The Oldest (Mtb/TB) and Newest (HIV/AIDS) Infectious Disease Pandemics

<table>
<thead>
<tr>
<th>Mtb/TB</th>
<th>HIV/AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>The tuberculosis (TB) pandemic is at least several millennia old. TB has caused more human deaths than any other infectious disease – with over a billion TB deaths estimated during the past few Centuries. <em>Mycobacterium tuberculosis</em> (<em>Mtb</em>) is a bacterial agent that is transmitted from person to person via the respiratory route. As a result, all household and close (face to face) contacts can be infected. <em>Mtb</em> is therefore capable of “generalized” spread in any “general” population.</td>
<td>The AIDS pandemic is less than a half Century old. It is estimated that there has been over 25 million AIDS deaths since this pandemic was first recognized in the early 1980s. The AIDS pandemic is comprised of several relatively separate and independent HIV epidemics. These epidemics involve persons who have unprotected sex with multiple and concurrent sex partners in open sex networks and in injecting drug users who share needles and syringes. HIV is thus not capable of “generalized” spread since it requires sex or blood contact.</td>
</tr>
</tbody>
</table>
Interaction between HIV and other infectious agents

• The only major HIV interaction identified is with *Mycobacterium tuberculosis* (*Mtb*), the cause of TB.
• About 90% of *Mtb* infections will NOT develop TB, but 60-70% of dually infected persons will develop TB. *Mtb* is the major opportunistic infection of HIV-infected persons.
• In 2008, some researchers, based on monkey studies, suggested that shistosome parasites that are prevalent in SSA may greatly increase susceptibility to HIV.
• If this finding can be confirmed in humans, this may prove to be another “facilitating” factor for HIV transmission but the major factor for epidemic HIV transmission remains having unprotected sex with multiple and concurrent sex partners within open or overlapping sex networks.

Consultant Report to WPRO on HIV associated TB – May 2000

• The public health implications of the interaction between HIV and Mtb infections are clear.
• The increase of HIV-related TB cases in SSA populations will overwhelm health care systems.
• HIV prevalence levels in Asian –Pacific countries range from less than 0.1% to 2-3% in Cambodia.
• Cambodia will likely have an increase from 30-50% in HIV-related TB by the end of this decade.
• Most of the other Asian-Pacific countries with current low HIV prevalence can expect to have a modest increase of HIV-related TB – from 5-10%.
Natural History of HIV Infection

- Human Immunodeficiency Virus (HIV) infection is likely lifelong, and severe immune deficiency will develop in half of HIV-infected adults by 9-10 years after infection and perhaps more than 90 percent after 15-20 years.
- Once sufficient immune damage develops, the infected person is susceptible to many cancers and infections, and these latter illnesses are indicators of the immune damage due to HIV and they constitute the diagnosis of Acquired Immune Deficiency Syndrome (AIDS).
- Annual progression rates from HIV infection to the development of AIDS are similar in Haiti, Thailand, Uganda, and “Western” countries (median of 10 years).
- Survival after the onset of AIDS is, in the absence of anti-HIV treatment, short and is usually less than 1 year in developing countries.
During the acute phase, the viral load is 2-3 orders of magnitude greater than at other stages.

Persons dually infected with HIV and Mtb will develop TB at varying levels of immunodeficiency.

Who is at Risk of Acquiring or Transmitting an HIV Infection?

As of late-2008, 0.5% of the total world population is infected with HIV.

The vast majority of all populations are not at any measurable risk of HIV, but the following persons due to their HIV-risk behaviors or specific exposure to HIV-infected blood are at some risk of acquiring an HIV infection:

- Faulty medical procedures, etc. (≤5%)
- IDU (≤10%)
- MSM (≤10%)
- Heterosexual networks (≥50%)
- HIV+ mother to infant (≤5%)
- Regular sex partner of HIV+ person (≤20%)

New annual HIV-infected persons (incidence)
Estimates and Projections of HIV Prevalence Numbers

<table>
<thead>
<tr>
<th>Estimated HIV prevalence in the 15-49 year old population</th>
<th>Millions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult HIV prevalence (%)</td>
<td></td>
</tr>
<tr>
<td>UNAIDS 2001</td>
<td></td>
</tr>
<tr>
<td>2001 9%</td>
<td>1</td>
</tr>
<tr>
<td>2003 7.5%</td>
<td>2</td>
</tr>
<tr>
<td>2005 6.5%</td>
<td>3</td>
</tr>
<tr>
<td>2007 5.8%</td>
<td>4</td>
</tr>
</tbody>
</table>

UNAIDS 2007 back-calculated curve

Global Distribution of Estimated Adult HIV Prevalence Rates, 2007

- 10 countries in Central America, Caribbean and Northern S America with HIV prevalence 1-3%
- 22 countries in SSA with HIV prevalence of 1-5% and 14 counties >5% - 25%
- As of 2008, only Thailand had an HIV prevalence >1% (1.4%) but Cambodia and several states in India had peak HIV prevalence about 1-2%

Source: UNAIDS 2008 report on the AIDS pandemic
Countries with the highest estimated HIV prevalence rates - 2007

Countries with the highest estimated numbers of persons living with HIV (HIV prevalence) - 2007
### Relative Severity of HIV Epidemics

<table>
<thead>
<tr>
<th>Country</th>
<th>*Total adult population</th>
<th>*Number HIV+</th>
<th>Percent HIV+</th>
<th>Severity index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japan</td>
<td>57</td>
<td>0.017</td>
<td>0.03</td>
<td>1</td>
</tr>
<tr>
<td>China</td>
<td>746</td>
<td>0.65</td>
<td>0.087</td>
<td>3</td>
</tr>
<tr>
<td>India</td>
<td>579</td>
<td>2.5</td>
<td>0.36</td>
<td>12</td>
</tr>
<tr>
<td>USA</td>
<td>149</td>
<td>0.7</td>
<td>0.47</td>
<td>16</td>
</tr>
<tr>
<td>SSA region</td>
<td>350</td>
<td>21.4</td>
<td>6.1</td>
<td>203</td>
</tr>
<tr>
<td>South Africa</td>
<td>25</td>
<td>4.7</td>
<td>18.8</td>
<td>627</td>
</tr>
<tr>
<td>Swaziland</td>
<td>0.5</td>
<td>0.17</td>
<td>33.4</td>
<td>1,113</td>
</tr>
</tbody>
</table>

* Number in millions

Only adult (15–49) HIV infections used to calculate this severity index. SSA has >80% of all HIV infections in infants and children - inclusion of these infections would make HIV severity in SSA even greater! Inclusion of HIV related TB would also make the disparity in severity even worst.

### Question

Why is sustained **epidemic** \((R_0 >1)\) heterosexual HIV transmission almost non-existent in most countries in the world but is so prevalent in many sub-Saharan African (SSA) countries and to a lesser extent in several Caribbean countries and in only a few countries in South and Southeast Asia?
"Perfect Storm" Conditions for Sexual HIV Epidemics in sub-Saharan Africa

- The overall prevalence of *facilitating factors* such as genital herpes, “dry sex” etc., is from 1 to 2 orders of magnitude greater in SSA populations compared to most other populations.
- The prevalence of *protective factors* that limit sexual HIV transmission (male circumcision and condom use), are low in most SSA populations.
- The median age of sexual debut (for boys and girls) in many SSA countries is about a decade lower compared to most other populations.

*Facilitating factors are not co-factors since they are not needed for HIV transmission, but they can “facilitate” or increase the risk of transmission.*

Data source: Selected DHS or population based surveys
THE Major “Perfect Storm” Factor – concurrency of sex partnerships

- From 20% to 40% of 15-49 year old males and females in many SSA countries have multiple long term (many months/years) concurrent sex partners within small (<10), but overlapping sex networks.

- When a large percent of sex partnerships in a population is concurrent, the size of HIV epidemics can be an order of magnitude higher compared to a pattern of mostly sequential monogamy.

- With concurrency (i.e., within a sex network), HIV is not trapped within a monogamous partnership after transmission occurs, but can spread immediately beyond a single partnership to infect others.  

CONCURRENCY and HIV TRANSMISSION

Based on:
(1) A model of concurrent sex partnerships on the spread of HIV in Uganda by Morris and Kretzschmar
(2) Diagrams by Steward Parkinson of Population Services International; and
Acute HIV infections (first 2-3 months) are more infectious than older HIV infections by 1 to 2 orders of magnitude!

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March

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Acute HIV infections (first 2-3 months) are more infectious than older HIV infections by 1 to 2 orders of magnitude!

If these two HIV discordant couples remain as couples, then the uninfected partner is at high risk of HIV infection from unprotected sex over the next couple of decades. Nevertheless, epidemic HIV transmission is slowed or stopped.

May

Based on:
(1) A model of concurrent sex partnerships on the spread of HIV in Uganda by Morris and Kretzschmar
(2) Diagrams by Steward Parkinson of Population Services International; and

Acute HIV infections (first 2-3 months) may be more infectious than older HIV infections by 1 to 2 orders of magnitude!
In populations where half or more are *Mtb* (+), virtually everyone is at some risk of *Mtb* infection, but the following contacts to a TB case are at much higher risk of *Mtb* exposure and infection:

- Household contacts
- Work and school contacts
- Health-care contacts
- Other close personal contacts

New annual *Mtb*-infected persons (incidence)

- About 5% of persons initially infected with *Mtb* will develop TB within the first few years of infection.
- About 90% of *Mtb*-infected persons will NOT develop TB.
- About 5% of persons infected with *Mtb* will develop TB many years to many decades after initial infection.
- Over 90% of HIV infected persons will develop AIDS and the majority of dually infected persons will develop TB.

Without treatment, about half of TB cases will die.

Death

TB
Countries with the highest estimated TB case rates - 2005

Countries with the highest estimated numbers of clinical tuberculosis (TB) - 2006
Interaction between HIV and Mtb infections

Geographical distribution of estimated HIV-positive TB cases, 2006.
For each country or region, the number of incident TB cases arising in people with HIV is shown as a percentage of the global total of such cases. AFR* is all countries in the WHO African Region except those shown separately; AMR* excludes Brazil; EUR* excludes the Russian Federation; SEAR* excludes India.

Source: WHO 2008 report on Global TB Control
Modeling TB in an African country with and without HIV infection

Population of 10 million with half (50%) *Mtb*+ and 15% HIV+

Of the 5 million *Mtb*+ about 10% (500,000) will develop TB during their lifetime (about half – 5% within 1-2 years after infection and another 5% during the remainder of their life - over a 50 year period

- 10,000 TB cases (HIV-) per year

- A total of about 57,000 TB cases per year with > 80% HIV+

Of the remaining 4.5 million *Mtb*+, 15% or 675,000 are also HIV+. About 70% of these dually infected persons will develop TB over about a 10 year period – i.e., when their CD4 cell counts have been reduced to about 350 or less

- 47,000 TB cases (HIV+) per year

This model does not include the increase in both HIV- and HIV+ TB cases that can be expected to develop from the more than 4 fold increase in ARI for *Mtb* from the 47,000 TB cases calculated above.

Modeling TB in an Asian country with and without HIV infection

Population of 10 million with 30% *Mtb*+ and 0.5% HIV+

Of the 3 million *Mtb*+ about 10% (300,000) will develop TB during their lifetime (about half – 5% within 1-2 years after infection and another 5% during the remainder of their life - over about a 50 year period

- 6,000 TB cases (HIV-) per year

- A total of about 7,000 TB cases per year with over 10% HIV+

Of the remaining 2.7 million *Mtb*+, 0.5% or 13,500 are also HIV+. About 70% (9,450) of these dually infected persons will develop TB over about a 10 year period – i.e., when their CD4 cell counts have been reduced to about 350 or less

- Close to 1,000 TB cases (HIV+) per year

This model does not include the increase in both HIV- and HIV+ TB cases that can be expected to develop from the 1,000 TB cases calculated above – about 40% smear +, i.e., infectious.
Global Distribution of New TB Case Rates - 2007

New TB cases – HIV negative
New TB cases – HIV positive

AFR

AMR

EMR

EUR

SEAR

WPR

Cases per 100,000 population

Global Distribution of New TB Cases - 2006

New TB cases – HIV negative
New TB cases – HIV positive

AFR

AMR

EMR

EUR

SEAR

WPR

Millions

[AFR]

[AMR]

[EMR]

[EUR]

[SEAR]

[WPR]

[85.4%]

[3%]

[1%]

[2%]

[5.6%]

[3%]
### Estimated TB Incidence in Selected African and Asian Countries - 2006

<table>
<thead>
<tr>
<th>Country/Region</th>
<th>Population (Million)</th>
<th>TB Incidence (Million)</th>
<th>TB Incidence per 100K Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Africa</td>
<td>49</td>
<td>0.454</td>
<td>114 (44%)</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>13.5</td>
<td>0.074</td>
<td>240 (43%)</td>
</tr>
<tr>
<td>Cambodia</td>
<td>14.6</td>
<td>0.071</td>
<td>500 (10%)</td>
</tr>
<tr>
<td>India</td>
<td>1.177</td>
<td>0.9</td>
<td>168 (1.2%)</td>
</tr>
<tr>
<td>China</td>
<td>1.332</td>
<td>0.3</td>
<td>99 (0.03%)</td>
</tr>
</tbody>
</table>

**Current impact of the HIV/AIDS and the Mtb/TB pandemics**
### Current Estimated Global Burdens of the Mtb/TB and the HIV/AIDS Pandemics

<table>
<thead>
<tr>
<th></th>
<th>Mtb/TB</th>
<th>HIV/AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Annual incidence</strong></td>
<td>Up to 100 million <em>Mtb</em> infections or &gt;250,000 per day - the majority in Africa and Asia. 9.2 million new TB cases</td>
<td>2.5 million HIV infections or about 7,000 per day, with close to 70% in sub-Saharan Africa (SSA).</td>
</tr>
<tr>
<td><strong>Prevalence</strong></td>
<td>Over 2 billion <em>Mtb</em> infections; 14.4 million TB cases; 0.5 million cases of multi-drug-resistant TB (MDR-TB).</td>
<td>Adult HIV prevalence about 30 million with close to 70% in SSA – extremely wide range of prevalence - from less than 0.1% to 25%.</td>
</tr>
<tr>
<td><strong>Annual deaths</strong></td>
<td>1.5 million TB deaths in HIV (-) people and 0.2 million in HIV (+) people</td>
<td>2.1 million AIDS deaths – includes 0.2 million HIV (+) TB deaths (ICD-10).</td>
</tr>
</tbody>
</table>

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**Population size with and without AIDS, South Africa, 2000 and 2025**

![Population size chart](attachment:image.png)

Source: UNAIDS 2004 Report on the global AIDS epidemic
A quarter-century after the recognition of AIDS, the SF Gay Men’s Chorus has suffered the deaths of 257 members - Those dressed in black, with their backs turned, represent (in 1993) those who had died. Today, all their backs would be turned because the obituary list is now 47 names longer than the chorus roster. As of mid-2006, only four men are left from the original 1978 Chorus of about 200 members. *SF Chronicle* file photo by Eric Muse

The conclusions and recommendations in this report are right on target and this is a superb report. However, AIDS is NOT the leading cause of death in the 15-44 year age group in Asia! It is (depending if traffic deaths are included or not), “only” about the 5th or 6th leading cause of death in this age group in Asia. WHO and UNAIDS have been alerted to this error, but as of September, no correction has yet been issued.
Have the Mtb/TB or HIV/AIDS pandemics peaked and if so when and why?

AND

The probable future of the HIV/AIDS and the Mtb/TB pandemics

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**Figure 1:** HIV incidence and prevalence in Kenya in people aged 15-49 years old

Source: Shelton et al Lancet, 367, April 8, 2006
The Most Likely HIV/AIDS Scenario in sub-Saharan Africa

This HIV scenario for SSA was developed in 2005 and is almost identical to UNAIDS' estimates released in late 2007!

This graph shows the peak annual HIV incidence and prevalence rates, as well as the number of AIDS deaths and the total number of the 15-49 year old population.

Source: Shelton et al. Lancet, 367, April 8, 2006
Three scenarios: baseline (solid lines), optimistic (dotted lines) and pessimistic (dashed lines).

Projections of global AIDS deaths (millions) - 2002 to 2030

UNAIDS 2007 estimate 2.1 million

A more likely scenario

Source: Mathers C. WHO Policy Working paper, October, 2005

Major Factors Responsible for Peaking of Sexual HIV Epidemics

1. Increase of more responsible sexual behaviors, i.e., sexual Abstinence and/or Being faithful
2. Increase of consistent Condom use for risky sex behaviors
3. Saturation of HIV infection in those with the highest risk pattern and frequency of sexual risk behaviors

All of the above, but perhaps saturation of infection may be the most important factor!
The sequence of annual estimates up to 2006 suggests (as in the data up to 2005) that all three major indicators of impact – TB incidence, prevalence and mortality per 100,000 population – are falling globally. Prevalence was already in decline by 1990, mortality peaked before the year 2000 and incidence began to fall in 2003. TB prevalence continued to fall globally between 1990 and 2006.

Source: WHO 2008 report on Global TB Control
E-mail comments received
March 21, 2007 from:

DA Henderson
Former Dean, John Hopkins
School of Public Health

[Your] book received and read with the greatest interest…
I am certain that in the short term there will be anger and rejection but, eventually, your contribution will be appreciated. I salute you for a remarkable piece of work…

I would hope that this will be made a requisite text for anyone interested in international health…