A REVIEW ON: SNAIL FEVER

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Summary

Schistosomiasis is one of the deadly disease which ranks second only to malaria as the most common parasitic disease, killing an estimated 280,000 people each year. Parasites penetrate the skin during contact with freshwater containing contaminated snails. The larvae migrate to the blood vessels where they mate and produce eggs.Twenty million schistosomiasis sufferers develop severe and sometimes disfiguring disabilities from complications from the disease, including kidney disease, liver disease and bladder cancer. It is a parasitic disease carried by fresh water snails infected with one of the five varieties of the parasite Schistosoma. Schistosomiasis is transmitted by contact with contaminated fresh water (lakes and ponds, rivers, dams) inhabited by snails carrying the parasite. It only takes a few seconds for these worms to penetrate human skin. From the skin, the parasites get into the bloodstream and infect whole body. Urinary schistosomiasis causes scarring and tearing of the bladder and kidneys and can lead to bladder cancer. Microscopic identification of eggs in stool or urine is the most practical method for diagnosis. A single dose of praziquantel has been shown to reduce the severity of symptoms in those re-infected with the disease. As with other major parasitic diseases, there is ongoing and extensive research into developing a schistosomiasis vaccine that will prevent the parasite from completing its life cycle in humans.

Key words: Bilharzia, Bilharziosis, Snail fever

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Introduction

Schistosomiasis is a parasitic disease caused by several species of fluke of the genus schistosomiasis.[1] It is a parasitic disease carried by fresh water snails infected with one of the five varieties of the parasite Schistosoma. Found predominantly in tropical and sub-tropical climates, schistosomiasis infects 207 million people in 74 countries worldwide, with a vast majority of the burden occuring in Africa. Schistosomiasis ranks second only to malaria as the most common parasitic disease. Schistosomiasis is transmitted by contact with contaminated fresh water (lakes and ponds, rivers, dams) inhabited by snails carrying the parasite. Swimming, bathing, fishing and even domestic chores such as laundry and herding livestock can put people at risk of contracting the disease. Larvae emerge from the snails and swim in the water until they come into contact with an individual and penetrate the skin. Once inside the body, the larvae develop into male and female worms which pair up and live together in the blood vessels for years. Female worms release thousands of eggs which are passed out of the body in the urine and feces. If people urinate or defecate in bodies of freshwater, the eggs migrate to snails where they eventually hatch and begin the cycle again. Some Schistosoma eggs, however, remain trapped in the body and migrate to specific organs (depending on the type of parasite) where they can inflict major damage. Urinary schistosomiasis causes scarring and tearing of the bladder and kidneys and can lead to bladder cancer. Intestinal schistosomiasis develops slowly, causing abdominal bleeding; enlargement of the liver, lungs and spleen; and damage to the intestines. A major indicator of the disease is blood in the urine and/or feces. [2]

Potent Fact

Female long worms can lay 200 to 2,000 eggs per day over a five-year period. [3]

History

1798	The first clinical description of epidemic haematuria is credited to the French army surgeon A J Renoult in Napoleon's army in Egypt
1847	The 3rd most important schistosome is S. japonica that causes Katayama disease. It is an ancient disease described by Dairo Fujii.[4]
1851	Schistosomiasis was first recognized in the time of the Egyptian pharaohs. The worms that cause the disease were discovered in a hospital in Cairo by Theodor Bilharz, a German pathologist. The disease was originally named bilharziasis after him. [3]
1902	The Scot, Sir Patrick Manson, who was one of the founders of the London School of Tropical Medicine, first suggested the existence of 2 species of human Schistosoma
1908	The first doctor who described the entire disease cycle was Piraja da Silva .[5,6]
1910	The science of palaeoparasitology is generally regarded as beginning with the discovery of S. haematobium eggs in 20th dynasty (1250-1000BC) Egyptian mummies by the British scientist and Professor of Bacteriology at Cairo Medical School, Marc Ruffer.[7]

1913	Various Japanese workers identified the worm and elucidating the life cycle in the snail.[8]
1915	Robert Leiper, helminthologist to the London School of Tropical Medicine, to formerly identify the intestinal schistosome S.mansoni in 1915, the same year he elucidated the life cycle of S.haematobium in the snail.[9,10]
1950 -1990	The number of dams in the world increased from 5,000 to more than 36,000. There has been a corresponding increase in schistosomiasis, especially in sub-Saharan Africa. [3]
2000 -2003	843,000 people were officially infected with schistosomiasis. The areas along the Yangtze River, which often get flooded, seem to be where many of the people get infected. The area is ideal for the snail to live and breed.[4,11]

Table no. – 1 History of Snail fever

Disease Impact

- Schistosomiasis is the most deadly NTD, killing an estimated 280,000 people each year
- Twenty million schistosomiasis sufferers develop severe and sometimes disfiguring disabilities from complications from the disease, including kidney disease, liver disease and bladder cancer
- Children with chronic disease can suffer from anemia and malnutrition, which can contribute to lost days at school and pervasive learning disabilities.[2]

Prevalence

- 207 million people worldwide
- A majority of the burden occurs in Africa.[2]

Geographical distribution and epidemiology

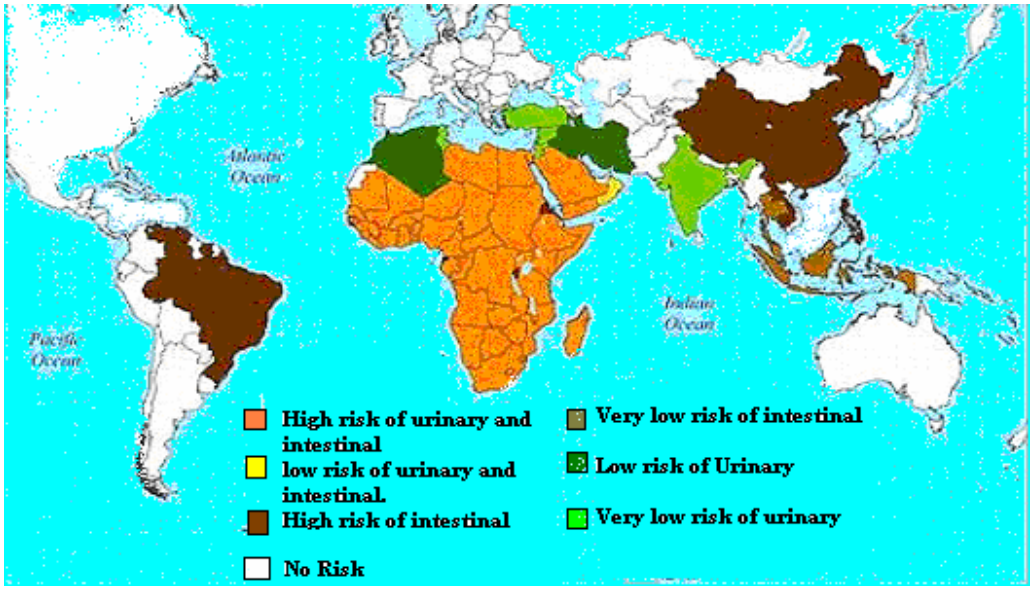

Figure no. 1 Geographical distribution and epidemiology

Quick Facts

- Found predominantly in tropical and sub-tropical climates
- Afflicts 207 million people in 74 countries worldwide
- Schistosomiasis is the most deadly NTD, killing an estimated 280,000 people each year
- A single dose of praziquantel has been shown to reduce the severity of symptoms in those re-infected with the disease. [2]

An estimated 779 million people are at risk of schistosomiasis, of whom 106 million (13.6%) live in irrigation schemes or in close proximity to large dam reservoirs.[12]

We present a systematic literature review and meta-analysis with the following objectives:

(1) To update at-risk populations of schistosomiasis and number of people infected in endemic countries

(2) To quantify the risk of water resources development and management on schistosomiasis.[13]

Using 35 datasets from 24 African studies, meta-analysis showed pooled random risk ratios of 2.4 and 2.6 for urinary and intestinal schistosomiasis, respectively, among people living adjacent to dam reservoirs. The risk ratio estimate for studies evaluating the effect of irrigation on urinary schistosomiasis was in the range 0.02-7.3 (summary estimate 1.1) and that on intestinal schistosomiasis in the range 0.49-23.0 (summary estimate 4.7). Geographic stratification showed important spatial differences, idiosyncratic to the type of water resources development. The development and management of water resources is an important risk factor for schistosomiasis and hence strategies to mitigate negative effects should be associated with underdeveloped countries and living near dam reservoirs.[14, 15]

Species –vise distribution [16, 17]

S. haematobium: Africa and Middle East: usually affects bladder diagnosed with urine examination.

S. intercalatum: central West Africa; uncommon.

S. japonicum: Southeast Asia and western Pacific countries; diagnose with stool examination.

S. mansoni: South America, Caribbean, Africa and Middle East; diagnose with stool examination.

S. mekongi: Southeast Asia; uncommon.

The disease is found in tropical countries in Africa, the Caribbean, eastern South America, southeast Asia and in the Middle East. Schistosoma mansoni is found in parts of South America and the Caribbean, Africa and the Middle East; S. haematobium in Africa and the Middle East; and S. japonicum in the Far East. S. mekongi and S. intercalatum are found locally in Southeast Asia and central West Africa, respectively.The disease is endemic to 74 countries, affecting an estimated 200 million people, half of whom live in Africa. A few countries have eradicated the disease and many more are working toward it. The World Health Organization is promoting these efforts. In some cases, urbanization, pollution and/or consequent destruction of snail habitat has reduced exposure, with a subsequent decrease in new infections. The most common way of getting schistosomiasis in developing countries is by wading or swimming in lakes, ponds and other bodies of water that are infested with the snails (usually of the Biomphalaria, Bulinus, or Oncomelania genus) that are the natural reservoirs of the Schistosoma pathogen.[1]

Life Cycle[19]

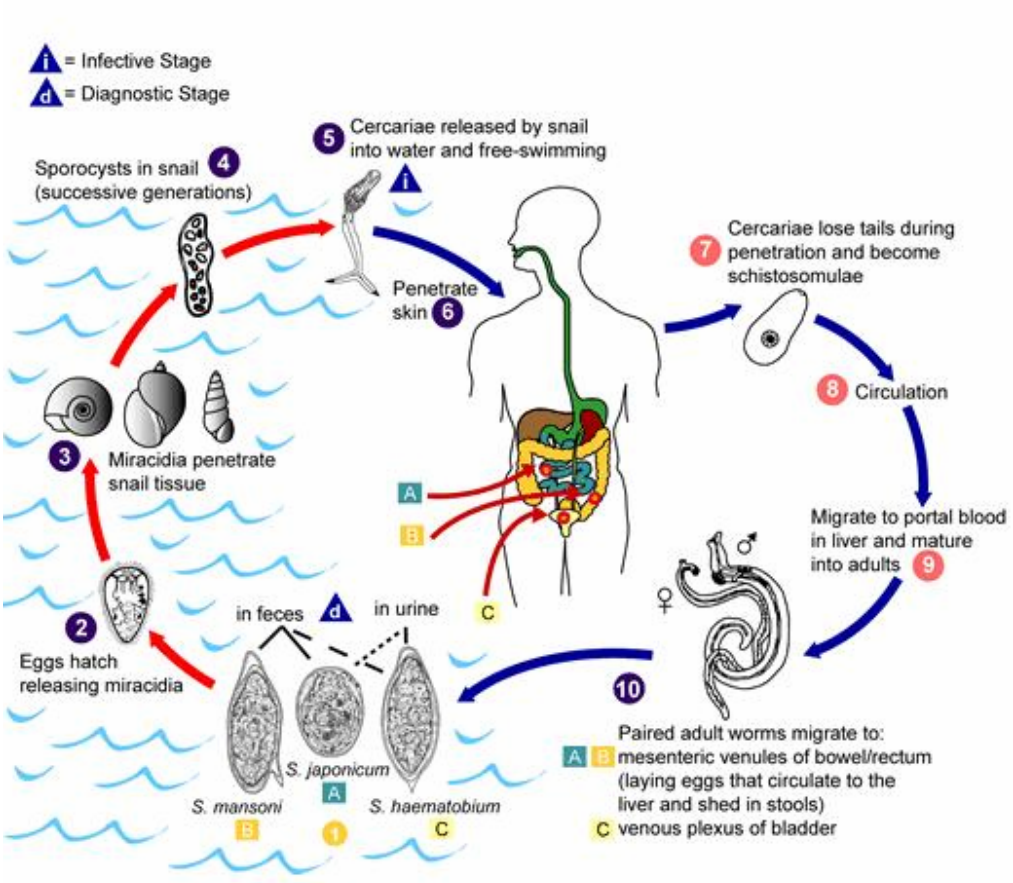

Figure no.-2 life cycle of Schistosomiasis

1. Eggs are eliminated with feces or urine.
2. Under optimal conditions the eggs hatch and release miracidia.
3. Eggs swims and penetrate specific snail intermediate hosts.
4. The stages in the snail include generations of sporocysts.
5. The production of cercariae.
6. Upon release from the snail, the infective cercariae swim; penetrate the skin of the human host.
7. And shed their forked tail, becoming schistosomulae.
8. The schistosomulae migrate through several tissues and stages to their residence in the veins.
9. The schistosomulae migrate through several tissues and stages to their residence in the veins.
10. Paired adult worms migrates to urine and feces

Transmission

Parasites penetrate the skin during contact with freshwater containing contaminated snails. The larvae migrate to the blood vessels where they mate and produce eggs. Some eggs travel to the bladder or intestines and are passed into the urine or stool. Others remain trapped in the body and cause damage to internal organs.[2, 19]

Pathophysiology

Acute schistosomiasis	Acute schistosomiasis (Katayama fever) is a systemic, serum sickness like illness that develops after several weeks in some, but not most, individuals with new schistosomal infections. It may correspond to the first cycle of egg deposition and is associated with marked peripheral eosinophilia and circulating immune complexes. It is most common with S japonicum and S mansoni infections and is most likely to occur in heavily infected individuals after primary infection[20]. Symptoms usually resolve over several weeks, but the syndrome can be fatal. Early treatment with cidal drugs may exacerbate this syndrome and necessitate concomitant glucocorticoid therapy. Tourists and travelers are most likely to present to EDs in this country with this syndrome; a history of contact with freshwater such as swimming, boating, rafting, or water skiing should be obtained. Mild maculopapular skin lesions may develop in acute infection within hours after exposure to cercariae. Significant dermatitis is rare with the major human schistosomal pathogens, probably because the invading and developing cercariae are minimally immunogenic. However, abortive human infection with schistosomal species that rely on other primary hosts may cause marked dermatitis or swimmer's itch. This self-limited process may recur more intensely with subsequent exposures to the same species.[21]
Chronic schistosomiasis	The pathology of chronic schistosomiasis, which is far more common than the acute form of the infection, results from egg-induced immune response, granuloma formation and associated fibrotic changes. Although cercarial and adult worms are minimally immunogenic, schistosomal eggs are highly immunogenic and induce vigorous circulating and local immune responses. (Eggs may require an intense immune response to aid their migration through the body.)Egg retention and granuloma formation in the bowel wall (usually S mansoni or S japonicum) may cause bloody diarrhea, cramping and, eventually, inflammatory colonic polyposis. Patients with heavy bowel wall involvement have an increased rate of recurrent salmonellal infection, generally with positive blood cultures and negative stool cultures. Unshed eggs, which are swept back to the portal circulation, lodge there and induce granulomatous reactions in the portal tracts. Heavy infestations are more likely to produce hepatic disease[22]. Eventually, severe periportal fibrosis in a characteristic pipestem pattern ("Symmer's pipestem fibrosis") may occur. Although hepatocellular function is spared, periportal fibrosis can lead to portal hypertension with the usual potential sequelae, including splenomegaly, ascites, esophageal variceal bleeding and development of portosystemic collaterals. Through these collaterals (or directly from the IVC in the case of bladder wall schistosomiasis), eggs can reach the pulmonary circulation. The resulting pulmonary granulomatosis and fibrosis can lead to pulmonary hypertension and frank cor pulmonale with a high mortality rate. Co-infection with hepatitis B or hepatitis C can accelerate hepatic dysfunction and raise the risk for hepatocellular carcinoma beyond that seen with hepatitis alone. In addition, gallbladder cancer may be associated with schistosomal infection. Egg retention and granuloma formation in the urinary tract (S haematobium) can lead to hematuria, dysuria, bladder polyps and ulcers and even obstructive uropathies. S haematobium infection is also associated with an increased rate of bladder cancer, usually squamous cell rather than transitional cell.[23]

Table no.-2 Pathophysiology

Figure no. - 3 Pathophysiology

Symptoms and Signs of Schistosomiasis

Above all, schistosomiasis is a chronic disease. Many infections are subclinically symptomatic, with mild anemia and malnutrition being common in endemic areas[24]. Acute schistosomiasis (Katayama's fever) may occur weeks after the initial infection, especially by S. mansoni and S. japonicum. Manifestations include:

- Abdominal pain
- Cough
- Diarrhea
- Eosinophilia extremely high eosinophil granulocyte (white blood cell) count.
- Fever
- Fatigue
- Hepatosplenomegaly the enlargement of both the liver and the spleen.
- Genital sores lesions that increase vulnerability to HIV infection. Lesions caused by Schistosomiasis may continue to be a problem after control of the Schistosomiasis infection itself. Early treatment, especially of children, which is relatively inexpensive, prevents formation of the sores.
- Skin symptoms: At the start of infection, mild itching and a papular dermatitis of the feet and other parts after swimming in polluted streams containing cercariae.[25]

Occasionally central nervous system lesions occur: cerebral granulomatous disease may be caused by ectopic S. japonicum eggs in the brain and granulomatous lesions around ectopic eggs in the spinal cord from S. mansoni and S. haematobium infections may result in a transverse myelitis with flaccid paraplegia.

Continuing infection may cause granulomatous reactions and fibrosis in the affected organs, which may result in manifestations that include:

- Colonic polyposis with bloody diarrhea (Schistosoma mansoni mostly)
- Portal hypertension with hematemesis and splenomegaly (S.mansoni, S. japonicum)

- Cystitis and ureteritis (S. haematobium) with hematuria, which can progress to bladder cancer;
- Pulmonary hypertension (S.mansoni, S. japonicum, more rarely S. haematobium)
- Glomerulonephritis; and central nervous system lesions.[26]

The urinary form of the disease is characterized by the presence of blood in the urine, which can lead to bladder cancer or kidney problems. The intestinal form of the disease is characterized by intermittent, bloody diarrhea, which can lead to serious complications of the liver and spleen. Those who get the disease are very weakened by it and are often unable to work. Within days of infection, people develop a rash or itchy skin. Fever, chills, cough and muscle aches can start within a month or two of infection. Most people have no symptoms during the early stages of infection. Infected individuals can contaminate their environment. The worm eggs in human excrement hatch on contact with water and release larvae. The tiny larvae must find a freshwater snail to survive[27]. Once inside the snail, the larvae divide several times and produce thousands of new parasites. The new parasites are excreted by the snails into the surrounding water. It only takes a few seconds for these worms to penetrate human skin. From the skin, the parasites get into the bloodstream. Within 30 to 45 days, they grow into long worms (12 to 16 millimeters in length). In intestinal disease, the worms live in the blood vessels that line the intestine. In urinary disease, they live in the blood vessels of the bladder. Only half of the eggs are excreted in feces or urine. The rest are trapped in the body tissues and do damage to vital organs. It is the eggs, not the worm, that damage the intestines, bladder and other organs.[28]

Laboratory Diagnosis

- Microscopic identification of parasite eggs in stool (S. mansoni or S. japonicum) or urine (S. haematobium).
- Serologic tests are useful to diagnose light infections where egg shedding may not be consistent and in travelers and others who have not had schistosomiasis previously. Antibody tests do not distinguish between past and current infection. Available test sensitivity and specificity vary, depending on the antigen preparation used and how the test is performed.[29]Microscopic identification of eggs in stool or urine is the most practical method for diagnosis. The stool exam is the more common of the two. For the measurement of eggs in the feces of presenting patients the scientific unit used is epg or eggs per gram. Stool examination should be performed when infection with S. mansoni or S. japonicum is suspected and urine examination should be performed if S. haematobium is suspected. Eggs can be present in the stool in infections with all Schistosoma species. The examination can be performed on a simple smear (1 to 2 mg of fecal material) [30]. Since eggs may be passed intermittently or in small amounts, their detection will be enhanced by repeated examinations and/or concentration procedures (such as the formalin-ethyl acetate technique). In addition, for field surveys and investigational purposes, the egg output can be quantified by using the Kato-Katz technique (20 to 50 mg of fecal material) or the technique. Eggs can be found in the urine in infections with S. japonicum and with S. intercalatum (recommended time for collection: between noon and 3 PM) [31]. Detection will be enhanced by centrifugation and examination of the sediment. Quantification is possible by using filtration through a nucleopore membrane of a standard volume of urine followed by egg counts on the membrane. Investigation of S. haematobium should also include a pelvic x-ray as bladder wall calcificaition is highly characteristic of chronic infection. Recently a field evaluation of a novel handheld microscope was undertaken in Uganda for the diagnosis of intestinal schistosomiasis by a team led by Dr. Russell Stothard who heads the Schistosomiasis Control Initiative at the Natural History Museum, London.[19] Photomicrography of bladder in S. hematobium infection, showing clusters of the parasite eggs with intense eosinophilia, Tissue biopsy (rectal biopsy for all species and biopsy of the bladder for S. haematobium) may demonstrate eggs when stool or urine examinations are negative.The eggs of S. haematobium are ellipsoidal with a terminal spine, S. mansoni eggs are also ellipsoidal but with a lateral spine, S. japonicum eggs are spheroidal with a small knob. Antibody detection can be useful in both clinical management and for epidemiologic surveys.[32]

Treatment

Schistosomiasis is readily treated using a single oral dose of the drug Praziquantel annually. As with other major parasitic diseases, there is ongoing and extensive research into developing a schistosomiasis vaccine that will prevent the parasite from completing its life cycle in humans. The World Health Organization has developed guidelines for community treatment of schistosomiasis based on the impact the disease has on children in endemic villages

- When a village reports more than 50 percent of children have blood in their urine, everyone in the village receives treatment.
- When 20 to 50 percent of children have bloody urine, only school-age children are treated.
- When less than 20 percent of children have symptoms, mass treatment is not implemented.[33]

The Bill & Melinda Gates Foundation has recently funded an operational research program the Schistosomiasis Consortium for Operational Research and Evaluation (SCORE) to answer strategic questions about how to move forward with schistosomiasis control and elimination. The focus of SCORE is on development of tools and evaluation of strategies for use in mass drug administration campaigns. Antimony has been used in the past to treat the disease. In low doses, this toxic metalloid bonds to sulfur atoms in enzymes used by the parasite and kills it without harming the host[34]. This treatment is not referred to in present-day peer-review scholarship; Praziquantel is universally used. Outside of the U.S., there is a second drug available for treating Schistosoma mansoni (exclusively) called Oxamniquine.Mirazid, an Egyptian drug, was under investigation for oral treatment of the disease up until 2005[35]. The efficacy of Praziquantel was proven to be about 8 times that of Mirazid and therefore it was not recommended as a suitable agent to control schistosomiasis. Experiments have shown medicinal castor oil as an oral anti-penetration agent to prevent schistosomiasis and that Praziquantel's effectiveness depended upon the vehicle used to administer the drug (e.g., Cremophor / Castor oil).[36]

Prevention

- Education campaigns about risks of getting infected by bathing in fresh water lakes and ponds
- Praziquantel is the primary form of treatment
- A single dose of praziquantel has been shown to reduce the severity of symptoms in cases of subsequent re-infection
- 200 million tablets have been donated by Merck KGaA for 2008-2017, but this is only 5% of the global need
- A schistosomiasis vaccine is currently in the early stages of development by Sabin's vaccine development team.[37]

Don't Drink the Water	Avoid swimming or wading in fresh water when traveling in countries where the disease is common. Drink safe water. Bath water should be heated for five minutes at 150 degrees. Water held in a storage tank for at least 48 hours should be safe for showering. Vigorous towel-drying after an accidental, brief water exposure may help prevent the parasite from penetrating the skin, but this method should not be relied upon to prevent exposure and disease.[38]
Eliminating or avoiding the snails	Prevention is best accomplished by eliminating the water-dwelling snails that are the natural reservoir of the disease. Acrolein, sulfate and niclosamide can be used for this purpose. Recent studies have suggested that snail populations can be

	controlled by the introduction or augmentation of existing crayfish populations; as with all ecological interventions, however, this technique must be approached with caution. In 1989, Aklilu Lemma and Legesse Wolde-Yohannes received the Right Livelihood Award for their research on the Sarcoca plant, as a preventative measure for the disease by controlling the snail. [39]
Prevention through good design	For many years from the 1950s onwards, civil engineers built vast dam and irrigation schemes, oblivious to the fact that they would cause a massive rise in water-borne infections from schistosomiasis. The detailed specifications laid out in various UN documents since the 1950s could have minimized this problem. Irrigation schemes can be designed to make it hard for the snails to colonize the water and to reduce the contact with the local population. [40,41]

Table no. – 3 Prevention

- **Conclusion:**

Snail fever is a deadly disease causing many complications including liver and kidney damage , anemia and malnutrition, and even cancer. A single dose of praziquantel has been shown to reduce the severity of symptoms in those re-infected with the disease.Prevention is best accomplished by eliminating the water-dwelling snails that are the natural reservoir of the disease. Acrolein, sulfate and niclosamide can be used for this purpose.Education campaigns about risks of getting infected by bathing in fresh water lakes and ponds will also be helpful. Swimming or wading in fresh water when traveling in countries where the disease is common must be avoided. Experiments have shown medicinal castor oil as an oral anti-penetration agent to prevent schistosomiasis and that Praziquantel's effectiveness depended upon the vehicle used to administer the drug.

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