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# **Adherence Redux**

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# **To Be Human Is To Err...**

- **People, on the whole, are not particularly adherent or compliant, with healthy, beneficial behavior.**
- **Nothing is unique or new regarding failure of patients to take antiretroviral therapy as directed**
- **Even public health issues – spread of disease to others – have been raised before.**
- **Our vocabulary has evolved: ignorant, vicious, recalcitrant, non-compliant have given way to Non-adherent.....**

# **Relevance of Adherence to Antiretroviral Therapy**

- **Fact: Combinations of three or more antiretroviral agents are highly effective in suppressing viral replication, restoring immune function, preventing emergence of opportunistic infections, preventing progression to AIDS and decreasing mortality.**
- **Fact: Medicine not taken is not effective.**
- **Fact: Ineffective therapy is linked to emergence of resistance.**
- **“Adherence is the achilles heel of antiretroviral therapy.”**

# **Adherence to Highly Active Antiretroviral Therapy Predicts Virologic Outcome at an Inner-City Human Immunodeficiency Virus Clinic – McNabb et al, 2001**

- **Prospective, observational , 3 month study.**
- **Inner city minority population (hx of IDU 58%, alcohol use 40%, psychiatric disorders 63%)**
- **Adherence measured by MEMS, pill counts and patient self-report**
- **Success = <400 copies HIV/ml**
  - **Adherence >95% -100%**
  - **Adherence 90-95% - 100%**
  - **Adherence 80-90% - 57%**
  - **Adherence 70-80% - 29%**
  - **Adherence <70% - 23%**

# **Consistency of Adherence to Antiretroviral Therapy Predicts Biologic Outcomes for HIV-Infected Persons in Clinical Trials – Mannheimer et al, 2002**

- **Prospective measurement of adherence related to therapeutic outcome among pts in salvage regimen post PI failure and treatment naïve pts in 3 arm study (PI based, NNRTI based and both PI & NNRTI containing regimen) over 12 months.**
- **Data for 540 participants to 12 months**
- **Self-report of 7 day pill adherence**
- **HIV < 50 copies at 12 months ( $\Delta$  CD4 cells)**
  - **100% adherent – 66% (  $\uparrow$  179 cells/ml)**
  - **80-99% adherent – 47% (  $\uparrow$  159 cells/ml)**
  - **1-79% adherent – 17% (  $\uparrow$  53 cells/ml)**

# Defining Adherence

- **Based upon studies of viral suppression over time, the taking of medication >95% of time should be the gold standard of adherence, although there is no universal definition.**
- **Adherence as continuous variable may not be applicable to antiretroviral therapy.**



# Measuring Adherence

- Adherence with medical appointments
- Patient self-report
- Prescription fill
- Pill count
- Spot blood or urine drug levels
- MEMS (Medication Event Monitoring System) cap



# MEMS Bottle and Lid



# MEMS 6 Cap in Cradle



# MEMS Problems

- **May under estimate adherence (if patient takes out multiple doses at same time)**
- **Multiple drug regimens require MEMS caps for each drug.**
- **Expensive system.**

# Predicting Adherence

# **Social Support and Patient Adherence to Medical Treatment: A Meta- Analysis – DiMatteo, 2004**

- Published work 1948-2001
- Elements of support:
  - Practical
  - Emotional
  - Unidimensional social support
  - Family cohesiveness
  - Family conflict
  - Married
  - Living with another adult
  - # of people in household

# **Antiretroviral Therapy**

## **Adherence in Brazil** — Nemes et al, 2004

- From *Qualiaids* – a multidisciplinary group in Brazil
- 1972 patients in 60 sites in Brazil interviewed
- Self-report of pill adherence over prior 3 days with >95% = adherent.
- Associated with non-adherence:
  - Care at facilities with less than 100 pts
  - Missed appointments
  - High pill burden
  - Less than 2 yrs of education

# **Medication Adherence Among HIV+ Adults – Effects of Cognitive Dysfunction and Regimen Complexity – Hinkin et al, 2002, 2004**

- **Study of 137 pts**
  - **Neuropsych battery**
  - **MEMS caps to assess adherence; >95% = good adherence**
  - **Mean adherence rate 80%; 34% > 95% adherence**
- **Dosage complexity – qd & bid vs tid: 84% vs 73% adherence, major effect in the cognitively impaired**
- **Predictors of adherence**
  - **Older Age (>50 yrs) = better adherence (mean 88% vs. 78%), or older pts 3x more likely than younger to be >94% adherent**
  - **Global NeuroPsych impairment, poor adherence**



# Cue-dose training with monetary reinforcement - Rigsby et al, 2000

- Pilot project with 55 subjects
- cue-dose training, cue-dose training + \$\$ (\$2 per correctly taken dose).
- During 4 wks of active intervention, cue-dose plus \$\$ group had significant improvement vs controls and cue-dose groups.
- At 8 wks after intervention period, adherence back to baseline for all groups.

# **Impact of a Patient Education Program on Adherence to HIV Medication – Goujard et al, 2003**

- “Ciel Bleu” randomized 367 pts on long term therapy & stable 3 drug HAART regimen to Standard of Care or Education program (3 or more 1 h sessions over 12 months).
- Adherence judged by self-report.
- Education group had higher adherence throughout, as did the control group at month 18.
- No improvement in CD4 counts or viral load – *but population was heavily experienced at entry*



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# **Conclusions and Recommendations**

- **Simplified HAART regimens will improve adherence.**
- **Decreased adverse effects will improve adherence.**
- **Patient characteristics and belief's will continue to have major impact on adherence.**

# Conclusions and Recommendations II

- **Establish trusting relationship.**
- **Individualize antiretroviral therapy.**
- **Screen for factors that are associated with non-adherence (depression, cognitive impairment, substance abuse, lack of practical and emotional support) and address before therapy.**
- **Prioritize adherence not only at initiation of therapy but at every visit thereafter.**
- **Remember, adherence likely to remain the “achilles heel” of antiretroviral therapy.**