INTRODUCTION

Dr Paddy Brock’s research is about the transmission of malaria by mosquitoes. Malaria is a big problem in Malawi and scientists at the Malawi Liverpool Wellcome Institute (MLW) are not only carrying out research into the prevention and cure of the disease but also have a programme of outreach activities to raise public awareness about how malaria affects the body and what people can do to reduce their chances of infection. This activity is one they use with students in Malawi.

AIMS

- To understand the cyclical way in which malaria is transmitted to humans by mosquitoes
- To encourage debate about the attitude of drug companies to research into malaria

MATERIALS

This piece of the MLW outreach kit consists of a set of discs illustrating steps in the malaria cycle which students have to put in the correct order. There are 3 sets of 5 images.

The discs can be found on pages 4 – 6 of this sheet. Copies of these discs can be printed and cut out.

STARTER

Ask the following question and by show of hands record the number of votes for each animal.

“What do you think is the most deadliest animal in the world”?

A great visual resource can be found here:

https://www.gatesnotes.com/Health/Most-Lethal-Animal-Mosquito-Week
DISCUSSION

HOW SERIOUS IS MALARIA?

Malaria is a mosquito-borne infectious disease of humans and other animals caused by parasitic protozoans (a group of single-celled microorganism) belonging to the genus *Plasmodium*. Malaria causes symptoms that typically include fever, fatigue, vomiting and headaches. In severe cases it can cause yellow skin, seizures, coma or death. The disease is transmitted by bites from mosquitoes, and the symptoms usually begin ten to fifteen days after being bitten. If not appropriately treated, people may have recurrences of the disease months later. In those who have recently survived an infection, re-infection typically causes milder symptoms. This partial resistance disappears over months to years if the person has no continuing exposure to malaria.

Malaria is typically diagnosed by the microscopic examination of blood using blood films, or with antigen-based rapid diagnostic tests. Methods that use the polymerase chain reaction to detect the parasite's DNA have been developed, but are not widely used in areas where malaria is common due to their cost and complexity.

HOW IS MALARIA TRANSMITTED?

The disease is transmitted most commonly by an infected female *Anopheles* mosquito. The mosquito bite introduces the parasites from the mosquito's saliva into a person's blood. The parasites travel to the liver where they mature and reproduce. Five species of *Plasmodium* can infect and be spread by humans. Most deaths are caused by *P. falciparum* because *P. vivax*, *P. ovale*, and *P. malariae* generally cause a milder form of malaria. The species *P. knowlesi* rarely causes disease in humans.

In the life cycle of *Plasmodium*, a female *Anopheles* mosquito (the definitive host) transmits a motile infective form (called the sporozoite) to a vertebrate host such as a human (the secondary host), thus acting as a transmission vector. A sporozoite travels through the blood vessels to liver cells (hepatocytes), where it reproduces asexually (tissue schizogony), producing thousands of merozoites. These infect new red blood cells and initiate a series of asexual multiplication cycles (blood schizogony) that produce 8 to 24 new infective merozoites, at which point the cells burst and the infective cycle begins anew.

Other merozoites develop into immature gametocytes, which are the precursors of male and female gametes. When a fertilised mosquito bites an infected person, gametocytes are taken up with the blood and mature in the mosquito gut. The male and female gametocytes fuse and form an ookinete—a fertilized, motile zygote. Ookinetes develop into new sporozoites that migrate to the insect's salivary glands, ready to infect a new vertebrate host. The sporozoites are injected into the skin, in the saliva, when the mosquito takes a subsequent blood meal.

METHOD

ASK STUDENTS TO ASSEMBLE THE SETS OF DISCS IN ORDER TO GIVE A COMPLETE MALARIA CYCLE.

The discs also include the Chichewa translation of each stage, which can be used as a starting point for discussion about the problems of malaria in African countries and issues about the priority given by drug companies to research into the disease.
Only female mosquitoes feed on blood; male mosquitoes feed on plant nectar, and do not transmit the disease. The females of the *Anopheles* genus of mosquito prefer to feed at night. They usually start searching for a meal at dusk, and will continue throughout the night until taking a meal. Malaria parasites can also be transmitted by blood transfusions, although this is rare.

**WHAT CAN BE DONE TO PREVENT INFECTION?**

The risk of disease can be reduced by preventing mosquito bites by using mosquito nets and insect repellents, or with mosquito-control measures such as spraying insecticides and draining standing water. Several medications are available to prevent malaria in travellers to areas where the disease is common. Occasional doses of the medication sulfadoxine/pyrimethamine are recommended in infants and after the first trimester of pregnancy in areas with high rates of malaria. Despite a need, no effective vaccine exists, although efforts to develop one are ongoing. The recommended treatment for malaria is a combination of antimalarial medications that includes an artemisinin. The second medication may be either mefloquine, lumefantrine, or sulfadoxine/pyrimethamine. Quinine along with doxycycline may be used if an artemisinin is not available. It is recommended that in areas where the disease is common, malaria is confirmed if possible before treatment is started due to concerns of increasing drug resistance. Resistance among the parasites has developed to several antimalarial medications; for example, chloroquine-resistant *P. falciparum* has spread to most malarial areas, and resistance to artemisinin has become a problem in some parts of Southeast Asia.

**WHAT ARE THE ECONOMIC IMPLICATIONS?**

The disease is widespread in the tropical and subtropical regions that exist in a broad band around the equator. This includes much of Sub-Saharan Africa, Asia, and Latin America. Malaria is commonly associated with poverty and has a major negative effect on economic development. In Africa it is estimated to result in losses of US $12 billion a year due to increased healthcare costs, lost ability to work, and effects on tourism. The World Health Organization reports there were 198 million cases of malaria worldwide in 2013. This resulted in an estimated 584,000 to 855,000 deaths, the majority (90%) of which occurred in Africa.
The mosquito ingests the gametocytes.

Gametocytes emerge from the blood cells and develop into gametes.

Male and female gametes fuse to become a zygote.

Zygotes develop into ookinetes.

Oocysts grow and rupture releasing sporozoites.

Sporozoites are injected into the blood stream.

They move through the stomach wall and develop into oocytes.

They migrate to the salivary glands.

Horn amanualaka makoza m'akazi amakumana mndi kunanuka zyugulwe.
Sporozoites are injected into the blood stream.

Sporozoites are carried to the liver infecting the liver cells.

The infected cells swell and rupture, releasing merozoites.

Merozoites are released into the blood stream infecting red blood cells.

The red blood cells swell with parasites and rupture.

Merozoites infect the liver cells

At this stage, some parasites change into male and female forms called gametocytes.

The mosquito ingests the gametocytes.
Standing water is a breeding ground for mosquitoes.

Eggs are laid onto the surface of the water.

Larvae hatch within 48 hours and live in the water.

After around 10 days they turn into pupa.

After 2 days they emerge as fully formed adults.
EXTENSION QUESTIONS

THESE CAN BE USED WITHIN THE SESSION TO STIMULATE DEBATE OR FOR HOMEWORK/INDEPENDENT STUDY TASKS.

- Why do you think that an effective vaccine for malaria has been so hard to develop?
- Genetic resistance to malaria drugs is spreading through malaria parasite populations worldwide – how do you think we might tackle this problem?
- How are changes in land use linked to disease outbreaks?
- Many dangerous infections in humans, like Plasmodium knowlesi, Ebola and Zika virus, come from animals – how do you think we can limit future infections that spillover from animals to human?

OTHER RESOURCES

SPECIFIC LINKS TO THE RESEARCH BEHIND AFTERGLOW CAN BE FOUND HERE:

http://www.voanews.com/content/malaysian-deforestation-driving-spike-malaria-strain/3124811.html
http://www.lshtm.ac.uk/newsevents/news/2015/deforestation_malaria_link.html
http://malaria.lshtm.ac.uk/MONKEYBAR

YOU CAN FIND OUT MORE ABOUT THE MLW MALARIA RESEARCH PROGRAMME AT:


OXITEC IS AN OXFORDSHIRE BIOTECH COMPANY THAT HAS DEVELOPED WAYS TO CONTROL INSECTS LIKE MOSQUITOES THAT SPREAD DISEASE AND DAMAGE CROPS THAT ARE SUSTAINABLE, ENVIRONMENTALLY FRIENDLY AND COST EFFECTIVE.

AS PART OF A PRESENTATION AT A ROYAL SOCIETY SUMMER EXHIBITION THEY PRODUCED AN ONLINE SIMULATION OF ONE SUCH METHOD BASED ON RELEASING GENETICALLY MODIFIED INSECTS:

http://sse.royalsociety.org/2012/exhibits/insect-control/
http://sse.royalsociety.org/2012/media/46644/mosquitoes2.swf

THE WELLCOME TRUST SANGER INSTITUTE IN CAMBRIDGE HAVE ALSO PRODUCED SOME EXCELLENT DOWNLOADABLE RESOURCES:

http://www.yourgenome.org/interactives/malaria-challenge

THE GATES FOUNDATION HAS A HUGE SELECTION OF EXCELLENT RESOURCES ON MALARIA SUCH AS:

SYLLABUS LINKS FOR PATHOGENS IN A-LEVEL BIOLOGY

**EDEXCEL SALTERS NUFFIELD**
Topic 8
Immunity Infection and Forensics

**EDEXCEL B**
Topic 6
Microbiology and Pathogens

**OCR B ADVANCING BIOLOGY**
Module 3
Cell division, development and disease control

**WJEC**
Component 3 option
Immunology and disease