

MEDMYST MAGAZINE

A Companion to Web Adventures at <http://medmyst.rice.edu>

1.5

DISEASE DISCOVERY



The idea of **One Medicine, One Health** means that we recognize that human, animal, and environmental health are closely related and intimately linked. Over 60% of all infectious diseases are zoonoses, or diseases transmitted from animals to humans. When a disease appears, it takes many people working together to discover the cause.

Learn about the One Health Initiative at:
<http://www.onehealthinitiative.com>

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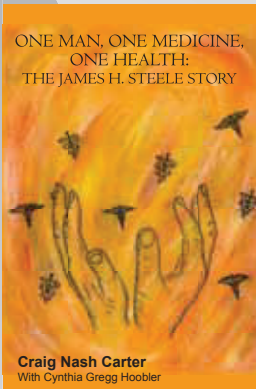
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MAN of STEEL

"YOU CANNOT HAVE GOOD PUBLIC HEALTH UNLESS YOU HAVE GOOD ANIMAL HEALTH. AND YOU CAN'T HAVE GOOD ANIMAL HEALTH UNLESS YOU HAVE GOOD PUBLIC HEALTH!"

-DR. JAMES H. STEELE



What's it like to be a one of the most influential persons in a new field? Dr. James Steele, who is now in his 90's, could give us some insights. He is known as the **Father of Veterinary Public Health**, or simply as **Big Jim** to his colleagues. His career involved discovering and controlling zoonotic diseases, and it took him all over the world. You can read about it in his recent biography, *"One Man, One Medicine, One Health: The James H. Steele Story"*.

While people have long known that animals transmit diseases to humans, knowing what to do about it hasn't always been so obvious. Take Dr. Steele's encounter with rabies. In 1950, the **Memphis, Tennessee** area was suffering from a rabies outbreak. Dr. Steele came up with

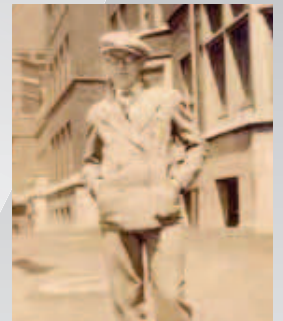
a plan of action: conduct a rabies awareness campaign, pick up stray dogs, and vaccinate the animals.

This successful intervention stopped the outbreak and became the **model for national and international rabies control**. As a doctor of veterinary medicine who went back to school to study public health, Jim became

the first head of the **Veterinary Public Health Division** at the **Centers for Disease Control and Prevention (CDC)** in Atlanta. He edited the *CRC Handbook Series in Zoonoses*, an eight volume set regarded as the best reference source in the field when it was published in 1979-1984.

Animals + Humans = One Health

Dr. Steele has always believed that animal health and human health should be united in one approach. Too often we forget how close our well-being is tied to that of animals, and the important role veterinarians play in protecting public health. Think of animal diseases such as **bird flu**, **anthrax**, **salmonella**, and **bovine tuberculosis**! They have devastating impacts when transmitted to humans.



Dr. Steele, Chicago, circa 1927

While Dr. Steele has been exposed to many diseases over his years of traveling throughout the world, the only thing he ever caught was avian influenza.



Dr. Steele at Michigan State, circa 1941

"In 1959, I came down with something I thought was malaria – but it turned out I became the first victim of avian influenza, the grandfather of all avian influenza viruses, H7N7" Steele said. "The CDC put me in the hospital and it took two years for me to come back to normal. Recently I was introduced as a 'man who seeks strange viruses and brings them back to us.'"

Photos are from the 2009 biography, *One Man, One Medicine, One Health: The James H. Steele Story* available on Amazon.com

WHAT IS A BSL?

A **BioSafety Level**, or **BSL** rating, is based on the degree of hazard associated with a **pathogen** and **what you will be doing** in a laboratory.

There are FOUR classification levels of laboratories ranging from the **least protected (BSL 1)** to the **most protected (BSL 4)**. In the United States, there are only seven labs that have a BSL4 rating!



Do you know that your school science lab could be categorized as a BSL 1 laboratory? This is the lowest safety level. People in this laboratory work with **pathogens** that are not very hazardous to them or the environment. Simple organisms such as **yeast** or **non-disease causing E. coli** are pathogens for BSL 1 labs. No special containment is necessary, so all work can be done on a lab table surface, but good lab safety practices are required. You already know one good laboratory practice: wash your hands when you're finished!

BSL 1

What other safety practices do you follow when doing science experiments?



PHOTO CREDIT: CDC/ Hsi Liu, PhD, MBA, James Gathany

If you work with pathogens like the **measles virus** or **hepatitis B virus**, then you'll have to work in a BSL2 laboratory. These pathogens are moderately hazardous to lab workers and the environment. Only workers that are trained to properly handle pathogens are allowed to work here. Often the use of a **biological safety cabinet**, a specially designed work space that protects the worker and the environment from pathogens, is required when working with BSL2 infectious material.

BSL 2



PHOTO CREDIT: CDC/ James Gathany

Scientists who work in a **BSL3 lab** deal with pathogens that can cause serious or deadly diseases, like **West Nile virus** and **SARS**. Inhaling aerosols, small airborne droplets of the pathogen, is a possibility, so work is done inside a biological safety cabinet or containment device. Any air that leaves this room first goes through a **special filter** and any waste that comes from this lab must be specially treated. All lab clothes must be decontaminated before washing. Access to BSL3 labs is only for **highly trained scientists** who have first had BSL2 training.

BSL 3



PHOTO CREDIT:
CDC/James Gathany

BSL 4

Imagine a **separate secure building** with its own ventilation system, air locks, showers, and **biosuits**. If you're working with dangerous pathogens, like **Marburg virus** or **Ebola virus**, then you must work in this lab. Pathogens handled here are dangerous and incurable, and have a high risk of being transmitted through small airborne droplets. A BSL4 lab uses the same precautions as a BSL3 lab and MORE. Work is conducted in a specially designed laboratory and workers wear air-supplied **biosuits**. People have to change out of their street clothes before entering the lab and must take a shower upon leaving. A BSL4 lab is so airtight and secure that it is referred to as "a submarine within a bank vault."

All biosafety level activities and facilities are designed with **SAFETY** in mind - to keep the worker, the environment, and the community safe! The three things that are specific to each BSL are:

- the personal protective equipment (**PPE**)
- special laboratory practices
- the laboratory facilities

Try your hand at selecting the appropriate PPE for each lab.

BIO-SAFETY LEVEL



Want to know more about what a scientist must do in order to work in a BSL4 laboratory?

Check out this web site from The University of Texas Medical Branch's Galveston National Laboratory for a great overview!

<http://www.utmb.edu/GNL/safety/BSL4Stickman.shtml>

MATCH THE PIECES OF PPE ILLUSTRATED BELOW BESIDE THE CORRECT BIOSAFETY LEVEL BY WRITING THE CORRECT NUMBER IN THE BLANK PROVIDED.

BSL-2: _____

BSL-3: _____

BSL-4: _____



ANSWERS: BSL-2: 2 5 9 BSL-3: 1 5 9 BSL-4: 4



EMERGING ZOOONOSES

A DISCOVERY-TO-CONTROL CONTINUUM CONUNDRUM!



Wow! Those are a lot of big words! Let's see if we can explain this continuum:

Emerging zoonoses are new diseases that are transmitted from animals or insects to humans. They are called "emerging" because they are diseases new to a certain area or

have never before been seen. This was the case with West Nile virus when it was first seen in New York City in 1999. West Nile was a completely new disease for North America at that time. Why are there emerging zoonoses? It is because pathogens adapt to changing environments...

A **continuum** is defined as a "continuous series". When we say "**discovery-to-control continuum**," we really mean:

- **recognizing** a new disease in a new setting
- **discovering** what the disease is
- figuring out **how to treat** the disease and contain it
- **preventing** the disease from occurring again
- **managing** the disease so that few people get it

There can be a lot of steps in the discovery-to-control continuum, and many different people who contribute their expertise. Let's take a quick tour of the **discovery** part of the continuum. The best way to think about this part is to ask yourself:

"What is going on here?"



1. People are sick
DOCTOR

Local clinicians and pathologists see sick people.



2. Animals are sick
VETERINARIAN

Veterinarians and farmers see sick animals.

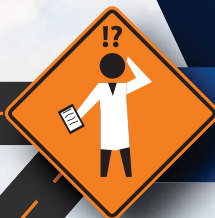
Basic research is needed to determine if this is an emerging zoonosis.

5. RESEARCH



Disease outbreaks may not always be obvious, especially when they first begin.

Epidemiologists figure out if a true outbreak or epidemic is occurring by collecting and analyzing data.



3. "Is this an outbreak!?"
EPIDEMIOLOGIST



4. What is the cause (pathogen) and how is it transmitted?
MICROBIOLOGIST

A series of tests in laboratories can help to identify the specific pathogen that is the cause. Microbiologists play a big part in this.

cell culture

serology

electron microscopy

sequencing

microbiology

These are the tools microbiologists use to figure out what pathogen is making people sick.





Aedes albopictus
Asian tiger mosquito

PHOTO CREDIT: Stephen Higgs, PhD, FRES
The University of Texas Medical Branch at Galveston



Aedes aegypti

PHOTO CREDIT: CDC/ Prof. Frank Hadley Collins,
Dir., Cntr. for Global Health and Infectious Diseases, Univ. of Notre Dame

Little known virus reveals mutation strategy for world fame

Chikungunya (Chick-kun-goon-ya) virus has taken up with a new **vector**, the Asian tiger mosquito. ***Aedes aegypti*** (Aye-dees uh-gyp-tie), Chikungunya's long-time partner, felt betrayed when she first heard about the **other** mosquito, ***Aedes albopictus*** (Aye-dees al-bow-pick-tus), also known as the Asian tiger mosquito.

According to reliable sources, "We never thought Chikungunya was a good match for the Asian tiger mosquito, but it seems that the virus is cleverly changing so as to be equally appealing to her. This new strategy has us worried."

As one scientist reported, "It seems that the **chikungunya virus has mutated its genetic material in a way that allowed it to better replicate in the Asian tiger mosquito.**" Does this mean Chikungunya is beginning its drive for global emergence?

Will Chikungunya be able to make itself a household name? Only time will tell.

I want to tell my side of the story. It seems that other viruses are getting all the attention, but I have the most interesting name—Chikungunya. And NO, I have nothing to do with chickens. My African name means "that which bends up," since people I infect have to bend over when they walk because I make their joints hurt so badly. I've also been known to give people fatigue, headache, nausea, vomiting, muscle pain, and rash, so you see I have a lot to offer.

While it is true that I have long been associated with *Aedes aegypti*, there is no huge loyalty there. I've got my own plans for achieving fame and that involves me getting out of the tropics and spreading my name. Right now I have my eye set on Europe, particularly Italy. *Aedes albopictus* just happens to share the same interest as me. In fact, she began spreading her name across the globe years ago! At first we weren't a great match, but I was willing to make some changes and now we're perfect for each other and ready to travel the world together.

As for remaining loyal to *Aedes albopictus*... we'll have to see. There are plenty of mosquitoes out there. Some may not be a perfect fit, but that hasn't stopped me yet.

Kiss of Death: Disease Discovery to Disease Control

from the *T. infestans* Point of View

Greetings, I am ***Triatoma infestans*** (also known as the kissing bug or assassin bug). Before 1909, life in Latin America was good for me. In countries like Bolivia, Argentina, Uruguay, Paraguay, Chile, Brazil and Peru, I pretty much had my way. I could hide during the day and come out at night to feed on the blood of animals or people. I tended to bite people near the eyes or lips while they slept.

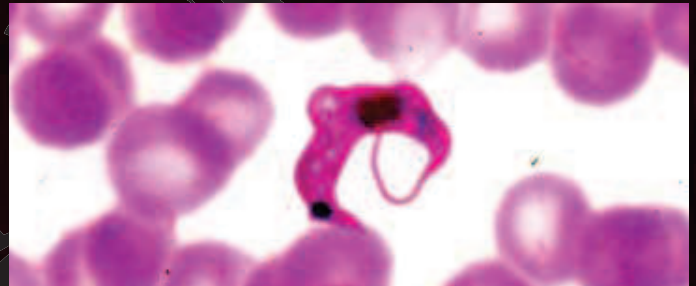


PHOTO CREDIT: CDC/Dr. Mae Melvin

The real culprit

I have a little surprise—a parasite (a **protozoan**) lives in me! When I suck blood from my victims, sometimes the victims are infected with the parasite because the parasite comes along for the ride in the blood. If I bite a person, I also leave feces behind, and the parasite can also hide there. When a person awakes and scratches the bite, they often spread the parasite to open cuts or places where the parasite could enter their bloodstream. So you see, I really don't cause any disease. I am just the vector.

Take a look at my traveling companion, ***T. cruzi***

The whole enchilada

Now this Dr. Chagas was one sharp dude. Most people would have been satisfied to make this discovery and call it quits, but not Chagas. He had to go and do something really remarkable. He published his research that described not only me (the vector) and cycle of the protozoan, ***T. cruzi*** (the parasite) in the digestive tract, but he went on to describe the clinical signs in humans and animals, and the animals that served as reservoirs for the disease. This pretty much spelled the end of the mystery about this disease. Again, the scientist gets naming rights—so **Chagas' disease** it is.

Armed with all these new revelations, it seems like everyone has been after me and my parasite companion ever since. Now people spray their homes and sleep under bed nets. The disease control strategy is to give me, ***T. infestans***, the kiss of death by eliminating me—the vector!

My cover is blown

In 1909, along came a young Brazilian doctor, named **Carlos Chagas (SHA-gus)**. He was assigned the task of controlling a malaria epidemic that had brought the building of a railroad in a rural region in Brazil to a halt. One night, the lead engineer in charge of constructing the railroad introduced him to me and some of my assassin bug friends.

Being the sharp scientist that he was, Dr. Chagas quickly discovered our parasite companion. He named the parasite **Trypanosoma (tri-PAN-oh-so-mah) cruzi (KRU-see)** or ***T. cruzi*** for short. **Dr. Oswaldo Cruz** was Dr. Chagas' mentor so ***T. cruzi*** was his name choice. (As a scientist, whoever makes a discovery pretty much gives them naming rights.)

Controlled but not out of the game

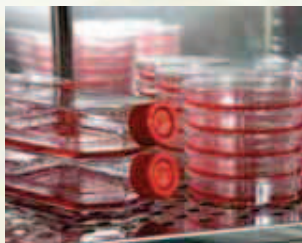
I am intrigued to see that **Chagas' disease** is not totally eliminated. With world travel of people and vectors now so easy—who knows, maybe I can get some new found fame. Never count me out!



PHOTO CREDIT: CDC/World Health Organization

CELL CULTURE

How do we grow cells in a laboratory?



Did you know it was possible to grow cells outside the body? In fact, this process called **cell culture** plays an important role in helping scientists identify specific diseases and

create vaccines. By using special dishes or flasks, and then storing the cells in an **incubator**, we can provide the right temperature and gas environment for cells to grow.

A special liquid called **media** is added to the containers, and it supplies all the nutrients the cells need. To prevent unwanted contaminants from getting into cells in culture, they are grown and handled in a **sterile environment**. This sterile environment is created with the help of a special enclosed workspace called a **biological safety cabinet**.

WHY CULTURE CELLS OUTSIDE THE BODY?

Viruses, and even some bacteria, can only grow and reproduce inside a living cell. Growing cells in the lab gives scientists a fast and easy way to grow a lot of the virus they are interested in studying. Before the discovery that cells could be grown in culture, scientists had to rely on chicken eggs and lab animals to isolate viruses.



To grow viruses in cells, the scientist adds some of the virus to the **media**. This allows the virus to come into contact with the cells so they can force their way inside and turn the cell into a **virus-making factory**! Another way scientists use cell culture is to make vaccines. **Vaccines** for many diseases, including polio, rubella, hepatitis A, and chickenpox, are made in cell culture.

HELa CELLS AND THE IMMORTAL HENRIETTA LACKS

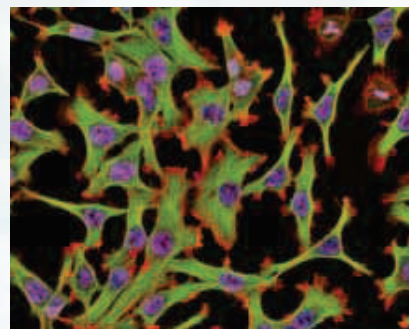
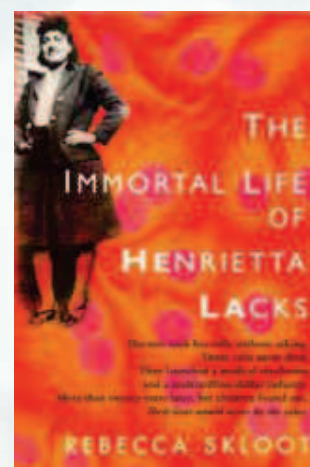


Photo of HeLa cells courtesy of Thomas Deerinck.

HeLa cells are a **cell line** that is commonly grown in laboratories. It all began in the 1951 when a 31 year-old mother of five, named **Henrietta Lacks**, was diagnosed with cervical cancer. Unfortunately she lost her battle with cancer, but before she died, scientists removed some of her cancer cells and began growing them in the laboratory. What they saw were cells that grew like none they had never seen before! This was because her cancer cells grew uncontrollably and never stopped dividing, unlike healthy cells. The scientist who grew the cells named them “HeLa”, short for **Henrietta Lacks**. The vast majority of biological research laboratories in the world have used these cells to grow many types of viruses. HeLa cells also played an important role in the development of the polio vaccine.

You might find it interesting to read about this important science discovery. This book raises some very interesting ethical dilemmas and tells a fascinating story about the contribution Henrietta Lacks made to medical science.



Courtesy of The Crown Publishing Group, a division of Random House, Inc.

Scientific Method:

A way of thinking



Mendel

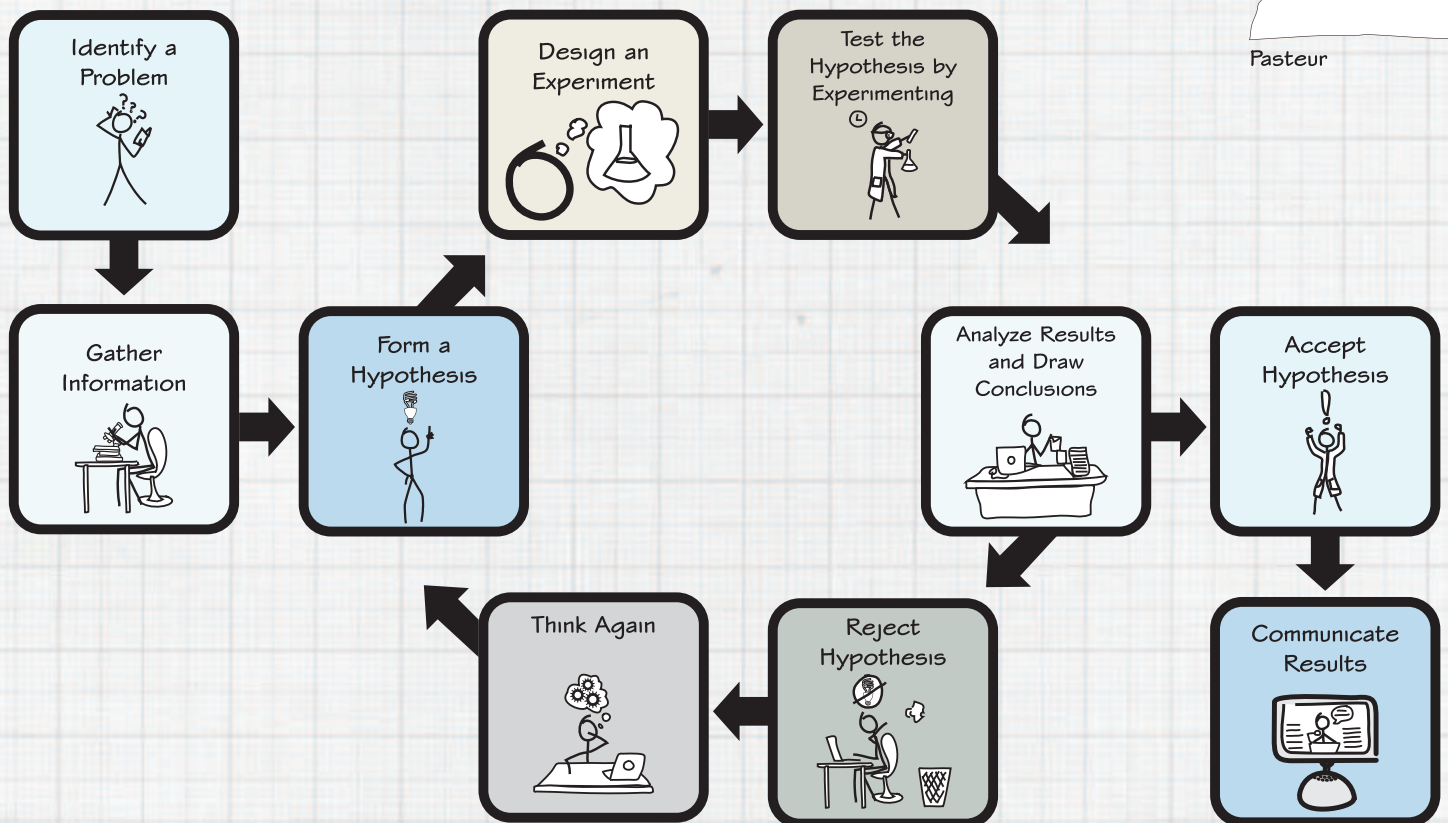
Science is not only facts, but it is a **way of thinking**. Although this method does not fit every situation, the diagram indicates a common process in science. If you have ever done a science fair project, you probably used these steps.

Gregor Mendel and **Louis Pasteur** are good examples of people who used the scientific method to solve problems. Are you familiar with their experiments? It would be fun to look them up.



Pasteur

Meanwhile, try your hand at applying this method to an everyday question. Maybe something as simple as, "Which types of exercise increases heart rates the most?"



What might be a good hypothesis to begin your investigation?

What is the dependent variable?

What are independent variables that you will investigate?

How would you set up an experiment to prove your hypothesis?

DO YOU THINK LIKE A SCIENTIST?

1. If you went to bed at 8:00 at night and set your wind up alarm to get up at 9:00 in the morning, how many hours sleep would this permit you to have?
2. Why can't a man living in Winston-Salem be buried west of the Mississippi?
3. If you had only one match and entered a room in which there was a kerosene lamp, an oil heater, and a wood-burning stove, which would you light first?
4. Some months have 30 days; some have 31; how many have 28?
5. If a doctor gave you three pills and told you to take one every half-hour, how long would they last?
6. I have in my hand two U.S. coins which total 55 cents in value—one is not a nickel. Please bear that in mind. What are the coins?
7. A farmer had 17 sheep—all but nine died. How many did he have left?
8. Divide 30 by $\frac{1}{2}$ and add 10. What is the answer?
9. An archeologist claims he found some gold coins dated 46 B.C. Do you think he did?
10. You have four nines (9,9,9,9). Arrange them to total 100. Each nine must be used once and only once.



ANSWERS

1. One hour. Wind up alarms cannot tell the difference between AM and PM.
2. Because he's living.
3. The match.
4. All of them.
5. One hour! At time 0, take a pill; at 30 minutes, take a pill; and at 60 minutes, take a pill.
6. 50 cent piece and a nickel. One is not a nickel, the other is.
7. Nine.
8. $30 / \frac{1}{2} = 60$; $60 + 10 = 70$.
9. No. Can't date something B.C. when you didn't know when B.C. was going to be.
10. $9/9 + 9/9$.