Malaria: Researching New Solutions

Secrets of the Sequence Video Series on the Life Sciences • Grades 9 — 12

Teaching materials developed by **VCU** Life Sciences

Virginia Commonwealth University

For Classroom Trial Testing

Video Description

"Secrets of the Sequence," Show 108, Episode 1
"Malaria" – approximately 8 minutes viewing time

It is one of the world's deadliest and least understood diseases. But researchers are using fruit flies as surrogate mosquitoes to analyze this tiny, tropical parasite. By breaking it down genetically, their work could lead to better anti-malarial drugs and vaccines and, potentially, to malaria-resistant mosquitoes.

Ward Television
Producer: Elizabeth Pearson
Associate Producer: Julie James
Featuring: Joe DeRisi, Biochemistry and Biophysics, University of California-San Francisco and David Schneider, Microbiology and Immunology, Stanford University
Lesson Author; Reviewers: Susan Walton; Catherine Dahl

National and State Science Standards of Learning

National Science Education Standards Connection

Content Standard A: Science as Inquiry

As a result of activities in grades 9-12, all students should develop:

- abilities necessary to do scientific inquiry.
- understandings about scientific inquiry.

Content Standard C: Life Science

As a result of their activities in grades 9-12, all students should develop an understanding of:

- molecular basis of heredity.

Content Standard F: Science in Personal and Social Perspectives

As a result of their activities in grades 9-12, all students should develop an understanding of:

- science and technology in local, national and global challenges.

Content Standard G: History and the Nature of Science

As a result of their activities in grades 9-12, all students should develop an understanding of Science as a human endeavor

Selected State Science Standards Connection

Use http://www.eduhound.com (click on "Standards by State") or a search engine to access additional state science standards.

Texas

Biology (4) Science concepts

The student knows that cells are the basic structures of all living things and have specialized parts that perform specific functions, and that viruses are different from cells and have different properties and functions. The student is expected to:

- identify the parts of prokaryotic and eukaryotic cells

Biology (6) Science concepts

The student knows the structures and functions of nucleic acids in the mechanisms of genetics. The student is expected to:

(A) describe components of deoxyribonucleic acid (DNA), and illustrate how information for specifying the traits of an organism is carried in the DNA

Virginia

BIO.1 The student will plan and conduct investigations in which

a) observations of living organisms are recorded in the lab and in the field;
b) hypotheses are formulated based on direct observations and information from scientific literature;
c) variables are defined and investigations are designed to test hypotheses.

BIO.6 The students will investigate and understand common mechanisms of inheritance and protein synthesis key concepts include:

f) the structure, function, and replication of nucleic acids (DNA and RNA);
h) use, limitations and misuse of genetic information;
i) exploration of the impact of DNA technologies.

Overview

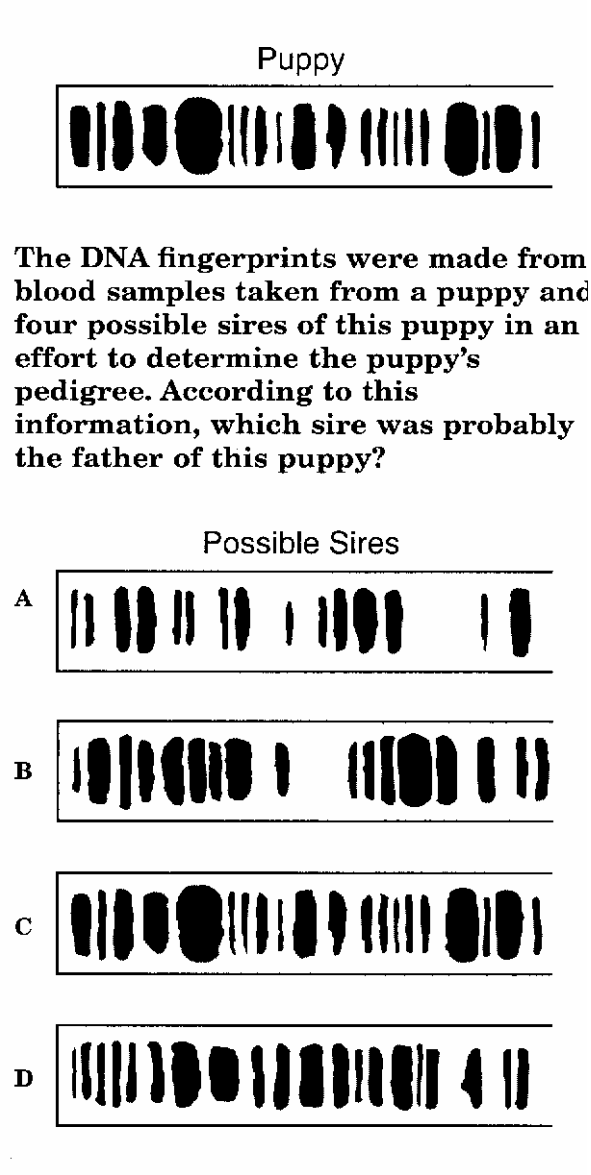
Malaria is a disease that most people think of as a thing of the past. When the media reports on mosquito-borne illnesses in the United States, we hear about West Nile Virus, not malaria. Yet, in many underdeveloped tropical countries malaria is on the rise, with 400 million cases worldwide reported annually that result in deaths. Many of these victims are children.

Why is malaria so hard to eradicate? One reason is the complicated life cycle of this parasite. Malaria can be caused by four microorganisms, with most victims being infected by *Plasmodium falciparum.* The mosquito is the vector, or agent of spread, for *Plasmodium.* Oocysts give rise to cells called sporozoites in the intestinal tract of the female mosquito. These cells migrate to the salivary glands. When the mosquito bites someone, the sporozoites are transmitted to the individual's blood and travel to the liver. In the liver they multiply and develop into the next state, the merozoites. The infected liver cells burst and the merozoites go into the bloodstream where they enter red blood cells and feed on the hemoglobin. In the blood cells the sexual gametocytes and asexual trophozoites are produced. Rupturing blood cells release the parasites to infect other cells. The parasites may be picked up by a biting female mosquito, after which the gametocytes will begin another generation in the mosquito's gut.

The word malaria is from the Italian for "bad air" because early scientists thought the disease was caused by swamp gases. *Plasmodium falciparum* was first observed in human blood in 1880 by Alphonse Laveran and named in 1887 by a British scientist. In 1897 a British doctor, Ronald Ross, established that the disease was transmitted by the female mosquito.

Quinine and later chloroquine were used to treat the disease. Using these drugs and the insecticide DDT, an effective war was waged against malaria in the 1930's and 40's. Unfortunately, chloroquine resistant strains of the parasite and DDT resistant strains of mosquitoes emerged in the 1960's. New drugs have been developed, but even newer drugs must be sought to keep pace with the growth of resistance by the parasite. It is hoped that study of the genomes of the parasite and mosquito will lead to effective control.

Testing: A sample multiple choice item from State Standardized Exams



Virginia Standards of Learning, Spring 2002 Released Test

Before Viewing

1. Ask students the following questions:
- What is malaria?
  Response: A disease caused by a microorganism and spread by mosquitoes.

- Is malaria still a problem in the world?

- Why isn't malaria a problem in the U.S?
  Response: It is mainly a tropical disease and the U.S. has excellent mosquito control.

2. Review the mosquito life cycle. A good animation is available at http://www.nature.com/nsu/malaria/malara_movie.swf.

3. Draw on the board or give students a copy of a flowchart or sequence chart for students to record and analyze the steps Dr. DeRisi used in his research design. (Flowcharts and sequence charts are available at http://www.eduplace.com/graphicorganizer/.) Ask students to identify the various steps and elements of Dr. DeRisi's research as they watch the video.

During Viewing

1. Start the video.

2. Pause as necessary to allow students to record the various steps to Dr. DeRisi's research. A good place to pause and summarize is after Dr. DeRisi says, "… and then ask the question, are they now more sensitive to the drug?" (5 minutes into the video). For a list of these steps, see the "After Viewing" section.

3. Resume the video and play to the end.

After Viewing

1. List and discuss the various aspects of Dr. DeRisi's research. Students will have some or all of the following:
   - Dr. DeRisi selected the problem of the role that various genes play in drug resistance by malaria parasites.

   - Studies the sequence of bases for the parasites.

   - Builds machines to test DNA in microarrays (these are the slides).

   - Determines which genes are on or off by adding samples colored with fluorescent molecules.

   - Finds out what the genes do by altering their environment and sees which genes respond by observing which ones change color.

   - Knocks out a gene to see if this makes the parasites more sensitive to drugs.

- Grows malaria in his own blood (an early step, but he doesn't discuss this until the end of his discussion)

2. Dr. DeRisi has developed lab protocols that could be patented and perhaps sold for millions of dollars. Yet, he offers this information for free on his lab's Web site. "There was a huge potential to make a lot of money. I was totally against that. Our whole deal was to make the technology more accessible, to level the playing field." (Dr. Joe DeRisi, "Populist Science" at http://mednews.stanford.edu/stanmed/2002summer/md-populist.html) Debate the pros and cons of his decision. Ask: Would you offer the protocols to the world at no cost? Or sell them?

3. Conduct the Student Activity, The Effect of Temperature on the Rate of Mosquito Larvae Development.

Teacher Notes for the Student Activity: The Effect of Temperature on the Rate of Mosquito Pupae Development

Students will conduct a controlled experiment to test the effect of an environmental factor – temperature – on the rate at which mosquito pupae develop.

Time

- 45 minutes to initially set up experiment
- A few minutes of observation daily over the two weeks needed for pupae metamorphosis.
- 45 minutes to discuss the completed experiment

Materials

- 30 mosquito pupae per group (available from Carolina Biological or other biological supply houses)
- 3 clear containers of the same size and dimensions, approximately 500 mlcheesecloth to cover the containers
- 3 rubber bands to secure the cheesecloth
- distilled water
- thermometers

Procedure

1. Develop a hypothesis with the class. The hypothesis should focus on the development of mosquito pupae into adults at various temperatures. Discuss possible designs for the experiment.
2. Identify locations in the classroom that are cooler or warmer than is typical in most of the room. These locations might include places nearer or further away from a heat source. Place each container in a location that provides the temperature conditions needed for that trial. Keep other conditions, such as light, as constant as possible.
3. Each day, have students record the number of pupae that have metamorphosed into adults.
4. At end of the study, destroy adult mosquitoes and any remaining pupae.

Student Handout: The Effect of Temperature on the Rate of Mosquito Larvae Development

In this activity you will conduct an experiment to determine the effect of environmental temperature on the rate at which mosquito pupae develop.

Materials

- 30 mosquito pupae
- 3 clear containers of the same size and dimensions, approximately 500 ml cheesecloth to cover the containers
- 3 rubber bands to secure the cheesecloth
- distilled water
- thermometers

Procedure

1. Develop a hypothesis and an experimental design with the class. The hypothesis should predict the effect of differences in temperature on the number of mosquitoes that develop. Complete the attached record sheet.
2. Label the three containers: one for cool temperature, one for room temperature, one for warm temperature.
3. Fill each container half full with distilled water.
4. Place ten mosquito pupae in each container.
5. Place each container in a location that provides the appropriate temperature conditions for that trial. Keep other conditions, such as amount of light, as constant as possible.
6. Each day record the number of pupae that have metamorphosed into adults in the table provided.
7. At the end of the study, destroy adult mosquitoes and any remaining pupae according to your teacher's instructions.

Analysis

1. To what extent did the data support your hypothesis?
2. If you were to conduct your experiment again, what would you do to improve the experiment?

Recording Sheet for the Effect of Temperature on the Rate of Mosquito Pupae Development

Independent variable _____

Levels of the independent variable _____

Dependent variable _____

Control _____

Constants _____

Hypothesis _____

Data Table

Number of Adult Mosquitoes

Day/Temperature	Cooler than typical	Typical room temperature	Warmer than typical
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
11			
12			
13			
14			

Additional Resources

Mosquito Bytes
http://whyfiles.org/016skeeter/

"The Transcriptome of the Intraerythrocytic Developmental Cycle of Plasmodium falciparum"
http://www.plos.org/downloads/malaria_plosbiology.pdf

Animation of malaria life cycle
http://www.nature.com/nsu/malaria/malara_movie.swf

Malaria Journal, an online journal
http://www.malariajournal.com/start.asp

Centers for Disease Control
http://www.cdc.gov/

"Portrait of a Serial Killer" article includes historic timeline for malaria
http://www.nature.com/nsu/021001/021001-6.html#

Dr. DeRisi's Web site, includes popular links and video clips
http://derisilab.ucsf.edu/

Web site for Microarray Technology
http://www.microarrays.org/

"Microarrays: Key to Malaria Cure?"
http://www.ucsf.edu/foundation/impact/archives/2000/31_10_derisi.htm

"Mission Bay Movers and Shakers - A Man Possessed with Curing Malaria"
http://pub.ucsf.edu/today/print.php?news_id=200109182

"Populist Science"
http://mednews.stanford.edu/stanmed/2002summer/md-populist.html

Ecological aspects of genetically modified mosquitoes, various articles
http://library.wur.nl/frontis/malaria/toc.html

Graphic organizers
http://www.eduplace.com/graphicorganizer/