- **Lecture 5…** **Tetanus & visceral leishmaniasis**
- **Objectives:** Have an idea about:-
  - Causative agents.
  - Epidemiology, Clinical features and Complications.
  - Management.
  - Prevention .
- **Tetanus**

Historically called **lockjaw,** is an acute, spastic paralytic illness caused by the neurotoxin produced by ***Clostridium tetani*** ,a motile, gram-positive, spore-forming obligate anaerobe whose natural habitat worldwide is soil, dust, and the alimentary tracts of various animals .

- **Tetanus neonatorum:** The Tetanus neonatorum is a form of generalized tetanus, typically manifests within 3–12 days of birth as progressive difficulty in feeding (sucking and swallowing), associated hunger, and crying. Paralysis or diminished movement, stiffness and rigidity to the touch, and spasms, +/- opisthotonos, are characteristic.
- **Opisthotonus :-** is an equilibrium position that results from unrelenting total contraction of opposing muscles, all of which display the typical **boardlike rigidity** of tetanus. the patient may assume an arched posture of extreme hyper-extension of the body **,**with the head and the heels bent backward and the body bowed forward with only the back of the head and the heels touching the supporting surface.
- The umbilical stump may hold remnants of dirt, dung, clotted blood, or serum, or it may appear relatively benign . Because tetanus toxin does not affect sensory nerves or cortical function, the patient unfortunately remains conscious, in extreme pain
- These seizures are characterized by sudden, severe tonic contractions of the muscles, with fist clenching, flexion, and adduction of the arms and hyperextension of the legs. Without treatment, the seizures range from a few seconds to a few minutes in length .

  DIAGNOSIS :

  The picture of tetanus is one of the most dramatic in medicine, and the diagnosis may be established clinically. The typical setting is an unimmunized patient (and/or mother) who was injured or born within the preceding 2 wk, who presents with trismus, other rigid muscles, and a clear sensorium.
- **Lab finding:-**
- A peripheral leukocytosis (secondary bacterial infection, stress of muscle contraction) .
- The cerebrospinal fluid is normal .
- Neither the EEG nor the EMG shows a characteristic pattern .
- ***C. tetani*** is not always visible on Gram stain of wound material, and it is isolated in only about **one third** of cases .
- ***Differential diagnosis:***
  - ***Rabies.***
  - ***Hypocalcemia.***
  - ***In neonates: neonatal sepsis.***

- **MANAGEMENT:**
  Aims:

1. Eradication of ***C. Tetani.***
2. Neutralization of all accessible tetanus toxin.
3. Control of seizures and respiration, palliation and provision of meticulous supportive care.
4. Prevention of recurrences .

TREATMENT:

1-Surgical wound excision and debridement are often needed to remove the foreign body or devitalized tissue that created anaerobic growth conditions.

- Surgery should be performed promptly after administration of **human tetanus immunoglobulin (TIG &** antibiotics).
- Excision of the umbilical stump in neonatal tetanus is no longer recommended .

2- Human tetanus immunoglobulin TIG :- should be given as soon as possible before the toxin can bind at distant muscle groups ,because Once tetanus toxin has begun its axonal ascent to the spinal cord, it cannot be neutralized by TIG.

- **If TIG is unavailable,** use of human IVIg may be necessary.
- Tetanus antitoxin: The usual dose of TAT is 50,000-100,000 units, with half given intramuscularly and half intravenously

3- ANTIBIOTICS: **Penicillin G** (100,000 U/kg/day divided every 4–6 hr IV for 10–14 days) remains the antibiotic of choice because of its effective clostridiocidal action and its diffusibility.

Metronidazole : appears to be equally effective. **Erythromycin** and tetracycline (for persons >8 yr of age) are alternatives for penicillin-allergic patients.

4-Management of complication:

- **COMPLICATION:**
- Aspiration of secretions & pneumonia may occurs before the 1st medical attention was received .
- The seizures may result in lacerations of the mouth or tongue, in intramuscular hematomas, rhabdomyolysis with myoglobinuria and renal failure, or in long bone or spinal fractures.
- Venous thrombosis, pulmonary embolism, are constant hazards .
- Excessive use of muscle relaxants may produce iatrogenic apnea
- Anticonvalcent, muscle relaxants and meticulous supportive care in a quiet, dark, secluded setting is most desirable. Because tetanic spasms may be triggered by minor stimuli, the patient should be sedated and protected from all unnecessary sounds, sights, and touch; and all therapeutic and other manipulations must be carefully scheduled and coordinated.
- Endotracheal intubation may be needed to prevent aspiration of secretions.

PREVENTION OF TETANUS

- WHO is engaged currently in a global elimination of neonatal tetanus campaign through maternal immunization with at least 2 doses of tetanus toxoid.
- Active immunization should begin in infancy with (DT a P) vaccine at 2, 4, and 6 mo of age, with a booster at 4–6 yr of age and at 10 yr intervals thereafter .(Td or Td a p) .

Leishmaniasis

Leishmaniasis are group of diseases caused by **intracellular protozoan parasites of the genus leishmania,** which are transmitted by ***phlebotomine sand flies*.**

multiple species of leishmania organism are known to cause human diseases involving the skin, mucosal surface of the visceral and reticulo endothelial organs.

Visceral leishmaniasis = Kalaazar:

- **Epidemiology :-** VL is caused by L. donovani in Africa, and by L. infantum in middle east, Mediterranean basin, and central Asia. The maintenance of leishmania in most endemic area is through a zoonotic cycle in which humans are only incidentally infected.
- The leishmaniases may occur sporadically throughout an endemic region or may occur in epidemic focuses
- The parasite is dimorphic ,existing as a flagellate promastigote in the insect vector, and an aflagellate amastigotes that resides and replicate within the macrophage of the vertebrate host, and are resistant to the hostile environment of the macrophage , replicate and eventually rupture the cell and goes to infect other macrophage.
- Cellular immune mechanisms determine resistance or susceptibility to infection with *Leishmania*.
- **Pathogenesis of kalaazar:-** The Resistance is mediated by expansion of the T helper 1 cell population, with interferon-γ production resulting in macrophage activation and parasite killing.Pt with active VL demonstrate minimal or absent leishmania specific CIM , but these responses resume after successful therapy.
- Within endemic area people who have had a subclinical infection can be identified by a positive DHR to leishmania Ag (Montenegro skin test)
- **CLINICAL MANIFESTATION OF VL**

VL typically affect children younger than 5 yr in new world and Mediterranean region , and older children and young adults in Asia and Africa. After inoculation of the organism in to the skin by the sand fly the child may have either of:

1-**Asymptomatic** infection or transiently sero-positive, but no clinical features.

2- An Oligo symptomatic Infection: the pt have mild constitutional symptoms (malaise, intermittent diarrhea, poor activity), intermittent fever, and mildly enlarged liver that mostly resolve without therapy, Or evolves into active kala-azar

- ***3-Active kala azar form:*** within 2-8 months about one fourth of infected pt develop high grade fever, marked splenomegaly, progressive cachexia ,gross muscles wasting, massive hepatosplenomegaly, pancytopenia, jaundice, edema,and ascites. Anemia may be severe enough to precipitate heart failure, bleeding episodes, especially epistaxis, are frequent.

The late stage of the disease often complicated by secondary bacterial infection which is frequently the causes of death.

- The classic clinical features of high fever, marked hepatosplenomegaly, and severe cachexia typically develop approximately 6 mo after the onset of the illness, but a rapid clinical course over 1 mo has been noted in up to 20% of patients .
- **Diagnosis of VL**

1-The clinical features of pronged fever, weakness, marked hepatosplenomegaly in pt who had potential exposure in endemic area.

2- lab finding: pancytopenia Hb 5-8 g/dl, WBCs 2000-3000 cells/μL

- & hypergamaglobulinemia >5 G/dl that is mostly immunoglobulin G (IgG).
- &L.F.T: mild elevation of hepatic transaminase.
- **Definitive Diagnosis of VL**
- smears or cultures of material from splenic, bone marrow, or lymph node aspirations are usually diagnostic. In experienced hands, splenic aspi-rationhas a higher diagnostic sensitivity, but it is rarely performed because of the risk for bleeding complications.
- Serological Testing: enzyme immunoassay, indirect fluorescence assay,
- ELISA: using a recombinant (K39) antigen 80-90% sensitivity& and 95%, specificity

TREATMENT OF VL:-

1-Nonspecificic treatment: Hospital admission, bed rest, antipyretic.

- Nutritional rehabilitation.
- Antibiotic for secondary bacterial infection.
- Blood transfusion for severely anemic pt , and platelets transfusion for pt with thrombocytopenia and bleeding tendency

2- Specific treatment: by **pentavalent antimony compound :**sodium stibogluconate (pentostam), and meglumine antimoniate , have been the mainstay of antileishmanial chemotherapy for more than 40 yr, Currently, **sodium stibogluconate** regimen is 20 mg/kg/24 hr IV or IM for 28 days, repeated course of treatment may needed in severely infected pt.

- An initial clinical response to therapy usually occurs in the 1st wk of therapy , but complete clinical healing , regression of splenomegaly &normalization of cytopenia is usually not evident for weeks to few months after completion of therapy.Cure rate of 80-100% can be expected. The side effects of antimony therapy are dose and duration dependent and commonly include fatigue, arthralgia, myalgia, hepatotoxicity (elevated hepatic trasaminase), cardiotoxicity(T-wave changes), mild hematological changes
- Relapses are common in pt who don't have effective antileishmanian cellular immune response such as those co infected with HIV. When clinical relapses occur, they are usually evident within 2 mo after completion of therapy.
- **Other drugs that can be used are :**
- ***Amphotricin B desoxycholate*** :0.5-1mg every other day for 14-20 doses.
    - Cure rate 100%.(side effect is renal toxicity).
- ***liposomal amphotricin B***: highly effective and less nephrotoxic. (90-100% cure rate)
- **Others**:-parentral Paromomycine.
- -Recombinent human interferon gama. used as an adjunct to antimony therapy
- -oral **miltefosine** 2.5 mg/kg /day for 28 days, demonstrated a cure rate of 80-90%.

PREVENTION OF VL:-

- Avoid exposure to the nocturnal sand flies by insect repellent and permethrin-impregnated mosquito netting.
- Control & elimination of the infected reservoir hosts (e.g., seropositive domestic dogs) .
- Early recognition and treatment of the case.
- A number of vaccines have been demonstrated to have efficacy in experimental models; !!!! Future vaccination.

References:

- Nelson Textbook of Pediatrics , 20 edition .
- Nelson essentials Textbook of Pediatrics , 7th edition.
- Illustrated textbook of pediatrics.