



Be Aware of Schistosomiasis

2015 Edition

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Fig. 1 Biomphalaria fresh-water snail.

Image source: Eduardo Rivera (Shutterstock)

THE HELPFUL DATEBOOK

It's noon, the skies are clear, it is unbearably hot and a caravan snakes its way across the Sahara. Twenty-eight people on camelback are heading towards the oasis named El Mamoun. They are tourists participating in 'La Saharienne', a popular excursion conducted twice weekly across the desert of southern Tunisia by an international travel club. In the boundless Sahara, they were living a fascinating experience, their senses thrilled by the majestic grandeur of the desert. After hours of riding, they reached the oasis and were dazzled to see a clear pond fed by a bubbling spring. The idea of jumping into the cool water to relieve the intense heat must have been exciting. There was a momentary pause at the pond's edge to test the water, then the tourists waded in. Although they had been warned never to wade or bathe in the freshwater in the tropics, the cool water was irresistible after travelling for so long under the scorching sun. The advice given at home was forgotten in the momentary relief of the refreshing oasis pond.

Milan – five months later. A pathologist was examining a cervical biopsy of a young woman suspected of having cancer. Under the microscope, he was amazed to see some peculiar worm eggs. There was no doubt in his mind that these were not the common worm eggs routinely seen in his work, but the eggs of the flatworm called *Schistosoma haematobium*.

The eggs of this worm damage the urinary and genital tracts which become inflamed and scarred. The disease, called Schistosomiasis (Bilharzia), is a languishing, debilitating illness which saps the physical and mental energies of its victims.

It was clear to him that this young woman must have spent some time in Africa or the Middle East where this type of worm is prevalent. When interviewed she confirmed that she had been in Africa, participating in one of the excursions organized by the club.

The young woman did not have cancer at all, but had contracted schistosomiasis while swimming in the oasis pond. When investigators began to fear that other members of her group might also be infected, her date book came to their aid. Many of her companions had exchanged addresses with this attractive young lady, and eventually all members of the group were contacted and examined. The toll was heavy – out of 28 persons, nine were added to the long list of travellers infected at El Mamoun.¹

THE LIFE OF THE FLATWORM

How did it happen? The swimmers hadn't noticed among the vegetation at the edge of the pond the presence of minute snails so small that a dozen would easily fit into a teaspoon. In some ponds and rivers as many as 1,000 can be found in a square metre. They are the freshwater snails belonging to the genus *Bulinus*, which serve as the specific hosts to the larval stages of the *Schistosoma haematobium* worm.

The Snail – The Creature Nurturing Infection

The eggs of the worm are eliminated via the urine of those infected. When an egg reaches freshwater, it hatches rapidly – see picture of the life cycle of the human schistosomes (1). The ensuing larva (an immature form of life called *miracidium*) is an oval shaped organism clothed with minute cilia (2) swimming in search of the *Bulinus* snail.

1. Although Schistosomiasis cases are no longer reported from Tunisia, this true story highlights how the disease can go undetected in unsuspecting travellers.

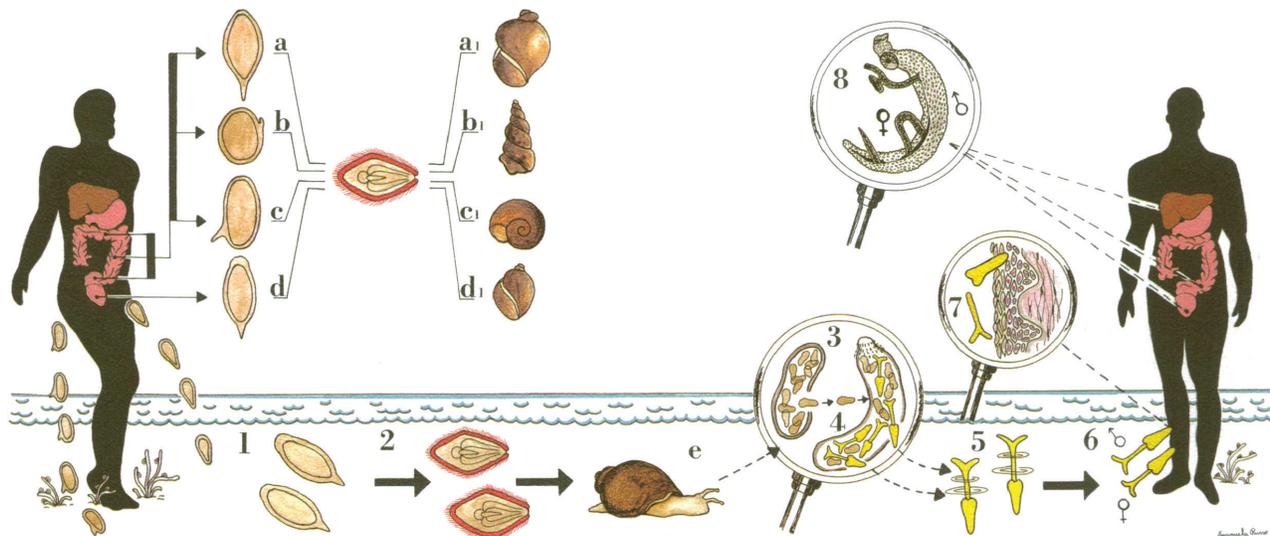


Fig. 2 Life cycle of human schistosomes.

The *miracidium* [Gr.: meirákon = young form of life] is attracted by the snail's mucous secretion and burrows into the soft tissue of the mollusc (e). Once inside, the *miracidium* transforms itself into an elongated, thin walled sack called mother *sporocyst* [Gr.: sporá = sowing, seed; kústis = sack] (3), which gives rise to about four hundred daughter *sporocysts* (4). Each one forms within its cavity numerous fork-tailed *cercariae* [Gr.: kerkos = tail], representing the early stages of maturing worms. A single *miracidium* may produce thousands of *cercariae* in only six weeks and this production may carry on in the snail for months.

The water in the pond of El Mamoun was teeming with this kind of microscopic life when our tourists arrived at the oasis. Previous visits to the oasis by Bedouins had left the pond infected, a legacy of the disease for the tourists to contract.

Like divers jumping from their boats, the *cercariae*, stimulated by the bright light and the high temperature of the day, abandon the snails. Seen under the microscope they look like miniature tadpoles, with a pear shaped buoy and a long tail ending in a y-shaped fork which acts as a propeller to move the organism through the water (5). They are now swimming in a desperate race against time, searching for a human host to ensure their survival. They will die within 48 hours if the search fails.

Attracted by the oily secretion lubricating the human body, they attach themselves to the skin with their oral suckers. They do not need to find a wound or break in the skin since they secrete an enzyme which splits the 'cement' holding the cells of the skin together (6). As soon as the *cercariae* start to penetrate the outer layers, they shed their tails (7) and burrow a tunnel through the epidermis.

Humans – The Sexual Life of the Worm

The tail-less *cercariae*, now called *schistosomulae*, then reach the lymph vessels which drain into the two major veins, allowing the *schistosomulae* of both sexes to reach first the lungs and then the liver, where they mature and mate.

The worms have a rounded and elongated appearance. In the animal kingdom they are placed under the group *Platyhelminthes* (Gr.: platús = broad; élmis = worm). They are greyish-white in colour and measure between 1/2 and 1 inch (1.2-2.5 cm) in length and have two suction discs for adhesion and feeding. They belong to the family of flukes or *Trematoda* (Gr.: tre – ma = hole) and are commonly called 'blood flukes' because they live in the blood vessels of mammals. The name for their genus, *Schistosoma* (Gr.: schistós = cleft, split; soma = body), indicates their difference from all other flukes: They are not hermaphroditic, but have two genders – male and female. When they mate, the edges of the larger male worm fold over to form a groove to hold the slender and longer female close to him (8). Then, tightly embraced, they leave the liver, swimming against the flow of the venous blood, to settle in the blood vessels surrounding the bladder and the adjacent organs in the genito-urinary system.

The reason? Since the only way to ensure the survival of the species is to get the eggs into freshwater, the worms live close to the natural openings of the human body – the bladder or the openings of the reproductive organs – so that the eggs can easily escape to the outside.

The human body doesn't suspect their presence because the worms disguise themselves with a coating of protein similar to that of the host. This coating fools the human's defense system,



Fig. 3 Electron micrograph of a male/female pair of adult schistosomes.

Image source: Natural History Museum, London

which otherwise would fight off foreign particles. Undisturbed, the worms may live for years producing an incredible number of eggs.

The Eggs – The Quest for Freedom

The eggs, which are oval-shaped with a spike protruding from one end, are deposited in large numbers in the tissue of the bladder. Some reach the innermost part through the tiniest of blood vessels. They are now only separated from the urine by a thin layer of tissue, which they pierce with the spike to allow them to fall into the urine. When the eggs are eliminated from the bladder and reach fresh water, they will hatch into *miracidia*, search out the snails, and start the cycle anew.

However, a great number of eggs remain trapped in the tissue. Unlike their shrewd parents, they are not able to cheat the defense system of the host. Immediately, they are surrounded by scores of white blood cells, the body's main defense system. These 'immune fighters', known as *phagocytes* (Gr.: phagein = to eat; kútos = cell), fend off whatever they recognize as foreign by grinding the invaders to bits and swallowing them up with enzymes. However, the *phagocytes* are powerless in their fight against so many giants, each one 10 times their size.

Not even with the help of larger cells, the *macrophages* (Gr.: macrós = big; phagein = to eat), which fuse to form giant cells, are able to turn the battle in favour of the host. They are only able to lay siege by completely surrounding the eggs forming *granulomas* (L.: granulum = small grain) in the bladder tissue. Within about a month the eggs die and their shells calcify into rigid structures forming polyps, nodules, and ulcers. Slowly these are replaced by fibrous scar tissue, making the bladder wall rigid and thicker causing constriction especially on the lower portion of the ureters (the tubes carrying urine from the kidneys to the bladder) impairing the outflow of urine. This produces back pressure, dilating the ureters and reducing the functioning of the kidneys. Finally the accumulation of waste in the blood poisons the human body resulting in death.

THE FLATWORM IN HUMANS

Of the thousands of different species of flatworms living as parasites in practically every kind of vertebrate, only 8 are responsible for the human disease schistosomiasis. Each species has a specific intermediate host a suitable species of freshwater snail, in which the larva undergoes further development:

- *Schistosoma haematobium* lives in the blood vessels of the bladder and genitalia. The eggs, characterized by a terminal spike (**d**), are passed with urine. The intermediate host snail belongs to the genus *Bulinus* which has a conical shaped shell, dark grey in colour measuring about 1 cm in length (**d1**). The infection caused by *S. haematobium* is found in Africa (including Madagascar) and the Middle East. Humans are the only known reservoir of this species, therefore, with improved sanitation and public health initiatives the prospects of eradication are excellent in communities who are infected with *S. haematobium* only.
- *Schistosoma mansoni* lives in the blood vessels surrounding the large bowel. The eggs, which have a lateral spine (**c**), are passed with the stools. The intermediate host belongs to the genus *Biomphalaria*, a snail with a flat disc-shaped shell (**c1**), dusky brown or reddish in colour with a diameter of 7-22mm. The infection caused by *S. mansoni* is endemic in Africa (including Madagascar), the Arabian peninsula, Brazil, Venezuela, and some Caribbean countries. Besides humans, *S. mansoni* also infects rodents and monkeys (baboons) in some endemic areas which contribute to maintaining the transmission cycle and making elimination more difficult.
- *Schistosoma japonicum* lives mainly in the blood vessels of the small intestine. The eggs, which have a rudimentary lateral spine (**b**) escape into the bowel and are passed with stools. The intermediate host is a small amphibious snail of the genus *Oncomelania* (**b1**). It has a turreted (tower-like) shell, dark olive in colour, measuring about 1cm in length. The infection caused by this worm occurs in China, the Philippines and in limited areas of Central Sulawesi, Indonesia. *S. japonicum* is primarily a zoonotic (animal) infection with multiple reservoir hosts: Rodents, dogs, cattle, water buffalo, pigs, horses, sheep and goats, making elimination efforts challenging and very costly.
- *Schistosoma mekongi* was identified in 1978. It is found along the Mekong River in Cambodia and Laos.

In countries where Schistosomiasis is endemic, avoid contact with fresh water. There will be situations where you will be tempted to disregard this simple advice. There is no risk in seawater.

- *Schistosoma malayensis* was identified in 1988 as the cause of human infection on peninsular Malaysia and Malaysian Borneo.
- *Schistosoma guineensis* was identified in 2003. It is found in western Africa, mainly in Cameroon, Equatorial Guinea, Gabon, Sao Tomé and Príncipe, Nigeria, Burkina Faso, and Mali. Mapping of this species is not complete.
- *Schistosoma intercalatum* is present in the Democratic Republic of the Congo. It is usually the sole transmission agent but can also be found in areas where *S. mansoni* and *S. haematobium* are present.
- *Schistosoma mattheei* is found in southern Africa (South Africa, Swaziland, Zambia) and primarily affects cattle, horses, sheep and antelopes, but can infect humans. It co-exists with *S. mansoni* and *S. haematobium*.

THE DISEASE – THE DAMAGE BY THE EGGS

The early signs of the disease caused by the different species of worms are similar. When the *cercariae* penetrate the skin, they produce itching and a localized rash at the point of entry which disappears within a day or two, followed by a symptomless period of 4 to 6 weeks during which the worms reach maturity. Towards the end of this period, you start to feel weak, suffer loss of appetite, experience night sweating, and have a pronounced rash resembling hives all over the body. A late afternoon fever lasting from 5 to 10 days is known as 'snail fever' or Katayama Fever. The French call it 'fièvre des safaris' (safari fever).

After a few months, when the infection is well established, the damage produced by the discharge of eggs into the tissues of the various organs will manifest itself in different ways based on the type of worm.

- The passage of blood in urine and frequent and painful urination are consistent symptoms of the disease caused by *S. haematobium*.
- Bouts of diarrhea with the passage of blood and mucous in the stools are the signs of the infection caused by *S. mansoni*. In the late stages of the illness, extensive fibrosis of the liver

(scarred liver) leads to the accumulation of fluids in the abdomen, producing a clinical picture similar to cirrhosis of the liver.

- The infection caused by *S. japonicum* follows a course similar to that of *S. mansoni*, but the disease tends to be more severe due to the large number of eggs produced by this species (an average of 3,000 eggs per female worm a day). Infection with *S. mekongi* and *S. malayensis* tend to be milder than *S. japonicum*.
- The infection by *S. guineensis* and *S. intercalatum* runs a rather mild course, sometimes without symptoms.

Schistosomiasis lacks the immediate effects of other tropical diseases. It is a chronic condition produced by the cumulative damage of repeated egg deposits, making you vulnerable to other infections, including HIV, and can be fatal. This silent drama unfolds slowly among populations in rural and agricultural areas. Even the suburbs of some African, Asian, and South American cities are infected. In many areas the disease is so common that it is regarded as a way of life. In fact, in some parts of Africa it is not considered unusual for a person to pass blood with urine. Today, it is estimated that 249 million people throughout the world, mainly in sub-Saharan Africa, are affected by the disease.

A MAJOR CONCERN

The worldwide demand for water requires new irrigation projects and the construction of dams has resulted in the spread of the disease where it previously did not exist.

A case in point is the construction of the Akosombo Dam in Ghana creating Lake Volta in 1965. The project displaced 80,000 people, mostly subsistence farmers and fishermen from 700 villages who were resettled into 52 new communities. In a short period after construction of the dam, the proportion of the population affected by Schistosomiasis jumped to 40% from the previous 5%.

In Egypt, construction of the Aswan Dam altered the balance between the two types of infection present in the country. Ecological changes favouring the spread of *Biomphalaria* snails, which harbours *S. mansoni* (affecting the liver and large bowel) increased, while the urinary form caused by *S. haematobium* decreased. With a successful national Schistosomiasis

A Brief History of Schistosomiasis:

It is believed that both schistosomes and snail hosts have been in contact with humans since our evolutionary origins. From the area of the Great Lakes in East Africa, the infection moved northward along the Nile and later reached the Middle East and West Africa through trade routes.

The movement of East African tribes contributed to spreading the disease to the south. From west Africa the infection was transported to the Americas by the slave trade and it became established in South America and some Caribbean Islands due to the presence of suitable snail hosts. Schistosomiasis was known to the ancient civilizations of Egypt, Mesopotamia, and China.

1500 B.C. The Egyptian Papyrus Ebers mentions remedies "to kill worms in the body causing blood in the urine". Calcified eggs of *S. haematobium*, found in two mummies of the XXth dynasty by Sir Marc Armand Ruffer in 1910 substantiate this evidence.

400 B.C. Ge Hong in his classic compendium of traditional Chinese medicine 'Zhouhou Beiji Fang', describes "water poison attacking man like 'shengong' [a poisonous insect], but invisible".

1851 Theodor Bilharz, a German physician working at the Kasr el Aini Hospital in Cairo discovered *trematoda* worms in the veins of a patient during an autopsy. He realized they were the cause of Schistosomiasis. In honour of his discovery, the disease is called Bilharzia, a term widely used in Europe.

► Important...

So what exactly is Swimmer's Itch?

In temperate areas, the *cercariae* of non-human schistosomes affect wild birds and ducks and are known to penetrate human skin.

After swimming in a lake a person may experience itching and a mild irritation of the skin. The *cercariae*, which have entered the wrong host, will not reach the blood circulation but will die at the point of entry.

This condition, known as Swimmer's Itch, is found all over the world.

control program, prevalence of both *S. haematobium* and *S. mansoni* infections are now on the decline.

In other desert areas such as Saudi Arabia and Iraq, the limited volume of water (ponds, small canals and temporary streams) makes prospects for eradication of the disease possible. Elimination of snails and treatment of infected persons in these areas are sufficient to block transmission.

In many countries, particularly in sub-Saharan Africa, the problem is still waiting to be solved. Rivers and lakes are an integral part of domestic life in rural communities where water is used for consumption, clothes washing, bathing, and playing. Only a combination of health education with the introduction of effective sanitation such as piped deep well water and the efficient disposal of human waste can prevent Schistosomiasis transmission.

TURNING TO HOPE

Since 1985 the WHO expert committee on schistosomiasis has recommended chemotherapy as the main control strategy against the infection. Large scale distribution of the drug praziquantel was officially adopted by the WHO assembly in 2001 and this strategy has been integrated into public health programs in many affected countries. Many non-profit organizations, such as the Carter Foundation and groups working to eliminate neglected tropical diseases have incorporated the distribution of praziquantel into their health care programs. Pharmaceutical companies

are also contributing with large drug donations. Since 2006, due to educational awareness programs and the yearly distribution of chemotherapy, many endemic countries have experienced a significant decrease in human infections. Some countries no longer report human infections and are awaiting evaluation and confirmation by the WHO that human transmission has been interrupted. See IAMAT's *World Schistosomiasis Risk Chart* for country details. However, the majority of endemic countries still require massive help with public health and improved sanitation, this is to say, chemotherapy campaigns must be combined with infrastructure improvements – safe water and sewage disposal – education, and snail control to achieve permanent success.

TREATMENT

The drug of choice for the treatment of Schistosomiasis is praziquantel, a compound effective against all species of schistosomes. The drug is well tolerated and fast acting.

Praziquantel paralyzes the worms, making them vulnerable to the body's defense mechanisms. However, successful treatment will improve but not solve the situation; treated persons can easily become re-infected. Prevention is still preferable to treatment since in the absence of obvious symptoms, irreversible damage may be done before the infection is detected.

The targets for the interruption of the transmission cycle are public education, improved sanitation and disposal of human waste, elimination of snails, and treatment of infected persons.

1902 The British physician Patrick Manson found schistosome eggs in the stools of a patient from Antigua suffering from intestinal schistosomiasis. This suggested to him that this form of the disease was caused by another species, which later was named *S. mansoni* in his honour.

1904 Fujiro Katsurada discovered a third species of schistosomes in Japan and named it *S. japonicum*.

1908 Pirajá Silva was the first doctor to describe the life cycle of the disease.

1909 Akira Fuginami and Hachitaro Nakamura proved that the schistosomes' entry route is through intact skin.

1913 Keinosuke Miyairi and Masatsugu Suzuki observed the penetration of *miracidia* into the specific snails, and by dissecting them, were able to describe the transformation of the *miracidium* into *sporocysts* and finally into *cercariae*.

1915 R. T. Leiper, working in Egypt, identified the two snail species which transmit *S. haematobium* and *S. mansoni*. The complete lifecycle of the major human schistosomes and their snail vectors was finally clarified.

PERSONAL PREVENTION

No drugs are available to prevent the establishment of the infection although progress has been made in the development of a vaccine for the schistosomes that affect domestic animals. Attempts to develop a vaccine for human schistosomes have not yet been successful.

The Golden Rules to Prevent Schistosomiasis

- In countries where Schistosomiasis is endemic, avoid contact with fresh water. There will be situations where you will be tempted to disregard this simple advice. There is no risk in seawater. See IAMAT's *World Schistosomiasis Risk Chart* for country details.
- If you are planning a trip into the jungle or desert, make sure it is a short one, so that you can withstand the heat and are not tempted to cool off in a pond or stream. Make sure you do not run out of purified water.
- If you must pass through streams or swamps, wear high waterproof boots or hip waders.
- Stay away from the banks of streams and rivers; snails abound in shallow water where they feed on organic waste and aquatic vegetation. Snail presence is minimal in the deeper ends of lakes, rivers, and streams where water tends to flow faster.
- Avoid contact with freshwater during peak daylight hours when the *cercariae* emerge from the snails and are most active.
- If you accidentally come into contact with freshwater, rub your skin immediately with rubbing alcohol and a dry towel to reduce the possibility of infection.
- If you are travelling overland by car, carry a pair of rubber gloves in case you have to dip your hands into a stream or pond to get water for the radiator.
- Water from a river or lake used for bathing and washing should be boiled or chlorinated.
- Water for washing and bathing is relatively safe if it has been stored for 2-3 days (the period generally accepted as the life span of *cercariae*), provided that the container is free of snails.
- Drinking water should be boiled or treated with chlorine tablets, as the *cercariae* may burrow through the mucosa of the mouth.
- Make sure vegetables are well cooked and avoid salads since the leaves may have been washed with infected water. For advice on water and food precautions, see www.iamat.org.

1978 Marietta Voge, David Bruckner and John I. Bruce confirmed that *S. mekongi* is a separate species from *S. japonicum*.

1988 *S. malayensis* was identified as a separate species from *S. japonicum* by G. J. Greer, C. K. Ow-Yang, and H. S. Yong.

2003 *S. guineensis* was identified as a separate species from *S. intercalatum* by a team of scientists from Cameroon, France, and England.

2009 & 2012 Research teams decoded *S. mansoni* and *S. japonicum* genomes (2009) and *S. haematobium* genomes (2012) opening up the possibility for new types of drug treatments.

Sources: Please contact IAMAT for references.

GUIDELINES FOR SNAIL IDENTIFICATION

It is not always easy, even for a trained person, to distinguish harmful snails from harmless ones. Snail features vary from continent to continent. The following hints will help you identify intermediate snail hosts. Always wear a pair of rubber gloves to hold snails for examination.

Africa

- Look for the dimensions of the snail. Harmful ones will have a shell less than 2 cm (3/4 inch) in length.
- Harmful snails are always in the water, either floating, lying on the bottom or attached to aquatic vegetation. Snails crawling on land are harmless.
- Harmful snails do not have an *operculum*, a 'door' attached to the foot which closes the opening of the shell when the snail retreats. In Africa, harmless snails have an *operculum*.

Harmful snails are divided into two major groups:

- 1) Snails with a flat, round shell like a disc or wheel belong to the genus *Biomphalaria*, which is the intermediate host of *S. mansoni*.
- 2) Snails with a conical shell ending with a sharp tip belong to the genus *Bulinus*, which transmit *S. haematobium*.

You may identify the harmful *Bulinus* species by holding the shell between your fingers with the opening facing you and the apex pointing upwards. You are dealing with a harmful species if the opening is to the left hand side. Shells with a right hand opening belong to harmless snails.

South America and Some Caribbean Islands

The only harmful species of snail present in the western hemisphere belong to the genus *Biomphalaria*. Except for *B. straminea*, they differ from the African species in that they are larger than 2 cm (3/4 inch) in length. They have a round, flat-shaped shell, dark brown, sometimes reddish in colour.

Southeast Asia

In southeast Asia, the snails transmitting schistosomiasis belong to the genus *Oncomelania*. They have a conical, turreted dark brown shell, usually less than 1 cm (1/2 inch) in length. You may notice that in this dangerous species the opening is to the right and when the snail retreats, the *operculum* will close the opening. You will find them either floating in water or crawling on land. 

genus *Biomphalaria*
(x 1.5 natural size)



genus *Bulinus*
(natural size)



Harmful snail
(left-hand opening)



Harmless snail
(right-hand opening)



genus *Biomphalaria* of the
western hemisphere
(natural size)



genus *Oncomelania*
(x 2.4 natural size)

