كلية : التربية للعلوم الصرفة

القسم او الفرع : علوم الحياة

المرحلة: دكتوراه

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اسم المادة باللغة العربية : علم النسج المرضية

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اسم المحاضرة الأولى باللغة العربية: الامراض الاستوائية

اسم المحاضرة الأولى باللغة الإنكليزية : SELECTED TROPICAL DISEASES

V. Leprosy

Definiton: Leprosy or Hansen disease is a slowly progressive infection caused by *Mycobacterium leprae* affecting the skin and peripheral nerves and resulting mainly in deformity, paralysis and ulceration. Though *M. leprae* is in most part contained in the skin, the disease is believed to be transmitted from person to person through aerosols from lesions in upper respiratory tract.

Pathogenesis:

- The bacillus is acid fast, obligate intracellular organism that does not grow in culture and it grows best at 32-34 0C of the temperature of human skin.
- Like *M. tuberculosis, M leprae* secrets no toxins but its virulence is based on properties of its cell wall. The bacilli thus produce either potentially destructive granulomas or by interference with the metabolism of cells. The bacilli are taken by alveolar macrophages; disseminate through the blood but grows only in relatively cool tissues of the skin and extremities.
- Classification based on host immune responses. Leprosy is a bipolar disease. Two forms of the disease occur depending on whether the host mounts a T-cell mediated immune response (tuberculoid leprosy) or the host is anergic (lepromatous leprosy). The polar forms are relatively stable but the borderline forms (border line-tuberculoid, borderline-borderline, and borderline-lepromatous) are unstable without treatment. It may usually deteriorate to lepromatous leprosy. Patients with tuberculoid leprosy form granuloma with few surviving bacteria (paucibacillary disease). The 48 hour leporine skin

test is strongly positive and this is effected largely by CD4 + type 1 helper T-cell that secretes IL-2 & interferon δ .

In contrast, patients with lepromatous leprosy lack T-cell mediated immunity, and are anergic to lepromin and have diffuse lesions (globi) containing foamy macrophages, stuffed with large numbers of mycobacteria (multibacillary disease). Lepromatous leprosy lesions lack CD4+ type I T-cell at their margins but in stead contain many CD8+ suppressor T-cell in a diffuse pattern. The CD8+ suppressor T-cell secrete IL-10, which inhibits helper-cells and may mediate the anergy seen in lepromatous leprosy. These CD 8+ suppressors T-cell also secrete IL-4, which induce antibody production by B-cell. Antibody production is not protective in lepromatous leprosy and rather the formation of antigen antibody complexes in lepromatous leprosy leads to erythema nodosum leprosum, a life-threatening vasculitis, and glomerulonephritis.

Tuberculoid leprosy	**Lepromatous leprosy**
Epitheoid granuloma without giant cell	Active macrophages, with every many bacilli(globi)
Dense zone of lymphocyte infiltration around granuloma	Scanty and diffuse
Nerves destroyed by granulomas	May show neuronal damage but not infiltrationor cuffing
No clear sub-epidermal zone	Clear sub-epidermal zone
Bacilli in granuloma are not seen	Numerous bacilli 5+ or 6+
Few macules + plaques with well defined edges	Macules, papules, plaques and nodulespresent with vague edges
Lesions distributed asymmetrically	Lesions distributed symmetrically
hair loss	*no hair loss*
Lesions are anesthetic	Lesions are not anesthetic

Nerve thickening often singly and early	Nerve thickening is symmetrical and late(stocking & glove patterns)
First manifestation may be neural	First manifestation never neuronal
Lepromin test is strongly positive	Lepromin test is negative

- Because of the diffuse parasite filled lesions lepromatous leprosy is more infectious than those with tuberculoid leprosy.

Table: **Differences between tuberculoid and lepomatous leprosy**

Clinical course and complications

- Lepromatous leprosy involves primarily the shin, peripheral nerves, anterior eye, upper airways (down to larynx), testis, hands and feet. The vital organs and the central nervous system are rarely affected presumably because the core temperature is too high for the growth of M.leprae.

VI. Syphilis

Definition: Syphilis is a systemic infection caused by the spirochete *Treponema pallidium,* which is transmitted mainly by direct sexual intercourse (venereal syphilis) and less commonly via placenta (congenital syphilis) or by accidental inoculation from the infectious materials.

- *T. Pallidum* spirochetes cannot be cultured but are detected by silver stains, dark field examination and immunofluorescence technique.

Pathogenesis:

- The organism is delicate and susceptible to drying and does not survive long outside the body.
- The organism invades mucosa directly possibly aided by surface abrasions following intercourse with an infected person, a primary lesion, an ulcer known as the chancre, develops at the site of infection usually the external genetalia but also lips and anorectal region. Within hours, the *T. pallidum* pass to regional lymph nodes and gain

access to systemic circulations. Thereafter, the disease is unpredictable. Its incubation period is about 3 weeks.

- Whatever the stage of the disease and location of the lesions the histologic hallmarks of syphilis are

A. Obliterative endarteritis

B. Plasma cell rich mononuclear cell infiltrates.

- The endarteritis is secondary to the binding of spirochetes to endothelial cells mediated by fibronectin molecules bound to the surface of the spirochetes. The mononuclear infiltrates are immunologic response.
- Host humeral and cellular immune responses may prevent the formation of chancre on subsequent infections with *T. pallidum* but are insufficient to clear the spirochetes.

Morphology: Syphilis is classified into three stages

Primary syphilis (chancre):

- Chancre appears as a hard, erythematous, firm; painless slightly elevated papule on nodule with regional lymph nodes enlargements. Common sites are Prepuce / scrotum in men-70%, Vulva or cervix in females -50%
- the chancre may last 3-12 weeks. Patients with primary syphilis who stayed for more than two weeks cannot be reinfected by a challenge.

Secondary syphilis:

- Almost any organ is involved (great mimickery). Widespread mucocutaneous lesions involving the oral cavity, plams of the hands and soles of the feet characterize it.
- There are also generalized lymphadenopathies mucosal patches (snail track ulcers) on the pharynx and genitalia, which is highly infectious.
- Condylomata lata: - which is papular lesions in moist areas such as axillae, perineum, vulva and scrotum, which are stuffed with abundant spirochetes.

- Follicular syphilitidis: - Small papulary lesion around hair follicules that cause loss of hair.

Nummular syphilitidis:- It is coin-like lesions involving the face and perineum

- Generalized lymphadenopathy and the uncommon swelling of epithrochlear lymph nodes have long been associated with syphilis.
- Though, asymptomatic, if untreated, secondary syphilis can relapse (latent syphilis) and more episodes of relapses may show a more granulomatous histology in skin lesions and progress to the next stage.

Tertiary syphilis:

The three basic forms of tertiary syphilis are:

1. Syphilitic gummas - there are grey white rubbery masses of variable sizes. They occur in most organs but in skin, subcutaneous tissue, bone, Joints and testis. In the liver, scarring as a result of gummas may cause a distinctive hepatic lesion known as hepar lobatum.

- Collapse of the bridge of the nose and palate can occur with perforation
- Osteitis and periosteitis may lead to thickening and deformity of long bones such as the sabre tibia
- Histologically, gummas look like a central coagulative necrosis characterized by peripheral granumatous responses. TheTrepanosomas are scanty in these gummas and difficult to demonstrate.

2**. Cardiovascular syphilis**

- This is most common manifestation of tertiary syphilis. The lesions include aortitis, aortic value regurgitation, aortic aneurysm, and coronary artery ostia stenosis. The proximal aorta affected shows a tree -barking appearance as a result of medial scarring and secondary atherosclerosis. Endartereritis and periaortitis of the vasa vasoum in the

wall of the aorta, is responsible for aortic lesions and in time, this may dilate and form aneurysm and eventually rupture classically in the arch.

3. **Neurosyphilis:**

- occurs in about 10% of untreated patients. The neurosyphllis comprises of

i. **Meningiovascular syphilis** – particularly in base of brain

ii. **General PARESIS of insane** it affects the cerebral artery with grey matter with subsequent atrophy.

iii. **Tabes dorsalis** – Result of damage by the spirochetes to the sensory nerves in the dorsal roots resulting in locomotion ataxia, Charcots joint, lighting pain and absence of deep tendon reflexes

Congenital syphilis

- This infection is most severe when the mother's infection is recent. Treponemas do not invade the placental tissue or the fetus until the fifth month of gestation (since immunologic competence only commences then) syphilis causes late abortion, still birth or death soon after delivery or It may persist in latent forms to become apparent only during childhood or adult life.
- The outcome of congenital syphilis depends on stage of maternal infection (i.e. the degree of maternal spirochataemia). In primary and secondary stages, the fetus is heavily infected and may die of hydrops in utero or shortly after birth. Liver and pancreas show diffuse fibrosis. The placentis is heavy, and pale with plasmacytic villitis. After maternal second stage, the effects of congenital syphilis are progressively less severe.
- Less dramatic visceral disease, papular lesions on skin and mucosae such as the nose snuffles, may be seen with Huchinton's teeth, and interstial keratitis.
- Children infected in utero who are sero -positive show no lesions until two or more years after birth are classified as having late congenital syphilis. The late congenital syphilis is distinctive for the triads: Interstial keratitis; Hutchinson teeth and Eight nerve deafness

VII. Malaria

Malaria is caused by the intracellular protozoan parasite called Plasmodium species and plasomodium Faliprium is the worldwide infections that affect 100 million people and kill 1 to 1.5 million people yearly. P.Falciparium and P.Vivax, P. ovale, and P.malarie represent 60%, 49 %, <1.0% and reported cases respectively in Ethiopia. P. falciparum cause high parasitmias, severe anemia, cerebral symptoms, and pulmonary edma and death.

Pathogenesis (P.Falciparum):

Infected humans produce gametocytes that mosquitoes acquire on feeding. Within these insects' body, the organism produces sporozites, which the mosquito transmits to human when it feeds.

③ Malarial sporozites after being released in the blood within minutes attach to a serum protein thrombosroridin and properidine located on the basolateral surface of hepatocytes. These sporozites multiply and release merozytes by rupturing liver cells.

③ Once released, P. falciparum merozites bind by a parasite lactin like molecule to on the surface of red blood cells

③ Within 2 to3 weeks of hepatic infection, merozites rupture from their host hepatocytes and invade erythrocytes establishing erytrocytic phase of malarial infection.

③ The merozites feed on hemoglobin grow and reproduce within erythrocytes. Repeated cycles of parasitemia occur with subsequent ruptures of these cells with resultant clinical manifestations such as chills, fever etc.

③ P. Vivax merozites however, bind by homologous lectin to the Duffy antigen on RBC so many cases who are Duffy negative are resistant to this infection.

③ HLA –B53 associated resistance in some Africans is related to the ability of HLA –B53 to present the liver stage specific malarial antigen to cytotoxic T-cells, which then kill malarial, infected hepatocytes.

③ Individuals with sickle cell trait are resistant to malaria because the red cells that are parasitized in these individuals are removed by the spleen.

③ Most malarial parasites infect new RBC & some develop to sexual form called gametocytes and the mosquito when it takes this blood meal the cycle continues.

Morphology:

③ Spleen enlarged upto 1000gm (normally 150grams) and this splenomegaly can be attributed to increased phagocytosis in splenic reticuloendothelial cells in chronic malaria. The parenchyma imparts grey or blue discolouration due to hemozoin.

③ Liver kuffer cells are heavily laden with malarial pigments, parasites, and cellular debris. Pigmented phagocytes may be dispersed through out bone marrow, lymph nodes, subcutaneous tissues and lungs.

③ Malignant cerebral malaria: Patients with cerebral malaria have increased amount of inter-cellular adhesion molecules (ICAM- 1). These patients manifest diffuse symmetric encephalopathy; brain vessels are plugged with parasitized red cells. There are ring hemorrhages related to local hypoxia. Cerebral involvement by *P. falciparum* causing 80% of childhood death is due to adhesion of the P. falciparum parasite to endothelial cells with in the brain.

Hypoglycemia- result from failure of hepatic gluconeogenesis & glucose consumption by the host and the parasite lactic acidosis -due to anaerobic glycolysis, non cardiogenic pulmonary edema, renal impairment, anemias etc

P. falciparum, the cause of malignant malaria produces much more aggressive and lethal disease than the other human malarias. This organism is distinguished from other malarial parasites in four aspects.

1) It has no secondary exoerythocytic (hepatic) stage

2) It parasitizes erythrocytes of any stage, causing marked parasitmia and anemia. In other types of malaria only subpopulations of erythrocytes are parasitized, and thus low

level parasitemias and more modest anemias occur. P. Vivax and P>Ovale attack immature erythrocytes while P. malarie attack senescent cells.

3) There may be several parasites in single erythrocyte

4) P. falciparum alters the flow characteristics and adhesive qualities of infected erythrocytes so that they adhere to the endothelial cells of small blood vessels frequently produce severe ischemia. Infected red cells sequester inside the small blood vessels at the same time P. falciparum infected RBCS may also adhere to uninfected red cells to form rosettes. The process of cytoadhernce and rosetting are central to the pathogenesis of falcparum malaria in the other three " benign" malarias sequestrations does not occur and all stages of parasites' development are evident on peripheral blood smears.

P. falciparum invades erythroytes of all ages and is associated with high level parasitemia whereas, P. vivax, P.ovale and P.malariae show predilection for either old red cells or reticuloytes & level of parasitmias seldom exceeds 2 percent.

Malaria in pregnancy

In pregnancy, malaria may be associated with hypoglycemia, fetal distress syndrome and low birth weight. Congenital malaria can occur rarely. P. falcparum malaria is an important cause of fetal death. Congenital malaria occurs in fewer than 5% of newborns.

Malaria in children

Most of the estimated 1-3 million persons who die of falciparum malaria each year are young African children. Convulsion, coma, hypoglycemia, metabolic acidosis and severe anemia are relatively common.

Transfusion malaria

Malaria can be transmitted by blood transfusion, needle -stick injury, sharing of needles by infected drug addicts, or organ transplants. The incubation period is short because there is no pre-erythrocytic stage of development**.**

Complications of malaria include:

Tropical splnomegaly syndrome (**Hyperreactive** malarial splenomegaly), Burkitt's lymphoma and EBV infection

Quartan malarial nephropathy

Black water fever

Algid malaria