PATHOPHYSIOLOGY & MANAGEMENT OF PATIENTS WITH HIV & AIDS

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Spr 2012

ININCIDENCE WORLDWIDE
– 2010
34 million people infected.
– 2009
1.8 Million AIDS related deaths
2.6 Million new infections

www.unaids.org retrieved 12/4/11

IN THE U.S.
– DECEMBER 2008;
1,178,350 PEOPLE LIVING WITH HIV
20% UNDIAGNOSED
CDC.GOV RETRIEVED 12/2/2011

– 2009 56,000 NEW CASES
LEWIS, DIRKSEN, & HEITKEMPER 2011
INCIDENCE IN US-TRANSMISSION

<table>
<thead>
<tr>
<th>Category</th>
<th>2007</th>
<th>% change</th>
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<tr>
<td></td>
<td>Male</td>
<td>Female</td>
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<tr>
<td></td>
<td>Male</td>
<td>Female</td>
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<tr>
<td>MSM</td>
<td>↓ to 62%</td>
<td>↓ by 5%</td>
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<tr>
<td>↑ risk heterosexual</td>
<td>↓ to 71%</td>
<td>↓ by 26%</td>
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<tr>
<td>IVD Use</td>
<td>↑ to 18%</td>
<td>↑ to 32%</td>
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<td>↑ by 6%</td>
<td>↑ by 13%</td>
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TRANSMISSION: EPIDEMIOLOGY OVERVIEW

↓ in white males who have sex with men (MSM)
↑ in racial & ethnic minority males who have sex with men

↑ in minority women
↑ in 19-29 year age group, especially in south and mid-west states
↑ in > 50 age group
  • Lack of prompt testing
  • Women > 50 y.o. dt heterosexual contact
MAJOR TYPES

HIV – 1
Group M - 10 subtypes, 90% of all cases worldwide
Group O (Now able to be detected with most routine HIV antibody tests)

HIV – 2
1% of cases worldwide
Slower progression
West Africa
79 cases in US, but most were African born

Rapidly changing nature (mutation) makes it challenging to develop vaccines

Genetic Promiscuity

ETIOLOGY & RISK FACTORS

Sexual Practices

Completely Safe
Autosexual
Abstinence
Mutually monogamous

Very Safe
Non-insertive

Probably Safe
Insertive w/ condoms

ETIOLOGY & RISKY BEHAVIORS

Sexual Practices that promote Disease Transmission

Under the influence (drugs, etoh)
Multiple partners
Sores in genital area
Oral receptive (possible)
Anal receptive
ETIOLOGY & RISK FACTORS

- Administration of blood or blood products
- Transplantation of tissue or organs
- Implantation of infected semen

EXPOSURE TO BLOOD

Use of injected drugs

- Absolutely safe
  - Do not inject!
- Very Safe
  - Sterilized or exchanged needles
- Probably safe
  - Clean with full strength bleach

EXPOSURE TO BLOOD

Use of injected drugs

- Occupational exposure
  - Accidental needle stick exposure
  - Report immediately
  - High risk exposures, combination ART for 4 weeks following exposure

Risky Co-factors
- geographical seroprevalence
- social setting
  - (alone vs group)
- frequency of injection
PERINATAL EXPOSURE

If untreated, @ 25% of babies born to HIV+ mothers become infected at birth. If mothers and or babies are treated, less than 2% of the infants become infected.

Risk ↑ in late stages of AIDS
• viral activity is ↑
• CD4+ titer is ↓

CDC Guidelines - September 25, 2006 & 2011
http://www.cdc.gov/ncidod/EID/vol10no11/04-0622_02.htm

PRENATAL HIV TESTING

Funds available in high prevalence states
Promotion of HIV testing for all pregnant women
“Opt-out”- voluntary
Routine rapid HIV testing is promoted at delivery if HIV status is unknown

>90% HIV status known before delivery
40% of all infected infants at birth due to HIV status of mother being unknown

Rapid HIV testing during labor with pharmacologic & OB interventions → ++ outcomes
CDC recommends testing conserving the “opt-out” provision

OTHER RISK FACTORS

Ulcerative STD’s
• Syphilis
• Herpes simplex
• Chancroid

Non-ulcerative STD’s
• Gonorrhea
• Chlamydia
• Trichomoniasis

Seroconversion
Occurs 1-3 months post-exposure when HIV antibodies are first detectable (window period) and the patient converts from HIV- to HIV +
S.T.A.R.H.S.

SEROLOGICAL TESTING ALGORITHM FOR RECENT HIV SEROCONVERSION

ABILITY TO DETERMINE WHETHER HIV INFECTION WAS RECENTLY ACQUIRED OR HAS BEEN ONGOING.

HELP IN MAKING DECISIONS REGARDING TREATMENT, WHAT CM’S TO WATCH FOR OR EXPECT AND WHEN TO SEEK HELP.

POST EXPOSURE PROPHYLAXIS

Health Maintenance Strategy

- Accidental exposure of health care and public safety workers
- Unprotected anal or vaginal intercourse
- Receptive oral intercourse with ejaculation
- Share needles with infected partner
- Single event exposure, i.e. rape
- Intention to stop high-risk behaviors

HIV LIFE CYCLE

#1 – Free virus
#2 – Virus binds to CD4 & fuses to T4 helper cell
#3 – Infectious virus penetrates cell
#4 – Reverse transcription
#5 – Integration
#6 – Transcription
#7 – Assembly
#8 – Budding
#9 – Immature virus leaves cell
#10 – Maturation – develop new virus
OVERVIEW OF PATHOPHYSIOLOGY

HIV destroys body's immune system by selectively attacking T-4 Lymphocytes, also macrophages & B cells

HIV indirectly affects CNS by neurotoxins produced by the infected macrophages

As CD4+ count ↓, body becomes more susceptible to opportunistic infections
**VIRAL LOAD & CD4+ COUNTS**

- CD4+ <200
- Viral load (10^2 to 10^7)
- Primary infection
- Latency
- AIDS

**PRIMARY HIV – CATEGORY A**

- Initial period
  - 50-70% symptomatic with “mono-like” symptoms
- Sudden, intense burst of HIV activity
  - Viral load > 1 mil
- New Test detects both antigen and antibody in window period.

- Starting antiretroviral Rx at this point may prevent damage to immune system
- False + are rare except in patients with lupus
- Rapid HIV tests +
  - Pre- & post-counseling waived
  - Results in 10-20 minutes

**SUSPICIOUS CASES**

- High index of suspicion
- Risky behaviors
- Clinical manifestations

- Offer HIV testing

- HIV-1 antibody enzyme immunoassay
  - If antibodies detected, (test is reactive) confirm with Western blot test
    - Identifies antibodies to 3 viral proteins
    - If 2-3 present, diagnosis of HIV is made
LATENCY PHASE

No CM's of disease … but…

CD4+ count ↓ from normal

(500-1600/µL) drops to 200 cells/µL

Remaining weakened CD4+ lose ability to contain the destructive nature of HIV

Viral load increases

Recurrent URI's

Fatigue

Candidiasis

Lymphadenopathy

AIDS PHASE

CD4 count <200

AIDS defining illness

Without antiretroviral therapy, death in 2-3 years

Opportunistic infection rate ↑↑

OUTCOME MANAGEMENT

Maintain Health

Initiate & maintain Antiretroviral Rx

Prevent infection
OUTCOME MANAGEMENT

Baseline & q 6-12 mos.
• CBC
• Chemistries

Annual Screening
• TB Skin tests/Chest x-ray
• Pregnancy & Pap; STD’s if sexually active
• Hep A & B to determine need for immunization; Hep B and/or C co-infection
• Testing for pathogens known to cause opportunistic infections
• CD4 & Viral load testing (every 3-6 months)

OUTCOME MANAGEMENT: INITIATE & MAINTAIN ART

Viral load is 5000-10,000
Evidence of clinical or immunologic deterioration (CD4 counts <500 mm3)
Viral load > 20,000 even without evidence of clinical deterioration
### ANTIRETROVIRAL AGENTS

<table>
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<tr>
<th>Nucleoside Reverse Transcriptase Inhibitors (NRTI’s)</th>
<th>Incorporate into viral DNA terminating its construction</th>
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<tr>
<td>Protease Inhibitors (PI’s)</td>
<td>Prevent assembly &amp; release of new virus particles</td>
</tr>
<tr>
<td>Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI’s)</td>
<td>Action is similar to NRTI’s; bind directly to reverse transcriptase</td>
</tr>
<tr>
<td>Entry Inhibitors-Fuzeon</td>
<td>Prevent HIV from entering healthy T cells in the body</td>
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### ANTIRETROVIRAL AGENTS

Nucleotide Reverse Transcriptase Inhibitors (NtRTI’s)

Combines with reverse transcriptase enzyme, preventing conversion of HIV RNA to HIV DNA.

### ADHERENCE

**Major cause of resistance is sub-therapeutic dosing**
- failure to take prescribed dose
- failure to take prescribed dose at prescribed intervals
- interactions with other drugs → ↓ blood levels of ART

**Factors affecting adherence**
- Complex dosing schedules
- Adverse side effects
- Unknown cross reactions
- Cost
- Access to Care
EVALUATION OF TREATMENT

Criteria
- ↓ HIV RNA (viral load) in blood
- ↑ # of T cells
- Appropriate clinical response

Generally, 1st treatment regimen of ART is Pt's. BEST CHANCE for SUCCESS, so Adherence is very Important!

Treatment Failure
- ↑ viral load with ↓ T-cell count
- Clinical deterioration
- New opportunistic infections

OPPORTUNISTIC INFECTION

When CD4 <200, causes decreased immune regulation leading to growth of previously controlled bacteria/virus/fungus, already present in the body, to develop into a source of disease/disability/death.

PREVENT OPPORTUNISTIC INFECTION

Pneumocystosis carinii
- Pneumonia (80%) at least once
- Prophylaxis when CD4+ count < 200mm³
  - Dapsone
  - TMP-SMX

Mycobacterium avium complex (60%) found to have active infection at death
- Prophylaxis when CD4+ count < 50 mm³

PPD with a CM’s of active Tb
- Prophylaxis with INH-9 mos
- Pyridoxine to prevent peripheral neuropathy

Flu & pneumonia vaccine
- Prevention of travelers diarrhea – Cipro
- Safer sex practices
- Food & water safety
- Skin & mucous membrane integrity
OUTCOME MANAGEMENT

Maintain Health

Initiate & maintain
Antiretroviral Rx

Prevent infection

NURSING CARE

Assessment

• Ask
• Believe
• Compile
• Differentiate

Communicate
Refer to specialized services

RESOURCE


http://hab.hrsa.gov/tools/palliative.html
### PAIN AND SYMPTOM MANAGEMENT IN RT VIRAL INVASION OF BODY TISSUES & ORGANS

**Opportunistic Infections**
- Cryptococcal meningitis → (headache)
- Mycobacterium Avium Complex (MAC) → visceral abdominal pain

**Effects of AIDS or Immune response to AIDS**
- Distal sensory polyneuropathy
- HIV related myopathy

**Effects of Medications**
- Peripheral neuropathy
- Headache
- GI distress

**Non-specific effects of chronic debilitating disease**

### COMMON LATE STAGE SYMPTOMS- AIDS DEFINING ILLNESSES

**Nutrition** < body requires
- Fatigue/Amenorrhea/weight loss/R&V&D
- Pain/Infections/Insomnia
- Depression/Impaired Cognition
- Sleep Pattern Disturbance
- Medication Side Effects

**Symptoms increased in patients with history of IVDA as mode of transmission**

### FATIGUE

- Muscular weakness
- Lethargy, Sleepiness
- Mood disturbance – depression
- Cognitive disturbance – difficulty concentrating

**Interventions**
- Fatigue diary for one week
- Avoid caffeine, smoking, alcohol
- Promote adequate sleep
- Promote adequate balance of rest/activity
- Promote energy saving procedures & exercise
PAIN
Alarmingly undertreated, especially in women
Significantly alters psychological well being and functional ability
Profound impact on quality of life
Pain management for injecting drug users

PAIN SYNDROMES/CAUSES IN HIV
Sensory peripheral neuropathy
Extensive Kaposi’s sarcoma
Headache
Oral and pharyngeal pain
Abdominal & chest pain
Arthralgia’s & myalgia’s
Painful dermatologic conditions

GENDER RELATED DIFFERENCES: WOMEN
↑ frequency & intensity
2 x as likely to be under-treated
Unique pain syndromes of gynecological nature r/t
• opportunistic infections
• CA pelvis & GU tract
2 x ↑ in radiculopathy & headache
SPECIFIC AIDS RELATED PROBLEMS

Invasive Cervical Cancer
- CIN – cervical intraepithelial neoplasia
- ↑ rate in women w/HIV
- Related to ↓ CD4+ counts

Kaposi’s Sarcoma
- HIV related KS-fulminant
- Disseminated throughout
- Unrelated to CD4+ count
- Can occur early in disease

AIDS dementia complex
- Very young & older pts.
- Anemia & weight loss
- < 12th grade education

HIV Wasting Syndrome
- 90% of people w/ HIV
- Profound wt. loss (>10% baseline) w/ chronic diarrhea, weakness, fever for >30 days

INVASIVE CERVICAL CANCER

Assessment
Early – cervical dysplasia
Post-coital bleeding
- Metrorrhagia
- Blood tinged vaginal discharge
Advanced Disease
- Back, pelvic, leg pain, edema of legs
- Weight loss
- Vaginal bleeding →anemia
- lymphadenopathy

Treatment
Minimally invasive procedures
Surgery
Internal radiation chemotherapy

AIDS RELATED KAPOSI’S SARCOMA

Assessment
Symmetrical, bilateral flat pink patches that look like bruises
Turn to deep violet or black lesions
Location:
- mouth, skin, mm’s
- Head, neck, torso, limbs, genitals
- Internal organs

Rx
- Depends on CD4+ count, CM’s, other diseases & functional ability
- Radiation, localized chemotherapy, cryotherapy
AIDS DEMENTIA COMPLEX
HIV ENCEPHALOPATHY

Cognitive Dysfunction
- ↓ concentration, memory
- Slowed thinking
- Impaired judgment

Motor Problems
- Leg weakness
- Ataxia
- Clumsiness

Behavior Changes
- Apathy, ↓ spontaneity, social withdrawal
- Irritability, ↑ activity
- Anxiety, mania, delirium

HIV WASTING SYNDROME

Incidence
- 90% of people with HIV infection

Profound involuntary weight loss with chronic diarrhea, weakness & fever > 30 days

Cause
- ↓ food intake
- Malabsorption
- Altered metabolism

Rx
- Replace low testosterone in men & women
- Stimulate appetite with megestrol & dronabinol
- Human growth hormone
WASTING SYNDROME

NEW ADVANCES

Four New Antiretroviral Agents approved by the FDA for HIV-1 infection:
- CCR5 co-receptor antagonists: Maraviroc (Selzentry)
- Integrase Inhibitor: raltegravir (Isentress)
- NNRTI's: etravirine (Intelence) & rilpivirine (Edurant)

www.hivguidelines.org retrieved 11/30/11

Worldwide efforts continue with many programs performing Clinical Trials to develop an HIV Vaccine
http://www.hivtreatmentispower.com/