CHAPTER 1

INTRODUCTION

1.1 General Introduction

Dermatitis is a form of skin rash or inflammation caused by an allergic reaction to chemicals (contact dermatitis) or a cutaneous inflammatory response associated with the penetration of the skin by cercariae, the free-swimming larval stage of non-human schistosomes (cercarial dermatitis or schistosome dermatitis) (Hoeffler, 1974).

Contact Dermatitis is an inflammatory condition caused by direct skin exposure to chemical with or without a requirement for ultraviolet light. There are two distinct types of contact dermatitis: irritant contact dermatitis (ICD) and allergic contact dermatitis (ACD) (Akhavan and Cohen, 2003). Sensitivity of the skin varies from individual to individual, and may vary in the same individual from time to time. ICD is an inflammatory reaction caused by chemical that result in direct cellular injury on the skin. The majority of cases of ICD are associated with soaps, detergents, solvents, acids, and alkali. There are two categories of ICD: acute reactions that develop within minutes to hours after exposure to very strong irritant chemical and cumulative reactions, which follow repeated contact with milder irritants. Since ICD is essentially an injury, individuals will develop an eruption when certain threshold of chemical concentration and frequency of exposure are exceeded (Akhavan and Cohen, 2003).

Whereas ACD, is an eczematous disease mediated through immune mechanisms and are acquired skin disorders that occur at sites of contact with small chemical haptens in individuals who have been previously exposed to, and immunologically sensitized to, a particular chemical. In contrast to ICD, only a small percentage of the population develops an eruption when exposed to chemical causing ACD. The most common chemical allergens causing this condition include nickel sulphate, found in everything from keys to clothing, as well as the pentadecycatechols, the active moiety in plants of the Rhus Family, which include poison ivy, poison oaks and poison sumac (Cohen, 1996). Active skin diseases, such as ICD which disturb the integrity of the body's epidermal barrier can be predisposing factors for ACD, that allow easier access of potential chemical allergens to the immune system (Akhavan and Cohen, 2003).

Cercarial dermatitis, commonly known as sawah itch in Malaysia, Swimmer's itch in North America, Europe and Australia and Kabura or Koganbyo in Japan. It is a skin rash caused by an allergic reaction to infection by larval trematode parasites of nonhuman schistosomes, mainly of birds and mammals. The schistosome cercariae of birds or wild mammals may accidentally come in contact with human skin, may penetrate human skin, but then die. These microscopic parasites are released from infected snails to swim in fresh and salt water, such as lakes, ponds, and oceans where swimming and other recreational activities are common. Cercarial dermatitis infections are found throughout the world. This can give rise to an allergic condition resulting in rashes. This reaction is caused by the release of antigens by the dying cercariae parasites in the skin. The species of schistosomes that occasionally infect man causing cercarial dermatitis are given in Table 1.1.

Table 1.1 Species of Schistosomes Causing Occasional Cercarial Dermatitis in Man (Adapted and Modified from Kumar and de Burbure, 1986)

Types	Geographical Locations	Definitive Hosts	References/Authors
Birds schistosomes			
1. *Austrobilharzia variglandis*	North America and Hawaii.	Parasites of waterfowl	Mileer & Northrup, 1926
2. *Microbilharzia sp.*	East Coast U.S.A. and Hawaii.	Parasites of gulls, ducks and marine wildfowl	Price, 1929
3. *Trichobilharzia ocellata*	Europe, Asia and North America.	Parasites of ducks	(La Valette, 1855) Brumpt, 1931
4. *Trichobilharzia physellae*	North America and Japan	Parasites of ducks	(Talbot, 1936) McMullen & Beaver, 1945
5. *Trichobilharzia stagnicolae*	The Great Lakes area of America.	Parasite of ducks	(Talbot, 1936) McMullen & Beaver, 1945
6. *Gigantobilharzia sp.*	-	Parasites of passerine birds.	Odhner, 1910
7. *Trichobilharzia brevis*	South East Asia	Parasites of birds	Basch, 1966
8. *Peseudobilharziella ionchurae*	Sabah, Malaysia	Parasites of birds	Fischthal & Kuntzm, 1973
Mammal – Ruminant schistosomes			
1. *Schistosoma bovis*	Africa, parts of Southern Europe and the Middle East	Normally infecting cattle, sheep and goats	(Sonsino, 1876) Blanchard 1895
2. *Schistosoma mattheei*	Central and Southern Africa	Normally infecting cattle, sheep and goats	Veglie & LeRoux, 1929
3. *Schistosoma margrebowiei*	Southern and Central Africa	Normally infecting antelope, buffalo and waterbuck	LeRoux, 1933
4. *Schistosoma curassoni*	West Africa	Normally infecting domestic ruminants has been reported, although this is disputed.	Brumpt, 1931
5. *Schistosoma spindale*	South East Asia	Ruminants, particularly cattle and water buffalo	Montgomery, 1906
6. *Schistosoma nasale*	South and South East Asia	Buffaloes and cattle (rarely sheep, goat or horse)	Rao, 1933
7. *Schistosoma incognitum*	India, Thailand, Indonesia, Malaysia.	Pig, dog, rodents	Chandler, 1926
Mammal – Rodent schistosome			
1. *Schistosoma rodhain i*	Parts of Central Africa	Normally infecting rodents & carnivores	Brumpt, 1931
2. *Heterobilharzia Americana*	Louisiana, U.S.A.	Raccoons and other mammals	Price, 1929
3. *Schistosomatium douhitti*	North America	Rodents	(Cort, 1915) Price, 1929

1.2 Diseases caused by schistosomes

The blood flukes of the genus *Schistosoma*, causes schistosomiasis or bilharziasis, one of the major diseases of mankind in tropical and subtropical countries. Schistosomiasis is endemic in 74 countries of the world (Shah and Agrawal, 1990). Vesical schistosomiasis, intestinal schistosomiasis, Asiatic schistosomiasis (Katayama disease) and cercarial dermatitis are the distinct clinical forms of schistosomiasis caused by different schistosome species. The majority of schistosomes caused zoonotic diseases involving either man or animal as reservoir hosts (Shah and Agrawal, 1990).

A literature search is done on diseases caused by schistosomes worldwide and in particular in paddy-growing countries of Asia. There are reports of schistosomiasis of man in the Southeast Asian countries of Indonesia, Philippines, Laos, Cambodia and Thailand, *Schistosoma japonicum* in Indonesia (Oemijati, 1976, Sudomo 1984, Hadidjaja, 1984, Harinasuta, 1984 and Izhar et al, 2002) and Philippines (Santos, 1976, Cabrera, et al, 1978, Harinasuta, 1984, Woodruff et al, 1987 and Herrin, 1986), *Schistosoma mekongi* in Laos (Kitikoon, et al, 1975, Woodruff et al, 1987 and Harinasuta, 1984) and Cambodia (Harinasuta, 1984), *Schistosoma japonicum*-like schistosome in Thailand (Harinasuta, 1984) and in Malaysia (Greer and Anuar, 1984, Harinasuta, 1984, Greer and Ow-Yang, 1985 and Woodruff et al, 1987), *Schistosoma sinensium* in Thailand (Baidikul et al, 1984 and Greer, Kitikoon and Lohachit, 1989) and *Schistosoma malayensis* in Malaysia (Greer et al, 1989, Shekhar and Pathmanathan, 1992a and Shekhar and Pathmanathan, 1992b). However we are only able to locate two published information on cercarial

dermatitis of man caused by animal schitosomes outside of Malaysia, in Assam by Narain, Mahanta, Dutta and Dutta (1994) and in Thailand by Kullavanijaya and Wongwaisayawan (1993). Most of the studies on cercarial dermatitis in paddy fields are from Malaysia (see Section 1.5 Introduction). The paucity of information from other Asian countries could be due to the records being published in their respective native languages and hence not available.

Schistosome cercarial dermatitis is an allergic syndrome in man and it is caused by the cercariae of non-human schistosomes (mammalian and avian species of blood flukes), which do not mature in the human host (Shah and Agrawal, 1990). It was Cort (1928) who first drew attention to the fact that the cercariae of birds and mammalian schistosomes, on contact with human skin, produces skin eruptions which leads to the development of dermatitis. In 1949 Oliver showed that cercariae of the non-human schistosome, *Trichobilharzia ocellata* can penetrate the skin causing papular eruptions in man. Olivier (1949) and Macfarlane (1949) considered the swimmer's itch as a sensitisation phenomenon that becomes more severe on repeated exposures to the invading cercariae (Shah and Agrawal, 1990).

Three major epidemiological types of schistosome dermatitis are recognized:

i) Dermal schistosomiasis caused by cercariae of birds of freshwater origin, which is acquired by persons swimming in fresh water lakes contaminated with the cercariae of avian schistosomes. The fresh water molluscs of the species *Lymnae, Stagnicola, Planorbis, Chilina* and *Polypylis* serve as the

intermediate hosts. The cercariae of avian schistosomes causing dermatitis are *Trichobilharzia* Skrjabin and Zakharow, 1920, *Gigantobilharzia* Odhner, 1910 and *Orientobilharzia* Dutt and Srivastava, 1955 (see Shah and Agrawal, 1990).

ii) Dermal schistosomiasis caused by cercariae of birds of saltwater origin, which is acquired by persons swimming in the seawater beaches with cercariae of avian schistosomes (*Microbilharzia* Price, 1929 and *Gigantobilharzia* Odhner, 1910). The marine molluscs are the intermediate host and release the cercariae which cause the infection (Shah and Agrawal, 1990)

iii) Dermal schistosomiasis caused by cercariae of non-human mammals, it is the result of the penetration of the human skin by *Schistosoma* Weinland, 1858 cercariae, which do not develop beyond schistosomula stage in the human. Examples of this form of dermal schistosomiasis are dermatitis caused by the cercariae of *S. spindale* Montgomery, 1906 affecting paddy farmers in Malaysia and Thailand, *S. bovis* Sonsino, 1876 (Blanchard 1895) causing dermatitis in Italy and *Orientobilharzia turkestanicum* Skrjabin, 1913 in Iran and Thailand (Shah and Agrawal, 1990).

1.3 Aetiology and Characteristics of Cercarial Dermatitis

Cercarial dermatitis manifests initially as itching accompanied by burning sensations, followed by the macular, papular and postural eruptions and eventually a severe dermatitis lasting for number of days. Initial exposure of the host to the non-human schistosome cercariae leads to a mild reaction but repeated exposures would result in a more severe reaction. A local anaphylaxis and cell mediated toxicity is thought to be responsible for this reaction (Shah and Agrawal, 1990).

Capron et al. (1982) has demonstrated that this reaction is associated with reagin like skin sensitizing antibodies in the serum. It has been further shown that both immediate and delayed hypersensitivity play important roles in the manifestations of schistosomal dermatitis. Within 30 minutes of exposure, the immediate hypersensitivity reveals itself in the form of prutitis (Shah and Agrawal, 1990). The chances of the development of skin lesions rise with an increase in the number of cercariae which die or are killed in the skin (Standen, 1953; Malek, 1980). This is followed by the development of small macules which subside within 10 hours of initial exposure (Shah and Agrawal, 1990). Most of the enzymes of the cercariae are secreted immediately on penetration through the outer layer of the skin (Standen, 1953; Malek, 1980). Cercarial secretions and excretions produce immunologic and toxic reactions. Damage due to penetration and movement of cercariae is believed to be highly localized (Bruce *et al*, 1970; Malek 1980). While penetrating the skin of different hosts a number of cercariae die, the number of dying cercariae depends on the degree of susceptibility of the host (Malek 1980).

The delayed hypersensitivity is highly noticeable in repeated exposures to the cercariae and manifests itself in the form of large papules within 6-15 hours of exposure. It is usually accompanied by the erythema, oedema and intense pruritis. Delayed hypersensitivity is species specific and is only seen with the species that had led to the initial reaction (Shah and Agrawal, 1990).

However, the parasites are limited to the epidermis layer, and are not found below the stratum germinativum. By 52 hours after the initial penetration by the cercariae, the cercariae are completely destroyed and the tunnel in which the cercariae rested is filled with exudates, leukocytes, lymphocytes, and an amorphous eosinophilic mass. The entire dermis shows much oedema, indicative of a well-marked inflammatory response. The marked erythema and even large urticarial wheals are produced in some individuals as a result of a strong allergic response of the individuals. Repair starts about 70 to 100 hours and is virtually complete by the fifth day. After the papules have disappeared some melanin-pigmented areas may remain. However, in most cases rubbing or scratching complicates the course of the dermatitis which cause the vesicle ruptures, and becomes pustular where secondarily infection occurs. In such cases the repair process is delayed a few more days (Malek, 1980).

1.4 The Life Cycle of Schistosome

The schistosomes are trematodes of the Family Schistosomatidae. There is no redia stage in the life cycle and all stages lack a muscular pharynx. The female adults produce non-operculated eggs. Both sexes have oral and ventral suckers. The male clasps the female in a longitudinal 'schist' or gynaecophoric canal so that the pair assume a nematode, worm-like shape ideally suited to live in a minor vessel of the portal or vesicular blood systems of the definitive, vertebrate host (Sturrock, 1993).

The general life cycle is shown in Figure 1.1. Egg laid in the blood vessel contains a fully developed larva (miracidium). These eggs could be lodged against the walls with the aid of spines and adhesive exudates. Lytic enzymes secreted by the miracidium diffuses through micropores in the egg shell to assist penetration of the blood vessel walls, a process possibly aided by phagocytic cells of the host's immune system (Doenhoeff *et al*, 1978; Sturrock, 1993). The operculated egg hatches when it reaches fresh/salt water, releasing miracidium. To develop further this larva, must penetrate the soft parts of a compatible fresh/salt water snail, the intermediate host, where it will be transformed into a primary sporocyst, usually near the point of penetration. Each primary sporocyst eventually produces a number of secondary sporocysts that migrate to the digestive gland ('liver') of the snail. In the digestive gland the secondary sporocyst grow and mature before producing large numbers of cercariae which break out of the snail tissues into the water. The cycle is continued if cercariae penetrates the unbroken skin of the definitive host and changes into a schistosomulum and enter the specific organ depending on the species and

grows into a mature adult. The cycle is completed with the pairing of the young male and female adults which then migrate against the blood flow of the hepatic portal system to the mesenteric or vesical veins, depending on the species of schistosomes (Sturrock, 1993).

In the case of cercarial dermatitis the schistosome cercariae penetrate man (non-definitive host) but die in the skin and are limited to the epidermal layer and are not found below the stratum germinativum. It is essentially a sensitization phenomenon (Margono, 1968).

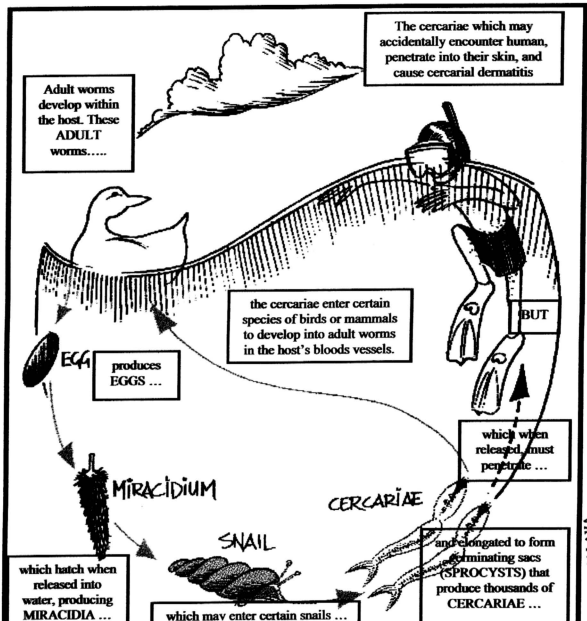

Figure 1.1: General Life Cycle of Schistosome causing (Cercarial) Dermatitis (adapted from EQC Bulletin December 1999)

1.5 Cercarial Dermatitis in Malaysia

Cercarial dermatitis is commonly known as the "sawah itch" because of its occurrence in paddy fields (sawah) and is found only in snail-infested paddy fields. In Malaysia cercarial dermatitis is an important cause of economic loss as many paddy fields are left uncultivated due to the presence of the parasite in the water (Inder Singh *et al*, 1997).

Buckley (1938) reported the first documented case of cercarial dermatitis in Malaysia in 1938. A skin infection called "sawah itch" has been known in Negeri Sembilan for some years, where it has been recorded from widely distributed areas in this state and also from the rice-fields adjoining the Tampin-Melaka road (Buckley, 1938). It was associated with paddy-cultivation and the disease is especially prevalent during the periods when the soil is being ploughed or "chankolled" prior to planting with rice seedlings, when the paddy field farmers spend hours each day with their legs submerged in the mud and water of the "sawah". The skin infection causes itching only in the ankles and legs and rarely on the back of hands and never anywhere else. The irritation dies down if the farmer does not re-enter the "sawah" on succeeding days but constant irritation would occur if succeeding re-entering the "sawah" occurs. It has been found that the cercarial dermatitis is caused by the cercariae of *S. spindale* (see Buckley, 1938).

In 1953 Sandosham reported the presence of dermatitis-producing cercariae in Malayan rice fields which led to the investigation by Basch in 1966. Basch found that cercarial dermatitis was localized in distribution in Malaya: although there were large areas of rice fields in western Selangor and in Kedah, dermatitis was unknown in these areas, and only occurred in the Kuala Pilah area. Two types of cercariae were identified: *Trichobilharzia brevis*, Basch, 1966 and *S. spindale* (Basch, 1966).

Sandosham and Lie (1969) reported that more than 30 species of Schistosomes cercariae are capable of causing cercarial dermatitis in man around the world. In Malaysia only two species have been shown to cause cercarial dermatitis namely *T. brevis* and *S. spindale* (Buckley, 1938: Sandosham, 1953, Basch, 1966; Krisnasamy *et al*, 1995). Sandosham and Lie (1969) believed that cercariae of other species may also be involved in causing cercarial dermatitis in Malaysia, but no systematic work was made to demonstrate this (Krisnasamy *et al*, 1995). Krisnasamy *et al*, (1995) implicated *S. spindale* as the only causative agent causing cercarial dermatitis among the paddy field farmers in the outbreak in the Malay village in Labu but the species might likely to be the cercariae of *Schistosoma nasale*, Rao, 1953. The cercariae was identified as such because of the presence of ova in the nasal scrapings from buffalo in this area (Krisnasamy *et al*, 1995). The intermediate host for *S. spindale* is the snail, *Indoplanorbis exustus*, whereas the intermediate host for *T. brevis* is the snail, *Lymnaea rubinosa*.

Schistosoma spindale was found to be the parasite of goat, *Capra hircus* and water buffalo, *Bubalus bubalis* (Krisnasamy *et al*, 1991), as well as in the paddy field rat, *Bandicota indica* (Inder Singh *et al*, 1992; Inder Singh *et al*, 1997). The goat and the Bandicoot rat were recorded as new hosts of the *S. spindale* in this country (Inder Singh, *et al*, 1997). Eggs of *T. brevis* were found in the droppings of adult ducks brought in to the Kuala Pilah market (Basch, 1966).

1.6 Objectives of Study

The main objectives of this study are to determine the occurrence and the causes of dermatitis amongst paddy field farmers in Kelantan where an outbreak of dermatitis had occurred.

To achieve the objectives, the following aspects are investigated:

1. Occurrence of dermatitis: to determine whether it is specific to paddy field farmers

2. Causes of dermatitis: to determine whether the dermatitis is caused by chemicals (fertilizers or pesticides) or by cercariae of non-human schistosomes.

The impact of dermatitis among the paddy field farmers was also evaluated by a visit to the area to determine if there were any changes in occupation and land-use in the infected villages.