Pioneer Science and the Great Plagues

Cheville, Norman F

Published by Purdue University Press

Cheville, Norman F.

Purdue University Press, 2021.
Project MUSE. muse.jhu.edu/book/84018.

For additional information about this book
https://muse.jhu.edu/book/84018
For a decade after World War II there had been concerns nationwide that the population was dumbing down. Then, in fall 1957, the Soviet Union launched its satellite Sputnik. Ban the Bomb movements appeared by banner-carrying activists. There was discontent about the “damaging effects” of modern science. The reality was that the nation was failing in science education. The National Defense Education Act of 1958 was passed by legislators and signed by President Eisenhower, who believed the U.S. was falling behind the Soviet Union in education. The Act led directly to biology textbooks that stressed the cell’s organelles and genes in life processes and evolution as a unifying principle of biologic change.

Evolution, clearly established in science for several generations, was no longer controversial among responsible citizens. The new discipline of evolutionary biology had been solidly built on the convergence of such diverse technologies as biology, anthropology, and physical chemistry. Darwin’s evolution through continual genetic change in species was being revolutionized by Stephen Gould’s stasis theory of punctuated equilibrium, preaching that there is a uniform, steady, gradual transformation of entire animal lineages—once a new species appears on the fossil record it becomes stable, with individuals showing all evolutionary change for most of its geologic history.

By the 1960s, the biological sciences were being transformed. Electron microscopy, protein chemistry, and DNA technology were being refined and used to explain how life processes work and how they are controlled by genes. The Romanian American George Palade combined biochemistry with electron microscopy of cellular structure to lay the groundwork for another new
discipline, cell biology. Together with Belgians Albert Claude and Christian de Duve, for discovering the protective cellular organelles they named peroxisomes and lysosomes, Palade won the Nobel Prize in 1974. There were leapfrog advances in technology and theory that began to link biochemistry, genetics, and virology into yet another new discipline, molecular biology.

In infectious disease research, scientists for the first time could see viruses inside the cell. Electron micrographs showed how viruses replicate within cellular organelles, solving problems in a few days that had been hanging around for decades. Scientists were publishing pictures of the ultrastructure of viruses and of how they attacked and killed cells. Influenza viruses could be seen attaching to cilia in the respiratory tract. Herpesviruses were photographed killing epithelial cells and in their sneaky move up the nerves to hide out in the brain. New adenoviruses were discovered that caused cold-like respiratory infections that could move into serious systemic disease in many species. To detect specific virus-infected cells under the light microscope, sophisticated labeling techniques were developed using antibodies complexed with fluorescent dyes.

In the next decades, Nobel Prizes in Physiology and Medicine were awarded for work done in the 1950s. Veterinarian Harry Rubin won the Lasker Award in 1964 for his discovery of the first cancer gene— src, short for sarcoma— showing that every cancer cell carried the virus and suggesting that it was a viral gene that drove the cell to malignancy. His work was done before cloning and genetic sequencing appeared, and it paved the way for the new field of viral oncogenesis. Rubin and his graduate student Howard Temin devised techniques to measure the virus in chick embryo cells in culture. The 1975 Nobel Prize went to Renato Dulbecco for his discovery of other new cancer-causing viruses and to Temin and David Baltimore, who had discovered reverse transcriptase, an enzyme that cancer viruses use to take over and control DNA metabolism. In 1976 the Prize went to Barry Blumberg for research on hepatitis B virus and Daniel Gajdusek for kuru.

Veterinary students bearing superb science credentials were highly qualified for biological research and began a transformation of veterinary science that not only attacked critical problems in animal health but burnished the reputation of the profession. Science and society were making a big transition. In a national poll taken four decades later, veterinarians were rated high as the “most trusted profession,” second only to nurses.
31. NEW PROGRAMS, NEW LABORATORIES: MALARIA, POLIO, AND NEW VIRUSES

After the war, the government’s World War II Malaria Control in War Areas program, located in Atlanta, Georgia, became a new agency under the U.S. Public Health Service dedicated to research and development for the control of malaria. Because malaria was still common in the South, the new agency remained in Atlanta. Named the Communicable Disease Center, its specialties were malaria, engineering, and entomology—nearly 60 percent of its staff and budget were dedicated to mosquito control.

From its beginning, the malaria control program at the Communicable Disease Center had a problem. DDT, short for dichlorodiphenyltrichloroethane and used in World War II to control mosquitos and body lice, was being used throughout the world. In 1945, dangers were recorded by U.S. Fish and Wildlife Service biologists, who warned that the use of DDT in marshes might be killing wild birds. By the 1960s, clues began to appear around the world that DDT was killing avian species and was also accumulating in soils and the tissues of wild animals. The food chain effect seemed ominous: plants accumulate toxins, herbivores get them from plants, carnivores from their food, and, finally, humans—if the rate of absorption is higher than the rate of loss.

The long struggle to legislate against the use of DDT began later when its effects were conspicuous: peregrine falcons and osprey began to disappear from their North American ranges along the Atlantic Seaboard. DDT was causing soft-shelled eggs, which were easily broken in the nest. Reproduction failed and bird populations declined. It took ten years, but DDT was finally banned for use. Alternative mosquito control chemicals appeared.

The Communicable Disease Center (now known as the Centers for Disease Control and Prevention—the CDC) quickly grew into related areas, and within a decade it was assigned new programs: venereal disease in 1957, tuberculosis in 1960, and immunization programs in 1963. To work at the center, veterinarians were commissioned officers in the U.S. Public Health Service, and the expertise gained in the science milieu of the laboratories provided leaders for the coming decades. Many of these veterinary scientists matured into international scientific experts.

Medical research was focused on polio when World War II ended. For two decades, infantile paralysis had crippled and killed children in the
developed countries of the world. Poliomyelitis virus attacked the brain and spinal cord, killing neurons that controlled muscles of the legs and diaphragm. Survivors were left crippled and, in severe cases, unable to breathe. Gruesome iron lungs, which compensated for paralyzed diaphragms, appeared in children’s hospitals. In the dog days of late summer, children were to avoid swimming pools, summer camps, and county fairs. Yet infantile paralysis seemed to be capricious, afflicting some children but not their siblings. Curiously, it seemed to occur more commonly in the cleanest households. Disturbing for scientists studying epidemiology, paralytic polio was practically unknown in Egypt and other countries with poor sanitation but widespread in developed nations—one of the worst outbreaks was during 1952 in Sweden.

Massive funding was available for research, but vaccine development was seriously hampered by one block: the difficulty in growing polio virus. The virus did not replicate in chick embryos, and assays in mice were not accurate. A polio-like virus from mice—discovered in 1937 by Max Theiler at the Rockefeller Institute—was a model for studying pathogenesis, but it was not all that helpful for the human infection. Human poliovirus would infect monkeys, which were a much better model, but they were costly to maintain. Polio research was laborious, time-consuming, and expensive, and for most scientists, unproductive. It required hundreds of rhesus monkeys imported from India on a massive scale. Veterinarians specializing in laboratory animals were required to care for all these experimental animals and a new field was born: laboratory animal medicine.

Rhesus monkeys were a serious danger to laboratory workers. Imported monkeys commonly had tuberculosis and measles acquired from their captors in India. They also carried a killer virus: their own version of human cold sores, a local infection of the lips and mouth that healed without treatment. Monkey B virus behaved like its close relative, human herpes simplex virus. The problem was that if transmitted to humans, monkey B virus caused an inescapable and uniformly fatal encephalitis for which there was no vaccine or treatment, and no survival. By 1960, monkey B had killed thirteen scientists and technicians working with monkeys, including three physicians and two veterinarians.¹

The inability to sustain isolated cells in the laboratory—in vitro in scientific lingo—was the limiting factor in polio research. The breakthrough came in 1952 when John Enders at Harvard Children’s Hospital published his report on the growth of poliovirus in the laboratory. He successfully perpetuated cells from
monkey kidneys by placing them in glass tubes containing a growth fluid that allowed the cells not only to survive but to support the replication of poliovirus. With Enders’s discovery, the race to produce a new polio vaccine was on. In 1955 the first polio vaccine was licensed. John Enders’s cell culture system had been the major medical discovery in polio research that led to the vaccine, and it won him the Nobel Prize.

The new technology to grow viruses in vitro—outside the living animal—had direct impacts on medical and veterinary science: cell cultures from pigs, calves, dogs, and cats were developed to isolate viruses from diseases in animals. New polio-like viruses were found that caused encephalitis in pigs, mice, and chickens. Vaccines based on cell culture technology quickly appeared against feline distemper, canine distemper, infectious hepatitis, and rabies in dogs.

In the next decade, the growth of high-population livestock operations would be possible because of vaccines produced against viruses of cattle and pigs. Cornell University established the Veterinary Virus Research Institute in 1950, renamed two years later as the James A. Baker Institute. Using the new cell culture technology, Cornell scientists discovered the causal viruses of several great plagues of cattle: virologist John H. Gillespie, James A. Baker, and Peter C. Kennedy reported the viral cause of infectious bovine rhinotracheitis—IBR for short—and pathologist Peter Olafson explained the pathogenesis of BVD—bovine viral diarrhea.

The close similarity of monkeys and other nonhuman primates to humans and the striking success in polio research was soon extended into other investigations. In 1962, several National Primate Research Centers were established by Congress, designed to be a national network of laboratories and scientists that specialize in studies of high-profile human diseases, ranging from autism to multiple sclerosis and other nasty neurologic disorders. The primate centers worked cooperatively with the National Institutes of Health as well as private foundations, industry, and other governmental agencies. For veterinarians whose science overlapped with medicine, the primate centers were a big stimulus. The New England Regional Primate Center associated with Harvard University had an outstanding Department of Comparative Pathology. Veterinary pathologists Ronald Hunt and Norval King discovered how cancer is caused by several primate viruses. Herpesvirus saimiri, an indigenous and noncytopathic virus of squirrel monkeys (Saimiri sciureus), when infecting other new-world monkey species (such as owl monkeys, spider monkeys, or marmosets), produced a
rapidly progressive cancer—a malignant T cell lymphoma that killed in thirteen to twenty-six days with massive invasion of body organs by malignant lymphocytes. The malignant cells did not contain the virus, only the viral genes.

Veterinarian Ralph Brinster at the University of Pennsylvania was developing new techniques for growing mouse embryos in cell culture and to manipulate embryos to study embryonic cell differentiation. One of the most celebrated veterinary scientists, Brinster founded a new discipline that dealt with transfer of foreign genes into mammals, transgenic stem cell implants, in vitro fertilization, and deletion of genes—knockout mice. He was elected to the National Academy of Sciences in 1987 and received the Presidential Medal of Honor from President Obama in 2010.7

32. COMPARATIVE MEDICINE: MODELS FOR LEUKEMIA

In 1908 two veterinarians, Vilhelm Ellermann and Olaf Bang, working at the Royal Veterinary School in Copenhagen, published a report that proved what field veterinarians had been telling them for some time, that avian leucosis—a form of leukemia in chickens—was a transmissible disease. Their disciplined experiments proved that to be true, and that whatever was causing the disease was much too small to be a bacterium. At the time, the status of human leukemia was vague; some physicians even suggested that human leukemia was not a “true tumor.” No one in medical science took leukemia in chickens seriously.

Close on the heels of the Danes was a report in 1911 from the Rockefeller Institute in New York City. Peyton Rous, also working with chickens, discovered that a tumor composed of fibrous connective tissue—the Rous sarcoma—was transmissible by a virus. No one in medicine thought much of that either. The response of the scientific community to these seminal discoveries on virus-induced cancers ranged from disinterest to disbelief.

To deal with continuing losses to the poultry industry from leukemia and lymphoma, the Bureau of Animal Industry established a poultry research laboratory in the 1930s in East Lansing—close to Michigan State University. The big poultry problem was the avian leukosis complex, a group of lymphomas and soft tissue tumors called big liver disease, range paralysis, and gray eye according to the organ in which the lymphoma tumors grew in the sick birds. At