Common Tropical Infections
Suma T K
Department of Internal Medicine, T. D. Medical College Hospital, Alappuzha, Kerala, India*

ABSTRACT
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Introduction: Certain diseases are more common in tropics probably because tropical climates are more conducive to these diseases and also because areas of poverty and primitive sanitation conditions are more common in the tropics. Tropical infections cause significant morbidity and mortality especially in less developed regions of the world.

Re-emerging infectious diseases are defined as those that are ‘due to the reappearance of, and an increase in the number of infections from a disease, which is known, but which had formerly caused so few infections that it had no longer been considered a public health problem’.

Discussion: For many emerging and re-emerging infectious diseases, changes in the pathogen and host environment play the primary role. Even minor ecological changes may significantly alter transmission and exposure patterns leading to sudden proliferation of disease. The recent epidemics of Chikungunya fever and the return of Dengue fever in India clearly shows the emergence of disease due to environmental changes and increased survival capability of mosquitoes. This article describes briefly salient points about Chikungunya fever and Dengue fever.

Keywords: Tropical infections, Dengue fever, Chikungunya fever.

*See End Note for complete author details

INTRODUCTION

The tropics are the part of equator bounded by the tropics of Cancer and Capricorn. Tropical diseases are illnesses that either occur uniquely in tropical and subtropical regions or, more widespread in the tropics. Certain diseases are more common in tropics probably because tropical climates are more conducive to these diseases and also because areas of poverty and primitive sanitation conditions are more common in the tropics. Tropical infections cause significant morbidity and mortality especially in less developed regions of the world.

The causative pathogens for the tropical infections include bacteria, viruses, parasites, and fungi. The various tropical infections caused by pathogens are given below. Some infections, such as measles, human immunodeficiency virus (HIV), and tuberculosis, though found throughout the world, are included in the list as they cause severe morbidity and mortality in tropical countries.

Emerging and re-emerging infectious diseases: Recently, infectious diseases have continued to emerge and re-emerge in a manner that defies accurate predictions. About 15 million (more than 25%) of the 57 million deaths worldwide are estimated to be related directly to infectious diseases. According to WHO, emerging infectious diseases are defined as those ‘resulting from newly identified and previously

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Corresponding Author:
Dr. Suma T K, Professor, Department of Internal Medicine, T. D. Medical College Hospital, Alappuzha, Kerala, India.
Phone: 98470 41205.  Email: sumatk@gmail.com
unknown infections, which cause public health problems either locally or internationally? SARS is an example of an emerging infectious disease. Re-emerging infectious diseases are defined as those that are ‘due to the reappearance of, and an increase in the number of infections from a disease, which is known, but which had formerly caused so few infections that it had no longer been considered a public health problem’. Anthrax is an example of a re-emerging infectious disease. The factors contributing to the emergence of new infections and re-emergence of infections include microbial adaptation, changes in human susceptibility to infection, climate and weather, changing ecosystems, human behavior and demographics, international travel and commerce, technology and industry, breakdown of public health measures, poverty and social inequality and even lack of political will.

For many emerging and re-emerging infectious diseases, changes in the pathogen and host environment play the primary role. Even minor ecological changes may significantly alter transmission and exposure patterns leading to sudden proliferation of disease. The recent epidemics of Chikungunya fever and the return of Dengue fever in India clearly shows the emergence of disease due to environmental changes and increased survival capability of mosquitoes. This article describes briefly salient points about Chikungunya fever and Dengue fever.

**Chikungunya Fever**

Chikungunya is a tropical disease caused by Chikungunya virus belonging to the genus Alpha virus and transmitted by Aedes mosquitoes. This disease typically consists of an acute illness with fever, skin rash, and incapacitating arthralgia. The word chikungunya, means “to walk bent over” in the African dialect Makonde, and refers to the effect of the incapacitating arthralgia.

**Epidemiology**

The first recorded epidemic of chikungunya occurred in Tanzania in 1952–53 and thereafter the infection has been documented in Burma, Thailand, Cambodia, Vietnam, India, Sri Lanka, and the Philippines. In 2001–2003, chikungunya virus re-emerged in Java, Indonesia, after a gap of 20 years. The first reported outbreak of chikungunya in India was in Calcutta in 1963 and later outbreak occurred in Barsi (Maharashtra) in 1973. The virus re-emerged in India in December 2005. Indian chikungunya outbreak actually followed the outbreak in the Indian Ocean islands and this may be related to the heavy tourist traffic between the two regions. The Indian and Indian Ocean outbreaks are caused by an African strain of chikungunya virus. Studies are underway to determine the genomic structure and virulence of Indian chikungunya virus isolates and to explain the re-emergence of the virus.

**Clinical manifestations**

Chikungunya fever affects all age groups and both sexes equally. The incubation period ranges from 3-12 days with an average of 2-4 days. Clinical onset is abrupt with high fever, headache, back pain, myalgia, and arthralgia. Arthralgia can be intense affecting mainly the extremities, frequently involving the small joints of the hand, wrist and ankles and may also involve the larger joints such as knee and shoulder. Erratic, relapsing, and incapacitating arthralgia is the hallmark of chikungunya. The pain may be severe enough to immobilize the patient and interfere with sleeping at night. It may persist for several months. The underlying mechanism of the crippling arthralgia is unknown. Arthralgia is rare in children. Skin manifestations such as a maculopapular rash predominating on the thorax, facial oedema, a bullous rash with pronounced sloughing, and localized petechiae occur in 40-50% of patients.

**Rare Manifestations**

Unlike dengue fever, hemorrhagic manifestations are uncommon in Chikungunya fever. When present they are mild and are more frequently encountered in Asian patients. These include epistaxis, bleeding from gums, sub-conjunctival haemorrhage and petechial/purpuric rash. Rarely, meningoencephalitis has also been described.

**Course of the Disease**

The fever is of short duration and usually resolves in three to four days. In some patients, a biphasic pattern of fever has been described with a febrile episode of four to six days, followed by a fever free period of a few days and then a recurrence of fever lasting a few days. Chikungunya is a self-limiting disease. In majority of the patients, the joint pains resolve in one to three weeks, but arthritis persisting for up to three years after the onset of illness has been documented. Indiscriminate use of corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs), especially aspirin and antibiotics may contribute to thrombocytopenia, gastrointestinal bleeding and gastritis. This may lead to dehydration, pre-renal acute renal failure, electrolyte abnormalities and sometimes hypoglycemia.
Diagnosis

During an outbreak in an endemic area, the diagnosis could be made by a detailed history and physical examination. The gold standard for the diagnosis of Chikungunya fever is viral culture, but this is seldom carried out as these facilities are available at selected centers only. Two main diagnostic methods are available, namely Reverse transcription-polymerase chain reaction (RT-PCR) and serology (IgM or IgG). RT-PCR is useful during the initial viraemic phase (day 0 to day 7) but classic serological methods are simpler (haemagglutination inhibition, complement binding, immunofluorescence, and ELISA). IgM is detectable after an average of 2 days by ELISA, immunofluorescent assay and persists for several weeks to 3 months. IgG is detected in convalescent samples and may persist for years. The sensitivity and specificity of these tests are poorly established, and so there is a possibility of false-positive reactions resulting from cross-reactivity with dengue or other Arboviruses.

MANAGEMENT

Chikungunya is a self-limiting disease and there is currently no effective antiviral treatment for chikungunya. Treatment is therefore purely symptomatic and is mainly based on non-salicylate analgesics and non-steroidal anti-inflammatory drugs. Ensuring adequate fluid intake, judicious use of paracetamol or NSAIDs for symptom relief can be helpful. As mentioned earlier, aspirin should be avoided due to its effect on platelets. Some clinicians have used hydroxychloroquine/chloroquine for treating the viral arthropathy of Chikungunya fever. Published evidence does not support the use of corticosteroids, antibiotics or antiviral drugs in the management of Chikungunya fever and indiscriminate use of these agents can be hazardous. Electrolyte imbalance, pre-renal acute renal failure, bleeding manifestations should be watched carefully and managed accordingly.

PREVENTION

Presently no vaccine is available for Chikungunya fever. Pending vaccine development, the only effective preventive measures consist of individual protection against mosquito bites and vector control. Patients with chikungunya fever should be advised to avoid being bitten by mosquitoes as the disease can be transmitted to others. Educating the community and public health officials, vector control measures such as elimination of breeding sites and spraying of insecticides should be initiated at the individual and community levels as this can be rewarding.

Dengue Fever

Dengue is an acute viral disease caused by a flavivirus, single-stranded, non-segmented RNA virus belonging to the family Arboviridae. This disease is characterized by fever, headache, muscle and joint pain, rash, nausea and vomiting. The most severe form of the disease is dengue hemorrhagic fever, which is characterized by thrombocytopenia, bleeding, and shock. The hemorrhagic form continues to be the leading viral hemorrhagic fever in the world.

Epidemiology

Dengue is the most important arthropod-borne viral disease of public health significance and has developed into one of the world’s major emerging infectious diseases with a global prevalence in more than 120 countries. The World Health Organization estimates that more than 2.5 billion people are at risk of dengue infection. First recognised in the 1950s, this disease has become a leading cause of child mortality in several Asian and South American countries. The first recognized dengue epidemics occurred almost simultaneously in Asia, Africa and North America in the 1780s. Dengue is transmitted by Aedes mosquitoes, particularly A. aegypti and less commonly A. albopictus. These mosquitoes travel well, particularly in cargo ships and the four subtypes of dengue virus have spread to most tropical and subtropical countries in their wake. During the last 200 years, spread of the disease has increased, reaching epidemic proportions during the last three decades. Since the late 1990s, dengue is the most important mosquito-borne disease affecting humans after malaria, with around 40 million cases of dengue fever and several hundred thousand cases of dengue haemorrhagic fever (DHF) each year.

Dengue virus is an arbovirus composed of single-stranded RNA. It has 4 serotypes, DEN-1, 2, 3 and 4. All serotypes can cause severe and fatal disease. Each serotype provides specific lifetime immunity, and short-term cross-immunity. The second infection with a different serotype becomes more severe. Genetic variation within serotypes has been demonstrated and some genetic variants within each serotype appear to be more virulent or have greater epidemic potential.

Clinical manifestations

Dengue virus infection may be asymptomatic or may cause undifferentiated febrile illness (viral syndrome),
dengue fever (DF) or Dengue Hemorrhagic fever (DHF) including dengue shock syndrome (DSS). Dengue fever could be with or without frank hemorrhage. DHF could present with or without shock. The clinical presentation depends on age of the host and the virus strain. The clinical spectrum of the disease is given below.

Undifferentiated fever

The first infection with dengue virus presents with an undifferentiated viral like illness. Maculopapular rashes may appear during the fever or during defervescence. Fever may be associated with nausea, vomiting, retro-orbital pain, intense headache, asthenia and myalgias.

- Positive tourniquet test
- Petechiae, ecchymosis, purpura
- Bleeding from mucosa, GIT, others
- Hematemesis, malena

3. Low platelet count (d”100,000/mm$^3$)
4. Objective evidence of capillary leakage
5. Elevated hematocrit (e” 20% above baseline)
6. Low albumin
7. Pleural or other serous effusions

b. Severity of DHF

Grade 1: Fever accompanied by non specific constitutional symptoms and a positive tourniquet test.
Grade II: Spontaneous bleeding in addition to the manifestation of Grade I patients, usually in the form of skin or other hemorrhages.
Grade III: Circulatory failure manifested by rapid and weak pulse with a narrow pulse pressure (<20 mm Hg) or hypotension with the presence of cold clammy skin and restlessness
Grade IV: Profound shock with undetectable blood pressure.

c. Danger signs in DHF: The four warning signs for an impending Dengue shock syndrome are i) Abdominal pain which is intense and sustained; ii) persistent vomiting; iii) abrupt change from fever to hypothermia, with sweating and prostration and iv) restlessness or somnolence. Increase in hematocrit and reduction in platelet count are also warning signals.

Dengue Shock syndrome: The identification of DSS requires all four DHF criteria and in addition evidence of circulatory failure manifested by: a) Rapid and weak pulse; b) Narrow pulse pressure (<20 mmHg); c) Hypotension for age < 5 yr- < 80 mmHg, > 5 yr- < 90 mmHg and d) Cold clammy skin, restlessness.

Unusual presentations:

These include encephalopathy, hepatic damage, renal failure and severe gastrointestinal hemorrhage. Seizures and coma have been reported in recent epidemics probably due to prolonged shock and bleeding within internal organs. Inappropriate use of water in treatment leading to hyponatremia may be responsible for features of encephalopathy. Subdural effusions have been observed in some cases. Fatal cases of encephalitis have been reported. Acute liver failure and renal damage usually occur at the terminal stage and may be associated with features of encephalopathy.
Pathogenesis of dengue hemorrhagic fever and dengue shock syndrome:

DHF is almost always found in individuals who had a previous exposure to at least one of the four serotypes of dengue virus. Release of vasoactive mediators from the infected monocytes results in increased vascular permeability and hemorrhagic manifestations that characterize DHF and DSS. In DHF there is an early suppression of bone marrow causing leucopenia and thrombocytopenia. Decreased levels of fibrinogen, prothrombin, factor II, VII, VIII, IX, X, XII, ATIII, protein C and S have also been reported. The levels of C3 and C5 are depressed, and C3a and C5a are elevated. The mechanism of thrombocytopenia in DF is controversial. It has been proposed that there is impaired megakaryocytic production and increased platelet destruction. The causes of platelet injury have been attributed to the virus itself, circulating antiplatelet antibodies, immune complexes and DIC. In addition platelet function abnormalities contribute to bleeding.

DIAGNOSIS

WHO clinical case definition:

Probable:
An acute febrile illness with two or more of the following:
- Headache
- Retro orbital pain
- Myalgia and arthralgia
- Nausea and vomiting
- Skin rash
- Hemorrhagic manifestations and
- Supportive serology or occurrence at the same location and time as other confirmed cases of DF

Confirmed:
Confirmation of DF is based on laboratory criteria
- Virus isolation from serum or tissue samples; or
- Demonstration of 4-fold or more rise in IgG and IgM antibody titers to dengue antigens in paired serum samples; or
- Demonstration of dengue antigen in tissue, serum, CSF by immunohistochemistry, immunofluorescence or ELISA; or
- Detection of genomic sequences by PCR

Management:
Dengue fever can be best managed at home, with an advice to take bed rest, consume plenty of oral fluids and paracetamol for control of fever. Patients should be advised to monitor platelets and hematocrit regularly at home and report to the hospital if there is persistent vomiting, or are unable to comply with medical advice. Patients with Grade II, III or IV illness should be hospitalized.

a. Intravenous Fluid Therapy for Dengue Fever:
Intravenous fluid therapy is the cornerstone for the management of Dengue fever. Crystalloids are used in fluid resuscitation. Dextrose, normal saline and ringer lactate can be used for fluid replacement. In Grades I and II, fluids are started at an initial rate of 6 ml/kg/hour for the first two hours and the patient is reassessed. If there is improvement in clinical features the fluid rates may be reduced to 3 ml/kg/h for the next 6 to 12 hours and discontinued after 24 hours. If no improvement during reassessment, fluid rates should be increased to 10 ml/kg/h. In grades III or IV, immediate volume replacement should be attempted with crystalloids at the rate of 10-20 ml/ kg/h for the first hour and the patient should be reassessed. In case of improvement the fluid therapy may be tapered of gradually over the next 24 to 48 hours.

b. Role of Platelet Transfusion in DHF:
There are no clear indications of platelet transfusion in Dengue fever. The World Health Organization recommends that platelets should be transfused only if the patient is bleeding or has a platelet count less than 10,000/cmm. Platelets should not be transfused blindly and decisions should be based on clinical judgment.

c. Role of Steroids in Dengue Hemorrhagic Fever:
It has been shown that corticosteroids have no clear indication or therapeutic benefit in the management of DHF or DSS.

Prevention:
Currently there is no licensed vaccine against dengue virus. Field testing of an attenuated tetravalent vaccine is currently underway.

CONCLUSION
The outbreaks of these diseases highlight the importance of monitoring vector borne diseases. Affordable, reliable rapid sero diagnostic tests that will be useful in the field setting are to be developed. Virology laboratory facilities are available only in few selected centers in India. There is an urgent need for setting up a nationwide network of reliable, high quality of virology laboratories and developing a surveillance
system for monitoring outbreaks of these diseases. Still the development of vaccine has to go a long way. With increasing urbanization and lack of hygiene, conditions facilitating breeding of the mosquito vector are ever increasing. A more drastic change in the outlook of the community and public health authorities with regard to hygiene and mosquito control measures is essential.

END NOTE

Author Information
Dr. Suma T K, Professor, Department of Internal Medicine, T. D. Medical College Hospital, Alappuzha, Kerala, India. Phone: 98470 41205

Conflict of Interest: None declared


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