Anal Symptoms and Their Clinical Assessment in Rectal Microbicide Studies

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‘I used dry condoms lubricated on the outside with KY, but when I heard that lubricants containing N9 spermicide were lethal to HIV I went over to ready lubed jonnies (condoms) for added protection. I now find that my arse (anus) becomes sore and inflamed and, at the same time rather numb so that sensation is lost’

Harry (Scunthorpe) 1991
14 Years Later……

- MSM actively seek lubricants that contain nonoxynol-9 (N-9) because they believe that N-9 may help to prevent infection by HIV.

- N-9 may actually enhance HIV infection.

- Because the rectal epithelium protects target cells in the submucosa from HIV, we conclude that lubricants containing N-9 should be avoided during rectal sex.

Phillips D M et al. Contraception. 2004:70(2);107-110. Lubricants containing N-9 may enhance rectal transmission of HIV and other STI’s.
• Importance of anal symptom perception in the assessment of candidate rectal microbicides
Overview

• Normal anal anatomy
• Common anal conditions
• Anorectal sexually transmitted infection
• Assessing anal symptoms in the context of rectal microbicide research
Anatomy
Normal Anal Canal

Normal Squamocolumnar Epithelial Junction

anus

rectum
Columnar and Squamous Epithelium

Shatlock et al. Nat Rev Microbiology 2003
Physiology
## Anal Sphincter

<table>
<thead>
<tr>
<th>Test site</th>
<th>Resting (mmHg)</th>
<th>Squeeze (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anal (male and female)</td>
<td>56</td>
<td>178</td>
</tr>
<tr>
<td>Pelvic floor (nulliparous)</td>
<td>-</td>
<td>15-20</td>
</tr>
</tbody>
</table>

Sensation

• Anal canal:
  Sensation to touch, pin-prick, heat, and cold
  Anal canal sensation is via the inferior rectal branch
  of the pudendal nerve

• Rectum:
  The rectum is only sensitive to distention by
  receptors in the rectal wall and pelvic fascia or
  surrounding muscle
  The sensory pathway for rectal distention is the
  parasympathetic system
Anorectal Pathology
Common Conditions

- Benign anal conditions highly prevalent in the general population
- 1.5 million anorectal preparations dispensed by prescription each year in US
- 80% of US population with anal symptoms self-medicate

Hemorrhoids

- Hemorrhoids are symptomatic hemorrhoidal tissue
- Prevalence 4% (10 million US)
- Peak 45-65
- Risk: ageing, pregnancy, straining at stool, portal hypertension
Anal Fissure

- Split in the anal epithelium
- Male = female incidence
- Younger > older
- Cause: trauma, previous surgery and scarring
- Site: posterior in 90% - anterior in 10%
Perianal Abscess

- 2 male: 1 female
- Peak 30’s to 40’s
- Cause: obstruction of anal crypts
- Site:
  - perianal > ischiorectal
  - intersphincteric
  - supralelevator
  - submucosal
Anal Fistula

- 2 male: 1 female.
- Peak age 40
- 9:100,000
- Cause: abscess in anorectal gland
- Fistula is sequelae in 7-40% of abscess' 
- 90% posterior, 10% anterior
Perianal Dermatoses/ Non-Specific Ulceration

- Dermatophyte
- Psoriasis
- Eczema
- Diarrhea
- Receptive anal sex
- Excessive wiping
Anorectal Diagnosis and Presentation

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Symptom/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fissure</td>
<td>Pain, bleeding</td>
</tr>
<tr>
<td>Fistula</td>
<td>Itch, pain, bleeding, discharge, swelling</td>
</tr>
<tr>
<td>Hemorrhoids</td>
<td>Itch, pain, bleeding, mass</td>
</tr>
<tr>
<td>Eczema</td>
<td>Itch, pain, discharge</td>
</tr>
<tr>
<td>Abscess</td>
<td>Pain, swelling, bleeding, discharge</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>Itch, pain</td>
</tr>
<tr>
<td>Dermatophyte</td>
<td>Itch, pain</td>
</tr>
</tbody>
</table>
Sexually Transmitted Infection
Anal Human Papillomavirus

- 50-75% of the general population exposed to anogenital HPV
- 1% develop clinical warts
- Site: perianal to transition zone
- High-risk HPV associated with the development of anal cancer
Gonococcal Proctitis

- Associated with female cervix infection in 35-50% mostly without RAI.
- 40% ONLY site in MSM - mostly with RAI
- Most often asymptomatic (90%)
Chlamydial Proctitis

- Cause of 15% of MSM proctitis
- Friable mucosa with mucopus
- Mostly symptomatic
Lymphogranuloma Venereum

- Proctocolitis with inflammation and granulomata formation with lymphoid hyperplasia
- Late: perirectal abscess, fistulae, rectal stricture/stenosis
- RAI or spread from posterior urethra (men)
Herpes Simplex Virus

- Primary infection may include distal 10cm of the rectum
- Systemic features
- Recurrent HSV limited to the anal canal and perianal area
- 60% seropositivity in STD populations
- Asymptomatic shedding
Primary Anorectal Syphilis

- Few reports in the literature
- Commonly asymptomatic chancre
- Rectal chancre very uncommon
# Anorectal STD Diagnosis and Presentation

<table>
<thead>
<tr>
<th>STD</th>
<th>Symptom/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonorrhea</td>
<td>Discharge, pain, tenesmus</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>Discharge, pain, tenesmus</td>
</tr>
<tr>
<td>Herpes simplex</td>
<td>Pain, bleeding, itch</td>
</tr>
<tr>
<td>LGV</td>
<td>Pain, bleeding, itch</td>
</tr>
<tr>
<td>HPV</td>
<td>Itch, bleeding, mass</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Mass, pain</td>
</tr>
</tbody>
</table>
U19 PI: Anton

- **Project 3 PI: Gorbach**

- **Specific Aim 1:** To describe behavioral features of anal intercourse that will affect microbicide utilization and administration.

- **Specific Aim 2:** To assess the level of and predictive accuracy of reported anal symptomology among women and men who practice anal intercourse and the effect of anal coitus on symptoms.

- **Specific Aim 3:** Quantify the acceptability of 5 different formulation types of anorectal products among target populations to prioritize formulation options for delivering a potential rectal microbicide in a pre-sex context.
Hypotheses

• Individuals who report RAI will report more anal symptoms than individuals who do not practice RAI.

• More individuals who report RAI will have clinical signs of anorectal conditions than individuals who do not report RAI. These signs will be evident through standard anoscopic clinical examination as well as by high-resolution anoscopic (HRA) imaging.

• Individuals who report RAI will have a higher prevalence of anorectal STI’s than individuals who do not report RAI.
Project 3: PI Gorbach

Aims

1. RAI (n=224) HIV + (n=112) HIV - (n=112)
2. No RAI (n=224) HIV + (n=112) HIV - (n=112)

Women (n=448)

1. RAI (n=224) HIV + (n=112) HIV - (n=112)
2. No RAI (n=224) HIV + (n=112) HIV - (n=112)

Men (n=448)
Project 3 Study Visit

• Consent

• Detailed computer assisted questionnaire covering:
  - Baseline demographics
  - Sexual lubricant use
  - Sexual behavior
  - General health with specific reference to anal hygiene practices, and current anal symptoms

• High-Resolution anoscopy
  - Anorectal STD testing
  - Image capture and lesion identification
# Baseline Symptom Assessment

<table>
<thead>
<tr>
<th>Symptom</th>
</tr>
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<tbody>
<tr>
<td>Swelling</td>
</tr>
<tr>
<td>Itch</td>
</tr>
<tr>
<td>Pain</td>
</tr>
<tr>
<td>Feeling like you had to poop or take a bowel movement or shit when there was nothing there</td>
</tr>
<tr>
<td>Constipation (not being able to have a bowel movement or poop/shit)</td>
</tr>
<tr>
<td>Diarrhea</td>
</tr>
<tr>
<td>Discharge/wetness from your butt</td>
</tr>
<tr>
<td>Burning inside your butt</td>
</tr>
<tr>
<td>Burning on the edge or outside your butt</td>
</tr>
<tr>
<td>Bumps/lumps on the inside of your butt</td>
</tr>
<tr>
<td>Bumps lumps on the outside of your butt</td>
</tr>
<tr>
<td>Irritation</td>
</tr>
</tbody>
</table>
Project 3 Study Visit

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  - Baseline demographics
  - Sexual lubricant use
  - Sexual behavior
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• High-Resolution anoscopy
  - Anorectal STI testing
  - Image capture and lesion identification
High-Resolution Anoscopy and Image Capture

- Rectum
- Anorectal transition zone
- Anal canal
- Perianal area
- Lesion/s
## HRA Abnormalities

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th></th>
</tr>
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<tbody>
<tr>
<td>Bleeding</td>
<td>Molluscum</td>
</tr>
<tr>
<td>Hemorrhoids</td>
<td>Fistula opening</td>
</tr>
<tr>
<td>Ulceration</td>
<td>Piercing/tattoo</td>
</tr>
<tr>
<td>Excoriation</td>
<td>Bruising</td>
</tr>
<tr>
<td>Discharge</td>
<td>Blistering</td>
</tr>
<tr>
<td>Condyloma accuminata</td>
<td>Condylomata lata</td>
</tr>
<tr>
<td>Swelling</td>
<td>Skin tag</td>
</tr>
<tr>
<td>Fissure</td>
<td>Abscess</td>
</tr>
<tr>
<td>Leukoplakia</td>
<td>Erythema</td>
</tr>
</tbody>
</table>
Summary

• Anal symptoms are common in the general population
• The anal canal will be the predominant source of symptom perception for candidate rectal microbicides
• U-19: prevalence of anal symptomatology related to RAI and the predictive value of anal symptoms for clinically apparent ano-rectal pathology
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