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Unit-V

TOPIC: HUMAN AFRICAN TRYPANOSOMIASIS OF THE CNS- DENGUE,INFLUENZA VIRUS

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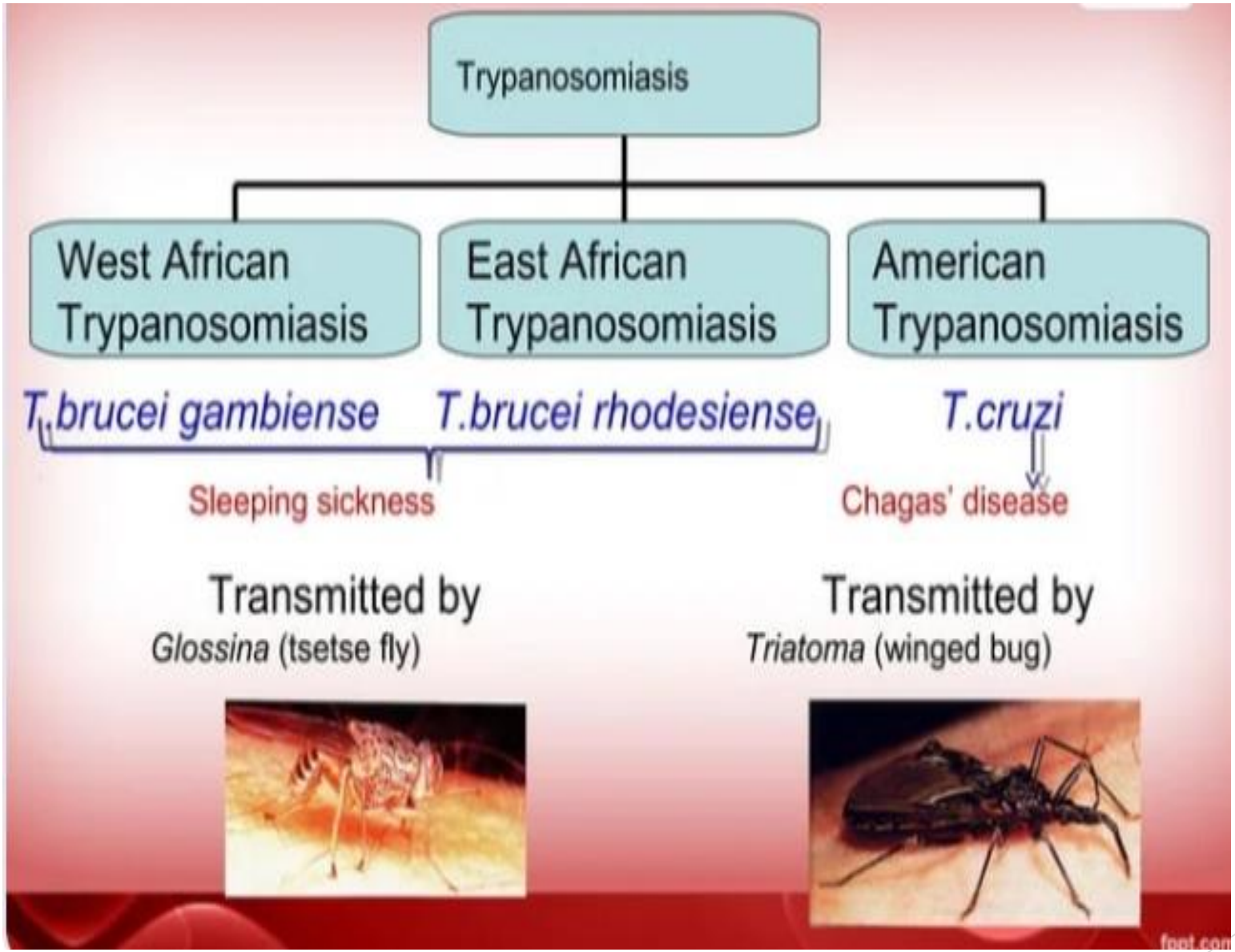
HUMAN AFRICAN TRYPANOSOMIASIS:

INTRODUCTION:

Human African trypanosomiasis is also known as Sleeping sickness is a vector- borne parasitic disease.

It is caused by the Protozoans of the genus Trypanosoma, transmitted by bites of tsetse flies (glossina) which have the acquired the parasite from infected humans or animals.

It mostly affect the central nervous system(CNS)


Trypanosomiasis
West African Trypanosomiasis
East African Trypanosomiasis
American Trypanosomiasis
T.brucei gambiense
T.brucei rhodesiense
T.cruzi
Sleeping sickness
Chagas' disease
Transmitted by
Glossina (tsetse fly)
Transmitted by
Triatoma (winged bug)

TRANSMISSION:

- HAT is mostly transmitted through tsetse flies. Other possible transmission ways are:
- mother-to-child: trypanosomes can cross the placenta and infect the fetus;
- mechanical transmission by other blood-sucking insects is possible, although its epidemiological impact is likely marginal;
- accidental infection in laboratories via pricks with contaminated needles; and
- transmission through sexual contact has been reported once.

STAGES:

- There are two recognized stages in the clinical presentation of HAT, namely the early hemolymphatic stage, and the late encephalitic stage when the CNS is involved.
- However, the transition from the early to the late stage is not always distinct in *rhodesiense* infection .
- The tempo of the disease is usually acute in *rhodesiense* disease — CNS invasion by the parasite occurs early, within a few months after initial infection — whereas *gambiense* infection is usually a slower, chronic infection, with late CNS infection lasting month to years.

FIRST STAGE:

- The onset is variable but usually occurs 1–3 weeks after the bite. Episodes of fever lasting 1–7 days occur together with generalized lymphadenopathy.
- The early symptoms tend to be non-specific: malaise, headache, arthralgia, generalized weakness, and weight loss .
- Multiple organs may then be infected , including the spleen, liver, skin, cardiovascular system, endocrine system, and eyes.
- This involvement underlies the wide spectrum of systemic dysfunction that may occur .

SECOND STAGE:

- The onset is insidious and the potential clinical phenotype is wide .
- The broad neurologic spectrum has been detailed elsewhere and the reported features can be grouped into general categories such as psychiatric, motor, and sensory abnormalities, and sleep disturbances.
- The mental disturbances may be subtle, and include irritability, lassitude, headache, apparent personality changes, and overt psychiatric presentations such as violence, hallucinations, suicidal tendencies, and mania .
- Motor system involvement may include limb tremors, tongue and limb muscle fasciculation, limb hypertonia and pyramidal weakness, choreiform and athetoid movements, dysarthria, cerebellar ataxia, and polyneuritis .
- Pout and palmar-mental reflexes may also be present.

- Sensory involvement may manifest as painful hyperaesthesia, pruritis, and also deep hyperaesthesia (Kerandel's sign), the latter being reported as particularly common in Europeans .
- The characteristic sleep disturbances include lassitude, distractibility, and spontaneous, uncontrollable urges to sleep, along with a reversal of the normal sleep-wake cycle in which daytime somnolence alternates with nocturnal insomnia.
- While these various features, including the sleep abnormalities, are typical of HAT, they are not individually diagnostic, since some of them may also be seen during other CNS infections.
- If untreated, the patient progresses to the final stage of the disease, which is characterized by seizures, severe somnolence, double incontinence, cerebral edema, coma systemic organ failure, and inevitable death.

DIAGNOSIS:

- Diagnosis involves 3 steps:
- screening for potential infection using serological tests (only available for *T. b.gambiense*) and clinical examination;
- confirmation by observing microscopically the parasite in body fluids; and
- staging the disease progression via clinical examination and analysis of cerebrospinal fluid obtained by lumbar puncture, if needed.
- Early diagnosis is important to avoid progressing to the neurological stage with more complex and risky treatment.
- The long, relatively asymptomatic first stage of *gambiense*-HAT is one of the reasons why active screening of exposed populations is done, to detect cases at an early stage and remove them as reservoir.

TREATMENT:

- Treatment choice depends on the disease form and the disease stage. The earlier the disease is treated, the better the prospect of cure.
- The assessment of treatment outcome requires follow up for up to 24 months with clinical assessment and laboratory exams including sometimes of cerebrospinal fluid, because parasites may remain viable and reproduce the disease many months after treatment.
- Treatment in the second stage requires drugs that cross the blood–brain barrier.
- All anti-trypanosomals are donated to WHO by the manufacturers and distributed for free to endemic countries. New WHO treatment guidelines for gambiense-HAT were issued in 2019. Six drugs are used:

In Gambiense HAT:

Pentamidine, intramuscular: in first stage, generally well tolerated by patients.

- Eflornithine, intravenous: much safer than melarsoprol, only effective in gambiense-HAT. It is generally co-administered with nifurtimox (Nifurtimox-eflornithine combination therapy, NECT) but can be used also as monotherapy. The administration is complex.
- Nifurtimox, oral: in second stage, only as a component of NECT, which is a shorter treatment with four-times fewer eflornithine infusions, safer and more effective than eflornithine alone. WHO supplies NECT free of charge to endemic countries in a kit containing all the material needed for its administration.
- Fexinidazole, oral: in first stage and non-severe second stage. To ensure efficacy, intake after a solid meal and under supervision of trained medical staff is required.

IN RHODIENSE HAT:

- Suramin, intravenous: in first stage. May provoke adverse effects including nephrotoxicity and allergic reactions.
- Melarsoprol, intravenous: in second stage. An arsenic derivate, it has many adverse effects, the most dramatic being the reactive encephalopathy which is 3–10% fatal.

DENGUE:

INTRODUCTION:

Dengue is a viral infection is caused by the dengue virus (DENV), transmitted to humans through the bite of infected mosquitoes.

About half of the world's population is now at risk of dengue with an estimated 100-400 million infection occurring each year.

Dengue is found in tropical and sub tropical climates worldwide, mostly in urban and semi urban areas.

Aedes mosquitoes, primarily including the female vectors *Aedes aegypti* and *A albopictus*, transmit the virus

ETIOLOGY:

- Dengue fever is caused by any of the four distinct serotypes (DENV-1 to DENV 4) of the single stranded RNA viruses belonging to the genus FLAVIVIRUS.
- Infection by the one serotype confers life long immunity to that serotype but not to others.
- Dengue fever is the fastest-spreading mosquito-borne viral disease worldwide, affecting over 100 million people annually.
- This disease also leads to 20 to 25,000 deaths, primarily among children, and is prevalent in more than 100 countries. Epidemics occur yearly in the Americas, Asia, Africa, and Australia.
- The dengue virus is maintained by the following 2 transmission cycles:
- Mosquitoes carry the virus from a nonhuman primate to another nonhuman primate
- Mosquitoes transmit the virus from human to human

- Whether the virus transmits from affected humans to mosquitoes depends on the viral load of the mosquitoes' blood meal.
- The primary vectors of the disease are female mosquitoes of the species *Aedes aegypti* and *Aedes albopictus*.
- Although *A aegypti* is associated with most infections, the geographic range of *A albopictus* is expanding. *A albopictus*, being more cold-tolerant, exhibits aggressive feeding behavior but does so less frequently, which may contribute to its increasing numbers.
- These mosquito species typically inhabit indoor environments and are active during the day. Modes of transmission include perinatal transmission, blood transfusions, breast milk, and organ transplantation.

STAGES:

- The disease is classified as either dengue or severe dengue.
- probable dengue: The patient lives in or has travelled to a dengue – endemic area. Symptoms include fever, nausea ,vomiting, rash ,myalgias, arthralgias,rash and leukopenia.
- warning signs of dengue: Dengue symptoms include abdominal pain, persistent vomiting, clinical fluid accumulation such as ascites or pleural effusion, mucosal bleeding, lethargy, liver enlargement greater than 2 cm, increase in hematocrit, and thrombocytopenia.

Severe dengue: Severe dengue is characterized by dengue fever accompanied by severe plasma leakage, hemorrhage, impaired consciousness, myocardial dysfunction, pulmonary dysfunction, and organ dysfunction, including transaminitis greater than 1000 IU/L.

- **Dengue shock syndrome clinical warnings:** Symptoms include rapidly rising hematocrit, intense abdominal pain, persistent vomiting, and narrowed or absent blood pressure.

SYMPTOMS:

- Sudden high fever
- Severe headache
- Fatigue
- Nausea and vomiting
- Diarrhoea
- Pain behind the eyes
- Mild bleeding such as nose bleed, bleeding gums,or easy bruising.

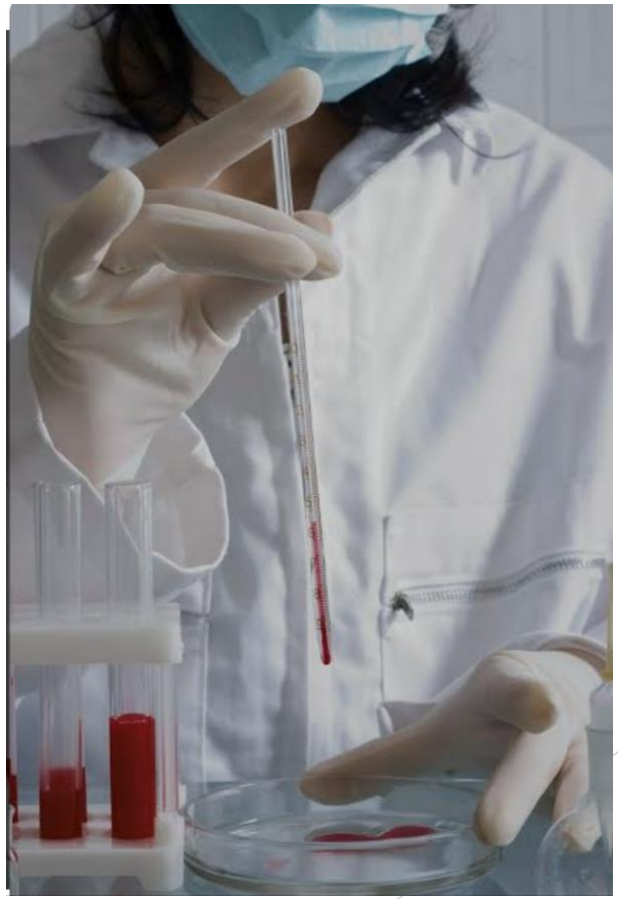
DIAGNOSIS:

- The dengue infection is difficult to diagnose without laboratory and radiology test because initially symptoms may be same as other disease such as malaria
- Test may include:

  Complete blood count

  Dengue serology test

  Dengue virus antigen detection.



TREATMENT:

- The treatment approach for dengue fever varies depending on the patient's illness phase. Patients without warning signs can typically be treated as outpatients with acetaminophen and sufficient oral fluids.
- In addition, educating patients about the warning signs and advising them to seek immediate medical attention if any of these signs occur is important.
- Presenting with warning signs of the disease, severe dengue fever, or having risk factors such as age, pregnancy status, diabetes mellitus, or those who are living alone should be evaluated for hospitalization .
- Individuals displaying warning signs can be started on intravenous (IV) crystalloids, with the fluid rate adjusted based on the patient's response. Patients in shock and not responding to initial crystalloid boluses may require colloids.
- Blood transfusion is indicated in cases of severe or suspected bleeding when the patient remains unstable despite adequate fluid resuscitation and hematocrit falls. Notably, it is essential to avoid administering aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), and other anticoagulants

INFLUENZA VIRUS:

- Flu or Influenza is a contagious respiratory illness that spreads from person to person through the air via coughs or sneezes or through contact with infected surfaces.
- It is caused by the group of continuously changing viruses called Influenza virus.
- Influenza virus change easily and often , they are unpredictable ,and they can be deadly.
- Influenza viruses are the members of the family Orthomyxoviridae.
- This family represents the enveloped viruses the genome of which consists of segmented negative-sense single stranded RNA segments.

TYPES:

- There are four types of influenza viruses: A, B, C, and D. Influenza A and B viruses cause seasonal epidemics of disease in people (known as flu season) almost every winter in the United States.
- Influenza A viruses are the only influenza viruses known to cause flu pandemics (i.e., global epidemics of flu disease).
- A pandemic can occur when a new and different influenza A virus emerges that infects people, has the ability to spread efficiently among people, and against which people have little or no immunity.
- Influenza C virus infections generally cause mild illness and are not thought to cause human epidemics.
- Influenza D viruses primarily affect cattle with spillover to other animals but are not known to infect people to cause illness.

Feature	Influenza A	Influenza B	Influenza C
Host Range	Humans, pigs, horses, birds, marine mammals	Humans only	Humans and pigs
Epidemiology	Antigenic shift and drift	Antigenic drift only	Antigenic drift only
Clinical Features	May cause pandemics with significant mortalities in affected young people	Severe disease, generally confined to elderly or high-risk, pandemics not seen	Mild disease, common in children, without seasonality
Genome	8 gene segments	8 gene segments	7 gene segments
Structure	10 viral proteins M2 unique	11 viral proteins NB unique	9 viral proteins HEF unique

SYMPTOMS:

- Fever,headache
- Chill,cough
- Body aches,
- Sore throat
- Running or stuffy nose(congestion)
- Tiredness or feeling run down
- Diarrhoea or vomiting.

DIAGNOSIS:

- Rapid influenza diagnostic tests (RID TS):

  Detect viral antigens quick but less sensitive.

- Reverse transcription polymerase chain reaction (RT-PCR):

  Highly sensitive and specific, detects viral RNA.

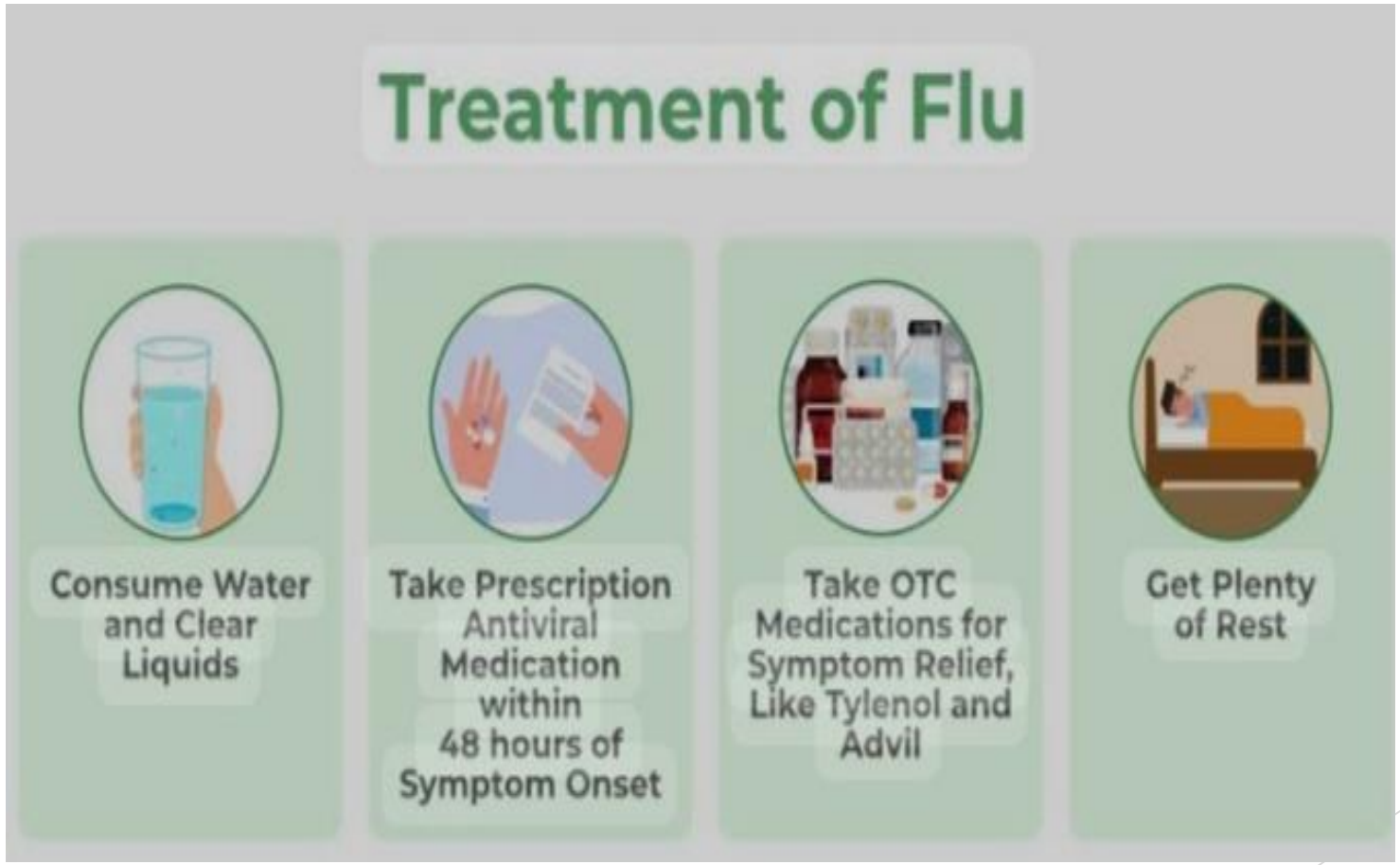
- Viral culture:

  Definitive diagnosis but takes longer.

- Serology:

  Detects antibodies, used for reterospective diagnosis.

TREATMENT:


Treatment of Flu
Consume Water and Clear Liquids
Take Prescription Antiviral Medication within 48 hours of Symptom Onset
Take OTC Medications for Symptom Relief, Like Tylenol and Advil
Get Plenty of Rest

REFERENCE:

- Buckingham and Flaw‟s, “Molecular Diagnostics: Fundamentals, Methods and Clinical Applications”, F.A. Davis Company; First edition, 2007.
- Trent, R. J. (2012). Molecular Medicine, Fourth Edition: Genomics to Personalized Healthcare. Academic Press.

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