

Reston's Hot Zone 20 Years Later

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Citation

C Berry-Cabán. *Reston's Hot Zone 20 Years Later*. The Internet Journal of Preventive Medicine. 2010 Volume 2 Number 1.

Abstract

In 1989, Reston, VA one of the most famous U.S. planned communities located about 10 miles from Washington DC stood at the epicenter of a potential biological disaster. This well-known story was narrated by Richard Preston in a bone chilling account related to the recognition and containment of a devastating tropical filovirus at a monkey facility the Reston Primate Quarantine Unit. This article reviews the antecedents leading up to the event, the role of the US Army in detecting Ebola and deploying a veterinary containment team and subsequent events since the initial outbreak.

INTRODUCTION

It was called the "Monkey House," a small stand-alone building located in one of the first office parks constructed in Reston, Virginia. Reston sits on land initially owned during the 18th Century by Lord Fairfax. In 1961, Robert E. Simon, having recently sold New York City's Carnegie Hall, bought most of the land and founded Reston on his 50th birthday April 20, 1964 naming it for his initials. Reston, an architectural dream, was the first modern, post-war planned community in the United States, sparking a revival of the new town concept that incorporated higher density housing to conserve open space, as well as promoting the mixed use of industry, business, housing, recreation and schools¹.

The careful planning and zoning within Reston provided common grounds, parks, large swaths of wooded areas with picturesque runs, wildflower meadows, golf courses, public swimming pools, bridle paths, a bike trail, lakes, tennis courts and extensive foot pathways²⁻⁴.

The first time I visited Reston in early 1980, it took me nearly an hour and a half by bus from the District of Columbia to make the 10 mile trip on the Virginia side of the George Washington Parkway down a stretch of Interstate 495 into Tysons Corner, then onto Leesburg Pike to Reston. Today the trip is much less time consuming due to new roads and access (and a metro train rail currently under construction).

Several years later I moved to Reston with my family. Reston was now coming into its own during the 1980s economic boom. Daily a new building seemed to materialize. As tenants moved in, older business parks often

converted to more mundane uses. By 1989, Isaac Newton Square consisted of approximately 20 brick and concrete small office buildings that housed an aerobics spa, police station, nail care salon, software firm and a diner.

By 1989, approximately 48,000 people resided in the community when Hazelton Research Products leased a structure at 1946 Isaac Newton Square West. The building was located just off Wiehle Avenue and a block North of Sunset Hills Road. Across the street, on Roger Bacon Drive, stood my offices. They christened the building the "Reston Primate Quarantine Unit." And it housed monkeys⁵.

THE EMERGENCE OF NONHUMAN PRIMATE QUARANTINING

The quarantining of monkeys in the US began in the 1940s and 1950s as increased numbers of nonhuman primates were imported to support disease research. Because many animals were caught in the African and Asian wilderness, there was potential for an animal or a group of animals to bring in new diseases that could pose a health threat to both humans and animals. During the 1960s and early 1970s, a number of African species were imported for infectious disease research including baboons, Vervets and Patas monkeys⁶.

At the same time, Asian species, predominantly macaques, also began being imported⁶. Several disease outbreaks occurred among imported Asian macaques which soon led to the recognition that many primate species carry simian hemorrhagic fever. While humans are not susceptible to simian hemorrhagic fever, it is highly infectious among monkeys, killing nearly 100% of those that come into contact with the disease.

Simian hemorrhagic fever is caused by Simian hemorrhagic fever virus (SHFV), which is currently classified as an arterivirus in the family Arteriviridae, order Nidovirales. In contrast to its closest relatives, the arteriviruses equine arteritis virus, lactate dehydrogenase-elevating virus, and porcine respiratory and reproductive syndrome virus, SHFV is almost completely uncharacterized. Thus far, SHFV has never been isolated from wild animals and all outbreaks have occurred within primate-holding facilities^{7,8}.

Until the 1990s, the length of quarantine varied from 40 to 90 days. The requirement for having three negative tuberculosis (TB) skin tests two weeks apart—at the beginning, midpoint, and end of the quarantine—required that most units quarantine monkeys for a 31 day period of isolation and observation. In addition to allowing time for serological or skin tests, this time period also allowed for the observation of any disease that might develop⁶.

The importation in 1967 of African green monkeys from Uganda to a laboratory in Marburg, Germany, resulted in the transmission of a previously unrecognized virus. A filovirus, this virus causes severe hemorrhagic fever both in humans and nonhuman primates⁹⁻¹¹.

The discovery of this first filovirus occurred after a number of laboratory workers in Germany and Yugoslavia who had handled green monkey tissues developed hemorrhagic fever. Thirty-one cases, including seven deaths, were associated with these outbreaks. Hence, the virus was named Marburg, after the city in which one of the outbreaks took place. It did not reemerge until 1975, when another case occurred in Johannesburg. Since then, there have been sporadic cases of Marburg hemorrhagic fever until two outbreaks killed about 150 people in the Democratic Republic of Congo between 1998 and 2000 and 227 fatalities occurred in Uganda in 2004¹².

Since 1948, the United States Public Health Service (USPHS) has had oversight of nonhuman primate imports. Because of the 1967 Marburg incident, as well as concerns about the risks of other potential zoonotic agents, the USPHS was prompted to consider a national quarantine program. Regulations enacted in 1975 required that all primates imported into the US must be quarantined for 30 days to ensure that they are disease free⁶.

The Ferlite Scientific Research, Inc., Monkey Farm was located approximately 40 km South of Manila. After monkeys were captured in the wild, they were taken to

Ferlite Farms which used open cages at their holding facilities; soon thereafter they were moved to individual cages. Ferlite exported about 1,500 monkeys a year to the US, mostly from coastal rain forests on the island of Mindanao.

THE RESTON EBOLA OUTBREAK

On October 2, 1989, 100 crab-eating macaques (*Macaca fascicularis*) were flown from Ferlite Farms, to Amsterdam via Tokyo and Taipei. From here they traveled to New York City and were then trucked down Interstate 95 to Reston. These monkeys were placed in Room F of the Hazelton facility to begin their quarantine period. The Hazelton facility already had about 500 macaque monkeys housed when this new shipment arrived.

In any transcontinental shipment of animals, some animals are expected to die due to the traumatic experience. However, this particular shipment began seeing a far larger number of deaths than expected.

By November 1, 29 of the 100 monkeys had died. Dan Dalgard, the Hazelton facility veterinarian dissected one of the dead monkeys searching for the cause of death. Inside, the body looked strange. Its inch-long soft spleen had tripled in size and grown hard as a rock. There was blood in the intestines. After conducting several other necropsies he diagnosed the deaths as being caused by simian hemorrhagic fever virus (SHFV).

The Hazelton facility veterinarian then sent samples of the monkey tissues to the United States Medical Research Institute of Infectious Diseases (USAMRIID) for a conclusive diagnosis. Located 80 km north of Reston at Fort Detrick, Maryland, USAMRIID was established in 1969, with the mission of developing medical defenses against biological warfare threats. While USAMRIID's primary mission is Soldier protection, its scientists and their research have provided numerous non-military benefits^{5,13}.

USAMRIID is the only laboratory within the Department of Defense capable of studying highly hazardous viruses that require maximum containment at Biosafety Level 4 (BSL-4). A biosafety level is the level of the containment precautions required to isolate dangerous biological agents in an enclosed facility. The levels of containment range from the lowest biosafety level 1 to the highest at level 4. Filoviruses are classified as Biological Level 4 agents based on their person-to-person, high mortality rate, transmission, potential for aerosol infectivity and absence of vaccines and

chemotherapy.

At 10,000 square feet, the USAMRIID BSL-4 facility is the largest biological containment laboratory in the US. When dealing with biological hazards at this level, the use of a Hazmat suit and a self-contained oxygen supply is mandatory. The entrance and exit of the laboratory contain multiple showers, a vacuum room, an ultraviolet light room and other safety precautions designed to destroy all traces of biohazards. Multiple airlocks are employed and are electronically secured to prevent both doors opening at the same time. All air and water service going to and coming from a Biosafety Level 4 laboratory undergo decontamination procedures.

The Hazelton veterinarian haphazardly followed proper laboratory procedures and sent the frozen samples wrapped in tin foil to USAMRIID. By the time the samples reached the lab, they had thawed out and were dripping fluids. An Army scientist examined the tissues and concurred with the finding of simian hemorrhagic fever.

While USAMRIID was analyzing the Reston samples, Hazelton lab workers began euthanizing the remaining animals in Room F. Over several days, however, sporadic deaths began occurring in several other rooms: soon 30 monkeys from a different Ferlite Farms shipment were dead.

Back at USAMRIID another researcher▯ using ELISA (Enzyme-linked immunosorbent assay), IFA (Immunofluorescence) and immunohistochemical staining discovered by electron microscopy that Ebola was responsible for the monkey deaths¹⁴.

The idea that a filovirus might burn through a ware-house ten miles from the capital of the US greatly disturbed the army scientists. Their first consideration was to identify the virus beyond question. At that time there were three filovirus tests. The first, Musoke, tested for Marburg. The second, Boniface, tested for Ebola-Sudan. The third, Mayinga, named for a mission nurse who died in Kinshasa, tested for Ebola-Zaire. When done correctly, a tested sample that matched a virus would glow under ultraviolet light.

Peter Jahrling, an Army civilian virologist decided to conduct the tests himself. The Marburg roused no glow in the monkey cells; the Ebola-Sudan made them glow a little; the Ebola-Zaire lit them up like light bulbs. It was conclusive▯ the Reston monkeys had Ebola-Zaire¹⁵.

Ebola is the poster child for virus outbreak scares because it

spreads extremely fast and kills most of its victims causing them to bleed uncontrollably. Since being featured in Richard Preston's 1994 book, *The Hot Zone*⁵ and several science-fiction movies such as *Outbreak*¹⁶, Ebola has become a household word.

The most well known epidemics of filovirus occurred in Zaire and Sudan in 1976¹⁷⁻²⁰. More than 600 cases were reported from these two outbreaks, with mortality rates of 88% in Zaire and 53% in Sudan. Both epidemics began with a first patient (called the index case) receiving treatment at a local medical clinic. The virus was transmitted by injections from used contaminated syringes.

When Ebola infects a human host, the person's immune system shuts down and the person dies from hemorrhages coming from all the body's orifices. Tissue oxygenation is interrupted, causing critical organ failure (parenchymal) or clinical shock. The infected person has a very high fever, accompanied by a bad headache. This early stage mimics malaria or typhoid and thus the disease often remains undiagnosed.

Then signs of Ebola start to appear. An Ebola patient can have blood standing in droplets on the eyelids and running from the tear ducts down the face. Blood can flow spontaneously from the nose, mouth, vagina, and rectum. The testicles swell up and are often destroyed. Ebola causes people to vomit masses of black blood with a distinctive appearance of "coffee grounds." As blood vessels burst and blood seeps into the skin, a spotty, bumpy rash spreads across the body, while small, star-like hemorrhages appear beneath the skin. There is incredible abdominal pain that cannot be relieved. Finally, after about 10 days, most sufferers mercifully fall into a coma and die.

Since 1967, 27 Ebola outbreaks have been reported. The largest outbreaks happened in 1967 in Zaire (280 deaths▯ 88% mortality) and in 1995 also in Zaire, resulting in 250 deaths from 315 cases (mortality rate of 81%). The most recent outbreak in February 2009 in Democratic Republic of the Congo resulted in 15 deaths from 32 cases (47% mortality rate)²¹.

Nonetheless, not one of these outbreaks resulted in a pandemic; in fact, just the opposite. Since the first documented filovirus outbreak in 1967, there have been approximately 1,500 fatalities²². Compared with other diseases, such as tuberculosis that is easily transmitted and quite pervasive, Ebola is quite rare. Indeed, the WHO

expects 30 million people to die of TB during the next ten years²³. Typhoid fever kills over 600,000 people per year²⁴; measles kills 1,000,000 people per year²⁵. Nonetheless, despite these realities, Ebola is seen as a predator on a killing spree.

On November 28, 1989 nearly six weeks after monkeys began dying in Reston, USAMRIID verified the Ebola finding. The following day, representatives from USAMRIID, the CDC, and the Virginia Department of Health met and developed an action plan. The CDC would handle people; USAMRIID would handle the monkeys and the monkey facility. Because of the threat that Ebola might spread to staff, Reston and the greater Washington, DC community, the Army determined that all remaining monkeys would be immediately euthanized. The first task was to determine how best to administer a solution to a building potentially full of Ebola.

COL Gerald "Jerry" Jaax was in charge of eradicating the virus. An initial entry team examined the buildings layout, entrances, exits, and unprotected openings. LTC Nancy Jaax (wife of COL Jaax), a veterinarian and pathologist, and COL C. J. Peters, chief of USAMRIID's assessment division and in charge of the Reston operation, conducted a walkthrough to determine the condition of the monkeys and what problems an operations team might encounter: blood, body fluids, as well as excited monkeys. Alarming, they also found that Hazelton staff and animal handlers were still working in the building without hazmat suits and most were unaware of the grave danger that they were in.

On November 30, LTC Nancy Jaax and another officer donned Hazmat suits and began to euthanizing 65 monkeys. Crab-eating Macaques males are considerably larger than females, weighing 5 kg to 9 kg compared to the 3 kg to 6 kg of female. Ketamine, a general anesthetic, was initially administered followed by xylazine▯ an analgesia and finally T-61, a euthanasia solution. By late afternoon, the monkeys were dead and liver and spleen samples collected. The remains were then triple-bagged for incineration or in some cases, a fuller evaluation at USAMRIID lab facilities. However, 450 monkeys remained alive.

Nearly a week later, on December 5, a group of 91 Tangos broken up into two-person teams entered the facility. 91 Tangos are animal care specialist that generally care, manage, treat, and clean government owned animals, with a primary responsibility of prevention and control of diseases transmitted from animal to humans. Consisting of mostly

young soldiers, most were unfamiliar with encapsulating suits, the tools they would be working with, the behavior of monkeys or of the full potential of the medical problem they were facing.

The same procedures used by LTC Nancy Jaax to put down the 65 monkeys were followed. The process was slow and the following day, one of the monkeys escaped. Efforts to net the animal were unsuccessful and only agitated the other monkeys. Shooting it was out of the question for fear that a loose round would end up somewhere unwanted. And, no one had thought of bringing a dart gun or other immobilizing device. Ultimately, it was decided to let the monkey roam freely and to try again the next day.

"Several of us spent the better part of a day trying to catch it. When we talk about the Reston incident, we compare the frustration of that day with the Hollywood version in the movie 'Outbreak,' in which an infected monkey was coaxed from a tree and captured within minutes. It is a great example of reality vs. Hollywood"²⁶. Finally the escapee was caught after it had jammed itself into a crevice leaving only its rump exposed. The creature was quickly euthanized.

That afternoon, building decontamination efforts began▯ chipping, scrubbing and bleaching. This continued for 11 days, followed by the introduction of *Bacillus subtilis niger*. Strains of the species *Bacillus subtilis* are used for sterilization control. This species produces spores resistance to dry heat or ethylene oxide and are used for testing the effectiveness of sterilization. When over exposed extensively to formaldehyde vapors, the *Bacillus subtilis niger* spores die. Their death presumes all bacteria and viruses to be dead⁵.

About 6:00 p.m. on December 18, electric fry pans, set on high, volatilized the formaldehyde crystals. For three days, the building was cooked. Finally it was determined that the building was decontaminated. Reston's three month ordeal with Ebola was over.

CONCLUSION

While the cleanout of the monkey house was going on, two out of the four monkey care takers were hospitalized. One had a heart condition; the other had high fever and nausea²⁷. Both men survived their illnesses unharmed. If these men were infected, it is hard to guess why Ebola-Reston did not cause in them the violent, hemorrhagic death it did in the monkeys. Perhaps a very tiny difference in the genetic code of the virus made it react differently within the systems of

humans and macaques.

And, indeed researchers discovered that this was a new species of Ebola virus, which they named Ebola-Reston^{15, 28, 29}. The new virus was highly pathogenic in monkeys but apparently not in humans. The researchers also dispelled the idea that filoviruses were found only in Africa, because the monkeys had been imported from the Philippines. The investigators documented a high likelihood of aerosol transmission outside a controlled laboratory setting, because the virus appeared to pass between rooms to infect susceptible monkeys. Specimens from animals that died or were killed to eradicate the outbreak yielded fertile ground for research in new Ebola virus detection and identification techniques and the virological and pathological events associated with infection.

Twenty years later there still is no standard treatment for Ebola. Currently, patients are provided supportive therapy consisting primarily of balancing the patient's fluids and electrolytes, maintaining their oxygen status and blood pressure, and treating them for any further complications.

In the aftermath of the Reston outbreak, Hazelton Research Products was purchased by Covance Inc., formerly Corning Incorporated. Headquartered in Princeton, New Jersey, Covance is a contract research organization that continues to conduct drug development and animal testing services. Monkeys continue to be housed in urban areas. Less than 13 km away, on Leesburg Pike, a Covance research facility continues to house monkeys.

In January 1997, unable to halt another outbreak of Ebola-Reston virus, Ferlite Scientific Research Farm killed 600 monkeys and soon thereafter permanently closed. In June 1995, the "Monkey House" was torn down. Even though the inside of the building was fumigated with formaldehyde and scrubbed with bleach several times, the closed facility remained unoccupied.

I remember touring the inside of the building in early 1992 when the accounting firm that I conducted business with suggested the site as a site to possibly site for my business and its 40 employees. By this time, however, the story of the "Monkey House" was well known and Ebola had made its way into our lexicon, so I politely declined the offer.

Shortly after the Reston facility was demolished, a new building built on the same site became a Kindercare. Today a Mulberry Child Care and Preschool sits at 1946 Isaac Newton Square West.

ACKNOWLEDGEMENTS

Many thanks to Kathryn C. Brue of Reston, VA, USA, who took a flawed manuscript and turned it into an interesting, readable article.

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