SCHISTOSOMES: BLOOD FLUKES

Schistosomes are diecious trematodes in which the sexes are separate. The male is

broader than the female, and its lateral borders are rolled ventrally into a cylindrical

shape, producing a long groove or trough called the gynaecophoric canal, in which

the female is held. It appears as though the body of the male is split longitudinally

to produce this canal—hence the name Schistosome (Greek schisto—split and —soma

body). Schistosomes were formerly called Bilharziaafter Theodor Bilharz who in

first observed the worm in the mesenteric veins of an Egyptian in Cairo. All ,١٨٥١

schistosomes live in venous plexuses in the body of the definitive host, the location

.(varying with the species (Fig. 9.2

:FIGURE 9.2: Morphology of Schistosomes

Male and female in copula. 1. Oral sucker

Ventral sucker 3. Uterus 4. Gynaecophoric .٢

canal 5. Testis 6. Caecum

Schistosomes differ from the hermaphroditic trematodes in many respects. They

lack a muscular pharynx. Their intestinal caeca reunite after bifurcation to form a

single canal. They produce non-operculate eggs. They have no redia stage in larval

development. The cercariae have forked tails and infect by penetrating the unbroken

skin of definitive hosts. Schistosomiasis (bilharziasis) is a water-borne disease constituting an important public health problem affecting millions of persons in ,Africa

Asia and Latin America. It is estimated that over 100 milion persons are infected

.with S. haematobium, S. mansoni andS. japonicum each

SCHISTOSOMA HAEMATOBIUM

History

This vesical blood fluke, formerly known as Bilharzia haematobiumhas been endemic

in the Nile valley in Egypt for millenia. Its eggs have been found in the renal pelvis

of an Egyptian mummy dating from 1250-1000 B.C. Schistosome antigens have been

identified by ELISA in Egyptian mummies of the Predynastic period, 3100 B.C. The

adult worm was described in 1851 by Bilharz in Cairo. Its life cycle, including the

.larval stage in the snail was worked out by Leiper in 1915 in Egypt

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Geographical Distribution

Although maximally entrenched in the Nile valley, S. haematobiumis also endemic

in most parts of Africa and in West Asia. An isolated focus of endemicity in India

.was identified in Ratnagiri, south of Mumbai by Gadgil and Shah in 1952

Morphology and Life Cycle

The adult worms live in the vesical and pelvic plexuses of veins. The male is 10

to 15 mm long by 1 mm thick and covered by a finely tuberculated cuticle. It has

two muscular suckers, the oral sucker being small and the ventral sucker large and

prominent. Beginning immediately behind the ventral sucker and extending to the

caudal end is the gynaecophoric canal in which the female worm is held. The adult female is long and slender, 20 mm by 0.25 mm with the cuticular tubercles confined

.to the two ends

The gravid worm contains 20 to 30 eggs in its uterus at anyone time and may pass up to 300 eggs a day. The eggs are ovoid, about 150 µm by 50 µm, with a brownish yellow transparent shell carrying a terminal spine at one pole (the terminal

spineis characteristic of the species). The eggs are laid usually in the small venules of the vesical and pelvic plexuses, though sometimes they are laid in the mesenteric

portal system, pulmonary arterioles and other ectopic sites. The eggs are laid one behind the other with the spine pointing posteriorly. From the venules, the eggs make their way through the vesical wall by the piercing action of the spine, assisted

by the mounting pressure within the venules and a lytic substance released by the eggs. The eggs pass into the lumen of the urinary bladder together with some extravasated blood. The eggs are discharged in the urine, particularly towards the end of micturition. For some unknown reasons, the eggs are passed in urine more during midday than at any other time of the day or night. The eggs laid in ectopic sites generally die and evoke local tissue reactions. They may be found, for instance

.in rectal biopsies, but are seldom passed live in feces

The eggs that are passed in water hatch, releasing the ciliated miracidia. They swim about in water and on encountering a suitable intermediate host, penetrate

into its tissues and reach its liver. The intermediate hosts are snails of Bulinusspecies

.in Africa. In India, the intermediate host is the limpet Ferrisia tenuis

Inside the snail, the miracidia lose their cilia and in about 4 to 8 weeks, successively

pass through the stages of the first and second generation sporocysts. Large number

of cercariae are produced by asexual reproduction within the second generation

sporocyst. The cercaria has an elongated ovoid body and forked tail (furcocercous

cercaria). Swarms of cercariae swim about in water for 1 to 3 days. If during that

period they come into contact with persons bathing or wading in the water, they

penetrate through their unbroken skin. Skin penetration is facilitated by lytic substances

.secreted by penetration glands present in the cercaria

On entering the skin, the cercariae shed their tails and become schistosomulaewhich

enter the peripheral venules. They then start a long migration, through the vena

cava into the right heart, the pulmonary circulation, the left heart and the systemic

circulation, ultimately reaching the liver. In the intrahepatic portal veins, the

FIGURE 9.3: Life cycle of Schistosoma haematobium. 1. Adult

male and female in copula in the vesical venous plexus. 2. Egg

.containing ciliated embryo passed in urine reaches water

.Miracidium hatches out of egg and enters the snail liver .٣

Development in snail—Sporocyst first generation. 5. Sporocyst .٤

.second generation. 6. Cercaria with forked tail released into water

Human infection by skin penetration

schistosomulae grow and become sexually differentiated adolescents about 20 days

after skin penetration. They then start migrating against the blood stream into the

inferior mesenteric veins, ultimately reaching the vesical and pelvic venous plexuses

where they mature, mate and begin laying eggs. Eggs start appearing in urine usually

to 12 weeks after cercarial penetration. The adult worms may live for 20 to 30 ١٠

.(years (Figs 9.3 to 9.6

.Humans are the only natural definitive hosts. No animal reservoir is known

Pathogenicity and Clinical Features

Clinical illness caused by schistosomes can be classified depending on the stages

:in the evolution of the infection, as follows

;i. Skin penetration and incubation period

ii. Egg deposition and extrusion; and

.iii. Tissue proliferation and repair

The clinical features during the incubation period may be local cercarial dermatitis

or general anaphylactic or toxic symptoms. Cercarial dermatitis consists of transient

itching petechial lesions at the site of entry of the cercariae. This is seen more often

in visitors to endemic areas than in locals who may be immune due to repeated

contacts. It is particularly severe when infection occurs with cercariae of nonhuman

FIGURE 9.4: S. haematobium: developmental stages

schistosomes. Anaphylactic or toxic symptoms include fever, headache, malaise and

urticaria. This is accompanied by leucocytosis, eosinophilia, enlarged tender liver

and a palpable spleen. This condition is more common in infection with S. japonicum

.(Katayama fever)

The typical manifestation caused by egg laying and extrusion is painless terminal

haematuria (endemic haematuria). Haematuria is initially microscopic, but becomes

gross if infection is heavy. Most patients develop frequency of micturition and .burning

FIGURE 9.5: Schistosoma in coupled

Cystoscopy shows hyperplasia and inflammation of bladder mucosa with minute

.papular or vesicular lesions

In the chronic stage there is generalised hyperplasia and fibrosis of the vesical

mucosa with a granular appearance (Sandy patch). At the sites of deposition of the

eggs, dense infiltration with lymphocytes, plasma cells and eosinophils leads to

pseudoabscesses. Initially the trigone is involved, but ultimately the entire mucosa

becomes inflamed, thickened and ulcerated. Secondary bacterial infection leads to

chronic cystitis. Calculi form in the bladder due to deposition of oxalate and uric

acid crystals around the eggs and blood clots. There may be obstructive hyperplasia

of the ureters and urethra. Schistosomiasis favours urinary carriage of typhoid .bacilli

Chronic schistosomiasis has been associated with bladder cancer, though a causative

.relationship is not proved

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FIGURE 9.6

Diagnosis

The eggs with characteristic terminal spines can be demonstrated by microscopic

examination of centrifuged deposits of urine. Eggs are more abundant in the blood

and pus passed by patients at the end of micturition. They can also be seen in

seminal fluid. They may occasionally be found in feces, or more often in vesical

.or rectal biopsies

A refinement of diagnosis by demonstration of eggs is to hatch shed eggs into

.motile miracidia

Another diagnostic method is by detection of specific schistosome antigens in serum or urine. Two glycoprotein antigens associated with the gut of adult schistosomes (circulating anodic and cathodic antigens, CAA and CCA) can be demonstrated by ELISA using monoclonal antibodies. The test is very sensitive and specific, but is available only in specialised laboratories. Skin tests are group specific and give positive results in all schistosomiases. The intradermal allergic test (Fairley's test) uses antigen from infected snails, from cercariae, eggs and

.adult schistosomes from experimentally infected laboratory animals

Several serological tests have been described but are not very useful. These ,include complement fixation, bentonite flocculation, indirect haemagglutination immunofluorescence, gel diffusion and ELISA. Two special tests are circumoval precipitation (globular or segmented precipitation around schistosome eggs incubated in positive sera) and “cercarien-hullen” reaction (development of pericercarial membranes around cercariae incubated in positive sera). Animal schistosomes can be used as antigens in these tests. Ultrasonography is useful .in diagnosing S. haematobiuminfection

Treatment

.Metriphonate is the drug of choice in schistosomiasis due to haematobium

Praziquantel is effective against all schistosomes and also against many other .trematode and cestode infections

Prevention and Control

.Prophylactic measures include eradication of the intermediate molluscan hosts

prevention of environmental pollution with urine and feces and effective treatment

.of infected persons

SCHISTOSOMA MANSONI

History and Distribution

The discovery by Manson in 1902 of eggs with lateral spines in the feces of a West

Indian patient led to the recognition of this second species of human .schistosomes

It was therefore named S. mansoni. It is widely distributed in Africa, South America

.and the Caribbean islands

Morphology and Life Cycle

S. mansoniresembles S. haematobiumin morphology and life cycle. The adult worms

are smaller and their integuments studded with prominent coarse tubercles. In the

gravid female the uterus contains very few eggs usually 1 to 3 only. The prepatent

period (the interval between cercarial penetration and beginning of egg laying) is

.(to 5 weeks. The egg has a characteristic lateral spine (Fig. 9.7 ٤

The intermediate hosts are planorbid fresh-water snails of the Genus .Biomphalaria

Humans are the only natural definitive hosts, though in endemic areas monkeys

.and baboons have been found infected

In humans the schistosomulae mature in the liver and the adult worms move

against the blood stream into the venules of the inferior mesenteric group in the

sigmoidorectal area. Eggs penetrate the gut wall, reach the colonic lumen and are

.shed in feces

Pathogenicity and Clinical Features

Following skin penetration by cercariae a pruritic rash may develop locally. During

the stage of egg deposition the symptomatology is mainly intestinal. This condition

is therefore known as intestinal bilharziasis or schistosomal dysentery. Patients

develop colicky abdominal pain and bloody diarrhoea which may go on intermittently

for many years.The eggs deposited in the gut wall cause inflammatory reactions

leading to micro-abscesses, granulomas, hyperplasia and eventual fibrosis. Ectopic

.lesions include hepatosplenomegaly and portal hypertension

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FIGURE 9.7: Schistosome eggs. 1. S. haematobium—Oval, with terminal spine, 2. —S. mansoni—Oval, with lateral spine. 3. S. japonicum

Roundish, with lateral knob. Small granules of tissue debris adherent

.to shell

Diagnosis

Eggs with lateral spines may be demonstrated microscopically in stools. Concentration methods may be required when infection is light. Proctoscopic biopsy snips

of rectal mucosa reveal eggs when examined as fresh squash preparation between

.two slides

Treatment

.Oxamniquine is the drug of choice

Prevention and Control

These are based on control of the snail hosts, prevention of fecal pollution and

.treatment of infected persons

SCHISTOSOMA JAPONICUM

Distribution

,Known as the Oriental blood fluke, S. japonicumis found in the Far East, Japan

.China, Taiwan, Philippines and Sulawesi

Morphology and Life Cycle

These are generally similar to the schistosomes described above. The adult worms

are seen typically in the venules of the superior mesenteric vein draining the ileocaecal

region. They are also seen in the intrahepatic portal venules and in the haemorrhoidal

.plexus of veins

The adult male is comparatively slender (0.5 mm thick) and does not have cuticular

tuberculations. In the gravid female, the uterus contains as many as 100 eggs at one

time and up to 3500 eggs may be passed daily by one worm. The prepatent period

is 4 to 5 weeks. The eggs are smaller and more spherical than those of S. haematobium

.and S. mansoni. The egg has no spine, but shows a lateral knob

Eggs deposited in the mesenteric venules penetrate the gut wall and are passed

in feces. They hatch in water and the miracidia infect the intermediate hosts, amphibian

,snails of the genus Oncomelania. Man is the definitive host but in endemic areas

natural infection occurs widely in several domestic animals and rodents, which act

.as reservoirs of infection

Pathogenesis and Clinical Features

Disease caused by S. japonicum is also known as Oriental schistosomiasis or Katayama

disease. Its pathogenesis is similar to that in other schistosomiases, but probably

.because of the higher egg output, the clinical manifestations are more severe

The acute illness consisting of fever, abdominal pain, diarrhoea and allergic

manifestations is called Katayama fever. It is an immune complex disease caused

.by antibodies to the schistosomulae, adult worms and eggs

In the chronic illness, the liver is the site maximally affected. There is initial

hepatomegaly followed by fibrosis. Portal hypertension leads to oesophageal varices

and gastrointestinal bleeding. The spleen is secondarily enlarged. Cerebral and

.pulmonary involvement may occur in some cases

.Diagnosis is by demonstration of the eggs in feces

Treatment

.S. japonicuminfection is more resistant to treatment than other schistosomiases

A prolonged course of intravenous tartar emetic gives good results. Praziquantel

.has also been reported useful

Prevention and Control

Prevention of fecal population of soil and water, treatment of infected persons and

snail control help to contain the infection. But the presence of animal reservoirs in

.endemic areas makes eradication difficult

SCHISTOSOMA INTERCALATUM

This species, first recognised in 1934 is found in West Central Africa. The eggs have

.terminal spines, but are passed exclusively in stools

SCHISTOSOMA MEKONGI

This species first recognised in 1978 is found in Thailand and Cambodia, along the

.Mekong river. It is closely related to S. japonicum

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HERMAPHRODITIC FLUKES: LIVER FLUKES

The adult forms of all hermaphroditic flukes infecting humans live in the lumen of

the biliary, intestinal or respiratory tracts. This location affords the parasites

considerable protection from host defense mechanisms and also facilitates dispersal

.of eggs to the environment

Flukes inhabiting the human biliary tract are Clonorchis sinensis, Fasciola ,hepatica

.less often Opisthorchisspecies, and rarely Dicrocoelium dendriticum

CLONORCHIS SINENSIS

History and Distribution

Commonly known as the Chinese liver fluke, C. sinensiswas first described in 1875

by McConnell in the biliary tract of a Chinese in Calcutta. Human clonorchiasis occurs

.in Japan, Korea, Taiwan, China and Vietnam affecting about ten million persons

Morphology and Life Cycle

Humans are the principal definitive host, but dogs and other fish-eating canines

act as reservoir hosts. Two intermediate hosts are required to complete its life ,cycle

the first being snail and the second fish. The adult worm lives in the human biliary

tract for 15 years or more. It has a flat, transparent, spatulate body; pointed anteriorly

and rounded posteriorly, 10 to 25 mm long and 3 to 5 mm broad. It discharges

eggs into the bile duct. The eggs are broadly ovoid, 30 µm by 15 µm with a yellowish

brown shell. It has an operculum at one pole and a small hook-like spine at the

.other

,The eggs passed in feces contain the ciliated miracida. They do not hatch in water

but only when ingested by suitable species of operculate snails, such as ,Parafossarulus

Bulimusor Alocinmaspecies. The miracidium develops through the sporocyst and

redia stages to become the lophocercus cercaria with a large fluted tail in about

weeks. The cercariae escape from the snail and swim about in water, waiting to ٣

get attached to the second intermediate host, suitable fresh-water fish of the carp

family. The cercariae shed their tails and encyst under the scales or in the flesh of

the fish to become, in about 3 weeks the metacercariae which are the infective stage

for humans. Infection occurs when such fish are eaten raw or inadequately processed

by human or other definitive hosts. Frozen, dried or pickled fish may act as source

of infection. Infection may also occur through fingers or cooking utensils contaminated

.with the metacercariae during preparation of the fish for cooking

The metacercariae excyst in the duodenum of the definitive host. The adolescaria

that come out enter the common bile duct through the ampulla of Vater and proceed

to the distal bile capillaries where they mature in about a month and assume the

.(adult form (Fig. 9.8

FIGURE 9.8: Life cycle of Clonorchis sinensis. 1. Adult fluke in biliary tract of humans or animals. 2. Eggs passed in stools reach water and are ingested by the first intermediate host snail. 3. Miracidium emerges from egg and penetrates into tissues of snail. 4. Sporocyst containing rediae. 5. Redia showing cercariae developing inside. 6. Cercariae leave the snail and swim about in water to infect the second intermediate host fish. 7. Encysted metacercaria develop in the muscles of fish. This is the infective form for .human or other definitive hosts

Pathogenicity

The migration of the larva up the bile duct induces desquamation, followed by hyperplasia and sometimes adenomatous changes. The smaller bile ducts undergo

cystic dilatation. The adult worm may cause obstruction and blockage of the common

.bile duct leading to cholangitis. Chronic infection may result in calculus formation

A few cases go on to biliary cirrhosis and portal hypertension. Some patients with chronic clonorchiasis tend to become biliary carriers of typhoid bacilli. Chronic .infection has also been linked with cholangiocarcinoma

Patients in the early stage have fever, epigastric pain, diarrhoea and tender hepatomegaly. This is followed by biliary colic, jaundice and progressive liver .enlargement. Many infections are asymptomatic

Diagnosis

The eggs may be demonstrated in feces or aspirated bile. They do not float in concentrated saline. Several serological tests have been described including

complement fixation and gel precipitation but extensive cross-reactions limit their

utility. Indirect haemagglutination with a saline extract of etherised worms has been

reported to be sensitive and specific. Intradermal allergic tests have also been

.described

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Treatment

Chemotherapy has not been very successful. Chloroquine and praziquantel have

been reported to be useful. Surgical intervention may become necessary in cases

.with obstructive jaundice

Prophylaxis

Proper cooking of fish can prevent the infection. Health education, proper disposal

.of feces and snail control measures help to limit the infection in endemic areas

OPISTHORCHIS SPECIES

Some species of Opisthorchis which resemble C. sinesiscan cause human .infection

O. felineus, the cat liver fluke which is common in Europe and the erstwhile Soviet

Union may infect humans. Infection is usually asymptomatic but may sometimes

cause liver disease resembling clonorchiasis. O. viverriniis common in Thailand where

.the civet cat is the reservoir host. Human infection is usually asymptomatic

FASCIOLA HEPATICA

Fasciola hepaticaor the sheep liver fluke was the first trematode to have been discovered

as early as 1379 by de Brie. It is the largest and most common liver fluke found

in humans, but its primary host is the sheep, and to a less extent cattle. It is worldwide

in distribution, being found mainly in sheep-rearing areas. It causes the economically

.important disease ‘liver rot’ in sheep

Morphology and Life Cycle

—The adult worm lives in the biliary tract of the definitive host for many years

about 5 years in sheep and 10 years in humans. It is a large leaf-shaped fleshy ,fluke

mm long and 15 mm broad, grey or brown in colour. It has a conical projection ٣٠

anteriorly and is rounded posteriorly. The eggs are large, ovoid, operculated, bile

stained and about 140 µm by 80 µm in size. They are laid in the biliary passages

and shed in feces. The embryo matures in water in about 10 days and the miracidium

escapes. It penetrates the tissues of intermediate host, snails of the genus .Lymnaea

In snail, the miracidium progresses through the sporocyst, the first and second

generation redia stages to become the cercariae in about 1 to 2 months. The cercariae

escape into the water and encyst on aquatic vegetation or blades of grass to become

metacercariae which can survive for long periods. Sheep, cattle or humans eating

watercress or other water vegetation containing the metacercaria become .infected

The metacercariae excyst in the duodenum and pierce the gut wall to enter the

peritoneal cavity. They penetrate the Glisson’s capsule, traverse the liver parenchyma

and reach the biliary passages, where they mature into the adult worms in about

.(months (Fig. 9.9 ٤-٣

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FIGURE 9.9B: Life cycle of Fasciola hepatica. 1. Adult in biliary tract of sheep

and humans. 2. Egg passed in stools reaches water. 3. Miracidium escapes

.and penetrates tissues of snail in which it develops successively into 4

Sporocyst and 5. Redia first generation and 6. Second generation. 7. Cercaria

released into water encysts on water plants to become 8. Metacercaria

which is infective to definite hosts by ingestion

FIGURE 9.9A

Pathogenicity

Fascioliasis differs from clonorchiasis in that F. hepaticais larger and so causes more

mechanical damage. In traversing the liver tissue it causes parenchymal injury. As

humans are not its primary host, it causes more severe inflammatory response. Some

larvae penetrate right through the liver and diaphragm ending up in the lung. Patients

present initially with fever, eosinophilia and tender hepatomegaly. Later they develop

a