Rectal Microbicides: The Basics

Date, Location
Your name, Your affiliation
This presentation

• Who is IRMA?
• Overview of the HIV epidemic
• New prevention technologies
• What are microbicides?
• Why do we need microbicides?
• Rectal microbicide research – the basics
• IRMA goals and objectives
• Rectal microbicide advocacy and you
IRMA is

Mission: support development of safe, effective, acceptable, and accessible rectal microbicides for all that need them

A global network of advocates, leading scientists, funders and policymakers from six continents – w/chapters in Peru and Nigeria

Secretariat
Report includes:

- Updated resource tracking & funding projections
- Overview IRMA activities
- Global context
- Updated Research snapshot
- Advocacy goals

From Promise to Product: Advancing Rectal Microbicide Research and Advocacy

Released
Microbicides 2010
May 23, 2010
Pittsburgh
De la Promesa al Producto:
Avanzando en la Investigación y Promoción de los Microbicides Rectales

Pittsburgh
Mayo 2010
Global context
# Global summary of the AIDS epidemic

*December 2008*

## Number of people living with HIV in 2008

<table>
<thead>
<tr>
<th>Category</th>
<th>Estimate</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>33.4 million</td>
<td>[31.1 – 35.8 million]</td>
</tr>
<tr>
<td>Adults</td>
<td>31.3 million</td>
<td>[29.2 – 33.7 million]</td>
</tr>
<tr>
<td>Women</td>
<td>15.7 million</td>
<td>[14.2 – 17.2 million]</td>
</tr>
<tr>
<td>Children under 15 years</td>
<td>2.1 million</td>
<td>[1.2 – 2.9 million]</td>
</tr>
</tbody>
</table>

## People newly infected with HIV in 2008

<table>
<thead>
<tr>
<th>Category</th>
<th>Estimate</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>2.7 million</td>
<td>[2.4 – 3.0 million]</td>
</tr>
<tr>
<td>Adults</td>
<td>2.3 million</td>
<td>[2.0 – 2.5 million]</td>
</tr>
<tr>
<td>Children under 15 years</td>
<td>430,000</td>
<td>[240,000 – 610,000]</td>
</tr>
</tbody>
</table>

## AIDS-related deaths in 2008

<table>
<thead>
<tr>
<th>Category</th>
<th>Estimate</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>2.0 million</td>
<td>[1.7 – 2.4 million]</td>
</tr>
<tr>
<td>Adults</td>
<td>1.7 million</td>
<td>[1.4 – 2.1 million]</td>
</tr>
<tr>
<td>Children under 15 years</td>
<td>280,000</td>
<td>[150,000 – 410,000]</td>
</tr>
</tbody>
</table>

The ranges around the estimates in this table define the boundaries within which the actual numbers lie, based on the best available information.

*2009 AIDS epidemic update*
### Regional HIV and AIDS statistics
#### 2008 and 2001

(First of 2 parts)

<table>
<thead>
<tr>
<th>Region</th>
<th>Adults &amp; children living with HIV</th>
<th>Adults &amp; children newly infected with HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Saharan Africa</td>
<td>22.4 million (20.8 – 24.1 million)</td>
<td>19.7 million (18.3 – 21.2 million)</td>
</tr>
<tr>
<td>Middle East &amp; North Africa</td>
<td>310 000 (250 000 – 380 000)</td>
<td>200 000 (150 000 – 250 000)</td>
</tr>
<tr>
<td>South and South-East Asia</td>
<td>3.8 million (3.4 – 4.3 million)</td>
<td>4.0 million (3.5 – 4.5 million)</td>
</tr>
<tr>
<td>East Asia</td>
<td>850 000 (700 000 – 1.0 million)</td>
<td>560 000 (480 000 – 650 000)</td>
</tr>
<tr>
<td>Latin America</td>
<td>2.0 million (1.8 – 2.2 million)</td>
<td>1.6 million (1.2 – 1.6 million)</td>
</tr>
<tr>
<td>Caribbean</td>
<td>240 000 (220 000 – 260 000)</td>
<td>220 000 (200 000 – 240 000)</td>
</tr>
<tr>
<td>Eastern Europe &amp; Central Asia</td>
<td>1.5 million (1.4 – 1.7 million)</td>
<td>900 000 (800 000 – 1.1 million)</td>
</tr>
<tr>
<td>Western &amp; Central Europe</td>
<td>850 000 (710 000 – 970 000)</td>
<td>660 000 (580 000 – 760 000)</td>
</tr>
<tr>
<td>North America</td>
<td>1.4 million (1.2 – 1.6 million)</td>
<td>1.2 million (1.1 – 1.4 million)</td>
</tr>
<tr>
<td>Oceania</td>
<td>59 000 (51 000 – 68 000)</td>
<td>36 000 (23 000 – 45 000)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>33.4 million (31.1 – 35.8 million)</td>
<td>29.0 million (27.0 – 31.0 million)</td>
</tr>
</tbody>
</table>

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**2009 AIDS epidemic update**

[UNAIDS Logo]

[World Health Organization Logo]
Condoms work.

So why do we need new strategies to halt the sexual transmission of HIV?
Here are some reasons for new strategies:

**Political opposition, resistance & inaction**
- Lack of educational & reproductive health programmes
- Lack of or poor social marketing
- Criminalisation by proxy

**Social barriers**
- Social stigma/Community response/Harassment
- Peer pressure & expectations
- Unbalanced gender relationships and roles
- Youth access/provision

**Structural barriers**
- Limited state and health services capacity
- Availability/Points of access
- Sex workers
- Incarceration
- Environmental
- Poverty/Cost

**Cultural barriers**
- Religious beliefs & values
- Moral values
- Misconceptions about semen

**Lack of or poor knowledge**
- Condom awareness
- Protective role of condoms
- Condom use

**Individual factors**
- Desire to conceive
- Poor negotiation skills
- Dislike of condom/Physical discomfort/Allergy
- Risk assessment
- Trust in sexual partner (required/expected)
- Sexual pleasure
- Mental health/Self esteem
- Alcohol/Drug use

**Rumors, myths & misconceptions**
- Efficacy/Quality
- Effect on sexual pleasure

Source: Roger Tatoud PhD, Senior Programme Manager, International HIV Clinical Trials Research Mgmt Office, Imperial College London & IRMA Steering Committee Member
And here are some more

Percentage of at-risk people with access to HIV prevention

- <20% Sex workers with access to behaviour change programmes
- 11% HIV+ pregnant women with access to PMTCT
- 10–12% Adults in Africa accessing HIV testing
- 9% Men who have sex with men with access to appropriate behaviour change programmes
- 9% Sexually active people with access to male condoms
- 8% Injection drug users with access to harm reduction programmes

New Prevention Technologies
What if we had a complete prevention tool kit?

**Prior to exposure**
- Rights-focused behaviour change
- Voluntary counselling and testing
- STI screening and treatment
- Male medical circumcision
- Preventive Vaccines
- Pre-exposure prophylaxis (PrEP)

**Point of transmission**
- Male and female condoms and lube
- ARV treatment to prevent vertical transmission (PMTCT)
- Clean injecting equipment
- Post-exposure prophylaxis (PEP)
- Vaginal and rectal microbicides

**Treatment**
- Improved ARV therapy
- Treatment for opportunistic infections
- Basic care/nutrition
- Prevention for positives
- Education & rights-focused behaviour change
- Therapeutic vaccines

ARV = antiretroviral
What is a microbicide?

• A product applied topically in the vagina or the rectum that can offer protection against HIV and, ideally, other STI pathogens
• Ideally would have a contraceptive version, and another to allow for pregnancy
• Formulated as a lubricant, gel, film, or vaginal ring
• A **rectal** microbicide (RM) might be delivered via suppository, douche, or an enema – in addition to a lube

**Microbicides are still in development**

**they are not available yet!**
## How would a microbicide work?

<table>
<thead>
<tr>
<th>Non-ARV-based</th>
<th>ARV-based</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Prevents HIV from entering healthy cells by creating a barrier between the cell and HIV</td>
<td>• Blocks specific proteins of HIV so that it cannot bind with a healthy cell</td>
</tr>
<tr>
<td>• In the case of a vaginal microbicide, could enhance the vagina’s natural defense system</td>
<td>• Blocks receptors on healthy cells so that HIV cannot bind with them</td>
</tr>
<tr>
<td>• Kills the virus by attacking it</td>
<td>• Deactivates key components of the HIV to inhibit replication</td>
</tr>
</tbody>
</table>
Comparing ARV-based and non-ARV-based microbicides

<table>
<thead>
<tr>
<th></th>
<th>ARV-based</th>
<th>Non-ARV-based</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Advantages</strong></td>
<td>More potent against HIV</td>
<td>Could work against HIV and other STIs</td>
</tr>
<tr>
<td></td>
<td>May be long lasting</td>
<td>Could be contraceptive</td>
</tr>
<tr>
<td></td>
<td>Not contraceptive</td>
<td></td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
<td>May be more toxic</td>
<td>May be less potent against HIV</td>
</tr>
<tr>
<td></td>
<td>May cause resistance</td>
<td>May need to be used at time of sex</td>
</tr>
<tr>
<td></td>
<td>Unlikely to protect against other STIs</td>
<td></td>
</tr>
</tbody>
</table>

Source: *Global Campaign for Microbicides*
Examples of how a microbicide might be delivered
Microbicides – the big picture

Source: Roger Tatoud PhD, Senior Programme Manager, International HIV Clinical Trials Research Mgmt Office, Imperial College London & IRMA Steering Committee Member
Anal Intercourse
Anal intercourse is a human behaviour.
Anal intercourse and women

- In absolute numbers, 7x more heterosexual women than gay men and MSM in the US practice receptive anal intercourse (AI) - a conservative estimate
  
  [Halperin DT.]

- Prevalence of AI among heterosexuals is not well defined
  - Varies regionally by age, population, co-risk
  - AI is relatively common globally, 5 – 10% in gen. pop. and up to 30-50% of women with other HIV risks engage in AI

- Unprotected AI may be a significant source of HIV transmission in many contexts, including those labelled as “heterosexual epidemics.”
Anal Intercourse
Gay men and other men who have sex with men (MSM)

- Anal intercourse is a common behaviour
- Most HIV infections due to unprotected AI
- Globally, MSM are 19x more likely to be infected with HIV than general population
- In North America, Western Europe, Latin America:
  - Gay men and MSM make up most HIV infections
- In many African, Asian and Latin American countries:
  - HIV among MSM significantly higher than general population
- Globally, only 9% of MSM in 2006 received any type of prevention
Compared to microbicides for vaginal use, rectal microbicides are in much earlier stages of development because of:

- Political and cultural reluctance to address anal sex among gay men, MSM and between women and men
  - Stigma
  - Denial
  - Homophobia
- Lack of understanding of need
- Scientific and biological challenges
- More complex safety issues – rectum very fragile
- Lack of adequate resources
## Biological challenges

<table>
<thead>
<tr>
<th><strong>Vagina</strong></th>
<th><strong>Rectum</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Most of the epithelium is 40 cell layers thick</td>
<td>Very fragile epithelium, 1 cell layer thick</td>
</tr>
<tr>
<td>Fewer CD4 cells than rectum</td>
<td>More inflammatory cells under surface (CD4 receptors)</td>
</tr>
<tr>
<td>Acidic pH</td>
<td>Alkaline, rather than acidic pH</td>
</tr>
<tr>
<td>Enclosed pouch</td>
<td>Open-ended tube</td>
</tr>
</tbody>
</table>
Anatomy 101

Mucosa of the Vagina and Rectum

Rectal mucosa

Vaginal mucosa

Mucosa of the rectum

Mucosa of the vagina
The anus and rectum

Source: Johns Hopkins Medicine
An act of unprotected anal intercourse is *10 to 20 times more likely* to result in HIV transmission than an act of unprotected vaginal intercourse.
Science
Clinical trials

- **Phase I**: Safety
- **Phase II**: Expanded safety
- **Phase IIb**: Proof of concept
- **Phase III**: Efficacy, large scale

[Diagram showing the relationship between phases with overlapping circles for safety and efficacy.]
The Product Pipeline

- **early-stage concepts**
  - pre-clinical testing
  - human safety trials
  - large-scale efficacy trials

Source: Alliance for Microbicide Development, with thanks to Anna Forbes
Research activities

• Pre-clinical/basic science
  – developing and testing products in labs and in animal studies

• Clinical trials – safety and efficacy
  – Are these RMss safe? Do they work?

• Acceptability & behavioural studies
  – What kinds of products would people use?
  – Who is having AI?
Research activities

• Baseline studies
  – What normally happens during AI?

• Formulation studies
  – How will different chemicals and substances be put together to make a safe, effective RM?

• Distribution studies
  – Where do RMs need to go?
## Research activities

<table>
<thead>
<tr>
<th>Section</th>
<th>Research project</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>The Microbicide Development Program (MDP)</td>
<td>2004–2010</td>
</tr>
<tr>
<td>2.2</td>
<td>Combination HIV Antiretroviral Rectal Microbicide (CHARM) Program</td>
<td>2010–2014</td>
</tr>
<tr>
<td>2.3</td>
<td>Microbicide Safety and Acceptability in Young Men</td>
<td>2010–2013</td>
</tr>
<tr>
<td>2.4</td>
<td>Combined Highly-Active Antiretroviral Microbicides (CHAARM) Programme</td>
<td>2010–2014</td>
</tr>
<tr>
<td>2.5</td>
<td>RMP-02/MTN-006: Phase I rectal microbicide safety and acceptability trial of topically applied tenofovir compared with oral tablet</td>
<td>2009–2011</td>
</tr>
<tr>
<td>2.6</td>
<td>MTN-007: Phase I rectal safety and acceptability study of tenofovir gel</td>
<td>2010–2011</td>
</tr>
<tr>
<td>2.7</td>
<td>Biomedical, social, and behavioural research funded by amfAR</td>
<td>2007–2010</td>
</tr>
<tr>
<td>2.8</td>
<td>Aptamer microbicide development program</td>
<td>2005–2011</td>
</tr>
<tr>
<td>2.9</td>
<td>Evaluating rectal safety and efficacy of microbicides in macaques</td>
<td>2008–2009</td>
</tr>
<tr>
<td>2.10</td>
<td>Assessing user preferences for rectal microbicide formulations: Gel vs. suppository</td>
<td>2005–2007</td>
</tr>
<tr>
<td>2.11</td>
<td>Assessing the rectal safety of sexual lubricants</td>
<td>2009</td>
</tr>
</tbody>
</table>

Source: From Promise to Product: Advancing Rectal Microbicide Research and Advocacy
Advocacy, Funding, IRMA and You
Advocacy goals

✓ Increase and diversify funding
✓ Increase research activities
✓ Increase knowledge
  - For instance:
    o Learn more about heterosexual anal sex
    o Learn more about anal sex behaviours and practices in general
Advocacy goals

Increase and diversify funding

RECTAL MICROBICIDE RESEARCH SPENDING BY YEAR (2000–2010), IN U.S. DOLLARS

Over the 11-year period of investments in RM research IRMA has tracked, the public sector has provided 97.3% of the funding (mostly from the U.S.), the philanthropic sector has provided 2.5% of funding, and the commercial sector has provided 0.2%.

Source: From Promise to Product: Advancing Rectal Microbicide Research and Advocacy
Advocacy goals

Projected funding needs

Source: From Promise to Product: Advancing Rectal Microbicide Research and Advocacy
Advocacy goals

• Develop Global Rectal Microbicide Development Plan
  – Every R&D dollar/euro needs to be spent smartly and strategically
  – Find consensus on research priorities among stakeholders
  – Coordinate research activities, from discovery through Phase III
  – Monitor progress
Advocacy goals

- Recruit researchers, advocates
- Recognise anal intercourse as an important driver in the HIV epidemic among gay men, MSM, and heterosexuals
- Address burden of HIV among gay men and MSM – particularly in the developing world
- Promote anal health
- Determine safety of lubricants for rectal use
  – http://tinyurl.com/lube-studies
MEN & WOMEN
DEMAND
RECTAL MICROBICIDES
What can you do?
What you can do in 5 minutes

• Join IRMA - sign up for IRMA listserv through website
• Read one fact sheet or news item from website or blog
• Join us on Facebook and Twitter
• Share web address and contact information w/another advocate, researcher, policy maker, potential funder

www.rectalmicrobicides.org
irma-alc.blogspot.com
What you can do in 30 - 60 minutes

• Join one of IRMA’s regular free teleconferences featuring world leaders in RM research, advocacy

• Read “From Promise to Product: Advancing Rectal Microbicide Research and Advocacy” or read one of the presentations from researchers, community members

• Talk to members of your community about your interest in rectal microbicides
Want to do more?

- Become your community’s rectal microbicide expert and spokesperson
  - Recruit new members, enlist organisational support for RMGs
  - Conduct presentations in your community – use this one as a template!
  - Write an article, a blog or a Facebook update on RMGs - IRMA will help!
Want to do more?

• Join one of IRMA’s working groups
  – Lubricant Safety
  – European Outreach
  – Communications
  – Fundraising

• Connect with IRMA ALC, IRMA Nigeria
  – irma-alc.blogspot.com
Special thanks to IRMA funders

- AIDS Foundation of Chicago
- amfAR – The Foundation for AIDS Research
- Broadway CARES /Equity Fights AIDS
- Elton John AIDS Foundation
Questions?
Thank you

• Your name
• Your affiliation
• Your email address

irma-alc.blogspot.com
rectalmicrobicides.org