

**Viral Outbreak: The Science of Emerging Disease**  
**2010 Holiday Lectures on Science**  
**Chapter List**

Lecture One

Dengue Fever: Breaking Epidemic Cycles

Eva Harris, Ph.D.

1. Start of Lecture One
2. Welcome by HHMI President Dr. Robert Tjian
3. Profile of Dr. Eva Harris
4. Dr. Harris first visited Nicaragua right after college
5. What is dengue fever?
6. Video: Managua: Rapid, Unplanned Urbanization
7. Dengue virus and vectors
8. Most dengue cases are asymptomatic
9. Rapid global spread of dengue
10. Animation: Dengue Fever Re-emergence in the Americas
11. Multiple types of dengue virus
12. Causes of dengue re-emergence
13. The immune response and severe dengue
14. A broad-based public health research approach
15. Pediatric cohort study to track dengue epidemics
16. Cohort study detects symptomatic and asymptomatic infections
17. Q&A: Would disease severity be worse if infected by all four serotypes?
18. Q&A: Would a live or a dead vaccine be better?
19. Q&A: Who funds your research programs?
20. Q&A: Is global warming helping spread dengue to the United States?
21. Spread of mosquito vector, spread of dengue
22. Large-scale mosquito control programs
23. Video: The Mosquito Life Cycle
24. Community-based mosquito education strategies
25. Video: Mosquito Vector Education Program in Nicaragua
26. Top-down and bottom-up approaches to mosquito control
27. A community-based mosquito control program
28. Measuring the effectiveness of community-based programs
29. Reduction of mosquito vectors by community-based programs
30. Building sustainable local capacity for vector control
31. Video: Health Brigades in Managua's Neighborhoods
32. Video: Mosquito Reggaeton, a Dengue Rap Song
33. Q&A: Does dengue fever only spread through mosquito vectors?
34. Q&A: What protects children who are infected but remain asymptomatic?
35. Q&A: Would putting screens in windows solve the problem?
36. Q&A: Do dengue symptoms differ between infants and adults?
37. Q&A: How is dengue spreading to the US? We don't use water barrels.
38. Q&A: Is dengue a rural problem?
39. Q&A: How do you control larvae if you can't afford to dump water?
40. Q&A: Are elderly people at greater risk from dengue?
41. Closing remarks by HHMI President Dr. Robert Tjian

## Lecture Two

### The Virus Hunter's Toolkit

Joseph L. DeRisi, Ph.D.

1. Start of Lecture Two
2. Welcome by HHMI Vice President Dr. Sean Carroll
3. Profile of Dr. Joseph DeRisi
4. Leading causes of death for children worldwide
5. Infectious disease is a major cause of child mortality
6. Video: Many Pathogens Affect Patients at a Nicaraguan Clinic.
7. How do you determine the cause of an infectious disease?
8. Koch's postulates for identifying an infectious agent
9. Viral plaque assay
10. Identifying viruses by their structure
11. Animation: Viral Geometry and Structural Diversity
12. Animation: Structure of Dengue Virus
13. Antibodies can recognize specific viruses
14. Classifying viruses by their genome type
15. Q&A: How can you stop viruses from spreading to other cells?
16. Q&A: What kind of antigens do viruses have?
17. Q&A: Where do secondary antibodies come from?
18. Q&A: Do lipid membranes come from other organisms?
19. Q&A: What are the advantages of different viral replication mechanisms?
20. Q&A: Are there innate defense mechanisms to detect viral DNA in the cell?
21. Concept of chip-based tool that can detect any virus
22. Animation: The Chemical Structure of DNA
23. DNA hybridization can detect viral DNA in a complex mixture
24. Replicating viral DNA in vitro
25. Kary Mullis's contribution to polymerase chain reaction
26. Animation: The Polymerase Chain Reaction (PCR)
27. Various PCR machines
28. Sanger method of DNA sequencing
29. PCR and sequencing for viral diagnostics
30. Virochip designed to represent all known viruses
31. Evolutionarily conserved sequences can identify unknown viruses
32. Animation: Running a Sample on a Virochip
33. Using the Virochip to identify viral pathogens
34. Q&A: How do you interpret the complicated pattern of Virochip output?
35. Q&A: Is Virochip ready for mass production as a diagnostic tool?
36. Q&A: How would you analyze a mixed sample of two viruses on a Virochip?
37. Q&A: Does Virochip analyze both RNA and DNA viruses?
38. Q&A: Can you use Virochip to find viruses that naturally attack cancer?
39. Closing remarks by HHMI Vice President Dr. Sean Carroll

## Lecture Three

### Fighting Viruses in the Lab and Beyond

Eva Harris, Ph.D.

1. Start of Lecture Three
2. Welcome by HHMI Program Director Dr. Dennis Liu
3. Profile of Dr. Eva Harris
4. Immune system as potential foe
5. Animation: Dengue Virus Enters Cell to Begin Infection
6. Antibodies neutralize viruses and tag them for destruction
7. Antibody-dependent enhancement (ADE) of disease symptoms
8. ADE leads to physiological changes that cause severe dengue
9. Maternal antibodies can cause ADE in infants
10. Engineering a mouse model for dengue research
11. Severe dengue can be induced by ADE in the mouse model
12. ADE mouse has high viremia and elevated cytokines
13. In vitro cellular model of ADE
14. Modified antibody can prevent ADE in vitro
15. Modified antibody can prevent ADE in mouse model
16. Modified antibodies work as therapy
17. Using the dengue mouse for basic and clinical research
18. Q&A: Can the modified antibodies be used as a vaccine?
19. Q&A: Can injected antibodies compromise you against other serotypes?
20. Q&A: Can this treatment be applied for other viral diseases?
21. Q&A: Wouldn't the dengue RNA be degraded in the cytoplasm?
22. Building research capacity in developing countries
23. Strategies for enhancing local scientific capacity
24. Transferring technologies and alternative techniques
25. An RT-PCR test to identify dengue subtypes
26. PCR test successes in the field
27. The impact of the Sustainable Sciences Institute
28. Video: Impact of Nicaraguan Dengue Project
29. Large cohort study reveals impact of influenza in Nicaragua
30. Improving clinical processes with technological advancements
31. Taking the fight against the diseases to the front lines
32. Q&A: Where does your motivation come from?
33. Q&A: How long does manual PCR take?
34. Q&A: Can dengue virus remain latent in the body?
35. Closing remarks by HHMI Program Director Dr. Dennis Liu

## Lecture Four

### Solving SARS and Other Viral Mysteries

Joseph L. DeRisi, Ph.D.

1. Start of Lecture Four
2. Welcome by HHMI President Dr. Robert Tjian
3. Profile of Dr. Joseph DeRisi
4. SARS: A global epidemic
5. Origin of SARS epidemic
6. Case definition of SARS
7. SARS spreads worldwide
8. Virochip identifies SARS virus
9. Sequencing confirms SARS is caused by a new coronavirus
10. SARS epidemic stopped in 6 months
11. SARS coronavirus originally came from horseshoe bat
12. Proventricular dilatation disease (PDD): Mysterious parrot disease
13. Virochip indicates bornavirus may cause PDD
14. Ultra-deep sequencing reads hundreds of millions of bases at once
15. Assembling sequences to get complete viral genome
16. Comparing sequences to known bornavirus genomes
17. Testing that the candidate bornavirus causes PDD
18. Q&A: What challenges did you face in developing the Virochip?
19. Q&A: Where did the index patient get SARS originally?
20. Q&A: Has treatment been developed for SARS?
21. Q&A: What makes SARS so much more transmittable?
22. Finding novel viruses in a Nicaraguan cohort
23. Bioinformatic filtering of deep-sequencing data to find viral DNA
24. Discovery of EV109, a novel enterovirus
25. Full-sequence analysis shows EV109 combines 3 viruses
26. Comparison of advances in DNA sequencing to advances in telescopes
27. Sequencing your personal genome
28. Sequencing all the microbes associated with humans
29. Q&A: Are there other sequencing technologies?
30. Q&A: Are we born colonized by bacteria and viruses?
31. Q&A: Can DNA chips be used to identify diverse HIV types?
32. Q&A: How does zoonosis occur?
33. Closing remarks by HHMI President Dr. Robert Tjian