كلية : التربية للعلوم الصرفة

القسم او الفرع : علوم الحياة

المرحلة: دكتوراه

أستاذ المادة : ا.م. د.لؤي حاتم علي

اسم المادة باللغة العربية : علم النسج المرضية

اسم المادة باللغة الإنكليزية : histopathology

اسم المحاضرة الأولى باللغة العربية: الاحتشاء

اسم المحاضرة الأولى باللغة الإنكليزية : Infarction

IX. Infarction

Definition: An infract is an area of ischemic necrosis caused by occlusion of either the arterial supply or venous drainage in a particular tissue.

Nearly 99% of all infarcts result from thrombotic or embolic events. Other mechanisms include [almost all of them are arterial in origin]**:**

• Local vasospasm

• Expansion of atheroma due to hemorrage in to athermotous plaque.

• External compression of the vessels. e.g trauma

• Entrapment of vessels at hernial sacks etc.

The development & the size of an infarct are determined by the following factors:

A. The nature of the vascular supply

B. The rate of development of occlusion

C. Suceptibility of the tissue for hypoxia

D. Oxygen content of the blood

E. The severity & duration of ischemia

A. The nature of vascular supply

The following organs have a dual blood supply.

• Lung → pulumonary artery → Bronchial artery

• Liver → hepatic artery → Portal vein

• Hand & forearm → Radial arteries → Ulnar arteries.

The effect of such a dual blood supply is that if there is obsrtuction of one of the arterial supplies, the other one may offset the rapid occurrence of infarction in these organs unlike the renal & splenic circulations which have end arterial supply.

Infarction caused by venous thrombosis is more likely to occur in organs with single venous outflow channels, such as testis &ovary.

B: Rate of development occlusion

Slowly developing occlusions are less likely to cause infraction since they provide time for the development of collaterals.

C: Tissue suceptibility to hypoxia:

The susceptibility of a tissue to hypoxia influences the likelihood of infarction. Neurons undergo irreversible damage when deprived of their blood supply for only 3 to 4 minutes. Myocardial cells die after 20-30 minutes of ischemia. Fibroblasts are more resistant, especially those in the myocardium.

D: Oxygen content of blood

Partial obstruction of the flow of blood in an anaemic or cyanotic patient may lead to tissue infarction.

E: The severity & duration of ischemia.

Types of infarcts:

Infarcts are classified deepening on:

A) the basis of their colour (reflecting the amount of haemorrhage) into:

1. Hemorrhagic (Red) infarcts
2. Anemic (White) infarcts

B) the presence or absence of microbial infection into:

1. Septic infarcts
2. Bland infarcts

1. Red infarcts occur in:

a) Venous occlusions as in ovarian torsion

b) Loose tissues such as the lung which allow blood to collect in infarct zone.

c) Tissues with dual circulations (eg. the lung), permitting flow of blood from unobstructed vessel in to necrotic zone.

d) In tissues that were previously congested because of sluggish outflow of blood.

e) When blood flow is reestablished to a site of previous arterial occlusion & necrosis.

2. White infarcts occur in:

a) Arterial occlusion in organs with a single arterial blood supply.

b) Solid organs such as the heart, spleen, & kidney, where the solidity of the tissue limits the amount of hemorrage that can percolate or seep in to the area of ischemic necrosis from the nearby capillaries.

Morphology of infarcts:

Gross: All infarcts are wedge-shaped with the occluded vessel at the apex and the periphery of the organ forming the base of the wedge. The infarction will induce inflammation in the tissue surrounding the area of infarction. Following inflammation, some of the infarcts may show recovery, however, most are ultimately replaced with scars except in the brain.

Microscopy:

The dominant histologic feature of infarction is ischemic coagulative necrosis. The brain is an exception to this generalization, where liquifactive necrosis is common.

Clinical examples of infarction:

A. Myocardial infarction

[a] Usually results from occlusive thrombosis supervening on ulcerating atheroma of a major coronary artery.

[a] Is a white infarct.

[a] Can cause sudden death, cardiac failure, etc...

B. Cerebral infarcts

[a] May appear as pale or hemorrhagic

[a] A fatal increase in intracranial pressure may occur due to swelling of large cerebral infarction, as recent infarcts are raised above the surface since hypoxic cells lack the ability to maintain ionic gradients & they absorb water & swell.

[a] Is one type of cerebrovascular accidents (CVA) or stroke which has various clinical manifestations.

C. Lung infarcts

[a] Are typically dark red & conical (wedge-shaped).

[a] Can cause chest pain, hemoptysis, etc…

D. Splenic infarcts

- Conical & sub capsular
- Initially dark red later turned to be pale.

XI. Shock

Definition: Shock is a state in which there is failure of the circulatory system to maintain adequate cellular perfusion resulting in widespread reduction in delivery of oxygen & other nutrients to tissues. In shock, the mean arterial pressure is less than 60 mmHg or the systolic blood pressure is less than 90 mmHg.

• Regardless of the underlying pathology, shock constitutes systemic hypoperfusion due to reduction either in cardiac output or in the effective circulating blood volume. The end results are hypotension followed by impaired tissue perfusion and cellular hypoxia.

• Adequate organ perfusion depends on arterial blood pressure (BP) which, in turn, depends on:

1. Cardiac output (CO)

2. Peripheral vascular resistance (PVR)

• CO = stroke volume X heart rate

In turn, stroke volume depends on:

a) Preload i.e. blood volume,

b) Afterload i.e. arterial resistance, &

c) Myocardial contractility.

• Therefore, shock (i.e. widespread decreased perfusion of tissues) occurs when the preload (i.e. the blood volume) is decreased, or when the afterload (the peripheral vascular resistance) is decreased, or when the myocardium fails to contract. These basic mechanisms of shock are used to classify it. Next, we will look at the classification of shock.

Classification of shock:

Shock can be divided into:

A. Hypovolemic shock

B. Cardiogenic shock

C. Distributive shock.

A. Hypovolemic shock

Definition: This is shock caused by reduced blood volume. Reduction in circulating blood volume results in the reduction of the preload which leads to inadequate left ventricular filling, reflected as decreased left & right ventricular end diastolic volume and pressure. The reduced preload culminates in decreased cardiac out put which leads to widespread tissue perfusion (shock).

Causes of hypovolumic shock include:

a) Haemorrhage

b) Diarrhoea & vomiting

c) Burns

d) Trauma

e) etc

The effect of haemorrhage depends on the rate and amount of blood loss. Hypovolumic shock is the most common type of shock in clinical medicine. A normal healthy adult can

lose 550ml (10%of blood volume) without significant symptoms. But loss of 25% or more of the blood volume (N=1250ml) results in significant hypovolemia.

B. Cardiogenic shock

Definition: This is shock that results from severe depression of cardiac performance. It primarily results from pump failure [myocardial failure].

™ Cardiogenic shock is hemodynamically defined as:

o DBP<60mm Hg

o Left ventricle filling pressure > 18mm Hg

o Cardiac index< 1.8 l/min/m2

o Usually pulmonary oedema coexists.

Causes of cardiogenic shock can be divided into:

A. Myopathic

B. Mechanical.

A) Myopathic causes of cardiogenic shock include:

1. Acute myocardial infraction. Usually shock occurs in this conditioin if ≥ 40% of the left ventricular mass & more on the right ventricle is involved by infarction.

2. Mycocarditis

3. Dilated cardiomyopathy/hypertrophic cardiomyopathy

4. Myocardial depression in septic shock

5. Etc….

B) Mechanical

i) Intracardiac

a) Left ventricle outflow obstruction E.g.Aortic stenosis, hypertrophic cardiomyopathy

b) Reduction in forward cardiac output E.g. Aortic or mitral regurgitation

c) Arrhythmia

ii) Extracardiac

This can be called obstructive shock. The extracardiac causes of cardiogenic shock can be caused by:

a) Pericardial tamponade (gross fluid accumulation in the pericardial space) results in a decreased ventricular diastolic filling → ↓CO

b) Tension pneumothorax (gas accumulation in pleural space)This decreases the venous return by creating a posit pressure.

c) Acute massive pulumonary embolism occupying 50-60% of pulumonary vascular bed.

d) Severe pulumonary hypertension (10 pulmonary hypertension).

C. Distributive shock

Definition: Distributive shock refers to a group of shock subtypes caused by profound peripheral vasodilatation despite normal or high cardiac output.

Causes of distributive shock

1) Septic shock – the commonest among the group & clinically very important.

2) Neurogenic shock

- Usually occurs in the setting of anaesthetic procedure [cephalo-caudal migration of anaesthetic agent] or spinal cord injury owing to loss of vascular tone & peripheral pooling of blood.

3) Anaphylactic shock

- Initiated by generalized IgE – mediated hypersensitivity response, associated with systemic vasodilatation & increased vascular permeability.

4) Endocrine shock

- This is a type of shock that typically occurs in adrenal insufficiency.

Next, we will discuss septic shock in some detail. But before discussing septic shock in detail it would be useful to know some aspects of sepsis briefly. Bactermia is the presence of viable bacteria in the blood as evidenced by blood culture. Septicemia is systemic infection

due the presence of microbes and their toxin the blood. Sepsis is a systemic response to severe infection mediated via macrophage-derived cytokines that target end organ receptors in response to infection. It is also called SIRS.

Septic shock

Definition: This is a kind of shock caused by systemic microbial infection, most commonly by gram – negative infection (endotoxic shock) but can also occur with gram – positive or fungal infections. Or It can be defined as sepsis with

1. Hypotention, arterial blood pressure less than 90mmHg or 40mmHg less than the patient's normal blood pressure,

2. Organ dysfunction, &

3. Unresponsiveness to fluid administration.

Pathogenesis of septic shock:

Septic shock has a mortality rate of over 50% ranking the first among the causes of death in intensive care units. It results from the spread & expansion of an initially localized infection like pneumonia into the blood stream.

Most causes of septic shock (~70%) are caused by endotoxin-producing gram-negative bacilli, hence the term endotoxic shock. Endotoxins are bacterial wall lipopolyschardes (LPS) released when cell walls are degraded. Analogues molecules in the walls of grampositive bacteria & fungi can also elicit septic shock. LPS bind with CD14 molecule on leucocytes, especially monocytes & macrophages, endothelial cells & others. Depending on the dosage of LPS – protein complex, initiation of a cascade of cytokine-mediated events take place.

The mononuclear phagocytes respond to LPS by producing TNF which, in turn, induces IL – 1 synthesis. TNF & IL-1 both act on endothelial cells to produce further cytokines like IL-6, IL-8, & secondary effectors like NO & PAF (platelet aggregating factor).

• High levels of the above molecules or mediators (TNF-α, IL-1, etc…) cause septic shock by acting on:

→ The heart – causing decreased myocardial contractility which results in low cardiac output,

→ Blood vessel – causing systemic vasodilation which decreases the peripheral arteries. The mediators also cause widespread endothelial injury & activation of the coagulation system resulting in DIC, &

→ Lung – causing alveolar capillary damage resulting in adult respiratory distress syndrome (ARDS).

Stages of shock:

Uncorrected shock passes through 3 important stages:

1) An initial nonprogressive phase

o It is also called a period of early compensatory period, during which compensatory mechanisms are activated & perfusion of vital organs maintained.

Mechanisms:

o A variety of neurohumoral mechanisms operate:

i) A decrease in cardiac output will stimulate peripheral & central baro receptors with subsequent intense sympatho-adrenal stimulation. This sometimes leads to up to 200 fold increase in plasma catecholamine level. The net effect is → Tachycardia, ↑HR → ↑ CO → Peripheral vasoconstriction → ↑ BP. This is a major autocompensatory response.

ii) The fall in renal perfusion stimulates the renin – aldosterone secretion mechanism → renal conservation of fluid.

2. Progressive stage (Established shock)

• This is characterized by tissue hypoperfusion with onset of worsening circulatory &metabolic imbalances including acidosis.

• There is a widespread tissue hypoxia.

• Anaerobic glycolysis results in excessive lactic acid production. The lactic acid reduces tissue PH & blunts vasomotor response. The hypoxic cells leak glucose leading to insulin-resistant hyperglycaemia and increased glycogenolysis. Impaired carbohydrate metabolism causes a fall in production of ATP, failure in function of Na+ - K+ ATPase, result in Na & water enterance into the cell, causing cellular swelling also called sick cell syndrome. Anoxic injury to endothelial cells results in DIC.

3. An irreversible stage

• A sage at which, even if hemodynamic disorders are corrected survival is not possible.

• Transition to irreversible damage is mediated via various mechanisms.

Morphology of septic shock:

• All organs are affected in severe shock. In shock, there is widespread tissue hypoperfusion involving various organs such as the heart, brain, & kidney. This leads to widespread hypoxic tissue necrosis. The widespread tissue necrosis manifests as multiple organ dysfunction [MODS]. Various organs may fail to perform their normal functions. And lungs may show ARDS or Shock lung.

Clinical course of shock:

• Patient with shock may manifest as having a weak and rapid pulse, tachypenia, & cool, clammy, cyanotic skin. In septic shock, the skin will initially be warm & flushed because of peripheral vasodilation. The patient may present with confusion, restlessnes, decreased urine output, coma, and death.

Immunodeficiency Diseases

The term immunodeficiency covers a group of disorders of specific immune responses, neutrophil, macrophage and natural killer cells functions, as well as defects in the compliment system that lead to impaired resistance to microbial infections.

Classification – These diseases are crudely classified into primary and secondary types.

1) Primary immunodeficiency diseases (exceedingly rare)

* These disorders usually manifest in early childhood and are almost always genetically determined. Though, some overlap exists primary immunodeficiency diseases are further divided into:

Deficiencies of antibody (B – cells) immunity. Eg. Infantile X-linked agammaglobinmea Transient hypogammaglobulinmea of infancy

Deficiencies of cell mediated (T-cell) Immunity

T-cell deficiencies are difficult to trace as T-cells affects B – cell functions Eg. Di George's syndrome:

Combined T-cell and B-cell deficiencies Eg Severe combined immunodeficiency disease (SCID).

2) Secondary immunodeficiencies States

These immunodeficiency states may be acquired secondary to various disease processes or drug effects

* Protein deficiency

Lack of protein leads to cell mediated immunity and hypocomplementamia

* Hematologic malignancies

Leukemia and lymphomas where normal functioning cell replaced by neoplastic ones here both humeral and cell mediated immunity are impaired

* Acute viral infection Especially infectious mononucleosis and misels cause temporary impairment of cell mediated immunity

* Chronic renal failure Probably due to toxic effects of accumulated metabolites that affects both B and T cell functions.

- Iatrogenic

Steroids etc for organ transplants, cytotoxic drugs or radiotherapy for the treatment of malignancies.

- Splenctomy

After staging operations of lymphomas or traumatic spleen rupture

Splenectomy leads to a characteristic immunodeficiency in which the patient is susceptible to infections by phylogenic bacteria especially pneumococal pneumonia.

- Acquired immunodeficiency syndrome (AIDS)

As a prototype example of secondary immunodeficiency states, AIDS is discussed in some detail below.

Acquired Immunodeficiency Syndrome (AIDS)

- AIDS is a retroviral disease characterized by profound immuno suppression that leads to opportunistic infections, secondary neoplasms and neurological manifestations.

Overview:

- Prevalence: Currently AIDS affects more than 40 million people all over the world and more than 90 % of the infections prevail in developing countries. Currently, the subSaharan Africa in general and South Africa, Ethiopia and Nigeria in particular shoulder the greatest burden of this pan endemic.

- Age: Mostly affected individuals are those aged between 15 and 49 years of age however, the epidemiology is quite different in children less than 13 years. Close to 2

- of all AIDS, occur in this age group presently where more than 90 % of this transmission results from transmission of the virus from the mother to the child.

- Sex: Women are more vulnerable than men:

Receptive sexual partners-

• Uterine, cervical and vaginal conditions that promote HIV transmission easily include cervical erosion, cervical ectopy, sexually transmitted diseases (STD), and cervical cancer.

• STD often goes unnoticed due to inaccessible anatomic locations.

• Menstruation: May make the transmission of HIV easier just before, during or after menstruation. It results in a large raw exposed area in the inner uterine lining to the virus

• Those with very low socio economic backgrounds are vulnerable to sex trade (HIV is said to be" the holocaust of the poor").

• Age of earlier sexual contact where the very young female genital linings are vulnerable to easy lacerations.

Modes of transmission:

- Sexual activities 75% of all world-wide transmission is heterosexual transmission
- Parenteral Transmission In intravenous drug abusers, hemophiliacs who received factor viii concentrates and random recipients of blood transfusion
- Mother to child transmission. About 25 –30% HIV, positive mother will transmit HIV to their infants. About 60% of this infection is transmitted during child- birth 25% during pregnancy and 15% during breastfeeding.
- Needle Pricking Accidental needle struck injury or exposure to non-intact skin to infected blood in laboratories accounts for about 0.3% risk of stereovision as compared to a 30% risk of accidental exposure to hepatitis B infected blood.

Etiology:

- HIV causes AIDS and HIV is a non-transforming retrovirus belonging to Lentivirus family. The retrovirus undergoes an unusual biologic process in which the genetic material in form of a single stranded RNA, can be converted to double stranded DNA by the effect of reverse transcriptase.
- Two type of HIV virus's HIV – 1 - USA, EUROPE, East & central Africa HIV - 2 - West Africa

II. Typhoid Fever

Definition: Typoid fever is an acute enteric disease caused by an obligate intracellular bacillus called Salmonella Typhi and this bacillus resides within mononuclear phagocytic cells of lymphoid tissues. **The disease is unique humans and it is characterized by fever, splenomegaly and neutropenia.**

Transmission: Feco-oral routes through contaminated foods

Carriers:

- convalescent carrier – for up to 6 months of infection
- Chronic fecal and chronic urinary carriers are associated with chronic cholecystitis and pyelonephritis respectively.
- S. mansoni and S. hematobium co-infections protract the course of typhoid fever.

Pathogenesis:

* Infection is by ingestion of the organism, (>10 to the power of 7) in 50% of cases penetrate the small intestine mucosa and reach the circulation with transient bacteremia
* The bacilli are taken by the lymphatic to lymph nodes and they are engulfed by mononuclear phagocytic cells.
* After a period of multiplication in these phagocytic cells, the organisms rupture the cells and invade the blood stream via the thoracic duct. The liver, gallbladder, spleen, kidney and bone marrow become infected during this second bactermic phase, characterizing the clinical features of the diseases.

The main pathological changes are found in the gastrointestinal tract particularly The Payer's patches, which are the sub mucosal lymphoid follicles in this tract. This invasion arises from the gall bladder. Payer's patches may show

f Hyperplasia in first week

f Necrosis in second week

f Ulceration in third week

f Healing in fourth week

* Typhoid ulcers are oval and are situated longitudinally along the long axis of the colon, which are in contra -distinction of tuberculous ulcers that are set transversally.

Clinical course:

Typhoid fever is a protracted disease that is associated with

ƒ Bactermia, fever and chills during the first week

ƒ Widespread reticuloendothelial involvement with rash, abdominal pain and prostration in the second week and

ƒ Ulceration of payer's patches with intestinal bleeding and shock during the third week

Complications may include:

ƒ Intestinal perforation: 3 – 4% and it is responsible to 25% of the death

ƒ Intestinal hemorrhage: 8% and usually seen between 14-21 days of illness

ƒ Acute cholecystitis, etc

III. Acute Osteomyelitis

Definition: It is an inflammation of the bone and marrow (osteo- means bone and myelo – marrow), commonly in children and adolescents

Route: Hematogenous spread – most common in long and vertebral bones extension from contagious site- otitis media, dental caries.

Direct implantation-compound fracture.

Etiology:

- All types of organisms possible; however, pyogenic organisms most notably Staphylococcus aurous represent 80 - 90% of pyogenic osteomylitis. Others include pseudomonas, Klebsiella, Salmonella in sickle cell anemic patients.

Sites:

- Any bone may be affected but the metaphysics of long bones (distal femur, proximal tibia and humorus) adjacent to actively growing epiphyses and the vertebral column are most often involved.

Pathogenesis:

* The location of the lesions within specific bones is influenced by the vascular circulation, which varies with age. In the neonate, the metaphysical vessels penetrate the growth plate resulting in frequent infection of the metaphysis, epiphysis or both.

* In children, localization of microorganisms in the metaphysics is typical.
* In adults, the epiphyscal growth plate is closed and the metaphysical vessels reunite with their epiphyses counterparts, which provide a route for bacteria to seed in the epiphysis and subchondral regions.
* The susceptibility of the metaphysis to acute osteomylitis is in part, explained by the dilated vascularature of the marrow spaces where sluggish blood flow provides an ideal site for multiplication of bacteria.

IV. Tuberculosis

Tuberculosis is a prototype example of granulomatius inflammation.
Tuberculosis infects one third of world populations and kills about three million people yearly and it is the single most important infectious disease.

Etiology: Mycobacterium tuberculosis and Mycobacterium bovis are the regular infecting rod shaped, acid fast and alcohol fast, strict aerobic, non-spore forming bacteria with a waxy coat. It has a slow generation time of 4-6 weeks to obtain a colony of mycobacterium tuberculosis. M. tuberculosis is transmitted by inhalation of infective droplets coughed or sneezed into the air by a patient with open tuberculosis, however, M. bovis is transmitted by milk from infected cows. Rarely, it transmits via breached skin surfaces and conjunctiva. M. Avium and M. intracellulare cause disseminated infection in 15%-24% of patients with AIDS.

Pathogenicity of the bacillus is related to its cell wall components. Pathogenicty of tuberculosis is attributed to its cell wall component.

1. Cord factor which is a cell wall glycolipid component is aviable on virulent strains
2. Lipoarabinomannan (LAM): It inhibits macrophage activation by interferonδ LAM induce macrophages to secrete TNF - α which causes fever, weight loss, and tissue damage and LAM also induce IL-10 which suppresses mycobacteria induced T-cell proliferation

3. Complement activated on the surface of mycobacteria may opsinize the organism and faclitate its uptake by macrophages complement receptor CR3 (mac-1 integrin) without triggering the respiratory burst necessary to kill the organisms.
4. M. Tuberculosis heat shock protein is similar to human heat shock protein and may have a role in autoimmune reactions induced by M. tuberculosis. The bacillus resides in phagosome, which are not acidified in lysosomes. Inhibition of acidification has been associated with urase secreted by the mycobacteria.

Who are those more susceptible to develop tuberculosis?

***ƒ* Race: North American Indians, black Africans and Asians are much more susceptible than others**

***ƒ* Age: Extremes of ages due to imperfect immune responses**

***ƒ* Immunologic and other host factors immunocompromized patients are more liable to develop tuberculosis. These include patients with steroid therapy or immunosuppressive drugs, HIV infection, diabetes mellitus, cirrhosis, malnutrition and damage of lung for example with silicosis etc.**

Pathogenesis:

Primary infection: Primary phase of M. tuberculosis infection begins with inhalation of the mycobacteria most often in the lower segment of the lower and middle lobes and anterior segment of the lower lobe of the lung. First, the organisms are phagocytosed by alveolar macrophages and transported by these cells to hilar lymph nodes. Naïve macrophages are unable to kill the mycobacteria, thus they multiply and lyse these host cells, infect other macrophages and sometimes disseminate through blood to other parts of the lung and elsewhere in the body.

- After few weeks T-cell mediated immunity is demonstrable by PPD reaction first the CD4 T cells interaction with macrophages secrete interferon, which activate macrophages to kill

intracellular mycobacteria through reactive nitrogen intermediates, including NO, NO2,HNO3.

- Second CD 8+ suppressor T-cells lyse macrophages infected with mycobacteria through a FAS -independent, granular dependent reaction and kill mycobacteria.
- Third CD4-CD8- (double negative) T cell lyse macrophages in a FAS dependant manner without killing mycobacteria. Lyses of these macrophages results in the formation of caseating granuloma and direct toxicity to the mycobacteria may contribute to the necrotic caseous centers. The primary infection of sub-pleural lesion, the intervening macrophage reactions within accompanying lymphangitis and the hilar lymph nodes caseous lesions is called primary complex (often called a Ghon focus).

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:

1- 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.

2- 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.

3- 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 .

4- 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

Because of the diffuse parasite filled lesions lepromatous leprosy is more -1
infectious than those with tuberculoid leprosy.