Overview of the activity

Students use the Malaria Challenge resource to research one of five different stages of the malaria lifecycle. Working in groups, they will identify different intervention methods that are used to target their chosen stage and discuss the pros and cons of these methods, considering their efficiency and cost. Once familiar with their chosen stage and its related interventions, students from each group form a new “expert group”. Here each student discusses their thoughts on their stage of the malaria lifecycle and then, as a group of “experts”, discuss what are the best strategies or intervention methods that could eradicate malaria. Each group feeds back their thoughts and finds out if their conclusions are the same as professional malaria researchers.

Estimated duration: 60-90 minutes
If class time is limited, students can be allocated to their groups before the lesson and prepare for the activity as a homework task by accessing the Malaria Challenge resource online to gather information on their allocated life cycle stage.

Running the activity

To run the activity you will require:
- Malaria Challenge resource
- Lifecycle Stage cards
- Teachers notes (one per teacher/facilitator)
- Student worksheet
- Expert group worksheet (one per group)
- Introductory PowerPoint or video
- Can malaria be eradicated? video
- Group discussion guidelines

Step 1: Introduction to malaria

Using either the Malaria Challenge video or PowerPoint presentation provided in the resource, introduce the students to the topic of malaria. Both resources provide information covering the key points of:
- what malaria is
- where it is a problem
- who is affected and why.

The resource also touches on issues such as how to diagnose and treat the disease and the problem of drug resistance.

After introducing the topic, introduce the activity to the students. Explain that they are going to become experts on the different stages of the malaria lifecycle and debate the best methods to eradicate malaria.
Step 2: Group research and discussion

Divide the class into five groups of 5-6 students. If you have more than 30 students in the class, form larger discussion groups of up to 8 students. Each group will randomly select a Lifecycle Stage card.

Stage 1: Transmission to human

Stage 2: Liver stages

Stage 3: Red blood cell stages

Stage 4: Transmission to mosquito

Stage 5: Mosquito stages

All members of the group must research the particular lifecycle stage they have been allocated using the Malaria Challenge resource. They should identify the stage’s relevance in the disease lifecycle and the prevention interventions that specifically target it. One suggested method is to allocate members of the discussion group specific research tasks, e.g. student A researches bed nets, student B researches anti-malarial drugs. This will ensure everyone in the group is familiar with at least one topic area and can therefore contribute to the discussion.

Students are recommended to use the Malaria Challenge resource to find out about the disease but additional information is available from the following websites:
- http://www.nothingbutnets.net
- http://www.rollbackmalaria.org/
- http://malarianomore.org.uk/malaria#

The group must discuss the advantages and disadvantages of the prevention interventions and how effective they could be at eradicating malaria. Before beginning the discussions, you should make the students familiar with the following guidelines. These are applicable throughout the activity for both research group and expert group discussions.
- Speak for yourself and not for others.
- Allow others to finish before you speak. Listen well.
- Ask questions as well as making statements.
- Explain what you think and feel.
- Respect differences in opinion – the world would be a boring place if everyone thought the same.
- Share your life experiences and knowledge.

By the end of their research and discussions each member of the group should be clear on the issues surrounding their chosen malaria stage and its prevention interventions. They are now “experts” and should have completed a worksheet with key points from their group discussions which they will use in the next step of the activity.
The Big Debate
Teachers’ notes

Step 3: The “expert conference”

Create new groups with an “expert” from each malaria stage as shown in figure 1. These newly formed groups will put forward their key findings on their particular stage of the malaria lifecycle and discuss what prevention interventions they believe could lead to the eradication of malaria.

Before starting, the discussion the group should nominate the following roles:

- **Spokesperson(s):** the person or persons who will speak on behalf of the group during the feedback session
- **Scribe:** the person responsible for taking notes on the discussion and completing the group worksheet

As a group, all of the students should put together an argument for the three best methods or techniques to eradicate malaria which the spokesperson(s) will present to the rest of the class. Emphasise to the students that methods still in development or undergoing trials can be championed as options as these represent areas for future development and research.

Step 4: Results feedback

All groups should feed back their three chosen methods for eradicating malaria. Encourage the students to explain and discuss why they chose some methods over the others. You can prompt them with questions such as:

- What are the main advantages of choosing method A over method B?
- Are there any limitations to the method and how could they be overcome?
- Why did you prioritise those particular three?
The Big Debate
Teachers’ notes

- Of your three methods which is likely to have the biggest impact?
- Of the methods you chose which is likely to deliver results first? Were there any methods that you think were not possible or feasible?

Record the answers from all of the groups on a flipchart or whiteboard using a table similar to the one below:

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
<th>Group 5</th>
<th>Group 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eradication method 1</td>
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<tr>
<td>Eradication method 2</td>
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<tr>
<td>Eradication method 3</td>
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</tr>
</tbody>
</table>

Are their similar ideas or is every group different? If there are differences in opinions, encourage the groups to explore these differences and try to come to a consensus.

**Step 5: What the real experts think**

To wrap up the session play the video of some of the world leaders in malaria research providing their opinions on how malaria could be eradicated.

Are the students’ opinions similar or different to the researchers?

The key message from this activity is that there are number of methods which could be used and at present there is no single solution that alone can eradicate malaria on a global scale.

**Supporting information for teachers**

The following information can be used by teachers and group facilitators to encourage debate during the group discussions or the feedback sessions.

**Key definitions (World Health Organization):**

*Malaria control:* reducing the disease burden to a disease level at which it is no longer a public health problem.
Malaria elimination: interrupting local mosquito-borne malaria transmission in a defined geographical area, i.e. zero incidence of locally contracted cases (although imported cases will continue to occur). Continued prevention measures are required.

Malaria eradication: permanent reduction to zero of the worldwide incidence of malaria infection.

Why eradicate malaria?
Over 3 billion people (almost half of the world’s population) are at risk of contracting malaria. Hundreds of millions of malaria cases and over 700,000 deaths due to the disease are reported every year.

In some parts of the world the number of malaria cases is decreasing due to the use of interventions, such as anti-malarial drugs, and effective mosquito control methods, such as the use of bed nets and insecticides.

Global malaria eradication is one of ultimate goals of the Roll Back Malaria initiative launched by the World Health Organization in 1998. Plans were made for all malaria endemic countries to actively work towards the reduction of malaria morbidity and mortality and ultimately eradicate malaria. These plans involved the help of supporting nongovernmental and community-based organisations, foundations, and research and academic institutions.
Stage 1: Transmission to human

What happens during this stage?
When an infected female mosquito feeds on a human hundreds of *Plasmodium* parasites, called sporozoites, are injected into the host in the mosquito's saliva. These parasites work their way through the epithelial cells and blood vessel walls to enter the bloodstream where they can be circulated around the body.

What are the symptoms?
There are no obvious symptoms of malaria parasite infection at this stage. There is only the physical evidence of mosquito bites on the surface of the skin. The mosquito also exhibits no symptoms of infection.

What is the critical point in this stage?
The mosquito bite is the critical point in this stage. If the mosquito cannot bite the host it cannot transmit the parasite.

What are the key prevention measures?
There are several ways of preventing mosquito bites. These include
- eliminating or killing the mosquitoes
- creating a barrier between the mosquito and the host.

Intervention 1: Insecticide spraying
Insecticides are chemicals that kill insects. They can be used to kill large numbers of mosquitoes.

Indoor residual spraying (IRS) is where insecticides are sprayed on the inside walls of houses in areas where malaria is present. Indoor residual spraying is most effective against mosquito species that rest indoors. It kills the female mosquito after it feeds on a person, reducing malaria transmission to other people in the home or community.

Insecticides such as dichlorodiphenyltrichloroethane (DDT) and pyrethroids are regularly used to reduce mosquito numbers. DDT is considered the most effective insecticide but due to its toxicity to other organisms only tends to be used indoors.

Image courtesy of Bonnie Gillespie, Voices for a Malaria free future
### Advantages

DDT is one of the longer lasting insecticides remaining effective for 6-12 months. Spraying needs to be carried out up to three times per year.

Indoor residual spraying (IRS) is cheap and cost effective. It costs an average of $3.60 per person per year.

Pyrethroids can be used for crop spraying and external use to protect areas surrounding the community.

Unlike some drugs that are used to treat malaria, insecticides are not specific to one species of *Plasmodium*. Because they kill all mosquitoes, they stop transmission of all *Plasmodium* species.

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### Disadvantages

DDT is a “persistent organic pollutant”. It accumulates in the environment through food chains and in the tissues of exposed organisms, including people living in treated houses.

DDT is controversial due to its long term toxicity and impact on the environment. Is it right to expose people to toxic compounds?

Overuse of insecticides, particularly in agriculture to protect crops, can contribute to the development of insecticide resistance in mosquitoes.

Will there be concerns over the environmental impact of insecticide use?

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### Intervention 2: Mosquito bed nets

Mosquito nets provide people with a physical barrier against mosquitoes at night. The most effective type of bed nets are insecticide treated nets (ITNs) and long lasting insecticide nets (LLINs) which provide both chemical and physical barriers to mosquitoes.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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</thead>
<tbody>
<tr>
<td>Mosquito nets can be used by more than one person.</td>
<td>Mosquito nets are only effective if they are used properly. In some cases, people who were given nets did not use them, resold them or did not replace them when they became damaged.</td>
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</tbody>
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Image courtesy of P Skov Vestergaard Frandsen
The Big Debate
Teachers’ notes

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<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>Because nets prevent mosquito bites, they stop transmission of all <em>Plasmodium</em> species.</td>
<td>Insecticide resistant mosquitoes have been reported in many areas of Africa, which could impact on the effectiveness of insecticide treated and long lasting insecticide nets.</td>
<td></td>
</tr>
<tr>
<td>When used by a large proportion of the community, insecticide treated nets can lead to a significant reduction in the number of parasites within the local mosquito population. This provides protection from malaria for the whole community, even those who do not sleep under nets.</td>
<td></td>
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<tr>
<td>Nets are cheap. One year’s protection from malaria with a long lasting insecticidal net ranges from $1.38 to $1.90.</td>
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</tbody>
</table>
Stage 2: Liver Invasion

What happens during this stage?
The sporozoite travels along the bloodstream to the liver. The parasite then invades hepatocytes, a type of liver cell. This process only takes a few minutes. Once inside the liver cell, the parasite undergoes many nuclear divisions to create tens of thousands of new parasites known as merozoites. These are released into the blood from the infected liver cell several days later.

What are the symptoms?
The liver stage of the malaria cycle is asymptomatic – there are no physical symptoms of infection by the Plasmodium parasite. This is thought to be because just a few of the millions of cells in the liver are being infected and therefore the immune system is unable to detect the infection.

What is the critical point in this stage?
The invasion of the liver cell is the critical point of this stage of the lifecycle because only a few hundred parasites enter the liver. Once inside the liver the parasites go on to increase their number one hundred fold. It is easier to interrupt the life cycle or interfere with the parasites when there are fewer of them present.

What are the key prevention measures?
Methods that can kill or prevent the parasite developing in the liver are key prevention interventions for this stage. This could be achieved through the use of anti-malarial drugs or a vaccine.

Intervention 1: Primaquine
Primaquine is an anti-malarial drug that is used to treat, but not prevent, malaria. It targets Plasmodium parasites that remain in a dormant state in the liver, known as hypnozoites.

To completely remove Plasmodium parasites from a patient, primaquine must be used alongside other drugs that treat the blood stage parasites (see stage 3). Taken together these drugs will eliminate parasites from the body and prevent a malaria relapse.

Primaquine is usually administered over a 14 day period and is mainly used to treat Plasmodium vivax and Plasmodium ovale infections.
The Big Debate
Teachers’ notes

### Primaquine

<table>
<thead>
<tr>
<th>Advantages</th>
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</thead>
<tbody>
<tr>
<td>Primaquine is effective against <em>Plasmodium vivax</em> and <em>Plasmodium ovale</em> infections.</td>
<td>Primaquine is not considered an effective treatment for <em>Plasmodium falciparum</em> infections because this species does not form liver hypnozoites. Therefore it would be useless for most malaria cases in Africa, where <em>Plasmodium falciparum</em> is most common.</td>
</tr>
<tr>
<td>To date no resistance to the drug has been reported.</td>
<td>Primaquine has side effects. It can cause severe reaction in people with a condition known as favism, where the patient is deficient in an enzyme called G6PD. In people with favism primaquine can cause intravascular haemolysis, a condition where the red blood cells rupture in the blood vessels.</td>
</tr>
</tbody>
</table>

### Intervention 2: Anti-malarial vaccine

A vaccine is a product given to healthy people to protect them from a disease. Vaccines have been used successfully to tackle and, in some cases eradicate, diseases caused by bacteria and viruses, e.g. smallpox. However, protozoan parasites, such as *Plasmodium*, are a lot more complex and harder to develop vaccines for.

The RTS,S vaccine is the only malaria vaccine currently available and is in phase 3 trials. It uses a recombinant protein that fuses part of the *Plasmodium falciparum* circumsporozoite protein or CSP (a protein found on the surface of the parasite) with a hepatitis B virus surface antigen. This surface antigen alerts the host’s immune system to the presence of the parasite. The host then produces antibodies and T cells that attack the parasite preventing it from infecting and developing inside the human liver.

Research into live attenuated vaccines is underway. These use whole *Plasmodium* parasites that have been modified so as they don’t cause malaria but still stimulate an immune response in the host. Once exposed to a modified parasite the host's immune system will quickly identify and destroy a wild type parasite if it enters the body.

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>A vaccine that targets the liver stage kills the parasites in the host before they reach the red blood stage where there numbers increase exponentially and are therefore much harder to manage and eliminate.</td>
<td>The RTS,S vaccine has not yet passed its final trial period, so is not yet publically available. If it does pass it could be available by 2015.</td>
</tr>
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Image courtesy of Bonnie Gillespie, Voices for a Malaria free future

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<table>
<thead>
<tr>
<th>Advantages</th>
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<tbody>
<tr>
<td>Phase II clinical trials conducted with over 2,000 children demonstrated that the RTS,S vaccine was protective for 18 months.</td>
<td>The RTS,S vaccine is currently only targeted to children and infants. At present adults are not vaccinated against malaria using RTS,S.</td>
</tr>
<tr>
<td>The RTS,S vaccine is designed for infants and children who are most at risk from malaria.</td>
<td>The RTS,S vaccine is not 100% effective. Some children in the trial went on to develop malaria even after vaccination.</td>
</tr>
<tr>
<td></td>
<td>To date no live attenuated vaccines have passed clinical trials.</td>
</tr>
</tbody>
</table>
Stage 3: Red blood cell stages

What happens during this stage?
Once in the bloodstream the merozoites start to invade red blood cells. Inside the red blood cells they undergo mitosis to form new parasites. One parasite can form up to 20 new merozoites. After 48 hours the infected red blood cell ruptures releasing the merozoites into the blood. Within a minute each of the new parasites will have entered a new red blood cell and the cycle starts again.

What are the symptoms?
The red blood cell stage of the malaria life cycle causes several physical symptoms in the human host that indicate infection by the Plasmodium parasite. These include fever, lethargy, nausea, muscle pains and cyclical chills and sweating.

Patients experience waves of fever every 48 hours. This is because the red blood cell invasion stage of the life cycle takes two days to complete. At the end of each full cycle the red blood cells burst releasing more parasites which cause the fever in the patient.

If the host has a very high parasite load they can show symptoms of severe anaemia, a decrease in the number of red blood cells in the body. This occurs because the host’s body is unable to replace the high number of blood cells being damaged by the Plasmodium infection.

What is the critical point in this stage?
The invasive merozoite stage offers a window of opportunity for the host’s immune system to attack the parasite. In the period when the merozoite exits one red blood cell and enters another it is temporarily exposed to the host’s immune system, outside of the protection of a red blood cell. Once inside the red blood cell the parasite is undetectable by the immune system.

What are the key prevention measures?
Methods that can kill the parasite or prevent it entering and developing in the red blood cell are key prevention interventions for this stage. The use of anti-malarial drugs or vaccines could target this stage of the malaria lifecycle.
**Intervention 1: Chloroquine and artemisinin**

Anti-malarial drugs are chemical compounds used to prevent or treat malaria. Different drugs target specific features of the parasite's biology. Chloroquine and artemisinin are two drugs that are used to treat malaria and both target the blood stages of the parasite.

It is common practice to use combinations of different drugs (combination therapies) as this increases the probability of successful treatment and there is less risk of the parasite developing drug resistance. It can often be more cost effective and may lead to fewer side effects.

Artemisinin combination therapies (ACT's) are currently recommended by the World Health Organization (WHO) as the first line anti-malarial treatment for *Plasmodium falciparum* malaria.

<table>
<thead>
<tr>
<th>Advantages</th>
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</thead>
<tbody>
<tr>
<td>Chloroquine and artemisinin treat the symptoms of the disease and kill the parasites.</td>
<td>Anti-malarial drugs do not prevent you from being infected by the parasite but prevent you being sick from the infection by killing the parasites. Once you finish taking the drugs you are no longer protected.</td>
</tr>
<tr>
<td>Chloroquine and artemisinin can be taken to prevent malaria, known as malaria prophylaxis. This is most common when travelling to malaria endemic countries for short periods of time. Pregnant women can be also given treatments several times throughout their pregnancy.</td>
<td>Malaria prophylaxis is expensive and it is unrealistic for people living in malaria endemic areas to be able to afford to continually take anti-malarial drugs.</td>
</tr>
<tr>
<td>Chloroquine is an extremely cheap drug making it accessible to some of the world’s poorest countries. A course of treatment for an adult can cost as little as $0.10</td>
<td>Chloroquine resistance is now widespread so the drug has limited effectiveness.</td>
</tr>
<tr>
<td>Artemisinin and its derivatives are effective anti-malarial treatments that destroy the younger forms of the parasite in the red blood cell preventing them from maturing and being released into the bloodstream.</td>
<td>Artemisinin combination therapies can cost less than US$1 for an adult treatment course. Although this is cheap it is still too expensive for many people in malaria endemic areas. For people in such areas, $1 may represent the total amount of money to spend on food and living each day.</td>
</tr>
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Advantages | Disadvantages
---|---
Artemisinin combination therapies are very effective. Currently more than 90% of malaria cases treated with artemisinin combination therapies make a full recovery. | The first cases of artemisinin resistance were reported in 2009 in the Cambodia Thailand border.

**Intervention 2: Anti-malarial vaccines**

A vaccine is a product given to healthy people to protect them from a disease. Vaccines have been used successfully to tackle and, in some cases eradicate, diseases caused by bacteria and viruses, e.g. smallpox. However, protozoan parasites, such as *Plasmodium*, are a lot more complex and harder to develop vaccines for.

Recently developed vaccines have targeted proteins on the surface of the parasite. Vaccines have been developed against apical membrane antigen 1 (AMA1) and merozoite surface protein 1 (MSP1). As with drugs, it is likely that combinations of multiple vaccine antigens are most likely to be effective. Trials with combinations are now under way.

Advantages | Disadvantages
---|---
Vaccines prevent children and adults from being infected with malaria. | So far no vaccine that targets the red blood cell stage of malaria has successfully passed through phase II clinical trials. Vaccines against apical membrane antigen 1 (AMA1) and merozoite surface protein 1 (MSP1) were not effective at protecting children from malaria infection.
Stage 4: Transmission to mosquito

What happens during this stage?
When an infected female mosquito feeds on a human they take up a sexual form of the parasite known as a gametocyte which develops inside red blood cells.

What are the symptoms?
There are no obvious symptoms of malaria parasite infection at this stage. There is only the physical evidence of mosquito bites on the surface of the skin. The mosquito also exhibits no symptoms of infection.

What is the critical point in this stage?
The mosquito bite is the critical point in this stage. If the mosquito cannot bite the host it cannot take up the parasite.

What are the key prevention measures?
There are several ways of preventing mosquito bites. These include:
- eliminating or killing the mosquito
- interfering with the mosquito life cycle to reduce or eliminate the population
- making the local environment unsuitable for them, so that they cannot survive or breed.

Intervention 1: larvae control
Adult mosquitoes are highly mobile and capable of detecting and evading intervention measures such as insecticides and bed nets. On the other hand, mosquito eggs, larvae and pupae are confined to small sections of water and can be easily targeted and eliminated.

There are two methods that can be used to control and eliminate larvae populations:
- The use of larvicides, chemical or biological agents (such as bacteria) that kill mosquito larvae.
- The use of biological controls such as larvae-eating (larvivorous) fish.
# The Big Debate

## Teachers’ notes

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>Chemical larvicides can be used to treat whole mosquito breeding sites to suppress the vector population. These strategies are most appropriate when permanent or temporary drainage of standing water is not possible.</td>
<td>Some chemical larvicides can be toxic to other organisms (including humans) and are therefore not recommended for natural bodies of water that form part of larger ecosystems such as rivers and lakes.</td>
</tr>
<tr>
<td>Chemical larviciding has proven to be a successful vector control. It was responsible for the eradication of <em>Anopheles gambiae</em> from rural communities on the Northeast coast of Brazil in the 1930s.</td>
<td>Resistance can develop to the chemical compounds making them less effective.</td>
</tr>
<tr>
<td>Microbial larvicides pose a low risk to human health and the environment. The toxins do not remain or build up in the environment or body tissues of animals that ingest them. They are not toxic and can be used in urban habitats.</td>
<td>Larvicides (chemical and microbial) can be short lived, lasting for just 1-2 weeks, and therefore regular application is needed.</td>
</tr>
<tr>
<td>The microbial larvicide <em>Bacillus thuringiensis israelensis</em> (Bti) is cheap to use costing less than $1 per year per person.</td>
<td>The effectiveness of microbial larvicides can be reduced by water pollution, high temperatures and exposure to sunlight.</td>
</tr>
<tr>
<td>Larvae eating fish can be used in natural rivers and streams but also in man-made structures such as wells, cisterns and barrels, providing protection to urban communities.</td>
<td>The introduction of non native fish can have a negative impact on other freshwater species and ecosystems.</td>
</tr>
<tr>
<td>Some species of larvivorous fish, such as the Nile tilapia (<em>Oreochromis niloticus</em>), are edible so can be farmed to provide additional revenue and food for the community.</td>
<td>Restocking is often necessary to maintain fish populations at levels high enough to continue to suppress the mosquito population. This can be expensive.</td>
</tr>
</tbody>
</table>
Intervention 2: Environmental management

One of the most effective methods of controlling or eradicating a vector population is the modification or manipulation of its habitats to prevent or discourage larval development and to reduce or eliminate contact with humans.

Techniques used to reduce or eliminate mosquito breeding grounds include:
- Draining areas of standing water
- Landfill
- Vegetation clearing from rivers and streams
- Drain cleaning in urban areas.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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</thead>
<tbody>
<tr>
<td>Successful large scale community projects, for example drain maintenance and clearance in urban areas, can significantly reduce mosquito populations and malaria transmission.</td>
<td>Large scale environmental management projects are time consuming and expensive.</td>
</tr>
<tr>
<td>Farmers and other community members can be trained in environmental management practices so the practice is sustainable and is continued in the future.</td>
<td>Different mosquitoes have different habitat preferences and behaviours. Environmental management interventions must therefore be matched specifically to the ecological requirements of the local vector population.</td>
</tr>
<tr>
<td>Environmental management has been shown to be highly effective at eliminating mosquito populations.</td>
<td>If projects are not maintained they will no longer work and the mosquitoes will return.</td>
</tr>
</tbody>
</table>

Image courtesy of Leonard Jan Bruce-Chwatt, Wellcome Library
Stage 5: Mosquito stages

What happens during this stage?
In the mosquito stomach the gametocytes mature into gametes. The female gametocyte turns into an egg and the male gametocyte matures into mobile sperm. The egg is fertilised by a sperm to form a zygote. This then develops into an ookinete which moves through the lining of the gut cell wall to form an oocyst in which thousands of new sporozoites are formed. These burst out and travel to the salivary gland where the cycle starts again.

What are the symptoms?
This stage takes place inside the mosquito so there is no impact on the human. A mosquito will only contain a small number of oocysts and so is unaffected by the parasite.

What is the critical point in this stage?
The critical point in this stage is the number of gametocytes taken up by the mosquito that go on to form ookinetes. As little as 10-100 gametocytes may be taken up and of these only 1-10 go on to mature, fuse, develop into an ookinete and form an oocyst. A single oocyst can form up to ten thousand sporozoites. If the ookinete formation is prevented this will stop the Plasmodium lifecycle from progressing.

What are the key prevention measures?
There are two main ways of interrupting the mosquito stage of the Plasmodium life cycle:
- kill or prevent ookinete formation inside the mosquito using a transmission blocking vaccine
- engineer mosquitoes that are unable to pass on the Plasmodium parasite or that are sterile and therefore unable to breed.

Intervention 1: transmission blocking vaccines
Transmission blocking vaccines target molecules called antigens on the surface of the parasite. These antigens stimulate the human immune system to produce antibodies which when taken up in a blood meal block the parasites development in the mosquito gut.

The vaccine does not stop the individual human from being infected by the Plasmodium parasite and developing symptoms of the disease but it does stop the parasite from being passed on to infect others in the community. If used by a significant proportion of the population a transmission blocking vaccine could eradicate malaria from a local community.

To date no transmission blocking vaccines have successfully passed clinical trials.
### Advantages

When used in conjunction with drugs or vaccines that target or kill the human stages of the parasite, a transmission blocking vaccine can help to prevent or reduce the spread of drug resistant parasites.

### Disadvantages

A transmission blocking vaccine does not reduce a person’s risk of becoming infected nor reduce the severity of the disease.

Will individuals be willing to accept some risk to benefit the rest of the community when there is no immediate benefit to themselves?

Is it ethically acceptable to vaccinate individuals with a vaccine that offers no protection from malaria but could interrupt the transmission cycle and protect other people from getting malaria?

There is a lack of interest from commercial drug companies in developing transmission blocking vaccines because its relevance is only to poorer countries where malaria is endemic.

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**Intervention 2: Engineered mosquitoes**

Researchers are looking at methods to genetically engineer mosquitoes that will reduce the transmission of *Plasmodium* parasites. These methods include:

- Identifying genes in the mosquito that are essential for the parasite to develop in the mosquito. Creating mosquitoes where these genes are mutated may block the parasites development in the mosquito and therefore block its transmission.

- Creating mosquitoes that produce transmission blocking antibodies that directly block parasite development.

- Creating sterile male mosquitoes that are unable to breed. The sterile mosquitoes compete with the wild males to mate with the females. If a female mates with a sterile male then it is unable to produce viable offspring, therefore reducing the population. Regular releases of sterile male insects can eventually eradicate a vector population. Males can be sterilised using radiation or chemical agents. Current research is looking at creating sterile male mosquitoes using transgenic technologies.

At present research into creating genetically modified mosquitoes that block *Plasmodium* transmission are...
in their very early stages. To date there have been no full scale sterile mosquito programmes due to limited funding and a lack of physical capacity to release millions of mosquitoes.

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<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sterile insect technique has been successfully used to eradicate the New World screwworm from North America. The New World screwworm feeds on living tissue of animals causing deep, pocket-like lesions in the skin.</td>
<td>It is difficult, expensive and time consuming to create genetically modified mosquitoes</td>
</tr>
<tr>
<td>Experimental work with sterile <em>Anopheles albimanus</em> has proved successful in El Salvador in 1971. By releasing 40,000 sterilised males daily into a 14-15 km² site the wild population was significantly reduced and no immature stages or adults could be detected after five months.</td>
<td>Sterilising male mosquitoes can reduce their fitness reducing their ability to compete with wild males.</td>
</tr>
<tr>
<td>Community attitudes to the release of large numbers of mosquitoes into a region can also be a challenge. Would you be happy if millions of mosquitoes were released into your local area?</td>
<td></td>
</tr>
</tbody>
</table>

**Further reading**


Kappe SHI, Vaughan AM, Boddey JA and Cowman AF. That was then but this is now: malaria research in the time of an eradication agenda. *Science*. 2010; 320: 862-866. Available online at: [http://www.sciencemag.org/content/328/5980/862.full](http://www.sciencemag.org/content/328/5980/862.full)