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ABSTRACT

The case-based study, which presents students with a dilemma that encourages exploration, is becoming a popular method for teaching biology. This Web-based report offers one such case study that asks readers to solve problems and make decisions based on information gathered as they engage with characters or situations in the story. The basis for the study narrative is antavirus, a topic of interest in the global scientific community. The story is broken into five sections: (1) It All Started Here: Old College Friends Return from a Dig; (2) Home Sick: Travelers Show Signs of Illness at Home; (3) What Hit Us? One is Dead and Another is Fighting for Her Life; (4) Of Mice and Men: Identifying the Source of the Infection Continues; and (5) Loose Ends and Law Suits: What are the Real Costs of a Disease? The study can be used as a single unit or it may be broken up and presented, as appropriate, throughout the semester. Included are extensive resources for both instructors and students who wish to try case-based investigations in their courses. (AS)

Souvenirs:
A Case Study for the 90s

Janet Yagoda Shagam
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&
BioQUEST Curriculum Consortium

Souvenirs:

A Case Study for the 90's

Case-based studies are becoming an increasingly popular method for teaching biology by introducing dilemmas which encourage student exploration. The case study **Souvenirs** is provided with extended resources for both instructors and students who wish to try case-based investigations in their courses.

Souvenirs offers carefully integrated clues about an emerging disease embedded in a rich social and ethical context. Students may develop a wide range of questions to explore the biological information on hand. In the process of answering these questions, students become involved in the dynamic and integrative thinking needed to solve problems scientifically in their own lives, not just in their life sciences courses.

Souvenirs is a realistic narrative developed to set the stage for student investigations. This case study involves resolving problems and making decisions based on the information gathered by readers as they engage with the characters or situations in the story. As they attempt to untangle the skein of information in this scenario, students have the opportunity to gain a practical level of understanding for the science needed to solve the problem.

Souvenirs can be used in introductory biology, microbiology, physiology or pathophysiology classes. In addition to intertwined life science themes, there are threads involving social, economic and political impacts of disease on a community.

Souvenirs :The entire case in five parts

It All Started Here: Old college friends return from a dig.

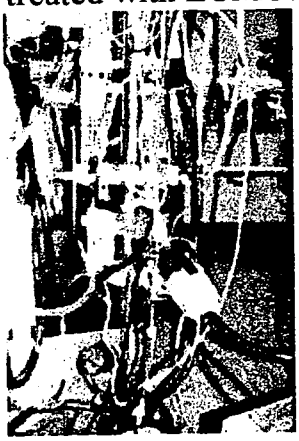
Home Sick: Travelers show signs of illness at home.

What Hit Us?: One is dead and another is fighting for her life.

Of Mice and Men: Identifying the source of the infection continues.

Loose Ends and Law Suits: What are the real costs of a disease?

Seriously ill patients may be treated with ECMO.



Teaching Notes

Summary of the case narrative

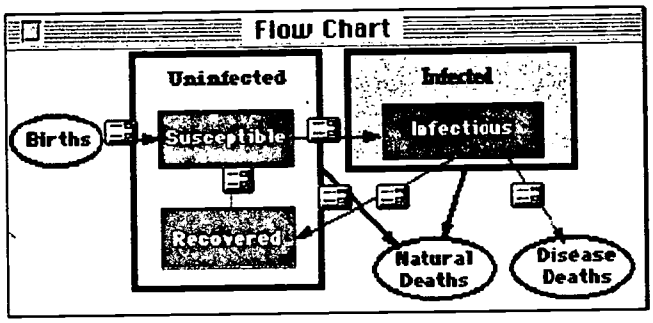
Why use Hantavirus in a case study?

Adaptation to your class

Student evaluation

References and web sites for using cases

Epidemiology modeling allows students to investigate diseases.



Ancillary Materials

Things to Ponder

Web Sites of Interest

Medical Data for Major Characters

Albuquerque Journal News articles

Computer Modeling and Simulations

Interviews with Hantavirus Survivors and Care Givers

Genomics and Hantavirus

The case and aspects of its use were introduced to the ASM membership at the 5th ASM

Undergraduate Education Conference in Atlanta this spring.

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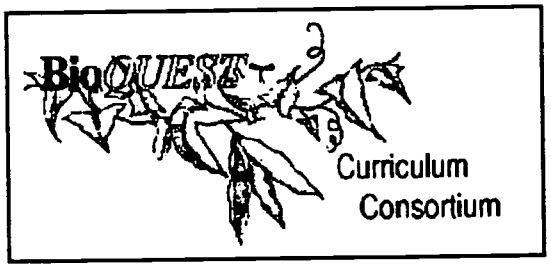
This is a collaborative project between the

and the



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last updated January 7, 1999 ds

Souvenirs

It All Started Here

It had been a wonderful week and a terrific break from the hum-drum life-style of the Chicago suburbs. The three women, all best friends from their college days, had planned for over a year to go on this archaeological dig sponsored as a fund raiser by their alma mater. Hilary, an elementary school teacher who suffered from asthma, was a bit concerned about working at such a high altitude. Ruth, a pharmaceutical chemist, was relieved to get away from her non-responsive colonies of laboratory mice. For Susan, this was just a bit of much needed R and R from her hectic life as a commodities broker. Although the dig had dried to dust, the participants stopped often to admire the yellow, pink and blue flowers covering the nearby hillsides.

The pot shards they had collected, carefully numbered and boxed, were now ready to be sent on to the museum. The friends placed the boxes, along with the plant material collected by the ethnobotanist, in the old storage shed at the site. Then they took the jeep for the one hour drive down the mountain to Santa Fe, where they spent their last afternoon in the Southwest shopping for jewelry and rugs. Because they had skipped lunch, they bought some fruit from a corner grocer. He explained in halting English that his family had just moved to Santa Fe from Argentina to start a new life. The fruit looked and tasted wonderful, though the old man coughed terribly as he waited on them. "I hope that's not catching!" Ruth thought to herself. Then she noticed a half-empty pack of cigarettes near the cash register and forgot the incident.

The next morning was hectic and with last minute packing and loading the truck. As a favor to the site-manager, Hilary and Ruth also cleaned the storage shed. It was apparent that the shed was home to many rodents and had not been cleaned for many months. Hilary and Ruth did the best they could in the time they had. Both hoped someone else would complete the cleaning before the next group arrived to work at the site.

The flight back to O'Hare was smooth, but crowded. Susan and Ruth sat together, but Hilary sat in the back so she could stretch out a bit better. Although the leg room was nice, it was annoying to sit right under the cabin air vent and in such close proximity to the bathrooms.

Home Sick

Sunday in Chicago for the three women was uneventful. They spent their time collecting the mail from the neighbor kid and catching up on laundry and bills before going back to work the next morning. Hilary had bought a beautiful hand-woven Navajo rug, which she shook out and displayed to family and friends.

Hilary began to feel ill late Sunday afternoon, with a fever, chills, and a dry cough. Since a cough was often a prelude to a long bout of asthma, Hilary used the nebulizer to insure a good dose of anti-inflammatory and bronchial dilating medications. She was also very thirsty. "It must be the result of my dry week in the Southwest and the canned airplane air," she thought to herself.

The next morning, feeling somewhat better, Hilary went off to work. It would be good to see "her" third grade kids after their spring break. However, by first recess Hilary was gasping for air. She was taken to the hospital and a substitute teacher took her place while the kids were out on the play ground. Hilary was pronounced dead at 7:28 Monday evening. Cause of death was listed as respiratory failure due to asthma.

Susan, whose morning always started with obituaries and coffee, screamed as she read Tuesday's paper. She immediately called Ruth. The phone rang 6 times. "Hello?" croaked Ruth.

"Ruth, have you seen the paper? Hilary died last night!" Susan sounded breathless, as if she had been running.

"Hilary...but we just saw her Saturday and she was feeling fine!" answered Ruth.

"You don't sound so great yourself... Are you O.K.?" asked Susan.

"Yeah, I just caught a cold on that flight from Albuquerque. When's the funeral? I can't believe this is happening."

What Hit Us?

The funeral, held three days after Hilary's death, was well attended. All the kids from Hilary's class were there, as well as assorted friends and family. Ruth still wasn't feeling great. Later that night she became feverish with muscle aches and chills. Nausea and vomiting hit about 2 AM. "Must be something I ate," Ruth thought to herself. She stayed home from work on Friday but felt well enough to go into the lab and check on the mice Saturday afternoon. However, by Sunday Ruth was very tired and ached all over - so she

called her doctor. The doctor on call suggested that she go to the emergency room if her symptoms worsened or make an appointment to see her regular doctor on Monday morning.

By Sunday evening Ruth's husband, seeing her struggle for every breath, insisted he take her to the hospital. A chest x-ray demonstrated a diffuse interstitial infiltrate. Since routine blood work also demonstrated decreased platelets, Ruth was immediately taken to intensive care. She was found to be hypoxemic, and required intubation and ventilation with a respirator. Despite intensive medical therapy, she developed shock with a low blood pressure and was placed on Extra Corporal Membrane Oxygenation (ECMO). Lab cultures for common respiratory bacteria came back negative, and her physician suspected a virus.

Fortunately for Ruth she was able to get appropriate treatment soon after her arrival at the hospital. Dr. Beatrice Gold was just the right person for the job - practical and hands on. Dr. Gold immediately recognized the seriousness of Ruth's symptoms and knew that to save her patient, aggressive measures had to be taken. She also did the appropriate immunology to back-up her diagnosis and started asking lots of questions. Ruth's husband did his best to answer them. Ruth managed to hang on. Three days on ECMO, a week in intensive care, and then two days after getting the hang of green Jell-O and yellow bouillon, Ruth was able to go home. However, a year later, she would still be having trouble with shortness of breath when trying to jog the trails around Lake Michigan.

Of Mice And Men

Dr. Gold particularly wanted to know if Ruth had been involved in any recent activity in a rodent infested area. The answer was yes - Ruth was involved in large scale rodent studies at the pharmaceutical company. She had also recently returned from a trip to the Southwest. Could she have been exposed there? In addition, there was Hilary's recent death. Could that be related to Ruth's infection? Hilary's next of kin were contacted and were very helpful. Autopsy samples were released and were processed for Hantavirus antigen and antibody.

Back in New Mexico, the site-manager had been found collapsed near the kiva and was now fighting for his life at University Hospital. A team from the CDC was dispatched to investigate the possible Hantavirus outbreak. They began by interviewing the organizers of the expedition and by compiling a list of other recent site visitors. No other out-of-state participants had become ill, nor were there any unusual health problems reported by passengers on the flight taken by the women. However, when the epidemiologists surveyed local hospitals for recent emergency admissions they found, in addition to the site-manager, the Santa Fe grocer in intensive care at University Hospital.

Mice from Ruth's lab were unavailable for testing, but several rodents captured near the archeological site tested positive for Hantavirus. Hilary's autopsy tissues were also positive for Hanta.

Loose Ends And Law Suits

Ruth's recovery was slow. She was out of work for several months and filed for short term disability to help with expenses during her recovery. Hilary's family hired a lawyer to file suit against the archeological dig, while Ruth and Susan filed a complaint with their college alumni association.

Hotels and businesses from Santa Fe to as far away as Tucson received inquiries about the outbreak. Many people were worried about a possible drop in business. News of the grocer's death circulated while nobody seemed to notice the recovery of the site-manager. There was some grumbling about tourists making things difficult for the locals. Meanwhile, rain clouds gathered as El Niño worked its way across the country.

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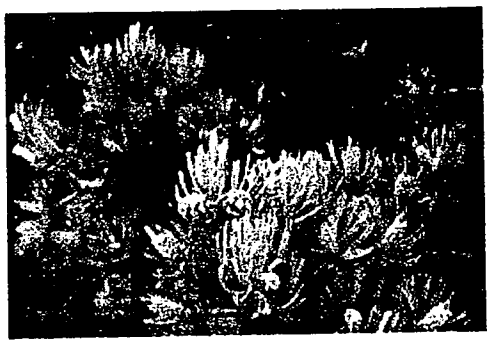

Summary of the Case Narrative

The study can be used as a single unit or it can be broken up and presented, when appropriate, throughout a semester. The first segment, **It All Started Here**, introduces the situation. A group of old college friends have just returned from an archeological dig. The scene is set, but the clues lead to a variety of topics including botany, ecology, allergy, epidemiology, demographics, travel and disease, southwestern archeology as well as an assortment of implied social and economic themes.

The three friends - Hilary, Ruth and Susan - have returned home and two will show signs of illness. In the section, **Home Sick**, various signs and symptoms are described. This forms the basis for inquiry about inflammation and anti-inflammatory drugs, the allergic response, sleuthing for a possible pathogen and the impact of confined spaces on the transmission of disease.

Before you know it, Hilary is dead and Ruth is fighting for her life in the **What Hit Us?** segment of the case study. Again more sleuthing for Hilary's cause of death - asthma or a deadly pathogen? To accomplish that task we have to apply a knowledge of biological molecules to clinical chemistry, immunology, microbial testing, pathology and physiology as well as evaluate lab results.

In the fourth section, **Of Mice and Men**, the source of the infection needs to be identified. Did the women get infected at work, on the airplane or while visiting the southwest? This leads students to consider epidemiological studies of disease as well as novel and new techniques used to match viruses in the field to disease in patients. To answer questions in this section students will become experts in genomics and immunology as well as have to evaluate clinical data from the new batch of sick people.

And since this is the 90's - no story would be complete without a law suite and some politically sensitive hackles being raised. In **Loose Ends and Law Suits**, the ability to immunologically identify the source and cause of an infection will have a direct impact worker's compensation and liability issues. The economic effects as well as feelings toward minorities and new immigrants will lend a sad bit of reality when the impact and cost of a disease on a community are discussed.

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Why use Hantavirus as the basis for a case study?

In 1988, Joshua Lederberg in a memo to Stephan Morse of Rockefeller University, states: "We need some high level policy attention to what needs to be done globally to deal with the threat of emerging viruses." At that time Hantavirus was specifically identified as a virus that needed to be watched for signs of global emergence. Although the pulmonary syndrome caused by Hantaviruses in the United States is a very rare and sporadic event it has, despite aggressive medical intervention, a very high mortality rate. In addition this disease is currently present in near epidemic proportions in Latin and South America as well as in the Far East and Russia. It would be both short-sighted and ignorant to assume that Hantavirus can not or will not become a larger problem in the United States. We need to understand everything about Hantavirus biology, epidemiology, prevention and treatment so that we limit its destructive global impact.

There are other, less pressing reasons, why Hantavirus is a good basis for a case study. Hantavirus is a "clean" model system. It is recent, the people involved or impacted by the disease are known and we were able to take advantage of recent advances in biotechnology and genomics to identify and potentially control the virus. In addition, due to the southwestern residency of two of the authors, we have access to unique resources to make this case study extremely full and realistic as well as a perspective that is both personal and respectful.

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Adaptation to your class

Souvenirs may be downloaded as is and distributed to students or you may rewrite segments to accommodate the specific needs and interests of your course. Students can be given the case study in sections, as a whole unit or they can work directly on the website. The case can be used in class, as an external assignment, as an extended group lab project, or as an independent project depending on your course needs. Unlike text material which is often quite linear, this case study allows you to introduce several related topics simultaneously.

Extensions to the case are available as well. These resources include additional medical data for major characters in Souvenirs, actual interviews with two Hantavirus survivors and two medical care providers, a list of newspaper articles from the Albuquerque Journal, a description of ECMO, scientific references, links to software that may extend case investigations, and links to other Internet resources. Things to Ponder, a set of directed questions, are offered as a place to start thinking about case possibilities. We urge you to have students develop their own questions. If you need to narrow the problem space, you can easily write your own or select certain questions for directed investigation when time is short.

The ethnic and social issues, although often not accommodated in our classes, should not be ignored. The reality is that the media and the press created "Navajo Flu", which lead to a massive invasion of privacy, a decline in tourist dollars in the area and a misplaced association of the disease to a specific people. This is no different than our historical linkage of syphilis, AIDS, leprosy and cholera to peoples who are disenfranchised due to ethnicity, sexual preference, economics or religion. We need to acknowledge the impacts of biologically linking a disease to a certain locale or country or a people based on prejudice.

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Student evaluation and case studies

Case studies are an open-ended teaching strategy used to encourage higher-order thinking, team-work and self-directed study.

The evaluation of student progress can take many different forms:

Small groups may present informal posters at various stages of their investigation to persuade others that their approach to the problem is sound based on methodology and gathered facts.

Perhaps, a formal poster session at the end of the project could be evaluated.

Students could give oral presentations or write reports to answer specific questions or to defend a hypothesis .

Portfolios could be required to demonstrate achievement and progress.

In addition the case study could support examination essays, short answer questions or multiple choice questions. If the case study is used to support or reinforce lecture material, it may not be practical or necessary to assign a grade to all case study activities.

Some instructors use a modified case study as an exam itself.

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References for Developing Our Case and Materials

Waterman, M.A. 1998. Investigative Case Study Approach for Biology Learning. Bioscene: Journal of College Biology Teaching 24 (1): 3-10.

Waterman, M.A. and E.D. Stanley. 1998. Investigative Cases and Case-Based Learning in Biology. A text module in the BioQUEST Library V (on CD-ROM). Academic Press: Philadelphia.

The authors wish to thank Dr. Margaret Waterman for sharing her manuscript on investigative case-based learning approach with us during the writing of this case.

Case Web Sites of Interest

Problem-Based Learning at the University of Delaware

Case Studies in Science

Kingdoms Entangled:Molecules, Malaria, and Maize A BioQUEST Case Study

Workshop Biology University of Oregon

Case It! Home Page

Additional References for Problem-Based Learning

Barrows, H.S. and R. Tamblyn (1980). Problem-Based Learning. Springer:New York.

Schmidt, H.G. (1993). Foundations of problem-based learning: some explanatory notes. Medical Education, 27, pp. 422-432.

Stepien, w. J., Gallagher, S. A. & Workman, D. (1993). Problem-Based Learning for traditional and interdisciplinary classrooms. Journal for the education of the Gifted (4), pp. 338-345.

Stepien, W., & Gallagher, S. (1993, April). Problem-Based Learning: As authentic as it gets. Educational Leadership, pp. 25-28.

Wilkerson, L. & Feletti, G. (1989) Problem-Based Learning: One approach to increasing student participation. In: A. F. Lucas (ed.) the Department Chairperson's Role in Enhancing College Teaching. New Directions for Teaching and Learning, no. 37, pp. 51-60. San Francisco: Jossey-Bass.

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Things to Ponder

What are some non-microbial causes of respiratory disease?

What different kinds of microorganisms can cause respiratory disease?

How are these microorganisms differentiated from each other?

What kinds of clinical tests can the patient be given to differentiate between fungal, bacterial, and viral agents?

Could Hilary and Ruth have been exposed to something at the same time and become ill five days apart?

Was Hilary's asthma a significant factor in her death? Did the use of inhalants contribute in any way?

How was Ruth's treatment a significant factor in her recovery? Why did Dr. Gold request the use of Extra Corporal Membrane Oxygenation (ECMO)?

Will Susan catch this disease?

Will it spread to the school children, people on the airplane or at the funeral?

Are Hilary's death and Ruth's disease related?

What about the illness(es) of the site-manager and the grocer?

Why didn't anyone else on the dig get sick?

What immunological tests could Dr. Gold have ordered to make her diagnosis?

What results will confirm the identity of the virus?

Will the tests reveal the virus, viral antibodies, or both?

What class(es) of antibodies might be found in a patient who has been ill for a

week? for three weeks?

What kind of virus is Hanta?

How does it infect cells and make new copies of itself?

How does Hantavirus enter the body and cause disease?

Is this typical of other viruses which cause respiratory infections?

Is it possible to identify the source of infection?

Can different viral isolates be differentiated antigenically or by nucleic acid sequence? How would this affect liability issues?

How is Hantavirus infection differentiated from other pulmonary diseases?

What kinds of drugs would you expect to be effective against the virus?

How is Hantavirus transmitted?

What are the ecological factors that might promote the transmission of this disease?

Would you expect some of the residents in this area to be seropositive for Hantavirus?

Would you expect some to be more likely to test seropositive for Hantavirus than others in this population?

If so, should the behaviors, cultural practices or other characteristics of the population be considered? (Is there a danger here?)

What are some economic factors that may contribute to or complicate evaluation of this disease?

Would you expect all or some of the rodents in this area to be seropositive for Hantavirus?

How are rodents involved in the transmission of Hantavirus?

Which rodents are commonly infected?

The outbreak of Hantavirus in the Four Corners area in 1993 followed an especially rainy winter. How are weather and Hantavirus connected?

In what parts of the world is Hanta found?

How might a recent arrival to the area (the grocer) be connected with the outbreak?

Does Hantavirus always cause respiratory infection?

Would you expect the same symptoms to occur if a Hantavirus from another location is involved?

How are the different hantaviruses related?

Were the organizers of the dig site negligent in allowing amateurs into the area without warning them about Hantavirus?

What precautions could the diggers have taken to protect themselves from the virus?

Would you expect the pharmaceutical company's rodent colony to become infected?

Should all lab rodents be screened for Hantavirus?

How could Hantavirus be prevented?

How could we develop a vaccine against Hantavirus?

Would a single type of vaccine be effective against all Hantaviruses?

How would you develop and test this vaccine?

Who should be vaccinated?

Should we provide a vaccine against Hantavirus for the general population or only those in high risk situations?

What strategies could a public health organization try to eradicate the disease in wild rodent populations?

How is the Hantavirus transmitted in the rodent population?

Would you expect to find rodents with pulmonary disease caused by Hantavirus?

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Web links

All About Hantavirus

Hantavirus Pulmonary Syndrome

Emerging Viruses Research Center Hantavirus Reference Laboratory

Phylogenetic tree (S segment) of genetically distinct Hantavirus species.

Guests: Dr. James C. Mills discusses Hanta Virus

All the Virology on the WWW

Viral Zoonoses

Hantavirus Pulmonary Syndrome United States, 1995 and 1996; Map of cases

Southwestern Archaeology Health Issues

Hantaviruses, with emphasis on Four Corners Hantavirus

Stalking The Deadly Hantavirus: A Study In Teamwork

One Year Later, The Hantavirus Investigation Continues

CDC slide of Hantavirus

Hantavirus Disease: symptoms, treatment

On The Trail Of a Killer Virus

Yahoo! News Health Headlines

Biology Student Inquires About Drugs on Trial for Treating Hantavirus

Ribavirin, Bradycor in Trial for Four Corners Hantavirus

If You Hear Hoofbeats, Don't Expect To Find Zebras.

Hanta virus Alert in South America Southern Cone

Social Inequalities and Emerging Infectious Diseases

Hantavirus "El Bolson" (Patagonia-Argentina)

Guarding Against the Most Dangerous Emerging Pathogens: Insights from Evolutionary Biology

Emerging Diseases Course Reference Page

Rapid and Specific Detection of Sin Nombre Virus Antibodies in Patients with Hantavirus Pulmonary Syndrome

Health: Warning--Killer Microbes Next 20 Miles

Hantavirus Transmission in the United States

Blood Cells and the CBC

Interpretation and Use of the Western Blot Assay

'Viral Chic': The Propaganda of Health Care in the United States

Ontario Plans to Continue Raccoon Vaccination Program

1998 Recommendations on Rabies Vaccines

Oral Rabies Vaccination of Raccoon

DNA Learning Center Cold Springs Harbor

The Institute for Genomic Research DNA Learning Center

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Medical Data

Hilary, Ruth, the grocer and the site-manager

Hilary: Caucasian, age 36, non-smoker, light alcohol consumption, chronic asthma. Has been taking Intol and Ventalin by nebulizer and oral prednisone for the past 36 hours to relieve asthma symptoms. Presents with shallow rapid breathing, dry unproductive cough, blue nail beds and lips.

Test Results

Blood Culture 3X	2 negative, 1 positive for staph epi
PO2	55
Serum lactate	2.7
Chest X-ray	not remarkable
Hematocrit	47

Ruth: Caucasian, age 37, non-smoker, light alcohol consumption, takes Prozac, takes an assortment of botanicals including blue green algae, St. John's Wort, and recently has been drinking a Southwestern tea made from chamisa. Presents with muscle aches, dry unproductive cough, shallow breathing and confusion.

Test Results

Blood culture 3X	all negative, 24 hours growth
Serum lactate	3.2
Platelets	75,000
Hematocrit	50
Chest X-ray	diffuse, interstitial infiltrate

Grocer: Caucasian, age 57, obese, heavy smoker, heavy drinker, hypertensive. Presents with deep productive cough, jaundice and confusion.

Test Results

Total bilirubin	4.3
hematocrit	27
Platelets	42,000
AST	750
ALT	175

Site-Manager: Hispanic, age 42, heavy smoker, presents with muscle aches, dry cough, shallow breathing.

Test Results

Blood culture 3X	1 negative, 2 with a mixture of propionibacterium and staph epi
Serum lactate	2.8
Platelets	81,000
Hematocrit	49
Chest X-ray	diffuse densities

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Newspaper Articles:

Albuquerque Journal http://www.abqjournal.com

May 27, 1993 Front page article

Mystery flu kills six in tribal area

June 3,1993 Front page articles

Puzzling epidemic slows its deadly pace

12th victim went downhill in two hours

Navajo grief, anger burst forth at funeral

Bubonic plague closes foothills picnic area

April29(?), 1998 Official identify victim of Hantavirus

April 30, 1998 Hantavirus kills N.M. man

May 3, 1998 Section B Hantavirus patient year's 2nd in N.M.

May 6, 1998 Physicians on Alert for Hantavirus

Family suspected man had Hantavirus

May 7, 1998 Physicians on alert for Hantavirus

May 8, 1998 Hantavirus patients battle for breath

Calls on Hantavirus flood health department

May 19, 1998 Six cats with plague heighten N.M. worries

May 20, 1998 Hantavirus not stopping N.M. tourists

May 29, 1998 Health Workers Spread Word About Hantavirus

June 16, 1998 TV, Radio Ads To Warn: Keep Mice Away

July 3, 1998 McKinley County Woman Diagnosed With Hantavirus

July 9, 1998 Hantavirus Victim's Condition Upgraded

July 10, 1998 Fourth Plague Case Confirmed

Hantavirus Case Sparks Claims

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Interviews and Notes

This case study is fiction, but it is based on real events and real people. Although Hantavirus is still a rare and highly sporadic disease in the United States, it has impacted the lives of many people in many different ways - death or survival from the disease being the two most obvious. Additionally it is important to remember the social and economic impacts of this disease on affected individuals and communities. The following interviews may help you to gain an appreciation for the complex interaction of these various factors:

Interview I	Interview II	Interview III	Interview IV
Suzanne	Nina	Dr. Diane Goade	Karen Milligan
Hantavirus survivor	Hantavirus survivor	Physician	ECMO Nurse

Interview I

Suzanne, who lives in Northern New Mexico, became ill with Hantavirus on December 1, 1995. She is not from the Four Corner's area nor is she a Native American. Her story is unusual in that she was one of three people, all of whom were expected to die from Hanta, to be treated at the University of New Mexico Hospital using ECMO. She and one other individual survived due to this "last ditch" treatment. As a result of this experiment, several other people, infected with Hantavirus during the 1998 season, have survived this overwhelming infection.

When and where do you think you were infected?

She became ill on December 1, 1995. She was probably infected at her 100 year old adobe home. There were mice in the home, due in part to its rural location, and because there was a grain storage area for her large animals near the house. In addition, because she was involved renovation, she was exposed to a lot of dust. " I knew there were mice because the cat would bring them in and I would dump them," she said.

How did you feel when you first became ill?

"On Friday morning I woke up not feeling right. I felt heavy, tired and emotionally strange." Her boyfriend, who was due to lead an elk hunt, asked if he needed to stick around. She told him that she would be fine and so he left for the weekend. Later in the day she felt feverish and achy. Several people at work had flu so she assumed she did as well. Later in the weekend the aches got worse. "My pelvis and lower back were just killing me," she said. It wasn't until early Monday morning when she went to bathroom, vomited and collapsed, that she called a friend for help and was taken to an emergency room in Raton. It was assumed that she had some form of pneumonia, but it wasn't until her mother raised the possibility of Hantavirus, was an other alternative considered. "I got worse and worse and I wasn't breathing." By 8 or 8:30 that evening she was loaded on a plane and transported to the University of New Mexico Hospital.

What happened at University Hospital?

She was conscious during the flight to the hospital, but had started to cough up bloody sputum. She lost consciousness as she was being loaded onto the ambulance. Close to death she was put on ventilator by 10 PM that evening and then on Extra Corporal Membrane Oxygenation (ECMO) by 2 or 3 AM in the morning. She was on ECMO for 4.5 days. She was unconscious during that time and for the week after she was taken off ECMO. She stayed a month in the hospital and was very weak and debilitated. She had trouble dressing, walking and eating. When she recovered enough to leave the hospital she stayed at a friend's home. " I could not return to my house because of its rural location and my level of disability. Also I could not emotionally return home. This was the place where I became sick and because my relationship with my boyfriend was falling apart, Hantavirus was a good excuse not to go back." She spent 6 weeks on a friend's couch. She couldn't do much. It was difficult to read, but she watched a lot of movies and got better at walking around.

Events after recovery

Three months after recovery from Hantavirus Suzanne was diagnosed with breast cancer. Due to her past experience she had a "high comfort level" with the diagnosis. In an attempt to calm her mother she said, "I might not have been here for this." She was able to go back to work a year and a half later - at first part-time and then as her stamina improved - full time as a veterinary technician. She still tires easily, has residual aches and pains and some skin discoloration due to bleeding as well as short term memory loss.

Epidemiology

After her diagnosis, mice were trapped and tested for Hantavirus. The virus isolated from the mice in her home were a genomic match to the virus that caused her illness. The house was never decontaminated, her former boyfriend still lives there and he has not had any unusual health problems.

How has Hantavirus changed your life?

"This was a near death experience. While sick I had a sense of lightness and well-being, there was no fear or depression." Suzanne says Hantavirus turned her life around- nothing bothers her anymore and where there was turmoil there is now direction and calm. Although she is not into formal religion she reads about faith and spiritualism. Suzanne says that she "is driven to be of service to others." She has recently spent some time in Albuquerque helping a Navajo family whose daughter required ECMO treatment for her Hantavirus infection. She visited with the family to help them and to help herself. "It has been good to patch in those two weeks when I was unconscious," she said. Suzanne, who feels that the community has shown her great support during her illness, was very surprised when the Navajo family stated concern about being socially ostracized, within the Navajo community, due to their daughter's illness.

Interview II

Nina, a medical technologist, lives in the southwest corner of Kansas. She became ill with Hantavirus on October 31st 1997 and feels that she was exposed to the virus on September 23rd - the day she helped a friend clean a basement. The basement was known to be infected with mice. As they entered the stairway to the basement Nina said, " this is a great place for Hantavirus." Because there had been three recent cases in the area they took precautions; they sprayed with bleach, did not sweep and moved only those objects that they needed. As it would turn out Nina would be the first person to survive a Hantavirus infection in Grant County, Kansas.

How did you feel when you first became ill?

Nina did not discuss her early symptoms during the interview but did say that when she was brought to the hospital a friend and co-worker told her "you are really sick." Although they has initially assumed pneumonia, her lab results suggested something more serious. They did not perform a PT, her platelets were down to 85-90,0000, there was a "left shift" and the presence of atypical lymphocytes. Blood cultures were negative. The diagnosis of Hantavirus was made based on the chest x-ray - B lines and infiltrate into tissue.

What happened at the hospital?

Nina was taken to a larger hospital with a more sophisticated intensive care unit. She had a blood lactic acid of 6.2. By Tuesday afternoon she was put on a ventilator and remained on this level of support care for 6 days. During that time she was conscious. She said that the 6 days on the ventilator were " interesting and not terrifying and that she knew that she had many people praying for her" She was conscious the whole time and participated in checking her own vitals. After 6 days on the ventilator she recovered quickly and went home.

Events after recovery

Nina still tires easily, but is able to work 32 to 36 hours per week in the hospital laboratory. She has had to adapt to less energy, finds stairs difficult though she can walk for miles. Exercise leaves her with deep muscle pains in her thighs that last for days. She says there maybe some short-term memory loss - " I think I am OK, but my friends and family tell me that I am forgetful."

Epidemiology

The basement where she got her infection was cleaned by a company that specializes in cleaning hazardous and biomedical waste. Mice were not trapped and there was no attempt to genomically link Nina's virus to the basement. Her friend, who cleaned the basement with her, did not become ill.

How has Hantavirus changed your life?

"Becoming ill with Hantavirus was a life changing event and I want something productive

to result from it. It was a fascinating experience. Patients have to learn a lot about themselves and science to help to communicate with their healthcare providers."

Interview III

Diane Goade, MD, a research physician at the University of New Mexico Medical School, has been involved with Hantavirus patients since 1993. She is currently working on the development of a genomic vaccine for Hantavirus, conducting a series of Hantavirus survivor studies as well as working on the mode of virus transmission in wild rodent populations.

What was it like over Memorial Day weekend of 1993?

"Well I had just completed an Infectious Diseases Fellowship and had just started my first week as an Attending Physician. There was a trickle of associated deaths - first 2 and by the time it hit 5 - we knew we were in trouble. We made an isolated ICU, we were completely covered in full body protection and we stayed there for 3 days. There was lots of fluid and blood, it was a completely helpless feeling to see somebody crash right before your eyes. But remember our treatment of Hantavirus is still pretty primitive - if you don't get them in time they still crash."

What did you feel or what did you think about during that time?

" I was - and you can quote me on this - scared shitless. Not only that, I had a 3 month old baby at home. So not only was I scared and tired, but I was also engorged and leaking milk all while confined in a Tyvec suite. If you ask my husband about that weekend he will tell you it was the weekend of the screaming baby."

How does treatment for Hantavirus at the University of New Mexico compare to other places in the country?

"We have the highest survivor rate and we are the only hospital to use Extra Corporal Membrane Oxygenation or ECMO. However, as I said before treatment is still primitive.

We need to get our patients early and we need to be aggressive. There is no catch-up period."

How far do patients travel for treatment at the University of New Mexico?

"Our patients come from all over the state, the Four Corners region, the Navajo Nation southern Colorado and the western pan handle of Texas."

There are some people that are critical of the attention that Hantavirus, a very sporadic disease, commands. How do you feel about that?

"Yes, Hantavirus is very rare in this country, but it is very deadly. It still has one of the highest mortality rates of any disease so it is important to understand everything about it. It is not a disease unique to the Southwest, it is found in other parts of the country and in other parts of the world Hantavirus is a significant problem."

You said earlier that your lab is in the process of developing a genomic vaccine. How will this vaccine be used?

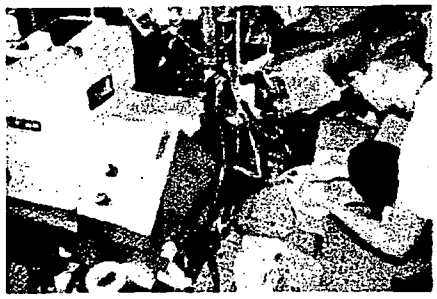
"Right now the vaccine is being tested in wild mice. Although it may be used to limit the virus in wild mice, its purpose will be to immunize high risk populations - people who have a high probability of being in contact with deer mice or their droppings. People who live in rural areas, ranchers, people who work in grain elevators."

If Hantavirus hadn't entered your life- what would you be doing now?

"Herpes viruses, I'd still be a virologist"

What do you want people to know about Hantavirus?

"I want people to know that it is a rare disease that can strike anybody. It can cut down people in the prime of their life. All it takes is exposure to infected rodent droppings, and those are - whether you like it or not - everywhere. To prevent this disease we need to be cautious, we need to prevent exposure and we need to have community education."

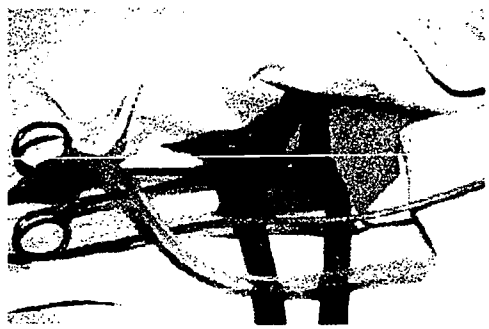


Interview IV

Karen Milligan, RN is an ECMO nurse at the University of New Mexico Hospital. She was trained and certified on ECMO in December of 1991, and is one of a dozen or so people who are ECMO certified in the state of New Mexico. Because ECMO is typically available only at major medical centers, all patients in the state requiring this technology, are treated at UNMH. To maintain her certification Karen is examined once a year and must pass a competency test every 3 months. The quarterly competency test includes an oral exam and a timed water drill. A bag of water is a model patient, and Karen is must be able to trouble shoot and repair the machinery within a fixed amount of time.

What does ECMO do; how does ECMO work?

"The technology was first available in the 1970's and is basically a heart/lung by-pass machine modified for long-term use. Typically it is used for term infants who have pulmonary hypertension, meconium pneumonia, beta hemolytic strep or a congenital diaphragmatic hernia. It is less frequently used for pediatric or adult patients, but in those situations usually some sort of trauma is involved."



ECMO uses 2 tubes. Blood is drained from a venous source, right atrium, and pumped through a circuit by an artificial heart pump. Gases are exchanged through an artificial lung, membrane oxygenator, and then the blood is warmed and returned to the patient through an arterial site. In adult ECMO the venous blood is typically drained from the right femoral vein and oxygenated blood is returned to the patient through the right femoral artery. Dialysis (to treat renal failure) and hemofiltration (to reduce excessive water retention) can be linked to ECMO. The patient is in a narcotic coma during treatment - receiving pain medication, sedatives and muscle relaxants/paralytics. The

muscle relaxants/paralytics may be lightened at least once every 24 hours to assess patient neurological status.

What is it like to be an ECMO nurse?

It takes two nurses to care for an ECMO patient - the bedside nurse and the pump nurse. "I am the pump nurse and the pump is my patient," Karen said. The bedside nurse measures blood gasses, monitors urine output, takes patient vitals and does general and neurological patient assessment at least once every hour. In addition the bedside nurse will maintain the airway and administer any other additional drugs. "My eyes never leave the pump. I must assess the activated clotting time of pump blood to make sure that clots do not form in the tubing. A proper clotting time - 180-200 seconds, can be adjusted with heparin. I also check and adjust blood gasses in the pump blood, check and if necessary remove clots from the tubing and adjust circuit blood pressure every 30 minutes. In addition I replace blood and platelets several times a day. Red blood cells and platelets get destroyed when they are run through and I need to compensate for the volume of blood that is in pump."

What do you think about when you are doing ECMO?

"I am totally focused on the circuit. I have to be able to notice small changes, because small changes can lead to a catastrophe. I can never leave the room without relief."

After a 12 hour ECMO shift- what are you like when you get home?

"I like intensive care nursing. I could do this all day for each of my 3 shifts per week. I think it is exciting to be involved in the use of this technology. I think most ECMO nurses feel the same way."

What was it like when you had the first Hantavirus patient?

"At that time we didn't know if person to person transmission was possible. We were all suited up in a hat, face protection and a gown. My first thoughts were " What the hell am I doing here and how can I get out of this room." I also thought that the pumps might explode because they had to rotate so fast to accommodate the adult patient. However, I got used to that."

In what ways is ECMO different for Hantavirus patients than babies?

"The tubing is bigger, the blood volume is bigger, but the hard thing is getting used to the large drug dosages. Emotionally it is different. With Hantavirus patients you think about their children and you notice that they may close to your age. Adults tend to be on ECMO for short amounts of time - days - babies tend to be on ECMO for extended periods, many weeks. Ethically ECMO is better accepted for use on babies than on adults."

Return to Index

Genomics and Hantaviruses

The study of genetics at the level of nucleotide sequences is called genomics. The genotype is the nucleotide sequence and phenotype is the resulting amino acid sequence of gene products.

The field of genomics is based on the ability to cleave and sequence DNA. The DNA fragments are of various sizes due to restriction enzyme specificity and the nucleotide sequence. Using sophisticated computerized computational methods, developed to create assemblages of hundreds of thousands of small DNA fragments, the sequence is determined by matching areas of overlap.

Recent advances in genomics have produced a revolution in our understanding of evolutionary relationships and the complex interplay of genetic and environmental factors on physiology and behavior. Genomics has also stimulated the discovery of new pharmaceuticals by revealing new biological targets for the development of drugs, vaccines and DNA based diagnostics.

In the ancillary Things to Ponder section, genomic analysis of Hantavirus is another facet of the story available for student exploration. Areas in the Hantavirus case study where genomics plays an important role include:

- identification of the pathogenic agent

- identification of the virus in patient sera

- the ability to link the source of infection to a specific geographic location

Through the National Center for Biotechnology Information, it is possible to find over 500 references to Hantavirus sequences. Using CLUSTALW Multiple Sequence Alignment Analysis of Hantaviruses isolated from rodents and humans throughout the country, students can defend the various medical and legal issues imbedded in the story.

A series of questions, linked to the DNA Learning Center at Cold Spring Harbor Laboratories, will be available to students who are interested in Hantavirus host range specificity, Old and New World Hantaviruses and issues pertaining to genetic conservation and the segmented genome.

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