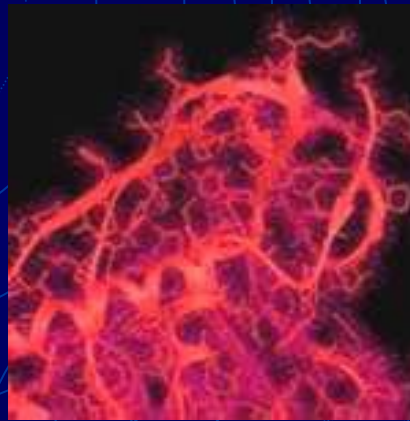
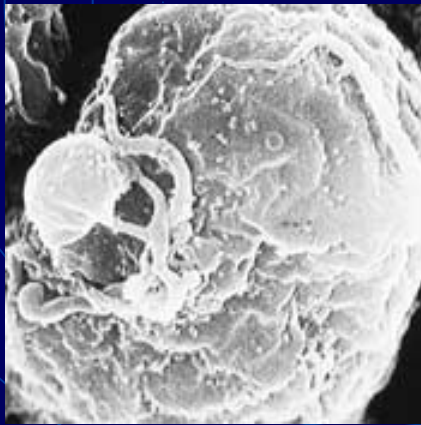


# Superinfections: *Real or Imagined Threat?*



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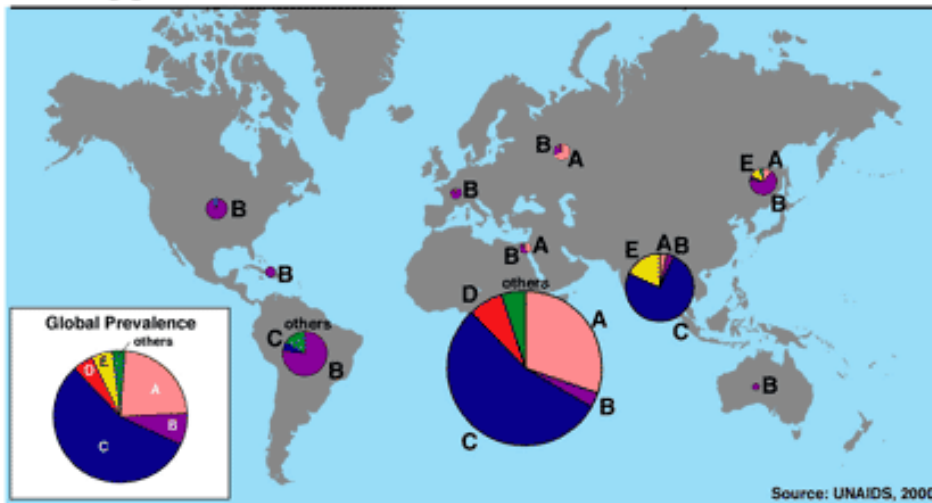
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# What is Superinfection?

- Coinfection vs. Superinfection
- HIV Classification: Type 1 with groups M, O, N plus 9 subtypes and Type 2.
- There is evidence that the global distribution of HIV is changing!

## Estimated Global Distribution of HIV-1 Subtypes



## The Theoretical Dangers of Superinfection:

- superinfected patients are more difficult to treat
- superinfected patients may see rapid progression to AIDS
- may have different viral load levels and transmission rates
- evolution of drug resistance through drug recombination
- finding a vaccine may be even harder!

# Background to the Superinfection Debate

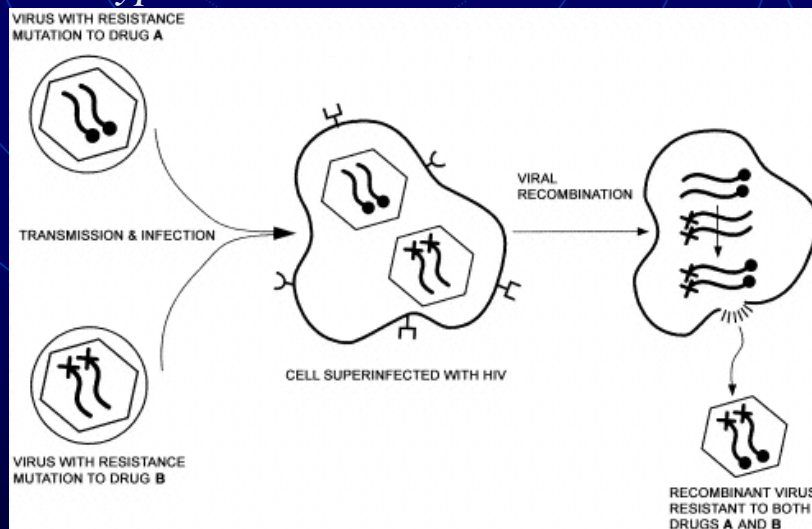
- Early Experimental Evidence:
  - early experiments showed that HIV superinfection was *theoretically* possible
  - in vitro studies
  - animal models- exposure to 2 different SIV strains caused the superinfected chimp to rapidly progress to full-blown AIDS
- Early Case Studies in Humans:
  - people infected by more than one strain had been documented but they were classified as ‘coinfections’
  - it was (and continues to be) difficult to test whether a person has a superinfection vs. coinfection due to the difficulty in est. onset time difference
  - for years there were simply no documented cases of proven superinfection
- Other Viral Diseases
  - superinfection is acutally quite common in viral infections
  - e.g. Epstein-Barr, herpesvirus, papillomavirus

# Critical Issues and Controversies: Is the superinfection threat real?

- Early in the AIDS epidemic, it was believed that infection by one strain brought about an initial immune response that protected the infected person from being infected from a second strain
  - 1998: Superinfection shown to be possible in chimps. HIV specialists assume that superinfection, even if it does occur in humans is probably rare. Many believed that there is only a brief window in which superinfection can occur.
- fast-forward to the last 2 years of HIV/AIDS research

# Is the superinfection threat real? YES

- Sept. 2002: First proven case of superinfection. 38 year old Genevan man was doing extremely well under HAART until he suddenly progressed rapidly to AIDS. Blood work showed that a second strain of virus (subtype B) had rapidly replaced his initial AE strain. Just weeks before viral rebound, he had unprotected sex in Brazil, where subtype B is dominant.
- April 2003: A patient was superinfected with a second virus from *the same subtype!*



→ Being reinfected with the same subtype as the first subtype DOES NOT confer protection (vaccine development will be very difficult indeed!)

→ superinfection more common than had been previously thought.

- July 2003: First proven case of superinfection and **recombination**. A superinfected woman's tests showed that her viruses had mixed and produced a hybrid that took over the original virus

# Problems and Implications

## 1. Policy Problems:

- the Stop AIDS Project in San Francisco had approved of unprotected sex between MSM partners of the same serostatus
- clearly this type of strategy needs rethinking

## 2. Treatment Difficulties

- treatment is especially difficult for superinfected patients who have one drug-resistant strain and one non-drug resistant strain
- also, evidence shows that superinfection causes rapid disease progression

## More Problems and Implications...

### 3. Vaccine Development Difficulties

- superinfection is even possible for 2 different viruses from the same subtype! Threat of superinfection and recombination.
- each HIV case is unique, “like a fingerprint”

### 4. Superinfection in the future will most likely increase b/c:

- a) Increasing # of people in the world living with HIV
- b) Increasing travel and mobility of people today
- c) Increasing rates of unsafe sex by those infected

“[Superinfections have] the potential to significantly affect the HIV pandemic in the future.”

- Jason T. Blackard, MD

# Proposed Solutions

## 1. Promote safe sexual practices, even between serocordant partners.

- initial pilot study by UCSF “Positive Partners Study of HIV-1 Superinfection” found that very few sexually active HIV-infected MSM are monogamous
- prevention efforts need to extend to those who are already infected

## 2. Campaign for public awareness of the dangers of superinfection

- there is a tendency for those already infected with HIV to think that having unprotected sex will not expose them to any further risks
- UCSF pilot study also found that partners who believed in superinfection were more likely to be monogamous and/or to use protection.

# Proposed Solutions

## 3. Constantly monitor the changing global distribution of HIV strains

- there are an increasing number of non-subtype B cases in the US
- national monitoring of the US strains by having clinics submit information to a national database; encourage national governments to do the same
- in resource-poor settings, concentrate on monitoring at high-traffic areas such as borders, sea coasts, roadside villages, and so on.

## 4. Consider each HIV case as very specific, much like a finger print

- treatment of each HIV infected individual may need to be very specific to their HIV case
- vaccine development will need to consider the possibility of recombination

# Many Studies are Still Needed

## 1. Clinical Studies

- Clinical studies are urgently needed to evaluate differences in: viral load, transmission rates, disease progression, treatment success and failure rates, vaccine implications, and drug resistance implication

## 2. Epidemiological Studies

- studies on the population level have thus far been largely weak or uninitiated
- there is an urgent need to assess the prevalence of superinfection in the general population.

# Conclusions

- The scientific data from the past two years and the data that is continuing to emerge to this present day suggests that superinfection is a phenomenon that is no longer just theoretical. Furthermore, the likelihood of superinfection will most likely increase in the future due to the increasing number of people living with AHIV, the increasing mobility and travel of people, and, in certain regions of the world, the increasing rates of unsafe sex by those infected. We need to deal with the real threat that superinfection poses.
- Superinfection concerns, up until recently, have been overly relaxed. HIV studies (both epidemiological and clinical) need to take a new direction to answer to superinfection uncertainties. Furthermore, policies today need to be revised to anticipate the increasing possibility that superinfection may significantly alter the future of the HIV pandemic.

