HIV / AIDS: THE HEART OF THE MATTER

David Jankelow
“to know syphilis is to know all of medicine, because of the multisystem involvement and variable manifestations of the disease”
HIV - protean disease of the era

• diverse manifestations & susceptibility to infection

in many respects to know AIDS is to know all of medicine!
2010: +34 million living with HIV worldwide; up 17% from 2001

Sub-Saharan Africa (12% global population); most affected region; with 68% of all living with HIV

Pandemic severe in RSA; 5.6 million affected!

“Represents the heart of darkness for any physician”, given the overwhelming implications in terms of mortality, morbidity & resources
• more effective Rx’s - longer survival, new complications of late-stage infection; HIV-heart disease

• growing group with acquired HD – tremendous global impact

• % develop clinically apparent disease relatively small; burden substantial in view of exceptionally high prevalence of HIV in Africa

• require cardiac Dx & Rx resources; screening to detect cardiac abnormalities early & base Rx on these findings
The heart is now key for the prognosis of HIV/AIDS pt's in developed countries, where cardiovascular disease is the most common cause of death, toppling even AIDS itself.

- mechanisms: direct myocardial & coronary HIV infection, autoimmune responses; adverse risk factor profile
- cardiac disease usually overshadowed by manifestations in other organs systems
- involvement at autopsy exceeds number with significant heart disease during life
• premature CAD with HIV/AIDS evoked concern in high-income countries (post-ART Rx era)

• most common cardiac manifestations Sub-Saharan Africa:
  - cardiomyopathy
  - pericardial disease (often TB)
  - pulmonary hypertension
  - endocarditis & valve abnormalities

• subclinical echocardiographic abnormalities independently predict adverse outcome & identify high-risk pt’s who can be targeted for early intervention & Rx
• cardiac complications occur late in the disease course

• clinical apparent in a small %

• very few clinical studies - based on autopsy & echocardiography

• poor information on the impact of Rx
- CHF; dyspnea often incorrectly attributed to lung disease – LV dysfunction
- echocardiography useful to identify the cause
- pericardial effusion
- RV dilation
- arrhythmias
- endocarditis
“Most of the cardiac problems are clinically unrecognized because they can easily be attributed to infectious disease complications or lung disease or things like that. All the signs and symptoms that you would associate with heart failure can sometimes be attributed to other causes. So what we've always pushed is that if you don't look, you don't know.”

Steven Lipshultz 2000
• study to assess incidence of unsuspected cardiac abnormalities in ambulatory VS hospitalized pt’s with HIV

• 60 hospitalized pt’s

• 40 (asymptomatic / early-stage disease) out-pt’s

• WHO: normal activity
  – minor LOW/ mucocutaneous manifestations/ zoster/ URTI’s
## Hospital Patients

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<tr>
<th>Condition</th>
<th>HOSPITAL</th>
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<table>
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Assessment of LV Function
fractional shortening =
EDD-ESD/EDD
Normal > 27%
27 of 60 hospital pt's had unsuspected cardiac abnormalities on echocardiography:

* pericardial effusion: 16 (17%)
* dilated RV: 16 (17%)
* LV dysfunction: 5 (5%)
Echocardiographic abnormalities & CD4

Significantly lower CD4 in pt’s with cardiac lesions:

u 166
u 402
u p<0.0001
Pericardial Effusion: 16 pt’s (16%)

- extremely low CD4 counts
- 11 small <10mm
- 3 moderate 10mm- 20mm
- 2 large >20mm
- 1 tamponade - pericardioscentesis - TB

- TB proven on pericardioscentesis / resolved with anti -TB Rx
- advanced immune deficiency
Cardiac tamponade due to a large pericardial effusion
resolution of a pericardial effusion after anti-TB Rx & oral steroids
Pericardial Effusion

- pre-HAART: common in advanced HIV-disease with prevalence rates up to 45%
- most are asymptomatic
- effusions small
- independent predictor of mortality & poor prognosis
asymptomatic pericardial effusion may signal end-stage HIV disease

- 231 pt’s; 5yr study
- pericardial effusion 12%/y
- 80% small
- shortened survival
- 36% (PE) vs 93% (6m)

Heidenreich; Circulation 95: Prospective Evaluation of Cardiac Involvement in AIDS
• idiopathic in the majority of HIV-infected pt’s (industrialized countries)

• in Africa, the majority of pericardial disease in HIV-infected people is caused by treatable microorganisms

• *M tuberculosis*: cause of large effusions in 86-100% of HIV-infected pt’s (Africa)

• non-HIV infected pt’s have other etiologies in 30–50%

• atypical Mycobacteria / pyogenic / lymphoma & Kaposi / Cryptococcus / Nocardia / viral infections
• HIV modifies the clinical presentation of TB pericarditis - high incidence of co-existing CMO

• histological pattern affected by the immune status with fewer granulomas with severely depleted CD4 counts

• lower incidence of effusive-constrictive disease

• less likely to present with ascites & more likely to have an effusion on echo
• small effusions: exhaustive search for the cause is unnecessary - not progressive

• usually no definitive etiology

• larger effusions - aggressive evaluation and Rx
TB pericarditis:

- no conclusive evidence for an optimal duration of Rx of extra-pulmonary TB in HIV-patient’s; 6-month’s Rx (WHO)

- access to HAART – timing & introduction of ART’s controversial

- potential problems: drug interactions & immune reconstitution

- advanced HIV / markedly CD4 (<100) – mortality benefit (early HAART)

- adjunctive steroids controversial; no significant mortality benefit in HIV +ve pt’s with TB pericarditis

- Investigation of the Management of Pericarditis in Africa (IMPI) Registry - expected to report its findings in the near future
pericardial effusions in HIV-infected pt’s are less frequent in the era of antiretroviral treatment

- HIV-HEART study: prospective & multicenter cohort
- small effusions in only 2 of 802 HIV+ve out-pt’s (2004-2006); 85.2% on HAART
- effective blockade of viral replication; reduced opportunistic infections, might explain the low effusion rate

Lind et al: Pericardial effusion of HIV-infected patients - results of a prospective multicenter cohort study in the era of antiretroviral therapy; European Journal of Medical Research 2011, 16:480
Left Ventricular Dysfunction

- Dilated LV: 6 patients’ EDD > 5.7 cm
- Mean EDD: 6.23 ± 0.51 cm
- LV dysfunction (FS < 27%): 5 patients
- Mean FS: 16.6 ± 4.2%
- CCF in 1 pt
Dilated Cardiomyopathy:

- common manifestation of late stage HIV infection – significantly improved survival

- trigger for HAART independent of CD4

- pre-HAART era: 15.9/1000pt’s (PM & echo)

- Africa: 9-57% (echo)

- LV dysfunction may occur in acutely ill pt’s (even outside setting of HIV) – distorted the figures
• CMO less frequent in developed countries, since introduction of HAART

• 8.1% - 1.8% : 7X pre-HAART (Pugliese et al: J infection 2000:40:282)

• no conclusive evidence that HAART reverses CMO

• myocardium remains healthier - preventing profound immunosuppression

• developing countries; availability of HAART scanty & role of other factors NB
• pathogenesis largely unknown—likely multifactorial
• direct infection of myocardial cells by HIV-virons (CD4-independent infection GP 120 & Tat),
• immune activation / co-infection with other viruses (coxsackievirus B3, CMV)
• as well as nutritional deficiencies, autoimmune factors (increased anti-α myosin antibodies), drug toxicity (AZT)
• pathology: myocarditis in > half of pt's
HIV-CMO associated with more advanced immunosuppression, CD4 counts: independently associated with death

- median survival: 101 (CMO) vs 472 days
- CMO (CD4 < 100)

Currie et al: BMJ 94
• Rx HIV-CMO is unclear

• afterload BB’s, aldosterone I’s: cornerstone of Rx of other types LV dysfunction

• remains unknown: role of inflammation & immune response

• children with HIV & LVEDD: LVEF after Rx with IVI IG’s; suggests that myocardial impairment is immunologically mediated

  – Lipshultz SE et al. Immunoglobulins and left ventricular structure and function in pediatric HIV infection. Circulation 1995;92:222
10 million children with HIV!

- prognosis of HIV-CMO worse than other non-ischaemic types


- children with vertical transmission of HIV

- even mild LV dysfunction associated with overall high mortality

- HIV-Heart study
**pulmonary hypertension & RV dilatation:**

*16 (16%) pt’s*

*RVEDD : 3.39 ± 1.37 cm*

*PAP : 46 ± 7.2 mmHg*

- did not occur in the absence of respiratory disease / LV dysfunction

- PHT - pneumonia / hypoxia / PCWP

- successful Rx - RV afterload - normal RV dimension
HIV associated pulmonary arterial hypertension (PAH):

- prevalence - 1/200 vs. 1/200000 (general pop); constant since the advent of HAART

- high mortality & progressive course; median survival 1.3 vs 2.6 years in HIV-ve matched controls

- association independent of 2° causes

- asymptomatic PASP is frequent; 35.2% of HIV pt’s PASP >30 mm Hg vs. 7.7% of non-infected controls
Pathogenesis not defined: pulmonary vessel endothelial proliferation & vasoconstriction triggered by pleomorphic cytokines (e.g., endothelin-1, IL-6, TNF) released by HIV-infected pulmonary macrophages - not potential targets for Rx.
• Rx HIV-PAH & role of HAART unclear

• few studies of the role of pulmonary vasodilators: Bosentan & prostacyclin analogues

• Swiss cohort study: HAART prolongs survival & reverses underlying physiology - RVSP-RAP PG 3.2 mm Hg in ART pt’s; 9.0 mm Hg in controls

• specific drugs: use of a ritonavir-boosted PI & Abacavir independently associated PAH
• HIV not associated with ↑ risk IE

• SA (prospective study of risk factors for IE),
  – only 1/92 pt’s HIV +ve
  – main factors: RVD in 76%, congenital HD, prosthetic valves, hx of IE

• high prevalence of both HIV & RHD (Africa); more cases of IE that are coincidentally HIV+ve

• IVI drug abusers – right-sided IE

• S Aureus (75% of cases); incidence of Gram-ve organisms & fungi – worse prognosis

• nonbacterial thrombotic endocarditis; in 3-5% of Western series (pre-HAART); predilection for pt’s with the wasting syndrome; not described in Africa
• overall incidence of unsuspected cardiac abnormalities (HIV infected pt’s) - 27%

• associated with late-stage infection

• depends on the stage of HIV disease

• degree of immunosuppression correlates with the presence of cardiac disease

• significantly lower CD4 counts (166 vs 402/ul)
• prospective, clinical registry: data from all de novo cases of HD presenting @ CH Baragwanath 2006–08

• largest study of the spectrum of cardiac manifestations of HIV/AIDS relative to de novo advanced HD in sub-Saharan Africa

• 518 of 5328 de novo cases of HD identified as HIV+ve (9.7%); 54% on HAART
196 cases HIV-CMO

- **viral load**: 110,000 vs. 19,000; \( P = 0.018 \)
- **CD4**: 180 vs. 211; \( P = 0.019 \)

**CMO**: most common primary dx attributable to HIV/AIDS:

- 128 (12.5%) cases pericarditis / effusion
- 42 cases PHT
- 14 cases CAD – AMI; IVUS - fresh thrombus & minimal underlying atherosclerotic disease; mean age 41y’s

196 cases HIV-CMO

- **viral load** 110,000 vs. 19,000; \( P = 0.018 \)
- **CD4** 180 vs. 211; \( P = 0.019 \)

- **introduction of HAART** more likely to be on HAART (64%) – cautious interpretation

- **immune reconstitution syndrome** higher than usual cardiac involvement – paradoxical inflammatory reaction

in agreement with other reports suggesting CAD in HIV/AIDS has a different pathophysiology than non-infected IHD pt’s

128 (12.5%) cases pericarditis / effusion
accelerated atherosclerosis in young HIV+ individuals without traditional coronary risk factors

- individuals with HIV infection are at risk for IHD events
- clinical presentations distinct
- ACS: more than a decade younger
- males; smokers; low HDL
- tend to have 1-vessel disease rather than MVD
- PCI: restenosis & stent related complications
mechanism of early atherosclerosis in HIV not well understood: vascular inflammation; viral effects; HAART; metabolic changes are important
overall effect of HIV infection is toward an atherogenic lipid profile:

• metabolic changes with HIV infection; 2-fold:

• early HIV stages, Tg’s predominantly, HDL & small, dense LDL’s

• after initiation ART & particularly associated with PI’s: LDL with little change in HDL

• Swiss HIV Cohort: LDL & TG’s 1.7–2.3X in pt’s on HAART
Lipodystrophy:

- uniform subcutaneous & peripheral fat loss, relative visceral fat - central adiposity, fat accumulation in the neck & dorsocervical region
- 20–35% within 12–24m’s after starting HAART
- combinations of HAART – lipoatrophy: PI’s & concomitant use of NRTIs, Stavudine & Didanosine
- prevalence DM & HT increased
uncontrolled HIV replication - □
CV risk & other non-AIDS complications

relative contribution of HIV vs. potential adverse effects of HAART to CHD risk, unclear

SMART study: randomized 5472 HIV+ve pt’s to strategy of viral suppression (continuous HAART) vs. drug conservation (intermittent Rx)

episodic Rx □risk of opportunistic disease / all cause death

continuous HAART: □risk of fatal / non-fatal CAD (HR 1.6)
TREATMENT OF CAD: existing recommendations in uninfected pt’s

- 2 particular aspects in HIV-pt’s:
  - potential role of HAART w.r.t CVD
  - Rx of hyperlipidaemia in HIV - goals same as for HIV-ve pt’s

- guidelines: HAART (asymptomatic pt’s) CD4 <350, with “individualized” Rx >350

- earlier HAART: high CV risk & other features (viral loads >100000/ml, \( CD4 >100/ul/yr \), hepatitis B/C or nephropathy)

- earlier initiation of Rx (higher CD4’s) improves CV risk ?
Treatment of hyperlipidaemia in HIV infected individuals
consider specific drug–drug interaction

PIs inhibit CYP3A4; NB Ritonavir

Simvastatin (contraindicated) as concentrations dramatically with PI – rhabdomyolysis

Atorvastatin lesser degree – lower doses

Pravastatin not metabolized by CYP3A4 - 1st line Rx

Roseruvastatin Atazanavir/Ritonavir & Lopinavir/Ritonavir; limit to 10mg

Rx of TG – fibrates

address traditional modifiable CVD risk factors (e.g. smoking); diet, exercise
CONCLUSION

• importance of cardiac involvement in HIV / AIDS, should not be overlooked

• shortness of breath; common; consideration of CMO / pericardial disease / PAH - echocardiography

• HIV will constitute an important cause of heart disease

• prevalence of older HIV individuals; by 2015 (CDC), over ½ of all HIV-pt’s will be >50 y’s

• chronic diseases, atherosclerosis, heart failure
• Importance of cardiac involvement should not be overlooked
• HIV will constitute an important cause of heart disease
• co-ordination between ID & cardiology – improve quality of care to develop an individualized Rx plan
• An important barometer of current & future impact of HIV/AIDS on the heart health of urban Africa

• HIV - CMO (3.7% entire cohort) & pericardial disease (2.4%): only minor contributors to overall burden of HD in the overall Heart of Soweto cohort (5328 de novo cases)

• PHT: 0.8%  HIV-CAD: 0.3%

• data is encouraging; 5.5m infected & 500 000 HIV-related deaths / yr;

• previous reports suggesting high levels of myocardial &/ pericardial disease

• expected ‘tsunami’ of cardiac disease α HIV-pandemic, has yet to arrive.

• HAART’s potential impact on premature CAD - still potential to truncate at least one of the many devastating consequences of this disease
Pericardial Disease

- pericardial effusions are rather common, occurring in up to 46% of AIDS patients
- common cause of clinical cardiovascular symptoms and signs
- most idiopathic.
- wide array of pathogens, often in conjunction with disseminated infection
- infections, neoplasias, myocarditis, endocarditis or myocardial infarct are possible etiologies.
• **HIV associated pulmonary arterial hypertension:**

• Unexplained HIV-pulmonary HT has a prevalence of 1/200 compared with 1/200 000 in the general population.

• **Unexplained primary pulmonary hypertension (PPH)**

• similar presentation to the non-HIV form
INFECTIVE ENDOCARDITIS

- HIV not associated with ↑ risk IE

- SA (prospective study of risk factors for IE),
  - only 1/92 pt’s HIV +ve
  - main factors: RVD in 76%, congenital HD, prosthetic valves, hx of IE

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Kaposi's Sarcoma

- most common AIDS-related neoplasm
- at autopsy, heart involvement is observed in 5-8% of pt’s with a widely disseminated form
- the epicardium and pericardium are most frequently involved

- AIDS-related large cell B immunoblastic lymphoma involving the atrial septum

- Malignant lymphoma presenting as a primary cardiac tumor is rare; however, its incidence is apparently increasing in HIV+ patients
Accelerated atherosclerosis has been observed in young HIV+ individuals without traditional coronary risk factors

- Despite the clinical benefits of protease inhibitors, complications such as lipodystrophy, insulin resistance, high levels of LDL cholesterol and TG develop in up to 60% of pt’s

- Angiographically proven advanced symptomatic coronary artery disease has been reported in men < 40 y’s, Rx with protease inhibitors

- Anecdotal information suggesting that the risk of angina and myocardial infarction is increased with HAART
VISUAL EVIDENCE OF SEVERE BODY CHEMISTRY CHANGES CAUSED BY PROTEASE INHIBITOR USE ("BUFFALO HUMP," "PROTEASE PAUNCH," AND "FACIAL WASTING")

- X-RAY OF ABOVE HUMP
- THREE PHOTOS OF SAME MAN
- BEFORE AND AFTER LIPOSUCTION
AIDS drugs and heart attacks

“New research raises the possibility that lifesaving AIDS drugs may also increase the risk of heart trouble, though experts say the medicines' benefits still far outweigh any hazard” CNN 10/03/02

CDC study - the overall risk is low, nevertheless, those on the drugs have about 5X the usual risk of MI’s

followed the health of 5,676 HIV+ people (1993 to 2001) – 13 MI’s (PI) vs 2 (no PI’s)

UCSCD: questioned whether patients have actually had more heart problems since the introduction of the drug combinations with protease inhibitors.

examined records of 36,766 HIV-infected pt’s - 1,800 hospital admissions for heart disease and strokes.

Concluded – a slight decline in heart disease & strokes following the introduction of PI’s
Cardiac lesions are common in acutely ill patients.

Table 2. Echocardiographic Findings in 70 HIV-Infected Patients

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<th>Hospitalized HIV</th>
<th>Ambulatory HIV</th>
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<tr>
<td>Mitral valve prolapse</td>
<td>0</td>
<td>3 (1)</td>
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</table>
• overall incidence of unsuspected cardiac abnormalities - 27%
• depends on the stage of HIV disease
• degree of immunosuppresion correlates with the presence of cardiac lesions
• CMO is associated with late-stage infection & CD4<200
• significantly lower CD4 counts (166 vs 402/ul)
• dilated RV & pericardial effusion - 26.7%
• dilated CMO - 8.3%

• limitation of this study - not prospective

• Currie et al (BMJ 1994) ; Heidenreich et al (Circulation 1995) : pericardial effusion / LV dysfunction is associated with shortened survival independent of CD4
Dilated Cardiomyopathy

- 8.3% of hospitalized patients had significant and unexpected severe LV dysfunction
- Many studies documented an association between AIDS & CMO
- Rare in control's with hematological malignancy and in drug users without HIV infection
- Probably a direct effect of HIV rather than cachexia
Currie et al: BMJ 94

- 296 pt's
- CMO in 13 (CD4 < 100)
- median survival 101 d's (CMO) as compared with 472 d's (normal hearts)
- independent adverse prognostic factor
What about children (10 million) with HIV??????

LV dysfunction common - prevalence of 5.7% ; 2-year cumulative incidence was 15.3%

- echocardiographic data - Pediatric Pulmonary and Cardiac Complications of Vertically Transmitted HIV Infection study:
  - mortality higher in children with LVFS
  - regular echo’s for HIV+ infants - help to single out those risk of dying, even when immune and neurological markers show no cause for alarm

- Circulation 2000
"The benefits of zidovudine during pregnancy in reducing vertical transmission of HIV outweigh the reported cardiac risks - a conclusion similar to that of other studies. Any decision not to initiate zidovudine therapy, or to stop it, should be made with great caution."

Infants born to women with HIV infection who were exposed to zidovudine (AZT) in the perinatal period appear to have no increased risk of cardiac abnormalities over those without such exposure.

No cardiac toxicity found among infants exposed to zidovudine - *N Engl J Med* 2000
Prevalence of congenital cardiovascular malformations in children of human immunodeficiency virus-infected women:
The prospective P²C² HIV multicenter study

No statistically significant difference in congenital cardiovascular malformation prevalence in HIV-infected versus HIV-uninfected children born to HIV-infected women
CONCLUSION

• observational study

• prospective published studies have tracked the incidence & course of HIV infection in relation to cardiac illness

• subclinical echocardiographic abnormalities independently predict adverse outcomes and identify high-risk groups who can then be targeted for early intervention and therapy
• Importance of cardiac involvement should not be overlooked
• HIV will constitute an important cause of heart disease

• Global estimates - 36 million people living with HIV infection & may rise to 120 million worldwide in next decade

• If there is a 8-10% incidence of symptomatic CHF over 5 years, then there will be about 3 to 12 million expected cases during this period!!!!!!!!!!
"The bottom line is, the people who are dying from AIDS don't matter in this world."

“When the philosopher Thucydides was asked when justice would come to Rome, he famously replied that it would come when those who are not injured are as indignant as those who are. So let us all feel indignant about the worsening HIV pandemic as if "we all have AIDS“ and let us make sure that the global AIDS fund turns this anger into action”

Gavin Yamey, deputy editor
William W Rankin, president

BMJ 2002;324:181-182 (26 January)
AIDS and global justice:
METHODS

- clinical examination
- ECG
- chest X-ray
- 2-D, M-mode, Doppler, colour Doppler echocardiography
- hemoglobin
- CD4+ T-lymphocyte count
DEMOGRAPHICS

• mean age 32 years (range 21-48 years)
• 57 males
• no alcohol / drug abuse
• no cardiotoxic medications
• no prior HT, diabetes, valve or IHD
## HEMOGLOBIN

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<td><strong>13.2 ± 2.3</strong></td>
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<td>&lt;12</td>
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<td><strong>p &lt; 0.01</strong></td>
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ECG’s of 60 hospital pt’s

- 24 pt’s (40%) - abnormal ECG

  * 18 minor ST/T
  * 2 RVH
  * 4 RV strain
  * 2 R axis
  * 2 RBBB
  * 1 L axis
  * 1 sinus bradycardia
  * 1 bigeminy
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AN OBSERVATIONAL STUDY

D Jankelow, Dept Internal Medicine, University Witwatersrand

- incidence of unsuspected cardiac abnormalities in ambulatory and hospitalized patients with HIV

- University of Witwatersrand, Ethics Committee
AIDS — Past and Future: “Living with AIDS is the politically correct euphemism. Dying with a potentially manageable HIV infection is the horrible reality. Can there be a more shameful medical emergency than 30 million patients' urgently requiring life-prolonging therapy and not getting it? Not only should existing antiretroviral drugs be provided, but massive efforts to explore all other potential therapeutic options should begin immediately”
NEJM 2002: 346; 710

'Aloof' Mbeki has a lot to learn – J Carter
11/03/02
• Barbaro et al, NEJM 98: 952 pt’s over 60 months follow-up
• 76 - CMO (8%)
• Incidence if CD4 ≤ 400 / AZT
• Myocarditis - 63
• HIV nucleic acid sequences - 58
• Active myocarditis in 36
• Coxsackie B 17%; CMV 6%; EBV 3%
• CMO - direct action of HIV on myocardial tissue / autoimmune process induced in association with other viruses.
Radiological features of the 60 hospitalized pt’s

- 35 pt’s (58%) abnormal CXR’s
  - lobar consolidation 12
  - infiltrates 5
  - bronchiectasis 4
  - pleural effusion 8
  - cardiomegaly 10
No evidence of any heart disease in the out-patient’s

- normal: cardiac examination
  ECG
  CXR
  ECHO
Pericardial Disease

- pericardial effusions are rather common, occurring in up to to 46% of AIDS patients
- common cause of clinical cardiovascular symptoms and signs
- most idiopathic.
- wide array of pathogens, often in conjunction with disseminated infection
- infections, neoplasias, myocarditis, endocarditis or myocardial infarct are possible etiologies.
• overall incidence of unsuspected cardiac abnormalities - 27%
• depends on the stage of HIV disease
• degree of immunosuppression correlates with the presence of cardiac lesions
• associated with late-stage infection & CD4<200
• significantly lower CD4 counts (166 vs 402/ul)
**pulmonary hypertension & RV dilatation:**

*16 (26.7%) pt’s*

*RVEDD : 3.39 ± 1.37 cm*

*PAP : 46 ± 7.2 mmHg*

- did not occur in the absence of respiratory disease / LV dysfunction

- PHT - pneumonia / hypoxia

- successful Rx - RV afterload - normal RV dimension
• unexplained primary pulmonary hypertension (PPH)
• similar presentation to the non-HIV form
• mechanism is uncertain
• not simply a phenomenon of immunodeficiency
Accelerated atherosclerosis has been observed in young HIV+ individuals without traditional coronary risk factors

- Despite the clinical benefits of protease inhibitors, complications such as lipodystrophy, insulin resistance, high levels of LDL cholesterol and TG develop in up to 60% of pt’s

- Angiographically proven advanced symptomatic coronary artery disease has been reported in men < 40 y’s, Rx with protease inhibitors

- Anecdotal information suggesting that the risk of angina and myocardial infarction is increased with HAART
initiating lipid lowering Rx: specific drug–drug interaction

- PIs inhibit CYP3A4; NB Ritonavir

- Simvastatin (contraindicated) as concentrations rise dramatically with PI use – rhabdomyolysis

- Atorvastatin lesser degree – lower doses in HIV-pt’s

- Pravastatin not metabolised by CYP3A4 - 1st line Rx

- Rosuvastatin concentrations Atazanavir/Ritonavir & Lopinavir/Ritonavir, limiting doses to 10mg

- Rx hypertriglyceridaemia – fibrates for Tg>5.6 mmol/l
<table>
<thead>
<tr>
<th>Condition</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pericardial effusion</td>
<td>119 ± 41</td>
</tr>
<tr>
<td>Dilated RV</td>
<td>184 ± 119</td>
</tr>
<tr>
<td>LV dysfunction</td>
<td>173 ± 113</td>
</tr>
</tbody>
</table>
• unexplained primary pulmonary hypertension (PPH)
• similar presentation to the non-HIV form
• mechanism is uncertain
• not simply a phenomenon of immunodeficiency
<table>
<thead>
<tr>
<th></th>
<th>HOSPITAL</th>
<th></th>
<th>OPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 (/ul)</td>
<td>254 ± 202</td>
<td>± 175 p &lt; 0.001</td>
<td>475</td>
</tr>
<tr>
<td>≤400</td>
<td>80%</td>
<td></td>
<td>35%</td>
</tr>
<tr>
<td>≤200</td>
<td>51.7%</td>
<td></td>
<td>7.5%</td>
</tr>
</tbody>
</table>
The patient in panel (a) had a normal right ventricle, with a triangular shaped filling chamber. The patient in panel (b) had a severely dilated right ventricle; the right ventricle had lost its normal shape and the right ventricular/left ventricular end-diastolic area ratio was more than 1. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.
• prevalence of older HIV individuals by 2015 (CDC), over \( \frac{1}{2} \) of all HIV-pt’s will be >50 y’s

• chronic diseases & atherosclerosis

• ultimately, HIV-specific adjuvant Rx in addition to ART that target key inflammatory & coagulation pathways, should be developed to mitigate premature HIV-associated CVD

• co-ordination between ID & cardiology – improve quality of care to develop an individualized Rx plan