Silent, Immunizing Ebola Infections

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- Impressive makeshift PPE.
- Potentially aided by asymptomatic immunity?
Evidence for Asymptomatic Infections
Gabon Ebola Outbreak, 1996

• Followed direct contacts of infectious cases
• 24 identified who did not experience any symptoms
• 11/24 developed immune responses
• Not infectious

Estimating the Symptomatic Proportion

• 11 of 24 (46%) of asymptomatic contacts were infected

• Does not directly give symptomatic proportion.

Example

• 1 cases infects 4 people, 2 symptomatic
Estimating the Symptomatic Proportion

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**Example**

- 1 cases infects 4 people, 2 symptomatic
- What’s the symptomatic proportion?
Estimating the Symptomatic Proportion

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Example

• 1 cases infects 4 people, 2 symptomatic

• What’s the symptomatic proportion? 2/4 = 50%

• What’s the proportion of asymptomatic contacts that were infected?
Estimating the Symptomatic Proportion

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• Does not directly give symptomatic proportion.

Example

• 1 cases infects 4 people, 2 symptomatic

• What’s the symptomatic proportion?
  want this  \( \frac{2}{4} = 50\% \)
  we estimate 20-60% based on available data

• What’s the proportion of asymptomatic contacts that were infected?
  have this  \( \frac{2}{8} = 25\% \)
  estimated at 46% in Leroy et al. 2000
Asymptomatic Infection: The Rule, Not the Exception

- Cholera
- Influenza
- Polio
- Pertussis
- Etc..

Potentially more important for Ebola because of high HCW risk.
Motivations for Understanding Silent Immunizing infections

• Projections
Given $R_0 = 2$
After 1 generation interval (15 days)

- Susceptible
- Infectious
- Immune
- Dead
After 2 generation intervals (30 days)
Contacts on survivors are “wasted.”

Eventually causes epidemic decline.

Not many survivors for highly fatal diseases.
Given $R_0 = 2$ and 50% asymptomatic
15 days

- Susceptible
- Infectious
- Immune
- Dead
30 days

- Susceptible
- Infectious
- Immune
- Dead
Contacts are “wasted” on immune individuals early in epidemic.

Immunity accumulates in small clusters with lots of risk (HCW & families).

Most immune individuals not survivors.
Effect of Silent Immunity on Outbreak Projections

Bellan et al. (2014) *The Lancet*. 

Projections consistent with CDC model.
Model Diagrams

Standard SEIR

\[ S \xrightarrow{\lambda} E \xrightarrow{\sigma} I \xrightarrow{(1-f)\gamma} R \]

SEIR with Asymptomatic Infection

\[ S \xrightarrow{s\lambda^*} E \xrightarrow{\sigma} I \xrightarrow{(1-f)\gamma} R \]

\[ \lambda^* = \lambda/s \]

Bellan et al. (2014) *The Lancet*. 
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Bellan et al. (2014) *The Lancet*. 
Effect of Silent Immunity on Vaccination

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Effect of Silent Immunity on Vaccination

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![Graph showing the relationship between cumulative cases and target vaccination coverage.](image)
Motivations for Understanding Silent Immunizing infections

- Projections

- Sample size calculations for vaccine trials
Sample size calculations for vaccine trials

Pre-existing naturally acquired immunity reduces effective sample size of study.
Motivations for Understanding Silent Immunizing infections

• Projections

• Sample size calculations for vaccine trials

• Leverage immune individuals in outbreak control
Leverage Immune Individuals in Outbreak Control

Identify immune individuals (survivors and asymptomatics), allocate them to front-line roles.

Similar to ring vaccination.
Two Critical Questions

• Are asymptotically infected individuals immune?

• Can we reliably identify them?

Must answer both of these before we can move forward on interventions.
Actionable Item 1: Domestic Studies

- Collect blood from contacts of Ebola cases in the US
  - Duncan’s family, Dallas nurses, NYC case
- Serology, PCR, other immunological assays
- Calculate the asymptomatic proportion

Duncan had > 70 contacts. If just two of them test positive, symptomatic proportion = 50%.

Can be done immediately, BSL-4 lab (RMNL) ready to do assays given samples.
Actionable Item 2: Animal Model Studies

- No NHP model for asymptomatic infection
- Collect blood from
  - EVD survivors
  - asymptomatically infected indiv.
- Give plasma or fractionated antibodies to NHPs, then challenge them
Actionable Item 3: Vaccine Efficacy Trials

- Baseline serum can help estimate asymptomatic proportion.
- Difference in Ebola risk in
  
  ![Diagram showing comparison between Vaccine and Control groups]

  in control arm indicates protective immunity.

- Any study of front-line workers → use serology to learn more.

MUST balance with risk of blood draws, resource scarcity
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Attribution:

Code: [http://ebola.ici3d.org/](http://ebola.ici3d.org/)

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