

**HIV/AIDS: The Total Body Effect
("Think HIV")**

**114th Annual Convention
New Orleans, LA
Nov. 1, 2009
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If not already, someday you will likely diagnose, misdiagnose, care for, have a relative or good friend who is HIV+

If not already, you may also become exposed to, or infected w/ HIV

You will most likely see....

- **Individuals - some w/ very high risk behavior - that are unaware that they are HIV+
You may be completely unaware of their high-risk behavior**
 - **Individuals that are in denial about their HIV status or at-risk behavior, e.g. "down low"**
 - **HIV+ individuals that are also being cared for by an "HIV Specialist", but are seeing you for other reasons**
 - **Or, you might be involved in an "exposure"**
- So.....what do you need to know????**

References

- <http://www.aids.gov>
- <http://www.aids-etc.org>
- <http://aidsinfo.nih.gov>
(Nov. 3, 2008 DHHS Guidelines)

- Hammer SM. Management of Newly Diagnosed HIV Infection.
N Engl J Med 2005;353:1702-10

In the U. S. alone.... (data thru 2006/7)

- ~1,100,000 currently HIV+
 - 56,000 newly infected each yr
 - >1/2: MSM
- Est. 20-30% (200 - 300,000) unaware of their HIV+ status; these are at very high risk for adding to the epidemic
- ~468,000 living w/ AIDS
 - 37,000 newly diagnosed each yr
 - 14,500 died (2007)
 - Cumulative deaths from AIDS: 583,000

Worldwide.... (data thru 2006/7)

- 33,000,000 living with HIV/AIDS
 - 2,000,000 dead (2007)
- 15,000,000 orphans

Milestones:

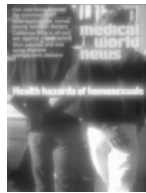
From the June 5, 1981 MMWR:

Pneumocystis Pneumonia - Los Angeles

“In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *P. carinii* pneumonia at 3 different hospitals in Los Angeles, CA. Two of the patients died. All 5 patients had laboratory-confirmed previous or current CMV infection and candida mucosal infection.”

Milestones:

- Over next few years, found to be due to a virus initially called HTLV-III
- Mid 80's: estimated 20 yrs for vaccine to become available
- 1985 - Ab testing available for screening U.S. blood supply



Milestones:

- Late 1980's/early 1990's - single drug rx
 - CD4 counts found to be useful markers for progression of disease - trt (though toxic, inconvenient, and short-lived) when CD4 < 500
 - Even later, commercial availability of viral "loads"
- 1996 - recognition that triple drug "cocktails" were quite effective at limiting rapid development of resistance, thereby controlling progression of disease
Downside: high pill burden, many side effects
- Currently: one pill/day!!!!

- A 32 y.o. caucasian female asks her gynecologist to test her for HIV as he is writing out her 3rd prescription for Diflucan ® within the past year
- Surprise!! Her HIV test is positive
- He promptly refers her back to you.

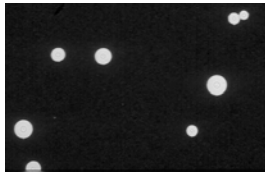
- After donating blood every year or so for the past decade, this time your patient is told that there is “a problem”. His screening test for HIV was found to be +.
- Now what?

- A 25 y/o male presents to your office - or the ED - with a 2-3 week history of fever, nonproductive cough and SOB with modest effort.



- A 30 y/o. AA male is brought to your office - or the ED - nearly unresponsive. His friend offers a history of progressive headache over the past week or so.
- Now what?

- Cryptococcal meningitis is the most common meningitis in HIV+ patients.
Clinical presentation may be insidious



- This 22 y.o. student develops high fever, severe sore throat, myalgias, diffuse adenopathy, and a rash, leading to a visit to your office
- PMH: "acute mono" when he was 13 y.o.
- You learn that he goes to college in North Carolina, is on the basketball team, and works as a cook in a local restaurant there.
- Exam as described. His pharynx is quite erythematous; a white exudate is noted on his tonsils.
- Strep screen and mono spot are negative
- CBC is 3400
- Now what??

**NEWLY APPRECIATED?:
Acute Retroviral Syndrome**

- Fever (96%), adenopathy (74%), pharyngitis (70%), rash (70%) myalgia (59%), thrombocytopenia (45%), leukopenia (45%), diarrhea (37%), headache (32%)
- 2/3 have a mononucleosis-like syndrome
- Incubation period: 1-6 weeks; resolves within 15 days (w/o treatment)
- D/D: mononucleosis, viral hepatitis, measles, rubella, 1^o HSV, secondary syphilis
- Though HIV Ab may be negative or indeterminate, this individual is likely to be highly contagious

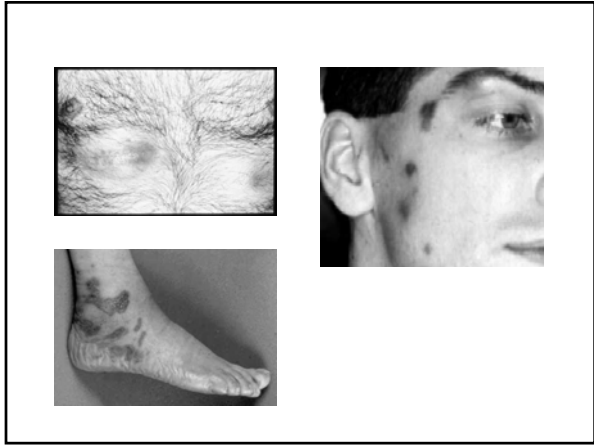
- It's September.
This 27 y.o. A.A. presents to the E.R. complaining of severe headache, fever and photophobia
- Past medical, surgical, and travel history unremarkable
- Exam: A & O x 3; obviously uncomfortable and photophobic. Her neck is stiff. She has a subtle macular rash and scattered adenopathy.

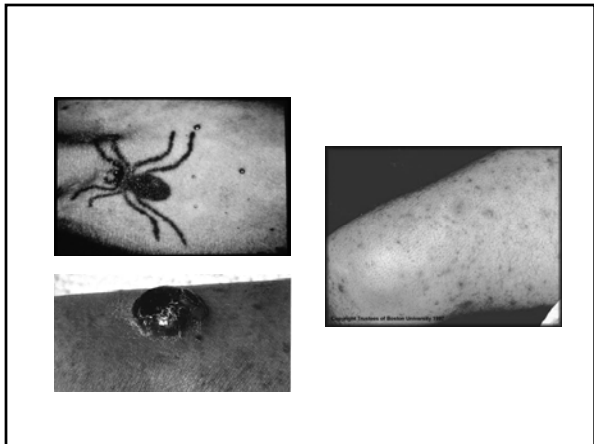
- CSF:
WBC's: 170; 96% lymphocytes
RBC's: 2
Glucose: 41 mg%
Protein: 62%

NEWLY APPRECIATED?: A Variation of the Acute Retroviral Syndrome

- **Differential of “aseptic” meningitis:**
 - Viral - this includes HIV!! (WNV as well)
 - Syphilis (HIV again)
 - Fungal, TB, rickettsia, other “hard to culture” organisms
 - previous antibiotics, parameningeal foci, medications

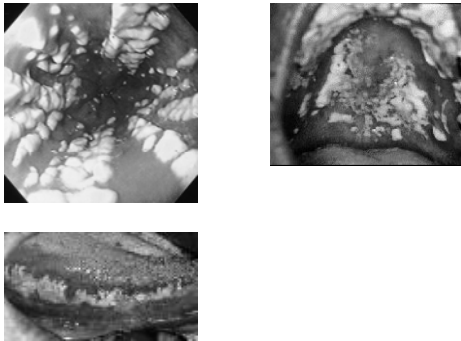
Remember - though HIV Ab may be negative or indeterminate, these folks may be highly contagious

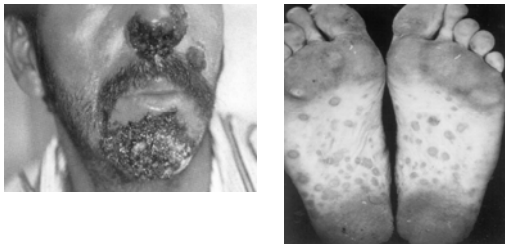




Other clues to possible HIV:

- Unusual presentation of a common illness
 - Bacteremic dx not usually seen
 - Pneumococcal pneumonia w/ bacteremia in a young person
 - Salmonella, shigella, campylobacter bacteremia
 - Presentation of an unusual illness
 - Uncommon dx
 - More advanced/severe dx than expected
 - Unusual age for illness
- TB, especially w/ unusual presentation
- Other STDs

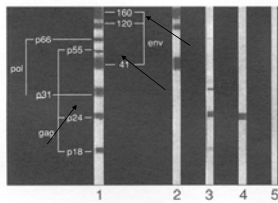




Diagnosis

- **Screening: ELISA antibody**
 - New: now recommended to be part of routine care
 - Likelihood of true positivity depends on patient population being screened
 - Most + within 6 - 8 weeks; almost all positive w/in 3 months
- **Confirmation: Western Blot**
 - Any two: p24, gp41, gp120/160 -> positive
 - one + band, or other + bands -> "indeterminate"
 - if low risk situation - usually false +
 - if high risk situation - may be early true +

Examples of Patterns of Western Blot Reactivity



DIAGNOSIS

1. Positive HIV-1 infection
2. gp160 immunization
3. Indeterminate or HIV-2 infection
4. Indeterminate cross-reacting antibody to p24
5. Negative

Two bands: p24, gp41, gp120/160 = true +

"Window phase"

- Screening tests are negative
- **NEWLY APPRECIATED?:** During this time frame, highly contagious
- Quantitative assay for HIV by PCR

The First Visit

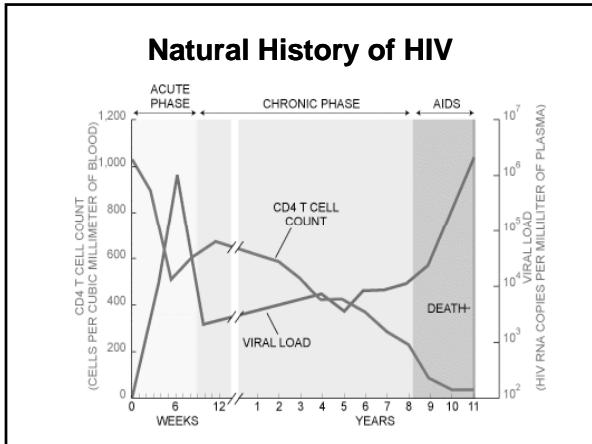
- Take history
- Review all data
- Discuss dx and prognosis
- Reassurance
- Support groups (careful!)
- Answer all questions, provide credible web sites

The First Visit

- May repeat ELISA/Western Blot
- CD4 count
- Quantitative HIV RNA (“viral load”)
- NEW: Genotype
- Also recommended:
 - VDRL
 - CMV, toxo IgG
 - hepatitis serologies
 - PPD (or other tests for TB exposure)

Clinical Course

- Without treatment, median time to develop “AIDS” is around 10 years
- Viral properties and host factors affect progression of disease
- Viral load - “how fast is the train going?”
 - correlates with degree of contagiousness
- CD4 lymphocyte count - “how long are the tracks?”
 - Reflects immune status
 - Correlates w/ development of opportunistic infections (OI's) and malignancies



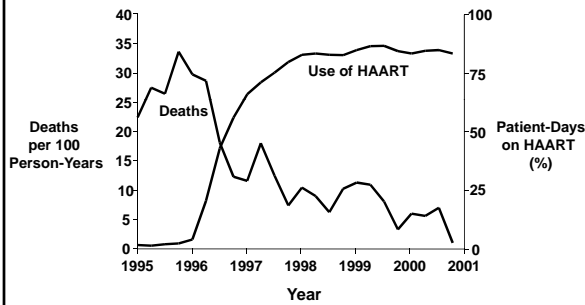
- ### The Second Visit
- Review lab results w/ pt
 - Answer ?'s
 - Physical exam
 - Oropharynx
 - Adenopathy
 - Rash
 - Condyloma
 - immunizations

- ### The Second Visit
- Repeat CD4 ct and viral load
 - Address lab results of concern
 - CD4 and viral load
 - Viral load - "how fast is the train going?"
 - CD4 count - "how long are the tracks?"
 - Hepatitis markers
 - PPD skin testing: >5mm induration is +; prophylaxis strongly recommended

**Treatment:
(ONLY WHEN PT READY)**

- **When:**
 - symptomatic, or "AIDS-defining" illness
 - Old: CD4 count < 200
 - NEW: CD4 count < 350 or even earlier
 - Pregnancy
 - HIV-associated nephropathy
 - ? Rapidly falling CD4 count,
 - ? Viral load > 100,000
- **What: HAART (Highly Active Anti-Retroviral Therapy)**
 - at least three drugs from at least two different classes of anti-retrovirals
- **Prognosis: usually reasonably good IF PT ADHERENT**

**Mortality vs HAART Utilization
HOPS Study**



**DHHS Guidelines for Initial RX of
Treatment-Naïve Patients (Nov. 3, 2008)**

- Emtricitabine (FTC)/tenofovir (TDF) (Truvada®) (2 NRTIs)
- +
- Efavirenz (EFV) (avoid in pregnancy) (NNRTI)
-or.....
- Atazanavir (Reyataz®)/r (PI)
- or
- Darunavir (Prezista®)/r (PI)
- or
- Fosamprenavir (Lexiva®)/r (PI)
- or
- Lopinavir (Kaletra®)/r (PI)

Note: TDF/FTC (Truvada®) + EFV (Sustiva®) = Atripla

Treatment

- **Goal:**
viral load < 50 copies ('undetectable')
increase in CD4 count
- **Failure:**
increase in viral load, followed by
decrease in CD4 count

Immune Reconstitution Syndrome

- An exaggerated inflammatory response to a previously relatively quiescent condition as a result of restoration of immune competence following initiation of HAART,
e.g. focal MAC dx
CMV vitreitis
TB
Cryptococcal meningitis
Hepatitis C
PML
HSV



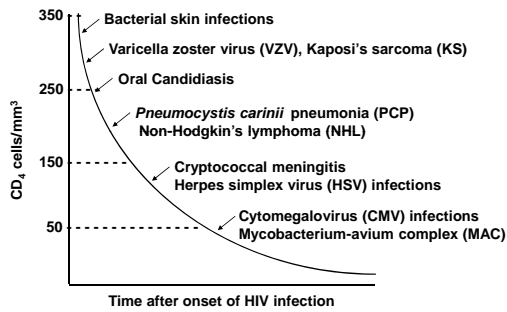
Immune Reconstitution Syndrome

- **Risk factors:**
 - Antiretroviral naïve
 - Starting HAART w/in 30 days of a diagnosis of an OI
 - Rapid decrease in HIV RNA level in response to Tx
- Tx includes continuing HAART, therapy of specific condition, and anti-inflammatory agents

Correlation of CD4 count to presentation of Opportunistic Infections

- Infections common in the non-HIV infected population tend to occur at higher CD4 counts.
At lower CD4 counts these same infections may develop, but often with more extensive or disseminated or recurrent disease (TB, HSV-1 or 2, H. zoster, various neoplasms, candidiasis)
- Infections rarely, if ever, seen in the non-immunosuppressed host tend to occur at the lowest CD4 counts, e.g. disseminated CMV, MAC
- Malignancies more common, even w/ "adequate" CD4 ct

Relationship Between CD₄ Count and AIDS Malignancies



Look for increase in tonsillar carcinoma in especially gay men

Opportunistic Infections/neoplasms relative to CD4 counts

- | | |
|---|--|
| ■ 200 - 500 and above | ■ 50 - 200 |
| ■ Pulmonary TB | ■ PCP |
| ■ Bacterial pneumonia | ■ Disseminated TB |
| ■ Oral/vaginal candidiasis | ■ Esophageal candidiasis |
| ■ H. zoster | ■ Cryptococcal meningitis |
| ■ Cervical CA, Kaposi's sarcoma, Hodgkin's lymphoma | ■ CNS toxoplasmosis |
| | ■ Cryptosporidium |
| | ■ Non-Hodgkin's lymphoma |
| | ■ Disseminated histoplasmosis, coccidioidmycosis |
| | ■ Lower |
| | ■ CMV, MAC |

Primary Prophylaxis against OI's*

PCP	CD4 < 200	TMP-SMX
TB	Previous + PPD or +PPD > 5mm	INH x 9 mos
Toxoplasmosis	+ serology w/ CD4 < 100	TMP-SMX
M. avium complex	CD4 < 50	azithromycin or clarithromycin

*can usually be d/c'd upon return of CD4 count above threshold parameters after ~3 months

■ The good news:

With a return of the CD4 count somewhat towards normal, the risk of OIs decreases significantly

■ The bad news:

Even with a return of the CD4 count towards normal, the risk of certain malignancies may not diminish

Additional comments/syndromes

- HIV accelerates progression of liver disease due to hepatitis B and C; the reverse may not be the case
- Other GI syndromes
- Endocrine Abnormalities
 - Adrenal insufficiency (meds, OIs)
 - Hypogonadism (OIs)
 - Altered glucose, insulin, and lipid metabolism (meds, esp. PIs)
- Wasting
- Neoplasms, including non-Hodgkin's lymphomas, anal and cervical CA
- Various hematologic presentations

■ While performing an office procedure, you manage to penetrate one of your gloves w/ the bloody scalpel blade.
Her HIV status is unknown/presumably negative.

■ Now what??

■ On the patient:
Hepatitis Bs Ag
Hepatitis C Ab
HIV Ab - time is critical

■ On yourself:
Hepatitis Bs Ag/IgG Ab
Hepatitis C Ab
HIV Ab

■ PEP hotline: 1-888-448-4911

■ While performing an office procedure, you manage to penetrate one of your gloves w/ the bloody scalpel blade.

■ Your worst nightmare: this patient has advanced HIV and is a terrible historian. It's Friday night.

■ Now what??

- **On the patient:**
 - Hepatitis Bs Ag (unless status already known)
 - Hepatitis C Ab (unless status already known)
 - ? HIV viral load/genotype
- **On yourself:**
 - Hepatitis Bs Ag/IgG Ab
 - Hepatitis C Ab
 - HIV Ab

- If you know the patient is + :**
- **What HAART is he/she on?**
 - **What is their “viral load”**
 - **PEP hotline: 1-888-448-4911**

- **Risk of seroconversion following a needlestick exposure to a HIV+ individual is approximately 2-3/1000 (0.3%); however, this is variable, depending on the nature of the exposure, e.g., bloody vs non-bloody, hollow bore vs non-hollow bore, etc...**
- **Note: there has been NO documented occupational injury leading to transmission of HIV since 2001!!**

- After partying way too much this past weekend in New Orleans, your pt calls you in a panic Monday am. He thinks he had unprotected sex the night previously, but can't remember the details. He sheepishly admits that his wallet was empty the following morning.
- Now what?

PEP hotline: 1-888-448-4911

Summary

- As a PCP, dealing w/ HIV is unavoidable. Relying on your ability to judge who is at risk is, at best, unreliable
- Undiagnosed HIV+ pts, particularly those recently infected, are at greatest risk for transmitting this infection
 - Be aware of the Acute Retroviral Syndrome
- Current therapy is simple, minimally toxic and highly effective for extended periods of time if pts are adherent
 - Be aware of the Immune Reconstitution Syndrome
- HIV testing is now considered part of routine care
 - In this setting, however, the risk for false +'s increases

Summary II

- Earlier treatment is now recommended by many
- Genotyping is now recommended before instituting Rx
- With current therapy, long term survival can be expected
 - Some therapies, as well as long term survival, increase the need to address cardiovascular risk factors aggressively
 - Even with return of CD4 towards or to normal, immune restoration may be incomplete

Thanks

?’s
