Human Immunodeficiency Virus Infection
John A. Bosso, Pharm.D.

MEN’S RULES #1
Learn to work the toilet seat.
You're a big girl. If it's up, put it down.
We need it up, you need it down.
You don't hear us complaining about you
leaving it down.

MEN’S RULES #2
Sunday sports. It's like the full moon
or the changing of the tides.
Let it be.

MEN’S RULES #3
• If something we said can be interpreted
two ways and one of them makes you sad
or angry, then we meant the other one
Epidemiology

- 1st cases recognized in Summer of 1981
- ~40 million infected worldwide (2001)
- 22 million deaths to-date, including 500,000 in USA (2006)
- 1 million people living with HIV/AIDS in USA (2006)
- 40,000 new HIV infections are expected this year
- HIV infection rates much higher in underdeveloped nations
  - >90% of new cases


Age-Related Issues
Human Immunodeficiency Virus Infection
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Geographic Variation
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Gender Issues
Race/Ethnicity Issues
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Etiology

- HIV-1
  - Accounts for 99.9% of cases in USA
- HIV-2
  - Less virulent
- “infects” CD4+ cells through receptor-mediated identification and entry
- With damage to CD4+ cells, the immune system is rendered dysfunctional

Human Immunodeficiency Virus

- A retrovirus
  - Endogenous genetic material is RNA
  - RNA must be transcribed to DNA for replication in human cells then back to RNA for translation into viral protein
  - Key enzymes are reverse transcriptase, integrase, and protease enzymes
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Life Cycle of HIV

Human Immunodeficiency Virus

- Transmission:
  - MSM 35%
  - IVDU 23%
  - Heterosexual transmission: 14%
  - Perinatal transmission accounts for 90% of peds cases
### Diagnosis

- **Enzyme-linked Immunosorbent Assay (ELISA)**
  - Detects antibodies against HIV-1
  - Ideally performed ≥ 2 mos after exposure
- **Western blot**
  - Also detects antibodies
  - Used to confirm ELISA
- **Viral Load (viral burden)**
  - Estimate of viral RNA in bloodstream measured as
    # viral particles/ml
  - Used as prognostic factor (esp in combination with CD4+ count)

### Clinical Course

- Varies from individual to individual
- Typical course includes
  - Acute phase
  - Asymptomatic phase
  - End-stage disease

### Acute Phase

- Widespread replication and dissemination of virus
- Asymptomatic or manifested by:
  - Fever - Weight loss
  - Fatigue - Adenopathy
  - Night sweats - Rash
- Can develop in days or weeks
- Mean duration: 14 days

### Acute Phase (con’d)

- HIV antibodies may not yet be established
  - HIV seronegative
- HIV seropositive:
  - 2 consecutive HIV ELISA antibody tests positive & confirmed
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Asymptomatic Phase

- Characterized by reduction in viral load and lack of clinical symptoms
- Steady-state or “viral set point” reached
  - Magnitude of viral set point relates to progression to AIDS and morbidity

Pre-AIDS Syndromes

- Persistent generalized lymphadenopathy
- Constitutional syndromes
  - Fatigue, low-grade fevers, night sweats, diarrhea
- Neurologic disease
  - Focal or diffuse encephalitis, ataxia, myelopathy
- Wasting syndrome
  - >10% wgt loss plus chronic diarrhea or chronic weakness/fever

End Stage Disease

- Viral replication exceeds immune response
- Characterized by:
  - Persistently elevated viral loads
  - Declining CD4+ counts
  - Anergy, anemia, leukopenia, thrombocytopenia
- AIDS dx’d on presence of CD4+ ≤ 200/mm³ or presence of specific opportunistic infections

AIDS Classification System*

<table>
<thead>
<tr>
<th>CD4 Particles/μl</th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥500</td>
<td>Asymptomatic, Acute HIV</td>
<td>Symptomatic, not A or C</td>
<td>AIDS indicator conditions</td>
</tr>
<tr>
<td>200-499</td>
<td>A2</td>
<td>B2</td>
<td>C2</td>
</tr>
<tr>
<td>&lt;200</td>
<td>A3</td>
<td>B3</td>
<td>C3</td>
</tr>
</tbody>
</table>

*1993 Revised surveillance Definition System
**AIDS Indicator Conditions**

- Bacterial infections
- Candidiasis
- Cervical Cancer
- Coccidioidomycosis
- Cryptococcosis
- Cryptosporidiosis
- CMV disease
- HIV related encephalitis
- Isoporiasis
- Wasting Syndrome

- Kaposi’s sarcoma
- Lymphoid interstitial pneumonitis
- Lymphoma
- Mycobacterium infections
- Pneumocystis carinii
- Pneumonia
- Leukoencephalopathy
- Salmonella septicaemia
- Toxoplasmosis (brain)

*1993 Revised surveillance Definition System

**HIV-Related Illnesses in Children**

- Often present with unexplained physical signs:
  - Hepatomegaly, FTT, weight loss, fever, splenomegaly, lymphadenopathy, LBW, eczema, parotitis
- Certain bacterial infections more common
  - Streptococcal, salmonella, MTB
- Kaposi’s sarcoma is rare

---

**AIDS-Defining Conditions Most Commonly Reported for Children <13 Years of Age, N=8,718, Reported through 1999, United States**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number</th>
<th>% of Cases*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumocystis carinii pneumonia</td>
<td>2900</td>
<td>33</td>
</tr>
<tr>
<td>Lymphoid interstitial pneumonitis</td>
<td>2061</td>
<td>24</td>
</tr>
<tr>
<td>Recurrent bacterial infections</td>
<td>1794</td>
<td>21</td>
</tr>
<tr>
<td>HIV wasting syndrome</td>
<td>1564</td>
<td>18</td>
</tr>
<tr>
<td>HIV encephalopathy</td>
<td>1462</td>
<td>17</td>
</tr>
<tr>
<td>Candida esophagitis</td>
<td>1372</td>
<td>16</td>
</tr>
<tr>
<td>Cytomegalovirus disease</td>
<td>838</td>
<td>10</td>
</tr>
<tr>
<td>Mycobacterium avium infection</td>
<td>709</td>
<td>8</td>
</tr>
<tr>
<td>Severe herpes simplex infection</td>
<td>422</td>
<td>5</td>
</tr>
<tr>
<td>Cryptosporidiosis</td>
<td>418</td>
<td>5</td>
</tr>
<tr>
<td>Pulmonary candidiasis</td>
<td>326</td>
<td>4</td>
</tr>
</tbody>
</table>

*1 diagnosis reported for some children

**Prevention of HIV Infection**

- Decreasing high-risk behaviors
  - Unprotected sex, IV drug use, decreasing mother-to-child transmission
- Vaccines
  - *Therapeutic*: augment immune response
  - *Preventive*: decrease infection potential
- Problems/challenges
  - Genetic diversity, rapid replication, high mutation rate
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Treatment of HIV/AIDS

- 3 classes of HIV inhibitors
  - Nucleoside reverse transcription inhibitors
  - Non-Nucleoside reverse transcription inhibitors
  - Protease inhibitors
- 3 potential antiretroviral regimens for treatment naive patients:
  - 1 NNRTI + 2 NTRIs
  - 2 NRTIs + 1 or 2 Pis
  - 3 NRTIs
- HAART or “potent combination therapy/potent antiretroviral therapy”

HIV/AIDS Treatment Guidelines

http://www.aidsinfo.nih.gov/guidelines/

The Newest Guidelines

Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

May 4, 2006

It is emphasized that concepts relevant to HIV management evolve rapidly. The Panel has a mechanism to update recommendations on a regular basis, and the most recent information is available on the AIDSinfo Web site (http://aidsinfo.nih.gov).

Address 1.) transmission 2.) diagnosis 3.) risk screening 4.) treatment, and 5.) adherence

Treatment of HIV/AIDS-2

- Initiating & Monitoring
  - CD4+ counts and viral load values used to guide initiation of and changes in therapy
  - Therapy recommended is symptomatic or in asymptomatic patients with CD4+ < 350/mm³ or viral load > 55,000 copies/ml*
- Goal of Therapy
  - Attain and maintain an undetectable viral load

*by RT-PCR or bDNA assays
Preferred Regimens
(ARV-naïve Patients)

• NNRTI-based
  – Efavirenz + (lamivudine or emtricitabine) + (zidovudine or tenofovir DF)
• PI-based
  – Lopinavir/ritonavir (Kaletra) + (lamivudine or emtricitabine) + zidovudine

http://www.aidsinfo.nih.gov/guidelines

Regimens That Should Not be Used

• Monotherapy (rapid development of resistance)
• 2-agent therapy (rapid development of resistance)
• ABC + TDF + 3TC (early failure)
• TDF + ddI + 3TC (early failure)

Components That Should Not be Used

• SQV hard gel cap as single PI (poor bioavailability)
• d4T + ddI (high incidence of toxicities)
• EFV in pregnancy
• APV oral solution (in certain populations due to high amount of exipient propylene glycol)
• d4T + AZT (antagonistic)
• d4T + ddC (additive peripheral neuropathy)
• ddI + ddC (additive peripheral neuropathy)
• AZA + IDV (potential additive hyperbilirubinemia)
• FTC + 3TC (similar resistance profile)
• Hydroxyurea (various)

Factors to Consider In Selecting/Initiating Therapy

• Patient’s willingness/readiness to begin tx
• Assessment of adherence potential
• Patient’s preference re: pill burden, dosing frequency, food & fluid considerations
• Severity of disease & AIDS-defining cond’s
• Potential ADRs
• Co-morbidities and other conditions (e.g., pregnancy)
• Potential drug interactions
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Treatment of HIV/AIDS-3

- Viral load should be monitored every 30 days after beginning tx and every 90 days thereafter
- Undetectable viral load associated with:
  - Decreased likelihood of development of resistance
  - Stronger immune system preservation & reconstitution

Treatment of HIV/AIDS-4

- Therapeutic failures
  - Previously undetectable viral load has increased or initial viral load is unresponsive
  - Initiate therapy with 3 or more new antivirals
- Addition of one extra drug to a failing regimen is inappropriate

Treatment of HIV/AIDS-5

- Challenges to therapy
  - Adherence
  - Complex, multi-drug regimens
  - Side effects
  - Drug Resistance
    - 10% of treatment naïve patients have drug-resistant strains
    - Most often with NRTIs (~7%), but also with NNRTIs (2.6%) and PIs (2.2%)
    - 1st drug resistance has become common
  - Drug Interactions

Pill Burden in Treating HIV

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Pills Daily</th>
<th>Times Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC/3TC/ZDV*</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>TDF/3TC/EFV</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>3TC/ZDV/EFV†</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>3TC/ZDV/NVP†</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>3TC/ZDV/LPV/rtv†</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>d4T/3TC/LPV/rtv**</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>d4T/3TC/NFV**††</td>
<td>14</td>
<td>2</td>
</tr>
</tbody>
</table>

*combination tablet, †3TC/ZDV combination tablet, ‡d4T and 3TC each given twice daily, ††NFV given as 10 tablets twice daily
Resistance Testing

- Recommended in cases of acute or recent HIV infection who:
  - Have been infected $\geq 2$ yrs prior to initiating tx
  - Have failed antiretroviral therapy
  - Are pregnant


Antiretroviral-Drug Interactions: Protease Inhibitors

- All are metabolized by, and inhibit CYP3A.
  - Ritonavir also induces CYP1A2 and glucuronyltransferase, and inhibits CYP2C9.
- Rank order of CYP3A4 inhibition
  - Ritonavir > indinavir = saquinavir (gel) = nelfinavir = amprenavir
- Metabolism of PIs is induced by rifampin, DPH, and autoduction (ritonavir, nelfinavir)
- Entire spectrum and significance unclear

Antiretroviral-Drug Interactions: NNRTIs


Antiretroviral-Drug Interactions: NNRTIs


Table 11. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation</th>
<th>Dosage</th>
<th>Food Effect</th>
<th>Drug Interactions</th>
<th>Half-Life (h)</th>
<th>Elimination</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir</td>
<td>Tablets</td>
<td>300 mg</td>
<td>Food effect</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamivudine</td>
<td>Tablets</td>
<td>150 mg</td>
<td>Food effect</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zidovudine</td>
<td>Tablets</td>
<td>500 mg</td>
<td>Food effect</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 17. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations

17a. Potentially Life-Threatening and Serious Adverse Events

- Seizures
- Rhabdomyolysis
- Adverse Drug Reactions

17b. Potentially Life-Threatening Adverse Effects (Lithium substituted under)

- Lithium toxicity
- Renal impairment
- Electrolyte abnormalities

http://www.aidsinfo.nih.gov/guidelines

PHMPR-732.bosso.HIV.rev7.07 14
http://www.aidsinfo.nih.gov/guidelines

http://www.aidsinfo.nih.gov/guidelines

Table 18. HIV-Related Drugs With Overlapping Toxicities

| Drug/Class | Neurologic | Cardiovascular | Gastrointestinal | Hepatic | Ocular | Renal | Skin | Other | Dose-Matched Agents | Neuraminidase Inhibitors | Fullingomide | Foscarnet | Lamivudine | Lopinavir/ritonavir | Didanosine | Zidovudine | Lamivudine | Abacavir | Tenofovir | Nelfinavir | Saquinavir | Ritonavir | Darunavir | Atazanavir | Indinavir | Nelfinavir | Saquinavir | Ritonavir | Darunavir | Atazanavir | Indinavir |
|------------|------------|----------------|------------------|---------|--------|-------|------|-------|---------------------|--------------------------|------------|-----------|-----------|------------------|-------------|--------|-----------|--------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| NNRTI      |            |                |                  |         |        |       |      |       |                    |             |            |           |                  |               |         |           |        |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Efavirenz  |            |                |                  |         |        |       |      |       |                    |             |            |           |                  |               |         |           |        |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Nevirapine |            |                |                  |         |        |       |      |       |                    |             |            |           |                  |               |         |           |        |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Stavudine  |            |                |                  |         |        |       |      |       |                    |             |            |           |                  |               |         |           |        |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Didanosine |            |                |                  |         |        |       |      |       |                    |             |            |           |                  |               |         |           |        |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Zidovudine |            |                |                  |         |        |       |      |       |                    |             |            |           |                  |               |         |           |        |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Lopinavir  |            |                |                  |         |        |       |      |       |                    |             |            |           |                  |               |         |           |        |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Ritonavir  |            |                |                  |         |        |       |      |       |                    |             |            |           |                  |               |         |           |        |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Darunavir  |            |                |                  |         |        |       |      |       |                    |             |            |           |                  |               |         |           |        |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Atazanavir |            |                |                  |         |        |       |      |       |                    |             |            |           |                  |               |         |           |        |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Indinavir  |            |                |                  |         |        |       |      |       |                    |             |            |           |                  |               |         |           |        |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Nelfinavir |            |                |                  |         |        |       |      |       |                    |             |            |           |                  |               |         |           |        |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |
| Saquinavir |            |                |                  |         |        |       |      |       |                    |             |            |           |                  |               |         |           |        |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |

Table 19. Drug Interactions Among Antiretrovirals and Other Drugs: PIs

<table>
<thead>
<tr>
<th>Drug Interaction</th>
<th>Antiretroviral Category</th>
<th>Other Drug Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indinavir</td>
<td>NNRTI</td>
<td>Nelfinavir</td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>NNRTI</td>
<td>Indinavir</td>
</tr>
<tr>
<td>Saquinavir</td>
<td>NNRTI</td>
<td>Ritonavir</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>NNRTI</td>
<td>Abacavir</td>
</tr>
<tr>
<td>Darunavir</td>
<td>NNRTI</td>
<td>Atazanavir</td>
</tr>
<tr>
<td>Atazanavir</td>
<td>NNRTI</td>
<td>Darunavir</td>
</tr>
<tr>
<td>Indinavir</td>
<td>NNRTI</td>
<td>Atazanavir</td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>NNRTI</td>
<td>Atazanavir</td>
</tr>
<tr>
<td>Saquinavir</td>
<td>NNRTI</td>
<td>Atazanavir</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>NNRTI</td>
<td>Atazanavir</td>
</tr>
</tbody>
</table>

Table 20. Drugs That Should Not Be Used With PI or NNRTI Antiretrovirals

<table>
<thead>
<tr>
<th>Drug Interaction</th>
<th>Antiretroviral Category</th>
<th>Other Drug Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indinavir</td>
<td>NNRTI</td>
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<td>Nelfinavir</td>
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<td>Indinavir</td>
</tr>
<tr>
<td>Saquinavir</td>
<td>NNRTI</td>
<td>Ritonavir</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>NNRTI</td>
<td>Abacavir</td>
</tr>
<tr>
<td>Darunavir</td>
<td>NNRTI</td>
<td>Atazanavir</td>
</tr>
<tr>
<td>Atazanavir</td>
<td>NNRTI</td>
<td>Darunavir</td>
</tr>
<tr>
<td>Indinavir</td>
<td>NNRTI</td>
<td>Atazanavir</td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>NNRTI</td>
<td>Atazanavir</td>
</tr>
<tr>
<td>Saquinavir</td>
<td>NNRTI</td>
<td>Atazanavir</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>NNRTI</td>
<td>Atazanavir</td>
</tr>
</tbody>
</table>

Table 16. Strategies to Improve Adherence to Antiretroviral Therapy

- Establish readiness to start therapy
- Provide education on medication dosing
- Review personal side effects
- Anticipate and treat side effects
- Utilize educational aids including pictures, pamphlets, and calendars
- Engage family, friends
- Simplify regimen, dosing, and food requirements
- Utilize team approach with nurses, pharmacists, and peer counselors
- Provide accessible, trusting health care teams

Public Health Service Task Force

Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States

July 6, 2006

It is emphasized that concepts relevant to HIV management evolve rapidly. The Task Force has a mechanism to update recommendations on a regular basis, and the most current information is available on the AIDSinfo Web site (https://AIDSinfo.nih.gov)
Human Immunodeficiency Virus Infection
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Prevention

- **Intrauterine transmission**
  - Treatment of mother & infant with zidovudine reduces transmission ~68%
  - Mother treated during pregnancy and delivery
  - Infant treated for first 6 weeks of life
- Use of “standard precautions” lowers risk of occupational exposure
  - Blood and other high risk body fluids considered/ handled as potentially infectious

Post-Exposure Prophylaxis (PEP)

- Lowers risk of transmission (~79%)
- Should be initiated within 1 to 2 hrs
- Offered in all cases of needlestick involving an HIV-positive patient
  - 30 day, 2 drug regimen (minimum)
    - Zidovudine & lamivudine
    - Zidovudine & emtricitabine
    - Tenofovir DF & lamivudine
    - Tenofovir DF & emtricitabine
- Unnecessary if source is urine or saliva

Pharmacist’s Role

- Simplify treatment regimens
- Stress medication adherence
- Explain administration in relation to time and nature of meals
- Identify and manage drug interactions
- Identify adverse effects and refer to treating MD

Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HIV and Recommendations for Postexposure Prophylaxis

Infectious Complications of AIDS

- Opportunistic infections responsible for ~90% of deaths in AIDS patients
- Consequence of loss of cell-mediated immunity
- Related to level of CD4+ cells
- Major opportunistic infections:
  - Pneumocystis carinii pneumonia
  - Candidal esophagitis, CNS toxoplasmosis or cryptococcosis
  - Mycobacterial disease
  - Herpes group viral infections

Opportunistic Infections

- PCP
- Toxoplasmosis
- Cryptosporidiosis
- Microsporidiosis
- TB
- Disseminated MAC
- Bact’l resp. infexe
- Bact’l enteric infexe
- Bartonella infexe
- Candidiasis
- Cryptococcosis
- Histoplasmosis
- Coccidiodmycosis
- CMV
- HSV
- VZV
- Human herpesvirus 8
- Human papillomavirus
- Hepatitis C

Opportunistic Infections as a Function of Immune Status

Candida Esophagitis

- Candida albicans is part of the normal flora in many people
- One of the more common indicator diseases/opportunistic infections
- Odynophagia (pain on swallowing) or dysphagia are the most common complaints
- Oral lesions are commonly found as well
- Treatment: generally treated with PO flucnazole
- Alternatives include irtraconazole and voriconazole
- Prophylaxis indicated for severe recurring episodes
Human Immunodeficiency Virus Infection
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Pneumocystis jiroveci Pneumonia

- Incidence has decreased because of prophylaxis
- Onset is insidious and presentation often subacute
- Treatment: TMP/SMX (alt: pentamidine)
  - ADR in AIDS patients:
    - TMP/SMX: rash, fever, leukopenia, ↑ serum transaminases, thrombocytopenia
    - Pentamidine: ↓ BP, ↑ HR, nausea, vomiting, hypoglycemia or hyperglycemia, pancreatitis, diabetes mellitus, ↑ transaminases, nephrotoxicity, leukopenia, cardiac dysrhythmias

Pneumocystis jiroveci Pneumonia

- Treatment (con’d)
  - Adjunctive steroid therapy decreases risk of resp. failure and increases survival
  - Alternatives to TMP/SMX or Pentamidine
    - Dapsone plus trimethoprim
    - Clindamycin plus primaquine
    - Atovaquone
    - Trimetrexate

Pneumocystis jiroveci Pneumonia

- Prophylaxis
  - Recommended for:
    - All HIV-infected patients who have already had PCP
    - HIV-infected persons with CD4+ count <200 (or CD4+ <20% of total lymphocytes) or with unexplained fever for > 2 weeks, or hx of oropharyngeal candidiasis

Pneumocystis jiroveci Pneumonia

- Prophylaxis (con’d)
  - TMP/SMX is preferred therapy
  - Confers cross-protection vs toxoplasmosis and many bacterial infections
  - Alternatives:
    - Dapsone
    - Dapsone & pyrimethamine & leucovorin
    - Aerosolized pentamidine
    - Atovaquone
Toxoplasma gondii Infections

- Seroprevalence in HIV-infected people living in large urban areas: 10-45%
- Case-defining illness in 2.1% of AIDS cases
- Transmitted to man through undercooked meats and via contact with cat feces
- Predilection for brain and eye
- Responsible for most focal intracerebral lesions

Cryptococcus Neoformans Infections

- Incidence: ~7% of AIDS patients in USA
- 4th most common infection in AIDS
- Most common life-threatening fungal infection
- Meningitis, pneumonia, disseminated disease
- Symptoms:
  - Fever, headache, malaise, etc

Toxoplasma gondii Infections

- Symptoms
  - Most frequently associated with CNS involvement
  - Fever, headache, seizures (10-25%), focal neurologic abnormalities (60-70%), mental status changes

Toxoplasma gondii Infections

- Treatment of CNS infections
  - Usually empiric in patients who are seropositive and have suggestive symptoms
  - Pyrimethamine plus Sulfadiazine
    - Response rate: ~85% with 4 wks tx
    - ADR: bone marrow suppression with pyrimethamine and sulfadiazine hypersensitivity reactions with sulfadiazine (both about 40%)
  - Relapse rate of as much as 100% after discontinuation of therapy
    - Secondary prophylaxis is recommended
- Primary prophylaxis
  - In HIV-infected, seropositive persons with CD4+ <100
**Cryptococcus Neoformans Infections**

- **Treatment:**
  - Amphotericin B (alt: fluconazole)
- **Maintenance therapy:**
  - Fluconazole
- **Prophylaxis:**
  - Only to prevent recurrence (prior episode)

**Mycobacterium Infections**

- **M. tuberculosis**
- **M. avium complex (MAC)**
  - In up to 40% of AIDS patients
  - Clinical syndrome: spiking fevers, diarrhea, night sweats, malaise, weight loss, anemia & neutropenia
  - Gastrointestinal infection: persistent diarrhea, abdominal pain, malabsorption syndrome, biliary obstruction

**M. avium complex (MAC)**

- **Treatment:**
  - Rifabutin, ethambutol, clarithromycin
- **Prophylaxis**
  - Primary px (patients with CD4+ < 50)
    - Clarithromycin or azithromycin
    - Discontinue when CD4+ > 100
  - Prevention of recurrence (2nd px)
    - May be discontinued with CD4+ count > 100-200
    - For 6 mos, asymptomatic & completed 12 mos px
    - Macrolide plus ethambutal ± rifabutin

**Herpes Virus Infections**

- **Herpes Simplex Viruses (HSV) 1 & 2**
- **Varicella-Zoster Virus (VZV)**
- **Cytomegalovirus (CMV)**
Herpes Simplex Viruses

- Manifestations/areas of involvement
  - Anorectal lesions (most common in homosexual men)
  - Genital
  - Orolabial
  - Esophagitis
  - Encephalitis (less commonly)

- Treatment
  - Acyclovir (alt: famciclovir or valacyclovir)
  - Suppressive tx for recurrent disease
  - Alternatives for acyclovir-resistant isolates
    - Vidarabine, foscarnet

Varicella-Zoster Virus

- Prevalence appears higher than in age-matched controls (immunocompetent)
- Typical clinical syndrome:
  - Radicular pain followed by localized erythematous rash and vesicles
- Treatment:
  - Acyclovir (alt: valacyclovir, famciclovir)

Cytomegalovirus

- Most common life-threatening viral infection in AIDS patients
- Manifestations:
  - Common:
    - Retinitis, esophagitis, hepatitis, GI involvement
  - Less common:
    - Radiculopathy, encephalitis, pneumonitis
- End-organ disease in ~ 45% when CD4+ < 50
Cytomegalovirus

- Retinitis
  - Most common CMV disease in AIDS
  - ~30% of AIDS patients
- Symptoms:
  - Painless, progressive loss of vision
  - Blurry vision, loss of visual acuity, "floaters"
  - Untreated, leads to blindness

Cytomegalovirus

- Treatment
  - Ganciclovir (IV)
    - Induction and maintenance phases
    - ADR: neutropenia & thrombocytopenia
  - Intraocular ganciclovir
    - Sustained release implants
    - Used in conjunction with oral tx

Cytomegalovirus

- Treatment
  - Foscarnet (IV)
    - Appears at least as effective as ganciclovir
    - Also administered in induction and maintenance phases
    - ADR: renal insufficiency, metabolic disturbances of calcium and phosphorus, anemia, thrombocytopenia, infusion-site reactions, nausea, vomiting, penile ulcerations, seizures
  - Other treatment options
    - Ganciclovir plus foscarnet
    - Cidofovir
  - Prophylaxis
    - Primary: not recommended
    - Secondary:
      - Ganciclovir (PO or IV), foscarnet, ganciclovir & foscarnet, cidofovir, valganciclovir
      - D/C if CD4+ count >100-200 for 6 mos and no active disease
Human Immunodeficiency Virus Infection
John A. Bosso, Pharm.D.

MEN’S RULES #4

Don’t ask us what we’re thinking about unless you are prepared to discuss such topics as baseball, the shotgun formation, or golf.