</td>
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<td>45</td>
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<tr>
<td>Diverticular disease</td>
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<td>9</td>
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<tr>
<td>Relapse</td>
<td>4</td>
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<td>10</td>
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<td>(Lactose intolerance)</td>
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<td>5</td>
</tr>
<tr>
<td>Pelvic sepsis</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3</td>
</tr>
<tr>
<td>New GI neoplasia</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>8</td>
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<td>-</td>
<td>4</td>
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<tr>
<td>Proctopathy</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>33</td>
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<tr>
<td>Other</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>5</td>
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</table>
Why do patients come and see a gastroenterologist?
What do you hope the outcome of a gastroenterological consultation will be?

- Return to normal
- Treatment
- Advice
- Explanation
- Research
- Information
- Reassurance

Male
Female

Gillespie AP&T 2007
What GI symptoms are important?
Which symptom is the worst?

- Leakage
- PR bleeding
- Wind
- Bloating
- Sleep disturbance
- Diarrhoea
- Constipation
- Pain
- Mucus
- Urgency
- Other

[Bar chart showing symptom worst by gender]

Gillespie AP&T 2007
GI symptoms: the Royal Marsden GI Unit algorithmic approach
## RMH algorithm v7 2011

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>Nausea</td>
</tr>
<tr>
<td>Bloating</td>
<td>Nocturnal need to defecate</td>
</tr>
<tr>
<td>Borborygmi</td>
<td>Pain - abdomen</td>
</tr>
<tr>
<td>Change in bowel habit</td>
<td>Pain - back (new onset)</td>
</tr>
<tr>
<td>Constipation</td>
<td></td>
</tr>
<tr>
<td>Diarrhoea</td>
<td></td>
</tr>
<tr>
<td>Evacuation</td>
<td></td>
</tr>
<tr>
<td>Flatulence (oral / rectal)</td>
<td>Tenesmus</td>
</tr>
<tr>
<td>Frequency of defaecation</td>
<td>Urgency</td>
</tr>
<tr>
<td>Incontinence / soiling / leakage</td>
<td>Vomiting</td>
</tr>
<tr>
<td>Loss of rectal sensation</td>
<td>Weight loss</td>
</tr>
<tr>
<td>Mucus excess</td>
<td></td>
</tr>
</tbody>
</table>

**Men**

Median 6 symptoms (range 1-16)

**Women**

Median 11 symptoms (range 4-16)

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Anorexia

Change in taste/saliva/smell

Dumping

Anorexia

Change in taste/saliva/smell

Dumping

Odynophagia

Reflux

Regurgitation

Wind/burping

Benton 2011
For each of the 35 symptoms:
• defined list of tests
• defined sequence of treatments
Based on the physiological model

Management of symptoms becomes straightforward

Identify each symptom accurately

Arrange appropriate tests to identify which physiological deficits are present

-> obvious treatment options
John

56 year old

- 2004  rectal cancer - anterior resection
- 2005  liver resection
- 2005  further liver resection + chemotherapy
- 2005  small bowel bypass
- 2006  para-aortic irradiation + 2\textsuperscript{nd} line chemotherapy
- 2006  ileal resection
- 2006  3\textsuperscript{rd} line chemotherapy
- 2008  hydronephrosis stented
- 2008  intra peritoneal chemotherapy
- 2008  bile duct stented
- 2008  cetuximab + chemotherapy
- 2009  further ileal resection + further chemotherapy

Referral: “unresponsive diarrhoea & weight loss”
• 9 months intractable symptoms
• Wind + cramps
• BO x 20 per day x 5 at night
• Incontinent most days
• Weight loss 25 kg in 4 months
• Feels terrible!

And!!!!
• Not diarrhoea
• It was steatorrhoea
Table 4  Questions to identify patients in need of specialist assessment

<table>
<thead>
<tr>
<th>Critical minimal questions indicating need for GI referral</th>
<th>Critical minimal indicators to consider endoscopic assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are they woken from sleep to defaecate?</td>
<td>Is the patient ≥5 years after radiotherapy (screening for second malignancy)?</td>
</tr>
<tr>
<td>Do they have troublesome urgency of defaecation and/or faecal leakage/soiling/incontinence?</td>
<td>Is there any rectal bleeding?</td>
</tr>
</tbody>
</table>
Follow the algorithm!

5 causes for steatorrhoea

1. Bile acid malabsorption
   (✓ SeHCAT scan 1%, Rx Colesevelam)

2. Small bowel bacterial overgrowth
   (✓ Duodenal aspirate, Ecoli, Rx ciprofloxacin 500mg bd 1 week)

3. Pancreatic insufficiency
   (✓ Faecal elastase <15, Rx creon)

4. Free fatty acid malabsorption
   (✓ 60g fat / day)

5. Miscellaneous
   (✓ Addisonian: synacthen test, Rx hydrocortisone + fludrocortisone)
Was back racing minis within a week

and

He continue racing them every weekend till 10 days before he died 9 months later!
£40 million wasted on ineffective or dangerous treatments annually

DOH 2010
Painful, rectal ulceration following APC for bleeding after prostate irradiation
Almost complete resolution of ulceration following 40 sessions of hyperbaric oxygen
Mr B

- Bowels open 10-18 times / day
- Normal - liquid stool
- Unable to attend meeting > 20 minutes
- Bowels open 3 times per night
- Tenesmus +++
- Wears nappies
Mr B

- some inflammation in his pouch
- no other abnormalities

**Treatment given**
- Normacol
- Toileting exercises
- Glycerine suppositaries

**After 6 weeks**
- Bowels open 4 times a day
- No urgency /Incontinence
- No nocturnal defaecation
Conclusions

1. Loads of patients
2. In loads of trouble
3. Seek them out
4. Develop referral pathways for expert care

Because
- Attention to detail allows management
- Do not make things worse!