malaria?

invades liver cells. Here the parasites multiply, then spill out into the bloodstream to cause illness.

The malaria problem is getting worse because the mosquitoes that transmit malaria are becoming resistant to insecticides, and the parasites are also increasingly resistant to anti-malarial drugs.

VACCINE SCIENCE

People naturally acquire immunity to an infection when they contract the illness and develop an immune response to it. The immune system can then fight off the same disease if it encounters it again. Vaccination mimics this process — the vaccine stimulates the immune system to generate a protective response against that pathogen if the individual is re-exposed to it.

The immune system responds to chemicals called **antigens** found in the disease-causing organism. A vaccine contains antigens from a specific disease-causing organism. It may contain whole pathogens which have been killed, weakened or inactivated, or fragments of the pathogen.

The malaria parasite can be weakened using radiation, but it is impractical to do this on a large scale because producing the parasites requires complicated rearing of mosquitoes. Another method for making a malaria vaccine is required.

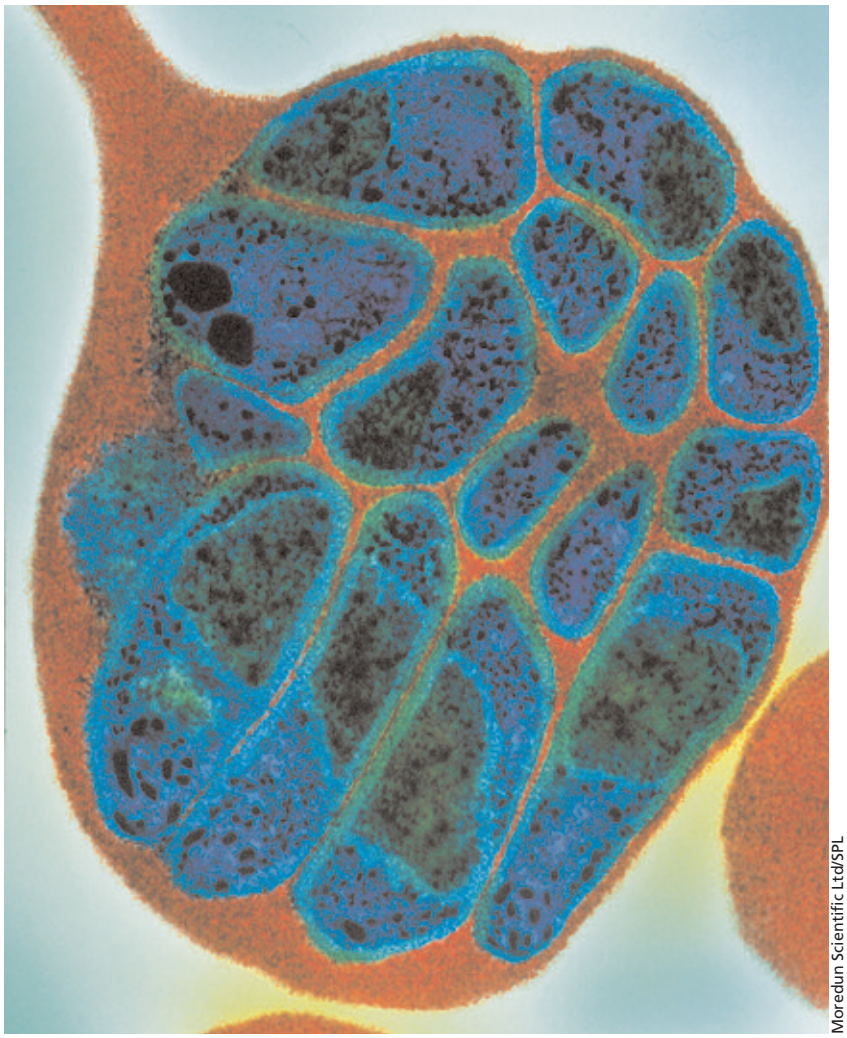
The immune system responds to pathogens in several different ways. Traditionally vaccines have been designed to provoke white blood cells called **B-lymphocytes** to make **antibodies**. These tag onto invading pathogens in body fluids, marking them for destruction by white blood cells and making it difficult for them to cause disease. However, because the malaria parasite spends a lot of its life cycle hiding inside human liver cells, antibodies alone may not be protective against malaria.

More recent approaches aim to use a different group of white cells called **T-lymphocytes** (T-cells). These normally monitor the surfaces of cells in the body and can detect cells that have foreign surface antigens — such as virus-infected cells and cancerous cells — as well as those infected with malaria parasites. The T-cells then kill them directly or help the immune response to remove the cells from the body.

VACCINES AGAINST MALARIA

The Malaria Vaccine Group at Oxford University has been working on a vaccine against malaria for 15 years. Led by Professor Adrian Hill, our group aims to design vaccines that will induce potent T-cell responses against the liver stage of malaria infection. These T-cells recognise malaria antigens on the surface of infected liver cells and destroy them, so preventing both infection in the blood and transmission to new people.

We are currently developing three different types of vaccine. The first is based on **DNA**. It uses a small loop of DNA called a **plasmid**, which contains genes for malaria antigens. Plasmids, which were first described in bacteria, are used in genetic engineering to transfer genes into new cells. They are able to get human cells to translate genes into



Moredun Scientific Ltd/SPL

Coloured electron micrograph of a human red blood cell infected with malaria parasites (blue) which have made this part of the cell swell.

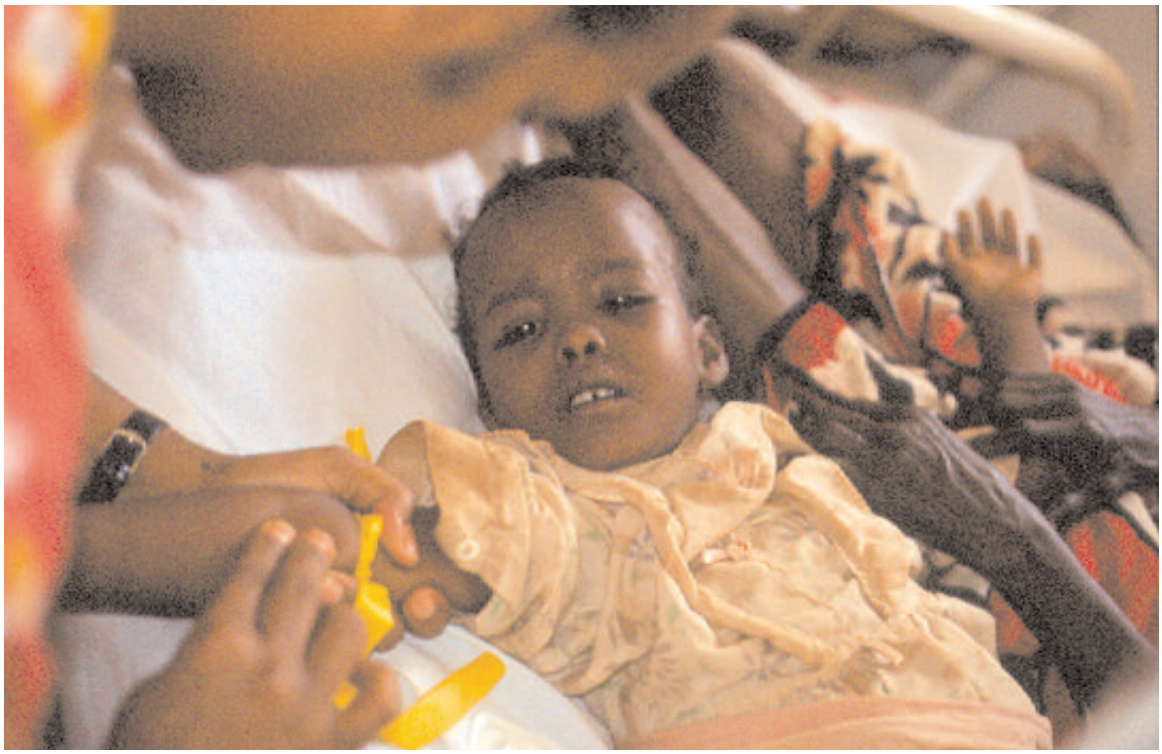
Table 1 *Some diseases which still have no effective vaccine*

Disease	Estimated annual deaths	Estimated annual cases
Malaria	1 086 000	300–500 million
Schistosomiasis	14 000	not available
Worm infestation	16 000	not available
Diarrhoea	2 213 000	~ 4100 million
Respiratory disease	4 039 000	~ 362 million
HIV/AIDS	2 673 000	~ 2 million

Source: *World Health Report 2000*, World Health Organization.

Sir Ronald Ross, a doctor in the Indian Medical Service, found malaria parasites inside mosquitoes, showing their role in the spread of the disease.

***Right:** A child in Somalia suffering from malaria.*



Crispin Hughes/Panos Pictures

Every 30 seconds a child somewhere in the world dies of malaria.

antigens because the plasmid also contains a signal to make products from the added DNA.

The other two vaccines contain weakened viruses that have been **genetically modified**. MVA (modified vaccinia virus ankara) and FP9 (fowlpox strain 9) viruses are harmless to humans but carry the same malaria antigen as the DNA vaccine. The viruses infect cells, which then produce malaria antigens on their surfaces. T-cells become sensitised to these malaria antigens and attack cells carrying them — including any liver cells infected by the parasite.

There are nearly 2000 cases a year of people returning to Britain from abroad with malaria.

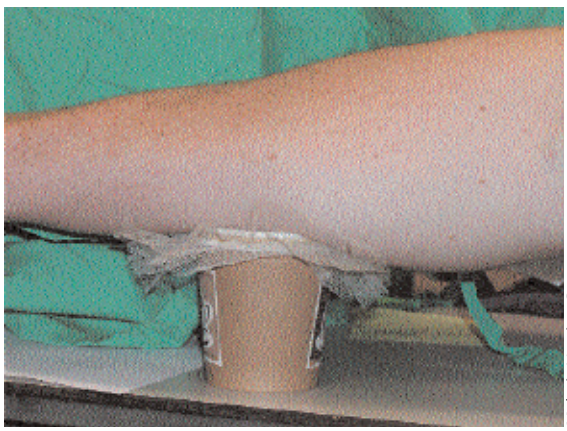
PRIME-BOOST VACCINATION

Mosquitoes spread not only malaria but also yellow fever and elephantiasis.

Each of these vaccines produces a weak immune response, but if they are given one after the other the immune response is much stronger and can protect against parasite infection. The theory is that one vaccine **primes** the immune system and the second vaccine **boosts** this response. The DNA and FP9 vaccines are good at priming the immune system and the MVA vaccine is excellent at boosting the response.

This discovery is significant for both human and veterinary medicine. It may be possible to develop vaccines of this new prime-boost type to prevent or treat diseases such as HIV, tuberculosis and viral hepatitis, and some cancers.

***Right:** A human volunteer being bitten by mosquitoes in the Oxford vaccine trials.*



Malaria Vaccine Group

HUMAN CLINICAL TRIALS

The Malaria Vaccine Group has conducted human clinical trials using various combinations of the DNA, MVA and FP9 vaccines. Trials are first carried out in the UK and, if the vaccines are safe and produce significant immune responses, small-scale studies are done in The Gambia in west Africa (where malaria is a major problem), before going on to large-scale field trials. Many different doses and strategies have now been tested in Oxford. The response to vaccination is measured by counting T-cell responses in the volunteers' blood. We are also researching the molecular mechanisms of how these vaccines function.

Vaccines are the only way to totally eradicate infectious diseases.

INFECTING VOLUNTEERS WITH MALARIA

It is important to see if a vaccinated person is protected against malaria. We infect volunteers using a safe, well-established procedure with a strain of malaria that can be treated by drugs. Each volunteer is bitten by five infected mosquitoes and we make sure that the mosquitoes have fed (they become swollen with blood). The volunteers then have blood

WEBSITES

The website of our Malaria Vaccine Group in Oxford
http://www.malaria-vaccines.org.uk

The website of the Malaria Vaccine Initiative, in Maryland, USA **http://www.malariavaccines.org**

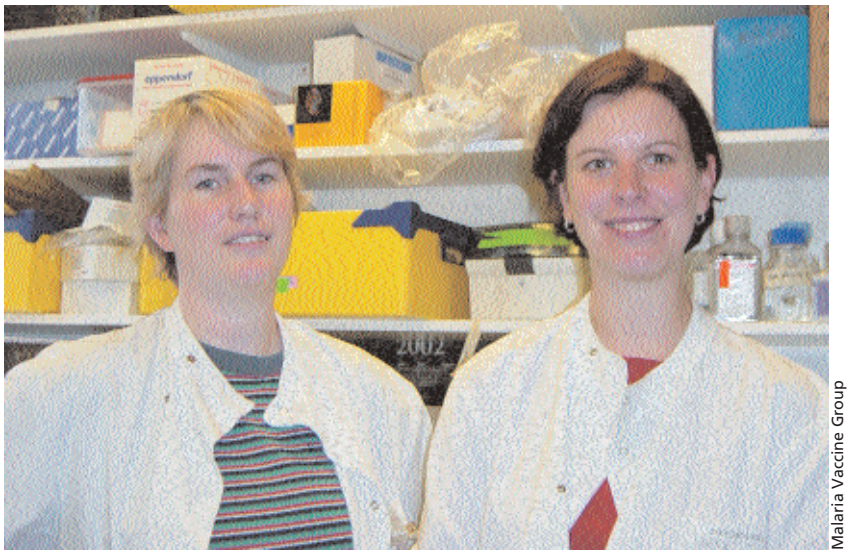
The World Health Organization website
http://www.who.int/en

The Wellcome Trust's malaria website
http://www.wellcome.ac.uk/malaria

samples taken twice daily and these are examined for the presence of malaria parasites. If a single parasite is seen the volunteer is immediately treated with chloroquine, a drug which kills the parasites. This type of malaria (*Plasmodium falciparum*) cannot recur after successful treatment, so the individual is cured.

RESULTS OF CLINICAL TRIALS

The trials have shown that vaccinated volunteers have significant immune responses in their blood and, more excitingly, some are completely protected against malaria. Large-scale field studies involving hundreds of people are currently underway in The Gambia. We hope that this scientific research will eventually enable malaria in Africa to be controlled.



Malaria Vaccine Group

Susanna Dunachie (right) and Anne Moore of the Malaria Vaccine Group.

Susanna Dunachie *is a medical doctor running the vaccine and challenge trials in healthy volunteers in Oxford.* ***Anne Moore*** *is a senior immunologist researching the immune mechanisms that make the vaccines work.*

The work of the Malaria Vaccine Group is funded by the Wellcome Trust and the Malaria Vaccine Initiative.

Shake that LED!

TRY this

Here's how to light up an LED (light emitting diode) without a battery, using your own wrist-power.

You will need:

- an LED — low-current ones are best;
- copper wire — about 50 m of thin, enamelled wire;
- a small, powerful magnet;
- an empty plastic 35 mm film container.

(If you have trouble finding any of these, ask your science teacher.)

WHAT TO DO

Wind a coil of wire around the film container. Keep the starting end of the wire free. (It helps if you fit the container with cardboard rings to contain the coil — see Figure 1.)

Scrape the insulation from the ends of the wire and solder on the LED.

Put the magnet in the container, put on the lid and shake it about.

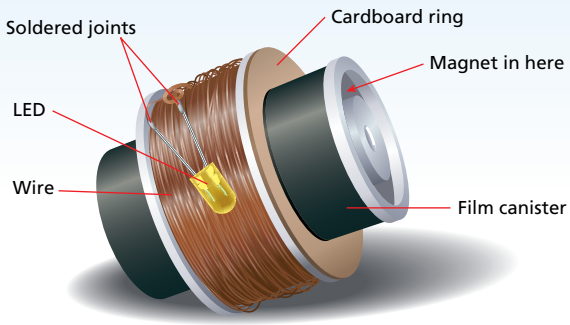


Figure 1
The end result.

HOW IT WORKS

You are generating an electric current by moving a magnet in a coil, just like in a bicycle dynamo. An induced current flows in the wire. When it flows in the right direction, it lights the LED.

Look out for an LED which lights up red or green, depending on the direction of the current. How do you think this will behave?

David Sang writes textbooks and is an editor of CATALYST.

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http://www.creative-science.org.uk