HIV 101: Fundamentals of HIV Infection and Applications of Antiretroviral Therapy

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Financial Relationships With Ineligible Companies (Formally Described as Commercial Interests by ACCME). Within the Last 2 Years:

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Planner/Reviewer 1 has no relevant financial affiliations to disclose. (Updated 09/22/21)
Planner/Reviewer 2 has no relevant financial affiliations to disclose. (Updated 09/28/21)

Pretest Question #1
At steady state, when an actively producing cell dies it is replaced by how many newly infected cells?
1. One
2. Twenty five
3. One hundred
4. One thousand
5. It depends on the viral load
BACK TO BASICS
How many HIV virions are produced a day in an infected person?

1. 1
2. ~1000
3. 570,342
4. ~1 million
5. >1 billion
ARS 2
At steady state, when an actively producing cell dies, it is replaced by how many newly infected cells?

1. One
2. Twenty – Five
3. One Hundred
4. One Thousand
5. It depends on the viral load
ARS 3

When should antiretroviral therapy be started? At a CD4 count of:

A. 200 cells/ul or less
B. 200 – 350 cells /ul
C. 350 – 500 cells /ul
D. 500 – 750 cells/ul
E. Any CD4 count
T cell "activation" is lower in treated than untreated adults, but consistently higher than "normal"

![Graph showing T cell activation levels](image)

Early ART Also Appears to Reduce Residual T Cell Activation during ART

![Graph showing early ART reduction in T cell activation](image)

Inverse Probability Weighted Cox Regression Multivariate Analysis

<table>
<thead>
<tr>
<th></th>
<th>Relative Hazard (HR)</th>
<th>95% Confidence Interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deferral of HAART at 351-500</td>
<td>1.7</td>
<td>1.4, 2.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female Sex</td>
<td>1.1</td>
<td>0.9, 1.5</td>
<td>0.390</td>
</tr>
<tr>
<td>Older Age (per 10 years)</td>
<td>1.6</td>
<td>1.5, 1.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline CD4 count (per 100 cells/mm³)</td>
<td>0.9</td>
<td>0.7, 1.0</td>
<td>0.083</td>
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</tbody>
</table>

- Results were similar when restricting the analysis to the 77% of participants with baseline HIV RNA data.
- Adjusted HR1 for deferred vs. immediate treatment was also 1.7 (95% CI, 1.4, 2.2; p < 0.0001)
- HIV RNA was not an independent predictor of mortality
START: 57% Reduced Risk of Serious Events or Death With Immediate ART

- Serious AIDS or non-AIDS event or death: 4.1% vs. 1.8% in deferred vs. immediate ART (HR 0.43; 95% CI 0.30-0.62; p<0.001)

Cost-Effectiveness of Early vs. Deferred ART

- Markov modeling approach
- Johns Hopkins HIV clinic database

<table>
<thead>
<tr>
<th>ART Initiation</th>
<th>Incremental Life-years Gained</th>
<th>Incremental Discounted QALY Gained</th>
<th>Cost Per Life-year Gained</th>
<th>Cost Per QALY Gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 &gt;100 vs 200-350</td>
<td>$10,074</td>
<td>0.75 (0.61)</td>
<td>$25,587</td>
<td>$31,326</td>
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</table>

- "Starting ART earlier ... rather than later ... is a cost-effective strategy (by the generally accepted benchmark in the US)."

Masedi and J.A. JAIDS 2005;39:962-969

Relative Time on Treatment...
Improved Clinical Outcomes With Rapid ART Initiation

- Universal recommendations for treating all HIV-infected persons
- Systematic review of 22 studies of rapid ART initiation (including 4 RCTs)

<table>
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<th>Characteristics</th>
<th>RR (95% CI)</th>
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<td>ART start within 90 days</td>
<td>1.35 (1.15-1.62)</td>
</tr>
<tr>
<td>Retained in care at 12 mos</td>
<td>1.11 (0.99-1.26)</td>
</tr>
<tr>
<td>Viral suppression at 12 mos</td>
<td>1.17 (1.07-1.27)</td>
</tr>
<tr>
<td>LTfu at 12 mos</td>
<td>0.66 (0.42-1.04)</td>
</tr>
<tr>
<td>Died by 12 mos</td>
<td>0.53 (0.28-1.00)</td>
</tr>
</tbody>
</table>

Expedited ART – Experience in Atlanta

- Grady reduced barriers, with goal to begin ART within 72hrs
- Pre-intervention days to ART = 22, Post-intervention days to ART = 4.
Conclusions

- Understanding HIV viral life-cycle is critical to understanding basis of ARV therapy
- Viral replication is very dynamic (1-10 billion new viruses produced a day) and is the driving force of HIV pathogenesis
- ARV therapy interrupts HIV replication completely, halting the most of the damage done by HIV
- ARV therapy protects uninfected cells from becoming infected and has no effect on cells already infected
- All ARV drugs target specific sites within the viral life-cycle

Posttest Question #1

At steady state, when an actively producing cell dies it is replaced by how many newly infected cells?
1. One
2. Twenty five
3. One hundred
4. One thousand
5. It depends on the viral load