Man jabbed with AIDS needle chops off own arm

A CRAZED HEROIN addict with AIDS stuck his needle into the arm of a firefighter, who immedi-
ately hacked off his own limb to stop the infected fluid from flowing into the rest of his body.
Quick but grusome act of self-mutilation saved his own life and amputated the limb.

by JOE FRICK

into the firefighter’s arm above the wrist.
“I saw a look of horror in Vincent’s face as he pulled the needle out,” recalls partner Henri Cuesney.
Then he ran wildly to the truck while the filthy lunatic stood there laughing.

Attacked

To everyone’s horror, Vincent grabbed a hatchet from the truck, put his arm on the side of the vehi-
cle and hacked it off between the elbow and the wrist.
Blood spurted out of the stump before firefighters and shocked onlookers.

Passed out

“We covered our hands with gloves and water-
proof coats and placed Vincent in the truck,”
notes Dr. Ingres.
“We believe he cut off the deadly virus.”

Bloodied and bandaged, Vincent was taken to the hospital near Le Havre, France, where Vincent barely survived following severe loss of blood.

Vincent was discharged from the hospital and faces attempted-murder charges.

Despite the ghastly loss of his arm, Vincent is happy to be alive, but he warns:
“All of us are in great danger as long as these drug addicts are walking the streets.”

Source: Slide from MPAETC “Train the Trainer” curriculum, 1989
Now, why would you have a stamp like that? I mean, what if you lick it and get infected?...
This May Be the Most Dangerous Time Yet!

AIDS

1980 Confusion
1980-2008 Hysteria / Ignorance
2008 Complacency
Adults and children estimated to be living with HIV, 2007

North America
1.3 million
[480 000 – 1.9 million]
Caribbean
230 000
[210 000 – 270 000]
Latin America
1.6 million
[1.4 – 1.9 million]
Western & Central Europe
760 000
[600 000 – 1.1 million]
Eastern Europe & Central Asia
1.6 million
[1.2 – 2.1 million]
Middle East & North Africa
380 000
[270 000 – 500 000]
Sub-Saharan Africa
22.5 million
[20.9 – 24.3 million]
East Asia
800 000
[620 000 – 960 000]
South & South-East Asia
4.0 million
[3.3 – 5.1 million]
Oceania
75 000
[53 000 – 120 000]

Total: 33.2 (30.6 – 36.1) million
Size and Course of The Epidemic Overestimated?

UN reports that they believe that the epidemic has been slowing for nearly a decade.

New HIV Infections  2.5 Million
Total with HIV Worldwide  33 Million

Source: AMA Morning Rounds, 11/20/2007
Why Are the Numbers Down?

The estimates on AIDS rates were mistaken because “data are tough to get”, and measuring “infectious diseases has always been a challenge in the global setting of low-income developing countries”

“This challenge also applies to other diseases like TB, polio, and childhood diarrhea”

Dr. Paul De Lay, Director of evidence, monitoring and policy for the U.N. Joint Program on HIV/AIDS.

Source: AMA Morning Rounds, 11/20/2007
Estimated Prevalence Rates for Adults and Adolescents Living with AIDS (per 100,000 population), 2005—United States and Dependent Areas

Note: Data have been adjusted for reporting delays.
* includes persons whose area of residence is unknown or missing.

Revised June 2007
Estimated Prevalence Rates for Adults and Adolescents Living with HIV Infection (not AIDS), 2006—33 States and 5 U.S. Dependent Areas

Note. Data from 33 states and 5 U.S. dependent areas with confidential name-based HIV infection reporting since at least 2003. Data have been adjusted for reporting delays.
Proportion of HIV/AIDS Cases among Adults and Adolescents, by Sex and Transmission Category 2006—33 States

Males
- Male-to-male sexual contact: 67%
- Injection drug use (IDU): 16%
- Male-to-male sexual contact and IDU: 12%
- <1%

Females
- High-risk heterosexual contact*: 80%
- Other/not identified †: 19%
- 1%

Note. Data include persons with a diagnosis of HIV infection regardless of their AIDS status at diagnosis. Data from 33 states with confidential name-based HIV infection reporting since at least 2003. Data have been adjusted for reporting delays and cases without risk factor information were proportionally redistributed. *Heterosexual contact with a person known to have, or to be at high risk for, HIV infection. †Includes hemophilia, blood transfusion, perinatal exposure, and risk factor not reported or not identified.
# HIV/AIDS Cases in Kansas 2007

<table>
<thead>
<tr>
<th>HIV/AIDS Cases</th>
<th>Cumulative AIDS Cases (through 12/07)</th>
<th>Cumulative HIV Cases (not AIDS) (through 12/07)</th>
<th>Grand Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Alive#</td>
<td>Alive %</td>
</tr>
<tr>
<td>HIV (no AIDS)</td>
<td>2821</td>
<td>1336</td>
<td>47.4</td>
</tr>
<tr>
<td>Prevalence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>38 Cases per 100,000</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ADULTS</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
<th>M:F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ratio</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cumulative AIDS Cases</td>
<td>2473</td>
<td>348</td>
<td>2821</td>
<td>7.1:1</td>
</tr>
<tr>
<td>Cumulative HIV Cases</td>
<td>868</td>
<td>245</td>
<td>1113</td>
<td>3.5:1</td>
</tr>
</tbody>
</table>

Data Source: Kansas HIV/AIDS Surveillance System 2007
AIDS (N=126)
- 56% White
- 29% Black
- 13% Hispanic
- 2% Other

2006 Kansas Population Estimates*
(N=2,764,075)
- 80% White
- 9% Black
- 5% Hispanic
- 6% Other

HIV (N=97)
- 52% White
- 29% Black
- 16% Hispanic
- 3% Other

*Other includes Asian/Pacific Islanders, Native Hawaiian/Pacific Islander, American Indian/Native Alaskan, and mixed races.

*2006 Kansas Population Estimates, KDHE, Office of Health Assessment, Center for Health and Environmental Statistics

Data Source: Kansas HIV/AIDS Surveillance System 2007
Living HIV/AIDS Cases Top Ten Counties in Kansas, by Date of Report, 2007

Data Source: Kansas HIV/AIDS Surveillance System 2007
Awareness of Serostatus Among People with HIV and Estimates of Transmission

- ~25% Unaware of Infection
- ~75% Aware of Infection

Accounting for:
- ~54% of New Infections
- ~46% of New Infections

- People Living with HIV/AIDS: 1,039,000-1,185,000
- New Sexual Infections Each Year: ~32,000

Marks, et al
AIDS 2006;20:1447-50
Late HIV Testing is Common
Supplement to HIV/AIDS Surveillance, 2000-2003

- Among 4,127 persons with AIDS*, 45% were first diagnosed HIV-positive within 12 months of AIDS diagnosis (“late testers”)

- Late testers, compared to those tested early (>5 yrs before AIDS diagnosis) were more likely to be:
  - Younger (18-29 yrs)
  - Heterosexual
  - Less educated
  - African American or Hispanic

*16 states

MMWR  June 27, 2003
Routine Testing

Routine one-time testing of everyone would cut new infections each year by just over 20%.

Every HIV-infected patient identified would gain an average of $1 \frac{1}{2}$ years of life.

Source: study by researchers at Duke and Stanford Universities and the Veterans Affairs Palo Alto Health Care System.
More is Better

- Earlier access to available medications – resulting in increased length of life
- Those who know they are positive tend to take more precautions to protect others
- On a population wide basis, such screening could reduce spread – because medications suppress viral load and reduce the chance of transmission
Revised Recommendations for HIV Screening in Health-Care Settings in the U.S.
New Guidelines for HIV Screening

- HIV screening is recommended in all health care settings, after notifying the patient that testing will be done.
- Separate written consent for HIV testing is not required.
- Prevention counseling is not recommended as part of routine HIV screening programs in health care settings.
- HIV screening should be included in the routine panel of prenatal screening tests for all pregnant women.
The CDC recommends that HIV screening be a routine part of health care for all:

- Individuals in the U.S. between the ages of 13 and 64
- Patients receiving care for tuberculosis (TB)
- Patients in care for other sexually transmitted diseases (STDs)
- Women who are considering conception and pregnancy
- Women who are pregnant
- Women in delivery who have undocumented HIV status at the onset of labor
- Infants born to mothers with undocumented HIV status.
Rapid HIV Testing: The “Waive” of the Future
Available HIV Rapid Tests in the United States

Six rapid HIV tests approved by the U.S. Food and Drug Administration (FDA) are commercially available for use in the United States

(listed in chronological order of their FDA approval dates):

• OraQuick Rapid HIV – 1 / 2 Antibody Test
• Reveal G2 Rapid HIV - 1 Antibody Test
• Uni-Gold Recombigen HIV Test - 1
• Multispot HIV-1 / HIV-2 Rapid Test
• Clearview HIV 1 / 2 Stat Pak
• Clearview Complete HIV 1 / 2
Rapid HIV Tests

Uni-Gold™ Recombigen® HIV Assay

OraQuick Advance

Clearview Complete HIV 1/2
When Is A Rapid Test Indicated?

- Obstetric admissions
- Healthcare worker occupational exposures
- Urgent care clinics and Emergency departments
- Public health settings
- Developing countries
- The primary Care office
Prenatal HIV Screening

Based on information presented in the MMWR – Both “opt-out” and prenatal maternal screening and mandatory newborn screening achieve higher maternal screening rates than “opt-in” prenatal screening

CDC recommends that clinicians routinely screen all pregnant women for HIV infection using an “opt-out” approach
Estimated Number of Perinatally Acquired AIDS Cases by Year of Diagnosis, 1985–2006—United States and Dependent Areas

Year of diagnosis

No. of cases


Note. Data have been adjusted for reporting delays and cases without risk factor information were proportionally redistributed.
Estimated Number of AIDS Cases, Deaths, and Persons Living with AIDS, 1985-2003, United States

- **AIDS** (yellow triangles)
- **Deaths** (blue diamonds)
- **Prevalence** (orange circles)

**Note:** Data adjusted for reporting delays.
“My daughter is not ready yet. Would you like to join me in watching a Short video on AIDS?”
WASHINGTON (Reuters) - Abstinence-only education programs meant to teach children to avoid sex until marriage failed to control their sexual behavior, according to a U.S. government report.
HIV Prevention Efforts

Abstain, Be faithful, Condoms, Counseling & testing

ABC

Circumcision

Diaphragsms

Exposure prophylaxis (MTCT, PEP, PrEP)

Female-controlled microbicides

Genital tract infection control

HSV-2 suppressive treatment

Immunization

I

H

G

F

E
Circumcision appears to reduce a man’s risk of contracting AIDS from heterosexual sex by half, United States government health officials said yesterday, and the directors of the two largest funds for fighting the disease said they would consider paying for circumcisions in high-risk countries.
WHO and UNAIDS announce recommendations from expert consultation on male circumcision for HIV prevention

28 MARCH 2007 | PARIS/GENEVA –

experts attending the consultation recommended that male circumcision now be recognized as an additional important intervention to reduce the risk of heterosexually acquired HIV infection in men.

Source: World Health Organization
Circumcision Effects

The impact of male circumcision on female partners was presumed to be beneficial…

- New findings in a randomized trial of discordant couples in the Rakai district of Uganda:
  - Did not provide protection for female partners
  - May increase the risk of transmission if the couple resumed sex before the circumcision wound was healed

During 2 years of follow-up, the annual incidence rate of HIV in wives of circumcised HIV+ men was 14.4 per 100 person-years vs 9.1 per 100 person years among women whose husbands remained uncircumcised!
Diaphragms Have Disappointing Results

7/13/2007

Large South African Study showed that using a diaphragm and lubricant alongside condoms did not reduce the risk of HIV infection further when compared to condom use alone.

One important note: Women in the diaphragm arm did not have an increased risk of HIV infection despite a significantly lower rate of condom use.
Disappointing Data from Anti-HIV Microbicide Trials

The 2007 IAS Conference provided new details about the two cellulose-sulfate trials that were halted earlier this year.
New Microbicides Under Development

- An estimated 60-80 different microbicide products are in various stages of development
  - 11 are currently in clinical trials
    - 2 are in on-going phase 3 trials
      - Carraguard – being studied in south Africa
        - A non-contraceptive gel
      - PRO-2000 – being studied in 4 southern African countries
  - Others are in pre-clinical testing

Source: Infections in Medicine, February 2008, pg.63-72
Vaginal Microbicide Gel Shows Promise

An experimental vaginal microbicide gel containing the AIDS drug tenofovir has proved safe and acceptable to women in phase two trials.

Microbicide Vaginal Gel with Tenofovir

- Study of 200 sexually active HIV-negative women in the US and India
- Designed to evaluate the gel’s safety, not its efficacy
  - The gel is safe to use
  - Well tolerated by HIV-negative women
- It is uncertain how long tenofovir can stay active after it is applied as a vaginal microbicide
- 12% indicated that it made sex more pleasurable
- 80% followed the experimental regimen and stated that they had no problem using it

Trichomonas Infection is Associated with Increased HIV Risk

- *Trichomonas vaginalis* is the most common nonviral sexually transmitted disease worldwide.
- The odds ratio of HIV acquisition among women infected with *T. vaginalis* was 2.74 in this nested case-control study of a general-population cohort, after controlling for hormonal contraception, other STIs and behavioral and demographic factors.

Effect of Herpes Simplex Suppression on Incidence of HIV Among Women in Tanzania

These data show no evidence that acyclovir (400mg twice daily) as HSV suppressive therapy decreases the incidence of infection with HIV.

HIV Prevention: HSV2 Suppression

- 3251 HIV-negative participants infected with HSV2
  - MSM from 3 US sites and 3 Peruvian sites
  - Women from Zimbabwe, Zambia and South Africa
- They were given placebo or oral acyclovir 400mg bid
- Adherence study was 94.3%
- Genital ulcers were reduced by 35% in the acyclovir arm

Source: The AIDS Reader, April 2008, pg 164
HIV Prevention: HSV2 Suppression

- Despite the decrease in reduction of ulcers there was no impact on HIV incidence:
  - 3.9 per 100 person-years in the acyclovir arm (75 events)
  - 3.3 per 100 person years in the placebo arm (64 events)

Source: The AIDS Reader, April 2008, pg 164
### Challenges in the Development of an HIV Vaccine

<table>
<thead>
<tr>
<th>Challenge</th>
<th>Impact on Vaccine Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral genetic diversity</td>
<td>Difficult to develop broad protection in light of high mutation rate and extensive viral diversity</td>
</tr>
<tr>
<td></td>
<td>Antibody and cellular response to specific isolates may not provide protection against all isolates</td>
</tr>
<tr>
<td>Evasion of immune system after infection</td>
<td>Down regulation of major histocompatibility complex 1 molecules on infected cells impedes immune system from recognizing infected cells</td>
</tr>
<tr>
<td></td>
<td>Early integration of viral genetic material into host cell DNA leads to long-lasting latent infection</td>
</tr>
<tr>
<td></td>
<td>Mutation of virus after infection allows for development of variants that can escape the control of the cellular immune system</td>
</tr>
</tbody>
</table>

Source: Infections in Medicine, February 2008, pg.63-72
# Challenges in the Development of an HIV Vaccine

<table>
<thead>
<tr>
<th>Challenge</th>
<th>Impact on Vaccine Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costly and complicated development</td>
<td>Costs prohibitive for widespread use in developing countries</td>
</tr>
<tr>
<td></td>
<td>Multiple injections with several different agents might be challenging to implement</td>
</tr>
<tr>
<td></td>
<td>Storage requirements often difficult to meet in resource-limited settings</td>
</tr>
</tbody>
</table>

Source: Infections in Medicine, February 2008, pg.63-72
Sperm Washing Found Effective

August 31, 2007

European study reported that sperm washing appeared to be a safe and effective method

- Study – 1,036 couples, reported that none of the HIV-negative women were infected with the virus after undergoing assisted reproduction with sperm from their partners that was carefully treated.
  - including interuterine insemination and in vitro fertilization - 533 pregnancies
  - 463 live births - all children HIV negative

Source: AIDS, September 2007
"I DON'T WANT TO GET YOUR HOPES UP, BUT I THINK WE HAVE EVERYTHING WE NEED TO MAKE S'MORES."
Technology is vital BUT…

– Diaphragm and female condom could reduce HIV incidence but experience with male condom use indicate that compliance will be a problem

– Circumcision could have a marked impact on the epidemic, especially if it is protective in both sexes, but service delivery is a challenge
Technology is vital BUT…

– A vaccine or microbicide with efficacy ≥50% could reduce incidence, but none exist
– PrEP and HSV2 interventions could reduce incidence but efficacy and feasibility unproven
– HAART will not significantly reduce HIV incidence unless widespread coverage and sustainability problems will develop if numbers of patients keep increasing

Behavioral disinhibition could offset the benefits
"That's the way I treat a virus!"
## 2008 Guideline Recommendations on when to Initiate HAART Therapy

<table>
<thead>
<tr>
<th>Clinical Condition and/or CD4+ Cell Count</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of AIDS-defining illness</td>
<td></td>
</tr>
<tr>
<td>CD4+ cell count &lt; 350 cells/mm³</td>
<td></td>
</tr>
<tr>
<td>Patients with HIV-associated nephropathy</td>
<td><strong>Antiretroviral therapy should be initiated</strong></td>
</tr>
<tr>
<td>Patients coinfected with hepatitis B virus*</td>
<td></td>
</tr>
<tr>
<td>Pregnant women**</td>
<td></td>
</tr>
</tbody>
</table>

* Where hepatitis B virus treatment (with fully suppressive antiviral drugs active against HIV and hepatitis B virus) is indicated.

** Consideration can be given to discontinuing antiretroviral therapy postpartum in women who do not require antiretroviral therapy for their own health


Recommendations for the Use of Antiretroviral Therapy (Hammer et al. JAMA. 2006)Available at: This article is also available at http://jama.ama-assn.org/cgi/content/full/296/7/827)
New Approaches to HIV Suppression

- First time since 1996 that more than one new category of drug introduced within the same year
- First drugs to target cellular targets
  - CCR5
  - CXCR4 inhibitors
- New antiretrovirals against novel targets
  - Integrase inhibitors
  - Maturation inhibitors
- New antiretrovirals in current categories
  - PIs active against resistant mutants
  - “Second generation” NRTIs and NNRTIs
HIV Replication Cycle and Sites of Drug Activity

1. Attachment
2. Uncoating
3. Reverse Transcription
4. Integration
5. Transcription
6. Translation
7. Assembly and Release

- **Attachment Inhibitors**
- **NRTIs**
- **NNRTIs**
- **Integrate Inhibitors**
- **Protease Inhibitors**

Licensure of Antiretroviral Agents by Year

- 1987: zidovudine (Retrovir)
- 1991: didanosine (Videx)
- 1992: zalcitabine (Hivid)
- 1994: stavudine (Zerit)
- 1995: lamivudine (Epivir) saquinavir (Invirase)
- 1996: ritonavir (Norvir) indinavir (Crixivan) nevirapine (Viramune)
- 1997: nelfinavir (Viracept) delavirdine (Rescriptor)
- 1998: efavirenz (Sustiva) abacavir (Ziagen)
- 1999: amprenavir (Agenerase)
- 2000: lopinavir/ritonavir (Kaletra)
- 2001: tenofovir (Viread)
- 2003: enfuvirtide (Fuzeon)
- 6/03: atazanavir (Reyataz)
- 7/03: emtricitabine (Emtriva)
- *8/04: lamivudine/abacavir sulfate (Epzicom) emtricitabine/tenofovir disoproxil fumarate (Truvada)
- 6/05: tipranavir (Aptivus)
- 6/06: darunavir (Prezista)
- *7/06: efavirenz/emtricitabine, tenofovir DF (Atripla)
- 8/07: maraviroc (Selzentry)
- 10/07: raltegravir (Isentress)
- 1/08: etravirine (Intelence)

*Fixed dose combinations of existing drugs
Earlier Start of ART: HOPS Cohort

• Prospective, dynamic cohort followed since 1993, N >8000

• In general, patients who started HAART at higher CD4+ cell counts experienced (≥ 95% of the time):
  – Lower mortality and incidence of OIs
  – Better CD4+ cell count responses to HAART
  – Lower odds ratio for renal insufficiency, neuropathy, and lipoatrophy

• Immunologic and safety benefits extended even to those who started therapy with CD4+ cell count 350-500 cells/mm³ and >500 cells/mm³

Lichtenstein KA et al. 13th CROI; 2006; Denver. Poster 769.
D:A:D: HIV and fatal malignancies

- Types and risk factors for AIDS-defining malignancies (ADM) and non-ADM studied in D:A:D\(^1\)
  - 23,447 HIV+ patients; 104,691 person-years of F/U
- Fatal non-ADM have become more common than ADM
- Incidence of both non-ADM and ADM increases with lower CD4+ cell count but is not affected by HIV RNA
- Current smokers had a 2.92-fold higher risk of fatal nADM than those who never smoked (risk for ex-smokers was 2.02-fold higher)
- Other cohorts have reported similar increases in nADM\(^2\)
  - HIV Atlanta VA Cohort study: 3051 patients followed since 1982
  - Annual incidence of prostate cancer has risen from 1/1000 before 2003 to 4.6/1000 since 2003 (p<0.00006)

Still A Ways To Go…
Clinical trials of investigational ARVs: 2008

<table>
<thead>
<tr>
<th>Drug</th>
<th>Target</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apricitabine (AVX754)</td>
<td>NRTI</td>
<td>III</td>
</tr>
<tr>
<td>KP-1461</td>
<td>NRTI</td>
<td>II</td>
</tr>
<tr>
<td>Etravirine</td>
<td>NNRTI</td>
<td>Approved</td>
</tr>
<tr>
<td>Rilpivirine</td>
<td>NNRTI</td>
<td>II</td>
</tr>
<tr>
<td>UK-453,061</td>
<td>NNRTI</td>
<td>I</td>
</tr>
<tr>
<td>Maraviroc</td>
<td>CCR5</td>
<td>Approved</td>
</tr>
<tr>
<td>Vicriviroc (SCH-D)</td>
<td>CCR5</td>
<td>III</td>
</tr>
<tr>
<td>PRO 140</td>
<td>CCR5</td>
<td>I</td>
</tr>
<tr>
<td>Raltegravir</td>
<td>Integrase</td>
<td>Approved</td>
</tr>
<tr>
<td>Elvitegravir</td>
<td>Integrase</td>
<td>II</td>
</tr>
</tbody>
</table>
## Cost-Effectiveness Ratios for Common Medical Interventions

<table>
<thead>
<tr>
<th>Treatment of</th>
<th>ICER*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enalapril for congestive heart failure</td>
<td>$10,904</td>
</tr>
<tr>
<td>Lovastatin to prevent coronary disease</td>
<td>$23,607</td>
</tr>
<tr>
<td>HIV antiretroviral therapy (CD4 &gt; 500)</td>
<td>$21,869</td>
</tr>
<tr>
<td>HIV antiretroviral therapy (CD4 200 - 500)</td>
<td>$26,848</td>
</tr>
<tr>
<td>HIV antiretroviral therapy (CD4 50 - 200)</td>
<td>$35,483</td>
</tr>
<tr>
<td>HIV antiretroviral therapy (CD4 &lt; 50)</td>
<td>$57,565</td>
</tr>
<tr>
<td>Screening mammography, women 40-79 years</td>
<td>$33,724</td>
</tr>
<tr>
<td>Renal hemodialysis</td>
<td>$56,206</td>
</tr>
<tr>
<td>Prostate specific antigen screening, men 50 years</td>
<td>$127,026</td>
</tr>
<tr>
<td>Coronary artery bypass surgery, men 50 years</td>
<td>$127,026</td>
</tr>
</tbody>
</table>

*ICER = incremental cost-effectiveness ratio

At least 3 million years of life have been saved in the United States as a direct result of care of patients with AIDS, highlighting the significant advances made in HIV disease treatment.
Reported TB Cases*
United States, 1982–2006

No. of Cases

Year

*Updated as of April 6, 2007.
TB Case Rates,* United States, 2006

*Cases per 100,000.

D.C.

- ≤ 3.5 (year 2000 target)
- 3.6–4.6
- > 4.6 (national average)
Tuberculosis: the Basics

Caused by infection with a bacteria

- *Mycobacterium tuberculosis*
- Spread like the common cold
- Respiratory droplets in the air
- Coughing, sneezing, talking, singing....
Clinical features

Latent TB infection progresses to disease when body’s immune system weakened
  ▪ Malnutrition
  ▪ HIV
  ▪ Other factors…

TB disease usually affects the lungs (pulmonary TB) but can affect any other part of the body (extrapulmonary TB).

Symptoms
  ▪ persistent cough for > 2-3 weeks
  ▪ weight loss
  ▪ fever
  ▪ night sweats
  ▪ coughing up blood
What Is Multi-drug Resistant TB (MDR-TB)?

• TB that is resistant to at least two of the best anti-TB drugs, isoniazid and rifampicin.
• These drugs are considered first-line drugs and are used to treat all persons with TB
Why Is there a Concern About Resistant TB?

Drug resistant TB results from inadequate TB control
Treatment of Drug Resistant TB

Treating MDR TB takes 3-4 times longer and Costs 100 times more
What *Is* Extensively Drug-Resistant TB (XDR-TB)?

- Relatively rare
- Resistant to almost all drugs used to treat TB including:
  - First-line (isoniazid and rifampicin).
  - Second-line drugs (fluoroquinolones).
  - One out of three injectable drugs (i.e., amikacin, kanamycin, or capreomycin).
Extensively drug resistant TB - XDR TB

- Difficult to diagnose
  - Time for culture
  - Special laboratories
- About 10% of MDR TB is XDR
- High fatality rate in people living with HIV
- Present in every region of the world
TB in Kansas: 2006

82 new TB cases (2.98 per 100,000) statewide in 2006:

- Up from 60 in 2005 but within the range we have seen in the past five years varying from 60 to 89 cases.
- Sedgwick County reported the most new cases with 25.
- Wyandotte County reported 10 cases.
- Johnson and Shawnee Counties each reported 8 new cases.
- No other county reported more than four cases in the state.
TB in Kansas: 2006

Of the 82 new TB cases reported statewide in 2006:

- 55 were among males and 27 were among females
- 13 cases were among black, non-Hispanics
- 18 were among Asians or Pacific Islanders
- 25 were among whites, non-Hispanic (plus one multi-racial)
- 24 cases were among Hispanics of all races.
- Only one case was reported in children under age 20, as compared with 3 cases in 2005
- 10 cases were reported in the age group 15-24
- 30 in the age group 25-44
- 32 in the age group 45-64
- 9 among people age 65 and older
- During 2006, there were five reported cases of HIV co-infection
"We always have at least one MDR-TB case that we are treating. This has been the case since around 2001…"

We always have varying degrees of drug resistance in the state.
We average around 10% INH resistance across the board.
We are currently nearing the end of treatment for a MDR case in Kansas City. She is a native of Peru, but came to us from Russia.

-Phil Griffin, Director, TB Section,
The Kansas Department of Health and Environment. 10/30/2007
TB Screening

- Still important to do TB skin test on a 6-12 month routine basis
- Frequency tied to TB risk factors
- Symptom review, not x-ray for prior PPD positives
Current Guidelines for QFT-G

From CDC:
- Can be used in all circumstances in which the tuberculin skin test is used.
- Negative results should be interpreted with caution, particularly in patients with impaired immune function and those at greater risk for severe TB disease.

Cost:
- Average cost of one test, including personnel costs, has been estimated between $35 and $120.
- Compared to $13 for each skin test.
- However, since it is more specific than skin tests, this may reduce the cost of follow-up X-rays and laboratory tests.
Tuberculosis Screening Flowchart

At-risk person

Tuberculin test + symptom review

Negative

Treatment not indicated

Positive

Chest x-ray

Normal

Possible Candidate for Rx of latent TB

Abnormal

Evaluate for active TB
Screening for Tuberculosis
Chest Radiograph

- To screen for active TB, obtain chest radiographs without waiting for TB skin test results
- But, advanced AIDS patients can have active TB and normal chest radiographs
The Links Between HIV & TB

• Often described as the “co-epidemic” or “dual epidemic”
• HIV affects the immune system and increases the likelihood of people acquiring new TB infection.
• It also promotes both the progression of latent TB infection to active disease and relapse of the disease in previously treated patients.
• TB is one of the leading causes of death in HIV-infected people.
The Impact of TB/HIV Co-infection

Each disease speeds up the progress of the other.
TB considerably shortens the survival of people with HIV/AIDS.
TB kills up to half of all AIDS patients worldwide.
People who are HIV-positive and infected with TB are up to 50 times more likely to develop active TB in a given year than people who are HIV-negative.
The Impact of TB/HIV Co-infection

TB is harder to diagnose in HIV-positive people.

TB progresses faster in HIV-infected people.

TB in HIV-positive people is almost certain to be fatal if undiagnosed or left untreated.

TB occurs earlier in the course of HIV infection than many other opportunistic infections.
An Extensive Problem

An estimated one-third of the 40 million people living with HIV/AIDS worldwide are co-infected with TB. Without proper treatment, approximately 90% of those living with HIV die within months of contracting TB. The majority of people who are co-infected with both diseases live in sub-Saharan Africa.
A Recent CDC Analysis…

• Reviewing data from 1993 through 2005 on 49 states and the District of Columbia…

• Reporting of HIV status among TB patients has increased since 1993, it has remained stable in recent years

• TB patients with highest HIV prevalence
  – Drug users
  – Homeless persons
  – Black
  – Correctional Inmates
  – Alcohol Abusers

MMWR, October 26, 2007
A Recent CDC Analysis...

• In 2005:
  • 9% of TB patients were also infected with HIV
  • Nearly 1/3 of TB patients (31%) had unknown HIV infection status
    - Of this 31% - ½ were not offered testing
    - This underscores the need for expansion of HIV testing and missed opportunities

MMWR, October 26, 2007
People with Tuberculosis and HIV Co-infection

WHO recommends that people with both TB and HIV complete their TB therapy prior to beginning ARV treatment unless there is a high risk of HIV disease progression and death during the period of TB treatment, defined as:

- A CD4 count <200/mm³
- The presence of disseminated TB
Active TB and HIV

1. Ensure completion of therapy (essential)

2. Treatment of TB/HIV is the same as for HIV-negative persons except:
   - Once-weekly rifapentine regimens cannot be used
   - Twice-weekly rifampin or rifabutin should not be used if the CD4 cell count is < 100 cells/ul

3. Be alert for drug interactions and paradoxical reactions
Summary Drug resistant TB

Drug-resistant TB poses a grave public health threat especially in high HIV prevalence settings.

XDR-TB strains have been found in all regions of the world.

XDR-TB occurs as a result of inadequate TB control programmes.

XDR-TB, if identified early, can be treated and cured but experience limited to low HIV prevalence settings.

Infection control measures must be strengthened.

XDR-TB underlines the need for investment in basic TB control plus development of new TB diagnostics, treatments and vaccines.
TB is Treatable and Preventable

TB can be prevented in people living with HIV by

- Isoniazid preventive therapy
- Intensified case finding
- Infection control
  - HIV care
  - Prisons
  - Workplace
What *Can* Be Done…

Strengthen TB services for people living with HIV/AIDS
Assemble outbreak response teams
Improve access to TB drugs
Develop international TB testing standards
Build capacity of health care providers to diagnose and treat TB
Support TB communication and education efforts
HIV and Hepatitis
<table>
<thead>
<tr>
<th>Hepatitis A</th>
<th>Hepatitis B</th>
<th>Hepatitis C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>What is it?</strong></td>
<td><strong>What is it?</strong></td>
<td><strong>What is it?</strong></td>
</tr>
<tr>
<td>A virus that causes inflammation of the liver. Does not lead to chronic (long term) liver disease.</td>
<td>A virus that causes inflammation of the liver. Can possibly lead to cirrhosis and liver cancer in chronic cases. Chronic (long term) for around 5% of adults who contract HBV. Chronic (long term) for about 90-95% of children infected with HBV at the time of birth.</td>
<td>A virus that causes inflammation of the liver. Chronic (long term) for around 65% of people who contract HCV. Can possibly lead to cirrhosis in approximately 5-10% of people who develop chronic hepatitis C infection and liver cancer in approximately 2-5% of people who develop cirrhosis.</td>
</tr>
<tr>
<td><strong>Incubation or Window Period?</strong></td>
<td><strong>Incubation or Window Period?</strong></td>
<td><strong>Incubation or Window Period?</strong></td>
</tr>
<tr>
<td>2-7 weeks. Average 4 weeks. <em>(incubation: from time of exposure until onset of disease/ window period: from time of exposure until antibodies can be detected)</em></td>
<td>6-26 weeks. Average 8-12 weeks. <em>(incubation: from time of exposure until onset of disease/ window period: from time of exposure until antibodies can be detected)</em></td>
<td>2-26 weeks. Average 6-9 weeks. <em>(incubation: from time of exposure until onset of disease/ window period: from time of exposure until antibodies can be detected)</em></td>
</tr>
<tr>
<td><strong>Transmitted By?</strong></td>
<td><strong>Transmitted By?</strong></td>
<td><strong>Transmitted By?</strong></td>
</tr>
<tr>
<td>Faecal – Oral contact. Contaminated food &amp; water or contaminated hand to mouth contact.</td>
<td>Blood to blood contact. Sexual contact. Infected mother to newborn baby.</td>
<td>Blood to Blood contact. Chronically infected mother to newborn baby – approximately 1-5% risk of transmission – low risk.</td>
</tr>
<tr>
<td><strong>Behaviours which place people at risk?</strong></td>
<td><strong>Behaviours which place people at risk?</strong></td>
<td><strong>Behaviours which place people at risk?</strong></td>
</tr>
<tr>
<td>Infected person’s unwashed hands coming into contact with food. Intimate or sexual contact with infected person (eg’oral/anal sex with infected person). Traveller’s to developing countries.</td>
<td>Sexual activity with infected person where there is contact with body fluids. Use of contaminated equipment when injecting drugs. Skin penetration (eg’ tattooing/body piercing) with contaminated equipment.</td>
<td>Use of any contaminated injecting equipment when injecting drugs. Receiving blood products (prior to February 1990 in Australia). Skin penetration (eg’ tattooing/body piercing) with contaminated equipment. Sexual transmission is unlikely unless there is blood to blood contact. People born in countries of high HCV background prevalence (probable transmission occurs via contaminated medical or cultural practices in country of origin).</td>
</tr>
</tbody>
</table>
# Prevalence - HBV, HCV, HIV

<table>
<thead>
<tr>
<th></th>
<th>Hepatitis B</th>
<th>Hepatitis C</th>
<th>HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Worldwide</strong></td>
<td>350 million</td>
<td>170 million</td>
<td>40 million</td>
</tr>
<tr>
<td><strong>In U.S.</strong></td>
<td>1.25 million</td>
<td>4.1 million</td>
<td>1 million</td>
</tr>
<tr>
<td>Coinfected-HIV</td>
<td>?&lt;5%,&lt;65,000</td>
<td>5-10%,</td>
<td>15-30%,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>150-300,000</td>
<td>150-300,000</td>
</tr>
<tr>
<td>Coinfected-HCV</td>
<td></td>
<td></td>
<td>15-30%,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>150-300,000</td>
</tr>
<tr>
<td>Coinfected-HBV</td>
<td></td>
<td></td>
<td>?5-10%,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>50-100,000</td>
</tr>
</tbody>
</table>
Epidemiology of HBV: United States

• 1.25 million in US have chronic HBV infection; highest incidence is in Alaska (6.4%)
• Local factors influence incidence and prevalence
  1. Ethnicity
  2. Immigration patterns
  3. IVDA
  4. High-risk sexual activity
• Increased incidence of infection in first generation children of families from high risk area
Impact of Vaccination Schedules in the US

- 1991 CDC published guidelines recommending universal vaccination of infants and children

- In period from 1990-2002, incidence of acute HBV decreased
  - 67% in all age groups
  - 89% in children < 20 years of age

MMWR 2004; 52; 1252
Thinking About Hepatitis B Treatment

- Chronic hepatitis B management is more like that of HIV than like that of hepatitis C:
  - Treatment aims at viral suppression more than eradication
  - Declines in HBV load and normalization of LFT’s are seen as favorable markers

- The NIH still mandates that HBV drugs are shown to be efficacious individually, so we have a series of single drug trials and know the effects of drugs individually, but not in combination
Hepatitis C Virus (HCV)

- Discovered in 1989 as a small RNA blood-borne virus with a large reservoir of chronic carriers worldwide
- Major cause of posttransfusion hepatitis prior to 1992
- Major cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma worldwide
- Prevalence is 1.8% of the US population
- 1990-2015: estimated 4-fold increase in the number of patients diagnosed with HCV in the United States

NIH Consensus Development Conference Panel Statement Management of Hepatitis C, 2002
Hepatitis C Basics

- “Chronic hepatitis C” is defined by a positive HCV RNA in a blood test
- 15-25% of people clear hepatitis C spontaneously (don’t have it): negative HCV RNA
- Longer time with HCV, older, heavy alcohol: more liver disease
- Five key genotypes in the U.S., which have variable genetic sequences (1a, 1b, 2a, 2b, 3a)
Approach to Treatment of Chronic Hepatitis C

- The decision to treat should be individualized, taking the following factors into consideration:
  - Patient’s age
  - Histologic severity of the disease
  - Comorbid conditions
  - Efficacy of currently available treatments
Any patient with chronic HCV infection can be treated.

Treatment is for 6-12 months and requires weekly subcutaneous injections and 4-6 pills by mouth every day.

Treatment has a lot of side effects.

The more liver disease a patient has, and if they have genotype 2 or 3 infection, affect how strongly treatment is recommended.

NIH Consensus Development Conference: Management of Hepatitis C 2002 Hepatology 36:S1-252
Interferon Adverse Effects

- Flu-like symptoms
  - fever, chills
  - headaches
  - myalgias, arthralgias
- Fatigue
- Anorexia
- Nausea/vomiting
- Diarrhea
- Thrombocytopenia
- Neutropenia
- Alopecia
- Injection site reactions
- Depression
- Mood swing/irritability
- Insomnia
- Impaired concentration
- Thyroid alterations
- Worsening diabetes
- Autoimmune disorders
The HIV-HCV Problem

In parts of the World (Spain),
>50% with HIV have HCV

HIV-infected individuals have shared risk factors for hepatitis A, B and C and should be vaccinated against HAV and HBV
HCV Transmission in the U.S.

Injecting drug use 60%
Sexual 15%
Transfusion 10% (before screening)
Unknown 10%
Occupational 4%
Other 1%*

* Nosocomial; iatrogenic; perinatal

Source: Centers for Disease Control & Prevention
The HIV-HCV Problem

- Liver disease is a frequent cause of morbidity and mortality
- Underlying liver disease clearly complicates management because:
  - Patients likely at increased risk of ART hepatotoxicities
  - Distinction between ART-related ALT abnormalities and hepatitis-associated fluctuations in ALT is problematic
  - Interactions between ribavirin and ART (ddI, d4T)
HCV-Related Deaths, U.S.

- Approximately 10-12,000 people die each year of HCV-related liver disease.
  - This number is expected to triple by 2020.
- HCV-related liver disease is the leading cause of death among persons with HIV disease.
Why Are More Patients With HIV / HCV Not Treated?
What Are the Contraindications to Interferon Therapy?

- Uncontrolled depression
- Ongoing alcohol use
- Underlying autoimmune disease
- Severe comorbid conditions (that would make it difficult to tolerate anemia)
Summary

- HIV and HCV have similarities but important differences
- HIV/HCV coinfection is common due to shared risk factors for transmission
- HCV infection can lead to cirrhosis, hepatic decompensation, and hepatocellular carcinoma
- Liver biopsy is to HCV what CD4 count is to HIV
- The serious consequences of HCV are becoming more evident, and disease burden is expected to increase
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under the heading KAAP