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 (Δ CD4 cells)
  - 100% adherent – 66% (↑ 179 cells/ml)
  - 80-99% adherent – 47% (↑ 159 cells/ml)
  - 1-79% adherent – 17% (↑ 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 a 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

- 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
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.