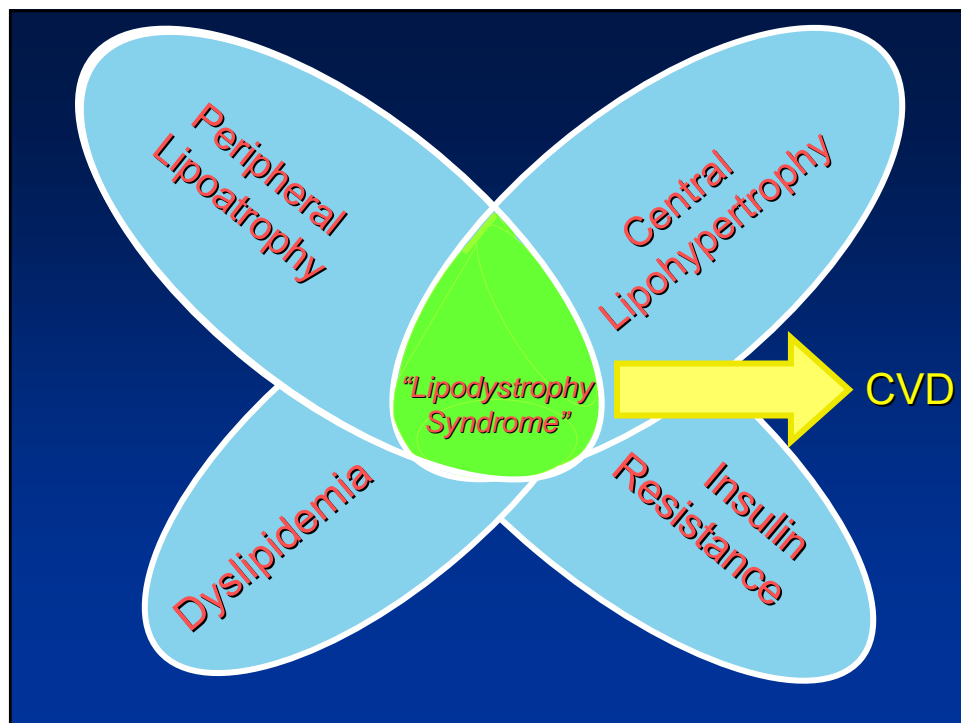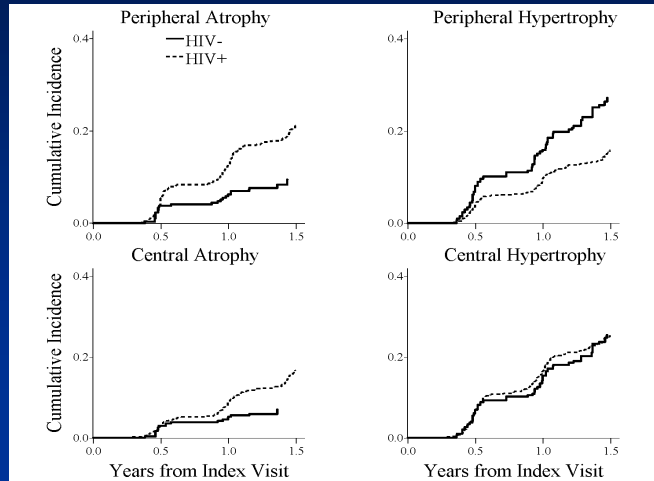# Fat and Metabolic changes in HIV infection: Contribution of Aging

Phyllis C. Tien, MD
October 29, 2007
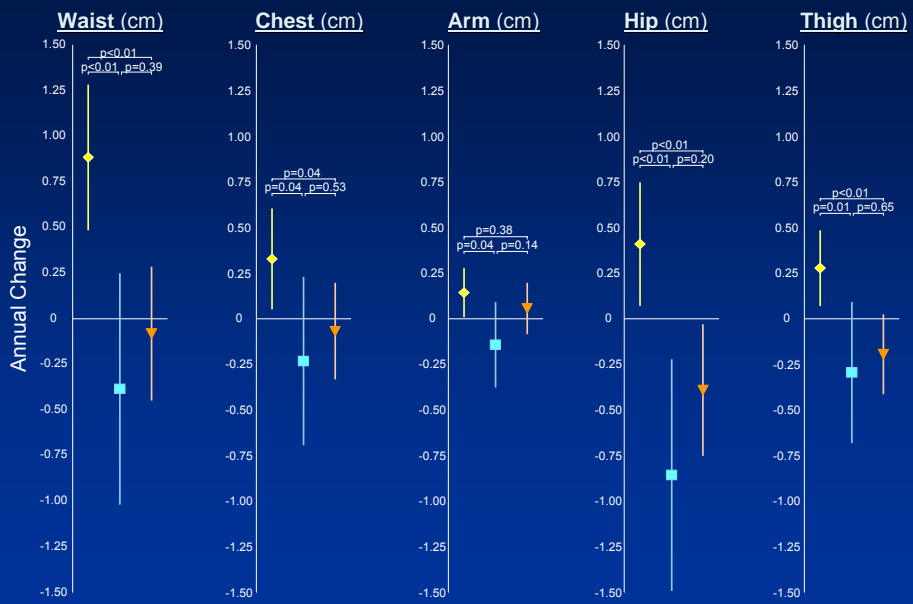
HIV+ women had more lipoatrophy; similar risk of central lipohypertrophy

Tien. PC et al JAIDS 2003



Stavudine discontinuation associated with slower annual loss in anthropometry in HIV+ women

Tien, JAIDS 2007

◆ HIV-uninfected     ■ use stavudine     ▼ discontinue stavudine

Older age is associated with more visceral adipose tissue (VAT) and less leg fat
in HIV-infected men and women

| % effect (95% CI) | Age (per decade) | |
| --- | --- | --- |
| | VAT | Leg fat |
| Men | 33 (23, 45) | -5 (-9, -1) |
| Women | 18 (2,35) | -6 (-14, 2) |

FRAM Investigators, JAIDS 2005, JAIDS 2006

# More VAT & less leg fat associated with higher TG

◆ 1st Tertile
■ 2nd Tertile
▲ 3rd Tertile
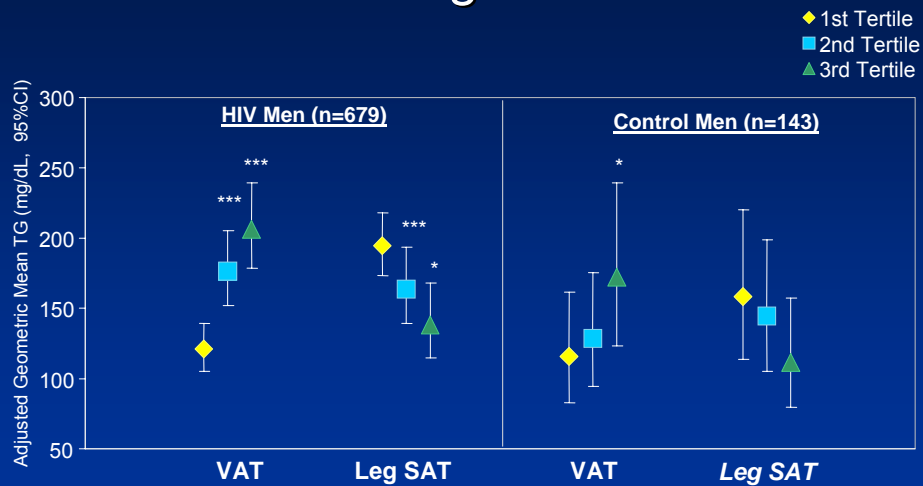


Wohl, CROI 2006

## In pre-HAART era, early ↓ HDL, later ↓ LDL, then ↑TG & VLDL.
## ↓ HDL may be more pro-atherosclerotic than ↓ LDL is protective

**Legend:** ■ Control  ■ HIV+  ■ AIDS

Bar chart (mg/dL) across categories: Triglycerides, Total Cholesterol, HDL Cholesterol, LDL Cholesterol, VLDL Cholesterol.

- Triglycerides: Control ~102, HIV+ ~110, AIDS ~202 (***)
- Total Cholesterol: Control ~182, HIV+ ~150 (**), AIDS ~150 (*)
- HDL Cholesterol: Control ~48, HIV+ ~30 (***), AIDS ~23 (***)
- LDL Cholesterol: Control ~120, HIV+ ~102, AIDS ~84 (**)
- VLDL Cholesterol: Control ~20, HIV+ ~22, AIDS ~40 (***)
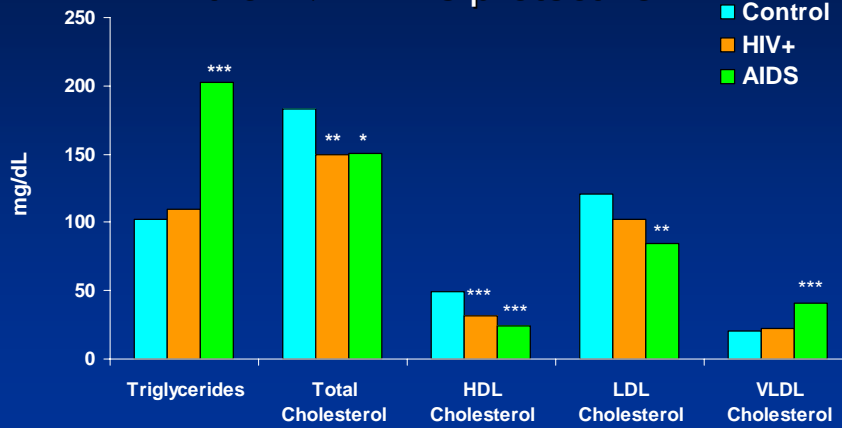
*P <0.05; **P <0.01; ***P <0.001 vs control
Grunfeld C et al. *J Clin Endrocrinol Metab.* 1992;74:1045.

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## HIV infection is associated with decreases in HDL and LDL; After HAART, HDL remains unchanged, LDL returns to preseroconversion values

| Lipid Measurements, mg/dL | Preseroconversion (n=50) Mean (95% CI) | HIV+ Prior to HAART (n=50) | HIV+ (on HAART) (n=43) |
|---|---|---|---|
| | | Mean change from preseroconversion (95% CI) | |
| Total Cholesterol | 201 (179 to 222) | -30 (-52 to -9) | 20 (-1 to 41) |
| HDL-C | 51 (46 to 57) | -12 (-19 to -6) | -9 (-16 to -2) |
| LDL-C | 122 (102 to 143) | -22 (-45 to 1) | -1 (-25 to 22) |

Riddler et al, JAMA June 11, 2003 vol 289, no. 22

## Ritonavir Based Drugs increase Triglycerides in HIV+ and HIV-
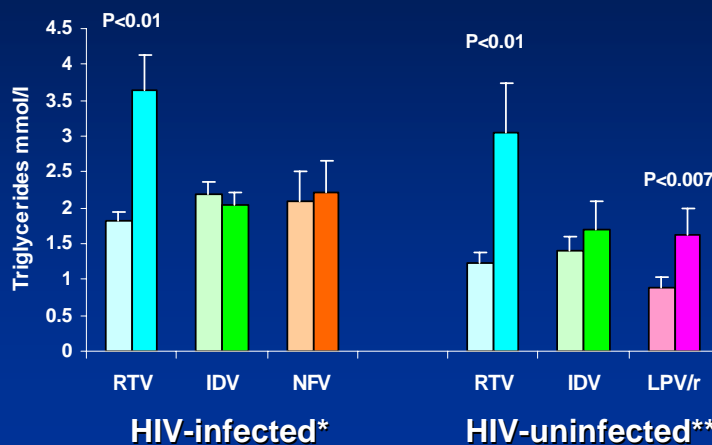


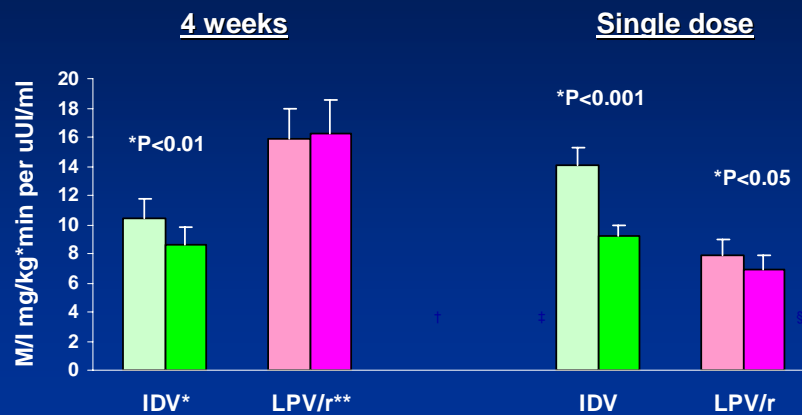*Periard et al; **Purnell et al, Noor et al, Lee et al.

## Summary

- HIV infection *per se* is associated with higher TG, lower HDL and lower LDL
- HDL remains low despite HAART
- LDL increase appears associated with a restoration to health phenomenon
- TG increase is associated with HIV and drug effect
- Age-associated changes in leg fat and VAT may worsen the lipid effect of HIV

## Other Infections Induce Insulin Resistance; HIV+ less insulin resistant

Plasma insulin (µU/mL)

- 400
- 300
- 200
- 100

p<0.01

Controls    HIV+
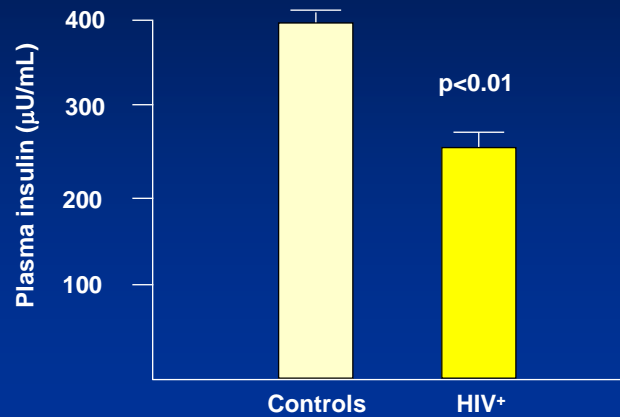
Hommes MJ et al. *Metabolism.* 1991;40:651.

## Decreased insulin sensitivity observed after single dose of PI acutely in HIV-; after 4 weeks of therapy, insulin sensitivity improves

**4 weeks**          **Single dose**

M/I mg/kg*min per uUI/ml

- 20
- 18
- 16
- 14
- 12
- 10
- 8
- 6
- 4
- 2
- 0

*P<0.01

*P<0.001

*P<0.05

IDV*    LPV/r**        IDV    LPV/r

†        ‡            §

*Noor *et al.,* **Lee *et al.,* †Noor *et al.,* ‡Lee *et al.*

## Regardless of type of HAART regimen, insulin levels increase over time
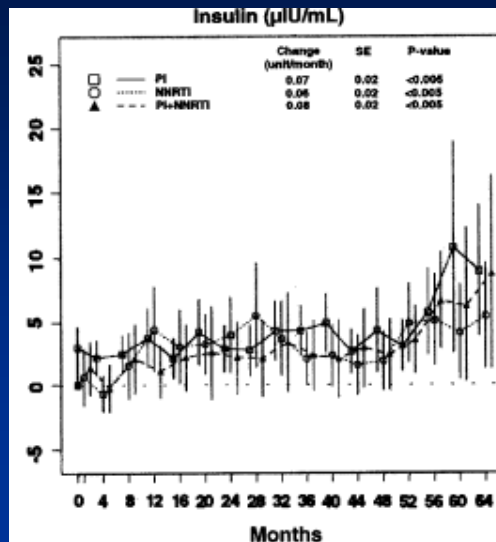


Longer cumulative exposure to NRTI is associated with increased risk of DM and more insulin resistance

Shlay JAIDS 2007; 44: 506-516

## Summary

- HIV infection *per se* does not appear to negatively affect insulin sensitivity
- There are differential effects of PI on glucose metabolism that may be acute
- Cumulative use of NRTI appears associated with DM and insulin resistance
- Older age (via aging *per se* vs reproductive aging) may worsen the disorders of glucose metabolism in HIV.

# Conclusions

- HIV infection, HAART use and specific antiretroviral drugs differentially contribute to fat and metabolic changes that portend an increased risk of CVD.
- Aging (somatic versus reproductive aging) may potentially worsen the HIV-associated fat and metabolic changes.

# Key unanswered questions for future research

- Further study on the role of
  - sex hormone levels (estrogen and androgens)
  - regional adipose tissue changes
  - Inflammatory markers

  on fat, metabolic, & CVD outcomes is needed.