



An Overview of Etiology, Types, Pathophysiology and Treatment of Dengue

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1. INTRODUCTION

Dengue is one of the most common mosquito-borne viral diseases affecting humans today. It is caused by the *dengue virus* (DENV), which is transmitted mainly by the bite of infected *Aedes aegypti* mosquitoes. The disease is often called “breakbone fever” because of the severe joint and muscle pain it causes.

The story of dengue goes back several centuries. Historical records suggest that dengue-like illnesses were described in China as early as the 10th century, but it wasn’t until the 18th and 19th centuries that major outbreaks were documented in tropical regions around the world. With the growth of trade and travel, the virus spread widely, especially in places where mosquitoes thrived.

In the present day, dengue has become a major global health concern. It is now found in more than 100 countries, particularly in tropical and subtropical areas of Asia, Africa, and the Americas. According to the World Health Organization (WHO), hundreds of millions of infections occur every year, and severe forms like dengue hemorrhagic fever and dengue shock syndrome can sometimes be life-threatening.



1.1 Background

The history of dengue stretches far back, long before modern medicine identified it. The earliest descriptions of dengue-like illness appear in Chinese medical writings from the Jin Dynasty (around 992 AD), where the disease was referred to as “water poison” and associated with flying insects. In the 17th and 18th centuries, major outbreaks of a dengue-like disease were reported in Asia, Africa, and the Americas — coinciding with the expansion of sea trade routes. The movement of ships carrying water barrels and goods also carried mosquito larvae, unknowingly helping dengue spread across continents.

The first scientifically recorded epidemics occurred in 1779–1780 simultaneously in Asia, Africa, and North America. However, it wasn't until the early 20th century that researchers began to understand the true cause of dengue. In 1906, the *Aedes aegypti* mosquito was confirmed as the main vector, and by 1943, the dengue virus had been isolated and classified. The discovery of the virus during World War II provided a new understanding of how it spread rapidly in tropical regions where soldiers were stationed.

During the mid-20th century, after the end of the war, rapid urbanization, increased population density, and poor waste management created ideal breeding conditions for mosquitoes. These factors contributed to the re-emergence of dengue as a major epidemic disease. By the 1960s and 1970s, dengue had become endemic in many Southeast Asian countries. The first recognized cases of severe dengue — then called “dengue hemorrhagic fever” — were documented in the Philippines and Thailand. Over time, dengue evolved from being a sporadic tropical illness to a continuous and serious global health concern.

1.2 Dengue in the Present Day

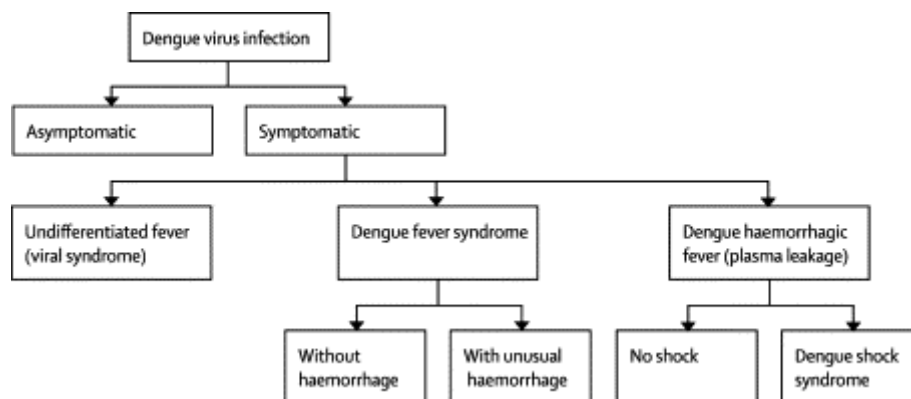
In the present era, dengue has become one of the fastest-spreading viral infections transmitted by mosquitoes. According to the World Health Organization (WHO), around **400 million people** are infected every year, with nearly **100 million showing clinical symptoms** and tens of thousands resulting in severe complications. The disease is now endemic in more than **100 countries**, including India, Sri Lanka, Thailand, Indonesia, Brazil, Mexico, and parts of Africa. The virus thrives particularly well in tropical and subtropical climates, where temperatures, rainfall, and humidity support mosquito breeding.

In India, dengue has become a seasonal threat that peaks during and after the monsoon months, when stagnant water provides ideal breeding grounds for mosquitoes. Every year, cities like Delhi, Mumbai, Chennai, and Kolkata experience a surge in dengue cases, putting pressure on hospitals and healthcare systems. Rural areas are not spared either, as increased travel and poor sanitation help the virus spread.

One of the major reasons dengue has continued to rise is **rapid urbanization** without proper waste disposal and drainage systems. Open water containers, old tires, flowerpots, and plastic waste often hold rainwater — becoming perfect nurseries for *Aedes* mosquitoes. Climate change has also worsened the situation, as warmer temperatures allow mosquitoes to survive longer and expand to new areas that were once too cold for them. In this way, dengue is not only a medical issue but also an environmental and social one.

2. Types of Dengue

Dengue is a viral disease caused by the *dengue virus (DENV)*, which has **four distinct but closely related serotypes** — DENV-1, DENV-2, DENV-3, and DENV-4. Each type can cause the same range of illnesses, from mild fever to severe and life-threatening conditions. Infection with one serotype provides lifelong immunity against that specific type, but only short-term protection against the others. This means a person can be infected up to four times in their lifetime by different serotypes.



Dengue classification

Clinically, dengue is classified into **three main types** based on severity and symptoms:

1. **Dengue Fever (Classical or Mild Dengue)**
2. **Dengue Hemorrhagic Fever (DHF)**
3. **Dengue Shock Syndrome (DSS)**

Each type differs in how it affects the body, the seriousness of symptoms, and the kind of care needed.

1. Dengue Fever (Classical Dengue)

This is the most common and mildest form of dengue infection. It is often mistaken for the flu because the symptoms are similar in the beginning. The infection usually appears **four to ten days after the mosquito bite**, and it lasts for about a week.

Symptoms:

- Sudden high fever (up to 104°F or 40°C)
- Severe headache and pain behind the eyes
- Muscle and joint pain (giving the name “breakbone fever”)
- Nausea, vomiting, and loss of appetite
- Skin rash appearing 3–4 days after the fever
- Fatigue and mild bleeding (such as nose or gum bleeding)

The fever usually follows a *biphasic pattern*, meaning it comes in two waves — it rises sharply, drops after a few days, and then returns again before finally subsiding.

Although most patients recover within a week, weakness and tiredness can linger for days or weeks. People often describe feeling drained or unable to work normally even after the fever ends. Proper rest, hydration, and fever control medicines like paracetamol are essential for recovery. Aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided as they can increase the risk of bleeding.

In general, **classical dengue fever** is not fatal, but it can develop into severe forms if not managed properly or if the patient gets infected again with a different serotype later in life.

2. Dengue Hemorrhagic Fever (DHF)

Dengue Hemorrhagic Fever is a more serious form of dengue that can develop after a person is infected for the second time by a different serotype. The body’s immune system reacts strongly, and this immune response causes damage to blood vessels, leading to leakage and internal bleeding.

Symptoms:

- High fever lasting 2–7 days
- Severe abdominal pain and persistent vomiting
- Bleeding from gums, nose, or under the skin
- Appearance of red or purple spots (called petechiae)
- Enlarged liver and signs of restlessness
- Low platelet count and plasma leakage
- In DHF, the patient’s condition may suddenly worsen after the fever starts to drop. This is known as the *critical phase*. It is the time when the body begins to lose plasma from blood vessels, causing dehydration, low blood pressure, and shock if not treated quickly.
- Laboratory tests play an important role in identifying DHF. Doctors monitor **platelet count** and **hematocrit level** (which measures the concentration of red blood cells). A drop in platelets and a rise in hematocrit usually indicate plasma leakage.
- Timely medical attention, fluid replacement therapy, and close monitoring can save lives. Without proper care, DHF can become fatal, especially in young children and people with weak immunity.

3. Dengue Shock Syndrome (DSS)

Dengue Shock Syndrome is the most dangerous and life-threatening form of dengue infection. It usually develops as a complication of DHF when the blood vessels lose too much plasma, causing a severe drop in blood pressure and leading to shock.

Symptoms of DSS:

- Intense stomach pain
- Continuous vomiting and restlessness
- Cold, clammy skin
- Rapid but weak pulse
- Difficulty breathing
- Bluish skin and confusion
- Very low blood pressure and weak pulse

When a person goes into shock, vital organs like the liver, kidneys, and brain receive less blood and oxygen, which can lead to organ failure if not treated immediately. DSS requires urgent hospitalization, intravenous fluid therapy, oxygen support, and sometimes blood transfusion in severe cases.

The critical stage in DSS usually occurs between the **third and seventh day** of illness. Early detection and supportive treatment during this period are essential to prevent death. Thankfully, with timely hospital care and improved awareness, the fatality rate of DSS has reduced significantly in recent years.

4. Serotypes of Dengue Virus

Apart from the clinical types, dengue is also categorized by its **four viral serotypes** — DENV-1, DENV-2, DENV-3, and DENV-4.

Each serotype has slight genetic and structural differences, but they cause similar symptoms. Infection with one serotype gives immunity against that type only, which is why secondary infections by another serotype can be more severe.

- **DENV-1:** Often linked with classic dengue fever; outbreaks have been common in Southeast Asia and South America.
- **DENV-2:** Frequently associated with severe forms like DHF and DSS; responsible for several large epidemics worldwide.
- **DENV-3:** Known to cause moderate to severe infections and is commonly seen in Asia and India.
- **DENV-4:** Less commonly found but can still cause outbreaks; tends to produce milder infections.

Because all four serotypes circulate simultaneously in many countries, the risk of multiple infections has increased, making dengue control even more difficult.

3. Pathophysiology of Dengue

The pathophysiology of dengue refers to the series of biological and physiological changes that occur in the human body after infection with the *dengue virus (DENV)*. Understanding this process helps explain why the disease causes high fever, severe pain, and in some cases, dangerous complications like bleeding and shock.

Dengue virus belongs to the *Flaviviridae* family and has four serotypes: DENV-1, DENV-2, DENV-3, and DENV-4. The virus is transmitted to humans through the bite of infected *Aedes aegypti* or *Aedes albopictus* mosquitoes. Once inside the body, it multiplies rapidly and triggers a complex immune response that can either protect or harm the individual, depending on various factors.

1. Transmission and Entry of the Virus

The infection begins when a female *Aedes* mosquito bites a person to feed on their blood. If the mosquito is carrying the dengue virus, the virus enters the bloodstream along with the mosquito's saliva. The saliva acts as a vehicle for the virus, helping it enter human cells without being immediately destroyed by the immune system.

After entering the body, the dengue virus targets **immune cells** such as dendritic cells, macrophages, and monocytes. These cells are part of the body's natural defense system, but the virus uses them to replicate. Once inside, the virus multiplies and spreads through the lymphatic system and bloodstream, reaching various organs such as the liver, spleen, and bone marrow.

The **incubation period** — the time between the mosquito bite and the onset of symptoms — typically lasts **4 to 10 days**. During this time, the virus multiplies quietly inside the body before the person begins to feel sick.

2. Viral Replication and Immune Response

Once the virus begins to replicate, the body's immune system immediately recognizes it as a foreign invader and starts defending itself. The immune cells release **cytokines**, which are signaling molecules that help coordinate the body's defense. However, in dengue, these cytokines are often produced in excessive amounts, leading to what is called a "**cytokine storm**."

This overreaction of the immune system is one of the key reasons why dengue causes severe inflammation and tissue damage. The cytokines increase the permeability (leakiness) of small blood vessels, allowing plasma (the liquid part of blood) to escape into surrounding tissues. This results in **plasma leakage**, a hallmark of severe dengue.

At the same time, the immune system produces **antibodies** against the virus. These antibodies help neutralize the infection during the first exposure. However, during a second infection with a different dengue serotype, the antibodies from the first infection may not completely neutralize the new virus. Instead, they attach to the virus and help it enter more immune cells — a phenomenon called **Antibody-Dependent Enhancement (ADE)**.

3. Antibody-Dependent Enhancement (ADE)

ADE is one of the most important mechanisms that explain why **secondary dengue infections** are often more severe.

When a person is infected for the first time with one dengue serotype, their body produces antibodies specific to that virus. These antibodies remain in the body for years. If the person later gets infected with a different dengue serotype, the old antibodies recognize the virus but cannot fully neutralize it. Instead, they bind to the virus and help it enter immune cells more easily through special receptors.

This process increases the number of infected cells, resulting in **higher viral loads** and an exaggerated immune response. The immune system releases even more cytokines, leading to severe inflammation, plasma leakage, and bleeding. This is why secondary dengue infections can progress to **Dengue Hemorrhagic Fever (DHF)** or **Dengue Shock Syndrome (DSS)**.

4. Vascular Leakage and Hemorrhagic Manifestations

One of the most serious complications in dengue is **plasma leakage** due to increased permeability of blood vessels. The lining of the blood vessels, known as the **endothelium**, becomes damaged by the excessive cytokines and viral attack. This allows fluid to leak out from blood vessels into surrounding tissues and body cavities, such as the abdomen and lungs.

As plasma leaks, the **blood becomes more concentrated**, leading to a rise in **hematocrit** levels (the proportion of red blood cells in blood). The reduced blood volume causes **low blood pressure** and poor circulation, which can eventually result in **shock**.

In addition, dengue affects **platelet production** in the bone marrow. The virus damages the bone marrow cells responsible for making platelets, and the immune system also mistakenly destroys existing platelets. A **low platelet count (thrombocytopenia)** increases the risk of bleeding.

This is why patients with severe dengue may show symptoms like:

- Bleeding from gums and nose
- Easy bruising or skin rashes (petechiae)
- Blood in vomit or stool
- Internal bleeding in severe cases

5. Liver, Kidney, and Organ Involvement

As the infection spreads through the bloodstream, various organs may be affected. The **liver** is one of the main organs impacted by dengue. The virus can cause inflammation of the liver (hepatitis), leading to elevated liver enzyme levels and sometimes jaundice.

The **kidneys** may also suffer due to reduced blood flow and dehydration caused by plasma leakage. In severe cases, this can lead to **acute kidney injury (AKI)**. The **heart** and **lungs** may experience fluid buildup, resulting in breathing difficulties.

This multi-organ involvement explains why dengue can become life-threatening when not treated in time. Early recognition and medical care are vital to prevent severe complications.

6. The Critical and Recovery Phases

Dengue infection typically progresses through **three distinct phases**:

a) Febrile Phase

This phase lasts for 2–7 days and is marked by high fever, headache, pain behind the eyes, and muscle and joint pain. The virus is actively multiplying in the bloodstream during this time.

b) Critical Phase

Around the time when the fever starts to drop, the patient enters the critical phase. This is when **vascular leakage** and **low platelet count** occur. If not managed properly, it can lead to DHF or DSS. Close medical monitoring is essential during this stage.

c) Recovery Phase

In this stage, the leaked plasma is reabsorbed back into the bloodstream, and the patient's condition gradually improves. Appetite returns, urine output increases, and platelet counts begin to rise. However, if excessive fluids were given during the critical phase, they can accumulate and cause swelling or breathing difficulties during recovery.

4. Treatment of Dengue

The treatment of dengue focuses mainly on relieving symptoms, maintaining fluid balance, and preventing complications because there is **no specific antiviral medicine** available for dengue virus infection. The care given to patients depends on the **type and severity** of the illness — whether it is mild dengue fever, dengue hemorrhagic fever (DHF), or dengue shock syndrome (DSS).

The main goal of dengue treatment is to **reduce fever and pain, prevent dehydration, monitor warning signs, and manage severe cases** in hospitals. Early recognition and proper supportive care can greatly reduce the risk of death.

1. General Approach to Treatment

Dengue treatment begins with **early diagnosis** and **clinical management**. As soon as dengue is suspected, patients should undergo blood tests to confirm infection and to check for platelet count and hematocrit levels.

Since the disease progresses in different phases — febrile, critical, and recovery — treatment also changes according to the stage of illness.

a) Febrile Phase (Mild Dengue)

This is the stage when patients usually experience high fever, headache, and body pain. During this phase, treatment is mainly **symptomatic and supportive**.

Care Includes:

- **Plenty of fluids:** Patients should drink plenty of water, fruit juices, and oral rehydration solution (ORS) to prevent dehydration caused by fever and vomiting.
- **Fever control:** *Paracetamol (acetaminophen)* is used to lower fever and relieve pain. *Aspirin and ibuprofen* should be avoided because they can increase the risk of bleeding.
- **Rest:** Complete bed rest is necessary to allow the body to recover and fight the infection.
- **Nutritious diet:** Light, easily digestible food like soup, fruits, and porridge help maintain energy levels.

The patient's temperature, urine output, and general condition should be monitored closely during this phase. If the patient begins to show warning signs such as severe abdominal pain, persistent vomiting, bleeding, or restlessness, hospital admission is necessary.

2. Hospital Management (Severe Dengue Cases)

When dengue becomes severe — in cases of **Dengue Hemorrhagic Fever (DHF)** or **Dengue Shock Syndrome (DSS)** — hospitalization is required for careful monitoring and treatment.

a) Fluid Replacement Therapy

This is the most important part of dengue management. In severe dengue, plasma leakage can cause dehydration and shock. The goal is to replace lost fluids and maintain proper blood circulation.

- **Oral rehydration:** For mild dehydration, patients are given ORS or electrolyte drinks.
- **Intravenous (IV) fluids:** For moderate to severe dehydration, IV fluids such as normal saline or Ringer's lactate are given under careful supervision.
- The amount and rate of fluids must be monitored closely to avoid overhydration, which can cause fluid buildup in the lungs (pulmonary edema).

b) Blood and Platelet Transfusions

In DHF and DSS, platelet levels often drop dangerously low. If the platelet count falls below **20,000/mm³** or if the patient has active bleeding, a **platelet transfusion** may be required.

In cases of severe bleeding, **whole blood or plasma transfusion** may also be necessary.

c) Monitoring Vital Signs

Patients in hospitals are kept under close observation. Doctors frequently check blood pressure, pulse rate, hematocrit levels, and platelet count. Early detection of warning signs helps prevent shock and organ damage.

d) Oxygen and Supportive Therapy

If the patient shows signs of breathing difficulty, oxygen therapy may be provided. In critical cases, intensive care units (ICUs) are used for continuous monitoring and management.

3. Home-Based Care for Mild Dengue

For most dengue cases that are not severe, **home treatment** under medical guidance is safe and effective. Family support plays an important role during this period.

Home Care Measures Include:

- Taking prescribed medicines only (mainly paracetamol for fever).
- Drinking plenty of fluids (ORS, coconut water, fresh juice, soups).

- Avoiding oily or spicy food that can upset the stomach.
- Monitoring temperature and warning signs every few hours.
- Visiting a doctor regularly for platelet and hematocrit check-ups.

Patients should immediately go to the hospital if they notice symptoms such as:

- Severe abdominal pain
- Persistent vomiting
- Bleeding gums or nose
- Drowsiness or confusion
- Cold, clammy skin or difficulty breathing

These are signs that the disease may be progressing to the critical phase.

4. Avoidance of Certain Medications

Some common medicines can worsen the condition of dengue patients, so they must be strictly avoided unless prescribed by a doctor.

- **Aspirin and NSAIDs (like Ibuprofen or Diclofenac):** These can cause stomach irritation and increase bleeding risk.
- **Steroids:** Unnecessary use can suppress the immune system and lead to complications.
- **Antibiotics:** Since dengue is caused by a virus, antibiotics are ineffective unless a secondary bacterial infection occurs.

Only medications prescribed by a qualified healthcare provider should be taken.

5. Nutritional and Supportive Care

Nutrition plays a key role in helping the body recover. During dengue, appetite is often lost, but patients should try to eat light and healthy food.

Recommended Foods:

- Fresh fruits like papaya, oranges, pomegranate, kiwi, and guava (rich in vitamin C and antioxidants)
- Soups and broths for hydration and strength
- Coconut water for natural electrolytes
- Papaya leaf extract (used traditionally and studied for its potential to increase platelet count, though not a proven cure)

Avoid: Processed, oily, or spicy foods that can worsen nausea or cause dehydration.

Proper rest is equally important. Patients should avoid heavy physical activity for at least two weeks after recovery because the body remains weak and platelets may take time to normalize.

6. Treatment of Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS)

In severe dengue cases, the focus is on **preventing shock and organ failure**.

Treatment Includes:

- Rapid fluid replacement through IV therapy
- Blood transfusion in case of severe bleeding
- Oxygen support and monitoring of urine output
- Managing electrolyte imbalances and maintaining body temperature
- Continuous hospital observation for at least 24–48 hours after the patient's condition stabilizes

DSS is a medical emergency. Immediate hospitalization and intensive care can make the difference between life and death. With proper management, most patients recover completely.

7. Emerging and Experimental Treatments

Although no specific antiviral drug exists for dengue, scientists are working on developing targeted treatments and vaccines.

a) Vaccine:

- The first dengue vaccine, *Dengvaxia*, is available in some countries. It provides partial protection but is recommended only for individuals who have previously been infected with dengue.
- Other vaccines, such as *TAK-003 (Qdenga)*, are being tested and approved in some regions, showing better safety and protection rates.

b) Antiviral Research:

Research is ongoing to develop antiviral drugs that can block viral replication or reduce the severity of infection. These include drugs targeting viral enzymes and immune-modulating therapies.

8. Psychological and Emotional Support

Dengue does not only affect the body but also causes stress and fear, especially in families with children or elderly patients. Constant worry about platelet counts, hospitalization, and the risk of complications can create anxiety.

Healthcare workers should reassure patients and their families, explaining that with early detection and proper care, dengue is fully curable. Emotional support, good nutrition, and rest contribute greatly to recovery.

9. Prevention as Part of Treatment

In dengue, **prevention and treatment go hand in hand**. Controlling the mosquito population and preventing mosquito bites are crucial steps in reducing new cases.

Preventive Measures:

- Remove stagnant water from pots, containers, tires, and tanks.
- Use mosquito repellents, coils, and nets.
- Wear long sleeves and light-colored clothing.
- Keep surroundings clean and dry.
- Participate in community awareness programs about dengue control.

When everyone contributes to mosquito control, the number of infections automatically decreases, reducing the burden on hospitals and families.

Conclusion

Dengue is one of the most widespread mosquito-borne viral diseases affecting millions of people across tropical and subtropical regions every year. It is transmitted mainly by the *Aedes aegypti* mosquito, which breeds in stagnant water found near human dwellings.

Historically, dengue has existed for centuries, but it became a major health issue during the 18th and 19th centuries as trade, travel, and urbanization expanded. Today, with rising population, climate change, and unplanned urban growth, dengue has spread rapidly across more than 100 countries.

The disease occurs in four viral forms known as serotypes — DENV-1, DENV-2, DENV-3, and DENV-4. Infection with one type gives lifelong immunity to that particular strain but not to others, increasing the risk of severe disease on subsequent infections.

Clinically, dengue presents in three major types — Classical Dengue Fever, Dengue Hemorrhagic Fever (DHF), and Dengue Shock Syndrome (DSS). While the mild form causes fever, rashes, and joint pain, the severe forms may lead to internal bleeding, low platelet count, and even shock if not treated promptly.

Pathophysiologically, dengue begins when an infected mosquito injects the virus into the bloodstream. The virus attacks immune cells, multiplies, and triggers a strong immune response. This leads to the release of inflammatory substances that damage blood vessels and cause plasma leakage. A second infection with a different serotype may worsen the immune response, resulting in severe symptoms.

Currently, there is **no specific antiviral drug** for dengue. Treatment is mainly supportive — managing fever, preventing dehydration, and closely monitoring blood parameters. Paracetamol is used for fever, while drugs like aspirin and ibuprofen are avoided because they may increase bleeding. In severe cases, hospitalization, fluid therapy, and blood transfusions become necessary.

Vaccines such as *Dengvaxia* and *Qdenga* have been developed to provide partial protection, but preventive measures remain the best defense. Controlling mosquito breeding sites, covering stored water, using mosquito repellents, and maintaining cleanliness in communities are simple yet effective ways to stop transmission.

Public awareness and timely medical attention play a vital role in reducing deaths and complications. Educating people about early symptoms — such as persistent fever, vomiting, bleeding gums, or sudden weakness — can help detect severe cases early.

Ultimately, the fight against dengue requires cooperation between individuals, communities, and health authorities. Everyone has a role in keeping the environment clean and preventing mosquitoes from breeding.

In conclusion, dengue is a preventable and manageable disease when knowledge, vigilance, and community action come together. Science and awareness have given humanity powerful tools to fight it — now it depends on how wisely we use them. By turning education into action, we can move toward a future where dengue no longer poses a threat to human life.

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