



Kunjin/West Nile Virus First Time in Western Hemisphere

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October 12, 1999 New York City, N. Y. Starting back around July 1999, residents in Queens, New York began calling their city's wildlife office to report various types of birds on the ground shaking, wobbling and disoriented. Then crows at the Bronx Zoo and surrounding areas kept dying. Dozens of them. Pathology tests showed mysterious lesions in the brains and hearts.

By August, doctors in New York's Flushing Hospital were seeing an increasing number of people with fever, mental confusion and severe weakness. The combination of symptoms was confusing because usually in cases of encephalitis, which is an inflammation of brain tissue, patients hallucinate, are out of control and sometimes have seizures. These new patients were disoriented, but were so weak they could not move.

By Labor Day, three Bronx Zoo flamingos, an Asian pheasant and a cormorant all died. Pathology tests showed the same heart and brain lesions found in the dead crows. Dr. Tracey McNamara at the Wildlife Conservation Society contacted the USDA's National Veterinary Services Laboratories in Ames, Iowa. There, researchers found virus particles that resembled a Flavivirus known in the United States as St. Louis Encephalitis. The St. Louis Flavivirus can only be transmitted by ticks and mosquitoes known as "vectors" in the medical community. For example, let's say a virus-carrying female mosquito bites a bird. Only female mosquitoes feed on blood. When birds are infected, their blood rapidly fills up with the virus for a week or so. If another mosquito comes along, bites the infected bird and then a human, the virus can get into the human system.



Photograph of *Culex pipiens* female mosquito,
courtesy Entomology Image Gallery.

By the end of September, human encephalitis cases were piling up in Manhattan, Queens, Long Island and Connecticut. And more dead crows were found in northern New Jersey. The New York Department of Public Health sent brain tissue from two of six fatalities to Dr. Ian Lipkin, Director of the Emerging

Diseases Laboratory and Professor of Microbiology and Molecular Genetics, Anatomy and Neural Biology and Neurology at the University of California-Irvine. By September 23rd, he and his California team announced the culprit was *not* St. Louis Encephalitis. It was a virus never before seen in the Western Hemisphere called Kunjin/West Nile Fever.

Interviews:

W. Ian Lipkin, M.D., Director of the Emerging Diseases Laboratory and Professor of Microbiology and Molecular Genetics, Anatomy and Neural Biology and Neurology, University of California-Irvine: "We have said it is a Kunjin/West Nile-like virus. (But so far) we only have a small percentage of the genome cloned.

FROM TWO OF THE BODIES FROM NEW YORK, OR THE BRAINS?

We've actually got sequence now from two brains, that's correct. But the sequences are virtually identical to the bird because we have compared them to sequences that have been obtained from the New York State Health Department and at least the regions that we've compared to date, there really doesn't appear to be any difference.

BETWEEN WHAT'S IN THE CROW AND THE PEOPLE?

That's correct. I would assume that we're talking about the same agent. The question is: where did it originate?"

What Is Behind Virus's Sudden Appearance in the United States?

BEFORE NOW, KUNJIN/WEST NILE VIRUS HAD ONLY BEEN IDENTIFIED IN AUSTRALIA, AFRICA, ASIA AND EUROPE. I TALKED ABOUT THE SUDDEN APPEARANCE IN THE UNITED STATES WITH DR. THOMAS MONATH, A HARVARD TRAINED VIROLOGIST AND ONE OF THE LEADING AMERICAN EXPERTS ON ARBOVIRUSES THAT SPREAD THROUGH TICKS AND MOSQUITOES.

Thomas Monath, M. D., Virologist and Arbovirus Specialist, OraVax, Cambridge, Massachusetts: "My first impression was, 'This is an incredible event!' In my career, there have been very few instances of such a dramatic emerging infection story. I've lived through a number of new viruses that have appeared, but to have an Old World virus like West Nile appear in North America is something we said could happen for many years, but sort of dismissed it as a low probability. So, I find it quite extraordinary. It's one of the biggest stories in virology of this century, certainly. And hopefully, it was a flash in the pan and we're not going to have to now suffer repeatedly from outbreaks of West Nile. But certainly, I am extremely interested and very shocked that this happened.

COULD THIS CURRENT ROUND THAT IS INVOLVING SO MANY DEATHS IN THE CROWS AND HALF A DOZEN DEATHS IN HUMANS WOULD THAT RESPONSE BE BECAUSE THE VIRUS HAS MUTATED? OR BECAUSE THIS WESTERN POPULATION OF BOTH BIRDS AND HUMANS HAS NO NATURAL IMMUNITY BECAUSE THE VIRUS HAS NOT SHOWN UP HERE BEFORE?

"I think we're clearly dealing with a strain of virus that has certain let's not call them mutations, but has a genetic sequence that directs the virus to be virulent for crows and to cause human illness. In some outbreaks of West Nile, there have been no illness in crows or other birds and illness in humans has been exceptionally mild, with no encephalitis cases or deaths. So, this is a variant of West Nile virus that is similar to others that have been described before, but has this capability of causing central nervous system infection.

SO IT IS MORE VIRULENT?

Looking at what's known today, I would conclude yes, this is a strain of West Nile on the more virulent end of the spectrum of virulence. But is probably not very different from other strains that have caused other outbreaks in the past. The case fatality rates in humans is a good measure here. In other words, of the people who got encephalitis, what proportion died? That would be an accurate way of looking, from a medical perspective, looking at the virulence of the virus. So, that lethality or case fatality rate, we call it, in this outbreak which is about fifteen percent or so is not different from the case fatality rate in the 1996 outbreak in Rumania. It seems to be similar to the outbreak coming out in Russia now from all reports. So, I think we are dealing with a virus of similar virulence."

West Nile Fever in Russia and New York At Same Time:

IN 1996 TO 1997, THERE WERE MORE THAN 500 CLINICAL CASES OF WEST NILE FEVER IN BUCHAREST, ROMANIA. AND THIS SEPTEMBER WHILE ALL THE CROWS WERE DYING AND DOZENS OF PEOPLE BECAME ILL IN NEW YORK, 559 CASES AND 33 DEATHS IN VOLGOGRAD, RUSSIA THE OLD STALINGRAD WERE ATTRIBUTED TO AN OUTBREAK OF WEST NILE FEVER AS WELL.

W. Ian Lipkin, M. D. and Microbiologist: "Now, if we can get access to the Russian isolates, that might give us a lot of information. So, we'll have to see if we can do that.

THE QUESTION THAT WAS RAISED SUNDAY AND MONDAY IN THE NEW YORK MEDIA AND REUTERS ABOUT THE FBI AND CIA LOOKING INTO THIS AS POSSIBLY CONNECTED TO A SADAM HUSSEIN EFFORT TO ENGINEER WEST NILE FEVER - IF THERE WAS AN ENGINEERED MUTATION IN A VIRUS, IS THERE ANY WAY THAT WE COULD TELL A DIFFERENCE FROM A NATURAL MUTATION?

That's an excellent question. If there is a sequence that is clearly present from another virus which looks like it was spliced in, yes, you could tell that. I have no idea if we'll find anything like that because we haven't yet sequenced to that extent. But, that would be evidence.

IS KUNJIN ITSELF A MORE VIRULENT, SLIGHTLY MORE VIRULENT, STRAIN?

No, it isn't. In fact, it's less virulent. But that doesn't really matter. When you work in viral pathogenesis which is the study of how viruses cause disease, you learn that very small changes in the sequence of a virus can result in marked changes of its ability to cause disease. This has been shown over and over again. So, the key is that we will need to analyze how this virus replicates, how it results in disease and so on.

THE CROWS SEEM TO BE LIKE THE CANARY IN THE CAGE FOR THE MINERS. I would agree that's an excellent analogy that's more or less the way we view it.

WE HAVE TO KEEP WATCHING THE BIRDS UP AND DOWN THE EAST COAST. WHAT WOULD BE YOUR GUESS, BASED ON YOUR MEDICAL EXPERIENCE, FOR WHAT MIGHT HAPPEN NEXT SPRING, SUMMER AND FALL? IS IT LIKELY THAT THIS KIND OF VIRUS COULD PERPETUATE ITSELF THROUGH THE WINTER AND RE-OCCUR IN THE SPRING?

It's something that concerns all of us. It's obviously something that worries us. But as to what the probability is, I don't know."

Will West Nile Fever Virus Spread in Spring 2000?

Thomas Monath, M. D., Virologist: "This is the \$64,000 question. The

possibilities are that the virus is able to over-winter or survive in the area of epidemic. So, the greater New York area, Connecticut, Long Island, New Jersey and so on. And then could re-appear next spring from a local reservoir. That's one possibility.

The other is that it's re-introduced by migratory birds coming from South America. In other words, the virus was here in North America this year, migratory birds got infected and took it south. Now, it gets re-introduced next year.

MOSQUITOES ACTUALLY SURVIVE THE WINTER?

Yes, *Culex pipiens* hibernate. (Species of mosquito associated with West Nile Fever). So, the mosquitoes go into protected, warm dark areas, cellars, tunnels where they can hibernate. They are inactive. They don't blood-feed. But they survive in the adult stage over the winter.

ANY POSSIBILITY THAT IF IT RE-EMERGES NEXT SPRING BASED ON THE HISTORY OF STUDYING THESE VIRUSES IN AFRICA AND EURASIA, THAT SINCE THEY DO MUTATE AND IT ALREADY HAS CAUSED SO MANY DEATHS IN CROWS AND HALF A DOZEN IN PEOPLE THAT IT COULD ACTUALLY BE WORSE NEXT SPRING?

It could go the other way, too. These viruses are very their genetic material is very plastic. Very high rate of mutation. I don't know. Theoretically you could propose that because new mosquitoes and new bird species were involved that that might put pressure on the virus to change quicker than in Africa and the Old World where it's become fixed in its host vector association. I think it's possible that involvement of new vectors and hosts could put pressure towards virulence, increased virulence in the virus. This is highly speculative."

Origins of the West Nile Fever Virus:

WHERE DID THE NEWLY EMERGING VIRUS IN NORTH AMERICA COME FROM IN THE FIRST PLACE? THE PROFESSIONAL CONSENSUS IS PROBABLY BY AN AIRPLANE TRAVELER FROM EURASIA, AFRICA OR AUSTRALIA. OR LESS LIKELY, AN ILLEGALLY IMPORTED BIRD OR A MIGRATING BIRD THAT GOT BLOWN OFF COURSE BY THE WEATHER.

BUT SINCE THE POSSIBILITY OF A BIOTERRORIST MANIPULATION OF THE VIRUS HAS BEEN RAISED, I TALKED WITH DR. ALAN ZELICOFF, SENIOR SCIENTIST IN THE CENTER FOR NATIONAL SECURITY AND ARMS CONTROL AT SANDIA NATIONAL LABORATORIES IN ALBUQUERQUE, NEW MEXICO. DR. ZELICOFF ALSO SERVES ON A GOVERNMENT PANEL OF EXPERTS WHO ARE TRYING TO COORDINATE WITH THE CENTER FOR DISEASE CONTROL TO DISTRIBUTE MORE INFORMATION TO ALL GOVERNMENT AGENCIES ABOUT DISEASE OUTBREAKS AMONG HUMANS, ANIMALS AND PLANTS. I ASKED HIM IF THERE WAS ANY REASON WHY WEST NILE FEVER MIGHT BE UNDER ANY CONSIDERATION BY SOMEBODY LIKE SADDAM HUSSEIN AS A VIRUS FOR ATTACK ON THE UNITED STATES?

Alan Zelicoff, M. D., Internal Medicine with a fellowship in Immunology and Rheumatology, Sandia National Laboratory, Albuquerque, New Mexico: "I think it is highly unlikely and the reason I think it is highly unlikely is that the efficiency of transmission, if one were to introduce this virus by mosquito or by bird the efficiency of the transmission into humans is still extraordinarily low. And it would strike me as far from optimal for a biological weapon used in a terrorist mode.

When we look at the Iraqi biological and chemical weapons program, the information that was gathered by UNSCOM brings up a number of peculiar surprises. We know that they had requested and received some small amount of

West Nile Fever virus, but we have no evidence that they produced it in large amounts, nor do we even find the capability that they were able to produce West Nile Fever in large amounts.

COULD YOU EXPLAIN HOW YOU KNOW THAT SADDAM HUSSEIN REQUESTED WEST NILE FEVER VIRUS AND WHERE WOULD HE GET IT?

I read that in the newspaper and I believe he got it by request from some supply house in the mid-1980s. I think it was perfectly easy to do that back then. It's now much more difficult to do so.

SO HE ACTUALLY GOT WEST NILE FEVER VIRUS FROM A LAB IN THE UNITED STATES BY PURCHASING IT IN THE 1980S?

That's my understanding, yes.

THAT RAISES THE QUESTION AGAIN, WHAT WOULD HE OR HIS MEDICAL COMMUNITY HAVE ON THEIR MINDS ABOUT WHY THEY WOULD PICK THAT PARTICULAR VIRUS?

That's a good question. There is a very thin line between working with dangerous pathogens for legitimate purposes, such as development of vaccine or understanding the fundamental physiology of the virus, and doing the same kind of research for purposes of developing a weapon. Unfortunately, it comes down to an issue of intent. There is no difference between the research that is done in the earliest stages between developing a biological weapon and doing legitimate medical research.

WHAT DO YOU THINK IN THE UNITED STATES WE CAN DO IN TERMS OF ANTICIPATING AND DEFENDING OURSELVES AGAINST BIOTERRORIST ATTACK WITH ANTHRAX OR SMALL POX?

Well, we have a multi-pronged approach and it is a combination of sensors that do continual monitoring of the air, an increasing reporting network specifically designed to make it easy for physicians and veterinarians to enter in data into a centralized data base over the internet. And then there is a healthy dose of intelligence that finds its way into the mix as well.

HOW DO WE MONITOR THE ATMOSPHERE?

One has to do it with more or less continuous sampling and in a way that does not result in a lot of false alarms. So, at the Department of Energy National Laboratories, there is a very robust program in developing small, inexpensive, automated sensors specifically designed to pick up the physical as well as chemical characteristics of the coatings on anthrax spores, many different virus types and also virtually all chemical weapons and materials. And that program which has been in existence now for about three years has made enormous gains and the first prototypes will probably actually be installed in certain high risk settings over the next year or so.

DO THESE DEVICES GO UP INTO THE AIR?

They literally just sample the air. So, they don't necessarily fly around, although they can. They are generally meant to be placed in single spots. They are called "point sensors." And they continuously monitor the air and feed that data automatically into an automated data base. And the nice thing about them is they have a low false alarm rate, much less than the smoke detector in your house. They require very little power and they can operate autonomously for months at a time.

THOSE ARE GROUND BASED SENSORS?

Ground, but they may be high up off the ground like in a building, for example. Our surveillance for infectious disease as well as infectious disease that is communicable from person to person needs to be beefed up substantially. The CDC has been arguing that point for many years, I think, quite correctly. And I believe that this is a wake up call that should enlighten all of us, including policy and decision makers that more effort needs to be put into disease surveillance as well as making it easy for health care practitioners, including veterinary health care practitioners, to report to a centralized data base that will

enable very rapid distribution of the information."

More Information:

The discovery of the Kunjin/West Nile virus in New York and surrounding communities underscores an issue of growing concern among public health experts the speed and frequency with which foreign microbes are entering the U. S. They are coming in through air travel, global tourism and international trade. For example, the number of malaria cases in New York has been going up a direct result of people bringing the disease back from the tropics. Humans make the problem worse by cutting down forests that force birds into more concentrated areas where disease can spread more easily.

This encephalitis outbreak and the associated human deaths show that when microbes are released into an environment where they have not been before, the microbes can be especially dangerous because what they infect has no immunity against them. According to the New York City Department of Health, 39 patients have been classified as laboratory positive cases of West Nile virus in New York City with six deaths and 168 cases under investigation.

Swine Flu Pandemic of 1918

Back in 1918, there was a world pandemic called "the swine flu" which killed an estimated **twenty million** people worldwide and more than half a million people in the United States. The reason was that a virus crossed over into pigs and then transferred into people who had no immunity. Could another pandemic occur?

Communication without delay has been stressed and hospitals have been asked to contact their particular State's Department of Health immediately if there are any suspected or confirmed cases of St. Louis Encephalitis or West Nile Fever virus. Individuals who find one or more dead birds should report the location to their local health department.

Websites:

<http://www.cdc.gov/>

<http://www.who.org/>

<http://www.health.state.ny.us/>

<http://www.state.nj.us/health>

<http://www.reutershealth.com/eline/open/1999101108.html>

<http://www.ent.iastate.edu/imagegal/diptera/culicidae/cxpipf.html>

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