2000 and Beyond: Confronting the Microbe Menace
1999 Holiday Lectures on Science
Chapter List

Lecture One
Microbe Hunters: Tracking Infectious Agents
Donald E. Ganem, M.D.

Lecture Two
The Microbes Strike Back
B. Brett Finlay, Ph.D.

1. Start of Lecture Two
2. Introduction by HHMI President Dr. Purnell Choppin
3. Introductory interview with Dr. Brett Finlay
4. Dr. Finlay describes objectives of this lecture
5. Demonstration: Size analogy of bacteria
6. How does one study bacteria?
7. Bacteria are everywhere
8. Role of bacteria in body
9. Cheek cell demonstration
10. Rate of bacterial reproduction
11. Video clip: Bacterial growth
12. Mortality rate and productivity loss from infection
13. List of the leading deadly bacteria
14. Susceptibility to disease
15. Disease kills more people than bullets do
16. Bacteria cause many diseases
17. Ulcers and other diseases caused by bacteria
18. How do bacteria spread?
19. Demonstration: Air transmission of bacteria
20. How do we fight bacteria?
21. Antibiotics: Penicillin structure
22. Origin of antibiotics
23. Antibiotic modes of action
24. Culture plate showing antibiotics' effect
25. Video clip: Penicillin killing *E. coli*
26. Antibiotics increased life expectancy by eight years
27. Bacteria can develop antibiotic resistance
28. How does antibiotic resistance develop?
29. Superbugs
30. Bacteria can share antibiotic resistance
31. Animation: Conjugation
32. Development cost of antibiotics
33. How should we use antibiotics?
34. Vaccines: Basic facts
35. Should everyone be vaccinated?
36. List of available vaccines in 1959, 1982, and 1999
37. How do we develop a vaccine?
38. Genomics of bacteria
39. Bioinformatics and the Human Genome Project
40. Who will win–humans or bacteria?
41. Student question: Why don't we have an AIDS vaccine?
42. Student question: Do disinfectants affect resistance?
43. Student question: Can we use viruses to kill bacteria?
44. Student question: What bacterial disease causes blindness?
45. Student question: How do we deal with biological warfare?

46. Student question: How does flesh-eating disease work?
47. Student question: How do resistances initially develop?
48. Student question: How do we treat different areas of the body?
49. Student question: Can we use antibiotics years later?
50. Student question: Can we modify antibiotics to overcome resistance?
51. Closing remarks by HHMI Vice President Dr. Joseph Perpich

Lecture Three
Outwitting Bacteria's Wily Ways
B. Brett Finlay, Ph.D.

1. Start of Lecture Three
2. Introduction by HHMI Vice President Dr. Joseph Perpich
3. Interview with Dr. Brett Finlay: Joy of scientific study
4. Lecture Three objectives
5. What is a pathogen?
6. *E. coli* introduction
7. Two types of *E. coli*: EPEC and EHEC (0157:H7)
8. *E. coli* infection via ground beef and vegetables
9. What does *E. coli* actually do?
10. What virulence factors does *E. coli* possess?
11. Bundle-forming pilus attaches to host
12. Animation: *E. coli* adheres to host using the pilus
13. Demonstration: virulence factor injected into host cell
14. Type III secretion system
15. *E. coli* injects its own receptors into the host cell
16. Virulence factor modifies cell signaling
17. Animation: *E. coli* injects receptor protein into host and binds to it
18. *E. coli* changes host cell cytoskeleton
19. Animation: *E. coli* causes pedestal formation
20. Electron micrograph of pedestal *in vivo*
21. Toxins as virulence factors; Shiga toxin in enterohemorrhagic *E. coli*
22. Evolution of pathogenic *E. coli*
23. Potential therapies to fight bacteria
24. Introduction to *Salmonella*
25. Microscopic view of live *Salmonella*
26. Virulence factors of *Salmonella*
27. Demonstration: Jell-O simulation of *Salmonella* invasion
28. Video: Living *Salmonella* invading a cell
29. Animation: *Salmonella* invading a cell
30. *Salmonella* needs to survive and multiply inside the host cell
31. Animation: *Salmonella* inside the host cell
32. Bacterial strategies for intracellular survival
33. Introduction to *Listeria monocytogenes*
34. Demonstration: Jell-O simulation of *Listeria* invasion
35. Intracellular lifestyle of *Listeria*
36. Video: Live *Listeria* moving inside the host cell
37. Regulation of virulence factor expression
38. The future of infectious bacterial diseases
39. Student question: Treatment differences for gram-positive and gram-negative bacteria
40. Student question: Why don't we have a cure for the common cold?
41. Student question: Lysosome avoidance by *Listeria*-type invaders
42. Student question: Is the actin used by bacteria the same as actin/myosin?
43. Student question: How do some pathogens mutate faster than others?
44. Student question: Are there harmless bacteria in humans that harm animals?
45. Student question: How do bacteria survive host cell death?

46. Student question: Jungles as a source for antibiotics
47. Closing remarks by HHMI Vice President Dr. Joseph Perpich

Lecture Four
Emerging Infections: How Epidemics Arise
Donald E. Ganem, M.D.

1. Start of Lecture Four
2. Introduction by HHMI Vice President Dr. Joseph Perpich
3. Interview with Dr. Donald Ganem: What I like about being a scientist
4. How do new epidemics arise?
5. New diseases arise from disruption of virus-host equilibrium
6. Genetic changes in viruses: Mutation and recombination
7. High rate of mutation in RNA viruses
8. Mutations that do not change the amino acid sequence
9. Why do RNA-based genomes have a higher mutation rate?
10. DNA proofreading mechanism
11. Consequences of an elevated mutation rate
12. Influenza virus: Protein and genomic structure
13. Pathology of influenza
14. Influenza epidemics caused by antigenic drift
15. Influenza pandemics caused by antigenic shift
16. Genetic basis of antigenic drift
17. Molecular structure of hemagglutinin
18. Genetic basis of antigenic shift
19. Origin of different influenza hemagglutinin types
20. Animation: Recombination of viral RNA in a host cell
21. Where does recombination take place in nature?
22. Environmental changes can cause new epidemics: Hantavirus
23. What environmental change was responsible for the hantavirus epidemic?
24. Human migration affects epidemic patterns: Smallpox
25. Why was smallpox so much more severe among Native Americans?
26. Lesson learned from rabbits in Australia
27. Myxoma virus as a rabbit-control agent
28. Less virulent myxoma strains emerge and maximize the spread of disease
29. Natural selection results in minimized susceptibility to disease
30. Comparing the myxoma virus in Australian rabbits and smallpox in Native Americans
31. What forces will shape the epidemics of the future?
32. Subtle changes affecting spread of diseases: Dengue fever and West Nile virus
33. Conclusion
34. Student question: Can we create a vaccine that covers all influenza strains?
35. Student question: How do DNA viruses mutate:
36. Student question: Can different species of bacteria and viruses trade genes?
37. Student question: How do researchers and health organizations share information?
38. Student question: Are some regions of the influenza genome more mutable?
39. Closing remarks by HHMI Vice President Dr. Joseph Perpich
40. Closing remarks by HHMI President Dr. Purnell Choppin