

Sexually Transmitted Infections...

What's Gender Got To Do With It?

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Gender Defined

- **Gender is NOT sex, i.e. biologically determined**
- **Gender refers to socially constructed roles and responsibilities assigned to men and women in a given culture.**
- Gender is very distinct from biologic sex, and gender roles differ across cultures



WHY consider Gender??

- **Gender roles and perspectives arise from a community's knowledge and belief**
- **Health messages that take into account gender are more effective AND help communities find acceptable ways to change existing beliefs or social norms**
- **STDs disproportionately affect women**

TARGETED MESSAGE



Health Behavior Communication

- Targeted to young females
- Used a supermodel that speaks to the GENDER role of being young and beautiful
- Focuses upon LOOKS – it's even written in the background

Applying Gender Roles to Sexually Transmitted Infections

**And their impact upon risk
behavior**

Social Factors that impact Gender Roles



And Facilitate STI transmission:

- **Economic forces**
- **Incarceration and homicide**
- **Intimate partner violence**
- **Power imbalances**
- **Fear of abandonment**



Economic Forces

- **Women usually earn less than men – creating power imbalances**
- **Educational attainment differences**
- **Single women head of households more often at or below poverty level**
- **Women may be pushed into decisions for economic reasons over health reasons**

Incarceration and homicide

- **1 out of every 3 African American males has been incarcerated**
- **Despite some decline, homicide rates among young males is high, 70% higher than a decade ago**
- **There are less males in the general population; some studies suggest 'competition' for men – even man sharing**

Intimate Partner Violence

- **Pattern of assault and controlling behavior used by one partner against another**
- **CAN include: physical, sexual, psychological attack, as well as**
- **Assaulted partner unwilling/unable to control sexual safety**
- **Often leads to social isolation, depression and substance abuse – all risk factors for STI**

Fear of Abandonment

“If I don’t ----- then he will:

(1) Leave me

(2) Not love me

(3) Find someone else

(4) All of the above

Sexually active Youth: Gender differences

● Teen Males

- Lower levels of depression
- Felt in control of their lives

● Teen Females

- Felt like a failure
- Depression
- Little control over life

Multiple roles of women



Working women



Health messengers

Gender roles can promote health or they can reduce it.



Caregivers



Warriors

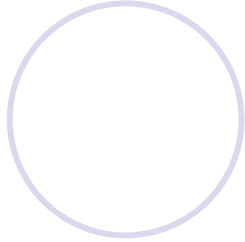
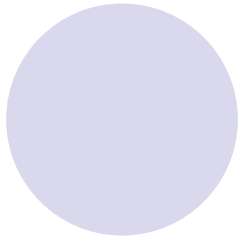
The slide features a decorative arrangement of six circles. The top row consists of three circles: the leftmost is an outline, the middle is a solid light purple, and the rightmost is a solid medium purple. The bottom row also consists of three circles: the leftmost is a solid medium purple, the middle is a solid light purple, and the rightmost is an outline. The text is centered over these circles.

Real Life Examples

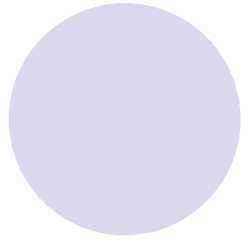
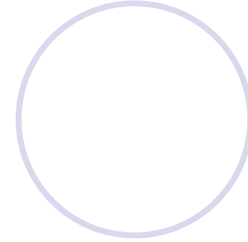
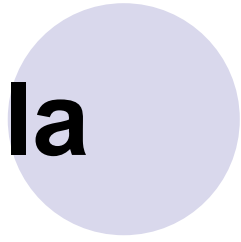
**How gender makes the
difference**

Case 1. Joella and Herpes

- Joella is a 35 y o woman of African and Cuban descent
- Has an on and off relationship with her boyfriend who travels for work
- Cares for her mother who had a heart attack
- Works an extra job to save money for school (wants to be a nurse)



Joella



- **Has yet another reunion with boyfriend**
- **After another breakup a month later she notes vaginal burning**
- **She presents to a local clinic with a distended abdomen and difficulty urinating**

Multiple roles for Joella

- **Problem with urine found to be due to an STI**
- **Active herpes lesions were found**
- **Not sure how to explain her work absence**
- **Confronts boyfriend**
- **When asked why he didn't use a condom, he said: "you didn't ask"**
- **Joella rushes from clinic to care for her mother**



Our Challenge

- **Using gender roles to adopt new health behaviors**
- **As culture is part of gender, identifying culturally acceptable changes**
- **Crafting effective health messages that reflect gender perspectives**
- **Increase awareness of gender impact upon behavior and behavior risk**

Resources to Learn More

- **Gender Equality: Resources**

- <http://www.undp.org/gender/resources.shtm>
!

- **Sex and Gender Differences**

- <http://orwh.od.nih.gov/pubs/sexgender.html>

- **Gender Norms and Adolescent Risk Behavior**

- http://www.fhi.org/en/RH/Pubs/Network/v17_3/nt1733.htm

Changing Gender Roles – Changing Women's Lives



“The most powerful agent of growth and transformation is something much more basic than any technique: a change of heart.” – John Welwood

Women's Health Seminar Series
Sexually Transmitted Infections
Office of Research on Women's Health

**Topical Microbicides:
Where are We?
What is on the Horizon?**

Roberta Black, PhD

Division of AIDS, National Institute of Allergy and
Infectious Diseases, National Institutes of Health,
Department of Health and Human Services

What is a Topical Microbicide?

- An active agent or cocktail of active agents that prevents or reduces transmission of HIV and/or other Sexually Transmitted Infections when applied vaginally and/or rectally
- Delivery could be in the form of a:
 - gel, cream
 - sponge
 - suppository
 - intravaginal ring or diaphragm
 - bio-engineered naturally-occurring vaginal bacterial species

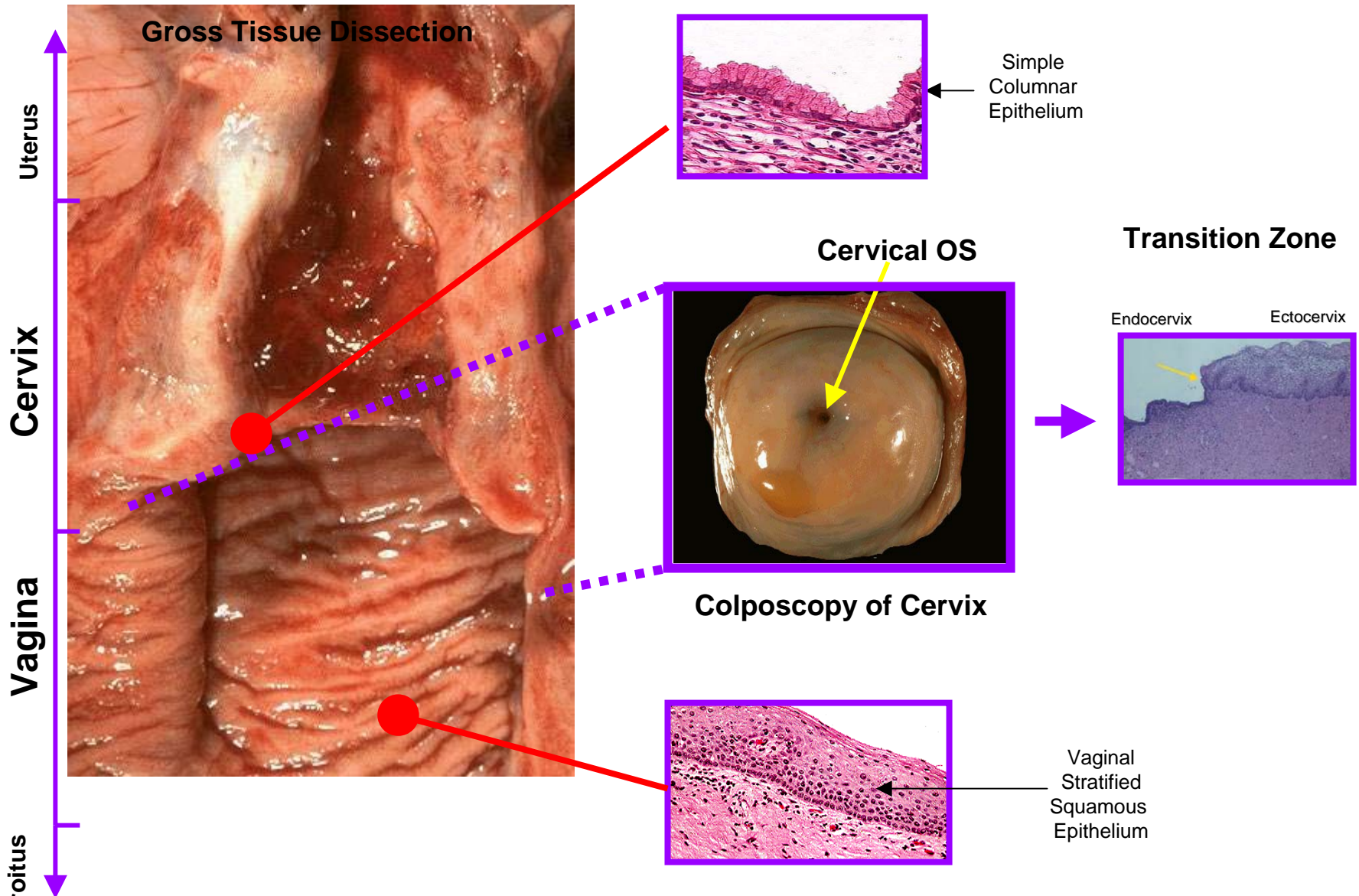


Where can I get a Topical Microbicide?

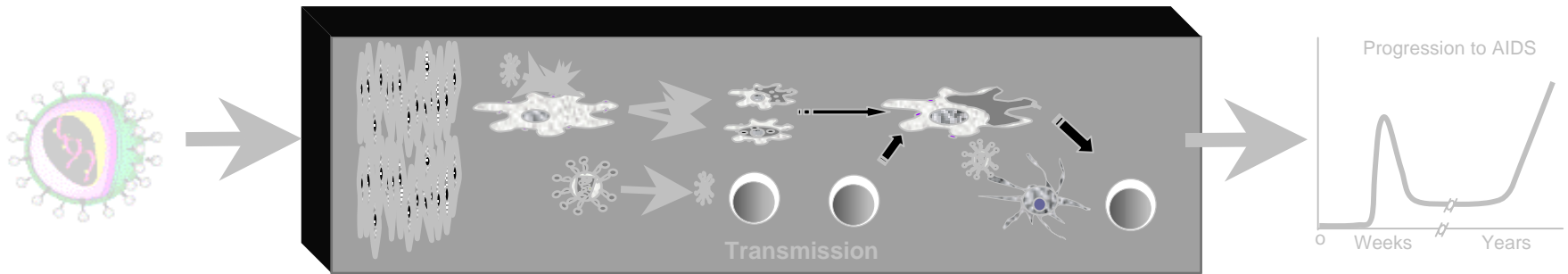
- No topical microbicides are available
- Proof of clinical effectiveness has not been documented
 - N-9 failure
 - Multiple Phase III effectiveness trials ongoing



What must a Topical Microbicide Protect?



Normal Vagina, Cervix bisected: evidence of chronic inflammation extending to the cervical OS



Vaginal Microenvironment

- Vaginal Microflora
 - *Lactobacilli* (~87%) with ~40% H₂O₂ Secreting
- Endogenous Factors
 - Defensins, SLIPI, Lactoferrin, TLRs, Others
- Physical Barriers
 - Mucous
 - Epithelial Cells
 - Vaginal pH (~4.0 to 5.0)
- Pre-existing STI

What are the characteristics of an ideal microbicide?

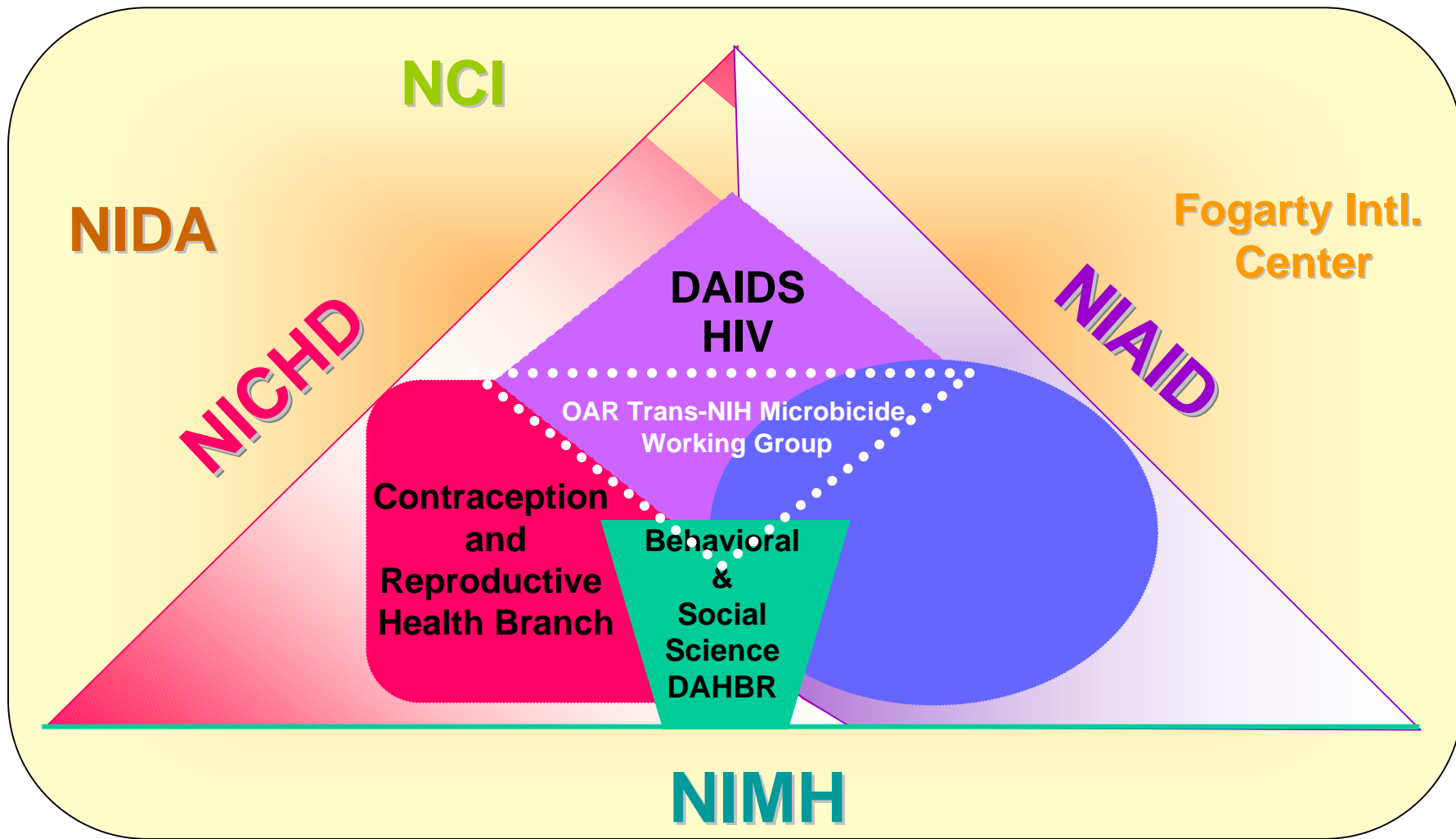
Acceptable	Unacceptable
Safety <ul style="list-style-type: none">• Multi-use daily• Long periods of time• Pregnancy	<ul style="list-style-type: none">• Cause epithelial disruption• Induce inflammation• Absorbed systemically• Interferes with vaginal defense mechanisms
Effect <ul style="list-style-type: none">• Fast• Long duration• Irreversible	<ul style="list-style-type: none">• Unstable• Interval between application and coitus short (before or after)
Acceptability <ul style="list-style-type: none">• Formulation stability• Acceptable to both sex partners• Unobtrusive/ pleasurable	<ul style="list-style-type: none">• Messy, leaky• Burning, itching• Cumbersome• Odor/taste?/ color?• Applicator trauma/discomfort



What are the characteristics of an ideal microbicide?

Acceptable	Unacceptable
<p>Availability</p> <ul style="list-style-type: none">• Contraceptive/non-contraceptive formulations• Low cost• Unlimited access• Ease of scale-up and GMP production	<ul style="list-style-type: none">• Costly for use and/or manufacturing• Regulated distribution (MD or health official)• Requires special storage/transport
<p>Uses</p> <ul style="list-style-type: none">• Vaginal and/or rectal• Unlimited use• Compatible with condoms and other STI preventatives	<ul style="list-style-type: none">• Complicated use
<p>Activity</p> <ul style="list-style-type: none">• Effect on STIs in ejaculate and cervicovaginal secretions• Broadly active: HIV + other STIs	<ul style="list-style-type: none">• Enhance growth of STIs or secondary pathogens• Affect vaginal (rectal) microbial ecology

National Institutes of Health Topical Microbicide Program



Topical Microbicides

*Preventing Sexually
Transmitted Diseases*



U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
National Institute of Allergy and Infectious Diseases

NIAID

Topical Microbicide

Strategic Plan



September 2003



U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
National Institute of Allergy and Infectious Diseases

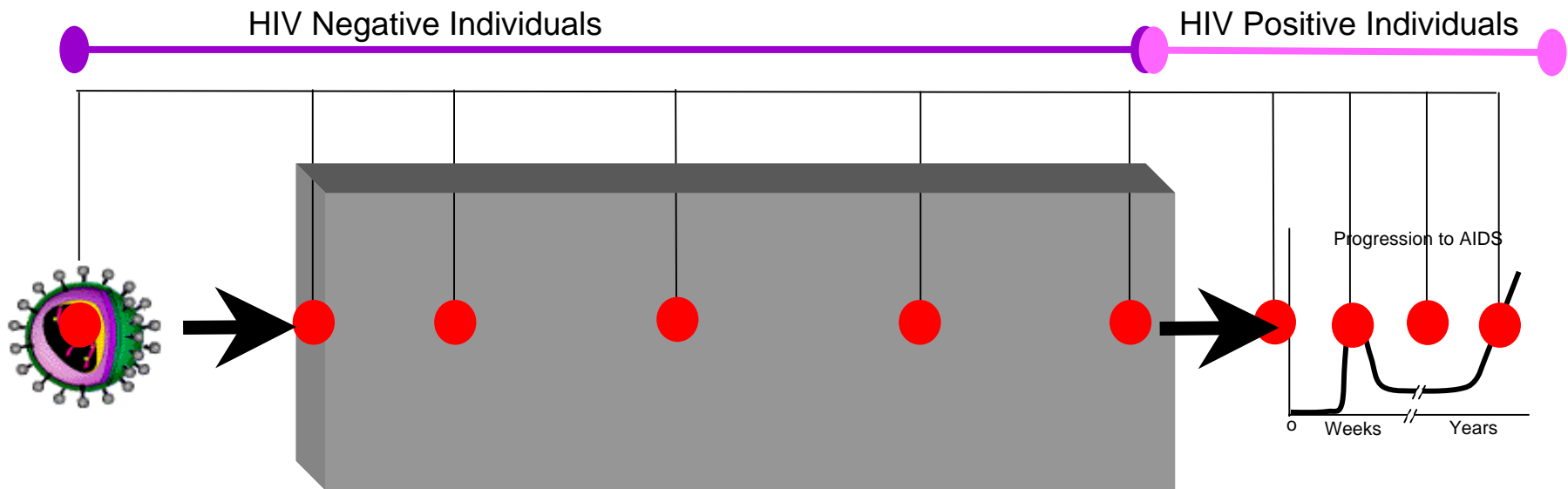
http://www.niaid.nih.gov/publications/topical_microbicide_strategic_plan.pdf

What is the Ultimate Goal of the NIAID Topical Microbicide Program?

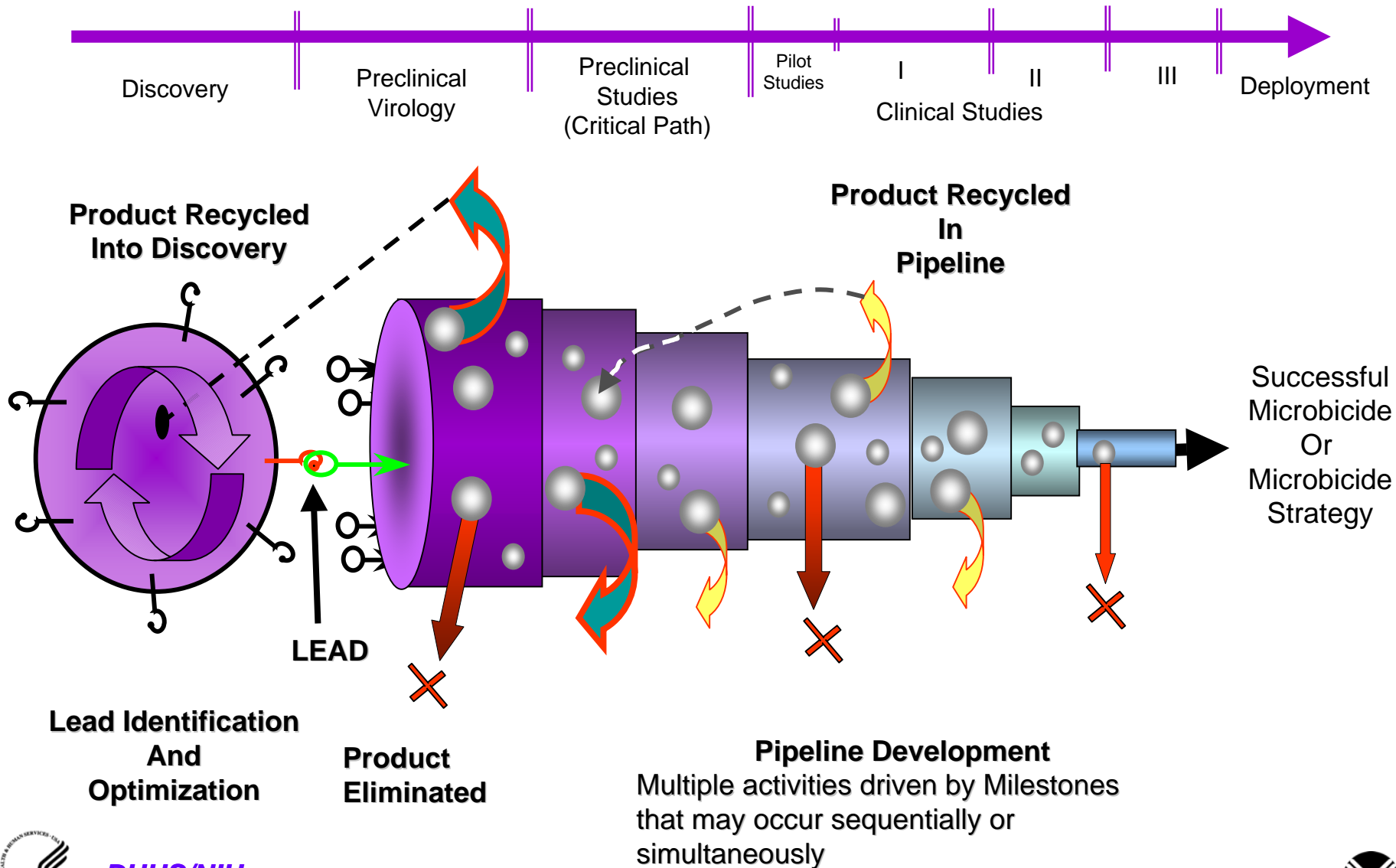
To identify safe, effective and acceptable topical microbicides to prevent HIV/AIDS and other STIs

- To provide proof of clinical efficacy for at least one candidate microbicide

Intervention Points for Microbicides in HIV Infection and Disease



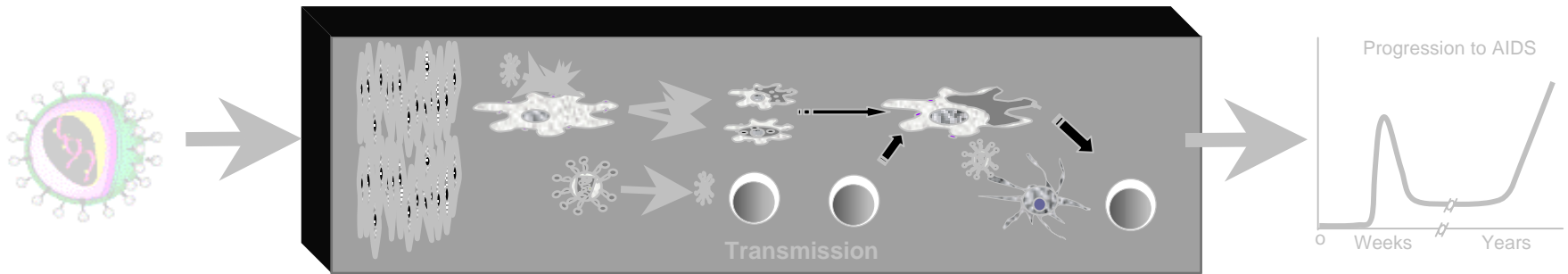
What are the Major Steps in Topical Microbicide Discovery and Product Development?



What is the Overall Strategy of the NIAID Topical Microbicide Program?

- Basic biomedical research
 - Guide design and evaluation
- Nonclinical product development
 - Identify and help advance the most promising approaches to clinical testing
- Clinical evaluation
 - Evaluate safety, efficacy and acceptability in populations most in need





Transmission

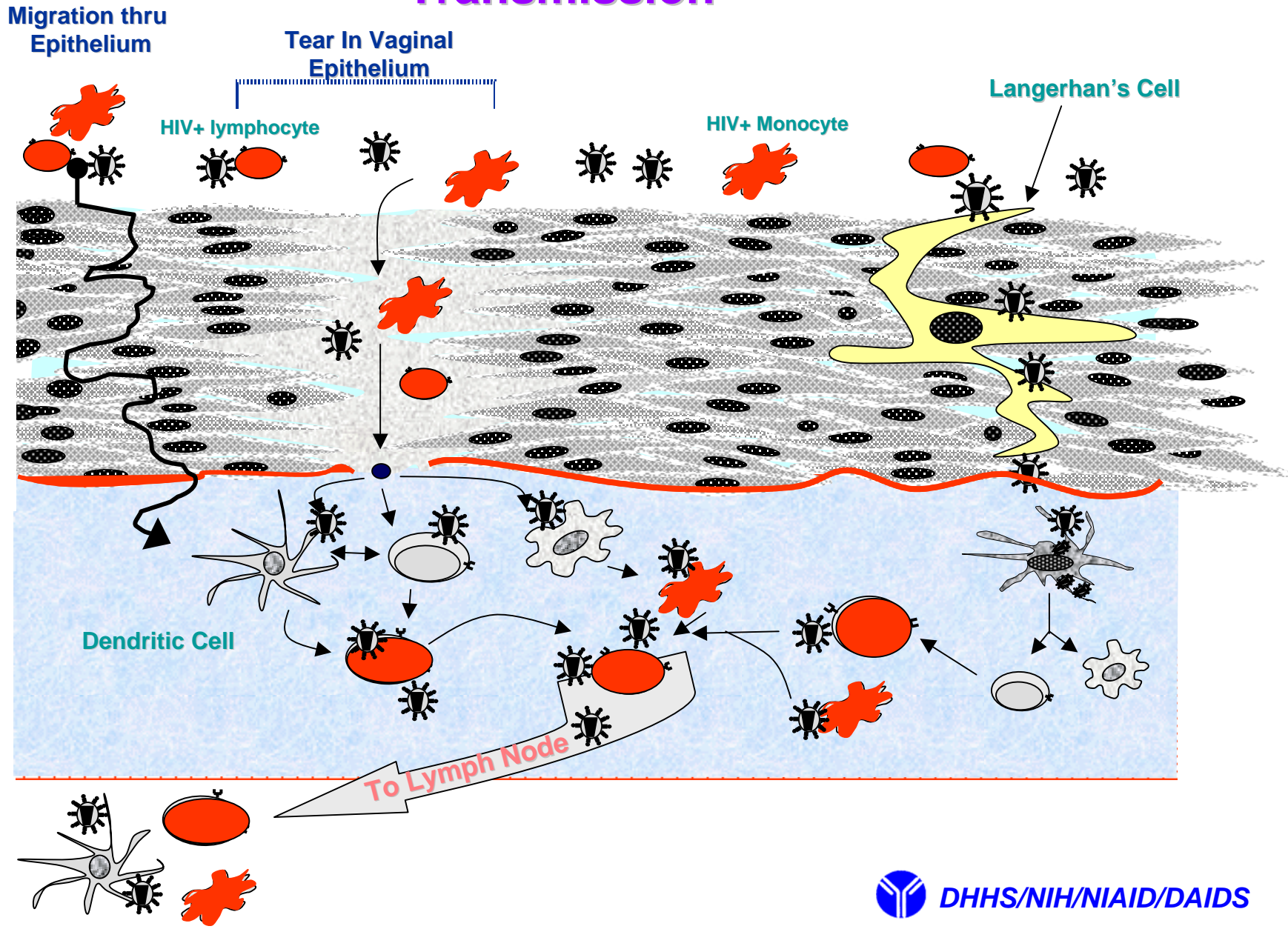
➤ Possible mechanisms of transmission are:

- Direct infection of epithelial cells,
- Transcytosis,
- Transmigration through the epithelium by infected cells or virus,
- Dissemination of virus by intra-epithelial Langerhan's cells,
- Breach of epithelial integrity- micro- and macro-trauma,

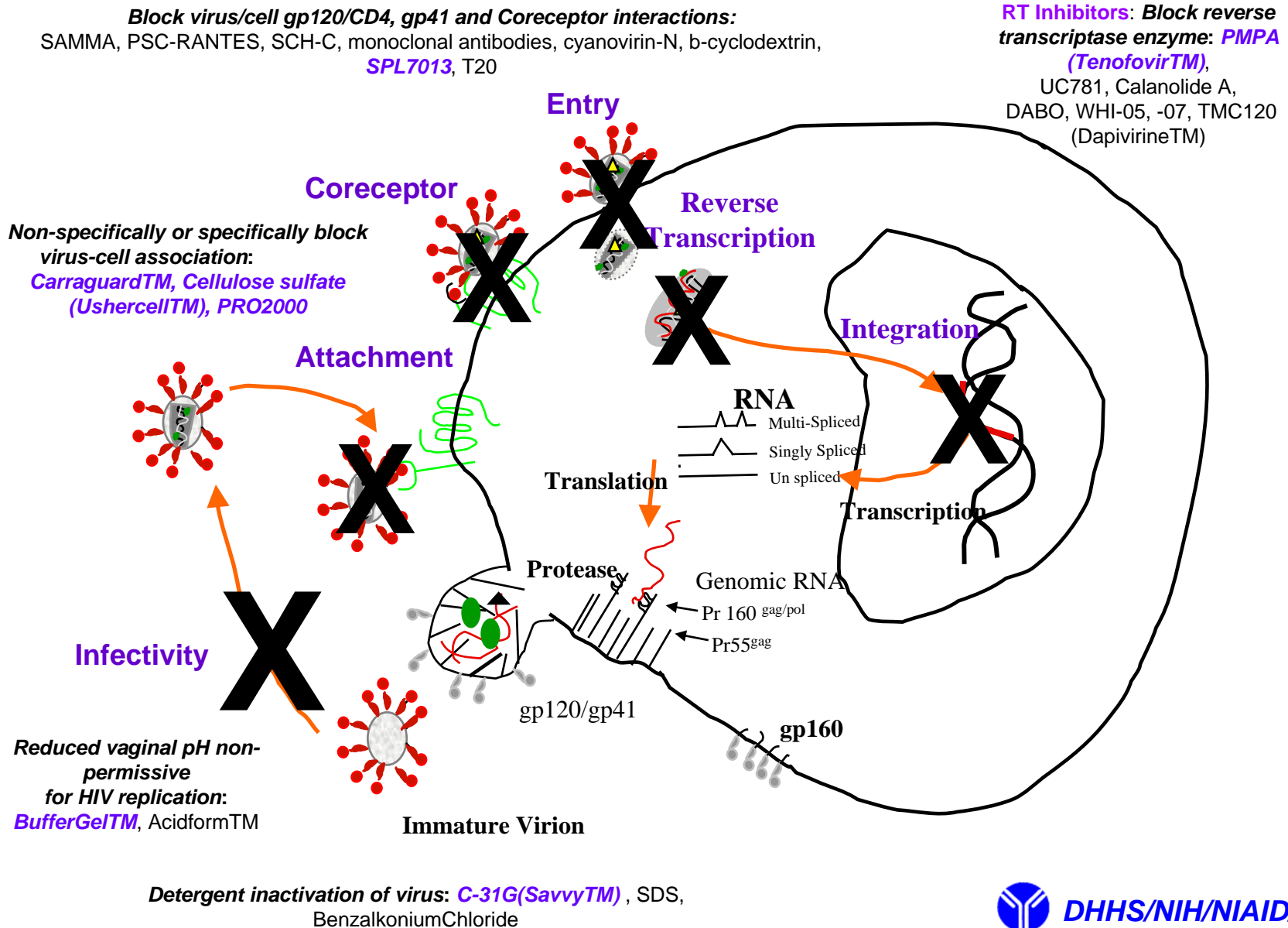
➤ Multiple cell types are involved in transmission.

➤ A two phase model of transmission has been proposed—local infection followed by dissemination.

Proposed Mechanisms for Cervicovaginal HIV Transmission



What are the Potential Targets in the HIV Replication Cycle?



The Integrated Preclinical Clinical Program for HIV Topical Microbicides (IPCP-HTM)

- The purpose of the IPCP-HTM program is to **promote** the **development** of a **safe** and **effective vaginal** and/or **rectal microbicide** using a **single** or **combination** microbicide strategy.
- **Hypothesis-driven Specific Aims** that reflect the **iterative linkage** between **discovery**, **preclinical** and **clinical** studies.

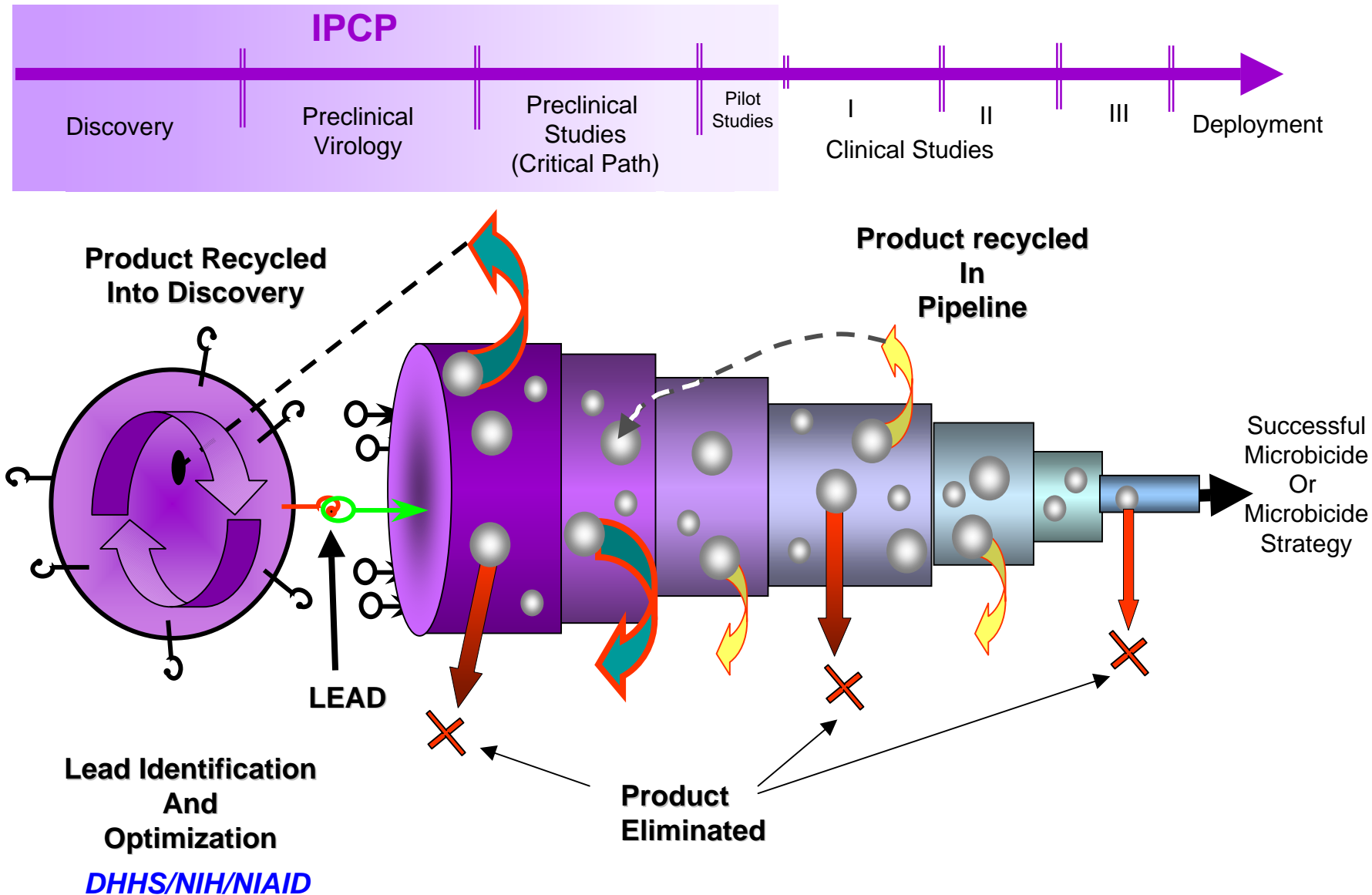


Integrated Preclinical/Clinical Program for HIV Topical Microbicides: Salient Features

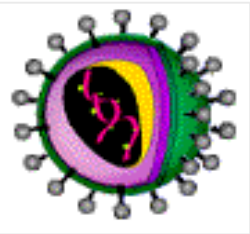
- Link research with product development and exploratory clinical evaluation for candidate optimization through multidisciplinary, multi-project cooperative agreements
- Requires involvement of the private sector



Where Does the IPCP-HTM Fit In? NIAID/NICHHD



Topical Microbicides Supported Through The IPCP-HTM Program



CELL-FREE VIRUS

Nonspecific

Polybigunaides (NICHD)

Specific

NCp7 Inhibitors (NICHD, in combination with CAP)

gp120/CD4 Interaction

- CV-N • BMS-38806 • CD4-IgG (PRO542)
- Monoclonal antibodies b12, 2G12, 2F5
- Optimized Dendrimers
- Cellulose Acetate Pthalate (NICHD)

Coreceptor Inhibitors

- CMPD 167 • TAK779 • AD-101
- PSC-RANTES • -2 RANTES

C-type Lectins

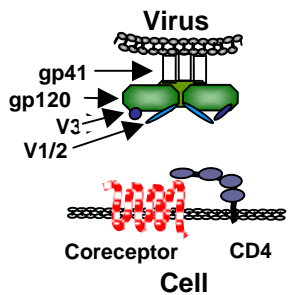
- Soluble mannans • Soluble DC-SIGN

Unknown

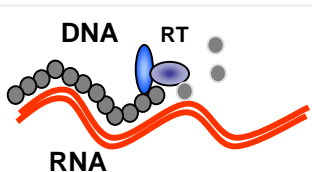
- bKLA, • TatCD • Flavins/Flavoids

RT INHIBITORS

- UC781 (V + R)
- PMPA (V)



ENTRY



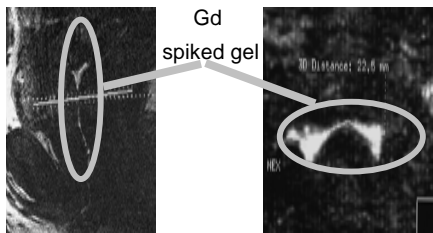
Other Approaches

Vaginal Defense –Lactobacillus delivered CV-N, CD4, RANTES peptides, slg anti-ICAM-1

Combination Microbicides: BufferGel with Dendrimers (SPI-7013 and Optimized Dendrimers)
CAP with NCp7 nucleocapsid Inhibitors and UC781 (NICHD)



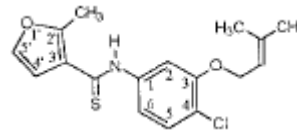
What Microbicides Are in the IPCP-HTM Pipeline Advancing to Exploratory Safety and Acceptability Trials?



Vertical Plane Traverse Plane

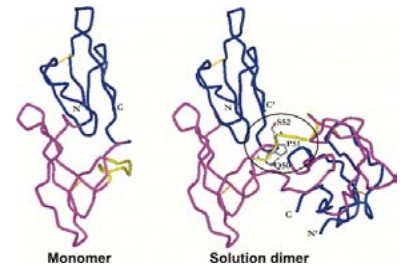
MRI

Distribution of Prototypic Formulations

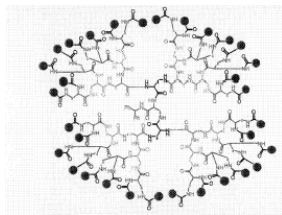


UC781

(Vaginal and Rectal)

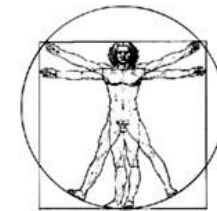


Cyanovirin-N



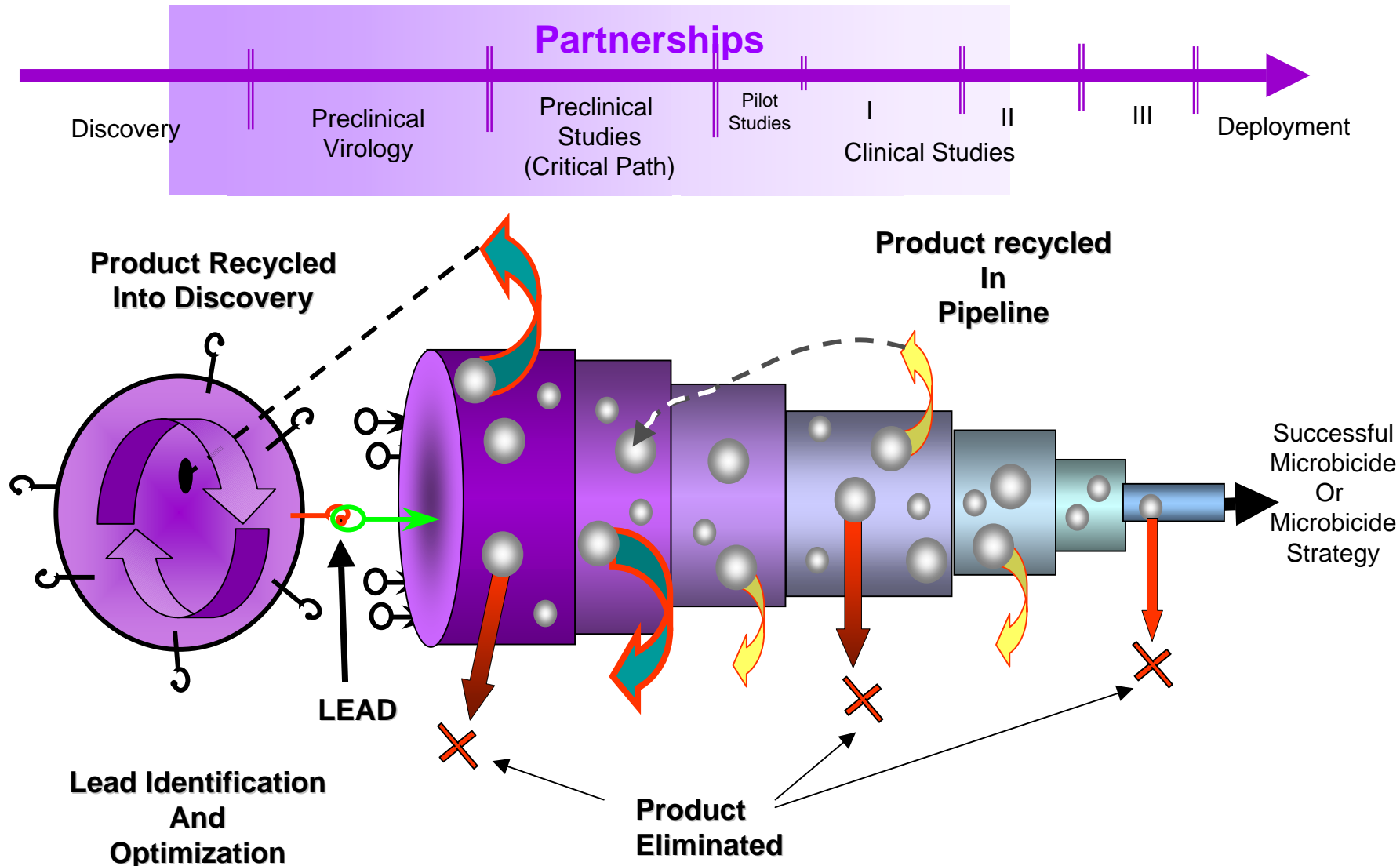
Dendrimers

(SPI-7013)



Behavioral (Acceptability)

Where Does the Partnership for Topical Microbicides Fit In?



Lead Identification
And
Optimization

DHHS/NIH/NIAID



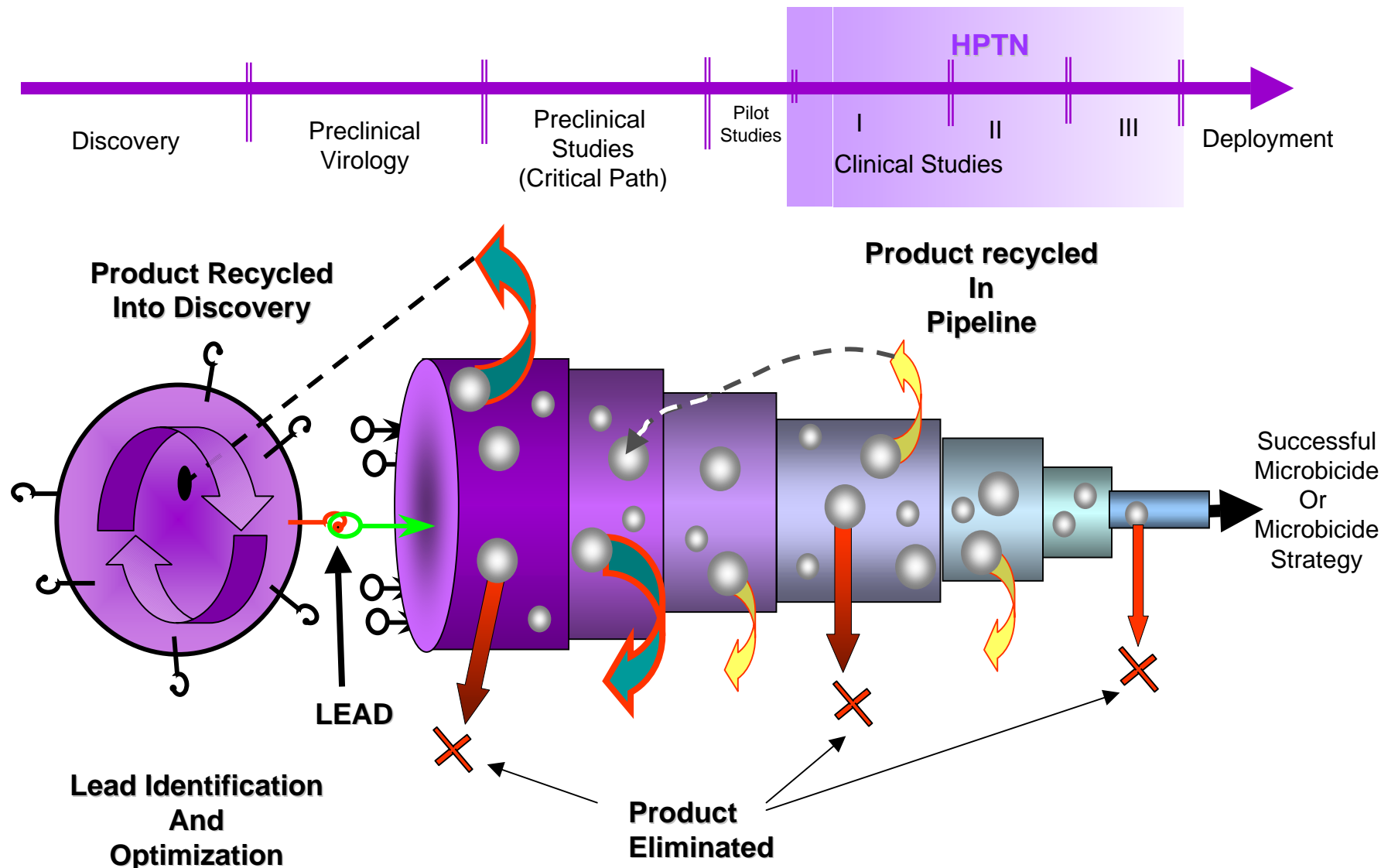


Partnerships for Topical Microbicides: Salient Features

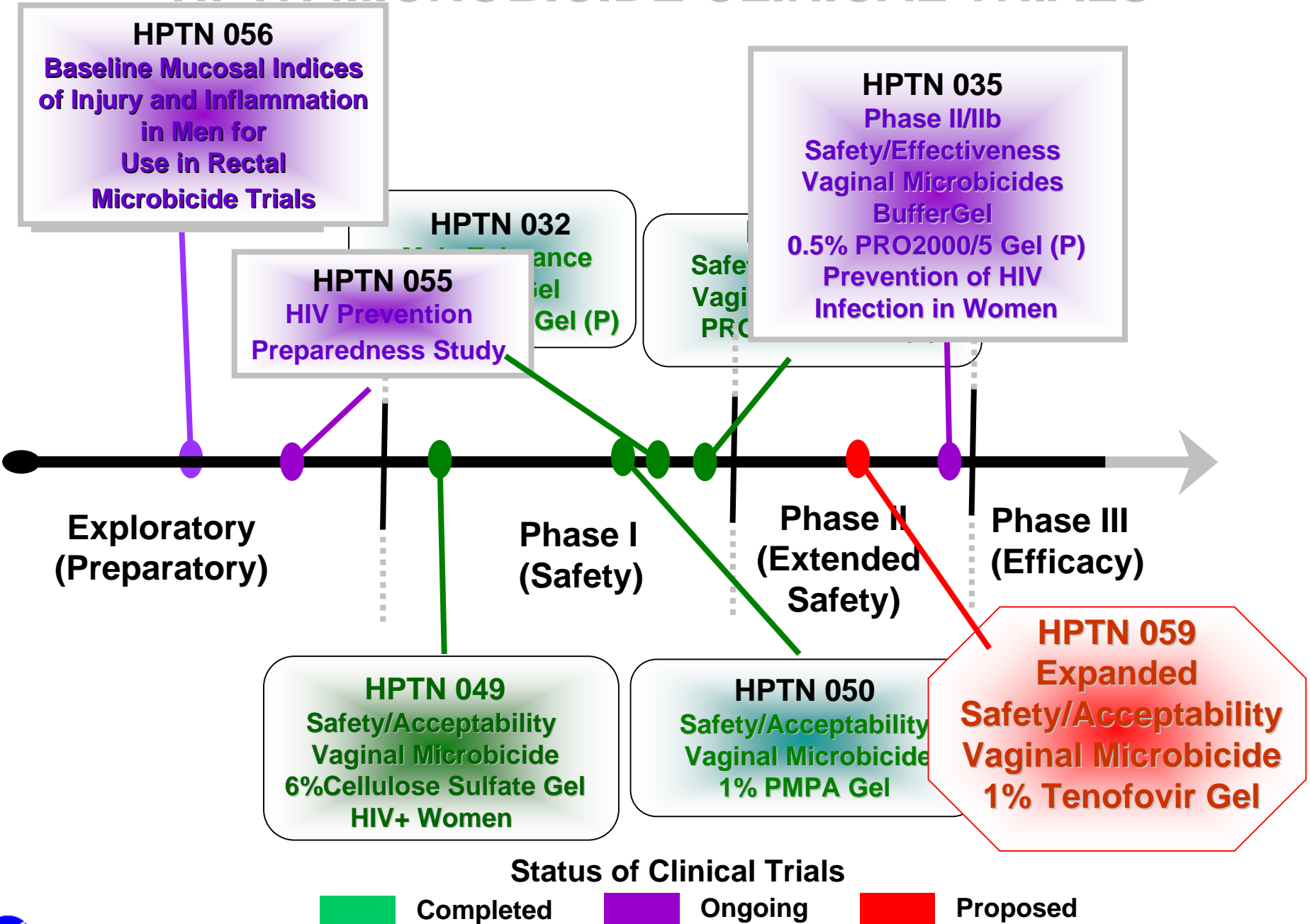
- Advance industry involvement
- Develop combination products
 - Some STIs enhance HIV transmission
 - “Duet” cervical barrier device (Gonorrhea, Chlamydia, Trichomoniasis, BV, HIV)
 - Aptamers (HPV, HSV, HIV)
 - Lactobacilli (BV, HSV, HIV)



Where Does the HIV Prevention Trials Network (HPTN) Fit In?



HPTN MICROBICIDE CLINICAL TRIALS



Status of Clinical Trials



Completed



Ongoing



Proposed



MICROBICIDE CLINICAL TRIALS

Characterization of Baseline Mucosal Indices of Injury and Inflammation in Men for Use in Rectal Microbicide Trials

Purpose: Identify mucosal indices valuable in the safety evaluation of rectal microbicides and to determine the sensitivity and variability of assays used to measure safety parameters

Study Site: Los Angeles CA, USA

Study Size: 16 MSM in 4 arms HIV + or – practicing or not practicing RAI

Duration: four months and each participant will be followed for six weeks

Design: Observational study with endoscopic collection of distal colonic and rectal tissue biopsies over a 6-week period

Will determine the variability and contrast the differences of a range of immunological, virological, and histopathological parameters in multiple rectal tissue biopsies collected at two sites in the recto-sigmoid colon (10 cm and 30 cm).

STATUS: ongoing

HPTN055

HPTN 056

HIVNET016A

Exploratory
(Preparatory)



Completed

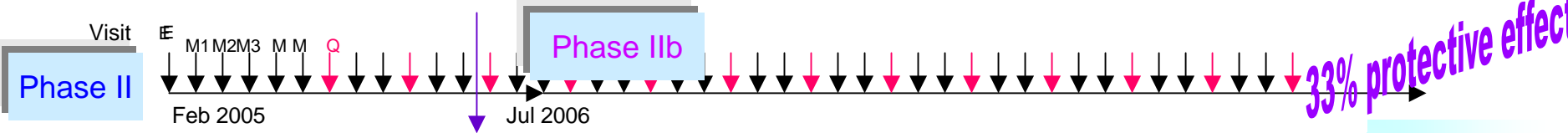


Ongoing



Proposed

HPTN 035: Phase II / IIb Trial of Vaginal Microbicides for the Prevention of HIV Infection in Women



DSMB \leq 12 mos.

M1, M2, M3 Monthly Visits:
Pelvic exam, safety labs with pregnancy and HIV tests (colposcopy for subset)

Quarterly Visits: Pelvic exams and HIV tests
Monthly Visits: Pregnancy test

192 incident infections

N = 200/~605

BufferGel

N = 200/~605

0.5% PRO2000 Gel

N = 200/~605

Placebo

N = 200/~605

No treatment

N = 100

Philadelphia, PA

N \approx 220

N = 700

Durban & Hlabisa, SA
Lilongwe, Malawi
Harare, Zimbabwe
Blantyre, Malawi
Lusaka, Zambia

N \approx 2200

- Primary endpoints:**
Safety
HIV infection
- Secondary endpoints:**
BV
Chlamydia infection
Genital ulcer disease
Gonorrhea infection
HSV-2 infection
Pregnancy
Syphilis infection
Trichomoniasis

Treatment regimen: Apply a single dose of the product intravaginally up to 60 mins before each act of vaginal intercourse

Participant follow-up: 12-30 mos.

MICROBICIDE CLINICAL TRIALS

HPTN 032

HPTN 059

Phase II Expanded Safety and Acceptability Study of the Vaginal Microbicide 1% Tenofovir Gel

Purpose: Assess the safety of tenofovir gel for vaginal use in HIV-uninfected women versus a placebo gel. .

Intervention: Daily use of tenofovir gel or placebo versus coital-dependent use

Study Sites: New York, NY, USA; Birmingham, AL, USA; Pune, India

Study Size: 200 women; 100 domestic sites, 100 international site

Duration: 6 months tenofovir gel exposure

Design: Phase II four arm, two site randomized, controlled trial comparing tenofovir 1 % vaginal gel used once daily and tenofovir 1% vaginal gel used prior to intercourse, to a placebo gel study, with 6 months tenofovir gel exposure and follow-up. Participants who are HBV positive will return to site at visits Weeks, 28, 32, and 36 (post product use). Participants in all four arms will receive ongoing condom counseling and free condoms.

STATUS: Planned—Activation May 2006



Completed



Ongoing



Proposed

MICROBICIDE CLINICAL TRIALS* (March 2006)

PHASE	TRIALS
1	ACIDFORM™/Amphora™
	Carraguard®
	Cellulose acetate 1,2-benzenedicarboxylate (cellacefate/CAP)
	Cellulose sulfate/CS
	Lime juice
	PC 815
	TMC120
	UC-781
	VivaGel/SPL7013™
1/2	Invisible Condom™
2	Cellulose sulfate/CS
	Praneem Polyherbal Vaginal Tablet
	Protected Lactobacilli in combination with BZK
	Tenofovir/PMPA gel (1%)
2/2B	Tenofovir/PMPA gel (1%) and PRO 2000 (0.5%)
	BufferGel™ and PRO 2000 (0.5%)
3	Carraguard®
	Cellulose sulfate/CS
	PRO 2000 (0.5% and 2%)
	Savvy™ (C31G)

*This table is an attempt to give a picture that is as accurate as possible of the microbicide candidates that have reached the clinical stages of testing. The trials that appear in this table may be (1) in the active planning stage, (2) ongoing, or (3) recently completed but with published analysis pending. For any modifications, please contact Carolyn Plesecia, email cplesecia@microbicide.org, tel. 301-587-3502.



ALLIANCE FOR
MICROBICIDE
DEVELOPMENT

SUMMARY: MICROBICIDE CANDIDATE COMPOUNDS AND PRODUCTS IN DEVELOPMENT

No. in Active Preclinical Development: 13

No. in Clinical Development: 16

TOTAL: 29



DHHS/NIH/NIAMD/DAIDS

Behavioral research in the microbicide clinical trial context: Interrelationship of Product Acceptability and Risk Assessments

Product Acceptability

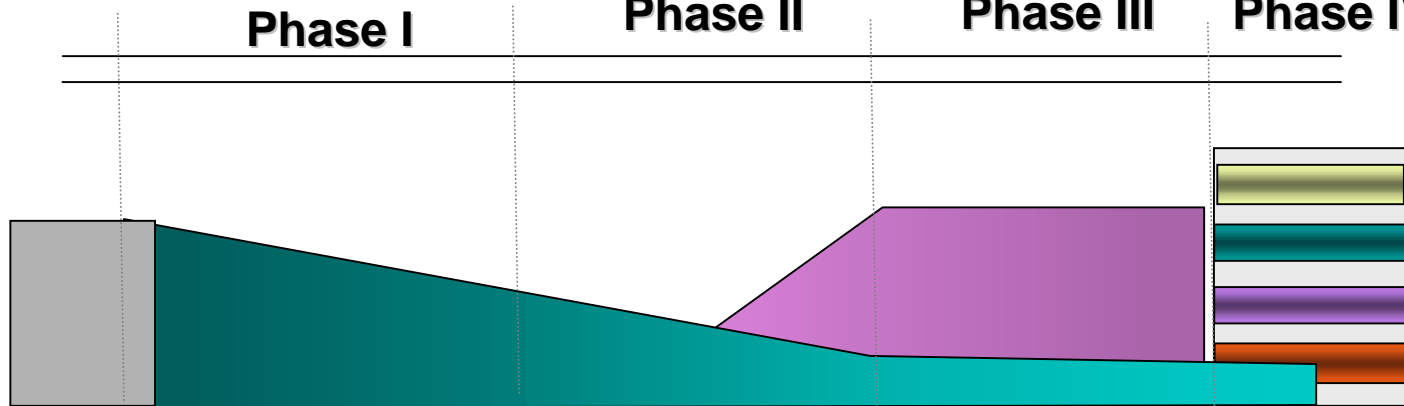
Risk Assessment

Phase I

Phase II

Phase III

Phase IV



Basic Research

- Vaginal Distribution
- But also...*
- Formulation Issues
- Preliminary acceptability considerations

Preliminary Trials

- Safety/efficacy
- But also...*
- Product acceptability
- How conditions of product use (e.g., context, frequency, etc.) affects acceptability
- Considerations for product improvement

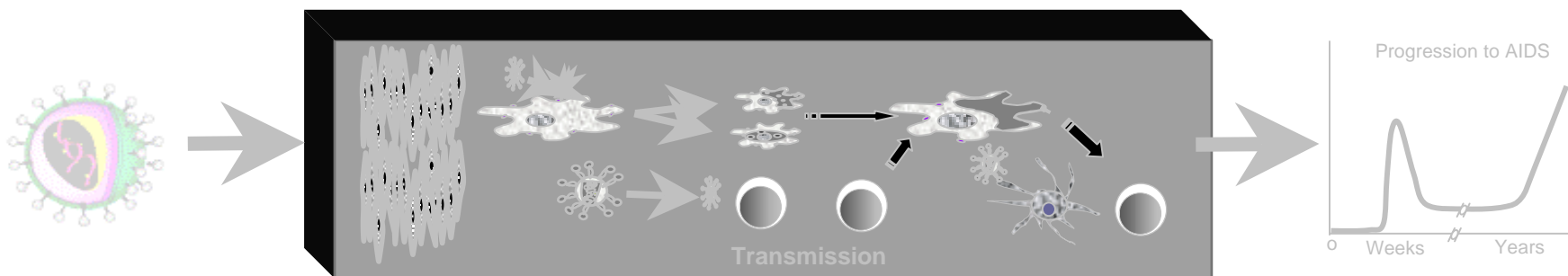
Larger Trials

- Safety of longer term use
- Expanded efficacy tests
- But also...*
- Assessment of infection risk
- Individual & dyad-level behaviors associated with product use
- How risk or product use behaviors affect efficacy

Marketing & Bridging Studies

- Longer term risks and benefits
- Efficacy outside the clinical trial context
- But also...*
- Reformulation to appeal to different populations
- Assessment of risks for different user groups

Challenges in Microbicide Development (but not all)



- ❖ Mechanism of transmission-cell-free virus, cell-to-cell- combinations thereof?
- ❖ What is an adequate demonstration of microbicide feasibility--- in vitro?---in vivo?
- ❖ Surrogate markers via cytokines, chemokines and innate factor measurement --- A microbicide *fingerprint* for safety?
- ❖ Role of formulation in discovery and advancement new microbicides
- ❖ Incorporation of behavioral and social science data (acceptability) into the development pipeline?
- ❖ Combination microbicides---What in vitro/ in vivo proof is needed and what are FDA requirements?
- ❖ ETC.!

PROOF-OF-CONCEPT FOR CLINICAL EFFICACY

Summary

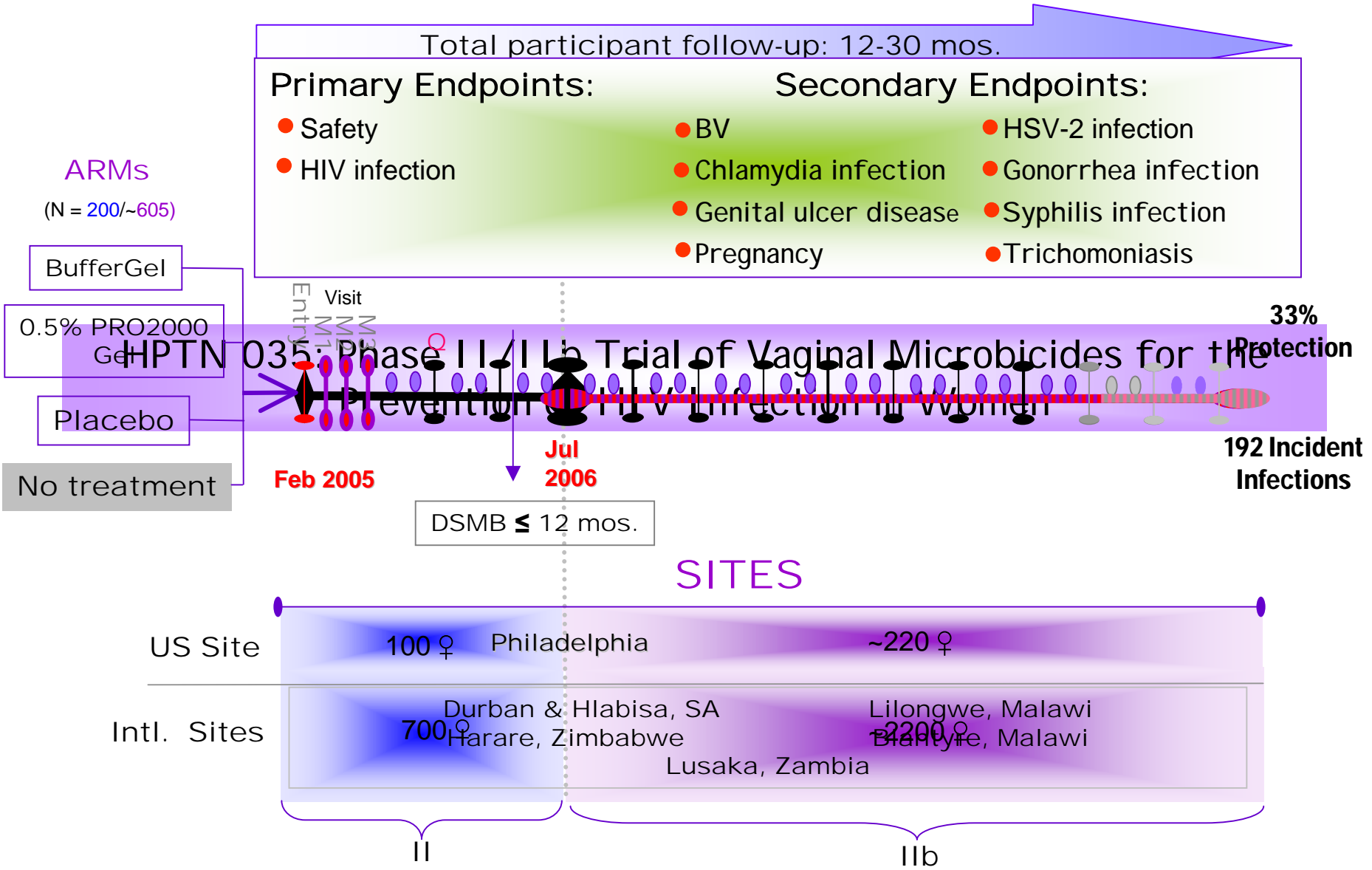
Lack of Proof-of-Concept for Microbicide acceptability, safety and efficacy is a key factor in today's microbicide development programs

Key Issues

- Preclinical pathway for selection and advancement
 - Relevant, predictive models for safety/efficacy
- Appropriate surrogate markers for safety
- Formulation/delivery

Resolution of key issues and gaps in microbicide development to formulate an effective critical pathway will ultimately depend upon implementing iterative basic, developmental and clinical research

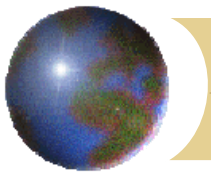






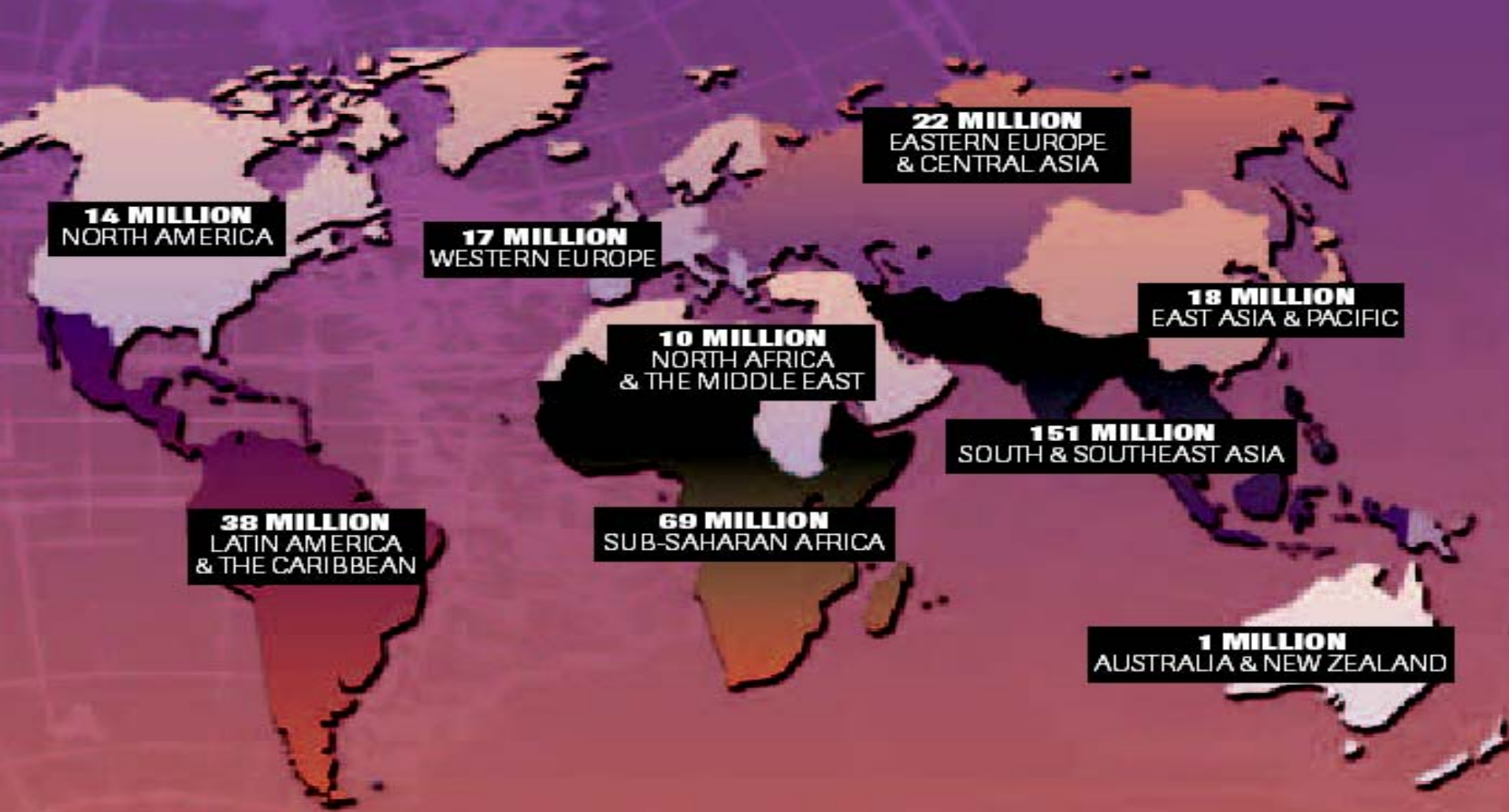
Prevention of Sexually Transmitted Infections in Adolescent Girls

**Craig Cohen, MD, MPH
University of California, San Francisco
Department of Obstetrics, Gynecology and
Reproductive Sciences**

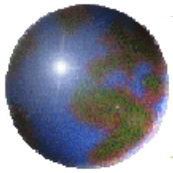


Sexually Transmitted Infections (STI) in Adolescent Girls

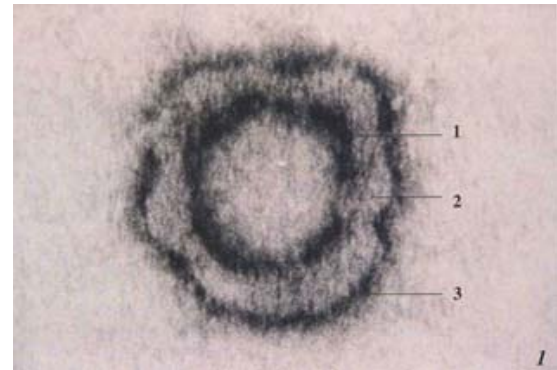
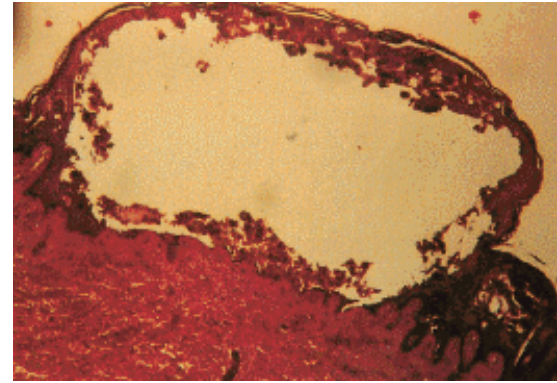
- Significant morbidity
 - ▣ Infertility, ectopic pregnancy, chronic pelvic pain
 - ▣ Perinatal infections
- Facilitate HIV transmission
 - ▣ Treatment and prevention may break the HIV chain of infection

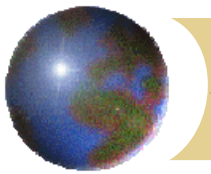


Estimated number of curable STI per year in 2000
Global total = 340 million

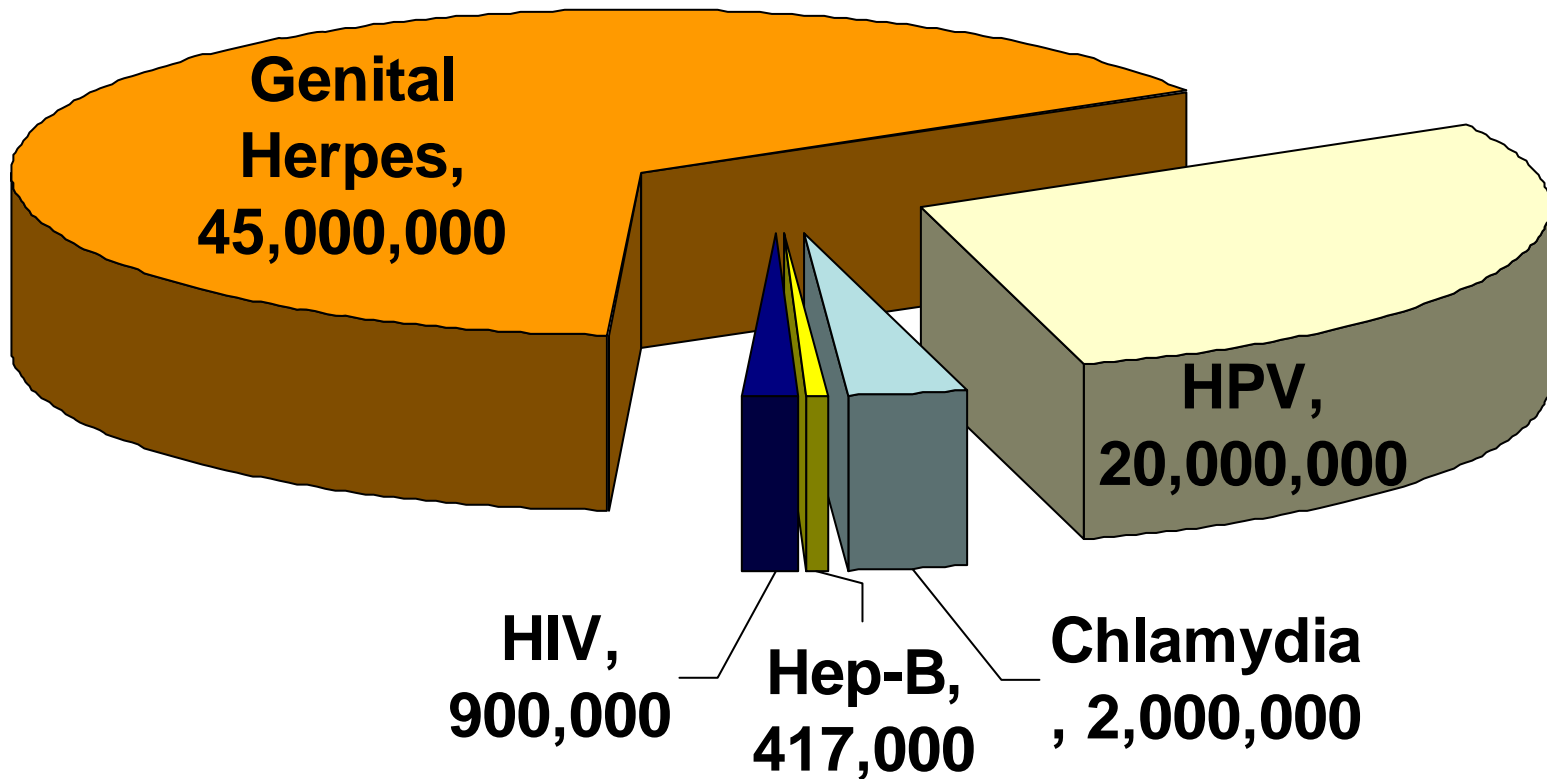


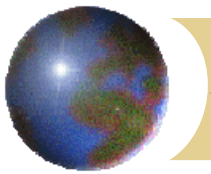
Genital Herpes





Prevalence of STI in the U.S. in 2000

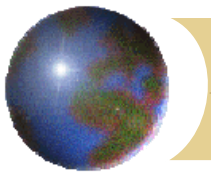




Per contact probability of HIV-acquisition

- HSV-2 associated with 2 to 4 fold increased risk of HIV acquisition

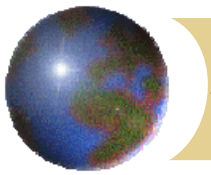
Probability per 1000 contacts	
Overall	1.1
HIV ⁻ & HSV-2 ⁺	2
HIV ⁻ & HSV-2 ⁻	0.4 [*]
HIV ⁻ & HSV-2 ⁻ & GUD	3.1
HIV ⁻ , HSV-2 ⁺ & no GUD	2
HIV ⁻ , HSV-2 ⁻ & GUD	0.4 [*]



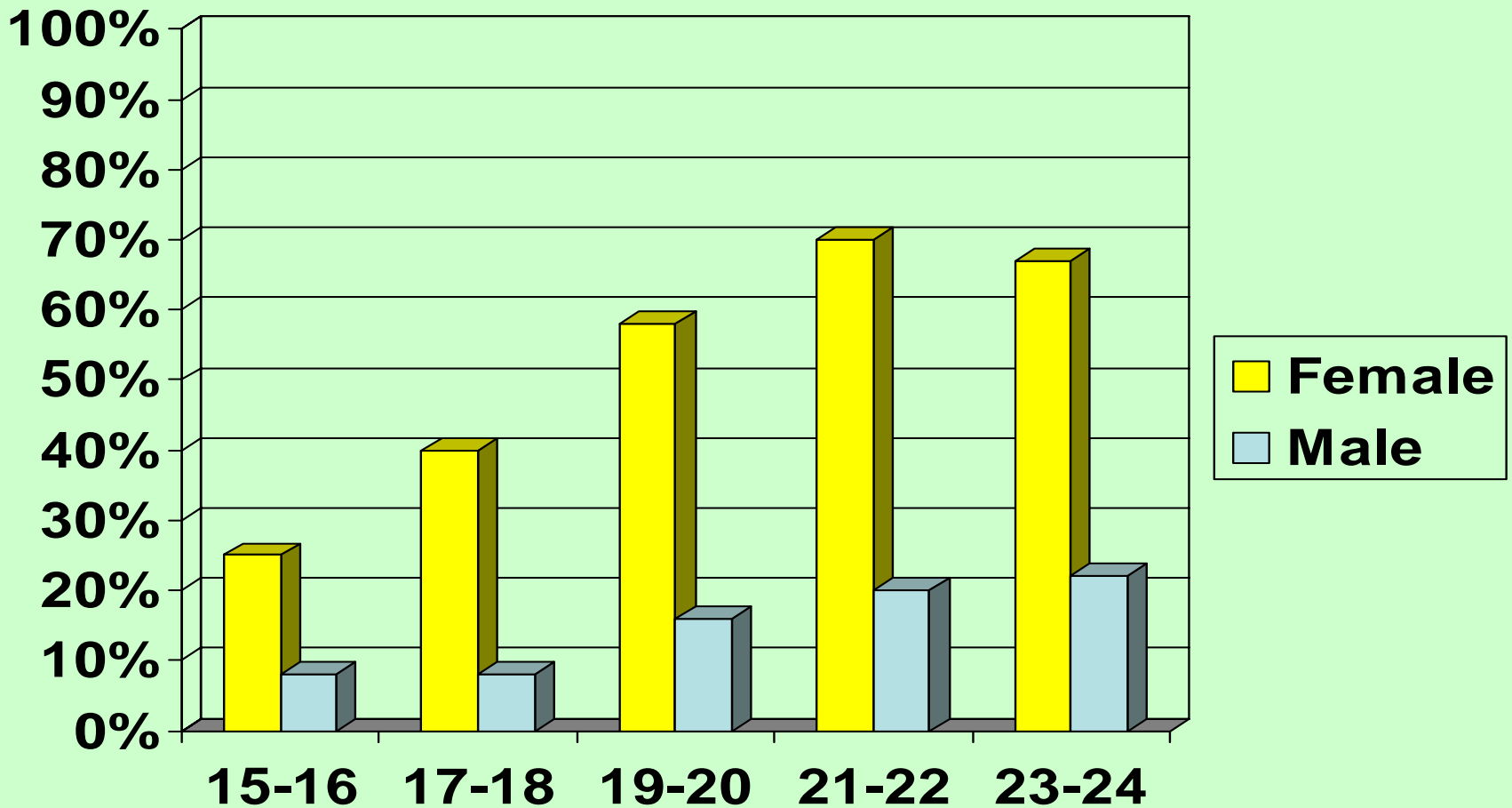
Per contact probability of HIV transmission

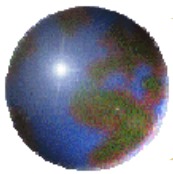
- HSV-2 associated with 5-fold increased risk of HIV transmission

Probability per 1000 contacts		
HIV Viral Load	HSV-2 ⁺	HSV-2 ⁻
<1700 per ml	0.1	0.04
1700-12,499	2.3	0.5
12,500-34,499	1.8	0.2
≥ 35,000	3.6	0.7

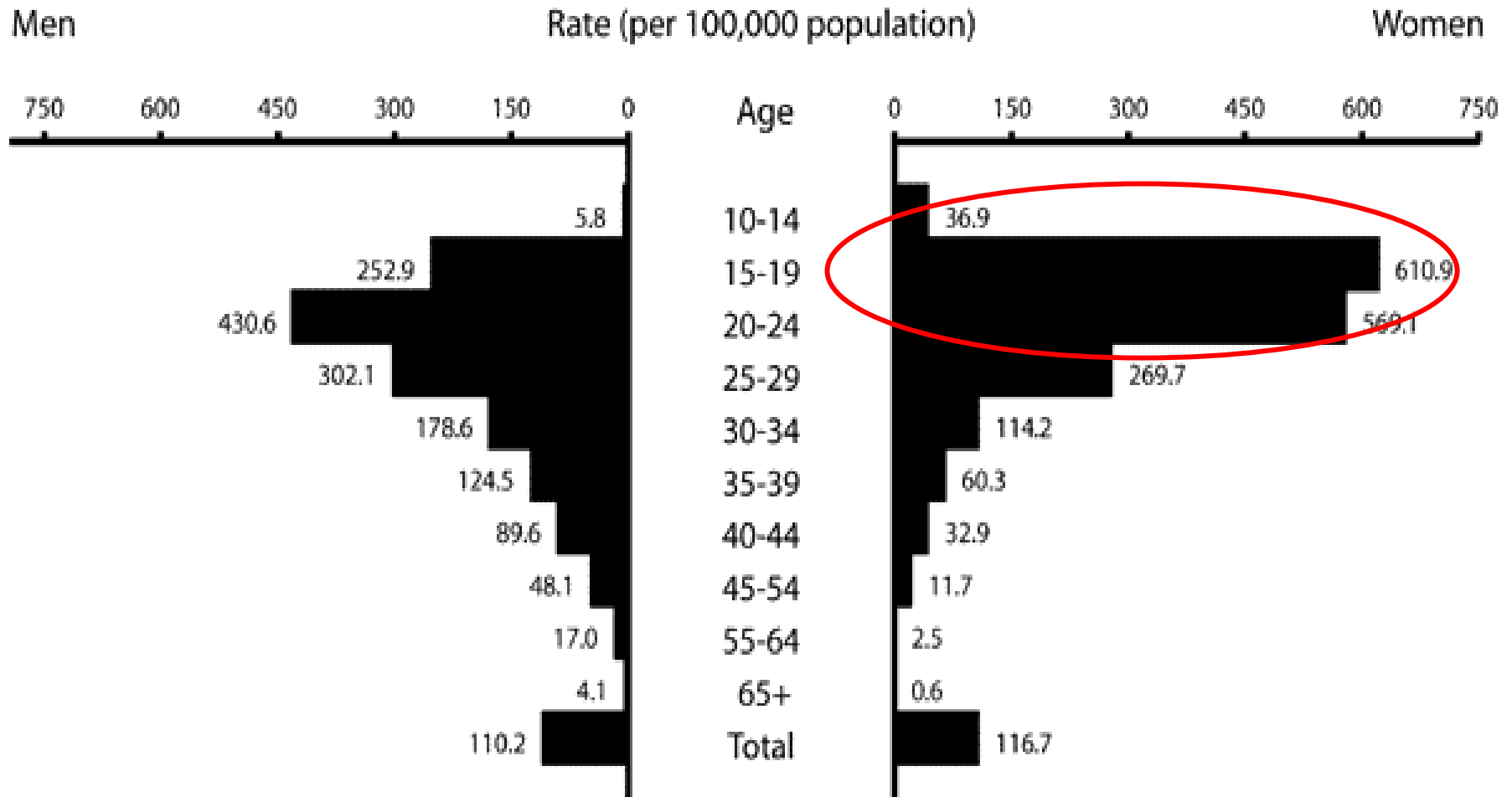


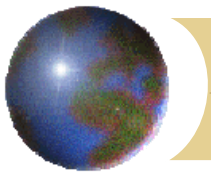
HSV-2 prevalence: Kisumu, Kenya





Gonorrhea - Age and sex-specific rates: United States, 2004





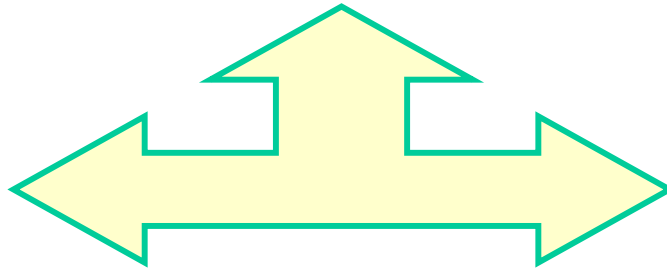
Overall Goal of KEMRI-UCSF Program

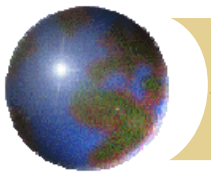
- Find STI & HIV prevention methods that work effectively and safely for adolescent girls and young women

Research

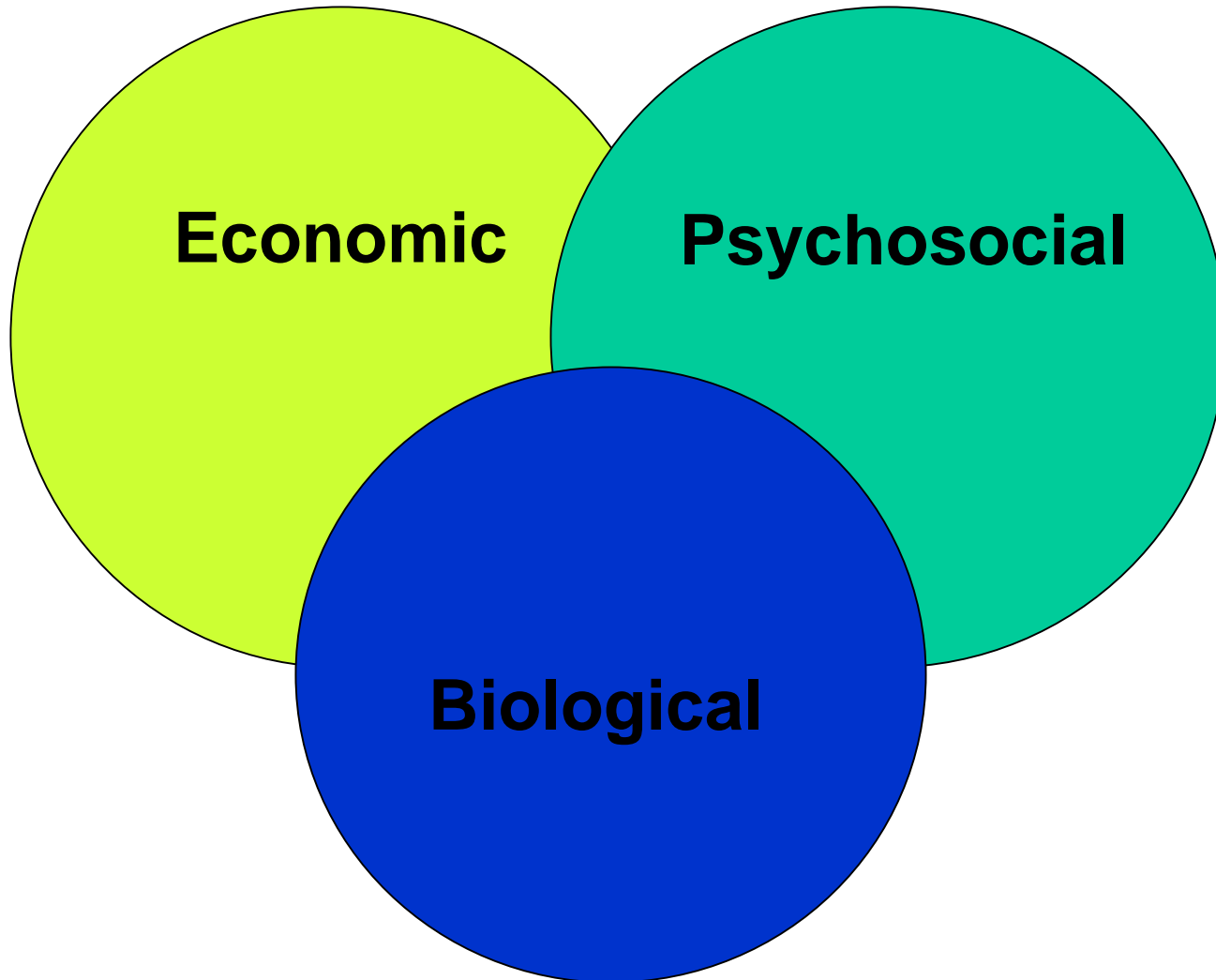
**Prevention &
Education**

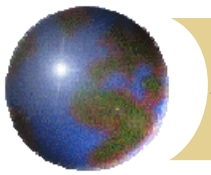
Care





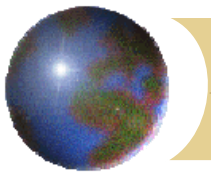
Vulnerability





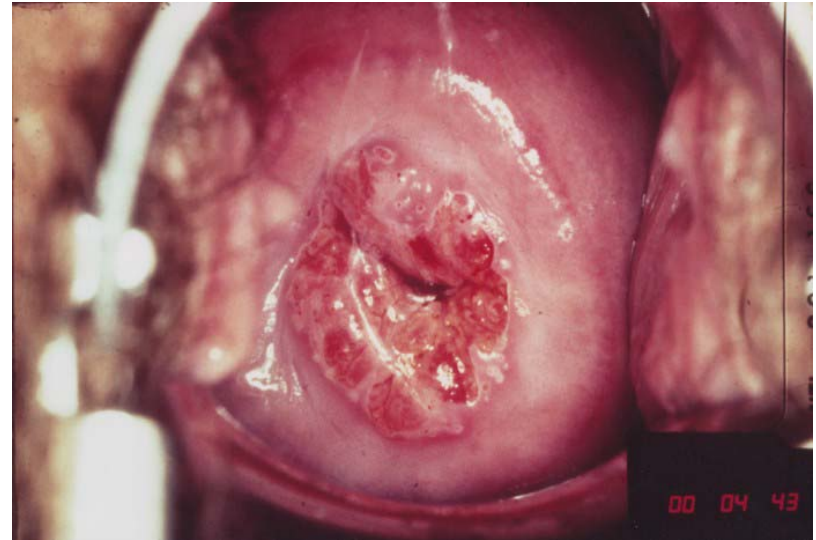
Psychosocial Vulnerability

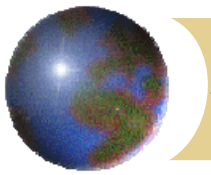
- ❑ Gender power imbalance
- ❑ Violence
- ❑ Non-consensual sex
- ❑ Imperception of risk
- ❑ Poor health seeking behavior
- ❑ Complexity of sexual network
- ❑ Inability to recognize symptoms of infection



Biological Vulnerability

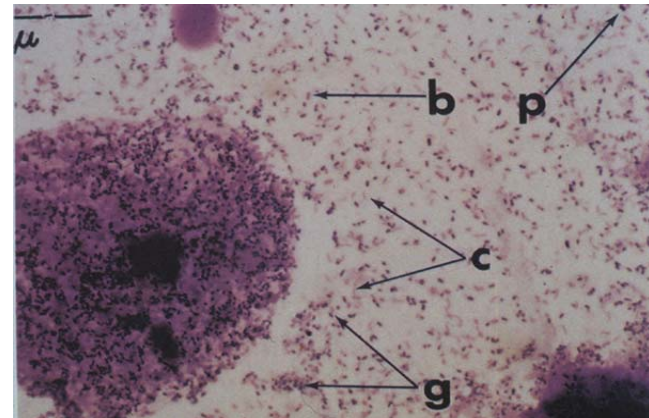
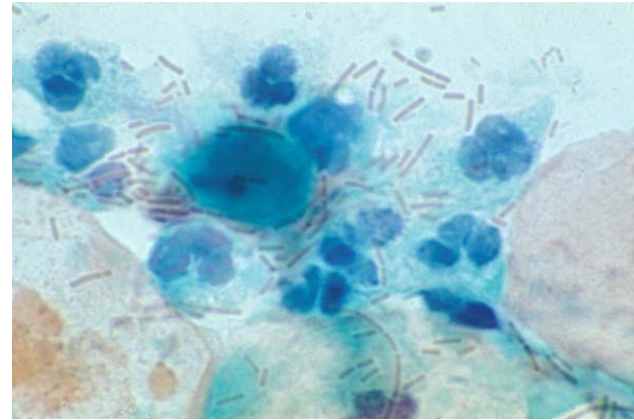
- Hormonal changes at puberty
- Immunological naivety
 - ❑ Immaturity of genital mucosal immune system
 - ❑ Lack of acquired immunity
- Cervical ectopy
 - ❑ Increased at puberty
 - ❑ Associated with increased risk of STIs and HIV
 - ❑ Ectopy associated with increased HIV shedding

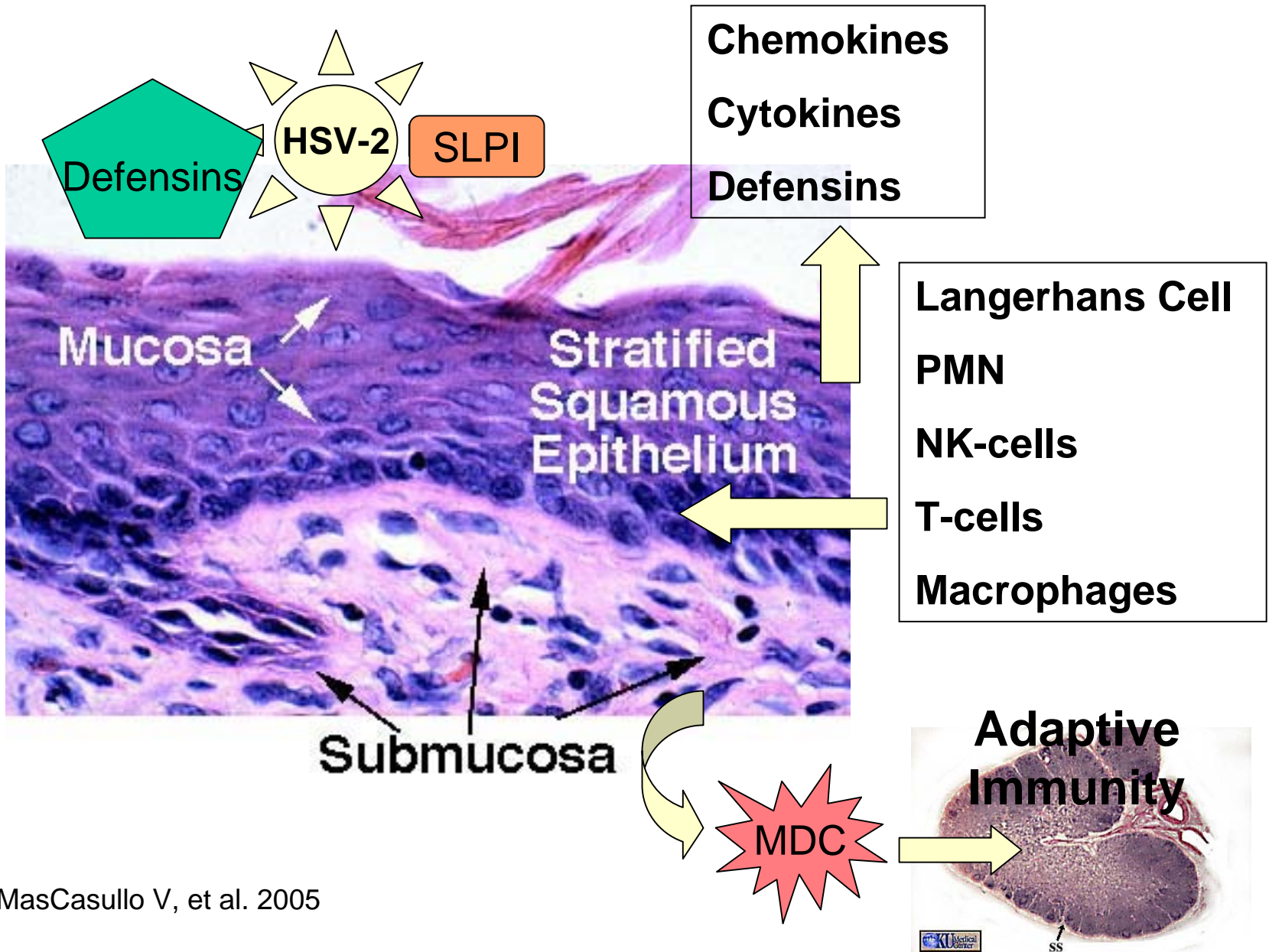
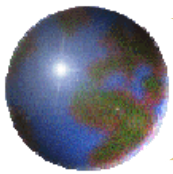


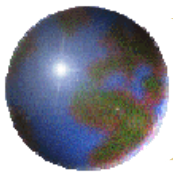


Biological Vulnerability

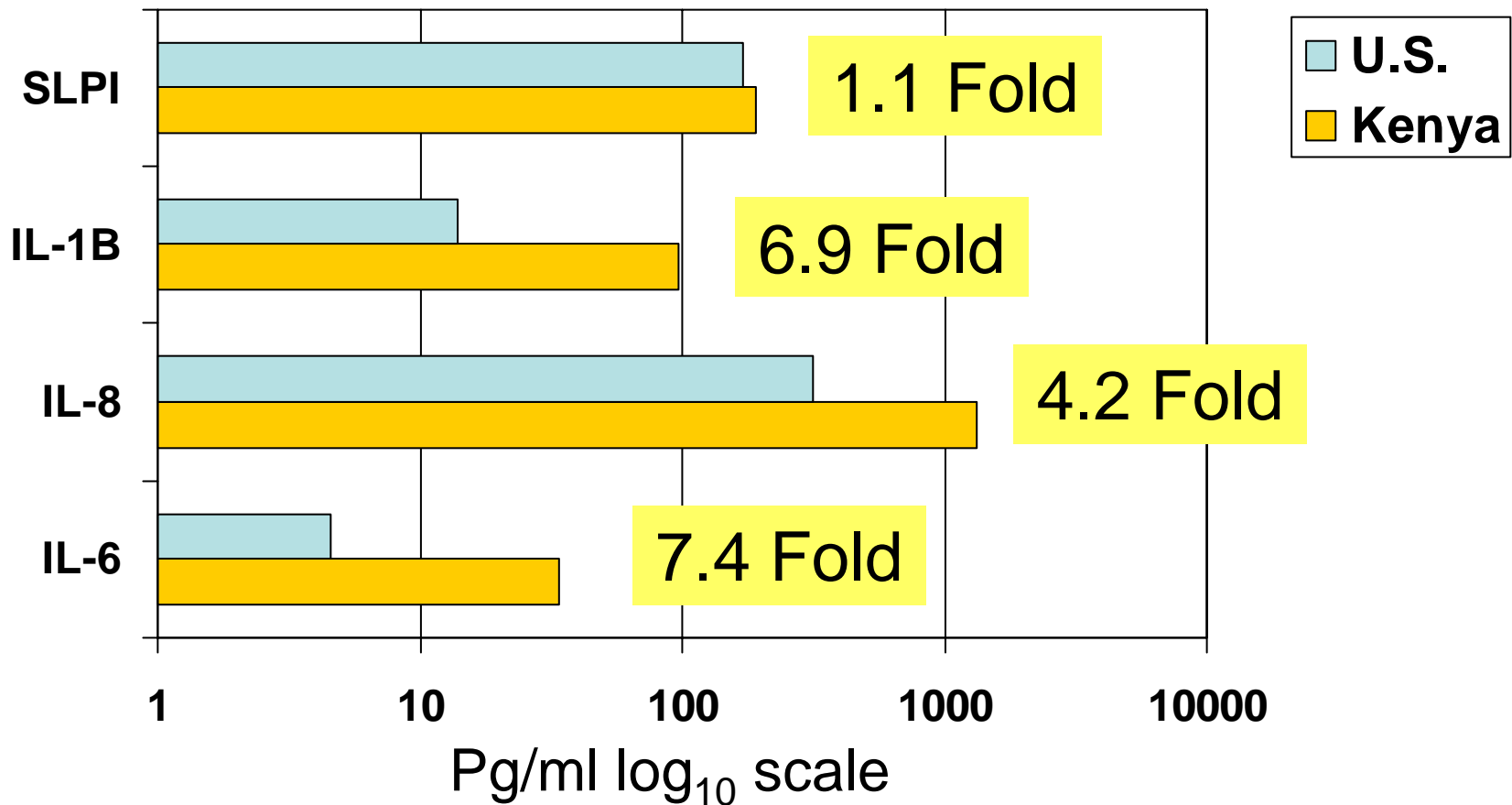
- Lack of normal flora
 - ❑ Normal flora predominantly *Lactobacillus* spp.
 - ❑ Higher pH
 - ❑ Normal flora inhibits HIV and STIs

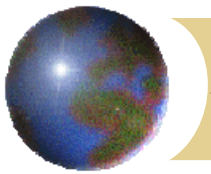






Are women in sub-Saharan Africa biologically more susceptible to STI & HIV?





Prevention

- Microbicides

- Barriers

 - Diaphragm

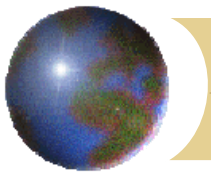
 - Condoms

 - Male

 - Female

- Vaccines

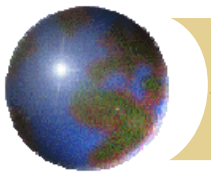




Hurdles: Involving Adolescent Girls in Research

- Community and Institutional Reticence
- Acceptability
 - ❑ Very few studies
- Adolescent sexual behavior
 - ❑ Intermittent intercourse
 - Most products are coitally dependent
 - ❑ Gender power dynamics

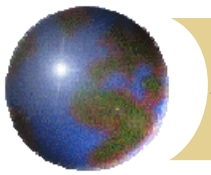




Suggested Solutions

- **Involve Local Communities**
 - ▣ Include Community Advisory Boards
 - ▣ Reach consensus
- **Build Trust**
 - ▣ Transparency
- **Expand Safety Trials**
 - ▣ Include adolescents
- **Bridging Studies**
 - ▣ E.g. vaccines





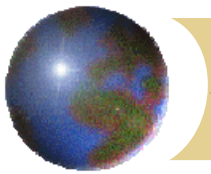
Building the Case for Microbicides

● Barriers to Condoms

- ❑ Less than half of all people at risk of HIV infection able to obtain condoms
- ❑ Only 4.9% of married women of reproductive age use them
 - 1.3% in Africa

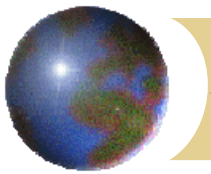
● Female-Initiated Methods

- ❑ May be used without detection during sex
- ❑ Require different gender power balance in sexual partnerships



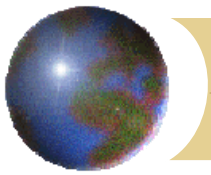
Why Microbicides are an Option

- Program Meta-Analysis: School-based HIV prevention programs for African youth
 - Programs targeting younger, primary school children more effective than targeting secondary school
 - For older youth (e.g., 16–18 years of age), programs did not affect a change in sexual behaviors, e.g.
 - abstinence and number of partners
 - one program was able to increase “reported” condom use



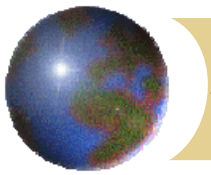
MEMA kwa Vijana: randomised controlled trial of >9,000 adolescents part of a sexual health program in rural Mwanza, Tanzania

- **Intervention comprised of:**
 - ▣ Teacher-led, peer-assisted sexual health education program for students in the last 3 years of primary school
 - ▣ Training and supervision of health workers in the provision of youth-friendly health services
 - ▣ Peer condom promotion and distribution
 - ▣ Wider community activities



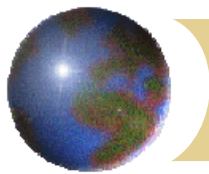
MEMA kwa Vijana: Summary of Results

	Knowledge	Behaviors	HIV/STI
Female	Improved	Little improvement	No change
Male	Improved	Some improvement	No change

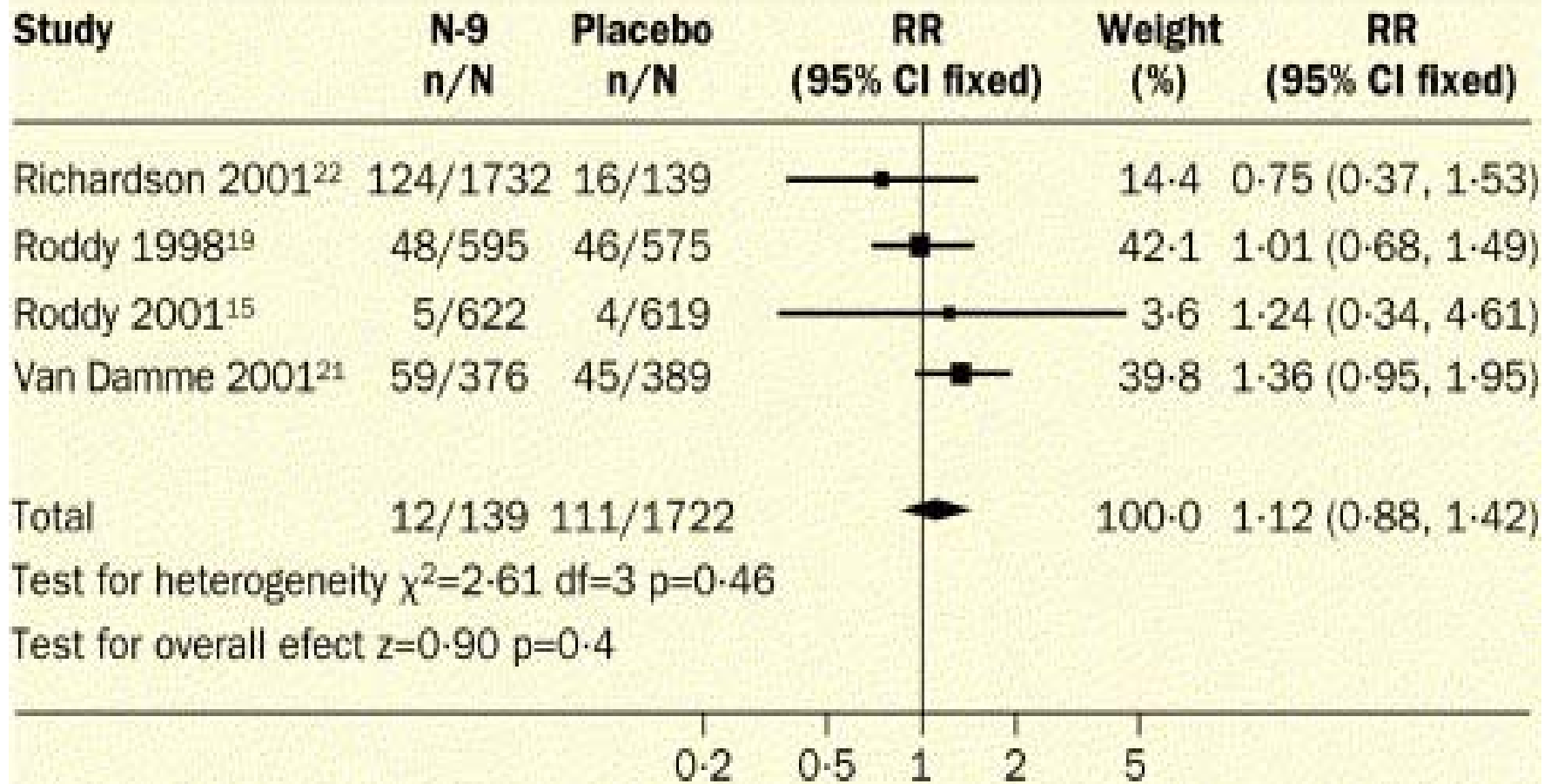


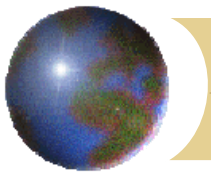
Interpretation of MEMA kwa Vijana

- Such interventions change knowledge & skills, but not risk taking, at least in the short-term
- The pressures for 'risky' sex are very strong within many African communities
 - Cultural norms, such as:
 - gender power relations
 - age-related power relations
 - marriage and fertility norms



Nonoxynol-9 meta analysis

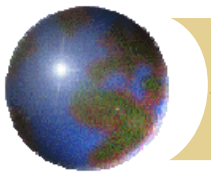




Hypotheses about N-9 failure

- Effect on innate and acquired immunity
 - Toxicity to vaginal/cervical epithelium
- Increased inflammation
 - Induced mucosal inflammation (cytokines) and decreased SLPI
- Very frequent usage in study population
- High dose of N-9 cause lesions that enhance HIV infection
- Less than optimal dosage with N-9 film





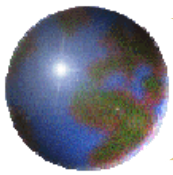
Research: Microbicide Safety Trial in Adolescent and Young Women

- Phase 1 randomized placebo controlled trial of the safety, and tolerability of a microbicide administered twice daily for 14 days

■ Two sites

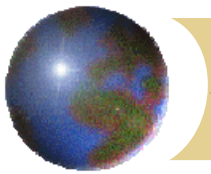
- Kisumu, Kenya
- San Francisco





Kisumu, Kenya

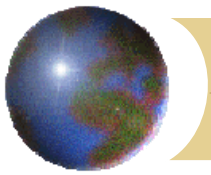




Groundwork & Community Building

- Formative Investigation of HIV and STI Preventative Research in Adolescent Girls
 - ▣ Engage parent forums at both school and church venues
 - ▣ Hold health talks focusing on HIV/STI prevention options and research in Kisumu schools
 - ▣ Develop Community Advisory Group
 - Adolescent females & parent/community leaders
 - ▣ Engage youth and parents in development of proposal
- Initiated Youth HIV/AIDS care program
 - ▣ Ages 14-21





Acknowledgements

● UCSF

- Katy Yanda
- Joelle Brown
- Jenell Coleman

● Kenya Medical Research Institute

- Elizabeth Bukusi

● Financial Support

- STI Clinical Trials Group (NIAID)
- Women's HIV Interdisciplinary Network (NICHD)
- CDC (PEPFAR)

● Other Support

- Office of Research on Women's Health



PERSPECTIVES FROM THE COMMUNITY- STI'S/HIV IN ADOLESCENTS AND YOUNG WOMEN

KATHY WOODWARD M.D.

DIVISION OF ADOLESCENT AND YOUNG ADULT
MEDICINE

CHILDREN'S NATIONAL MEDICAL CENTER
WASHINGTON D.C.



PERSPECTIVES FROM THE COMMUNITY – WHAT NO ONE EVER TALKS ABOUT

- Adolescent and young women have higher biologic risks for STI's/HIV.
- Communities of color have the highest rates for STI's/HIV.
- Survival sex – a commodity to trade for food, shelter, drugs, “love”, jewelry and clothes – among street youths/runaways, GLBT youth, and youth with special needs.
- That you can have an STI/HIV and not know it.
- That there is more to worry about than pregnancy, UTI's and yeast infections.
- The media does not show the reality of STI's/HIV.



SEXUALLY TRANSMITTED INFECTIONS

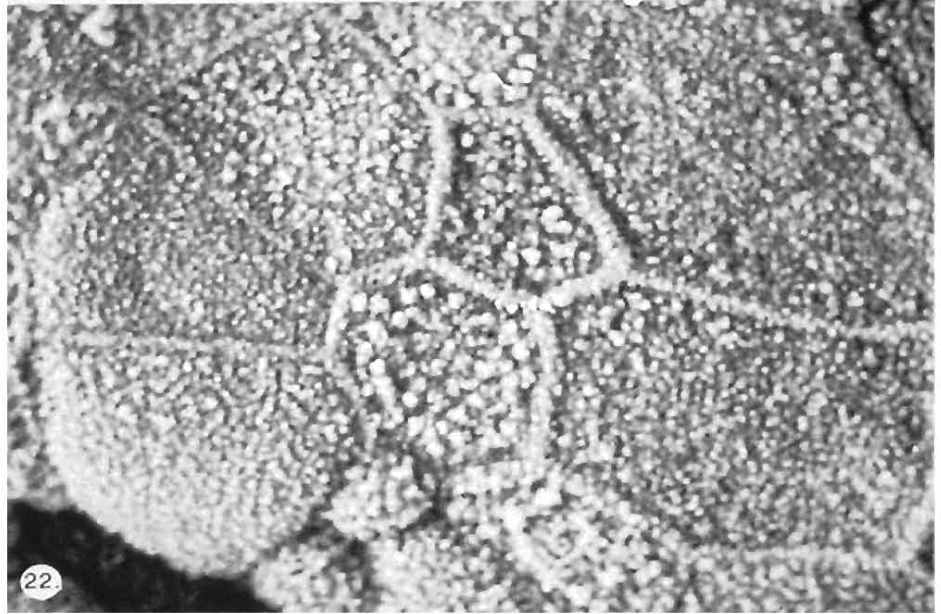
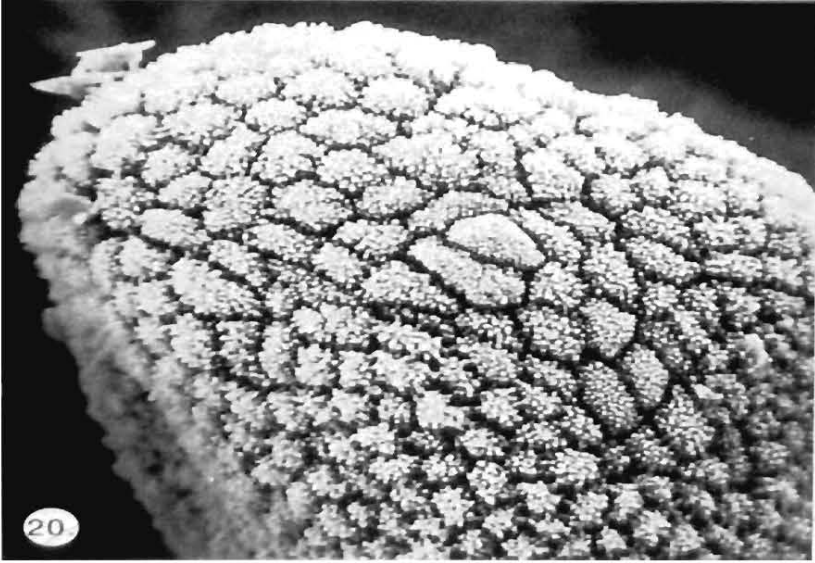
- Adolescent females are at higher risk:
 - Biologic immaturity
 - Cognitive immaturity - early and middle adolescents may not have abstract thought and believe they are invulnerable.
 - Social/Behavioral risks - inconsistent condom use, limited access/knowledge about healthcare services, increased number of sexual partners, adolescent health seeking behavior shaped by concerns of confidentiality, costs, and denial of health problems (many STI's asymptomatic), sexual abuse and dating violence, homelessness/substance abuse/poverty = survival sex, younger females with older male partners



YOUTH AND STI'S/HIV

- Adolescent females are at higher biologic risk for STI's and HIV/ AIDS because of biologic immaturity.
- Teens have significant areas of cervical ectopy and more anovulatory menstrual cycles. The lack of progesterone produces less mature cervical mucus.





PERSPECTIVES FROM THE COMMUNITY

WOMEN'S HEALTH IS NOT JUST PREGNANCY, UTI'S AND YEAST INFECTIONS

- The focus on pregnancy prevention must include condoms.
- Every vaginal discharge is not a yeast infection.
- Every genital exam is not a “pap smear”.
- Condom use with casual partners but not steady partners is not safe.
- Condom use should not be a marker for relationship trust.



plan B[®]
(LEVONORGESTREL)
(2 tablets, 0.25 mg)



SEXUALLY TRANSMITTED INFECTIONS

○ GONORRHEA

- Non-Hispanic Blacks account for 3/4's of all reported GC cases among 15-19 year olds. The Black GC rate is 2,635.3/100,000, seven times that for AI/AN 346.3/100,000, over eleven times the rate for Hispanics 223.7/100,000 and over 23 times the rates for Whites 114.3/100,000 and Asian/PI 93.2/100,000/

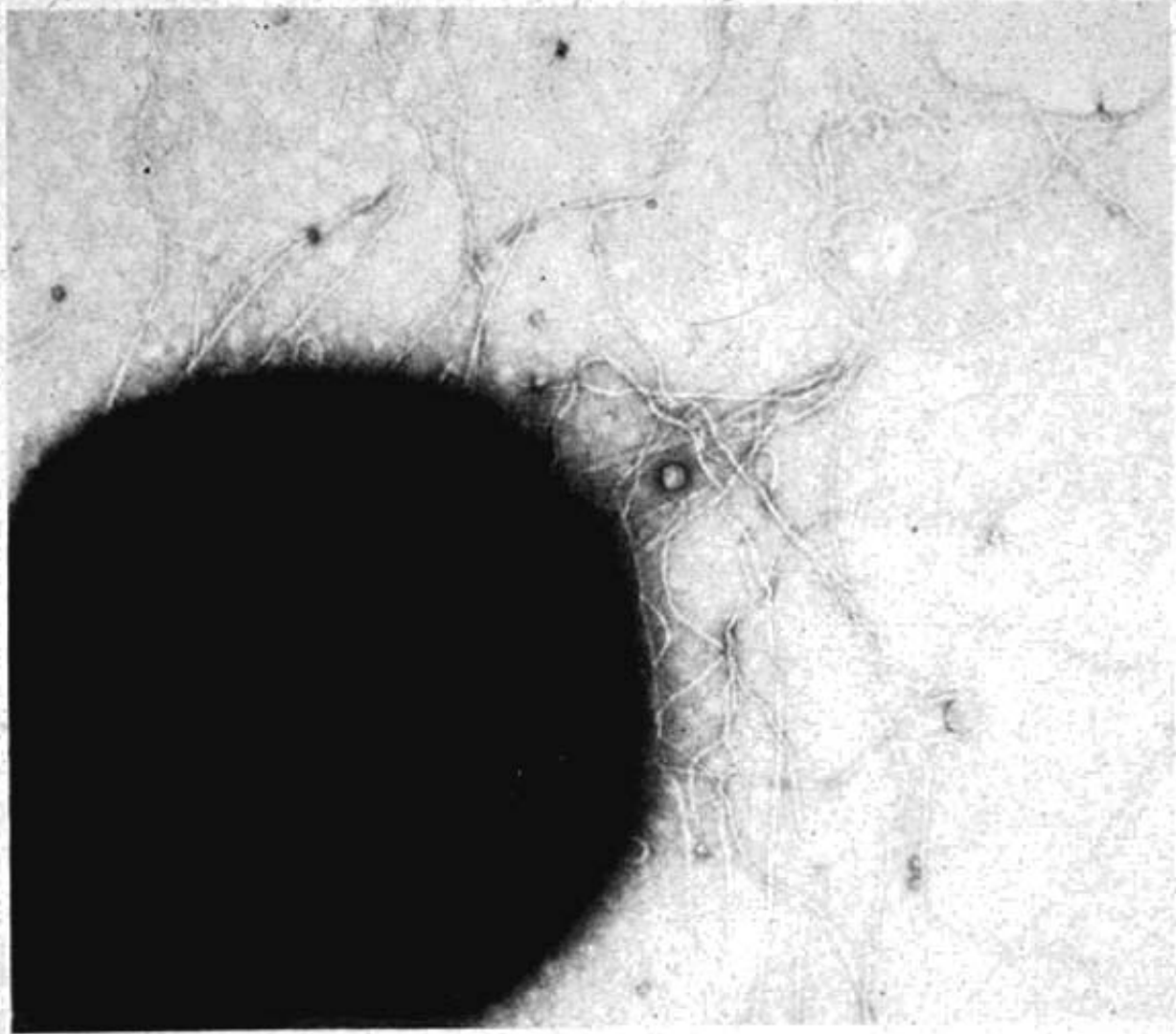


FIG. 53-2. Negative stain electron micrograph of T₂ colonies of *Neisseria gonorrhoeae* showing pili projecting from the surface of an individual gonococcus. (Approximately 50,000; Courtesy of Dr. John Swanson)

GONOCOCCAL CERVICITIS

Cervicitis symptoms include a red and inflamed cervix with an unusual discharge

Normal cervix



Cervicitis



GONOCOCCAL PHARYNGITIS

- The Gonococcus (GC) bacteria can be spread to the tonsils by oral sex.
- GC can live silently in the throat without causing pain, but can be spread to sexual partners.





SEXUALLY TRANSMITTED INFECTIONS

○ CHLAMYDIA

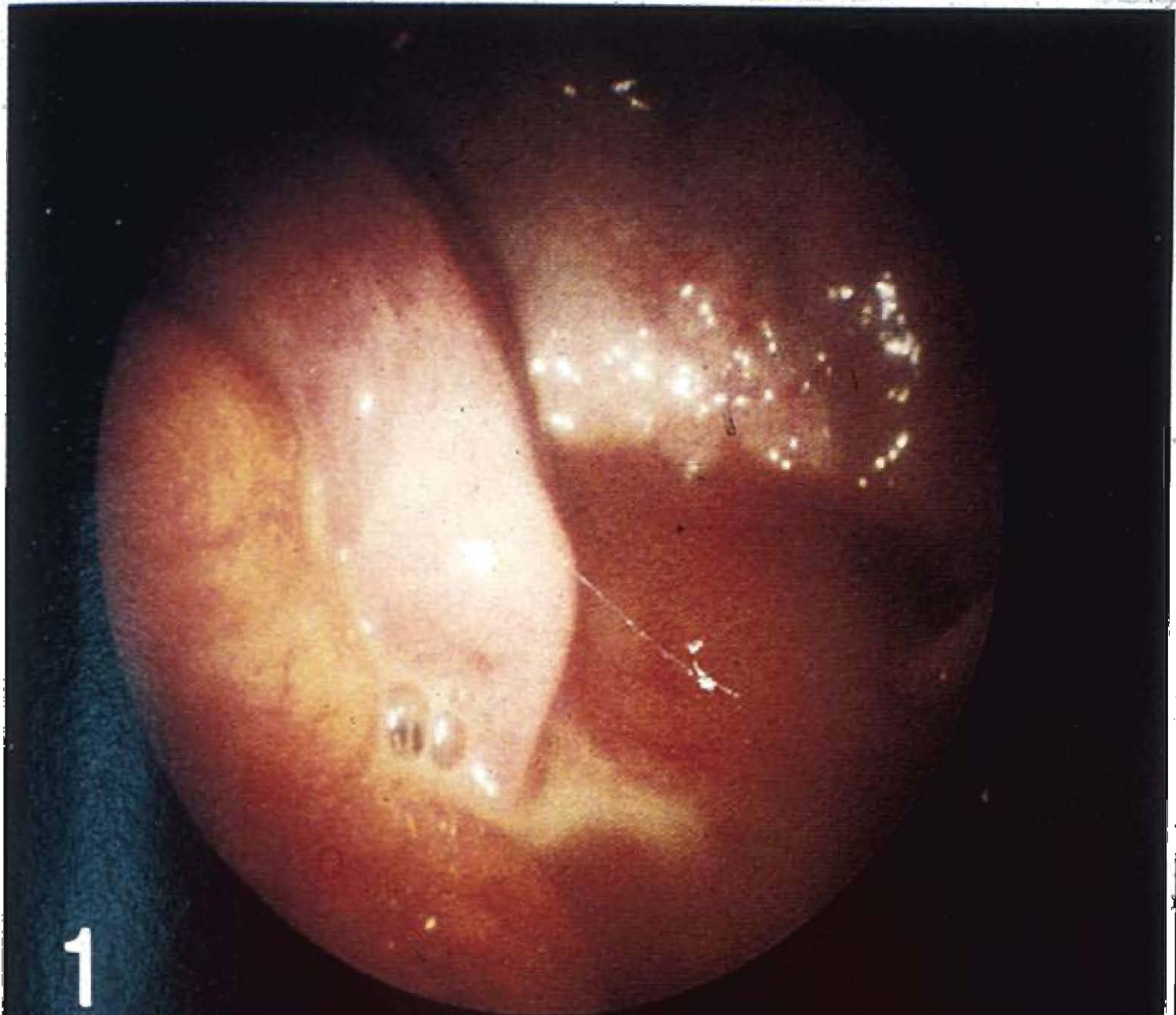
- For most STI's the rate of infection has been decreasing among youth 15-19 years old. There was a 33% increase in chlamydia rates between 1996 and 2001.
- Adolescents 15-19 years old account for 37% of all the chlamydia cases in the US.
- The reported prevalence rate for 15-19 year old non-Hispanic Blacks is 4,957.2/100,000, twice the rate of AI/AN 2,522.4/100,000; three times the rate of Hispanics 1,547.1/100,000 and seven times for Whites 689.0/100,000 and Asian/Pacific Islanders 567.1/100,000. (STDS, 2001-CDC, 2002)





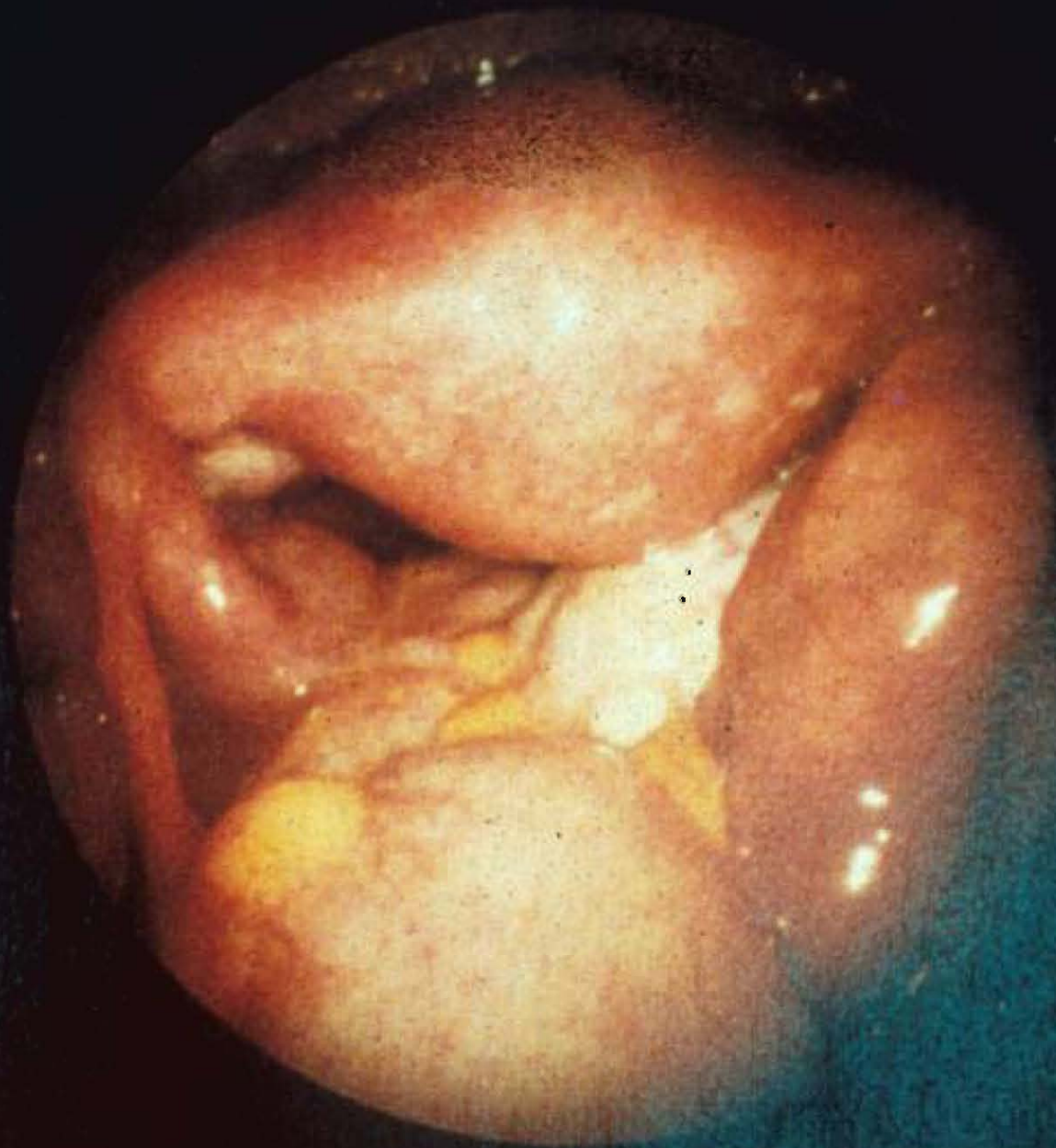
SEXUALLY TRANSMITTED INFECTIONS

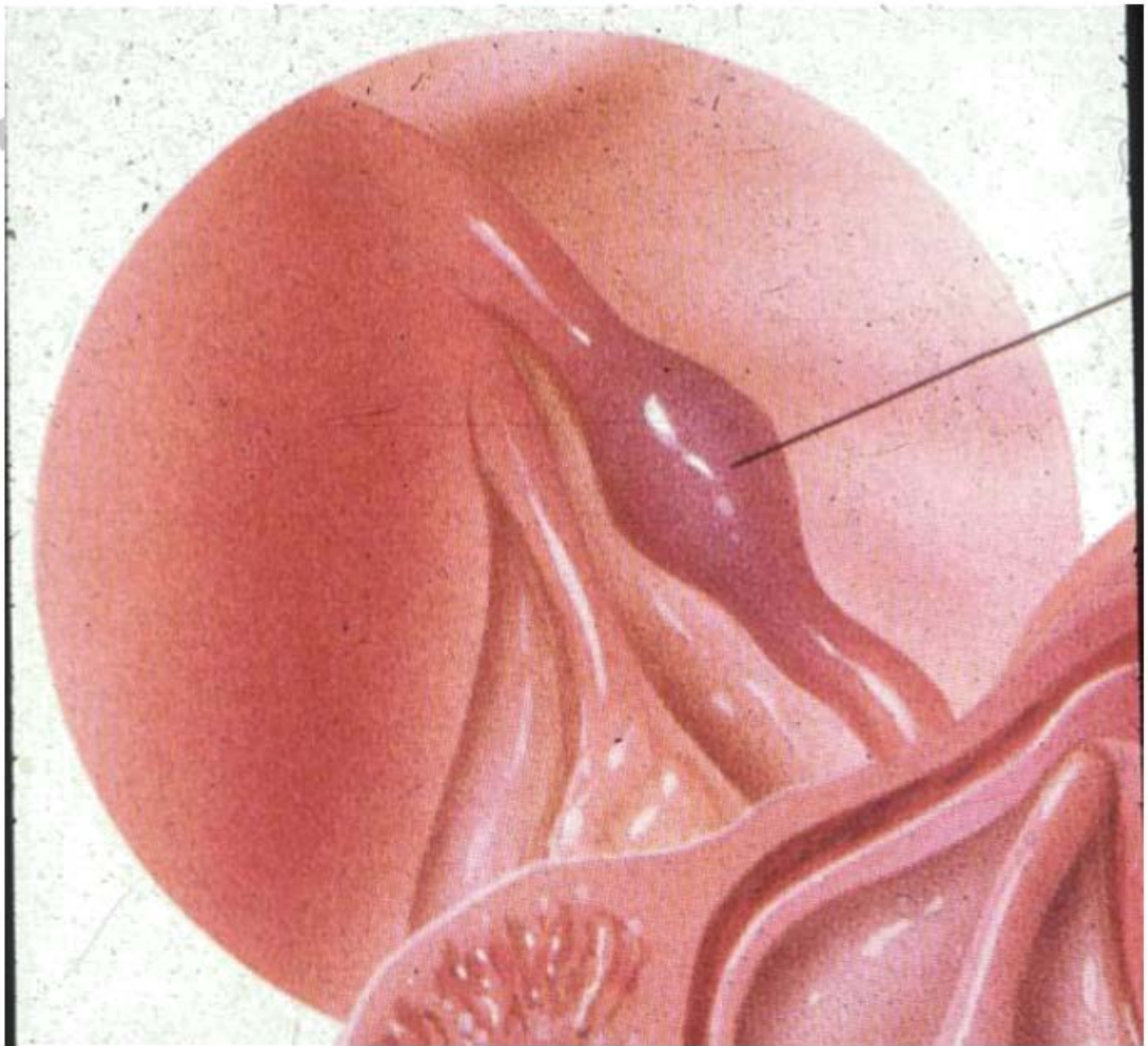
- Pelvic Inflammatory Disease (PID) caused by gonorrhea, Chlamydia and mixed bacterial infection. Severe lower abdominal pain, associated with vaginal discharge, dysuria, and fever. Must have abdominal pain, cervical motion tenderness and adnexal tenderness on exam.
- PID may be associated with RUQ tenderness (peri-hepatitis) or Fitzhugh-Curtis Syndrome, which can be caused by GC or chlamydia salpingitis.
- Chronic pelvic pain, increased risk of ectopic pregnancy and infertility can occur after PID.



1

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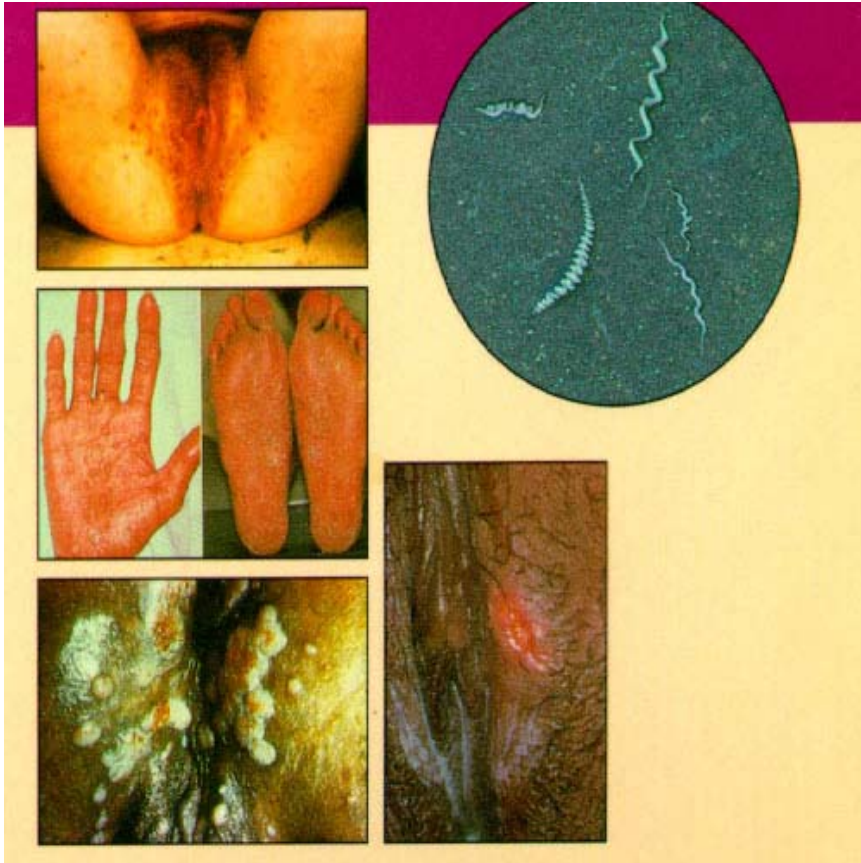




SEXUALLY TRANSMITTED INFECTIONS

- SYPHILIS
- Syphilis is less common than GC in all ages, including adolescents.
- The syphilis rate decreased in 15-19 year olds from 6.1/100,000 in 1996 to 1.9/100,000 in 2001. (STDS, 2001-CDC 2002)
- Black adolescent females have the highest rate of syphilis of adolescent women 13.3/100,000, which is 6-13 times higher than the rate for other teen women.

● ● ● | SYPHILIS





SEXUALLY TRANSMITTED INFECTIONS

- The only viral STI's reported to the CDC are HIV/AIDS and Hepatitis B (and C). Human papilloma virus (HPV) and herpes simplex virus (HSV) are not reportable. Data on these two STI's must be estimated from surveillance data STD clinics and physician offices.
- HPV has become the leading viral STI pathogen with one half million to one million new cases each year. Spread by cutaneous and mucous membrane contact, HPV has been linked to genital cancers (50% of all cervical cancers caused by HPV16/18), and increasing rates of rectal squamous carcinomas in males and females.



HUMAN PAPILLOMA VIRUS (HPV) ORAL LESIONS





SEXUALLY TRANSMITTED INFECTIONS

- The herpes simplex virus (HSV) has two types; HSV Type 2 is usually associated with genital herpes.
- Seroprevalence data of HSV Type 2 from the late 1970's was 0.96% among whites 12 to 19 years of age which increased to 4.5% by the mid-1990's. This is a five fold increase.
- Seroprevalence in the mid-1990's among black adolescents was 8.7%, nearly twice the rate among whites. (Fleming, et.al.,1997)



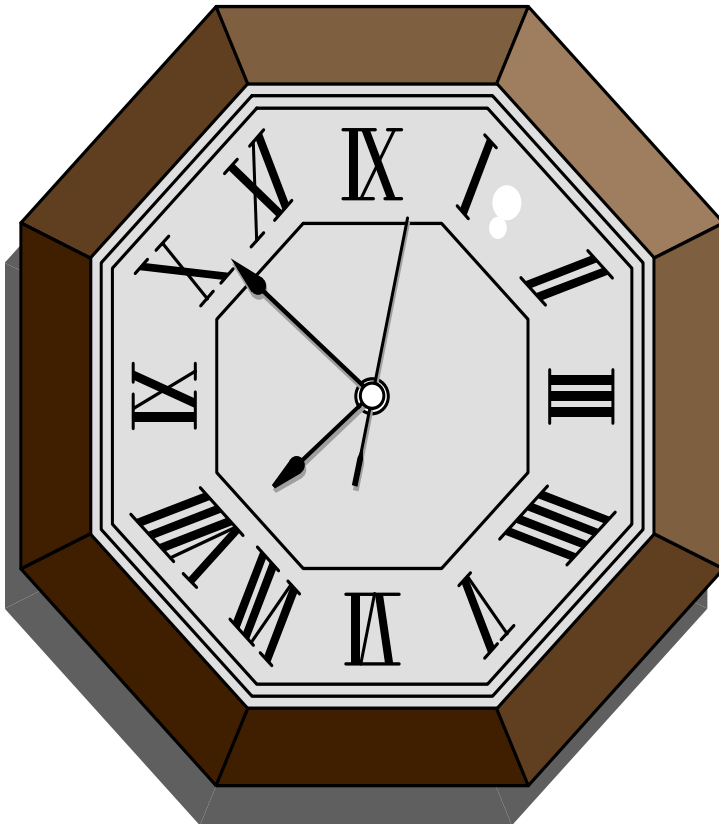
Figure 9. Herpes simplex lesions.

ORAL HERPES



- By age 6 years 90% of children have antibodies to HSV 1 from cold sores/fever blisters. *So no one's mouth is a "virgin" for HSV.*
- HSV 1 can cause genital infections. HSV 2 can cause new oral infections.

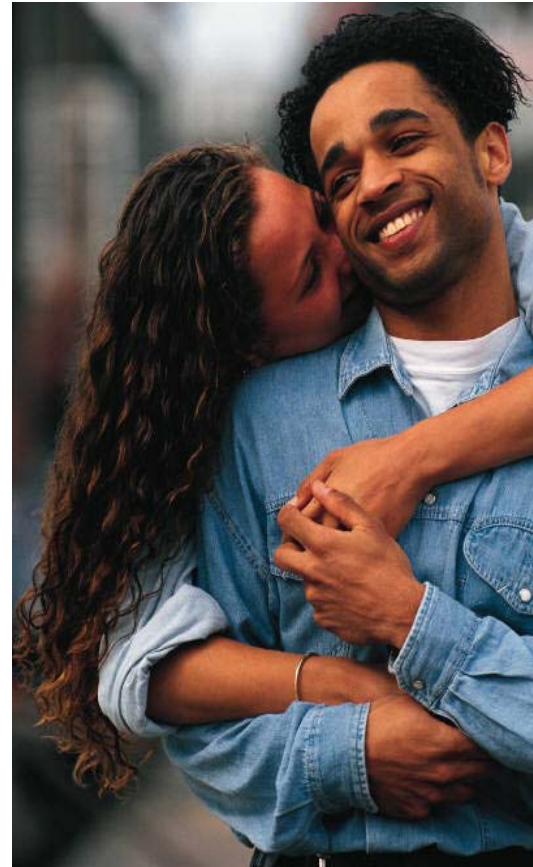
YOUTH AND HIV/AIDS



- Globally, every 14 seconds a youth becomes HIV infected.
- 6,000 youth each day become infected. The majority are young women.
- In the U.S. 2 youths every 30 minutes become HIV infected. There are 20,000 new infections each year to youth under the age 25 years.

YOUTH AND HIV/AIDS

- African- American men are 50% of all the new HIV in the U.S.
- African-American women make up 64% of all the new HIV cases in the U.S.
- Pediatric HIV cases fell from 745(1995) to 150 (2002), but the majority were African-American.





HIV - COLLEGE OUTBREAK

- The North Carolina Dept. of Health and Human Services noted an increase in new HIV cases in men under 30 years old. In male college students 18-30 there were 6 cases (2000), 19 cases in 2002, 29 cases in 2002 and 30 cases in 2003. African-American males represented 73/84 of these new cases (88%).



HIV - COLLEGE OUTBREAK

- The Health Department found two newly infected students (HIV PCR+, Elisa -, High viral load) and traced their sexual network to 69 linked HIV cases. There were 61 college students and 8 men outside of college.
- Among the 84 new cases in North Carolina - 73 were black and 11 were white. The cases involved 33 colleges in North Carolina, 2 colleges in South Carolina, and one each in Georgia and Florida.



HIV-COLLEGE OUTBREAK

- In the year before their diagnoses, 4% of the men reported sex only with women, 58% had sex only with men, and 33% had sex with both men and women.
- In the sample of 84 men - 40% of the college men with HIV reported having had sex with women. Dr. Peter Leone, a study co-author states, “a substantial number of heterosexual college women are at significant unrecognized risk for HIV infection.” Yes, the CDC has discovered “the down low”



SPECIAL ADOLESCENT POPULATIONS

- Adolescents who engage in multiple high risk activities may increase the risk of pregnancy, STI's and HIV/AIDS in their peer group and the adult community.
- In the NSFG 1995 study, females reporting voluntary intercourse before the age of 16 years, 7% stated their partners were 20-22 years old, and 6% stated their partners were 23 years old or older. (Abma, et.al.)



ADOLESCENT SPECIAL POPULATIONS

- Adolescents who initiate sexual intercourse at earlier ages are more likely to report that the sexual activity was non-voluntary.
- In the NSFG, 16% of teens younger than 16 years old reported that their first intercourse was non-voluntary, compared to 7% of those whose first intercourse occurred at 16 years of age or older. (Abma, et.al.)
- Females ages 13-24 have the highest rates of reported rapes and sexual assault. The chances are 1 in 4 that a women will be sexually assaulted by age 20 years.

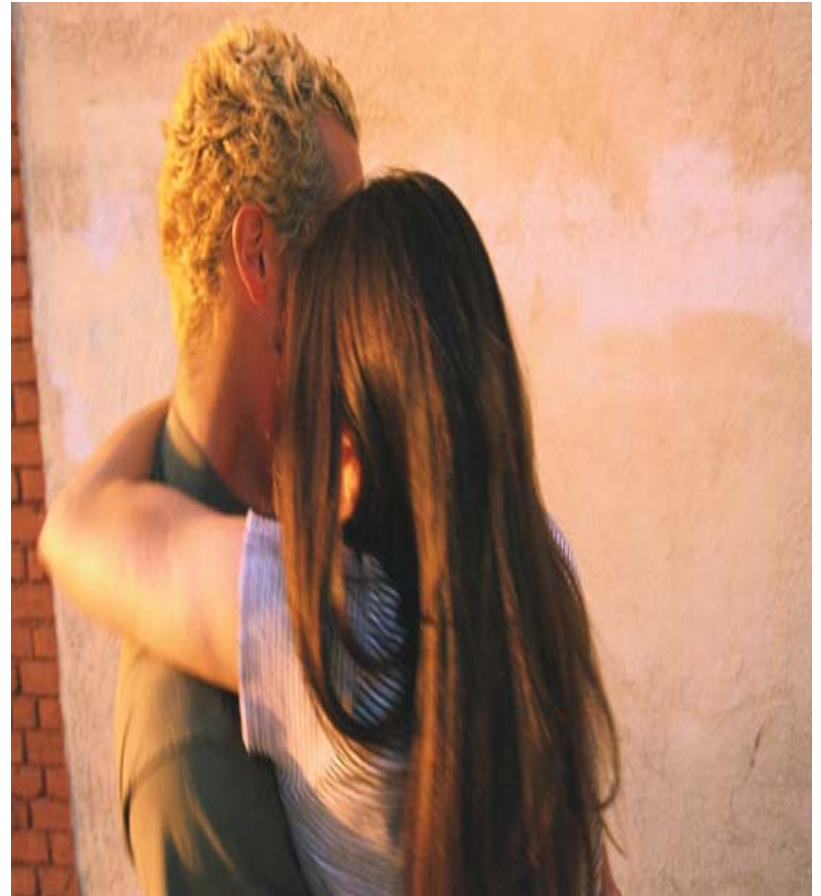


ADOLESCENT SPECIAL POPULATIONS

- Adolescent runaways or street youth represent a high multiple risk group that may be engaged in substance abuse use/addiction and may use sex to barter or sell to support themselves (survival sex).
- Adolescents in the GLBT community may also engage in multiple high risk sexual behaviors with peers and adults.
- Developmental delayed adolescents and mentally ill adolescents may also be homeless, involved in alcohol/drug use and engage in survival sex with peers and adults. (Knopf, et.al.)

TODAY'S ABC's

- A = ABSTINENCE
- B = BEHAVIOR/
BE FAITHFUL.
Don't use drugs or
alcohol. They change
your CHOICES.
- C = COMMUNICATE/
CHOICE/CONDOMS.



HIV PREVENTION

- Is there a comprehensive sex education message for the MTV, Hip-Hop, video game, celebrity impressed, bling-bling conscious youth?
- Can the internet, peer educators, and the media help in STI and HIV prevention?





THE MEDIA AND REALITY

- The only 100% way to avoid pregnancy, sexually transmitted infections (STI's), and HIV/AIDS is not to have sex or abstinence.
- When will the OC, Desperate Housewives, Grey's Anatomy, and MTV Spring Break talk about the reality of STI's/HIV and pregnancy for “girls gone wild”?
- Condom use must be more prominent in the media. Teachable moments – 1) Clinton/Lewinsky; 2) “Why did Kobe have to hit ‘that’ raw?”; 3) How did two doctors have an unintended pregnancy (ectopic) on Grey's Anatomy?





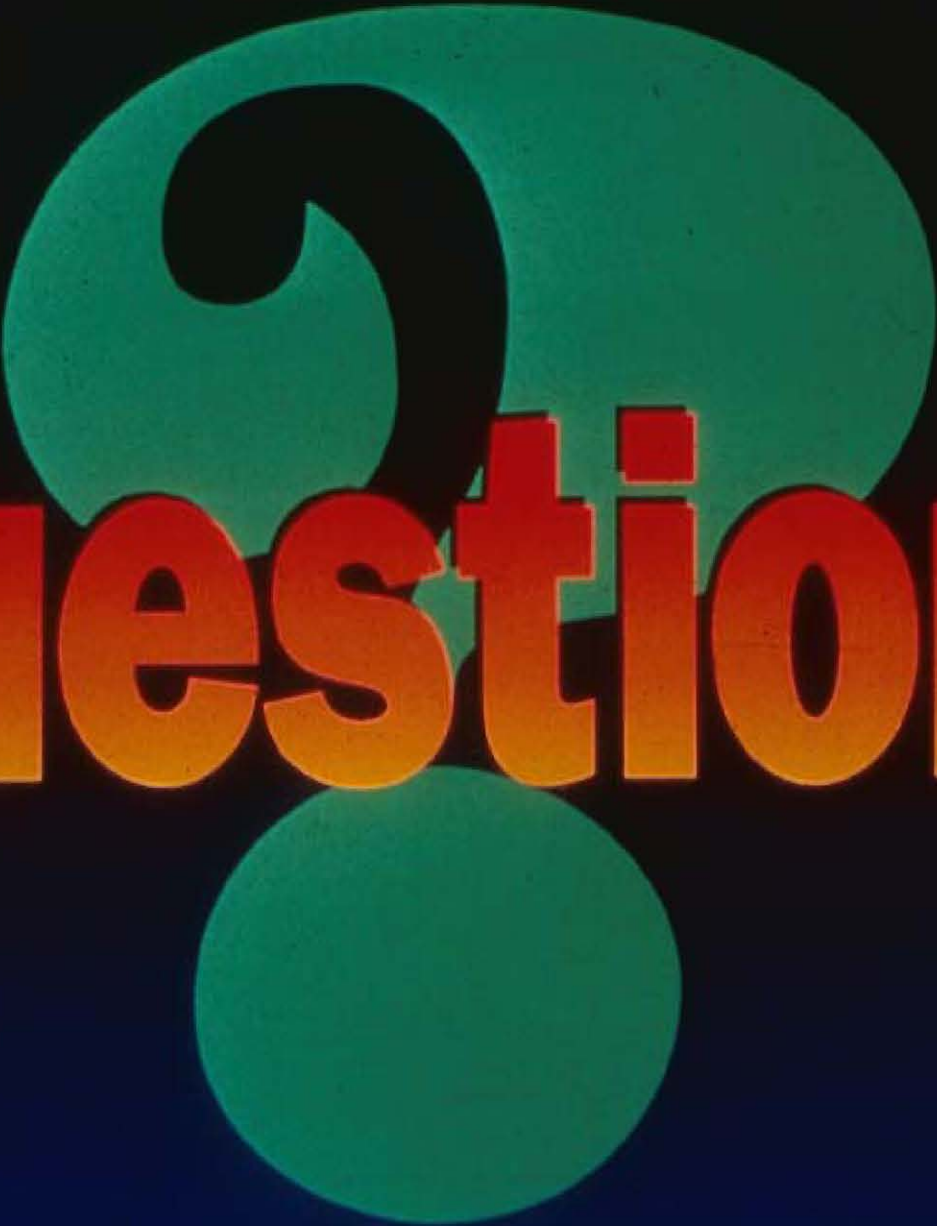
WEB SITES FOR YOUTH AND PARENTS

- WWW.IWANNAKNOW.ORG THE AMERICAN SOCIAL HEALTH ASSOCIATION SITE FOR TEENS
- WWW.NIAID.NIH.GOV/FACTSHEETS/STDINDO.HTM - NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES FACT SHEET ON STD'S
- WWW.HEALTHYDEVIL.STUAFF.DUKE.EDU/INFO/HEALTHINFO.HTML - DUKE UNIVERSITY WEB SITE FOR COLLEGE STUDENTS
- WWW.CDC.GOV/HEALTH/WOMENSMENU.HTM - CDC'S WOMEN'S HEALTH HOME PAGE ON STD'S
- WWW.TEENWIRE.COM PPFA TEEN WEBSITE



PERSPECTIVES FROM THE COMMUNITY WOMEN'S HEALTH

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Questions