

***The DNA Files:***  
***Unraveling the Mysteries of Genetics***

As heard on National Public Radio

**Planet of the Bugs**  
**The Never-Ending Tale of DNA and Infectious Disease**

**Hosted by John Hockenberry**

Transcript

SoundVision Productions  
2991 Shattuck Avenue, Suite 304  
Berkeley, California 94705-1872  
(510) 486-1185  
feedback@dnafiles.org  
<http://www.dnafiles.org>

For further information about genetics and these programs, as well as the producers who brought you this series, visit the project web site at [www.dnafiles.org](http://www.dnafiles.org).

Send your questions about genetics and this project to [feedback@dnafiles.org](mailto:feedback@dnafiles.org).

**Funding for this series was made possible by generous grants from The National Science Foundation and the Alfred P. Sloan Foundation.**

*Last reviewed for accuracy: February 2002.*

**JOHN HOCKENBERRY:** This is *The DNA Files*; I'm John Hockenberry. I'd like you to pause right now and take a look around you- carefully, if you happen to be in your car.

What do you see?

I have no idea what you're seeing. But I do know what you're not seeing: you're not seeing the millions and millions of tiny living creatures on you and in you and everywhere around you. We're surrounded by these microscopic critters- the microbes- our entire life.

**STANLEY FALKOW: You know, we come out of the womb, we're sterile, and the first living thing we come in contact with is not our mother, its not the attending physician, its the microbes that are in the birth canal. You are colonized with microbes; you have billions of these creatures with you from the minute you're born till the day you die**

**JOHN HOCKENBERRY:** Scientists these days are learning how humans and microbes deal with each other at a genetic level. We'll tell you about our Planet of the Bugs: The Never-Ending Story of DNA and Infectious Disease when we return with *The DNA Files*

• • •

**JOHN HOCKENBERRY:** Mutant killer microbes that antibiotics cannot beat have been a problem in hospitals for more than two decades. Now the genetic revolution is helping us understand how these pathogens propagate ... how their DNA is eluding our best efforts to control them. Antibiotic resistance has the makings of a public health crisis, as Leda Hartman reports.

**LEDA HARTMAN:** The battle cry of the newborn, here in the neo-natal intensive care unit at the University of Virginia hospital. In 1991 it was a battle~~ground~~, where doctors fought off an outbreak of methicillin-resistant staphylococcus-aureus, or MRSA, in eighteen infants. They all survived, but several years later another U.VA patient was not as lucky. Dulcey Fowler died after MRSA bugs infected a surgical wound in her hip. Her widower Michael explains:

**MICHAEL FOWLER: She was particularly vulnerable, especially with her very compromised immune system with the arthritis drugs, to such an invasion by mrsa bugs, if there were any around at the clinic**

**LEDA HARTMAN:** Around 800,000 antibiotic-resistant infections are recorded in U.S. hospitals each year. Of those, about a third are caused by staph-a, the single-cell microbe that can produce a range of nasty infections, from boils to blood poisoning. When the microbe develops resistance to antibiotics, it can turn deadly, killing from 10% to 25% of its victims. Dr. Bill Jarvis investigates superbug outbreaks for the Centers for Disease Control. He explains how bacteria can adapt to antibiotics ... and outwit them.

**BILL JARVIS: in some episodes, it's development of an enzyme that will eat up the antibacterial. Another is to hide the target where the antibacterial has to get, or modify the structure of that target, so that the antibiotic no longer fits correctly.**

**LEDA HARTMAN:** Some antibiotics are designed to jam a bacterium's internal machinery, fitting onto and binding the ribosomes that build essential proteins. Over time, some bacteria may develop a small pump that repels the antibiotic. Other bacteria might grow thicker cell walls over several generations, eventually keeping the antibiotic out. It's survival of the fittest. Bill Jarvis.

**BILL JARVIS: and we need to realize that our antibiotics are very precious. And if we use them when they're really not necessary, they may no longer work**

**LEDA HARTMAN:** So how do these bugs get so nasty? Some inherit genes that confer resistance, some acquire them in random mutations and others collect new traits through gene swapping. Bacteria are asexual, but in one process akin to mating, microbes join together and transfer bundles of their DNA through tiny tubes. In other cases, microbes simply pick up naked DNA from their environment. If the new DNA contains resistance genes, then the bacteria, plus all their descendants, are free to multiply even when antibiotics are present.

Of course, you don't have to go to a hospital to get a superbug infection like MRSA. But contaminated equipment and patient movement in hospitals help spread it around, says epidemiologist Dr. Barry Farr.

**BARRY FARR: And that means if you control spread, you have a much lower rate than places that aren't doing this**

**LEDA HARTMAN:** Here in Dr. Farr's hospital in Virginia, people with antibiotic resistant infections are put into isolation rooms, clearly marked with signs like the one nursing coordinator Eve Gianetta is pointing out.

**EVE GIANETTA - And what that means, it tells you that you need to wear a mask when you go in, you need to wear gloves and you need to wear a gown. And when you're finished you need to wash your hand**

**LEDA HARTMAN:** Controlling spread is an effective way of eliminating an outbreak, but it's expensive, and Farr says many hospitals are reluctant to implement the commonly accepted CDC guidelines, a decision he calls penny-wise and pound-foolish ... especially in terms of the human cost.

**BARRY FARR: As we let it get worse, patients are more likely to fail. They're more likely to die, and we have to pay more. And that's been shown in study after study. And we're allowing that to happen systematically - as a society**

**LEDA HARTMAN:** In the United States, superbugs are responsible for 40 percent of all hospital-acquired infections. Farr points to Denmark, where rigorous spread-control measures in one recent study cut their proportion to less than 1 percent. And when antibiotics were eliminated from Danish pig and chicken feed by government order, resistance levels of particular types of bacteria decreased dramatically in the livestock. Two million pounds of antibiotics were produced in the United States in 1954. Today, it's 50 million pounds – and almost half of those are given to animals.

Soap and hot water, new drugs, and reducing antibiotic use are all part of the solution. In the meantime, methicillin-resistant staph-a and other superbacteria are alive and kicking in the very places we go to get well, our hospitals.

For *The DNA Files*, I'm Leda Hartman.



**JOHN HOCKENBERRY:** Welcome to *The DNA Files*. I'm John Hockenberry.

Today we're going to take a look at DNA and infectious dis- (he coughs) -sorry, excuse me- we're going to look at DNA and infectious diseases. (he snuffles.) Scientists, you know, are making remarkable discoveries about DNA these days. What light can these discoveries shed on -(he sneezes) - sorry... the mysterious world of microbes- all those bacteria and viruses and yeasts and protozoa with whom we share the planet? (he sneezes again). Sorry, I seem to have picked up a bug somewhere... its very annoying.

Actually it was much worse yesterday. I was sick, the kids were sick, everyone in the house was sick. This happens a lot. I guess the kids pick up germs at daycare or the playground. So yesterday afternoon while I was lying on the couch sneezing and feeling sorry for myself, I had this dream.

[Dream music starts]

I dreamed I was going to get rid of all the microbes in my house once and for all:

[clinking of bottles and cans]

**JOHN:** Okay I'm lining up the weapons here on the table: Disinfectants. Germicides. I've got Antibiotics. Fungicides. Antimicrobial soap. Sprays, pills, powders, ointments- rubbing alcohol, that's gotta do something. What's this- ant poison? - why not, let's kill 'em/... I'm piling up every lethal substance I can find ...and now... I'm going to attack! I'm going to blast every germ in the house -I'm going to kill them all! Every last one of them!

[doorbell rings]

Wait, someone's at the door. [calling] Who is it? This is not a good time...

[doorbell rings persistently]

Oh all right, all right, I'm coming. Just when I was all set for a little population control. I hate that.

[door opens]

Hello?

**PETM:** Hello Mr. Hockenberry. I see I have arrived in the nick of time

**JOHN:** Excuse me? Who are you?

**PETM:** My name is not important. What's important is that I am a spokesperson for P. E. T. M. - People for the Ethical Treatment of Microbes. And you, sir, are about to commit a terrible crime

**JOHN:** People for the Ethical Treatment of Microbes? I never heard of you.

**PETM:** Of course not. No one pays attention to microbes except when they want to kill them. Just look at those disgusting chemicals you're playing with

**JOHN:** But microbes are, you know, germs. They make people sick.

**PETM:** Ha! Germs- Bugs-Infections- the language of prejudice! Us versus Them! Do have any idea how important microbes really are? Do you realize how much you depend on them?

**JOHN:** What do you mean?

**PETM:** Did you have toast for breakfast this morning?

**JOHN:** I think so, yes.

**PETM:** And what do you suppose made the bread rise when it was baking

**JOHN:** Um.... the yeast?

**PETM:** Yeast, exactly, a microbe. Microbes make wine and cheese and beer, too. Without them you'd have to eat broccoli three times a day. And what's more you wouldn't be able to digest it. If it weren't for the bacteria in your intestines you couldn't digest anything. You'd starve to death.

**JOHN:** I never thought of that.

**PETM:** I doubt you could think at all without microbes. Have you ever heard of mitochondria?

**JOHN:** Mitochondria? Now they're those little things inside our cells that help the cell make energy?

**PETM:** They're indispensable. They used to be bacteria, you know; they moved into the cells of plants and animals ages ago, and we've kept them on as servants. You see, Mr. Hockenberry, humans and microbes have always lived together. There's no Us versus Them. We're just one happy family

**JOHN:** Some family, and I'm sick. And never mind me, look around the world- the plagues, the epidemics. Every year tuberculosis, AIDS, and malaria kill more than 5 million people - poor people, mostly, who can't afford medical care. In developing countries half of all deaths are caused by infections.

**PETM:** Admittedly there rough edges. It's not easy to make a happy family. But in the long run our destiny is to accommodate each other, to evolve in harmony. Look at the big picture! Lift up your eyes! See the light

**JOHN:** Hey, wait a minute! You're not a spokesperson for P.E.T.M. You're not a person at all! You're a...you're a microbe!

**PETM:** No, wait, listen to me.

**JOHN:** Get out! Get out!

[sci-fi music and shrieks, fading as we return to the studio]

**JOHN HOCKENBERRY:** Okay, it was only a bad dream.

It's left me a lot to think about, though. The spokesperson for People for the Ethical Treatment of Microbes may be imaginary, but she does make a point: humans and microbes have been living side by side for a long, long time. Call it a war, call it a dance, call it a game- whatever you call it, the relationship between Us and Them is old and complex. We've both developed elaborate strategies for dealing with each other. So lets look at these strategies – theirs and ours. Lets see what the new discoveries in DNA can tell us. We'll begin with bacteria. These are simple one-celled organisms. Under a microscope some look round, some are rod-shaped, others are curved. They have no mouths, no eyes, no ears; they simply absorb nutrients and other chemicals from the environment around them. When its time to reproduce, they divide; they split in two and start over again.

Simple though they are, bacteria are successful. They established themselves on earth long before humans came along, and they can thrive almost anywhere. Some live at the bottom of the oceans, others on mountaintops; some are at home in ice, some in boiling hot springs. You might say bacteria are the dominant form of life on our planet.

Dr. Stanley Falkow is a professor of microbiology at Stanford University. Right this minute he's fly-fishing on the Bitterroot River in Montana. Lewis and Clark came this way about two hundred years ago. A hundred years later a man named Howard Ricketts set up a laboratory here to study Rocky Mountain spotted fever, a sometimes fatal bacterial infection spread by ticks living in the woods, or on dogs. Today the lab is run by the National Institutes of Health, and this is where Dr. Falkow works in the summer... when he's not fishing.

**STANLEY FALKOW: I really find it historical, Lewis and Clark in 1805, Ricketts in 1905, and now its not quite 2005 but I can't help thinking that the organism that Ricketts discovered here, they've now sequenced the chromosome of this, I don't what Ricketts would have thought of that. So we're in an era of discovery all based on genomics. What's amazing is that this organism that causes this disease, as well as typhus and other diseases transmitted from insects to humans, they are the closest know relatives to those things that live in animal cells called mitochondria.**

**JOHN HOCKENBERRY:** Now, mitochondria are useful; our cells need them to make energy. Rocky Mountain spotted fever we could do without. Yet they're genetically related; they have a lot in common.

**STANLEY FALKOW: Bacteria, you know, they're very simple creatures. All they want to do is grow. A bacterium, which is one, wants to become bacteria, which is more than one. A very simple goal in life. Give them an opportunity to do so and they will. Don't blame the bacteria for doing what they evolved to do.**

**JOHN HOCKENBERRY:** So if bacteria are just trying to divide and multiply, why do some of them- the bad ones- make us ill? Well, sometimes it's because they're competing with other cells in our body – they're hogging space and stealing nutrients. Sometimes they happen to produce chemicals that are toxic from our point of view. Now, this doesn't mean the microbes are deliberately trying to poison us. You could just as well say it's an accident. Lets look, for example, at *Vibrio Cholerae*, the microbe that causes cholera. This is a diarrheal illness. The World Health Organization estimates a quarter of million people around the world are infected each year. The bacteria lives in water and likes to attach itself to the shells of crustaceans.

**RITA COLWELL: Cholera is an interesting bacterium in its ability to attach to chitin.**

**JOHN HOCKENBERRY:** Dr. Rita Colwell is a microbiologist and Director of the National Science Foundation.

**RITA COLWELL: What is chitin? It is that hard shell you see in crabs, the white structure that gives rigidity to the animal. The bacterium produces a toxin that allows it to anchor itself to a surface. We assume that *Vibrio Cholerae* has a powerful chitinase, an enzyme that breaks down this hard shell to the elements**

**JOHN HOCKENBERRY:** The cholera bacterium is especially fond of a microscopic shrimp-like creature called a copepod. It lives on the shell of the copepod doing no harm to humans...until we swallow it.

**RITA COLWELL: Now in humans, we don't have chitin, but the bacterium when we swallow it tries to behave as if we are one large copepod. And so it attaches to our gut, produces toxin which interferes with our sodium-potassium balance; there's an out-flushing of water, diarrhea, and the loss of as much as 16**

**liters of fluid, so you could see a cholera victim so dehydrated that he or she would look skeletal – leading to death from shock.**

**JOHN HOCKENBERRY:** Horrible as this is, you can see its basically an accident. The microbe does something which it assumes is perfectly reasonable; Vibrio Cholerae can't tell the difference between a shrimp and a human. On our side, we're just trying to flush out a poison; we're responding in a way which might be reasonable if only we didn't over-do it.

In America we haven't had a cholera epidemic since the 19th century. We won't find the bacteria in our tap water at home, because our water treatment plants get rid of them. We're lucky. Most people in the world are not so lucky:

**GARY SCHOOLNICK: Look at these, aren't they beautiful...Look at these.**

**JOHN HOCKENBERRY:** Gary Schoolnick- professor of medicine, microbiology and immunology at Stanford Medical School. He's looking at photos of his last trip to Bangladesh.

**GARY SCHOOLNICK: This is the delta just at the decline of the monsoon season. So the delta empties into the Bay of Bengal. During the monsoon season it floods. Seventy percent of the entire country is underwater during monsoon season.**

**Let me show you another thing... this map. This is the map of Bangladesh. And it shows this enormous delta area. What I wanted to show you are these red circles**

**JOHN HOCKENBERRY:** The red circles sprinkled across the map are research sites where Schoolnick and his colleagues are continually sampling the water. They know the water chemistry changes as the floods come and go.

**GARY SCHOOLNICK: During the year, depending on how much fresh water comes down from the Himalaya foothills, this water will either have a lot of salt – and a heavy influence from the Bay of Bengal – or it will become relatively fresh during the rainy season. So any microorganism living in this water has to adjust to these ancient periods dictated by the monsoon season. See this device?**

**JOHN HOCKENBERRY:** Dr. Schoolnick holds up a little plastic disc. It looks more like a child's toy than a scientific instrument. But this is what researchers use to collect Vibrio Cholerae in the water.

**GARY SCHOOLNICK: Its about 4 inches in diameter and it is a circular disc with a hole in the center through which a fishing line can be threaded. And it can be suspended at any depth in the river. We leave it there for two weeks, come back, and by that time there's a bio-film on the surface of this. It's scraped off, brought back to the lab in Dacca, the capital of Bangladesh, preserved, and then eventually sent by Federal Express to our laboratory here.**

**JOHN HOCKENBERRY:** A bio-film is a slimy substance which bacteria make. You might think of it as an apartment house for microbes. Dr. Bill Costerton is Director of The Center for Bio-film Engineering at Montana State University:

**BILL COSTERTON: The bio-film is made of 15 percent bacteria and about 85 percent of slime- we can't think of a more polite word than slime, it's actually a polysaccharide, and its very slimy.**

**JOHN HOCKENBERRY:** We encounter bio-films all the time, Costerton points out. You know that slippery film that forms on the tiles of a shower stall? The plaque that grows on your teeth? The slimy stuff you feel when you pick up a rock that's been sitting in a pond? These are all bio-films. Nearly all bacteria which live in water, the way cholera does, form bio-films attached to a surface- a rock, a plant, a piece of plastic- whatever they can find.

**BILL COSTERTON:** And so the bacteria can actually sit on the surface, and that slime collects any nutrients that might be going by. They do very well in the slime because they're protected from all kinds of host defenses and antibiotics as they grow in the slime.

**JOHN HOCKENBERRY:** The bacteria in a bio-film are not only safe and well fed; they're also packed very close together. And like neighbors in a crowded apartment building, when they bump into each other they exchange information – genetic information.

**BILL COSTERTON:** While they're in the bio-film community they get really, really interactive. They're passing bits of DNA back and forth. They exchange plasmids, which are also little pieces of DNA, while they're in the bio-film. And in fact they can trade genes that will make them resistant to toxins in the environment or antibiotics in the individual. When the lights go out in the bio-film, all sorts of pretty sexy things happen (laughs)... So it is in fact a pretty good party going on there...

**JOHN HOCKENBERRY:** Back at Stanford University, Dr. Schoolnick will be waiting to examine those bio-film samples collected in Bangladesh. He'll look for changes in the state of the genes: which ones turn on, which ones turn off, as the water around them changes. Eventually, he hopes to learn exactly how the microbe interacts with a real-world environment.

**STANLEY FALKOW:** In the real world a microorganism in essence knows where it is by constantly testing the complexity of environment

**JOHN HOCKENBERRY:** Stanley Falkow.

**STANLEY FALKOW:** The organism in essence knows where it is by constantly testing the temperature, the pH, the kind of gases it comes into contact with; and depending on the environment it expresses some genes, and it turns them on and it turns them off depending on the environment. So we need to know when it's on, how long it's on, and what the gene product does after it's produced.

**JOHN HOCKENBERRY:** This is complicated business-so complicated, Falkow says, the human mind can't follow it without a lot of help from computers. But if we can learn how microbes work at the genetic level, then we should be able to find new ways to influence them.

Of course, we're already influencing microbial genes. Not by high-tech DNA manipulation, but through a low-tech sort of natural selection. We humans have always done this, and always will. So says Amherst College biologist Paul Ewald: he points out that if a microbe spreads by human contact- one person sneezing or coughing or shaking hands with another person- then it can't afford to make its host too sick. It relies on the mobility of the host to get around.

**PAUL EWALD:** But if an organism is transmitted by water, then the mobility of the infected host is pretty close to irrelevant. Because if somebody is knocked flat by a diarrheal disease like cholera or dysentery, the organisms are shed into the clothing or the bed sheets and somebody else takes those bed sheets out and

**washes them. If they take the materials to wash in a canal, and other people come to the canal to get drinking water, then those organisms can reach thousands of persons even if the original infected individual is not mobile at all. So what one expects is that waterborne infections should be much more harmful than the ones that are not transmitted by water. And that's what one finds**

**JOHN HOCKENBERRY:** Fortunately, Ewald says, there's a lot of genetic variation in a population of microbes. Some variations are less harmful to us than others. So when we clean up the water supply- when we make water transmission difficult for the microbe- we're favoring the less toxic ones. We're encouraging the microbes that depend more on the mobility of their host. The idea is that evolution-with a nudge from us- will gradually alter the gene pool.

**PAUL EWALD: And the evidence from the Latin American outbreak of cholera that began in 1991 provides strong support for this idea. Because when cholera got into countries like Chile, which have a low potential for waterborne transmission, it evolved within a few years towards a mild equilibrium with the host. And in the United States, by the way, the trend reflects the trend in Chile; the organism now is extremely mild here**

**JOHN HOCKENBERRY:** Wow. An infection that becomes less dangerous over time! I think that's what the P.E.T.M spokesperson was trying to say in my dream: she claims that if we live together long enough, we'll learn to get along. And that really does happen. But, Ewald says, the opposite can happen too: mild microbes can evolve into real killers. It just depends on what strategy is best for microbe:

We're going to take a short break. When we come back: Chickens that fight microbes.

• • •

**JOHN HOCKENBERRY:** This is *The DNA Files*. I'm John Hockenberry.

**MIKE DOYLE: I'm Mike Doyle, I'm a professor of food and microbiology at the Center for Food Safety at the University of Georgia. These are some of the chickens we use in our studies...**

**JOHN HOCKENBERRY:** Most of the chickens in this room harbor a microbe known as campylobacter; it doesn't make them sick, but- like Salmonella- it causes a food-born illness in people. Campylobacter infections are actually more common than Salmonella.

**MIKE DOYLE: We have spent over a year trying to identify chickens, among thousands of chickens, that don't carry Campylobacter. And it's hard to do because 90 to 95 percent of chickens at one time or another will carry Campylobacter. And we came about with about 10 different chickens that didn't carry Campylobacter. We fed Campylobacter to those chickens, and in the end we found about 5 that still didn't carry it**

**JOHN HOCKENBERRY:** Five out of a couple thousand is not a lot. But those few birds-those happy few- may be very useful.

**MIKE DOYLE: We think those chickens probably have protective bacteria in their intestinal tracts that prevent Campylobacter from colonizing them. So we**

**have dissected several of these animals and have isolated from them what appear to be friendly bacteria that produce anti-microbials to Campylobacter.**

**Yeah, this one here is a good one ...and one of those white ones is a good one...  
There are two colored ones here that appear to be protected from Campylobacter.**

**JOHN HOCKENBERRY:** Friendly bacteria- scientists call them pro-biotic bacteria- are like those mild strains of cholera Paul Ewald told us about. We don't create them; they occur naturally. But Doyle hopes he can produce enough of these microbes to use them a weapon; perhaps they can put in into chicken feed to protect other birds. Like most researchers these days, Mike Doyle will use DNA to identify the microbes he's hunting for. This is a new way of doing things, and it's a very big deal.

**ROBERT TAUXE: This business of identifying exactly what kind of organism it is is undergoing a major revolution now.**

**JOHN HOCKENBERRY:** Dr. Robert Tauxe is Chief of the Food-born and Diarrheal Branch at the CDC- the Centers for Disease Control in Atlanta.

**ROBERT TAUXE: For many years it was basically an attempt to figure out what sort of environment the microbe would be able to grow in. You would have a series of different small environments on glass plates called Petri dishes. Some would have salt, some would have sugar, some would have other things present and the question would be could that bacteria grow in that environment or not? And basically by answering a series of questions about whether a microbe did or didn't thrive in a particular environment, you could decide what kind of bacteria it was**

**The next stage in identifying the microbe was the realization that a microbe would have particular substances on its surface. Like the feathers on a bird. So for example, the bacteria E.coli - which was one of the very first to be discovered, because all of us have it all of the time in our intestinal tracts - those E.coli can be defined by what substances they have on their surfaces. So when we have something like E.coli O157H7, the formula is referring to different proteins and sugars that the bacteria actually puts on its coat, its surface. It's like the feathers of the bird, when we see that its O type 157 and the H type 7 we say aha, that's that type of E.coli. That's a bad actor, that particular type**

**JOHN HOCKENBERRY:** This method, the traditional way of identifying a microbe, may be good enough for your doctor. It says: Hey, the patient has E.coli 0157. But for public health officials, this isn't enough. Thousands of people in America become ill from this infection each year; the public health folks want to know exactly which variety of E.coli 0157 they're dealing with. They want to know the genetic fingerprint.

**ROBERT TAUXE: If we have a way of fingerprinting bacteria then we have a way of comparing the strains that come from different people. There's E.coli 0157 happening in the States all the time. Some of the cases may be among people who all were exposed to the same food, or exactly the same swimming pool, or some common source that they have in common that we would like very much to identify and control. So for us, the ability to fingerprint the strains, within the big group of E.coli 0157, turns out to be a really useful tool**

**JOHN HOCKENBERRY:** The CDC fingerprints DNA the same way forensic laboratories do when they examine, say, blood from a crime scene. They wind up with a picture that looks like bar codes, or as banding patterns.

**ROBERT TAUXE:** And just like with spots of blood at a crime scene, we are able to say with ecoli0157, this strain with this banding pattern and this strain with a different banding pattern, are pretty different and they're not likely to be closely related. Or we could say that this strain which came from one person, and this strain which came from another person, they have the same banding pattern -- gee, lets find out what those people have in common and what they've been eating or doing. This is now making a difference in public health. We're finding outbreaks that would have been missed before

**JOHN HOCKENBERRY:** Identifying and tracking genes is also the key to our annual bout with the flu. Flu is a virus, not a bacteria, but from a researchers viewpoint, it's still just DNA. Flu viruses normally live inside animals, but mutant strains will often break out and jump to human hosts. Scientists all around the world keep a lookout for these genetic mutations. Every year the CDC- the Centers for Disease Control in Atlanta-tries to predict which strain is most likely to appear in this country, so vaccines can be made ahead of time.

Now, flu can be life threatening to the elderly, to infants, or to people with compromised immune systems. For most of us, however, it's only a nuisance. You might wonder why scientists spend so much time worrying about it. One reason is the memory of the terrible epidemic that appeared in 1918- the so-called Spanish Influenza,

Historians aren't sure how many people died from it, either; some say 20 million worldwide, others calculate more like 40 million. In any case, this particular flu killed more people more quickly than any disease ever known. Scientists still don't know what was unique about the Spanish Flu. Something genetic, perhaps, something in the DNA which turned it into a killer-- but what? We don't know. Could it come back, could some other genetic variation of the common flu turn deadly? Yes. As far as we know, it could happen. So the search for a vaccine is not trivial.

**JOHN HOCKENBERRY:** Vaccines stimulate our immune system, our body's oldest line of defense against microbes. The immune system has devised all sorts of way to poison, bake, eat and otherwise eliminate microscopic invaders. We have specialized proteins- called antibodies-that lock onto to the microbes if they recognize them, making them larger and easier targets for the cells heading out to destroy them. Some of the symptoms we feel during an infection, like fever and inflammation, are produced by the immune system rather than the microbes. An infection is really a series of moves and counter-moves between host and microbe.

**STANLEY FALKOW:** It's not as if there's a big cataclysmic fight, but rather it's like an orchestration

**JOHN HOCKENBERRY:** Stanley Falkow.

**STANLEY FALKOW:** The organism comes in and senses the host from a variety of biochemical signals; and the organism in sensing this, begins to turn on specific genes. The host is basically doing the same thing. It begins to pick up the scent of the incoming organism, and begins to mobilize particular genes. The more aggressive the organism becomes, the more aggressive the host becomes. The organism senses the aggressive nature of the host and turns on another set of genes, and so forth and so on, back and forth. And the whole

**scenario is based, for the organism, on getting in and replicating; and the idea for the host is to prevent it**

**JOHN HOCKENBERRY:** Falkow notes out that if a microbe were so aggressive as to immediately overwhelm the immune system and kill off the host, it would be defeating its own purpose. It wouldn't have anywhere to live.

**STANLEY FALKOW: By the same token if the host is too quick at eliminating the organism, that may be good, but it is also worthwhile for the host to be able to mount a lasting immune response, so that if it sees the organism again it will be able to neutralize it**

**JOHN HOCKENBERRY:** This, basically, is what a vaccine does: it introduces a sample of a microbe into our body- just enough so our immune system learns to recognize it, and is ready to deal with it the next time it shows up.

The strategy works well against some microbes- smallpox and polio, for example. It looks like vaccines have actually eliminated smallpox from the planet. Yet so far we haven't figured out how to make vaccines work with diseases like TB or AIDS. And flu? Well, if you've ever a flu shot, you know its.... iffy.

Flu, like HIV, is a virus. From a human standpoint, viruses are perhaps the most unpopular type of microbe. The word itself is Latin for poison. Like bacteria, viruses come in a variety of shapes. If you could see one - which is unlikely, they're much smaller than bacteria - you might find yourself looking at a sort of miniature lunar landing craft. This high-tech, Star Wars vehicle contains nothing at all except a little dab of genetic material- DNA or RNA. You'd soon get bored watching it, since most of the time the virus does nothing at all. It doesn't eat or breathe or reproduce or do any of the things we associate with life. It appears to be dead.

But when it happens to land on the surface of a cell, it springs into action. It punches through the surface like a hypodermic needle and injects its genes into the cell. Once inside, they hijack the DNA of the cell and force it to make replicas of the virus. This is great for the virus, but a nightmare for the cell, which eventually bursts open as the viral replicas make their exit.

Any cell can be attacked by a virus. Remember those bad E.coli - the E.coli 0157 - which produce toxins that makes us sick? Robert Tauxe says it's not really their fault:

**ROBERT TAUXE: The reason E.coli 0157 makes those toxins is that at some point in the past, the E.coli were infected themselves with a virus that brought the genetic material that codes for making those toxins in the E.coli. Until that happened it may be that the E.coli could cause a little mild diarrhea, probably not a very severe illness at all. When they became infected with the virus themselves, they acquired this ability to produce a very powerful poison that can kill people**

**JOHN HOCKENBERRY:** So bacteria can be victims. Just as often, though, they're the aggressors. They attack each other all the time, by making the chemicals we call antibiotics. Antibiotics are the microbial equivalent of rat poison or tear gas: something to dump on the competition to mess them up. Sure, the antibiotics we get from a doctor look like they're made in a lab someplace, and they are; but they're based on the chemicals bacteria naturally make in order to damage other bacteria. Why would bacteria do this? Because life is tough and overcrowded in the their world, sort of like life in New York. Bacteria are in fierce competition with each other.

Ever since we humans discovered antibiotics -around the time of World War Two- we've considered them bacteria's greatest gift. Antibiotics are good at killing bacteria, we love antibiotics. We love antibiotics, perhaps, a little too much...

**JOHN HOCKENBERRY:** Here's Dr. Dawn Motyka a general practitioner who hosts a public radio show on KUSP-FM in California:

**DAWN MOTYKA: Welcome to Health Matters, I'm Dr. Dawn Motyka, and I'd love to talk with you. Lets go to our next call. Hello, you're on the air**

**JOHN:** (on phone line) Hello, Dawn, this is John from Brooklyn. You do a great service - (coughs)

**Dawn Motyka: Are you calling about your cough**

**JOHN:** I am calling because basically I've got a house full of flu, my wife is sick, my kids are sick, I'm looking for some antibiotics. And not only that, I want a carpet-bombing program to eliminate every single germ in my body. I've had it; I want these creatures out of me.

**DAWN MOTYKA: I'm concerned that you are mistaken in wanting that to happen. If you've got what you think is a virus, you're asking for nothing but trouble taking an antibiotic. You aren't going to touch a viral infection with an antibacterial**

**JOHN:** So the only real sure-fire cure for a viral infection is basically jumping off the Brooklyn Bridge?

**DAWN MOTYKA: Well that would work**

**JOHN:** Well what puzzles me then, is my impulse is to call up a doctor and say, I want an antibiotic.

**DAWN MOTYKA: Mm-hmm**

**JOHN:** Either I'm getting the wrong message from the health--care system, or I'm just an idiot

**DAWN MOTYKA: I'm not gonna venture an opinion. I have to tell you, sometimes you get worn down as a physician because people are demanding antibiotics, and sometimes you just give in because you're busy and you wont get in trouble with the patient for giving them an antibiotic, but you'll get in trouble for not doing it, they'll go next door and get it from your competitor...and then tell everybody what a terrible doctor you are. And those sorts of considerations are in your mind sometimes**

**JOHN:** Well then what are the consequences to the body for using antibiotics-?

**DAWN MOTYKA: - inappropriately? It's evolution in action. What we do, when we take an antibiotic, is we kill off say 99 percent of the bacteria, the 99 most sensitive bugs. And there are a few in there that are a little bit stronger, a little bit more resistant; and those guys survive. Well then, you hit them with another days worth of erythromycin. And kill off 99 percent of those. And if you take your erythromycin for long enough, you kill all the bacteria, and there's nobody left to reproduce. But if you leave behind just one bug- one survivor- it can divide, and then those two divide. And before you know it you've repopulated the entire human body with bacteria, which are now survivors of erythromycin. They know how to fight that antibiotic. And they'll just go out and spread to other people. They can actually trade that genetic information, bacteria will trade genes, and**

**they'll...this is why we don't use penicillin for skin infections anymore, because the bacteria learned how to fight penicillin and they traded that information. And the reason is people didn't finish their meds**

**JOHN:** Well, I'll go back to-

**Dawn Motyka: - comfort measures**

**JOHN:** - sneezing and phlegmy life here in Brooklyn but thank you very much.

**Dawn Motyka: Bye- bye**

**JOHN:** And lay off the scotch, right?

**DAWN MOTYKA: Bye. I'm Dr. Dawn Motyka, and I'd love to talk with you at (gives phone numbers**

**JOHN HOCKENBERRY:** Drug resistance caused- as Dr. Motyka says- by people not finishing their meds- has become a serious obstacle in treating tuberculosis. The disease itself has been around a long time; Tuberculosis was known to the ancient Greeks and Egyptians. In the 18th and 19th centuries it became one of the leading causes of death in Europe and America, thanks to overcrowded cities with poor hygiene.

People still get tuberculosis in this country: one person in every five or six thousand is known to be infected. It's easy to catch, since the bacteria can survive for months lurking on doorknobs or silverware or wherever they land when somebody with active TB sneezes or coughs. Very few people who're infected will actually get sick, though. Our immune system is good at walling off the bacteria; it surrounds them in a sort of capsule which keeps them from spreading- sometimes for years, sometimes forever. And if they do break loose and start to grow again, antibiotics can kill them.

So, while tuberculosis is a major public health problem in many countries, in America it's become less and less common. Scientists talk about eliminating it altogether. Yet in the late 80s and early 90s there was a sudden resurgence. Researchers discovered that a lot of TB patients were not taking their medicines. No wonder: it's a complicated regime, with lots of pills over a long period of time. To make sure people take their meds, someone has to pay regular visits to the patient's homes. This is now known as DOT- directly observed treatment.

Recently, my friend Jon Kalish followed a caseworker for the National Tuberculosis Center in New Jersey as she went on her rounds in the city of Newark.

**JON KALISH:** It's a bright sunny Friday morning as social worker Rebecca Stevens stops at a senior citizen housing project. In the course of her day she'll visit six TB patients including two HIV positive men and a 30 year-old drug abuser. She has three elderly clients, including Ben, the 64 year-old retired cook who lives here. In addition to his TB medication, Stevens brings Ben small plastic containers of grape juice. Like most people, Ben doesn't know when he got exposed to TB but he's that unlucky one in ten of those infected who get sick. Ben has his suspicions about where he caught the TB bug.

**BEN: It wasn't inside. It was on the street. There was a couple people that I thought had it. They coughed all the time and, you know, spit. Stuff like that. But I would never say something about it**

**JON KALISH:** You didn't suggest that they go get tested?

**BEN: No. No**

**JON KALISH:** Ben swallows four pills at once with some grape juice.

**BEN: Ah! Oh, boy**

**JON KALISH:** Ben grimaces as the medicine goes down. He clearly does not enjoy taking pills. He is now one month into his treatment. Like all TB patients, he spent the first few weeks that the disease was transmissible in quarantine. In his case the quarantine consisted of time on a TB ward at a hospital in Newark and some time at home. All TB patients in New Jersey are on DOT, the first two weeks of which are mandated by state law.

In Newark patients have the choice of coming in to a clinic to take their meds or being visited at home by a social worker. Ben, like the majority of TB patients in Newark, chose to take his medicine at home.

**BEN: At first, I wanted to stop. But since it was helping me-- I seen it was helping me. So, it's no problem. I be glad to see her come when she comes. Every day she comes and gives me my medicine. She talks nice and she out the door**

**JON KALISH:** As Stevens leaves, she gives Ben a five-dollar gift certificate for the supermarket and two packets of medicine for the weekend, which she hopes Ben will take on his own. TB patients like Ben who don't like taking pills are common, which is why directly observed treatment is necessary. People with active TB start off on four antibiotics and over a period ranging from six months to a year they eventually go down to a two-drug regimen. Dr. Lee Reichman is executive director of the National Tuberculosis Center in Newark. He explains how several antibiotics work together to kill the TB bacteria.

**LEE REICHMAN: It's like the old razors they advertised on television. The first razor takes off most of the beard, the second razor takes off the ones the first one misses and the third one takes off the ones that the second one misses. That's why we treat with multiple drugs for tuberculosis**

**JON KALISH:** The antibiotics kill the TB bacteria and relieve the symptoms of the disease, which include chest pain, coughing up blood or phlegm, fatigue, fever and weight loss. But the drugs must be taken well past the elimination of the symptoms in order to eradicate the tuberculosis bacteria. If TB isn't treated, people can die of meningitis, heart failure, internal hemorrhaging and just not being able to breathe. Fieldworker Rebecca Stevens herself tested positive for TB infection in 1992. She was treated with an anti-biotic for a year.

**REBECCA STEVENS: Thank G-d I only had to take one pill per day so it was like a vitamin. But when you're taking 12, 13-some patients are taking as much as 30 pills per day because they have other problems that they have to take medication for, and that's a lot of pills to take and I can understand that they're getting tired of taking those pills**

**JON KALISH:** There are legal consequences for not taking your medicine In New Jersey. Patients can be confined to a hospital and forced to take their medication. It is a drastic measure used for a very small number of patients. In California, instead of being sent to a hospital, TB patients who don't take their meds are sent to jail.

The medical consequence is that normal TB can turn into Multi Drug Resistant TB, which is much harder and much more expensive to cure. In New Jersey it costs \$5,000 to treat someone with

standard TB using directly observed therapy but it costs around \$200,000 to treat one person with MDR-TB because there are often lengthy hospitalizations and sometimes surgery to remove part or all of an infected lung. An MDR-TB patient may have to take as many as eight drugs for as long as two years.

Dr. Reichman notes that although MDR-TB is on the decline in New Jersey, it's on the rise globally. Progress made in this country, he says, shouldn't lull us into a false sense of security because the disease is still very much out there. Which is why Rebecca Stevens is out there every day trying to make sure her patients take their meds.

[Stevens knocks on front door several times, talks with someone from shelter off mic, footsteps going up stairs "Eugene! Eugene!" ... more footsteps going upstairs, knock on door, footsteps going down stairs]

For *The DNA Files*, I'm Jon Kalish in Newark, New Jersey.

**JOHN HOCKENBERRY:** So...even in these high-tech times, a simple, hands-on human intervention is often the key to success. Our headlines always seem to be about glamorous new multi-million dollar technologies. Nothing wrong with that. Yet basic public health measures- old-fashioned things like quarantines and sewage treatment plants and clean water supplies- can save just as many lives.

(sfx: boat ambience arriving at Ellis Island: PA says: Ellis Island, American Museum of Immigration...if you wish to visit, please make your way down through the gangway area...Ellis Island is our stop.)

**JOHN HOCKENBERRY:** The other day I paid a visit to Ellis Island with Dr. Howard Markel, a pediatrician and medical historian at the University of Michigan. Between 1890 and 1927 seventy-five percent of all the immigrants to this country came through here. This was, in a sense, our national immune system.

**HOWARD MARKEL: This is the great hall; let's go out into the center. Think about how the sound must have traveled when- I think the record was 15 thousand in one day, and the noise. There was labyrinth of fences, where they were inspected for visas and medical issues. It was a very orderly process**

**JOHN HOCKENBERRY:** It came out of a progressive idea, that through science one could control the impact of all the microbes of all those people

**HOWARD MARKEL: 15 million people**

**JOHN HOCKENBERRY:** So what microbes were they looking for?

**HOWARD MARKEL: The biggies, the quarantineable diseases: cholera, plague, smallpox, typhus.**

**JOHN HOCKENBERRY:** All diseases that had created extraordinary problems in Europe, How long would people have to wait for the results of these tests - hours, days?

**HOWARD MARKEL: It depends. Cholera cultures take a couple days. The Wasserman test takes a day. They had a great system: if they suspected somebody of having something other than just pink eye or a sty, they would keep them across the way in the contagious disease hospital for about five days and see what developed**

**They'd stamp your passport right here, you'd hear kachunck! Kachunk! ...And it would echo through here, the sound meaning you're free. There's a finality to that. But for those who had a problem they would have to stay here some days. And the immigrants referred to Ellis Island as the isle of hope and the Isle of tears**

**JOHN HOCKENBERRY:** Ellis Island may be closed now, but anyone who wants to immigrate is still supposed to get a documented medical checkup. This doesn't apply to undocumented immigrants, of course, or to business travelers or tourists. More and more people are traveling all over the world these days. As people move, microbes move with them. And as we move into new places and cut down trees and change the environment, and perhaps the climate, we create new opportunities for the microbes. Suddenly we encounter new diseases- or at least they seem new to us.

**STANLEY FALKOW: There is this concept that infectious disease have been conquered somehow and that antibiotics have done it. And in my lifetime its been announced by several Nobel Laureates and by several Surgeon Generals of the United States. And it simply ain't true. Infectious diseases are still the leading cause of death and misery in the world. We have not conquered them and we're a long way from doing it**

**JOHN HOCKENBERRY:** Well, but what about DNA? Now that the Human Genome Project is complete, and we have a list of all our genes, aren't we going to discover new strategies against infection? Of course we are; we've talked about some of them during this program. But human genes don't exist in a world of their own. On the contrary: we are surrounded by an ocean of microbial genes, always interacting with us, an incessant back-and-forth, parry-and-thrust.

**STANLEY FALKOW: One of the things that's going to happen in the future is there's going to be a second human genome project, and that human genome project is going to be sequencing all the organisms that are part of the normal flora in humans- in the mouth, in the intestines. With the combination of the human genome and microbial genomes you'll have a kind of parts list of everything that's there in principle, and it'll begin to make sense**

**JOHN HOCKENBERRY:** John: Well... I've decided to revisit that little nightmare I had at the beginning of this show- the one that launched this investigation. And this time, as I replay the fantasy, things are a bit different

[same dream music used in the original sequence]

**JOHN:** I imagine I'm still angry about getting sick all time, but I no longer think I can eradicate all the germs in the world. I'm just going to find a new approach, a more mature approach... lets see... clean up the kitchen counter here and put this sponge in the dishwasher. And I'm going to throw out this old disgusting smelling cutting board and get a new one, what else? Oh yeah, make an appointment with the doctor: I need to find out whether I've got a virus or a bacteria before thinking about antibiotics. Don't want to encourage drug resistance or-

[the doorbell rings]

Doorbell again. Gosh, I wonder who that could be?

[door opens]

Yes?

**PETM:** It is I.

**JOHN:** So it is: the spokesperson for People for the Ethical Treatment of Microbes.

**PETM:** Alive and well as always. So what about it, John, have you learned to see things my way?

**JOHN:** Up to a point. I'm not mad at you. I don't think you're out to get me, not on purpose anyway. And I do appreciate your many good points

**PETM:** So we can be friends?

**JOHN:** Well, we do seem to be inseparable. Call it family, call it friends. We're stuck with each other. Naturally on those occasions when you make me sick, I'm going to try and wring your neck. Sound fair enough?

**PETM:** Fair enough. Shall we shake on it?

**JOHN:** Sure, why not, I'll shake your hand--just wait a second though...

**PETM:** What's the matter? What are you doing?

**JOHN:** Hang on, I'm just looking for the surgical gloves...I need them.

**JOHN HOCKENBERRY:** I'm John Hockenberry. Thank you for listening to *The DNA Files*.

## **CREDITS:**

This series, *The DNA Files*, was produced by SoundVision Productions with funding by the National Science Foundation and the Alfred P. Sloan Foundation.

This program, **Planet of the Bugs: The Never-Ending Tale of DNA and Infectious Disease**, was produced by Larry Massett, and engineered by Robin Wise. The feature on Tuberculosis was produced by Jon Kalish and engineered by Robin Wise. The program editor was Loretta Williams, and our host was John Hockenberry.

The opening feature, "Hospital Superbugs," was produced by Leda Hartman, and edited by Gemma Hooley.

*The DNA Files* is: Managing Editor, Rachel Ann Goodman. Science Consultant, Sally Lehrman. Research and Production support by Adi Gevins and Noah Miller. Technical and Music Director, Robin Wise.

Original music composed by Jesse Boggs and performed by the Stanford Woodwind Quintet, Joel Schoolnick, Ingebord Saatdjian, Anton Schwartz, Tom Hayashi and Jesse Boggs.

Project Director, Jude Thilman. Marketing by Murray Street Enterprise. Legal services by Walter Hansel and Spencer Weisbroth.

You can visit our website at [www.dnfiles.org](http://www.dnfiles.org). Send your responses and letters to [feedback@dnfiles.org](mailto:feedback@dnfiles.org). For tapes and transcripts, call 866-DNA-FILE (866-362-3453).

The Executive Producer is Bari Scott.

This has been a SoundVision Production, distributed by NPR, National Public Radio.