Safety Evaluation of Re-designed Multi-Use-Nozzle Jet Injectors

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Jet Injector Safety Concerns

- 1968 : concern of risk (visible blood on nozzle)
- 1984: HepB outbreak in 1 clinic (!).
- 1985: animal studies prove risk
- 1987: WHO restricted application
- 1996: WHO :“multidose jet injectors not recommended”
- 2001: Epidemiology in Brazil suggests HepB associated to vaccination with jet injectors*

- New generation designs with protector cap:
  - used in field (n=3000) **
  - safety not yet demonstrated

*Souto et al., 2001. Pan Am J Public Health 10(6) 2001; ** Dimache et al., 1997. Vaccine 15, 1010

How to evaluate risk of use?

- HepB >> HIV > HepC (viremia)
- Transmission is by blood
- Measure the amount of blood transmitted

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  - Sensitive assay for blood
  - Limit of Detection

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- Calculate risk

How much blood is safe ?

- 10^9-10^{11} HBV DNA copies/ml = 1-100 HBV/pL*
- 10 pL smallest volume for transmission of HBV**
- Needle-stick injury(10^6 pL): of HBe+ve = 30% risk of HBV***

Use blood-banking methods to determine if safe for injection

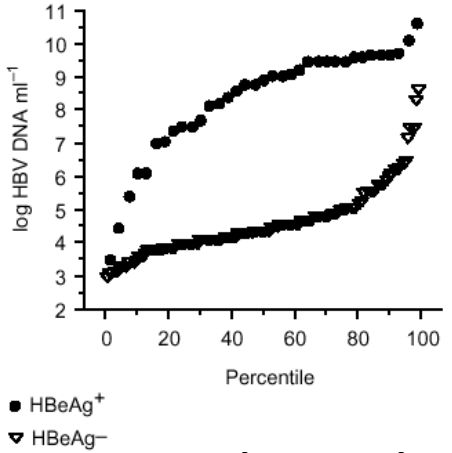
* Lindh et al. 2000 J. Vir. Hep. 7, 258. ** Feinman et al. 1984. J. Virol. Meth. 8, 199

*** Beltrami et al. 2000 Clin. Microbio Rev 13, 385

Blood Banking Approach

- ELISA method to determine if blood 'acceptable'
  - use PCR method >> sensitivity than commercial ELISA
- Use blood from high viremia carriers

Dilute until PCR negative

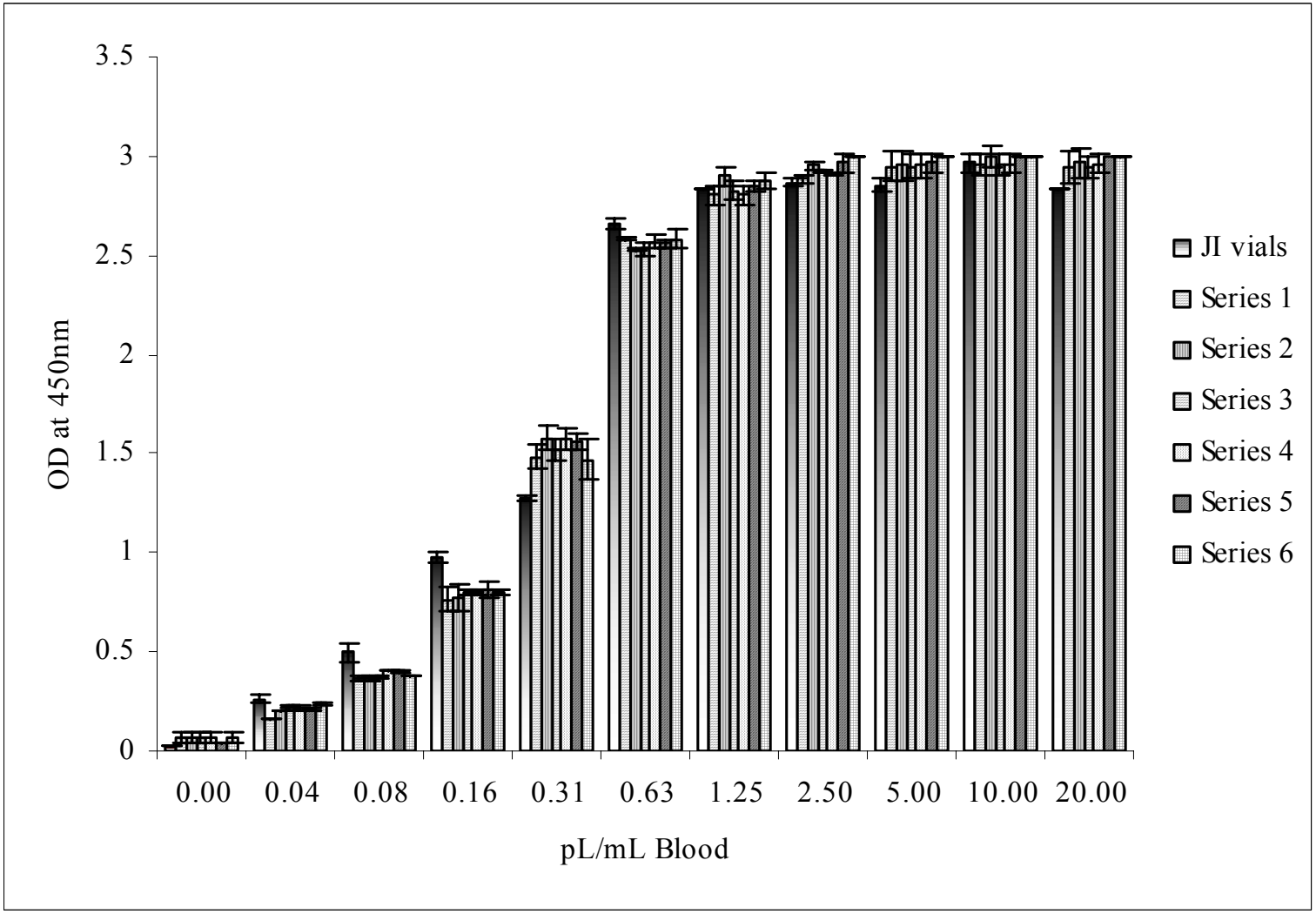


- Determine volume of blood from most viremic carriers which represents accepted risk (no detection of HBV)

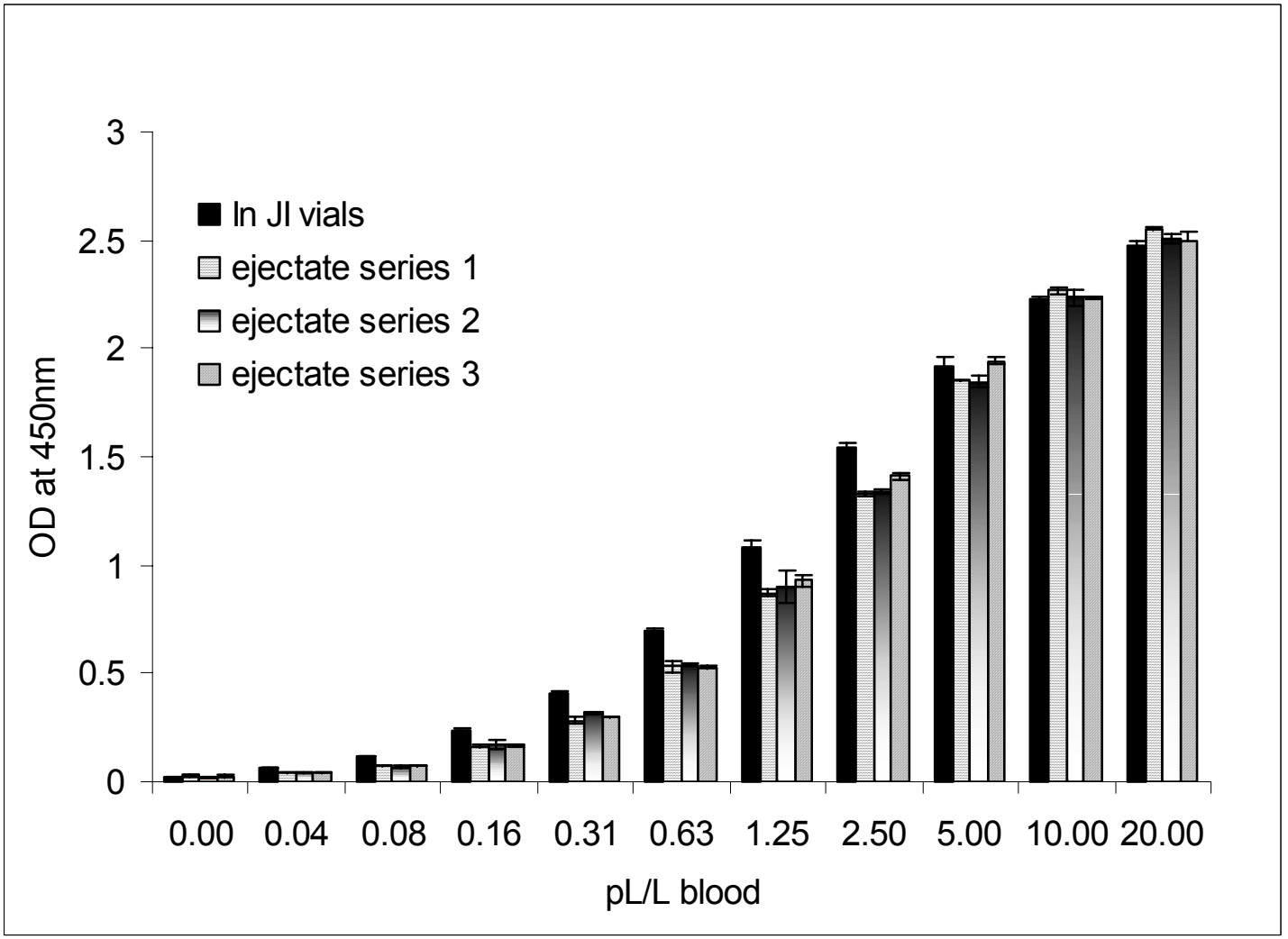
Assay for blood contamination

- Use serum albumin as indicator of blood volume
- Sensitive ELISA Assay developed by Dr Abuknesha, King's College (UK)
- Need to demonstrate:
  - Reliability, linearity and sensitivity
  - No risk of False Negatives
  - No risk of False Positives

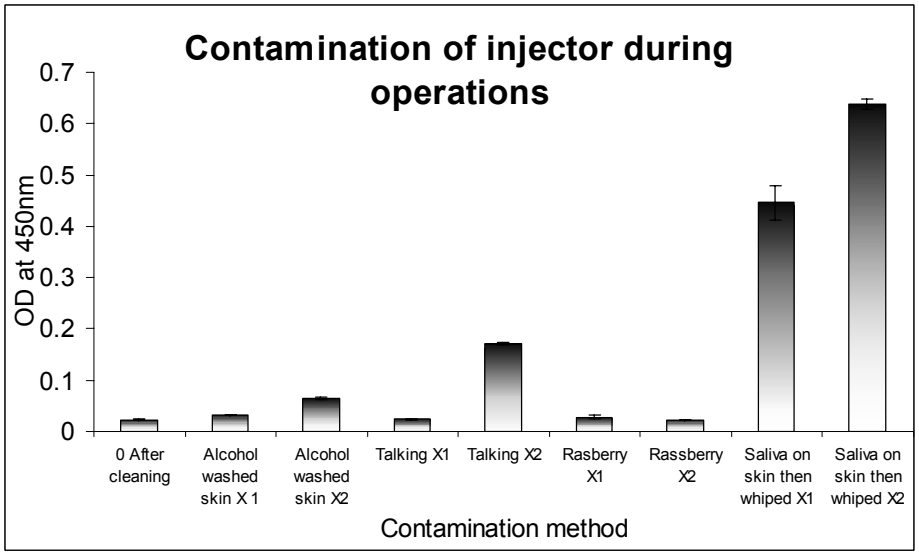
Sensitivity, Reproducibility

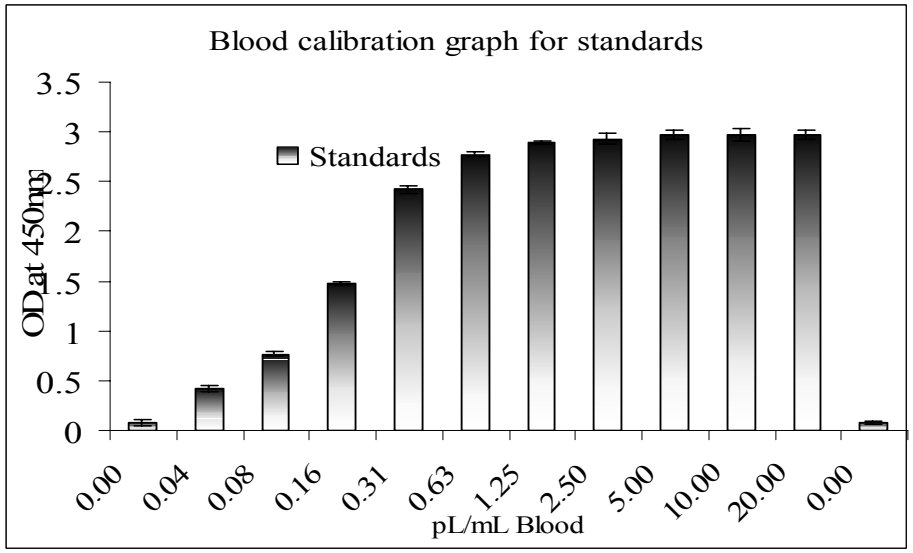


Modified Dynamic Range



Risk of False Positives

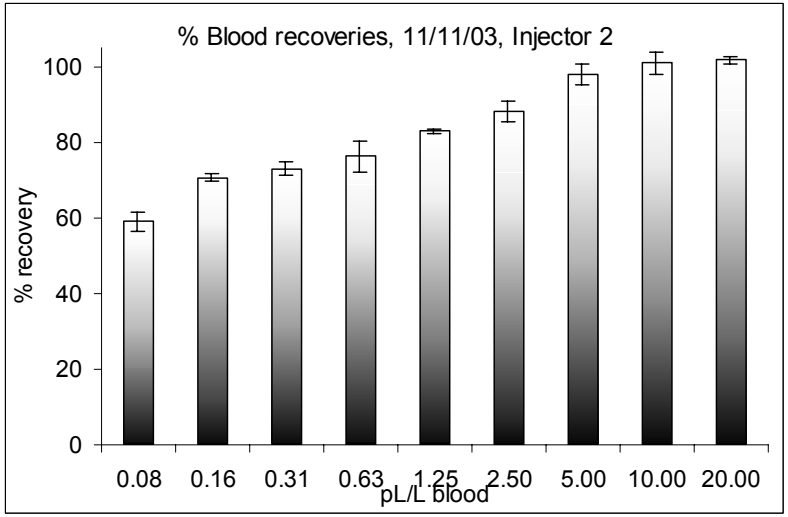




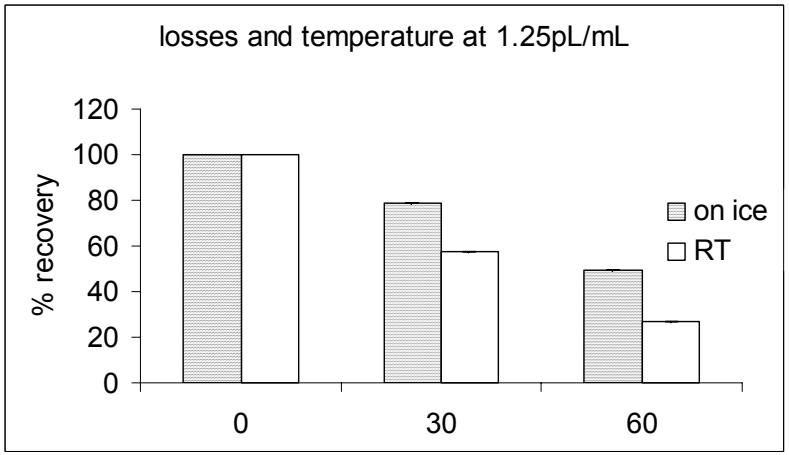
Albumin is found in saliva, skin-cells etc., and presence does not prove blood

The signal level resulting from ‘non-blood’ contamination is low

Risk of False Negatives



Risk of loss of signal due to binding of albumin to collection tube



Loss of signal at low signal level dependent on time and temp. Set operational specs.

Clinical trials to determine safety

- Use HepB +ve population. Test ejectate for HBV by PCR.
- Use any population. Test ejectate by blood assay

- How many safe injections do you have to give to consider the device safe ?

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What is the risk from immunization

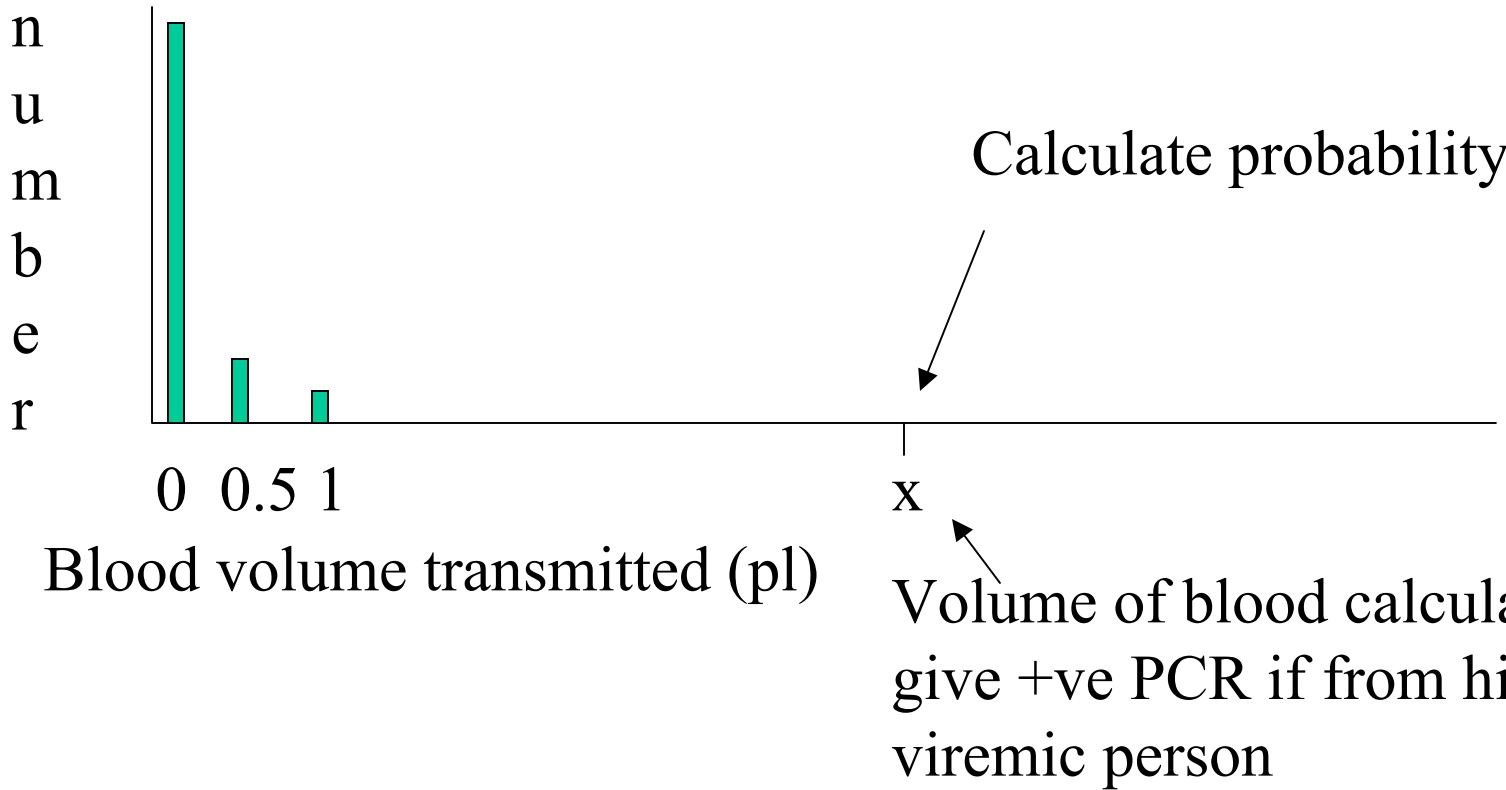
- 1999: 8 million HepB infections due to unsafe injection practice (WHO).
  - 2-10% from immunization: 0.8 million cases
  - 1500 million immunizations → 1 per 2000 risk

- 2003: only auto-disable syringes should be used in immunization (WHO-UNICEF policy)
  - what is current risk ?
  - Only from sharps disposal

Required level of safety

- Are YOU prepared to receive an injection from the device KNOWING the previous recipient is HBV positive ?
- Need v. good risk data (eg >1:100000)
- Clinical trial of 100000 volunteers ?
    - device must be sterilised between each injection !

Statistical solution



Future Steps

- To move forward we need to know:
  - 'safe' volume of blood of worst case patients
  - an idea of level of contamination (pl)

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- Committee of experts
  - how many injections need to be given for safety to be demonstrated ?
  - What 'device' tests are needed

Implementation

- Device safety not sufficient
- Reliability
- Cleaning procedures
- Autoclave issues
- Supply of jet injector
- Immunization program ‘buy-in’
- Public perception