HIV Monitoring Technologies for Resource-Limited Settings

Integration of New Monitoring Technologies into ARV Rollout Plans

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Adults & Children Estimated to be Living with HIV/AIDS, END 2003

- **North America**: 790,000 – 1.2 million
- **Caribbean**: 350,000 – 590,000
- **Latin America**: 1.3 – 1.9 million
- **Western Europe & Central Asia**: 520,000 – 680,000
- **North Africa & Middle East**: 470,000 – 730,000
- **Sub-Saharan Africa**: 25.0 – 28.2 million
- **Eastern Europe & Central Asia**: 1.2 – 1.8 million
- **East Asia & Pacific**: 700,000 – 1.3 million
- **South & South-East Asia**: 4.6 – 8.2 million
- **Australia & New Zealand**: 12,000 – 18,000
Estimated no. of Adults & Children newly infected with HIV during 2003

North America
36,000 – 54,000

Caribbean
45,000 – 80,000

Latin America
120,000 – 180,000

Western Europe
30,000 – 40,000

North Africa & Middle East
43,000 – 67,000

Sub-Saharan Africa
3.0 – 3.4 million

Eastern Europe & Central Asia
180,000 – 280,000

East Asia & Pacific
150,000 – 270,000

South & South-East Asia
610,000 – 1.1 million

Australia & New Zealand
700 – 1,000
Antiretroviral Therapy

- The introduction of ART especially HAART changed the outlook of HIV infection in the developed world
  - Reduction in mortality
  - Reduction in morbidity
  - Improvement in quality of life
Mortality and frequency of use of combination antiretroviral therapy including a protease inhibitor among HIV-infected patients with fewer than 100 CD4+ cells/mm³, according to calendar quarter, from January 1994 through June 1997.
Rates of cytomegalovirus infection, *Pneumocystis carinii* pneumonia, and *Mycobacterium avium* complex disease among HIV-infected patients with fewer than 100 CD4+ cells/mm³, according to calendar quarter, from January 1994 through June 1997.
Effects of Changes in Antiretroviral Therapy on Course of HIV Infection

The world has increasingly realized that the benefits of ART must be extended to all mankind. The need for ART in resource limited-settings is a moral imperative which cannot be ignored.
ART in Resource-Limited Settings

- Worldwide 6 million people are estimated to be in immediate need of ART
- Less than 400,000 people outside the advanced countries of North America and Western Europe are estimated to be on ART
  - Most of these are in middle income countries like Brazil
  - Sub-Saharan Africa has a miniscule number of people on ART compared to the magnitude of the epidemic
The scale-up of ARV in resource-limited countries is therefore the only way to go.
There has been a fusion of purpose among various actors in the HIV/AIDS arena which has brought ARV roll out into reality

- The international community
  - Western governments and leaders
  - Multinational organizations
  - Charitable and humanitarian organizations

- Resource-limited countries
  - Political commitment
  - Civil society
  - NGOs, etc
Initiatives assisting roll-out of ARVs

- UN Global Fund to fight AIDS, tuberculosis and malaria
- WHO 3-by-5 campaign
- President’s Emergency Plan for AIDS Relief (PEPFAR)
- National governments
  - Brazil & Thailand initiatives
  - South African “Operations Plan for Comprehensive HIV/AIDS Care, Management & Treatment for South Africa
- Humanitarian Organizations
  - Medicine San Frontier, etc
ARV Roll Out: Barriers

- Cost and Supply of ARVs
- Infrastructure to deliver ARVs
- Monitoring of ART
Monitoring of ART

- Clinical
  - Always required-body weight, organ specific evaluations and patient well-being
  - ? Can it wholly or partially replace aspects of ART monitoring
    - Evidence that it can be used to some extent-Haiti-experience
    - On-going research such as the Development of Antiretroviral Therapy in Africa (DART Study)-Uganda and Zimbabwe
Monitoring of ART

- **Laboratory**
  - Toxicities-organ specific and general
  - CD4 T-Lymphocytes
  - HIV RNA viral load

- **Challenges**
  - Cost of technology-equipment, reagents, maintenance, staff salaries, QA/QC
  - Lack of expertise and training of lab personnel
  - Diverse levels of health providers delivering ART
Monitoring of ART: Toxicities

- Bone marrow, liver, renal, pancreatic, biochemistry, etc
  - Standard equipment available up to various levels of the health delivery infrastructure
    - Rationalization of the use of these tests
      - Eg choice of tests at start of ART
      - ? No routine tests or limited choice of routine tests
      - ? Symptom driven choice of routine test
    - A referral system for patients or specimens
Monitoring of ART

CD4 T-Lymphocytes

- Standard technology (flow cytometry)-limited availability and penetration
  - Cost US$25-US$40/test
- Low-cost assays (manual CD4 assays-Dynal, Coulter, Capcellia)
  - What is their place in the ARV roll-out?
    - When to institute prophylaxis (in addition to clinical, WHO staging, etc)
    - When to start ART
    - Suspected ARV failure
    - Routine assays- ? Every 6 months or yearly
Monitoring of ART
Plasma HIV RNA Viral Load

- **Molecular assays**: expensive and not widely available
  - US$60-$100/test
- **Low-cost assays**: ultrasensitive rt (Cavidi) and p24 assays
  - What is their place in the ARV roll-out?
    - When to start ART
    - Suspected ARV failure
    - Routine assays- ? Not recommended
Monitoring of ART

Other

- P24 antigen-claims
  - Cheaper than HIV RNA tests
  - Requires less expensive equipment
  - That newer assays may give data in a variety of clinical settings comparable to HIV RNA

- β2-Macroglobulin

- Etc…
Hierarchy of Laboratory Setup
Reference → Provincial → District
ART Monitoring in Resource Limited Settings Conclusion

- Large number of patients in each setting
- Variability in resources
- Cheaper tests need to be truly cheap
  - Cost-instrumentation, reagents, etc
  - Infrastructure required-technician training, QA/QC
- Tailor tests to level of health care
- National guidelines must address the issue of monitoring of ART explicitly