HIV/AIDS: Past, Present, Future

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Disclosure Statement

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Objectives

1. Review the history of HIV/AIDS
2. Learn from the past regarding the role of hospice and palliative care in management of HIV
3. Review mortality trends for HIV/AIDS

• When did CDC report the first cases of AIDS?
  A) 1981
  B) 1982
  C) 1991
  D) 1992

1981: First Cases Recognized

• The CDC publishes a report from Los Angeles of five young homosexual men with fatal or life-threatening PCP pneumonia.

• PCP and KS turn out to be two of the major "opportunistic infections" that kill people with AIDS.

1982

• The CDC calls the new disease acquired immune deficiency syndrome or AIDS.

• AIDS is seen in people with hemophilia.
AIDS Timeline

- AIDS-related illnesses have killed more than 30 million people since 1981.

- An estimated 1.1 million Americans are among the 33 million people worldwide who are now living with HIV.

1991-1992

- The red ribbon is introduced as a symbol of AIDS solidarity.
- Magic Johnson announces he is HIV positive.
- Queen lead singer Freddy Mercury dies of AIDS.
- AIDS becomes the leading cause of death in U.S. men aged 25-44.
- The FDA licenses the first rapid HIV test.

When was AZT approved?

A) 1986
B) 1987
C) 1989
D) A & C

Drug Development

- 1987 AZT
- 1989 ddI
- 1991 ddC
- 1992 FDA approved combination use of AZT and ddC
- 1995 first protease inhibitor
- 1996 first non-nucleoside reverse transcriptase inhibitor
- 1997 1st time the number of deaths from AIDS drops in US

1996-1997

- A treatment breakthrough: The AIDS drug cocktail -- highly active anti-retroviral therapy or HAART
- Decreased HIV viral load to undetectable levels.
- AIDS deaths decline by more than 40%.
Epidemiology

- After rapidly increasing since the 1980s, the annual rate of death due to HIV disease peaked in 1994, decreased rapidly through 1997, and became almost level after 1998.

1998-2000

- Side effects of HAART increased
- Treatment failures increased
- Newer drugs started to develop

HIV Medicine

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Changing mortality rates and causes of death for HIV-infected individuals living in Southern Alberta, Canada from 1984 to 2003

HIV Medicine

AIDS Related Diseases
1. Gastrointestinal:
   Symptoms:
   - Diarrhea
   - Wasting
   - Abdominal pain
   - Infections
   Pathogens: Candida albicans, cytomegalovirus, Microsporidia, and Cryptosporidia.

Opportunistic Oral Yeast Infection by Candida albicans in an AIDS Patient

Source: Atlas of Clinical Oral Pathology, 1999

AIDS Associated Disease Categories
2. Respiratory:
   Partial list of respiratory problems associated with AIDS:
   - Bronchitis
   - Pneumonia
   - Tuberculosis
   - Sinusitis
   - Pneumonitis

AIDS Associated Disease Categories
3. Neurological:
   Opportunistic infections, tumors of central nervous system, and AIDS dementia complex (Memory loss, motor problems, difficulty concentration)

AIDS Associated Disease Categories
4. Skin and mucocutaneous Disorders:
   - Kaposi's sarcoma
   - Herpes zoster (shingles)
   - Herpes simplex
   - Thrush
   - Invasive cervical carcinoma

5. Eye Infections:
   - CMV retinitis
   - Conjunctivitis
Extensive lesions of Kaposi’s sarcoma in AIDS patient.
Source: AIDS, 1997

Non-Hodgkin’s Lymphoma & ascites in AIDS patient
Source: Tropical Medicine and Parasitology, 1997

2008
• The CDC announced that improved surveillance showed HIV in America is worse than we’d thought: 1.1 million infected, up 11% from 2003.

2009-2010
• Polls indicate that Americans no longer consider AIDS a major problem.
• New infections continue to soar. Over half are in men who have sex with men, but 31% are in heterosexuals. African Americans -- 12% of the U.S. population -- get 45% of new HIV infections.

Take Away Points
• History repeats itself. Hospice played a significant role in early days of HIV and palliative medicine will play significant role in the future.
• Physicians who were managing HIV/AIDS patients in the past used to have expertise in both HIV and palliative care. Now these two fields have separated creating a gap

HIV - Present
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Disclosure Statement

Dr. Merlin has disclosed no relevant financial relationships.

Current Treatment Guidelines

- ART initiation:
  - Recommended in patients CD4 < 500 cells/mm3
  - should be considered in all patients
  - in certain conditions regardless of CD4

http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf
http://www.iasusa.org/guidelines/

Current Treatment Guidelines

- Therapy is lifelong
- First line regimens: choice of TDF/FTC/EFV, ATV/r + TDF/FTC, DRV/r + TDF/FTC, Ral + TDF/FTC – low pill burden, minimal side effects

http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf
http://www.iasusa.org/guidelines/

Life Expectancy

- Approaching normal:
  - Best scenario: 10 years less lifespan than normal
  - Starting ART when severely immunodeficient: 10-20 years worse than that

A 20 year old with a new diagnosis of HIV and a CD4 count of 500 cells/mm3 starting ART can expect to live to age 63 based on current data


Medical Comorbidities

- Cardiovascular disease
- Metabolic syndrome
- Non-AIDS-defining malignancies
- Renal disease
- Frailty
- Osteoporosis
- HIV/HCV Coinfection

Psychiatric Comorbidities

- 41% for depression and other mood disorders, 21% for anxiety, and 21% for substance abuse

Chronic Pain

- Chronic pain: 39-55%
- Recent study:
  - 154 ambulatory HIV-infected patients, 49% reported pain, of whom 51% had moderate to severe pain
  - Pain associated with psychological symptoms


Blueprint for HIV Treatment Success

Ulett et al. AIDS Pt Care STDs (in press).

Blueprint at a Population Level


Take Home...

- Most patients with HIV should be on ART
- Patients on ART should lead long lives
- This assumes retention, adherence
- In addition to HIV-related morbidity, patients with HIV have a variety of comorbidities that must be addressed

Take Home...

- Opportunities for palliative care:
  - Symptoms associated with comorbidities; pain
  - Health behaviors (retention/adherence)
  - AIDS-related morbidity; advanced care planning; end-of-life care
HIV and Palliative Care: Future Trends

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Disclosure Statement

Dr. Selwyn has disclosed no relevant financial relationships.
Changing Demographics of HIV/AIDS in the United States

- Increasing concentration of HIV infection among racial-ethnic minorities, particularly African-Americans and Latinos
- Growing discrepancies in survival by demographic and HIV risk category.
- ‘Grim democratization’ of pre-HAART era now replaced by disparities in health outcomes related to underlying social inequalities.
- Aging population of HIV ‘survivors’ (e.g., chronic disease, co-morbidities, polypharmacy)
- Challenges for both disease-specific and palliative care: how to avoid double standard of “HAART for the rich, palliative care for the poor”?

Palliative Care and HIV

- Decreased HIV mortality rates = increased prevalence of HIV/AIDS
- Prolonged survival = greater need for ongoing care
- Prolonged survival in symptomatic patients = greater need for palliative medicine interventions
- “Conversion of death to disability”
- Difficult in acceptance of death in the era of HAART
- Increased mortality risk in vulnerable populations
- Increasing co-morbidities and ‘aging cohort’ effects
  → Increasing need for palliative care for patients living with HIV/AIDS

Special Challenges for Palliative Care for HIV/AIDS in the HAART Era

- Pain and symptom management
- End-of-life issues
- Changing prognostic indicators
- Role of HAART
- Pain management in drug users
- Co-morbidities
- Aging population
- Pharmacologic interactions
- Changing therapeutic paradigms
- Social context and stigma of HIV/AIDS


- Opportunistic infection era
  - Crisis management
  - Treatment of opportunistic infections
  - Palliative care
  - Primary care
- Antiretroviral era
  - Focus on viral pathogenesis
  - Specialization and medicalization of HIV care (‘HIV specialist’)
- Chronic disease era
  - HIV disease management
  - Co-morbidities and aging
  - Primary care

Changing Pattern of Mortality in Patients with AIDS, 1985-2010
Standardized Rate Ratios of AIDS-Defining and Non-AIDS-Defining Types of Cancer; ASD and HOPS Cohorts vs. General Population (SEER)*, 1992-2003

*Adapted from Patel et al, Annals of Internal Medicine, 2008

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Need for New Prognostic Criteria for Advanced HIV/AIDS

National Hospice Organization Criteria (1996):
- CD4+ nadir < 25 cells/mm
- HIV RNA > 100,000 copies/ml
- disseminated MAC (untreated)
- serum albumin < 2.5 g/dl
- AIDS-defining conditions
- advanced HIV-related dementia
- visceral Kaposi's sarcoma
- CNS lymphoma
- severe cardiomyopathy
- PML
- cryptosporidiosis
- severe wasting
- toxoplasmosis
- chronic severe diarrhea
- advanced HIV-related dementia

How account for HAART?
- Clinical Challenges in an Aging HIV-Infected Population
- How account for HAART?
- e.g., documented failure to respond to or tolerate an adequate trial of antiretroviral therapy (?) Additional criteria suggestive of short-term mortality:
  - impaired activities of daily living
  - clinically significant cognitive impairment
  - serious medical co-morbidity
  - life-threatening malignancy, end-stage cirrhosis/liver failure, renal failure not on dialysis, and/or other organ system failure

Need for current-era prospective studies to define changing clinical trajectory and indicators of mortality risk.

Causes of Death and Predictors of Mortality: Montefiore HIV Palliative Care Program

Patients referred to HIV Palliative Care Program: n=230
No. of deaths: 120 (54%)
Causes of deaths:
- *Selwyn PA, J Palliative Med, 2003
- Shen JM, JAIDS, 2005

Predictors of mortality: ↑ Age, ↑ impairments in activities-in-daily living, ↓ Karnofsky (P < 0.0001 for all), not CD4+ count, viral load, or HIV disease stage

Co-morbidities and HIV Disease
- Metabolic issues
- Diabetes
- Dyslipidemia
- Cardiovascular disease
- Renal disease
- Hepatitis B & C
- Non-AIDS defining cancers
- Pulmonary disease
- Psychiatric illness

Clinical Challenges in an Aging HIV-Infected Population
- Immune senescence
- Lower CD4 counts at diagnosis
- Lower time to viral suppression on HAART
- Slower rate of CD4 increase on HAART
- Shorter survival after diagnosis
- Higher rates of co-morbid illness
- Polypharmacy/pharmacokinetics
- Age-related cognitive deficits/dementia
- Frailty, osteopenia/osteoporosis
- Social isolation
- ‘Premature aging’

Estimated numbers of persons living with AIDS, by year and selected characteristics, 2003-2008, United States*

*Adapted from DHHS, HIV/AIDS Surveillance Reports, 2005-2009

Adapted from CP Martin et al, Am J Med, 2006
**Psychosocial Issues for Palliative Care in the Era of HAART**

- From ‘fate’ to ‘tragedy’: the universal becomes selective
- Renewed isolation/ostracism of the dying: death as reminder of the fallibility of HAART
- Empowerment, guilt, and blame: new hope for success/greater possibility for failure
- Medicalization of AIDS challenge to patient-provider communication
- Need to focus on goals of care
- Bereavement needs of long-term survivors
- Caring for caregivers

**Clinical Issues in Palliative Care for End-Stage Liver Disease from HCV**

- decisional capacity/advance directives
- hepatic encephalopathy
- ability to maintain p.o. intake
- substance abuse history
- family history of HCV, HIV, and/or substance use
- ‘aging cohort’ effects (co-morbidities)
- symptoms: fatigue, ascites/peripheral edema, pain (risk of NSAIDS, acetaminophen), bleeding (coagulopathy, varices), pruritus, hypogonadism
- altered hepatic drug metabolism (e.g. opioids, benzodiazepines)
- possibility and reality of liver transplantation

**HIV and HCV: Implications for Mortality and Palliative Care**

- HIV ~ 1 million
  - ~ 15-18,000 deaths/yr
  - ~ 50,000 new infections/yr
- HCV ~ 2.7 million
  - ~ 10-12,000 deaths/yr
  - ~ 40,000 new infections/yr
- HIV → ↑ HCV progression/mortality
- Effective HIV treatment → ↑ HCV morbidity/mortality in co-infected patients surviving longer with HIV
- Liver failure increasingly significant cause of death in co-infected patients
- Palliative/end-of-life care increasingly involves HCV-related issues in co-infected patients

**Conclusion: Challenges for Palliative Care for AIDS in the Era of HAART**

- Attending to palliative care needs within ‘curative’ paradigm of HAART in which patients are not ‘supposed’ to die
- Addressing complicated pain and symptom management issues in chronically ill, aging, patients over extended period of time
- Managing iatrogenic complications, co-morbidities, drug interactions, and co-existing substance use disorders
- Maintaining focus on psychosocial needs to patients/families with progressive, incurable illness
- Overcoming the false dichotomy of HIV-specific and palliative care paradigms: beyond ‘either…or’, to ‘both…and’
- Goal: Providing integrated care across the continuum of HIV/AIDS, improving quality of life, treatment outcomes, and end-of-life care for patients and families
2012 AAHPM & HPNA Annual Assembly

Patient: MT*

Background…
- 58 year old male, dx'd HIV+ 1998, HCV+ 2000
- Former IDU on MMTP, chronic alcohol use
- Lives with 84 year old mother
- No hx of OIs, CD4+ nadir ~ 350 cells/mm3
- No hx of OIs, CD4+ nadir ~ 350 cells/mm3
- No consistent HAART usage
- Repeatedly declined follow up for evaluation of HCV
- Admitted to hospital x 2 in 2001 for bacterial pneumonia
- Readmitted for bacterial pneumonia and oral thrush in 2002

*Pseudonym

Patient: MT

Hospital Admission…
- Treated for pneumonia with good response
- Noted to have clinical stigmata of cirrhosis, with mild ascites and peripheral edema
- Pt 70 K, INR 1.7, albumin 3.1, bilirubin 1.3
- Referred to HIV skilled nursing facility for rehab care and initiation of HAART
- Started on TDF/3TC/ATV/r, FLU

Patient: MT

2 months later…
- CD4+ ↑ 400 cells/mm3, VL < 75 copies/ml
- HCV genotype 1a, VL > 3 million copies/ml
- Evaluation by GI consult: cirrhosis probably too advanced to qualify for HCV Rx, but willing to perform biopsy; pt declined
- Started on spironolactone/Na+ restriction, with good clinical response
- Tolerated all meds well, d/c'd home after 4 month stay in nursing home, with primary care follow up through MMTP

Patient: MT

6 months later…
- Readmitted to hospital with mental status changes (forgetfulness, intermittent disorientation, strange behavior), ammonia level = 90 mmol/L. Complete neuro workup ↑ Dx = hepatic encephalopathy, precipitated by dehydration
- Treated with lactulose and fluid management → improved mental status
- D/C'd home with outpatient follow up

Patient: MT

6 months later…
- Readmitted from home to HIV SNF, after several additional episodes of waxing and waning mental status, 'failure to thrive,' elderly mother no longer able to care for him
- Required lactulose 30-45 cc tid-qid to maintain mental status
- Remained on supervised HAART, with excellent response, CD4+ consistently > 500 cells/mm3, VL undetectable
- Increasing peripheral neuropathy sx, requiring oxycodone, gabapentin
- Able to go home to spend weekends with mother every 6-8 weeks, though would often return with worsened mental status, at times after having consumed alcohol

Patient: MT

6 months later…
- Increasingly frequent episodes of worsening mental status and/or ascites
- Requiring careful titration of lactulose, diuretics, fluids, Na+ intake
- Methadone dose decreased due to apparent oversedation
- Continued excellent HAART response
- Occasional episodes of decreased p.o. intake, with worsening mental status when unable/unwilling to take p.o.lactulose → lactulose enemas
- Agreement with health care agent (ex-wife) that pt needed indefinite long-term care; no longer feasible to consider D/C home
Patient: MT
6 months later…
- Addition of rifaximin due to progressively worsening mental status
- Family meeting to address issues of feeding, routes of administration of lactulose, decisions about rehospitalization; decided to pursue primarily palliative care plan, to remain at SNF
- Several episodes of decreased mental status, anticipatory meetings with family re: likelihood of imminent death, followed by pt's unexpected and unexplained return to 'baseline', over several months
- Treatment of probable aspiration pneumonia, metatarsal osteomyelitis
- Two episodes of epistaxis, treated with nasal packing, Vitamin K
- Continued calibration of fluids, diuretics, monitoring of electrolytes

Patient: MT
4 months later…
- Pt becoming more generally somnolent, no longer ambulatory, significantly decreased p.o. intake
- No longer taking p.o.meds consistently
- Decision to D/C HAART
- Decision to D/C methadone and oxycodone, convert to SQ MS continuous infusion
- Unable to take lactulose or rifaximin; given overall deterioration, decision to not continue lactulose enemas
- D/C blood draws; intermittent IV diuretics if felt to be able to provide palliative benefit

Patient: MT
2 weeks later…
- Progressive somnolence; occasional agitation and/or dyspnea. Rx'd with low dose SQ benzodiazepines
- Attentive skin and mouth care
- SQ scopolamine for pre-terminal respiratory secretions
- Pt died peacefully with family at bedside

Patient: OP*
Background…
- 51 y.o. male, dx'd HIV+ 1993, severe chronic alcoholism
- Poor engagement and adherence with care
- Minimal HAART exposure due to chronic substance use/loss to follow up
- Unstable living situation
- Family unable to care for him
- Admitted to hospital in early '04 with severe dementia, psychomotor retardation, incontinence, inability to walk

* pseudonym

Patient: OP
Initial work-up…
- CD4+ 80 cells/mm3
- HIV RNA 450,000 copies/ml
- MRI of brain = consistent with severe ADC
- LP: non-diagnostic
- No evidence of acute OI's or other pathology (besides advanced HIV disease)
- Patient bedbound, severely demented, able to be fed with assistance; requiring 24 hr. nursing care

Patient: OP
One week later…
- Little improvement in symptoms
- No acute complications
- With family's assent, pt discharged to HIV skilled nursing facility
- Intention for 'terminal care'
Patient: OP

Evaluation at HIV skilled nursing facility...
- Review of HIV history suggested no adequate trial of HAART
- Pt assessed to be able to take p.o. medications safely with assistance
- Discussed with family, suggested that in supervised environment pt’s symptoms might benefit from HAART
- Agreed to medication trial: started on TDF/FTC/EFV, tolerates medications well

Six weeks later...
- Pt receiving intensive nursing care, bedside PT
- Slow improvement in mental status: responding slowly to questions, starting to interact with staff
- CD4+ ↑ 140 cells/mm³
- HIV RNA ↓ 28,000 copies/ml

Six weeks later...
- Pt starting to feed self with fingers, speaking spontaneously in monosyllables
- PT notes improving strength and coordination
- CD4+ ↑ 230 cells/mm³
- HIV RNA ↓ 1400 copies/ml

Four weeks later...
- Pt walking with assistance
- Eating without assistance
- Return of fluent, appropriate speech
- Family and staff talk about ‘miracle’ recovery

Patient: OP

Eight weeks later...
- Pt becoming involved in group activities, excursions
- Family started to take pt out on day trips
- After returning from one such trip, a nurse’s aide noted alcohol on pt’s breath
- When confronted, pt admitted he had stopped at local tavern for a beer after family had dropped him off
- Restrictions placed on day passes: only permitted to leave with ‘responsible adult’

Two weeks later...
- Next time returned from day pass with brother, both pt and brother had alcohol on breath
- Team meeting with pt and family: no further leaves except for medical appointments
- Mandated AA meetings at facility
- Supervised disulfiram treatment as condition of remaining in facility
- Pt advised that further substance use would result in involuntary discharge

Patient: OP

Four weeks later...
- Pt noted to have absconded through first floor window of facility; returned several hours later with florid disulfiram reaction (sweating, flushing, abdominal cramping)
- Psychiatric consultation: pt deemed capable to make decisions, though somewhat lacking in judgment, not felt to warrant involuntary hospitalization or commitment
- Nursing and medical staff conflicted about necessary action, especially given pt’s remarkable recovery (most recent CD4+ 350 cells/mm³, HIV RNA < 50 copies/ml)
- After one more episode of elopement and alcohol use, pt was involuntarily discharged to homeless shelter (family unable to take him)

Two weeks later...
- Pt found walking down the middle of the street, disoriented and disheveled
- Brought to psych ER, admitted to inpatient unit
- After several weeks in hospital, discharged to locked long-term psychiatric facility
- Uncertain follow up for HIV medical treatment