Lecture # 8
Building specialized knowledge: HIV

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Outline

• Biological interactions
• Social aspects of the epidemic
• Programmatic actions
• Current challenges

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Retroviruses

CD4+ T cell

Macrophage

CXCR4

CD4

CCR5

CCR2

M-tropic HIV isolate (R5)

T-tropic HIV isolate (X4)

RANTES

MIP-1β

MIP-1α

Cytotropism

SDF1

CD4+ T cell

CD4

Macrophage

CXR4
**HIV transmission**

- **SEXUAL**
- **BLOOD-BORNE**
- **VERTICAL** - intrauterum, birth, breast feeding

**HIV genital shedding**
- associated factors -
  - higher HIV plasma viral load
  - acute infection
  - more advanced clinical status
  - cervicitis/urethritis

**HIV genital acquisition**

Hu J, 2000; Deeks S, 2011; Moir S, 2011
Immune response in HIV acute infection

HIV infection - Natural history

Early signs and symptoms of HIV disease

- Prolonged fever
- Weight loss
- Chronic diarrhea
HIV and cancer

Outline

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CUMULATIVE GLOBAL ESTIMATE (Dec 2012)

- People living with HIV: 35.3 million
- New HIV infections (2011): 2.3 million
- AIDS deaths (2011): 1.6 million
- Cumulative AIDS deaths: 43.9 million

UNAIDS, 2013
Outline

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Programmatic actions

- Primary prevention
  - safer sex
  - harm reduction interventions
  - prevention of mother-to-child transmission

Brazilian National ART Program

- universal access to medication distributed free of charge - SUS
- launched in 1991 - zidovudine (AZT)
- progressively incorporated new ARVs
- 1997 - combined therapy (HAART)
- local production of generic ARVs
- 2008 - compulsory license - efavirenz
- 2013 - “test and treat” strategy
Antiretroviral therapy

- Reverse transcriptase inhibitors
  - nucleoside/nucleotide analogues: AZT, 3TC, ddI, abacavir, tenofovir
  - non-nucleoside analogues: nevirapine, etravirine, elvitegravir

- Protease inhibitors - saquinavir, ritonavir, lopinavir, fosamprenavir, atazanavir, darunavir

- Fusion inhibitors - enfuvirtide, maraviroc

- Integrase inhibitors: elvitegravir

Virological and immunological outcomes of successful ART

- Suppression of blood viral replication → undetectable viremia

- Immune restoration

- Reduction/suppression of viral replication in tissues - CNS, genital tract, others

- Remarkable reduction in HIV genital shedding

Brazilian response to HIV/AIDS

- Main peculiar features:
  - Historical momentum
  - Legal foundations

Brazilian Constitution 1988

"Health a right of citizens and a duty of the State."

SUS basic principles
Brazilian response to HIV/AIDS
- main peculiar features -

- historical momentum
- legal foundations
- combined interventions in prevention and care

HIV testing and counseling

Promoting condom use
Care responses

- Health service and laboratory networks
  - Reference hospitals
  - Day hospitals
  - Outpatient clinics
  - ART distribution units
  - Labs – CD4 cell counts, HIV viral loads, HIV genotyping

Brazilian response to HIV/AIDS
- main peculiar features -

✓ historical momentum
✓ legal issues
✓ prevention and care interventions
✓ governmental commitment
✓ strong civil society involvement (NGOs and private sector)

Berkman, 2005; Nunn, 2012
Brazilian response to HIV/AIDS
- main peculiar features -

- historical momentum
- legal issues
- prevention and care interventions
- government/civil society commitment
- human rights perspective
Brazilian HIV epidemic - trends

- territorial spread

- changes in the proportional distribution of different exposure categories
Distribution of AIDS cases in men aged 13 and over, according to exposure categories and year of diagnosis.
Brazil, 1983 - 2009*

Brazilian HIV epidemic - trends

- territorial spread
- changes in the proportional distribution of different exposure categories
- male-female ratios

AIDS male-female ratios, Brazil

Male-female ratios in AIDS cases according to year of diagnosis, Brazil, 1986-2008
Male-female ratios in AIDS cases in individuals aged 13-19, according to year of diagnosis, Brazil, 1986-2008
Clinical outcomes

- Reduced morbidity
  - incidence of opportunistic infections

- Reduced morbidity
  - progression to AIDS
  - hospital admissions
  - day hospital use
Clinical outcomes

- Reduced mortality (AIDS-related deaths)

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MDGs and HIV/AIDS

UNAIDS, 2013

Global HIV epidemic - trends

UNAIDS, 2013
Outline

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Current challenges - 1

- Regional discrepancies - local epidemics
- Late diagnosis
- Uptake and retention in care

Global new HIV infections
AIDS mortality in Brazil

Global AIDS-related deaths

Late entry into HIV care

Table 1. Clinical and immunological status of HIV-infected adults 15–59 years of age upon entry into HIV care in public health care facilities in Brazil.

<table>
<thead>
<tr>
<th>Year</th>
<th>2013-2014</th>
<th>2015-2016</th>
</tr>
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<tbody>
<tr>
<td>Clinical</td>
<td>67%</td>
<td>57%</td>
</tr>
<tr>
<td>T1</td>
<td>97%</td>
<td>92%</td>
</tr>
<tr>
<td>T2</td>
<td>91%</td>
<td>88%</td>
</tr>
<tr>
<td>T3</td>
<td>84%</td>
<td>81%</td>
</tr>
<tr>
<td>T4</td>
<td>75%</td>
<td>70%</td>
</tr>
</tbody>
</table>

Grangeiro A, 2011

Page 21
HIV/AIDS care cascade - Brazil

Current challenges - 2

- ART sustainability
- highly vulnerable populations
- adherence to ART
Current challenges - 3

- coinfections - HCV, HPV
- comorbidities - mental health
- HIV drug resistance
- chronic AIDS - lypodistrophy, cardiovascular risk

Number of people on ART

Figure 4. Number de pacientes na ART, Brasil, 1999-2013

Number of people on ART

Figure 6.1: Percentage of people eligible who are receiving antiretroviral therapy (based on 2010 WHO guidelines) in low- and middle-income countries, by region, 2010-2012

- Coinfections – HCV, HPV
- Comorbidities – mental health
- HIV drug resistance
- Chronic AIDS – lypodistrophy, cardiovascular risk
Outcomes of chronic ART

Deeks S, 2011

Current challenges - 4

- Stigma and discrimination
  - need to address more vulnerable populations
  - targeted prevention and care initiatives
  - need to face structural dimensions of vulnerability to HIV acquisition and disease development
  - recent retrenchment in human rights-based response in Brazil

Malta C, 2013; Reis RK, 2013

HIV stigma and discrimination

UNAIDS, 2013
Important strategies

- Scaling up HIV testing
- Scaling up early ART - test and treat
- Use of combined HIV prevention technologies - behavioral, structural and biomedical approaches
- Integrating HIV care and other health care programs

Prevention of HIV sexual transmission

- STI detection and treatment
- Microbicides
- Cervical barriers (vaginal diaphragms)
- HIV testing and counseling
- Immunization (HIV vaccine)
- ART prophylaxis (PEP, PrEP, Truvada)

HIV integration

- Tuberculosis care
- Sexual and reproductive health care
- Primary care
- Antenatal and child care
- Non-communicable diseases