EMERGING APPROACHES TO TACKLE NEGLECTED DISEASES

FROM MOLECULE TO END PRODUCT

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Emerging Approaches to Tackle Neglected Diseases: From Molecule to End Product

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ISBN (Online): 978-981-5196-86-3

ISBN (Print): 978-981-5196-87-0

ISBN (Paperback): 978-981-5196-887

First published in 2024.

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PREFACE

This work will lead to an extensive debate as it covers an interesting topic. I feel compelled to share my knowledge, analyses, and conclusions after working for numerous years in the field of pharmacy. I have written many papers and book chapters on various aspects. Perhaps this description will increase the knowledge of the issue and initiate a discussion that could result in significant ideological transformations. There are two reading categories for this book. First off, it can be read by individuals with little to no prior knowledge of science. Professionals from academia and government organizations are the second set of readers. It is hard to believe that all members of the scientific community will comply with the concepts and ideas presented in this work. But I do hope that the knowledge and information provided will serve as a guide for all the sections of society.

Neglected tropical diseases (NTDs) are a diverse collection of 20 illnesses that are primarily found in tropical regions and impact more than 1 billion people who reside in underdeveloped communities. Numerous pathogens, such as viruses, bacteria, parasites, fungi, and toxins, are responsible for their development. More than one billion people suffer from terrible health, along with social, and fiscal effects of these diseases. There are 12 chapters in the book. The introduction to neglected diseases is broadly introduced in Chapter 1 of this book. The strategies to overcome the impact of neglected diseases on the world are discussed in Chapter 2, which also provides a step-by-step process to handle such conditions. The current therapeutic strategy for leprosy, dengue, lymphatic filariasis and dracunculiasis, helminthiasis, Chagas disease, neurocysticercosis and leishmaniasis, rabies, trematodiasis, Buruli ulcer and trachoma is introduced in Chapter 3 to 10, respectively, along with an account of the possible disease mechanism, transmission and management protocols.

I wish a lot of people read this book. In order to escape the mistakes of the past, we must alter course and begin utilising knowledge built up by scientists.

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CHAPTER 1

Neglected Tropical Diseases

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Abstract: Neglected tropical diseases (NTDs) are a widespread category of communicable illnesses that thrive in tropical and subtropical environments. More than a billion people are affected by these illnesses, which annually drain billions of dollars from developing nations' economies. The most severely impacted populations are those who lack access to basic sanitation, live in poverty, and are in close proximity to disease vectors, domestic animals, and livestock. The World Health Organization (WHO) is a United Nations department focusing on public health issues. NTDs pose a significant threat to public health both globally and in India. Lymphatic filariasis (LF), Visceral Leishmaniasis (VL), Rabies, Soil-Transmitted Helminthic Infections (STH), and Dengue are the principal parasitic and associated infections that the World Health Organization (WHO) has designated as neglected tropical diseases (NTDs). These neglected diseases represent a concern to millions of underprivileged Indians who live in deplorable conditions. The current chapter examines the common NTDs in India, their prevalence, the state of control strategies, and obstacles and prospects for NTD eradication.

Keywords: Communicable diseases, Diseases of poverty, Epidemiology, Global burden, Integrated control, Mass drug administration, Neglected Tropical Diseases, Poverty, Risk factors, World Health Organization.

1. INTRODUCTION

Neglected tropical illnesses are a serious issue for public health since they affect almost one billion people worldwide [1]. Regardless of the fact that these illnesses have been known for centuries, many nations, especially low- and middle-income ones (LMIC), are still working to eradicate NTDs [2]. The WHO classified seventeen significant parasite infections and associated disorders as neglected tropical diseases. These illnesses disproportionately affect the underprivileged and

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poor populations of countries in Africa, Southeast Asia, and South America [3 - 5]. A massive campaign aimed at public health control and elimination of these diseases is closely related to neglected tropical diseases (NTDs), a group of tropical infections [6 - 8].

The three main types of diseases in India are communicable diseases, maternity and child health issues (which collectively account for around half the burden), and non-communicable disorders [9]. Thus, both the diseases of the industrialized world (such as diabetes mellitus and cardiovascular diseases) and the ailments of the underdeveloped world (such as infectious and neglected diseases) have been observed in India [10]. The recurrence of previously curable illnesses like leishmaniasis, malaria, and other vector-borne diseases has a major impact on underprivileged and rural populations. However, these diseases have received little attention globally because they primarily affect the poorer sections of the population. Thus, it will be appropriate to state that neglected diseases are a category of infectious and parasitic illnesses that often receive little attention from the pharmaceutical industry and mainly afflict the poorest members of society [11].

Upon the introduction of the Millennium Development Goals (MDGs) in the early 2000s, the NTD framework was initially put forth. HIV/AIDS, TB, and malaria were expressly included in the MDG's list of global infectious diseases, leaving out numerous tropical diseases with significant worldwide recurrence and disease burden. In response, 13 bacterial, protozoal, and helminthic “neglected” infectious disorders were grouped as NTDs. Later, WHO divided the NTDs into two groups: (1) individuals treated with preventative chemotherapy and transmission control (PCT) and (2) those demanding novel and rigorous disease management (IDM). The seven PCT-related illnesses were grouped based on the idea that they may all be treated at the same time with a “rapid-impact package” of drugs by mass drug administration (MDA; also known as preventative chemotherapy), as shown in Fig. (**1**) [12].

Schistosomiasis, lymphatic filariasis (LF), onchocerciasis, and trachoma were among the PCT disorders, as were the three major soil-transmitted helminth (STH) diseases (ascariasis, trichuriasis, and hookworm) [7]. As worldwide control and elimination operations gained significance internationally, the WHO formed a Department of NTDs and eventually added 18 major tropical illnesses to the NTD list. WHO has recently increased this figure to 20. In this book chapter, we review the public health initiatives for the control and eradication of NTDs, discuss current worldwide developments, and map a course for the future.

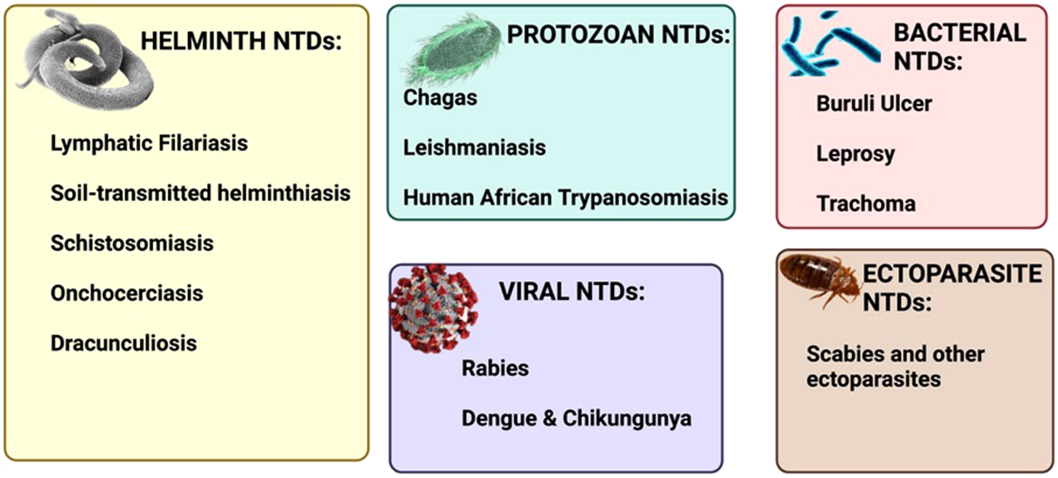

Fig. (1). A compendium of Neglected Tropical Diseases. Much attention is given to previously neglected diseases such as malaria, HIV/AIDS, and TB. In contrast, schistosomiasis and soil-transmitted helminthiasis continue to be overlooked; this also includes zoonosis diseases from the interactions of humans and their animals.

2. EPIDEMIOLOGY AND RISK FACTORS

To end the neglected tropical diseases for the achievement of goals incorporated in sustainable evolution, a protocol, namely 2021-2030 Neglected Tropical Diseases, has been adopted by the WHO Director-General and the Director of the Department of Control of Neglected Tropical Diseases.

The primary objectives of the year 2030 for neglected tropical disease awareness are listed below:

● Individuals needing therapy for NTDs decreased to 80-90% in particular areas.

● Approximately ten nations are in the process of eliminating NTDs.

● The most defined diseases, such as yaws and dracunculiasis, must be eliminated.

● All the matters related to NTDs, such as Disability-Adjusted Life Years, need to produce a 70-75% decline [13].

A ground plan helps in monitoring various distinct infections as well as setting standard targets for multiple factors, which includes decreased vector-instilled NTDs mortality within the limit of 70-75% along with the promotion of maximum ingress in supplying water as well as cleaning and sanitation procedure in various areas where NTDs is in the native range. The high expense of

CHAPTER 2

Strategies to Overcome the Impact of Neglected Diseases on the World

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Abstract: Neglected tropical diseases (NTDs) are highly prevalent in Sub-Saharan Africa. In the World Bank's definition of poverty, nearly all people suffer from at least one NTD. Among the most widespread NTDs are malaria, HIV, and soil-transmitted helminths like lymphatic filariasis, schistosomiasis, trachoma, and onchocerciasis. A recent study suggests that NTDs may influence the evolution of HIV and AIDS, malaria, and tuberculosis. These interactions may be influenced by epidemiological, immunological, and clinical factors, which may impair the prognosis for those with HIV/AIDS, TB, or malaria. World Health Organization (WHO) suggests five main strategies for preventing and controlling NTDs for public health-intensified case management, vector control, preventive chemotherapy, sanitation, the provision of safe water, veterinary public health, and hygiene. Despite only using one method and doing it locally, to control, and eliminate the NTDs, these methods can be used as a mark for achieving the Sustainable Development Goals as they are mainly found in disadvantaged regions and environments. The development of pilot projects and initiatives can help achieve the Millennium Development Goals. The poor and marginalised could gain from innovative treatments for neglected diseases (particularly parasite infections) based on sustainability concepts and knowledge of key factors affecting health.

Keywords: AIDS, Epidemiological, Immunological, Neglected tropical diseases, Tuberculosis, World Health Organization.

1. INTRODUCTION

A collection of infections known as neglected tropical diseases (NTDs) are the most common among low-level income people in developing nations, particularly in Africa, the Americas, and Asia. Because neither medication and diagnostics de-

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velopers nor public health programs have adequately addressed certain ailments, they are categorized as neglected diseases. At least 100 of the 149 nations and territories where NTDs are recorded have two or more endemic diseases, with 30 having six or more [1]. In all afflicted regions, NTDs now result in unacceptably high levels of human misery and death. For instance, the overall impact of NTDs in sub-Saharan Africa is comparable to the worldwide burden of both malaria and tuberculosis. Many NTDs also increase the lethality of diseases like HIV/AIDS and TB through co-infection. Although there are several preventative strategies and medical treatments for these illnesses in high-income nations, they are not easily available in low- and middle-income nations. The NTDs that the World Health Organization (WHO) has prioritized have been grouped despite their varied medical profiles because of their propensity to co-exist geographically and because they share some characteristics [2]. Combining various diseases makes it easier to calculate their combined burden and relevance to public health and elevates their profile to help with resource collection. Despite the prevalence of NTDs, funds granted for research and treatment of other diseases including HIV/AIDS, TB, and malaria have typically outpaced that of NTDs. Recently, considerable efforts have been made to combat NTDs as the global health community has recognized their significant burden. The WHO's plan to eradicate, eliminate, or control 10 NTDs was supported by the London Declaration, which was signed in 2012 by governments, nonprofit organizations, pharmaceutical firms, and the WHO [3]. Diagnostics are very crucial to determining the extent of transmission, assisting in the timing of the termination of MDA programs, confirming the end of transmission, and monitoring to ensure sustained elimination. When determining whether a disease is present or absent and assisting in the selection of a course of therapy, diagnostics offer objective and quantitative data. Diagnostics are needed to identify specific patients to administer therapy for NTDs such as leprosy, sleeping sickness, leishmaniasis, and Chagas disease that are not managed by MDA. Additionally, the first of the seven top research priority for Chagas disease, leishmaniasis, and human African trypanosomiasis (HAT) identified by the WHO's Special Programmes for the Research and Training in Tropical Diseases (WHO/TDR) is diagnostics for case detection and characterization, includes the tests to drug resistance and for a cure. Therefore, resolving the diagnostic requirements for these NTDs has emerged as a top priority to accomplish the goals of the London Declaration [4]. It will be vital to form alliances with many other sectors capable of taking effective action. Lowering of NDs will ultimately help communities suffering from poverty to develop sustainably, and it also helps the countries affected by these diseases experience greater economic growth [5].

As they say “Prevention is better than cure”, preventive measures need to be taken to reduce the impact of NDTs on the world.

2. IMPACT OF NDTs

NTDs have high rates of morbidity but low rates of mortality. (World Health Organization. Department of Control of Neglected Tropical Diseases, n.d.) According to the data, about $1/6^{th}$ of the population is suffering from NTDs and we can say about a billion people are suffering from NTDs and an extra 2 billion are at risk of developing NTDs. Consequently, around 185,000 people pass away every year. People frequently carry many NTDs at once, which can cause severe deformity, disability, blindness, and starvation because of infection [6]. NTDs' health consequences negatively impact economic development, educational success, cognitive development, agricultural production, and food security. NTDs are endemic to about 150 nations worldwide. However, middle and low-income nations in America, Africa, Latin, Asia, and Africa bear the lion's share of the burden of NTDs. Due to the incidence and effect of NTDs, those living in urban slums and rural regions are among the most exaggeratedly spoilt, due to no access to clean water, good sanitation, health services, and suitable housing. Since they are more likely to be exposed to NTDs and encounter hurdles to treatment more frequently, particularly those who live in remote locations, children and women are most at risk for infection [7].

2.1. To Defeat the Impact of NDTs on World's Health and Economy

Several approaches partake bee, effective in limiting and, in about cases, even eliminating various NTDs. The four selected NTDs cause considerable morbidity, and might even lead to death and all have a significant economic impact on the already impoverished populations they affect. We believe that the economic impact of COVID-19 on these populations will be severe and long-lasting. There have been several effective approaches in limiting and, in some cases, even eliminating various neglected tropical diseases (NTDs) [8]. Here are a few examples:

2.1.1. Mass Drug Administration (MDA)

MDA involves distributing preventive medications to large populations at risk of specific NTDs. This approach has been successful in controlling diseases like lymphatic filariasis and schistosomiasis [9].

2.1.2. Improved Sanitation and Hygiene

Enhancing access to clean water, and proper sanitation facilities, and promoting good hygiene practices can significantly reduce the transmission of NTDs like soil-transmitted helminthiasis and trachoma [10].

CHAPTER 3

Current Therapeutic Strategies for the Management of Leprosy

Inderjeet Verma[1,*], Dhirender Singh[1], Meenakshi Dhanawat[2] and **Sumeet Gupta[1]**

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Abstract: The chronic infectious condition known as leprosy is brought on by the bacteria *Mycobacterium leprae*. Peripheral nerves and the skin are frequently attacked, which can result in impairments. The incidence of *M. leprae* infection has decreased in endemic countries as a result of the WHO's multidrug therapy (MDT) program for leprosy treatment, but there is still active transmission as evidenced by the high rate of newly reported cases. It is critical to diagnose leprosy as early as possible, hence clinical examination and research are required. Leprosy has six subgroups, according to the Ridley-Jopling classification: Tuberculoid (TT), Borderline Tuberculoid (BT), Borderline-borderline Mid-borderline (BB), Borderline-lepromatous (BL), Subpolar Lepromatous (LLs), and Polar Lepromatous (LLp). Based on the type of therapy, leprosy is categorised into paucibacillary (PB) and multibacillary subtypes (MB). Skin scraping smears are still the preferred laboratory test for leprosy diagnosis. Depending on the type of leprosy, whether it belongs to the PB or MB group, the course of treatment with Multi-Drug Therapy (MDT) is modified. Rifampicin and dapsone are the recommended regimens for the treatment of PB type, whereas rifampicin, dapsone, and clofazimine are recommended for MB-type patients. To identify an efficient MDT treatment and stop the spread of the illness, a correct leprosy diagnosis must be made by both a physical examination and a laboratory analysis.

Keywords: Dapsone, Laprosy, *Mycobacterium leprae*, Multi-Drug Therapy, Rifampicin.

1. INTRODUCTION

Leprosy, a highly infectious chronic disease discovered by Gerhard Armer Hansen of Norway in 1873, is still a big issue in many parts of the world [1]. *Mycobacterium leprae* an acid-fast rod-shaped bacillus is the main causative

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agent of leprosy which primarily affects the skin and peripheral nerves, but also the muscles and other body parts [2, 3]. In the current scenario, leprosy is globally one of the principal causes of non-traumatic peripheral neuropathy. Despite developments in neglected countries, mostly in Southeast Asia and the Americas leprosy still remains widespread in a number of areas [4]. From 2005 till 2014, globally the count of reported cases remains unchanged, as a result, leprosy remains widespread in many areas even after a decade [5]. In 2019, over 1000 new cases were reported in 13 nations, which is more than 95% of new cases.

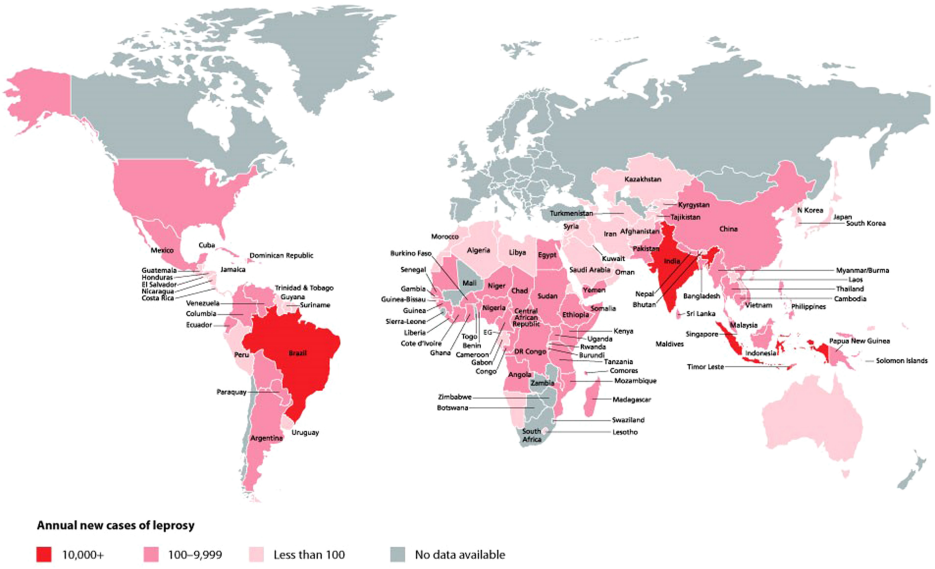

Fig. (1). Geographical distribution of leprosy cases. Courtesy of WHO. (10,11).

2. EPIDEMIOLOGY

In 1966, the first global data was published on the disease prevalence, (however, in 1953 in Rio de Janeiro(Brazil), the first-ever expert committee (WHO) on leprosy was formed. In those days, the expected figure of leprosy globally was more than 10 million even though the disease was underestimated. The leprosy cases remained stable till 1980, ranging from 10-12 million [6, 7]. From 1982 onwards, the initiation of multi-drug therapy leads to sharp decline in cases of leprosy. (5.5 million till 1991) [8]. This encouraging number inspired the members of the 44th meeting of the World Health Assembly (WHA) to pass the 44.9 resolution with the intention to eliminate leprosy as of the year 2000 *i.e*, the cases should be less than 1/10,000 population [9]. This initiation will result in a significant decrease in the number of cases from 719,219 million to 265,661 million from 2000 to 2006. Unfortunately, this decrease in annual cases reached a

plateau after 2006. From 2017 onwards, there was a slight decrease in the number of cases [10].

Among the newly reported cases, India comes at number one with a 60% share, however, Brazil and Indonesia come next with 13% and 8% share respectively [11]. The number of cases continues to fall, still in some parts of the world, where the prevalence of this disease is very normal, including India, Nepal, Brazil, Bhutan, Tanzania, Mozambique, Madagascar, and the western Pacific. A very few cases were identified in the USA each year [12] (Fig. **1**).

2.1. Etiologic Agent, the *Mycobacterium leprae* (*M. leprae*)

M. leprae, which is the main causative agent is an acid-fast bacillus, which has not yet been cultured *in vitro,* however, the bacterium was successfully grown *in vivo* into the footpads of mice [13, 14]. The bacterium is notorious and slow in growth with an exponential time of 14 days [15, 16].

Sequencing of *M. leprae* revealed a substantial number of pseudogenes and less than 50% coding capability. The rest 50% genes from *M. leprae* are used to define the minimal gene set necessary for this mycobacterial pathogen to survive *in vivo* as well as genes that might be important for leprosy infection and pathogenesis [17].

A recently discovered mycobacterium called *M. lepromatosis* is characterised as a causing agent for disseminated leprosy, but its significance is not yet unclear [18, 19].

2.2. Genetic Determinants of Host Response

The possibility of developing leprosy and the disease's clinical course is influenced by human genetic factors [20]. In single-nucleotide polymorphism (SNP) association analyses, a low lymphotoxin-producing allele (LTA) was identified as a major genetic risk factor for early-onset leprosy [21]. Additionally, it has been proposed that SNPs in the vitamin D receptor (VDR), IL-10, TNF, HLA, IFN genes and TLR1 may be linked with sickness and/or the onset of reactions in other genes [22 - 25]. In the promoter sequence shared through two genes, PARK2, which codes for the E3-ubiquitin ligase known as Parkin, and PACRG, linkage analysis have shown polymorphic threat factors [26]. Additionally, a study reveals that NOD2 genetic variations are linked to leprosy susceptibility and the emergence of responses (type I and type II) [27].

CHAPTER 4

Emerging Therapy for Dengue

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Abstract: There are over 60 countries where dengue fever is endemic, and 2.5 billion people could get sick from it. An RNA virus belonging to the Flaviviridae family that causes acute viral disease dengue is transmitted by Aedes mosquitoes. The presenting signs may be asymptomatic fever with severe implications such as hemorrhagic fever and shock. The most common symptoms are acute-onset high fever, cutaneous rash, hemorrhagic episodes, myalgia and circulatory shock. Although oral symptoms are seldom the primary presenting sign of dengue infection, they may occur in certain cases. Early and precise diagnosis is necessary for lowering mortality. Dengue virus infections are typically self-limiting, but in tropical and subtropical countries, dengue infection has become a public health threat. A detailed explanation of dengue virus infections, clinical symptoms, diagnostic techniques, and preventative measures are all included in this book chapter.

Keywords: Aedes aegypti, Dengue, Fever, Immunological, Virus infections.

1. INTRODUCTION

Dengue is a fever infection that, in extreme circumstances, can be severe. It is brought on by one of four different serotypes of the flavivirus (DV-1 to DV-4) [1]. Aedes aegypti and the virus spread by Aedes albopictus mosquitoes, which are carriers of the virus among humans [2]. The precise pathophysiology of severe dengue disease remains unknown, despite the fact that it is now well-acknowledged that the pathogen virulence, host genetic makeup and host immune system are all factors in the fast deterioration observed in certain patients [3]. In the tropics, dengue is a serious public health issue because of its increased occurr-

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ence. With waves of outbreaks occurring after each rainy season, dengue infections are closely related to seasonal climate change [4]. Thousands of people could be impacted by an outbreak. This results in a large mortality rate in many afflicted locations, which is prevalent primarily among early childhood and working-age adults. The inability to treat specific cases, the lack of a vaccine for prevention, the existence of four different virus serotypes, each of which has the capacity to independently cause fatal disease, and difficulties in managing the vector population are the main causes dengue infection [5].

Other than supportive treatment and prudent hydration therapy, dengue fever has no specific treatment. Over the past 50 years, clinical studies have evaluated a variety of therapy options with varying degrees of success. The “critical time” or risk window for dengue, during which the patient may suddenly deteriorate, is only between 48 and 72 hours long [6]. A fatal outcome is unlikely if the patient is properly handled throughout this stage. Still, this necessitates constant observation and flexible management evaluation. In simple dengue, there are no aftereffects if the patient recovers from the orchitis, oophoritis, and encephalitis, which can have a long-term impact on a very small percentage of cases. For a brief period, infections shield against different dengue virus serotypes, but not against the same serotype [7]. Due to the limited resources in developing nations, close monitoring and treatment of epidemics are quite challenging when hospitals are overburdened with patients. Additionally, there are limited evidence-based therapy plans that target the specific pathophysiological aspects of the disease. Due to ignorance, a lot of patients arrive at the hospital late, often in shock, and their management is challenging. Many efforts are now focused on preventing transmission by managing vector populations due to practical challenges of treating an established dengue infection [8]. To stop the spread of the disease, a variety of vector control techniques have been tried, including physical (removing breeding grounds), chemical (using insecticides and larvicides), and biological (using microorganisms like Bacillus thuringiensis). However, the mosquito can reproduce in clear stagnant water in between the trunk and the leaves, making this a difficult task [9]. It is quite impossible to remove such environments. Nevertheless, despite these difficulties, certain curative and preventive techniques have been found recently to lower the mortality linked with dengue infection.

An update on dengue is given in this book chapter, including information on the disease's etiopathogenesis, diagnostic standards, treatment options, and research directions.

1.1. Classification

Despite these challenges, several preventative and therapeutic strategies for reducing dengue disease and preventing death have been studied in recent years. This review updates knowledge on dengue in relation to a number of crucial areas, including the disease's epidemiology, history, and preventive strategies, as well as potential directions for future study.

The three types of dengue fever listed in the 1997 classification are undifferentiated fever, DF, and DHF. Grades I through IV were added to the DHF division, as shown in Fig. (**1**).

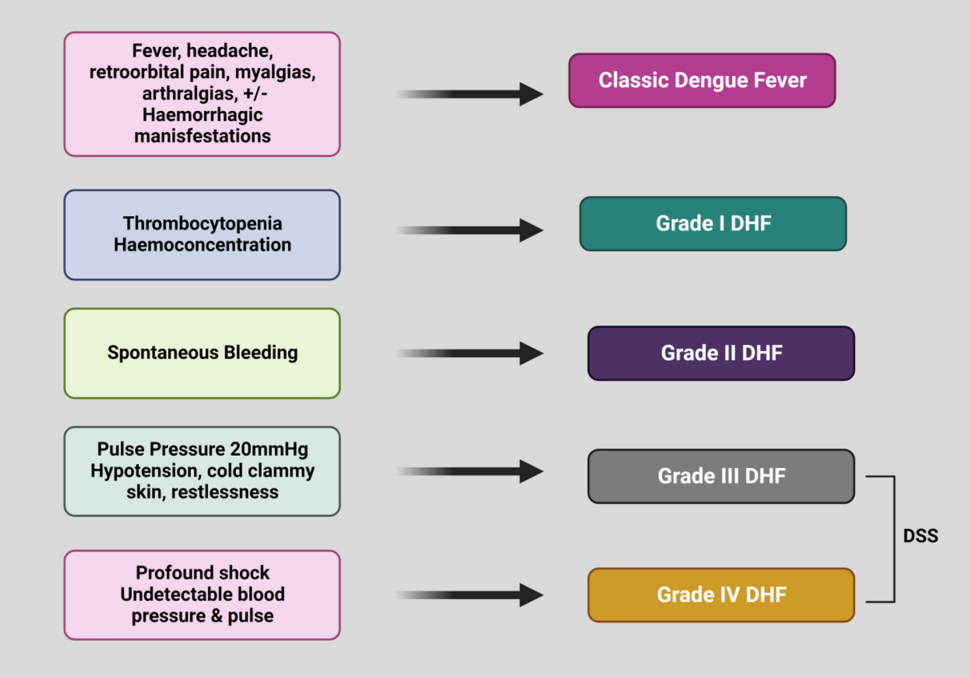

Fig. (1). WHO classification of Dengue infections and grading of severity of DHF.

Grade I: Having only minor bruises.

Grade II: Uncontrollable bleeding elsewhere and into the skin.

Grade III: Medical indications of shock.

Grade IV: Strong pulse, shock, and the inability to take a blood pressure reading. In this instance, grades III and IV make up DSS [10, 11].

CHAPTER 5

Lymphatic Filariasis and Dracunculiasis

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Abstract: In poor nations, helminthic illnesses are a major source of social, economic, and medical problems. These parasite illnesses affect a large number of people, and there are not enough effective treatments available. It is necessary to step up research on novel medications and treatments to address this pressing need. The lymphatic system is hampered by lymphatic filariasis, which can result in aberrant body part growth and cause discomfort, severe disability, and social stigma. As of 2018, there were 51 million cases, a 74% decrease from the 2000 commencement of the WHO's Global Programme to Eradicate Lymphatic Filariasis. With 27 cases documented in 2020, the devastating parasite disease dracunculiasis is almost completely eradicated. The transmission cycle takes between 10 and 14 months to complete after infection. The aim of the book chapter is to focus on pathogenesis, diagnosis, available treatment, and measures to eradicate these infections caused by helminthic parasites, which have been declared as neglected diseases by the World Health Organization.

Keywords: Dracunculiasis, Helminthic disease, Lymphatic filariasis, Neglected disease, WHO.

1. INTRODUCTION

Lymphatic filariasis is a condition brought on by a borne parasite that results in parasitic infection. It also goes by the name of elephantiasis, a painful and severely disfiguring condition. A neglected tropical illness is lymphatic filariasis (LF). When filarial parasites are transferred from mosquitoes to humans, infection results. Infection, which is often acquired in childhood, frequently causes subtle harm to the lymphatic system.

This parasitic condition, which is brought on by tiny, thread-like worms, is regarded as a neglected tropical disease (NTD) on a global scale. Only the human lymphatic system is home to these adult worms. The lymph system keeps the

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body's fluid balance in check and aids in the immune system's ability to combat illnesses [1]. People can develop lymphedema and elephantiasis, which results in a hydrocele, a protrusion in a man's scrotum. The leading global cause of irreversible impairment is lymphatic filariasis [2].

2. CAUSES AND TRANSMISSION

Infection with nematodes (roundworms) from the family Filariodidea, which are categorized as parasites, results in lymphatic filariasis. These thread-like filarial worms are classified into 3 categories:

a) *Wuchereriabancrofti*, which causes 90% of cases,

b) *Brugiamalayi*, the majority of the remaining cases are caused by this,

c) *Brugiatimori*, is the third one [1].

The skin is where mature parasite larvae are implanted so they can enter the body. The transmission cycle is subsequently completed when the larvae travel to the lymphatic vessels where they develop into adult worms [1].

Lymphatic filariasis is spread by a variety of mosquito species, including the Culex mosquito frequently available in semi-urban as well as urban areas. Anopheles mosquito in remote areas and the last one is the Aedes, which resides on endemic Pacific islands [1].

Microfilariae are larvae that are immature in nature and capable of circulating in the blood with distinct nocturnal periodicity, are produced by the adult. Typically, the worms produce microfilariae for 5-8 years of their life. Mosquito bites are the main method of transmission for lymphatic filariasis [3].

Although they appear healthy on the outside, people with circulating microfilariae spread the virus to others through mosquitoes. Chronic filarial swellings cause significant illness in those who have them, but they no longer spread the infection. In India, *Wuchereriabancrofti*, a species, accounts for 99.4% of cases while *Brugiamalayi* is only 0.6 percent of the problem. The filarial worms in the adult stage reside in the lymphatic system's channels. A crucial component of the body's immunological defense system, the lymphatic system is a network of lymph nodes along with lymph veins that maintain the balance of fluid between blood and the nearby tissues [3].

3. LIFECYCLE

The larval stage of filarial nematodes takes place in mosquito vectors (the

intermediate host), and the adult stage takes place in humans (the definitive host). When an infected mosquito bites, it spreads the infection. During a blood meal, the contagious larvae (third-stage larva; L3s) penetrate the bite wound before moving to the lymphatic artery and lymph nodes, where they develop into adult worms (Fig. **1**). Approximately 50,000 microfilariae can be produced each day by the female worm after mating. Then, depending on the type of parasite, millions of microfilariae are sporadically discharged into the host's blood circulation from the lymphatics. The lifespan of adult lymphatic filarial parasites is 5–10 years, whereas the lifespan of microfilariae is 6–12 months [4].

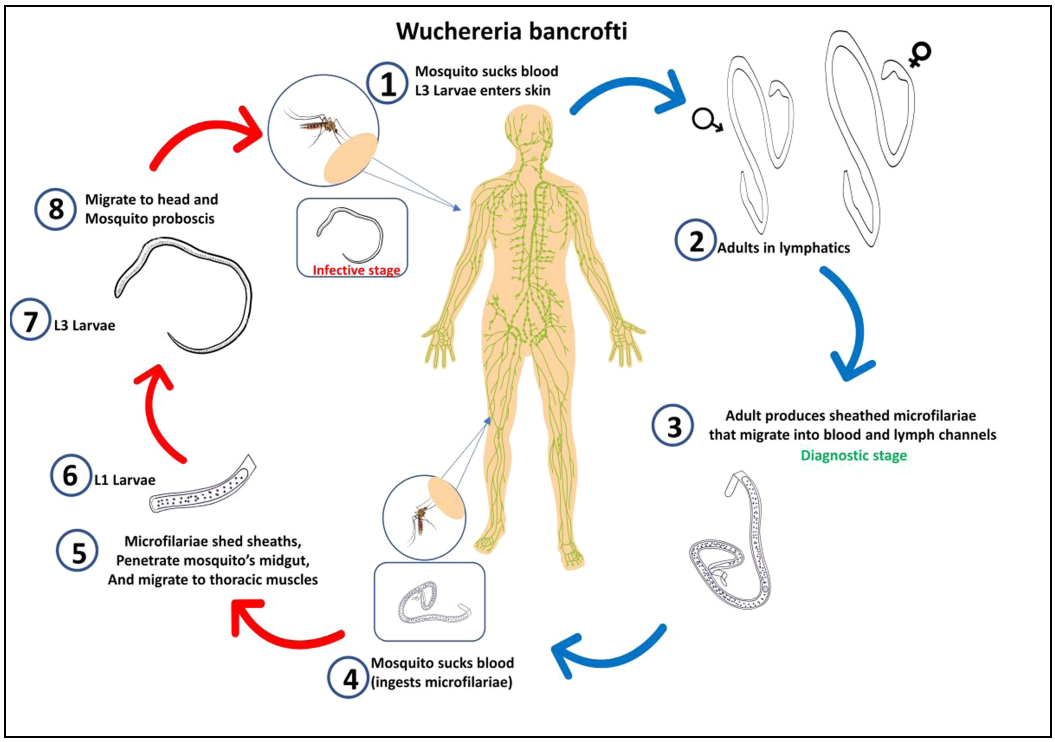

Fig. (1). Lifecycle of wuchereria bancrofti causing lymphatic filariasis.

Microfilariae are consumed by infected people after mosquito bites, their sheath gets shredded and it passes through the entire stomach wall and finally reaches the thoracic muscles. After a short span of time, these convert in the larvae which is the first stage and later mature into larvae that are responsible for causing infection. These infectious larvae then move to proboscis of the mosquito and through subsequent biting, they get transferred from person to person. A weakened lymphatic system may arise from infection, which is often acquired throughout childhood without any obvious symptoms [5].

CHAPTER 6

Current Therapeutic Strategies for Soil-Transmitted Helminthiasis

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Abstract: Soil-transmitted helminths [STH] are described as neglected tropical disorders (NTDS) since these impose terrific distress and disability, nevertheless, they can be eradicated or controlled. The pervasiveness of STH is more usual in rustic/bucolic areas than in city areas. STH signifies the worms present in the intestine provoking infection in humans and are transmitted/ conveyed *via* unhygienic/ dirty soil. "Helminth" denotes a parasitic worm and the causative agents/ chief species that can harm humans are the hookworms (*Ancylostomaduodenale* and *Necatoramericanus*), whipworms (*Trichuristrichiura*) and roundworms (*Ascarislumbricoides*). Various features namely, Hypersensitivity reaction (Type -1), the response of defective Th2, mucosal inflammation, volvulus, obstruction of small bowel and intussusception, blood loss in the mucosa, anaemia, *etc*. are involved in the pathophysiology of STH. To control mortality and morbidity, WHO has recommended population-based, specific, and target-based approaches. The medications recommended by WHO are Albendazole, Levamisole, Mebendazole, and Pyrantelpamoate as a single dose. Preclinical studies are being carried out on the ayurvedic and herbal treatments employing medicinal plants for STH infections as these are compatible with the body and have fewer side effects. The infection is now considered a major public health issue; the major role played by poor sanitation and hygiene in addition to this is certain environmental conditions. Thus, soil-conveyed helminth infections have a primary influence on socio-economic progress and advancement of society where occurrence rates are higher as such acquired infections influence the performance of adults to do work properly and provoke absenteeism amongst school-going children.

Keywords: *Ancylostomaduodenale*, *Ascarislumbricoides*, Adult parasitic worm, Cytokines, Anaemia, Anthelminthic, Deworming, Hypersensitivity reaction,

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Health education, Hookworm infection, Interlukin, IgE, Larvae, Lumbricoides, Mucosal inflammation, *Necatoramericanus*, Roundworm, Sanitation, STH, Soil transmitted Helminth, *Trichuristrichiura*, Th2 response, Unhygienic, Volvulus, Whipworm.

1. INTRODUCTION

Soil-transmitted helminths signify the worms present in the intestine provoking infection in humans and are transmitted/ conveyed *via* unhygienic/ dirty soil. Helminth infections passed on by the soil are the most prevalent illness, spread universally, and influence the most deprived and underprivileged population. These are conveyed by eggs existing in the faecal matter of humans, which in turn infect the soil present in moist and warm areas where hygiene and cleanliness are inadequate. Children infected by parasitic worms are generally deprived of micronutrients and exhibit physical or cognitive degeneration. The infection acquired by helminths is also common in pregnant women. It results in anemia and the possibility of carrying a newborn in pregnant women with lesser weight at the birth time [1]. About 1.5 billion humans or 24 percent of the population of the world acquire soil-conveyed helminth infections globally [2].

"Helminth" denotes a parasitic worm and the causative agents/ chief species that can harm humans are the hookworms (*Ancylostomaduodenale* and *Necatoramericanus*), roundworms (*Ascarislumbricoides*) and whipworm (*Trichuristrichiura)* [3]. The roundworm and whipworm largely affect children, while hookworm influences both children and youthful grown-ups. Soil-transmitted helminth species (STH) are usually categorized as a group since these require alike processes of diagnosis and act in response to a similar class of medicines. A parasitic worm in the intestine with specific features is Strongyloides stercoralis and this parasite needs distinctive procedures in comparison to other helminthiases conveyed by soil and not normally identified [4].

Soil-transmitted helminths are also described as neglected tropical disorders (NTDS) since these impose terrific distress and disability; nevertheless, they can be eradicated or controlled. The pervasiveness of STH is more usual in rustic/bucolic areas than in city areas [5]. Helminth infections are extensively prevalent in the subtropical and tropical regions with utmost numbers happening in America, East Asia, sub-Saharan Africa, and China [6]. More than 267 million kids of the kindergarten age group and greater than 568 million children going to school reside in the premises where these parasitic worms are rigorously transmitted and such children are in great need of medication and precautionary interventions [7]. Nearly 576 to 740 million humans worldwide are acquiring infection with hookworm. About 807 to 1221 million humans in the world are prone to infection from Ascaris, a roundworm. Closely 604 to 795 million people

account for worldwide illness with whipworm [8].

STH illness is likely to instigate chronic disease silently. The worm burden is not evenly dispersed among the populace globally. Only a small number of humans bear a heavy load of worms, while most people harbor a smaller number of severe infections [9]. It is significant to determine the proportion of infected humans having a higher load of parasitic worms since they are more prone to disability risk. These intensely infected humans having higher worm loads are the chief source of infectivity in an environment and the spread of infection. Soil-conveyed helminth infections have a primary influence on socio-economic progress and advancement of society where occurrence rates are more as such acquired infections influence the performance of adults to do work properly and provoke absenteeism amongst school-going children [10].

2. CLINICAL FEATURES OF HELMINTHIASIS

The clinical features of soil-transmitted helminthiasis [STH] occurring through *Ascarislumbricoides, Trichuristrichiura*, *Ancylostomaduodenale, and Necatoramericanus* are summarized and represented in Fig. (**1**) [11 - 15].

2.1. Mode of Transmission of Helminth Infection

Helminths passed on into the soil are conveyed by the eggs that are transmitted in the faecal matter of humans having an infection with parasitic worms. The worms on attaining an adult stage thrive in the intestine where they get a favorable environment to generate thousands of eggs per day. If the human host acquires infection from worms defecates in public places (preferably near the plants in fields or garden premises) or if the faecal matter of an infected individual is employed as fertilizer, eggs are put down onto the soil. One gram of faecal matter from a human carrying an infection can hold up to 100 parasitic eggs. The soil in overcrowded areas lacking satisfactory cleanliness and hygiene gets contaminated by eggs [16]. This can occur by various means:

• Eggs of worms are ingested from unhygienic and polluted water sources;

• Eggs of worms get affixed to fruits and vegetables that are swallowed when the fruits and vegetables are not cautiously washed, cleaned, peeled, or properly cooked;

• Eggs of worms are consumed by kids playing in the infected soil and after that place their dirty fingers unknowingly in their mouths without cleaning and washing hands [17].

Additionally, the eggs of hookworms hatch in the soil, producing immature

CHAPTER 7

Current Therapeutic Strategies for Neurocysticercosis and Leshmaniasis

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Abstract: The most prevalent parasite condition affecting the brain, neurocysticercosis (NCC), is a well-known contributor to new seizures all over the world including India. The only prevalent cause of acquired epileptic seizures in underdeveloped nations, whereas active epilepsy is a common cause in affluent nations, that is cysticercosis, a parasitic ailment of the neurological structure in humans initiated by the larval stage of the tapeworm *Taenia solium*. The location of the cysticercus affects the pathogenesis, natural history, clinical symptoms, and therapy. For instance, the primary clinical signs and symptoms differ depending on the type of disease. Seizures or headaches are generally the first symptoms of parenchymal NCC. Leishmaniasis is brought on by parasites of the genus *Leishmania* in the *Trypanosomatidae* family which is among the most neglected tropical infectious diseases. Over 20 different *Leishmania* protozoa types can cause the complex vector-borne disorder leishmaniasis, which has a variety of clinical presentations ranging from localised skin ulcers (cutaneous leishmaniasis) to a systemic illness that can be fatal if left untreated (visceral leishmaniasis). There is not a single effective Leishmaniasis treatment available now for all species and symptoms. Furthermore, the present therapeutic approaches frequently do not lead to a parasitological cure and recurrence in the context of immunodeficiency (*i.e.*, HIV) is an emerging area that needs further research. So, this review is a discussion of a combination of all aspects related to Leishmaniasis, and how to use old treatment methods such as monotherapy along with modern strategies to combat this major health issue all over the world.

Keywords: Acquired epileptic seizures, Conventional drugs, Cutaneous leishmaniasis, Cysticercosis, Leishmaniasis, Mucocutaneous leishmaniasis, Neurocysticercosis (NCC), Neurocysticercosis (NCC), Neglected disease, Recent strategies, *Taenia solium*, Visceral leishmaniasis.

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1. INTRODUCTION

Cysticercosis, a parasitic disease of the nervous system in humans caused by the larval stage of the tapeworm *Taenia solium*, is the only common cause of acquired epileptic seizures in the developing world, where active epilepsy is a common cause in developed countries [1 - 3].

All over the world, including India, neurocysticercosis (NCC) is the most predominant parasite ailment affecting the brain and a common recognizable cause of new seizures. NCC was the cause of epilepsy (at least one seizure in the five years prior to the survey) in at least a third of the patients, in a community survey of more than 50,000 persons in the district of Tamil Nadu, southern India [4]. According to the findings of the survey, there are 1 in 1000 cases of active epilepsy in India that are caused by NCC. Therefore, NCC is the cause of active epilepsy in at least 1.2 million Indians [5]. Solitary cysticercus granuloma (SCG), initially discovered in 1989, is the most prevalent ailment in India, appearing in up to 60% of NCC patients [6, 7].

The pathogenesis, regular history, clinical signs, and executives differ in the area of the cysticercus [8]. For instance, the real clinical signs shift between various types of illness (Table **1**). Parenchymal NCC regularly causes seizures or migraine. Ventricular NCC most frequently gives obstructive hydrocephalus. Subarachnoid NCC can offer hydrocephalus, meningitis, stroke, or central neurologic discoveries. Blended structures are likewise normal. Because of the intricacy of analysis and the board, the American Culture for Tropical Medication and Cleanliness (ASTMH) and the Irresistible Infections Society of America (IDSA) consented to mutually foster rules for the determination of NCC [9]. The Neurocysticercosis Classification and Neuroimaging According to Parasite's Location, Appearance with the Surrounding Host Tissue is shown in Table **1**.

Table 1. Neurocysticercosis Classification and Neuroimaging According to Parasite's Location, Appearance with the Surrounding Host Tissue.

Form[1]	Characteristic on Neuroimaging	Histopathology
Parenchymal[2]		
Nonviable calcified	Nodular calcifications Size:<20 mm in diameter (often 1–5 mm). With or without context oedema.	Calcified granuloma. With or without context inflammation and/or gliosis.
Single, small enhancing	Cystic or nodular enhancing lesion. Size: <2 cm.	Single parenchymal parasites. With context inflammation. Variable opacification. Absence of the cyst fluid.

(Table 1) cont.....

Form[1]	Characteristic on Neuroimaging	Histopathology
Viable parenchymal	Vesicular lesions. With evidence of associated contrast enhancement. High-definition imaging of scolex.	Parasites with intact cyst wall, vesicular fluid and scolex. With variable amounts of inflammation.
Extraparenchymal[3]		
Intraventricular	Cysticerci within the ventricles. Obstructive hydrocephalus or loculated hydrocephalus	Viable Cysticerci within the ventricles. Obstructive hydrocephalus
Subarachnoid	Cysticerci in the Sylvian fissure, in the basilar cisterns, or interhemispheric spaces. Strokes or meningitis without discrete cysts.	Cysticerci in the subarachnoid space mostly with arachnoiditis, and vasculitis. The cysticerci are in clusters with racemose May lack a scolex.
Spinal	Cysticerci within the spinal subarachnoid area. Intramedullary cysticerci within the spinal cord.	Subarachnoid cysticerci with attendant arachnoiditis. Intramedullary cysticerci analogus pathologically to parenchymal cysticerci.

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging.

[1]With the exception of single enhancing lesions that are also viable, which are classed with single enhancing lesions, patients with more than one form are classified according to the form found lower on the chart. Ocular cysticercosis is separately classified.

[2]Refers to cysticerci in the parenchyma of the brain. Small cysticerci that are present in the gyri above the cerebral convexity respond clinically similarly to parenchymal cysticerci and are categorized with them. Large parenchymal cysticerci (>20 mm) and several inflammatory parenchymal cysticerci with diffuse cerebral edema are rare types of neurocysticercosis.

[3]Refers to cysticerci outside of the brain parenchyma in the central nervous system.

2. THE PARASITE

Taenia solium is a dichotomous zoonotic cestode. The grown-up stage is a 2-4 m long tapeworm that lives in the small digestive tract of people. In nature, *T. solium* tapeworms have no other known end hosts. Likewise, with all cestodes, the gravid proglottids at the terminal end of the worm are loaded up with eggs, which are the wellspring of larval contamination or cysticercosis. The normal transitional host is the pig, which conceals larval blisters in any piece of its body. People become contaminated with blisters through unintentional ingestion of infective *T. solium* eggs through waste oral defilement (Fig. **1**).

CHAPTER 8

Current Therapeutic Strategies for Buruli Ulcer

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Abstract: The skin is a multifaceted organ with varied functions, but its exposure to various environmental conditions, including exposure to ultraviolet light, trauma, and infections, makes it more prone to ulcers. Ageing, poor lifestyle, and certain diseases, like obesity, hypertension, diabetes, *etc*., further exaggerate the cause. Skin ulcers are wounds (sores) often caused by reduced blood flow leading to absolute loss of the epidermal layer along with parts of the dermis or subcutaneous fat, and thus have tremendously slow healing affinity. Buruli ulcer (BU), or Bairnsdale is a type of necrotizing skin ulcer mainly caused by the bacterium, *Mycobacterium ulcerans*, and characterized initially by the formation of papules or nodules (edematous lesions), which further progresses to chronic skin ulceration as a result of epidermal hyperplasia, collagen destruction, and vascular damage in the underlying dermis and subcutis. It is considered one of the 20 neglected diseases of the skin by the World Health Organization (WHO). Although scattered in more than 33 countries, its prevalence is the highest in West Africa and this incidence has risen manifold during the last few years, which might be due to deforestation, artificial topographic alterations, and increased manual agriculture. Mycolactone, a polyketide-based immunosuppressive macrolide, is considered the major factor responsible for the pathogenesis of the disease. Its high toxicity dampens the immune system, causing extensive tissue destruction mainly in skin cells and minute blood vessels, leading to ulceration and skin loss. Generally, a combination of rifampicin with streptomycin, amikacin, clarithromycin, or ciprofloxacin along with oral prednisolone for eight weeks is specified as a first-line treatment. Surgery to remove necrotic tissue, BCG vaccination for short-term protection, and physiotherapy to promote healing are also found beneficial. To combat this deadly disease, enhanced public education and awareness through outreach initiatives is a must as prevention is always considered better than cure. Further studies in this area may be helpful in investigating more treatment regimens along with various ways by which the occurrence of Buruli ulcer can be avoided. The present study is therefore designed to compile all relevant literature, which can serve as an important lead for further investigations in this area of research.

Keywords: Antibiotics, Buruli ulcer, *Mycobacterium ulcerans*, Skin ulcer.

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1. INTRODUCTION

The skin is the most external part of the human body [1], comprising an intricate, complex network that is meant to defend our body from the direct attack of foreign particles, harmful rays, radiations, or entry of any kind of detrimental incursion. The skin tends to keep the human body safe and secure from the attack of injurious substances, pathogens, UV light, chemicals, and mechanical injury [2]. It consists of many layers that have a different moderately acting role to perform. Apart from safety, it performs miscellaneous functions that include excretion, defense mechanism, different climates, variations in extremes of temperature range, and protection. Being a complex organ, it is continuously exposed to environmental elements, the most important being ultraviolent light, trauma, and infections [3]. The skin is quite susceptible to disorders and diseases, especially microbial infections, which include cellulitis, erysipelas, impetigo, folliculitis, furuncles and, carbuncles and many more [4]. In substantial cases, it can also be affected due to the administration of some allergic food or, creams or any other product and gets infected. Skin infections are considered the 28th most common diagnosis in hospitalized patients [5]. Skin diseases are actually very hazardous as it imparts a lot of pain, tenderness, inflammation, redness, swelling and soreness to the patient. Most of these skin diseases have already been claimed, and understood, and required medicines are prepared to cure the particular disease. But the irony is that despite being common, they are not considered a noteworthy problem due to the myth that these are benign, not very critical, can cause minor nuisance, and ultimately are not fatal or life-threatening.

2. ULCERS

Ulcer can be clearly understood as a wound in which the epidermal skin layer is completely lost, affecting the surface tissue causing disintegration of the epithelial layer with eroded mucosa and extremely slow healing tendency. The incidence and intensity of ulceration is on a great rise due to varying factors such as stress, psychosocial conditions, age, alcohol consumption, population density, smoking, obesity, and diabetes, which at the same time elevates the risk factors for atherosclerotic occlusion [6]. Skin ulcers generally develop due to poor circulation, metabolic disorders, and bacterial infections, representing a difficult clinical problem and a major public health concern. Persistent wounds and ulcers affect more than 1% of the population with diverse etiologies, and their prevalence is estimated to rise significantly in the upcoming years [7]. Superficial skin ulcers may herald a primary disease ranging from acute to chronic, turning into malignant [8]. Ulcer changes further into acute wounds or *vice-versa* by proper treatment, thereby removing its underlying etiology and ultimately reversing its chronic nature [9]. Skin ulcer leads to a deep depression with a raised

and inflamed outer border, with the surrounding skin showing discoloration, turning black as the tissue dies. Skin ulcer initiates slowly and gradually worsens giving a burning or itching sensation, disintegrating the skin tissue, and eroding away.

2.1. Types of Ulcers

Ulcers can be classified into the following four types:

2.1.1. Decubitus Ulcers

Decubitus ulcers, popularly known as pressure ulcers, pressure injuries, or bedsores, are localised skin and soft tissue injuries causing damage to the underlying tissue. They generally occur as a result of constant pressure exerted on the skin for a prolonged period of time, decreasing the blood flow to the affected area, which can be fatal, leading to tissue damage. This class of ulcer tends to affect bony areas of the body, which are vulnerable to friction. The parts of the body more susceptible to this category of pressure ulcers include the back, tailbone, elbows, ankles, ischium, trochanter, sacrum, heel, malleolus and occiput [10].

2.1.2. Venous Ulceration

Venous ulceration, also termed varicose ulcer and stasis ulcer, is the most devastating effect of chronic venous disorders, resulting in more than 80 percent of lower extremity ulcerations with reduced mobility and financial constraints [11]. There are multiple reasons responsible for causing venous ulcers, such as poor blood circulation in the lower extremities, such as legs, varicose veins, obesity, trauma, age factor, sedentary lifestyle, lack of movement, and pregnancy, which can be contributing factors for the development of these ulcers.

2.1.3. Arterial Ulcers

Arterial ulcers, arterial wounds, or ischemic ulcers typically occur due to poor delivery of nutrient-rich arterial blood to the lower extremities, such as legs, ankles, and feet. Due to this poor perfusion, there is a depletion of oxygen content in the overlying skin and tissues, killing them and eventually turning them into an open type of lesion. The inadequate delivery of blood consequently leads to minor cuts, which do not cure easily, eventually causing necrosis, tissue damage, ulcer formation, and infection. Atherosclerotic disease is the major contributing factor apart from diabetes, vasculitis, gangrene, thalassaemia, and sickle cell disease.

CHAPTER 9

Current Therapeutic Strategies for Trachoma

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Abstract: As a result of persistent follicular conjunctivitis brought on by *Chlamydia trachomatis* and consequent corneal scarring, about 6 million people have irreparable blindness. *Chlamydia trachomatis* is a bacterium that causes trachoma, an eye infection. Early signs include eyelid itchiness and irritation, whereas advanced signs include swollen eyelids, pus oozing from the eyes, photophobia (light sensitivity), discomfort in the eye, and vision issues. Using the SAFE strategy, the WHO is driving an international campaign to eradicate Blinding Trachoma. Trichiasis surgery, antibiotic treatment for infection, hygiene promotion on the face, and environmental changes to improve air quality are all part of this. The best antibacterial medication for widespread distribution is oral azithromycin.

Keywords: Antibiotics, Eyelids, Hygiene, Trachoma, Vaccine.

1. INTRODUCTION

Trachoma (truh-KOH-muh), which is caused by specific *Chlamydia trachomatis* serovars [1 - 3], is the most prevalent blindness caused by infection [4]. An infection-related inflammatory conjunctivitis is known as “active trachoma.” [5, 6]. Repeated bouts [7 - 9] of active trachoma scarring on the eyelids may cause trachomatous trichiasis (TT), in which one or more eyelashes are redirected to touch the eye. The discomfort from TT is terrible [10 - 15]. It can be fixed with surgery. If left untreated, it may cause corneal opacification, blurred vision, and blindness.

Your eyes are impacted by trachoma. *Chlamydia trachomatis* bacteria is the cause of it. Trachoma can be disseminated through direct contact with an infected person's eyes, eyelids, nose, or throat secretions. Handling contaminated objects, including handkerchiefs, has the potential to spread the disease [16 - 18].

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The eyes and eyelids may first feel mildly uncomfortable and irritated due to trachoma. Then, your eyelids can swell and start to drain pus (Fig. **1**). Blindness may develop from trachoma if it is not treated [19].

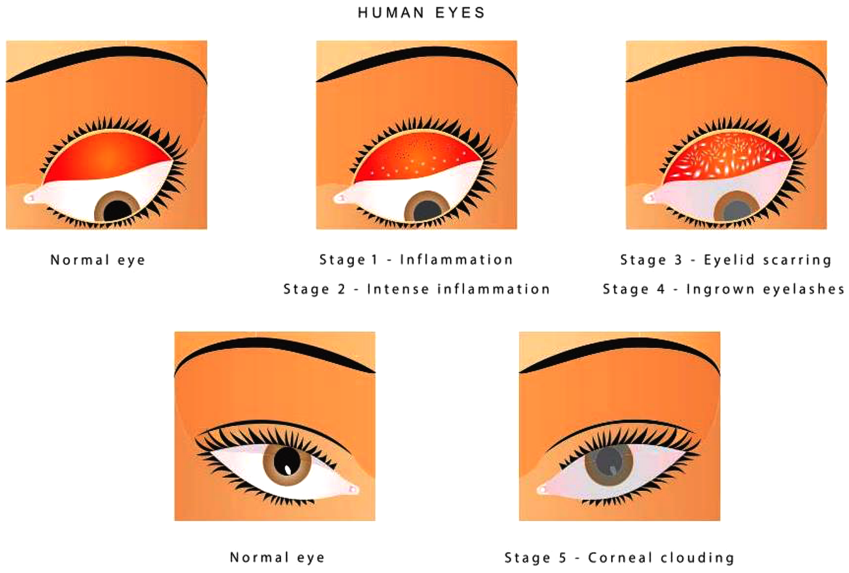

Fig. (1). Progression of trachoma [20].

The most commonly diagnosed form of blindness in the world is trachoma. Eight five% of trachoma cases happen in undeveloped areas of Africa, where the disease is very prevalent. In areas where the disease is prevalent, trachoma infection may be present in 60% or more of children under the age of five.

Trachoma problems may be avoided with early treatment [19].

2. CHLAMYDIA TRACHOMATIS

It is a gram-negative, intracellular, obligatory *Chlamydia trachomatis* bacteria. Its only known natural host is humans [15]. The most prevalent bacterial lymphatic system infections (serovars A–C) and sexually transmitted infections (STIs) in the globe are caused by several chlamydial serovars. (serovars L1 to L3) [18].

2.1. Symptoms and Signs

Trachoma often affects both eyes and signs and symptoms may include:

- Mild eye itching and irritation;
- Mucus- or pus-filled eye exudate;

- Swollen eyelid;
- Photophobia;
- A headache;
- Crimpsoneye; and
- Loss of vision.

Infection is particularly prone to affect young children. However, the illness advances gradually, and the more agonising symptoms cannot show up until adulthood [21].

2.2. Stages of Trachoma

According to the World Health Organization (WHO), trachoma develops in five stages [5]:

2.2.1. Follicular Inflammation

When seen under a magnifying glass, the inner surface of your upper eyelid will reveal five or more follicles, which are tiny bumps containing lymphocytes, a kind of white blood cell, in the early illness (conjunctiva).

2.2.2. Severe Inflammation

The top eyelid may thicken or enlarge at this point, and your eye is now highly contagious and inflamed.

2.2.2.1. Scarring on the Eyelids

Recurrent infections cause scarring on the inner eyelid. The scars typically appear as white lines when magnified. You could develop a malformed, inward-slanting eyelid (entropion).

2.2.3. Twisted Eyelashes (trichiasis)

Your eyelashes curl inward and rub against the transparent outside of your eye as a result of the distorted inner lining of your eyelid (cornea).

2.2.4. Cloudy Cornea (Opacity)

An inflammation that most frequently appears under your top lid affects the cornea. The cornea becomes clouded as a result of ongoing inflammation that is aggravated by scratching from the in-turned lashes.

Your upper lid exhibits all trachoma symptoms more severely than your lower lid. A disease process that starts in childhood can carry over into adulthood if no action is taken.

CHAPTER 10

Current Therapeutic Strategies for Food Borne Trematodiases

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Abstract: Food-borne trematodiases are among the neglected tropical diseases caused due to liver flukes (*Clonorchissinensis*, *Fasciolagigantica*, *Opisthorchis vivernii*), lung flukes (*Paragonimus* spp.) and intestinal parasitic flukes (*Echinostoma spp.*) infections and is an emerging public health problem. They are mostly found in developing countries and in areas where they are present, they aggravate poverty. However, they are no longer being neglected because of their broad geographical distribution, a wide range of infected people, and measures available to control several neglected tropical diseases. WHO estimates that every year two million people are suffering from disability and death due to these neglected diseases. The treatment of food-borne trematodiases, a neglected disease, is important for preventing the progression of clinical diseases and reducing the associated morbidity. In the present chapter, we will discuss the food-borne trematodes' life cycle, associated symptoms, diagnosis and various strategies used in treating food-borne trematodiases. Currently used chemotherapeutic drugs, their safety, therapeutic profile, and resistance developed are summarized here. Furthermore, emphasis is given to developing a broad-spectrum trematocidal drug with high safety and efficacy.

Keywords: Artesunate, Artemether, Chemotherapy, Diagnosis, Food-borne trematodiases, Geographic distribution, Lifecycle, Mefloquine, Praziquantel, Symptoms, Therapeutic strategies, Triclabendazole, Tribendimidine.

1. INTRODUCTION

Food-borne trematodiases are one of the neglected tropical diseases caused by intestinal, lung, and liver parasitic fluke infections. The parasites included are *Clonorchis*, *Fasciola*, *Paragonimus*, and *Opisthorchis* [1]. The life cycle of these parasitic flukes is known to be complex because of their presence in different

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definitive hosts or one or two intermediate hosts. In humans, infection due to food-borne trematodiases spreads by eating contaminated food. The infection produces various lung and liver diseases and every year, two million people suffer from disability and death worldwide due to these diseases [2].

The first food-borne trematode was discovered in 1760 in Germany during the postmortem examination of a female body. Then it was found to be a parasitic worm that belongs to the genus *Fasciola* [3]. The *Clonorchis sinensis* infection was first time reported in 1874 during the postmortem examination of a 20-years-old Chinese woman that showed oozing out of small size, dark coloured vermicular-looking bodies from the bile duct. In 1879 and 1892, the first report of *Paragonimus sp.* and *Opisthorchis felineus* infection appeared, respectively [4]. After these discoveries, more than hundreds of food-borne trematodes have been isolated and identified that are present in humans and affect domestic animals. Lung and liver fluke organisms pose more problems in people compared to intestinal flukes [5]. Foodborne trematodiases are endemic in various places in the world, particularly in rural places among low-wage earners, school children, and women of child-bearing age. In spite of changes in eating habits, health education, environmental alteration, industrialization, and the use of broad-spectrum antihelmintics, this disease is among the major public health problems [6]. In this chapter, the life cycle of food-borne trematodes, their geographical distribution, symptoms, diagnosis, and different treatment strategies for food-borne trematodiases have been described.

2. THE LIFE CYCLE OF FOOD-BORNE TREMATODES

Food-borne trematodes can be found in each organ of their definitive hosts and have complex life cycles that also involve different larval types. The complete life cycle of food-borne trematodes is described in Fig. (**1**). Their life cycle includes different hosts including vertebrate definitive hosts, humans, an invertebrate, the first intermediate host (mollusk), and the second intermediate host having an encysted metacercarial stage. In humans or domestic animals, following sexual reproduction, eggs are produced and released *via* feces or sputum [7].

Eggs of the parasites from infected humans or animals reach the freshwater bodies *via* contaminated feces. This may occur due to the defecating habits of humans in an unhygienic manner or the human feces used as fertilizer. These food-borne trematodes are mainly present in animals such as cats, dogs, foxes, rodents, and pigs, which are the definitive hosts for *C. sinensis,* whereas *F. hepatica* are mainly present in domestic ruminants. Once the eggs reach fresh water, their development occurs and miracidium is released that enters into the aquatic snail known as the first intermediate host. After several weeks, the development of

miracidium into cercariae takes place. They are then released into the freshwater environment, attach, penetrate, and encyst in the form of metacercariae in the second intermediate host. By ingesting metacercariae, food-borne trematode infection is achieved through eating raw fish, freshwater crabs, and aquatic plants or by drinking contaminated water [8].

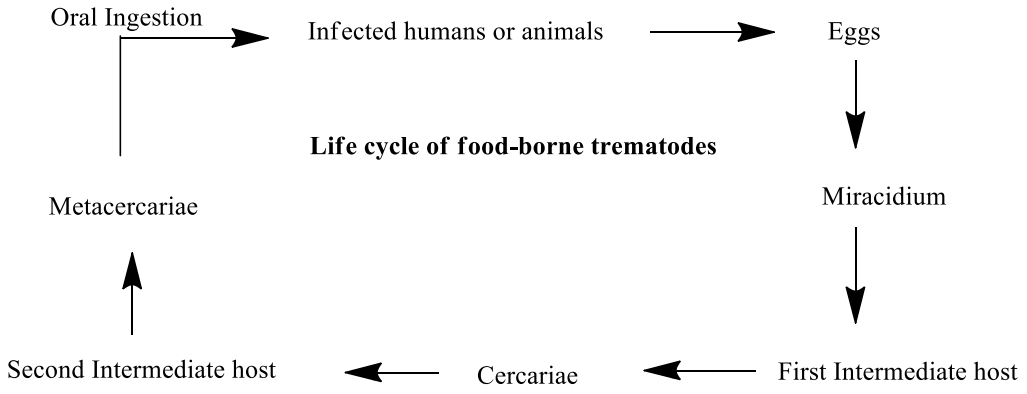

Fig. (1). Life cycle of food-borne trematodes.

3. GEOGRAPHIC DISTRIBUTION

The food-borne trematodiases transmission is restricted to those areas where the first and second intermediate hosts present together under conditions requiring appropriate environmental factors and where humans usually eat raw, undercooked fish and similar aquatic products [8, 9]. The number of infectious cases varies according to the trematode species. Worldwide, more than 200 million people were found to be at risk of *C. sinensis* infection, more than 15 million have been infected, and over 1.5 to 2 million showed complications. China has the maximum number of *C. sinensis* infected people, that is, around 13 million [10]. Around 20 million people have been found to be infected with *Paragonimus sp.* and 293 million people are at risk [11]. With *Opisthorchis viverrini*, 10 million people are infected [12] and with *Fasciola sp.* between 2.6 to 17 million people are found to be infected globally [13]. Approximately 3.5 billion people are found to be infected with different species of intestinal flukes [14].

4. SYMPTOMS

According to WHO, the public health burden due to food-borne trematodiases is because of morbidity rather than mortality because most of the early and light infections mostly go unnoticed. In case of chronic infections, severe morbidity

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Ms. Prerna Sharma currently serves as an assistant professor at Shri Krishna Ayush University, Kurukshetra. With 11.8 years of teaching experience, her expertise lies in the standardization of herbal plants and formulations. Her research focuses on pharmacognostical and phytochemical investigation of Indian medicinal plants. She has to her credit 50 research and review publications in reputable national and international journals, along with 40 copyrights, 2 patents, and participation in over 30 national and international conferences and workshops. Ms. Sharma has been honored with the Young Research Scientist Award by SPER and TIPA in Thailand.

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Bhawna Chopra

Dr. Bhawna Chopra, a distinguished academic and researcher in Pharmaceutical Sciences, focuses on the therapeutic potential of natural compounds. She holds a Bachelor's degree in Pharmacy from Guru Gobind Singh College of Pharmacy and a Master's degree from ISF College of Pharmacy. Her Ph.D. is from IK Gujral Punjab Technical University. With over 15 years of teaching experience, she received the Women Pharma Personality Award at the National Pharma Summit 2022. She is recognized as a Highly Cited Researcher by Elsevier and serves on editorial boards, including Bentham Science Publishers. She is an active member of professional organizations such as APTI, ISTE, and SPER, with over 85 publications, patents, and copyrights.

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