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I INTRODUCTION

I.1 FILARIASIS

The perfectly wholesome existence of mankind in this hostile world is often swayed by a bewildering array of infectious agents which invade, persist and propagate in the human body by virtue of their ingenious evasive strategies that result in severe ailments. The incidence of most of the infectious diseases are closely linked with poverty, inadequate health services, lack of safe water supply and poor sanitation. Their spread and recurrence are further favoured by low housing standard and the adverse climate in the tropics, where three quarters of the world population live. About half a billion people world wide are now infected with one or more of the tropical diseases such as malaria, schistosomiasis, filariasis, trypanosomiasis, leishmaniasis and leprosy [1].

Filariasis is a debilitating infectious disease of great public health importance in the tropics, afflicting more than 100 million people all over the world [1]. A cure for this disease has been elusive from any means. But the general paucity of knowledge on the causals, lack of early diagnostic kits, lack of drugs or vaccines are the bottle
necks for the control of filariasis. Impetus towards investigations on the fundamental and applied aspects of filariasis, employed throughout the world in coordination with WHO's special programme on Tropical Diseases Research may together contribute to better means for the global elimination of the scourge from this planet.

I.1.1 Epidemiology

Filariasis is endemic in many tropical and subtropical countries and the incidence is high in Africa, Asia, parts of Latin America, Indonesia and East Mediterranean regions (Box 1) [2-4]. About 985 million people are estimated to be at the risk of infection and more than 107.6 million to be infected with various filariases, which remain as a scourge in 76 countries [1,4]. India is highly endemic to filariasis (Box 2) and barring a few ancient records, the relevant epidemiological information is available only from the beginning of this century [5,6]. There were 14 million infected people in 1980 [7] which increased to 30 million in 1990 [1]. Due to thickly populated habitation coupled with poor sanitation and low housing standard, every third person in India faces the risk of exposure to filarial infection [6,8]. Kerala, a coastal state of south-west India, where the present work carried
Box 1

Distribution of the lymphatic filariasis

Wuchereria bancrofti

Brugia malayi

B. timori
Box 2

Distribution of lymphatic filariasis in India

Filaria map of India (1958) (Indian Council of Medical Research, 1971).
- AREA SURVEYED: *W. bancrofti*
- AREA SURVEYED: *B. malayi*
- AREA KNOWN TO BE FILARIOUS
Box 3

Map of Kerala showing endemic regions of filariasis

(Areas with Bancrofti infection)

(Areas with Malayi infection)

(Areas with Brin infections)

(Based on N.F.C.P surveys)
out is one of the world's high endemic belts of lymphatic filariasis (Box 3) [8,9].

I.1.2 Filarial parasites

The occurrence of lymphatic filariasis was described as early as in 16th century [10,11]. But the cause was attributed to the filarial parasite only in the second half of the 19th century [11,12]. Filariae form a group of long thread-like, insect vector-borne nematode parasites, infecting virtually all vertebrate species including man. Of the many species of filariids, only eight are known to infect man. Wuchereria bancrofti, Brugia malayi and B. timori are the three lymph dwelling filariids causing lymphatic filariasis in 90 million people [1,4]. Onchocerca volvulus, living in subcutaneous nodules, elicit painful dermatitis and ocular damage afflicting an estimated 18 million people [1], is a leading cause of blindness in the tropics [13]. The other four filarial species, Loa loa, Dipetalonema perstans, D. streptocerca and Mansonella ozzardi cause relatively benign infections [4,11].

I.1.2.1 Life cycle

All filariids have similar life cycle. A typical life cycle of a representative filariid, W. bancrofti is
Box 4

Life cycle of *Wuchereria bancrofti*
shown in the Box 4 [14]. The adult worms live in the lymphatic vessels, body cavities or skin of the vertebrate host. The female worms are ovoviviparous, produce large number of prelarval young ones called microfilaria (mf). These circulate in blood or tissues until ingested by the hematophagous vector in which the mf pass through three stages of development to reach the infective stage (L3) in 12-14 days, and transmitted into new host during the subsequent blood meal. The arthropod host is necessary for cyclical development and the mf circulating in the blood are unable to cause infection or develop into adult. The L3 find their way into specific niches in the definitive host, and develop into mature worms in about 8 to 12 months [12,15]. Mature adults often live for years while mf survive only for months. Thus filarial worms of several developmental stages can be present simultaneously in a single host living in an endemic area where transmission occurs continuously [16].

I.1.2.2 Transmission

The transmission of filariasis from one host to another by insects, which was accidentally discovered by Patrick Manson [11,12] synchronizes with the periodic rhythm of the mf and blood feeding habit of insect vectors. Different filarial species are transmitted by different
vectors. *W. bancrofti* which causes bancroftian filariasis is transmitted by mosquitoes mainly of *Culex*, *Aedes* and *Anopheles* species [17-19]. *B. malayi* and *B. timori* which cause brugian filariasis are transmitted by *Anopheles* and *Mansonii* mosquitoes [4,19]. *O. volvulus* which causes onchocerciasis is transmitted by *Simulium* black flies [19]. The epidemiological patterns of filarial infection/transmission are determined by the local vector bionomics, vector-parasite relationship, flight range, life span and parasite yield characteristics of vectors [19]. However, most natural infections are acquired over a period of weeks to months by repeated exposure to small numbers of L3 (trickle infection) [20], but susceptibility of the hosts is the other determining factor in their development.

**I.1.3 Aetiology**

**I.1.3.1 Susceptibility to infection**

Man is known to be a permissive host of eight filarial species. But the epidemiological studies in areas where filariasis is endemic have revealed their differential susceptibility to infection both within the entire population as well as within families [20,21].

*Endemic normal* is the most successful proportion of a holoendemic population who remain amicrofilaraemic and
without any clinical evidence of diseases for decades [20,22,23].

**Tropical pulmonary eosinophilia** (TPE) occurs in a minority of amicrofilaraemic endemic individuals who become allergically hypersensitive to parasite antigens is characterized by asthmatic attacks and chronic lung fibrosis [22-25].

**Filarial patients** are the other most susceptible group of endemic population and remain fully permissive to filarial infection within whom the L3 invade, grow and develop into adults.

**Asymptomatic microfilaraemia** is a state in which the infected people are exclusively devoid of any clinical manifestations for years, but remain as carriers, the most vulnerable group who transmit the disease intermittently among the population. Some of them elicit lymphatic inflammation or lymphangitis commonly called as filarial fever [22].

**Symptomatic patients** produce the diverse clinical manifestations of chronic filarial infection.

### I.1.3.2 Disease

The chronic stages of lymphatic filariasis are characterized by the various irreversible manifestations [22]. In general, the clinical symptoms caused by Brugian
and Bancroftian filariasis are common except for milder difference [22,26,27].

**Hydrocoele** is a swelling of the peritoneal lining that surrounds testicles leads to lymphatic blockade in the retroperitoneal areas resulting in the accumulation of hydrocoele fluid in this closed sac leading to enlargement of the scrotum [22,28].

**Elephantiasis**, the bulky solid enlargement of legs, arms, breasts or external genitalia is the most common disease of lymphatic filariasis [22,29]. This morbid state is formed only in tissues which have become persistently oedematous first as pitting and then as nonpitting oedema with loss of skin elasticity and fibrosis, resulting in anatomical and functional blockade of lymphatics of these extremities [22,29,30]. Lack of personal hygiene and cleanliness may lead to secondary bacterial or fungal infection in patients resulting in the formation of carbuncles and open sores generally giving a repulsive appearance to the elephantoid organs [22].

**Chyluria** is a chronic state characterized by the excretion of chyle in the urine. This is caused by the blockade of retroperitoneal lymph nodes below the cisterna chyli, resulting in the efflux of intestinal lymph directly into the renal lymphatics, producing a milky urine. The condition is painless but large amount of nutrients is
excreted leading to weight loss or even death [22].

I.1.3.3 Pathogenesis

Although the diverse manifestations of lymphatic filariasis are well described, the mechanism underlying the pathogenesis is poorly understood. Three main phases of the disease have been identified [22] as follows:-

**Incubation phase:** Normally asymptomatic, begins with the invasion of L3 and lasts until the L3 attain maturity in the definitive host.

**Inflammation phase:** Characterized by mild intermittent fever, pain and inflammation in the joints of extremities, starts when the mature female commences releasing mf.

**Obstructive phase:** Marked by blockade of different lymphatic vessels leading to diverse obstructive lesions is characterized by chronic filarial morbidities that develop years after repeated acute attacks.

Simple physical blockade by the adult filariae is not the only cause but some factors contributed by the living and/or dead worms coupled with the interaction of host's immune effector mechanisms may be responsible for
lymph drainage malfunction [22]. Instead, other factors such as changes in the texture of lymphatic endothelium [22], the major histocompatibility complex (MHC) restricted antigen presentation of host's immune system [22,31,32], different anatomical habitats of parasites [22,27] and other environmental factors [22] may also have their own contributions in the pathogenesis of filariasis. The evidences are meagre to explain any transplacental transfer of infection from an infected mother to the offsprings [33-35].

I.1.4 Immunological aspects

I.1.4.1 Immune response

Patients with all forms of lymphatic filariasis show both humoral and cell mediated immune responses. Increased antifilarial antibody production has been observed on infection with various filarial species [36-38]. Filarial antigen specific IgG, IgM and IgE antibodies [39] and recognition of parasite antigens by different IgG subclasses with respect to various clinical status have been determined [40,41]. Further, a significant correlation of antifilarial antibodies to developmental stages have been noted [42,43]. Similarly, cell mediated immune response have also been observed in filarial infection involving macrophages
[44,45] and B and T lymphocytes [46-48]. Promotion of adherence of macrophages and lymphocytes to mf and L3 of *B. malayi* by the monoclonal antibodies produced against the surface antigens of the respective larvae have been noted [49,50]. Besides that, production of lymphokines [48,51,52] including interleukin [47,53] has also been demonstrated.

I.1.4.2 Immunopathology

Although there is immune response against the filarial parasite, there is evidence to show definite immunological correlations in different groups of patients. Despite the TPE patients, who are extremely hypersensitive to all filarial antigens [22,24,54], show elevated levels of antifilarial antibodies of all classes, markedly IgE, the patients both symptomatic as well as asymptomatic showed low humoral and cell mediated immune responses [39,55,56]. The hyporesponsiveness is apparently limited to filarial antigens [55-58]. A relatively lower antibody response as an element of specific humoral immunosuppression was observed in microfilaraemic patients [57], while an elevated total and specific IgE antibodies and IgE mediated allergic reactions were also observed in patients [59,60]. Lymphocytes studied *in vitro* showed little response to adult and mf antigens in both bancroftian and brugian filarial patients [55-58,61,62]. Studies on onchocerciasis [63-65]
and with animal models [65-67] have further substantiated the findings of antigen specific immunosuppression in filariasis.

Such unresponsiveness occurs not because the patients failed to become sensitized to filarial antigens, but because various modulatory mechanisms develop which specifically suppress response to antigens. The mechanisms described include, serum suppressor factors (circulating antigens) [62,68], T lymphocyte suppression [65] and parasite specific T cell anergy [46] that develop following a transient, initial phase of vigorous responsiveness to parasite antigens [66,69]. But these abnormalities are thought to revert to normal after treatment with DEC [70].

I.1.4.3 Protective immunity

The endemic normals generally show specific cellular as well as humoral immune response to filarial antigens [20,23,71-73]. This indicates the development of an acquired immunity to filarial infection in an endemic population exposed to mosquito bite and hence to the invasion of L3. But the studies on protective immunity in human population is hampered by the difficulties in distinguishing the uninfected individuals who are truly immune and the infected individuals who are harbouring undetectable (occult) infection [20,71,72]. However, a clear
picture on this may be useful to formulate means to develop protective immunity to filarial infection.

I.1.4.4 Immunoevasion

Despite the highly evolved human immune effector mechanisms, the filarial parasites successfully persist in the human body, by virtue of strategies they attained through long evolutionary processes. A variety of complex evasive strategies of parasites have been recognized, all mostly related to parasite surface [73-76]. The "antigenic variation" within the parasite surface has been established beyond doubt as an evasive strategy of protozoans [77]. "Antigenic disguise" by blocking antigens [74,78] or antibodies of host origin [79] is also known to be another evasive mechanism. Further, the reduced MHC restricted antigen presentation in patients [80], accompaniments of parasitic infection to the CD4+ T cell subpopulations [81] and the other host modulatory mechanisms have also been considered in this respect. However, single or multiple immune evasive strategies may have been developed by these parasites, but observations usually raise more questions than answers. A definite knowledge on the evasive strategy with respect to the filarial surface is an important step towards combating filarial infection.
I.2 ANTIFILARIAL MEASURES

I.2.1 Diagnosis

Visual identification of mf by light microscope in blood smear taken at night is the diagnostic method routinely used in field surveys [19]. A 20 cmm thick blood smear is taken on a glass slide by finger prick during night, air dried, stained with Giemsa and observed under a microscope. However, this approach does not reveal prepatent infection, which are the most important indicators of monitoring active transmission, nor does it reveal amicrofilaraemic or occult infections that may be responsible for major disease manifestations at a later stage [2]. Hence highly sensitive immunological tests are being developed for accurate diagnosis of filariasis.

Immunodiagnosis: The immunodiagnostic tests depend basically on the detection of filaria-specific antibodies or antigens in the body fluids [2,20]. These techniques may also be modified for quantification of worm burden, determination of aetiology of filaria related syndromes and the effectiveness of treatments [2]. Although the IgG4 antibody show enhanced specificity [82], all the antibody detection tests even at Ig subclass levels will, however, share the major disadvantage of being unable to discriminate between past
exposure and current infection and the magnitude of the response bears no relation to parasite burden [2,20,83,84].

Attention has also been recently focused on detection of parasite antigen in the body fluids of patients [2,4]. Ever since the report by Frank in 1946 [85], attempts have been made by many workers to demonstrate filarial antigenemia in blood [86-93], urine [59,94] and other body fluids [4,95]. But the problems encountered with this approach for immunodiagnosis include, difficulties in producing specific immunological probes, epitope sharing between parasite and host antigens and complexing of parasite antigens with antibodies [4,20].

The less sensitive older immunological techniques [96,97] have now been replaced by highly sensitive techniques such as fluorescence immunoassay [87,98], radioimmunoassay [99] and enzyme immunoassay [88,100-103] for immunodiagnostic tests. Despite the intact parasites and crude undefined somatic extracts of adult and developmental stages, the increased sensitivity of these modern techniques have brought with it the need to identify and isolate parasite antigens or antibodies as assay reagents of equally high specificity for accurate diagnosis. Antigens of Brugia and Wuchereria species have been tried by many workers [77,84,102,104,105] for such use. Further progress has also been made in the development of monoclonal antibodies
15

[106-109]. Yet none of these reagents is available for mass survey of filariasis, because of high cost, requirement of trained man power and resulting in of the undefinable false results [2]. However, there is always an expectation for cheap and readily available immunodiagnostic reagents and techniques which are convenient to be undertaken in the field tests.

I.2.2 Treatment

DEC (1-Diethylcarbamyl-4-methylpiperazine), first introduced in 1947 [110] is still the only drug of choice for human use in the control of filariasis [111]. A dose of 6 mg DEC/kg body weight per day in three divided doses for 12 days is usually followed [2]. DEC is a microfilaricide and if given in large enough doses, also kills adult worms [112]. Experimental evidences suggest that action of DEC on the surface of mf [113-115] enhances both the cellular and humoral attacks and subsequent clearance of mf [112,116-118]. However, the rapid DEC-induced destruction of mf in heavy infections is often associated with severe side effects [112,118]. New drugs are being developed for effective chemotherapy to filariasis [1,118]. But it is well understood that once manifested, except surgical interventions no existing medicine can cure the chronic filarial morbidities [22]. Hence the treatment should have to be
started early before the development of any clinical symptoms. This requires accurate identification of the patients at an early stage for effective launching of chemotherapy.

I.2.3 Control

Filariasis is an occupational hazard which can be controlled by improving the conditions of housing [119,120], sewage disposal and water supply [121]. These seems not applicable in the tropical world. The use of insecticides and larvicides [122,123] for vector control or personal protection against mosquito bites by repellents or bed nets are useful to some extent in preventing transmission. However, improved methods are being developed for controlling vectors and despite chemotherapy, vaccination gain significance in controlling filariasis [124].

I.2.4 Vaccine

Vaccine will be the best answer for filarial infections [124]. The basic principle is that, sensitization of host with parasite antigen, who elicit a high secondary response during subsequent infection so that the pathogens are eliminated successfully [24]. The observations on the protective immunity, resistance to reinfection [125-131] and the experimental vaccination induced protection [132-134]
support a positive thinking towards the development of an antifilarial vaccine. The vaccines can be effective in the immunological intervention of infection, disease or transmission of filariasis [24].

The art of deliberate immunization against infectious diseases has been practiced for centuries. The earlier wild type live vaccines were then replaced by attenuated and irradiated vaccines [135-138]. Parasite extracts of developmental stages have also been used [133,139]. However, these vaccines evoke undesirable side effects as they have impurities, which need to be eliminated to enrich the active determinants for effective use. Attempts have been made in purifying and defining the antigens with potentially protective functions [4]. But yet no vaccine to filariasis is available for human use even after the best efforts [124]. The difficulty in getting the human filarial parasites for extensive studies and the complexity of even highly purified filarial antigens by having different types of epitopes, some of which may produce variety of untoward responses in the host [140,141] are the major problems encountered with the development of a vaccine. However, vaccines for human use need to be more antigenically defined and once purified, useful epitope specific monoclonal antibody production or removal of the disadvantageous epitopes by protein engineering can be made
to get a functionally safe vaccine [141]. Although it looks good in theory, the reality is that it is much more difficult than was first envisaged. But once succeeded, these vaccines will be safer, cheaper and more efficacious as prophylactic than drugs [124]. Joint use of drug as well as vaccine is expected to be more successful and hence both will be running mates in effective filariasis control programmes [124]. However, there is an urgent need for highly purified filarial antigens for the formulation of an immunodiagnostic kit or a vaccine.

I.3. SURFACE ANTIGENS

The antigens of greatest importance in lymphatic filariasis are those related to immunodiagnosis, protective immunity and immunopathology [2,22,23]. Intact filarial parasites and crude somatic extracts continue to be used virtually for all studies examining the diagnostic utility or immune response of patients with filarial infection [2]. These antigen preparations will be of highly complex, contain hundreds of proteins and glycoproteins and the particular antigenic determinants in these extracts useful for specific diagnosis or responsible for triggering protective or pathological immune responses are unknown. Thus, until defined antigens are available, the nature of
immune response in filariasis will remain ill-defined and nonspecific [2].

Analysis of either surface or excretory-secretory (ES) antigens of filarial parasites received much attention, since these antigenic molecules which are being released out or exposed to the host's effector mechanisms, involve directly in the host-parasite interaction [142]. Considerable progress has been made on the studies of ES antigens of both human and nonhuman filarial parasites [143-146]. The ES antigens have been shown to be less complex than the somatic extracts of adult parasites and appear to be a subset of the antigens found in the crude somatic extract [2]. Evaluation on the use of ES antigens for immunodiagnosis or other immunological studies have been undertaken as major targets of many research groups. But recent attention has been focussed on the cuticular surface of filarial parasites to identify potentially useful candidate antigens, which remain as a less explored area of much promise.

The research on the cuticle of nematodes has been going on for more than 120 years [147,148] and the use of electronmicroscopy in the past decade has led to considerable advances in the knowledge on the structure of nematode cuticle. The recent ultrastructural studies on the adults [149] as well as mf [150] of B. malayi, adult of D.
immittis [151] and B. pahangi [152] gave detailed information about the fine structure of filarial cuticle. Considerable similarities and variations have been shown in the structure of cuticle between species and stages of the same species [147,148,153,154]. However, all the filarial nematodes are bounded by a multilayered cuticle and owe much of their success in parasitic mode of life.

Despite structure, detailed information on the basic composition of cuticle is available only for a few species of nematodes [155-157]. The major protein components of cuticle are collagen-like, localized in the basal layer and inner cortex. Other noncollagenous proteins are found in the outer cortical and epicuticular layers [158-160]. Besides these, the recent observations on the permeability and nutrient uptake [161,162] metabolic turnover and dynamics [163-166] and antigenicity [160,166-168], revealed that the filarial cuticle despite being inert and impermeable, serves as a functionally active component. With these pieces of information, over the past few years, attempts have been made by many workers to isolate and characterize the surface antigens from many species of filarial nematodes, which improved the growing trend in understanding the importance of surface antigens of filarial parasites.
I.3.1 Importance of surface antigens

**Vaccine target:** The filarial parasites are highly successful in evading the host's immune effector mechanism. As the mechanisms described in this connection such as antigenic variation and/or antigenic disguise are all closely related to the parasite surface [73-79,140,169], a close examination on the antigenic nature of surface molecules may pave way for understanding the intrinsic ability of filarial parasite to protect itself from the host's effector mechanisms and to identify definite accessible determinants of exposed molecules on the surface which will presumably be a critical step towards initiating immune rejection [133,137,140, 170-173].

**Chemotherapeutic target:** The interaction between parasite surface and drug during chemotherapy are complex and highly varied [112]. Studies on these surface molecules will be highly valuable to achieve rational drug development, that target filarial surface lend themselves to exploitation by drugs [112-118].

**Inducers of immunopathology:** Investigations on the surface antigens of filarial parasites will be useful in the identification of responsible antigenic determinants with
which the host effector mechanisms interact and contribute immunopathological consequences \[2,22\].

**Diagnostic reagent:** Highly purified surface antigens are recognized as useful tools for the immunodiagnosis of human filariasis \[174,175\]. Once purified, monoclonal antibodies can also be produced to get highly specific reagents \[106-109\].

Hence, research on the isolation, purification and characterization of filarial surface antigens is now a field of prime interest.

### I.3.2 Surface antigens of human filarial parasites

The inaccessible habitats of human filarial parasites have highly restricted their availability for extensive studies \[2\]. The development of techniques for rearing these difficult human filarial species in laboratory animal models increased the availability of parasite materials for such use. Brugian filariids have been reared in the animals such as mouse \[176\], jirds \[177\] and primate hosts \[178\] whereas, rearing of *W. bancrofti* in *Macaca* and *Presbytis* species \[179\] of monkeys were also reported to be successful. Isolation of surface antigens from these filarial parasites while retaining all their functional properties for immunological studies is a difficult task and
## Box 5

### Surface antigens from the human lymphatic filarial parasites, species and stages

<table>
<thead>
<tr>
<th>Species</th>
<th>Stage</th>
<th>Relative molecular mass (K=000)</th>
<th>Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>B. malayi</strong></td>
<td>Adult</td>
<td>15 K</td>
<td>Water-soluble</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20 K</td>
<td>Water-soluble glycoprotein</td>
</tr>
<tr>
<td></td>
<td></td>
<td>29 K</td>
<td>Water-soluble glycoprotein</td>
</tr>
<tr>
<td></td>
<td></td>
<td>65-75 K</td>
<td>2ME&lt;sub&gt;b&lt;/sub&gt;-soluble collagen bands</td>
</tr>
<tr>
<td></td>
<td></td>
<td>100, 100 K</td>
<td>2ME-soluble collagen bands</td>
</tr>
<tr>
<td></td>
<td></td>
<td>15-29 K</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>65-110 K</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>17, 31, 44 K+</td>
<td>Multiple related antigens</td>
</tr>
<tr>
<td><strong>B. malayi</strong></td>
<td>Microfilaria</td>
<td>17 K</td>
<td>2ME-soluble</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25 K</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>35-40 K</td>
<td>Partially 2ME-dependent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>65-75 K</td>
<td>Triplet of cross-reactive antigens</td>
</tr>
<tr>
<td></td>
<td></td>
<td>70, 75 K</td>
<td>Recognized by IgG monoclonal antibody (&quot;MF-1&quot;)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>110 K</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>110 K</td>
<td>Recognized by IgM monoclonal antibody (&quot;AA.3.44&quot;)</td>
</tr>
<tr>
<td><strong>B. malayi</strong></td>
<td>Infective larva</td>
<td>15-120 K</td>
<td>Resemble <em>B. timori</em> and <em>B. malayi</em> antigens</td>
</tr>
<tr>
<td><strong>W. bancrofti</strong></td>
<td>Adult</td>
<td>15, 20, 29 K</td>
<td>Homologous with <em>B. malayi</em> antigens</td>
</tr>
<tr>
<td></td>
<td></td>
<td>51-67 K</td>
<td>Differ from <em>B. malayi</em> antigens</td>
</tr>
<tr>
<td><strong>W. bancrofti</strong></td>
<td>Microfilaria</td>
<td>17 K</td>
<td>13 K undetermined, 17 K antigenic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13, 17 K</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>34, 43, 51, 59 K</td>
<td></td>
</tr>
<tr>
<td><strong>W. bancrofti</strong></td>
<td>Infective larva</td>
<td>17 K</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>17, 24, 43, 51 K</td>
<td></td>
</tr>
</tbody>
</table>
the paucity of materials from these parasites has necessitated the use of radioisotopic techniques to define antigenic molecules on their surface [142]. Over the past few years, surface antigens from different stages and species of human filarial parasites such as *B. malayi* [142,180], *B. timori* [175] and *W. bancrofti* [181] have been studied by many workers and a list of which was reviewed recently by WHO (Box 5) [4].

**I.3.3 Surface antigens of nonhuman filarial parasites**

However, getting sufficient human filarial parasites from natural sources or model hosts pose difficulties and has led to the use of antigens from nonhuman filarial parasites [2]. Such studies investigated the use of *Setaria digitata* [182], *Dipetalonema vitae* [183], *O. gibsoni* [184], *Litomosoides carinii* [185], *Dirofilaria immitis* [186] and *B. pahangi* [187,188]. The close antigenic homologies observed between the human and nonhuman filarial species [4] justified the use of the heterologous antigens for immunodiagnosis [2,174,175,182] and as vaccines to develop protective immunity through the concept of "zooprophylaxis" [189].

*S. digitata* (Linstow, 1906) a filarial nematode dwelling in the peritoneal cavity of cattle, *Bos indicus* [190-192] (Box 6) has been used in this laboratory to study
The parasites dwell in the peritoneal cavity of cattle, *Bos indicus*. The female has a length of 70–90 mm and 0.5–0.7 mm breadth. The male has a length of 40–50 mm and 0.2–0.4 mm breadth.
the biochemical and immunological determinants of filarial infection. It has close similarity to the human filarial parasite *W. bancrofti* in their morphology [192], histology [193], response to drugs [112] and antigenicity [182]. The studies on their biochemical nature have recently been reported from this laboratory [194-197]. Studies on the nature of excretory/secretory materials of *S. digitata* [198], its origin and antigenicity [199,200] and cross-reactivity to *W. bancrofti* patients serum [201] have also been established in this laboratory. But lack of knowledge on the surface antigens of *S. digitata* had led to attempt the present work.

I.3.4 Present work

The present work on the *surface antigens of filarial parasites* was proposed to achieve the following.

i) **Isolation and analysis:** To isolate and to analyse the antigenicity, relation to somatic antigens, effect of heat on antigenicity, natural shedding, surface carbohydrate and developmental transformation of surface antigens of *S. digitata*

ii) **Purification and characterization:** To purify the individual surface antigens of *S. digitata* in their
native form and to characterize them based on protein composition, antigenicity and *in situ* localization using immunoaffinity purified antibodies.

iii) Cross reactivity and application: To analyse the antigenic cross reactivity of surface antigens of *S. digitata* with *W. bancrofti*, and to evaluate their application in the immunodiagnosis of bancroftian filariasis.

I.3.5 Scope of the work

The work is expected to offer a better understanding of the characteristics of surface antigens of *S. digitata* and their use in the detection of human filariasis.