

## HIV p24 Ag Screening of U.S. Blood and Plasma Donors

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### Outline of Presentation

- Review of data and events preceding implementation of p24 Ag screening
- Overview of observed yield of p24 Ag and HIV NAT in whole blood and plasma donor screening sectors
- Analysis of RNA load relative to p24 Ag signal: required sensitivity of NAT to safely discontinue p24 Ag screening

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### Projections of p24 Ag yield prior to mandated implementation

- Early studies of SC plasma donor panels
- National HIV-Antigen Study (0/515,494)
- TSS p24 Ag study (0/8,597 HR donors)
- 3 case reports of p24 Ag+/Ab- US donors
- Thailand: 1.6/10,000 p24+/Ab- units
- REDS WP/IR projections: 5-10 Ag+/Ab- units per 12 million annual blood donations

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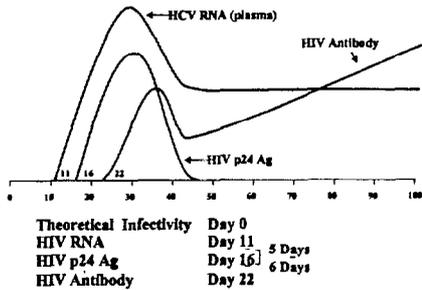
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### HIV markers during early infection




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### Cost-effectiveness of p24 Ag screening of whole blood donors

- Yield: 5-10 p24Ag+/Ab- donations per year
- Prevent: 10-15 recipient infections per year
- Cost: \$3-5 per unit; \$60 million per year
- Cost effectiveness:
  - HIV antibody screening: \$3,600/QALY
  - HIV p24 Ag: \$2.3 million/QALY

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### Magnet Effect Concerns

- High risk donors could donate more frequently to access more sensitive HIV test
- 15% of anti-HIV positive donors test seekers
- 3% of seronegative donors test seekers
- P24 test only detects 30-50% of WP units
- Formal analysis by REDS indicated magnet effect unlikely to offset benefit of WP closure

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### Decision to implement

- 6/95 BPAC: 9 to 6 vote against licensure
- 7/95 Letter from Congressman Shays
  - Projections underestimate yield (50-100/yr)
  - Inappropriate consideration of cost-effectiveness
  - Inappropriate influence of blood banking "industry"
- 8/95 FDA memo requiring implementation by 3/96 (blood and plasma donations)

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### Experience with p24 Ag

- Yield lower than projected:
  - ~1 in 10 million whole blood donations
  - reflects declining HIV incidence and bias in donation during p24Ag+ WP
- No evidence of magnet effect
- 0.02% p24 RR rate (RNA-/no SC)
- False positive p24 Ag neutralizations

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### Why was HIV yield overestimated ?

- Model assumed donations during p24 antigenemia would occur at same rate as following HIV antibody seroconversion
- However, donors may not donate during antigenemia or earlier in HIV infection:
  - not feeling well, physical symptoms, risk behavior

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### p24 Ag vs HIV RNA (NAT)

- MP NAT screening for HCV and HIV RNA implemented in 1998-2000
- Retrospective studies of SC plasma panels: MP-NAT at >10,000 gEq/mL > p24 Ag
- Prospective screening of plasma and blood donors: all p24Ag+/Ab- donations and Ag+ controls detected by MP-NAT

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### HIV Viremia preceding Ab seroconversion: p24 Ag, MP- and ID NAT Fiebig et al. AABB 2000

- 146 serial donations from 43 SC plasma donors (Alpha/BCP)
- Ortho/Coulter p24 Ag; Abbott & GSC Ab
- NGI PCR (UltraQual/SuperQuant)
- 94 RNA+/Ab- specimens
- Multivariate longitudinal regression model to estimate DT and p24 Ag intercept

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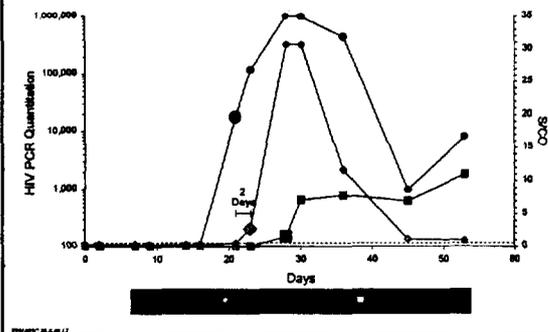
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### HIV panel 6240 – Virologic/Serologic Profile




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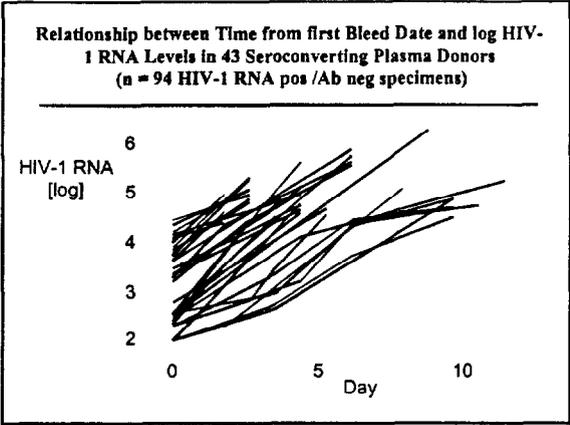
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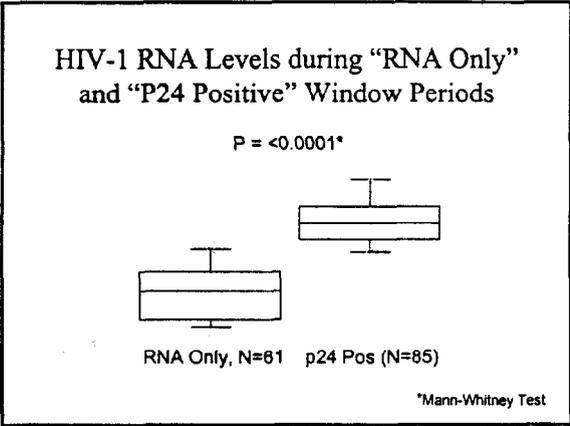
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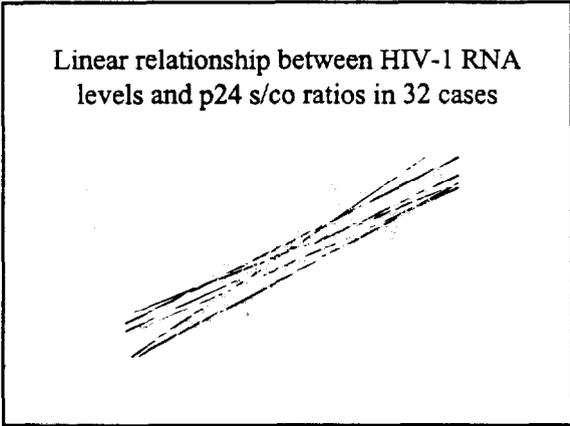
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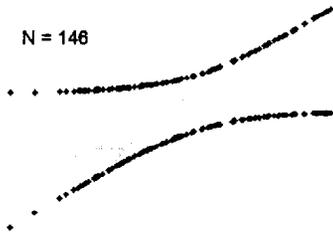
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95% Prediction Limits for Relationship of HIV RNA levels and p24 s/co ratios

N = 148



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HIV p24 Ag and RNA detection

- p24 antigen becomes positive at level of 10,000 RNA copies/mL
- Pooled NAT will need to detect <10,000 RNA copies/mL in the individual donation to:
  - replace p24 antigen testing
  - increase detection of HIV infected donors

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Conclusions

- 1995 projections overestimated yield (and cost-effectiveness) of p24 Ag screening
- False positive neutralization problem
- MP-NAT screening makes p24 Ag screening redundant
- Recommend discontinuing p24 Ag screening once HIV-MP NAT routine

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