HIV Infection Through Breastfeeding Model with Threshold Delay

Redouane Qesmi

York University, Canada

Joint work with J. Heffernan and J. Wu

Summer 2010 Thematic Program
on the Mathematics of Drug Resistance
in Infectious Diseases

July 22, 2010

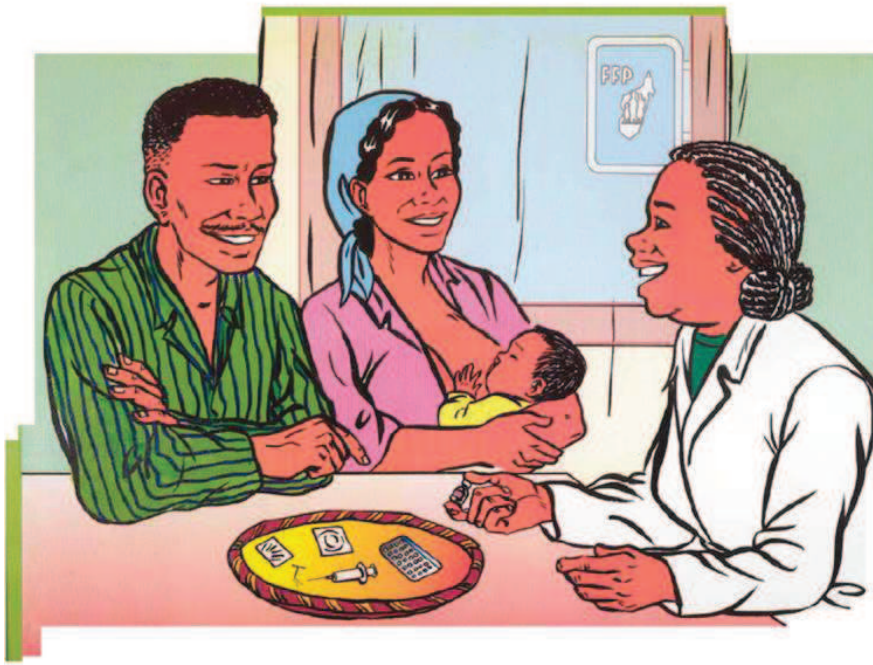
What is it about?

HIV and breastfeeding

- Breastmilk of HIV infected women contains HIV virus
- Risk of transmission is cumulative: The longer the baby is breastfed the greater the risk of infection
- breastfeeding is therefore dangerous for infants of HIV infected women

WHO: Breastfeeding and HIV International Transmission Study

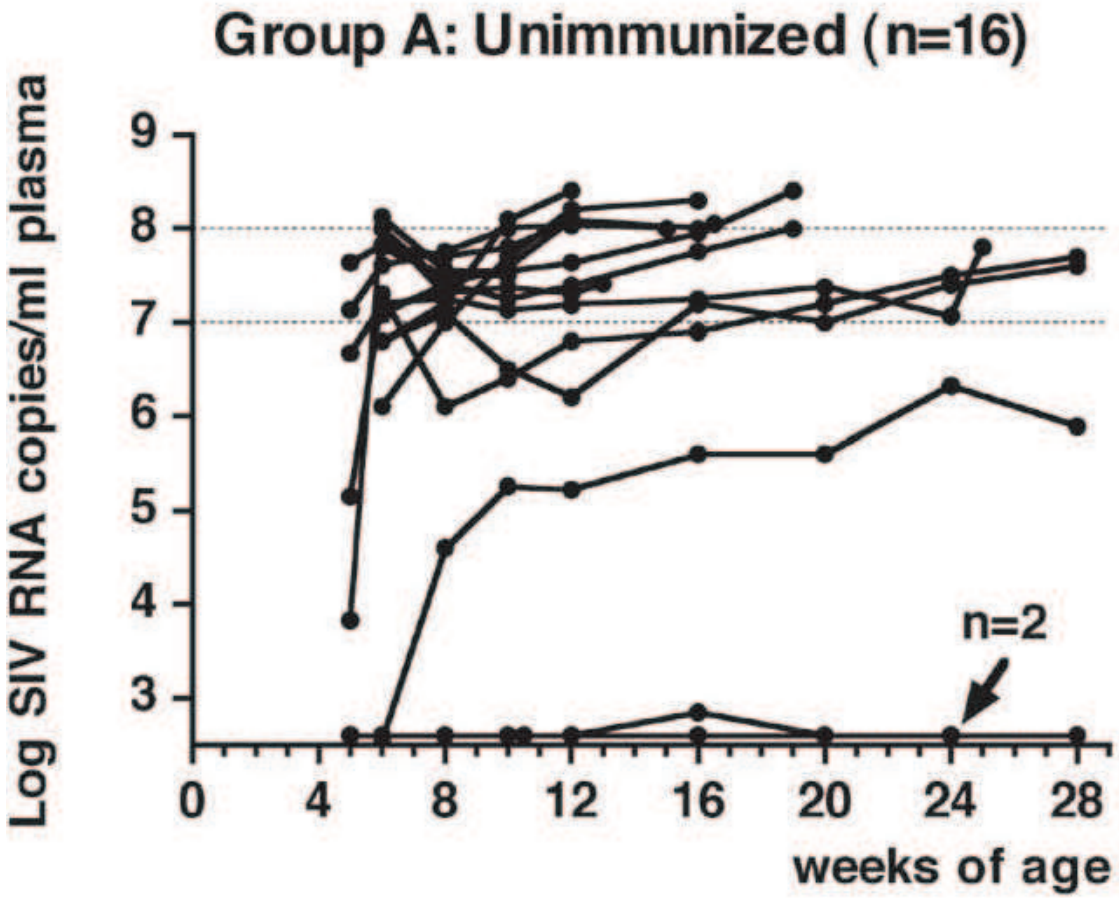
- An estimated 430 000 children were newly infected with HIV in 2008
- More than 5 million children infected since beginning of epidemic
- Mostly in sub-Saharan Africa.



Infant macaques and SIVmac251 Koen, et al., J.Acq. Immu. Defi. Synd. 2005

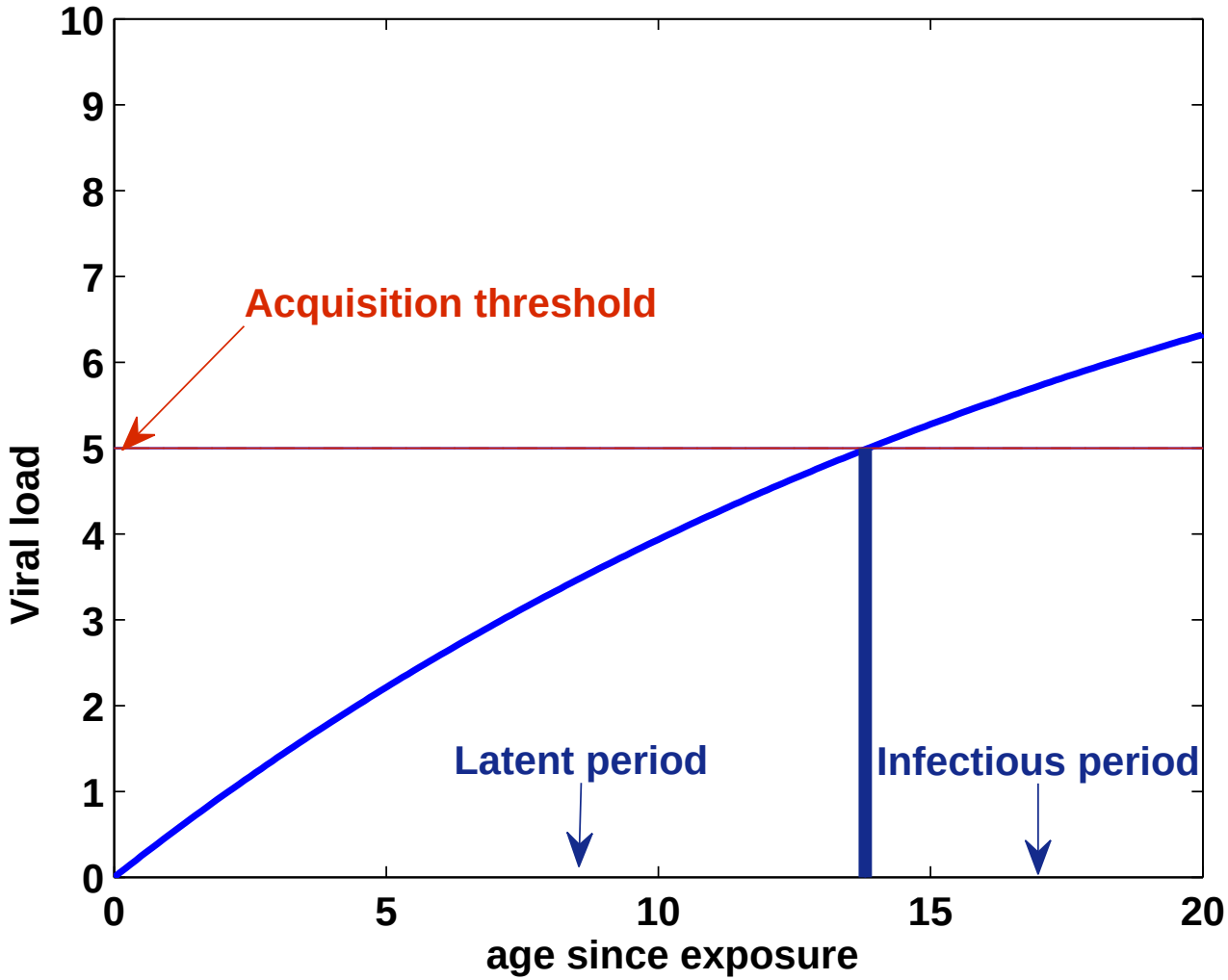
- 16 infant macaques were handheld and bottle-fed SIVmac251.
- A total of 15 times (3 times per day for 5 consecutive days).
- 14 became persistently viremic.
- 11 of 14 that became infected had persistently high viremia and developed simian AIDS within 24 weeks of infection.

Plasma viral RNA



The virus quickly increased; Viremia can be detected as early as 23 days after intravenous infection.

Diagram-Disease categories



A viral dynamic formula

- $V(t, a)$: the viral load which have spent a time a, in an infected infant, at time t;
- A : the minimum viral load above which the infection occurs;
- $I(t)$: Infected individuals at time t.

A viral dynamic formula ($V(t,a) < A$)

- The dynamic of the viral load during the early stage is governed by

$$\frac{dV}{dt} + \frac{dV}{da} = rV(t,a) + F(I(t)),$$

- r is the rate of the virus growth;

- $F(I(t))$ express the additive viral load due to multiple exposures to the virus:

$$F(I(t)) = \frac{bcI(t)}{kI(t)+1}$$

A viral dynamic formula ($V(t,a) < A$)

- The dynamic of the viral load during the early stage is governed by

$$\frac{dV}{dt} + \frac{dV}{da} = rV(t,a) + F(I(t)),$$

- r is the rate of the virus growth;

- $F(I(t))$ express the additive viral load due to multiple exposures to the virus:

$$F(I(t)) = \frac{bcI(t)}{kI(t)+1}$$

The full model

- Let, for $t \geq 0$, $\tau(t)$ be the first instant for which an exposed baby become infected.
- Then $\tau(t)$ satisfies

$$\Delta(\tau(t), I_t) = 0,$$

where

$$\Delta(s, \phi) = ce^{rs} + \int_{-s}^{0} e^{-ru} F(\phi(u)) du - A$$

and

$$I_t(\theta) = I(t + \theta) \forall \theta \in [-max(\tau(s), s \geq 0)] \ .$$

The full model

$$
\begin{cases}
\dfrac{dS}{dt} & = & \pi - \beta S(t) I(t) - dS(t) \\
\dfrac{dE}{dt} + \dfrac{dE}{da} & = & -\delta(a) E(t,a), \text{ if } t \geq 0 \text{ and } 0 \leq a \leq \tau(t), \\
\dfrac{dI}{dt} + \dfrac{dI}{d\theta} & = & -\alpha I(t,\theta), t \geq 0 \text{ and } \theta \geq 0, \\
\Delta(\tau(t), I_t) & = & 0
\end{cases}
$$

$$
E(t,0) = \beta S(t) I(t) \quad \text{and} \quad I(t,0) = E(t,\tau(t)).
$$

Reduction on the characteristic lines: **A model with threshold delay**

$$\begin{cases} \dfrac{dS}{dt} & = & \pi - \beta S(t) I(t) - dS(t), \\ \dfrac{dI}{dt} & = & \beta e^{-\int_0^{\tau(t)} \delta(s) ds} S(t-\tau(t)) I(t-\tau(t)) - \alpha I(t), \\ \Delta(\tau(t), I_t) & = & 0. \end{cases}$$

More simplification: A model with state-dependent delay

$$\begin{cases} \dfrac{dS}{dt} &= \pi - \beta S(t)I(t) - dS(t), \\ \\ \dfrac{dI}{dt} &= \beta e^{-\int_0^{\sigma(I_t)} \delta(s)ds} S(t-\sigma(I_t))I(t-\sigma(I_t)) - \alpha I(t), \end{cases}$$

$\sigma : C \longrightarrow \mathbb{R}^+ \in C^1$ is a decreasing function such that

$$\sigma(0) = \frac{1}{r} \ln(\frac{A}{c}).$$

Basic reproduction number

$$R_0 = \frac{\beta\pi}{\alpha d} e^{-\int_0^{\sigma(0)} \delta(s)ds}$$

where

$$\sigma(0) = \frac{1}{r} \ln(\frac{A}{c}).$$

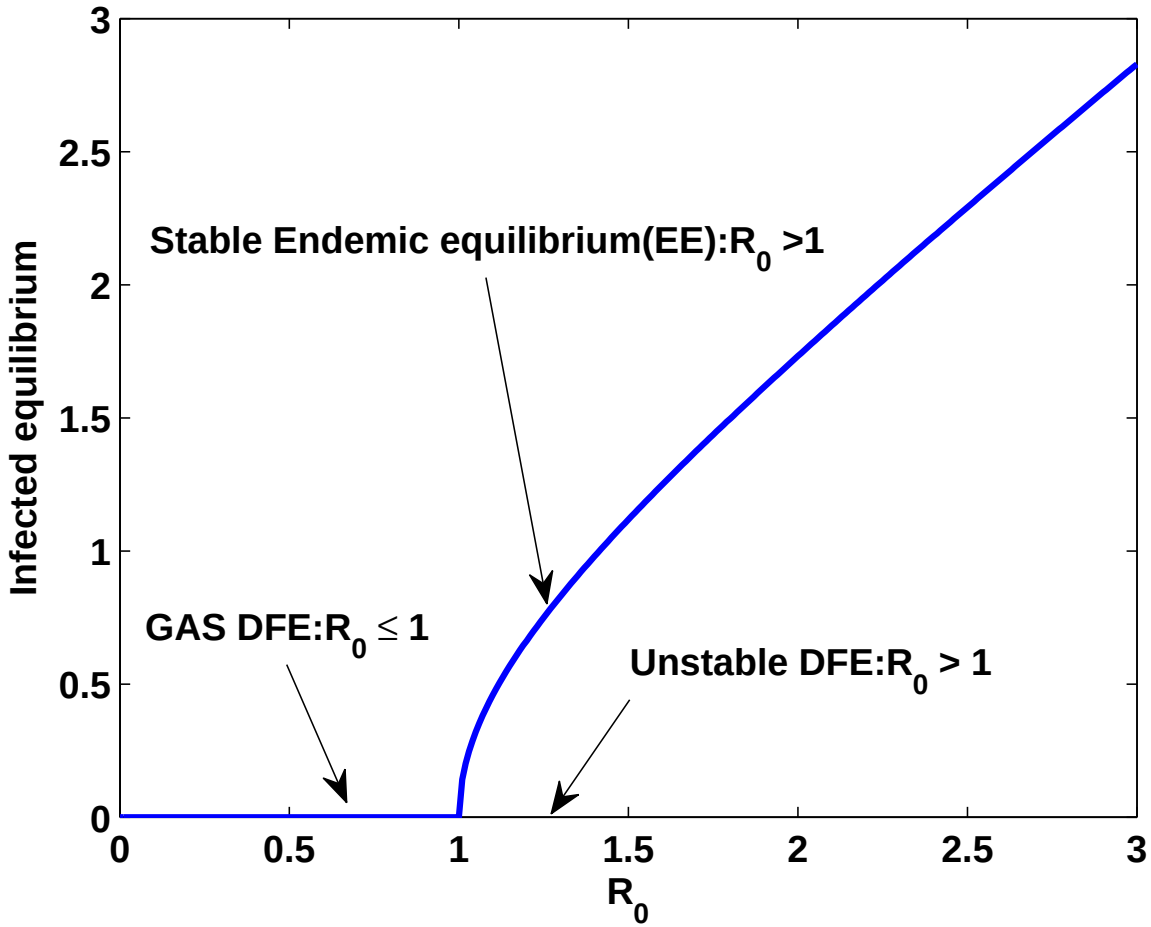
- $\frac{\beta\pi}{\alpha d}$ gives the reproduction number of the basic SI model in the absence of the delay and the exposed population.
- $e^{-\int_0^{\sigma(0)} \delta(s)ds}$ describes the survival probability of exposed infants of the initial population to HIV.

The SDDS has always a DFE: Stability

- If $R_0 \leq 1$ then the DFE is locally asymptotically stable
- If $R_0 > 1$ then the DFE is unstable
- If $R_0 \leq 1$ and $\delta(\sigma(0))\sigma'(0) > -\frac{\beta}{d}$ then the DFE of the system is GAS.

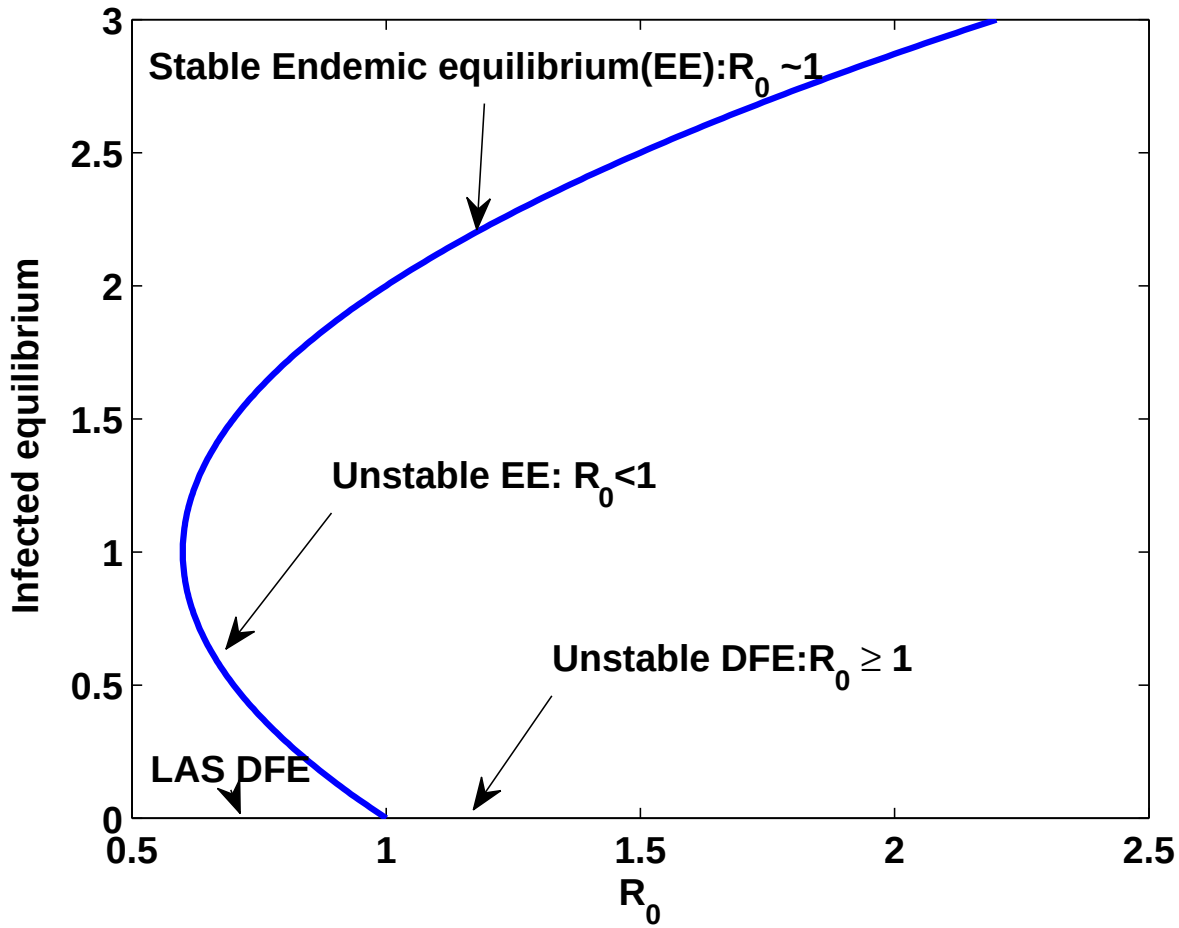
Case $\delta(\sigma(0))\sigma'(0) > -\frac{\beta}{d}$: Transcritical bifurcation

The SDDS system undergoes a transcritical bifurcation, i.e.



Case $\delta(\sigma(0))\sigma'(0) \leq -\frac{\beta}{d}$: Backward bifurcation

The SDDS system undergoes a backward bifurcation, i.e.



Implications

The disease dies out if

$$\frac{\beta\pi}{\alpha d} e^{-\int_0^{\sigma(0)} \delta(s)ds} \leq 1 \text{ and } b < \frac{\beta}{d} \frac{rA}{(A-c)\,\delta(\frac{1}{r}\ln(\frac{A}{c}))}$$

- Decreasing the duration of breastfeeding or decreasing the infection rate are effective at reducing $R_0 < 1$, but may not be successful in eradicating the disease.

- Introduction of antiretroviral drug regimens to prevent mother-to-child transmission of HIV should be accompanied by interventions to minimise the risk of subsequent transmission via breastfeeding.

Limitations-Future Works

- Get data and numerical study of the model with threshold.
- Study the impact of each parameter such that number of exposures, viral load due to exposures, threshold to get infected,... etc.
- Divide infected population into infected infants and mothers.
- Study the impact of vaccines for uninfected infants and drugs for infected mothers.
- Get a job soon...

Limitations-Future Works

- Get data and numerical study of the model with threshold.
- Study the impact of each parameter such that number of exposures, viral load due to exposures, threshold to get infected,... etc.
- Divide infected population into infected infants and mothers.
- Study the impact of vaccines for uninfected infants and drugs for infected mothers.
- Get a job soon...

Thank you!