IMMUNOGLOBULIN PATTERN IN CEREBROSPINAL FLUID OF PATIENTS WITH ACUTE BACTERIAL MENINGITIS

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THE MASTER DEGREE IN BACTERIOLOGY

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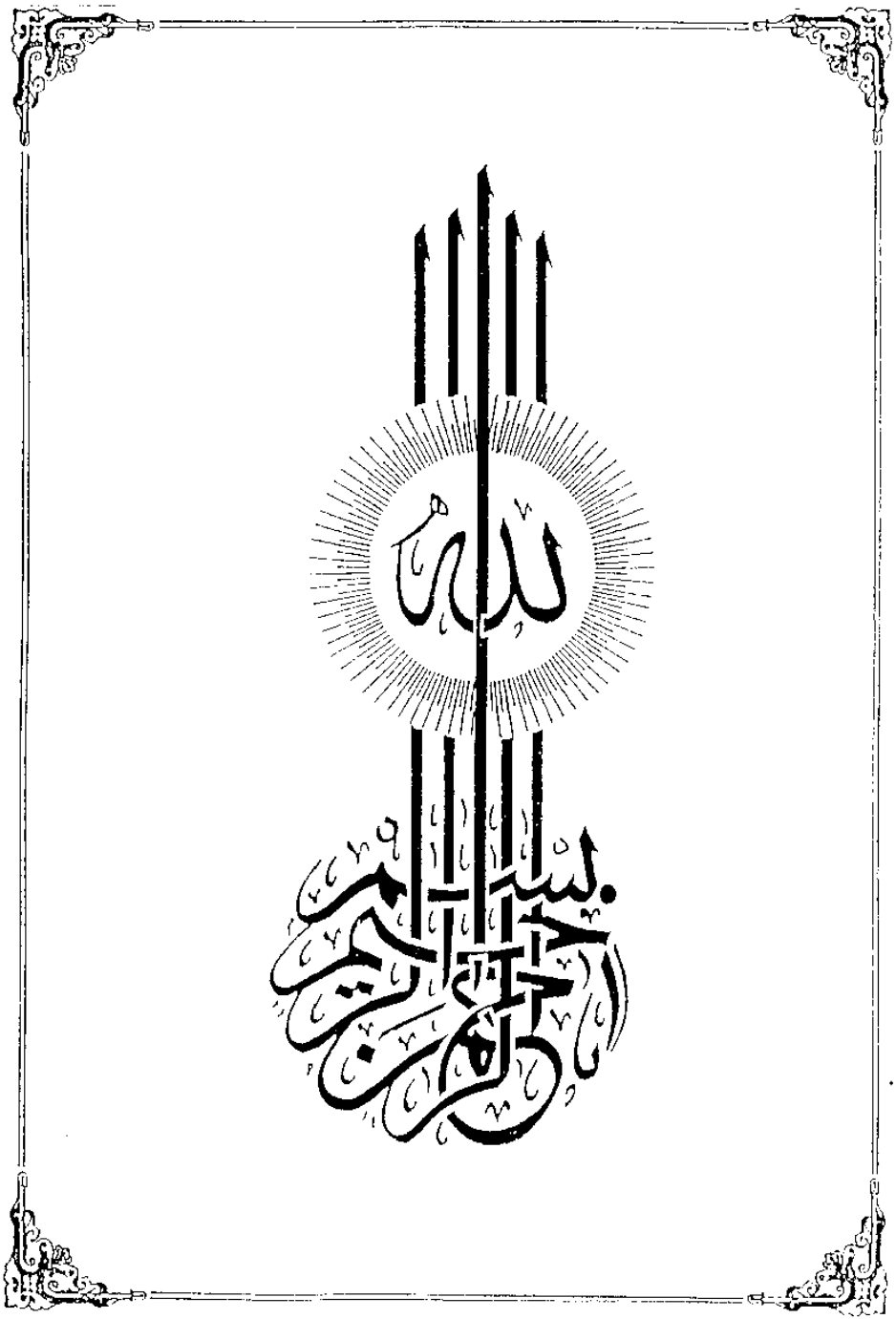
INDEX



Meningitis:

Definition and Causes

Meningitis

Definition:

Meningitis is an inflammation of the arachnoid, the pia mater, and the intervening cerebrospinal fluid.

Since the subarachniod space is continuous through the brain, spinal cord and optic nerves, infection in this space extends throughout the cerebrospinal axis unless there is obstruction of the subarachnoid space (*Scheld, 1994*).

Causes of meningitis:

Meningitis can by produced by many causes that can be collected in the following groups:

I- Bacterial meningitis:

It can be caused by any bacterium gaining entry to the subarachnoid space, but the most common organisms involved are Haemophilus influenzae type b, followed by Neisseria meningitidis and Streptococcus pneumoniae (*Tunkel et al., 1990*).

II- Viral meningitis:

Viruses constitute the majority of numerous infective agents that produce aseptic meningitis (*Beghi et al., 1984*).

In outline, the clinical syndrome of aseptic meningitis consists of fever, headache and other signs of meningeal irritation, and a predominantly lymphocytic pleocytosis with normal CSF glucose. (*Adams and Victor, 1989*).

Causes of Aseptic Meningitis:

The majority of cases are due to viral infections of which the most common are the enteroviral infections: echovirus, Coxsackie virus, and nonparalytic poliomyelitis. Mumps is the next most common, followed by Herpes simplex (type 2), lymphocytic choriomeningitis (LCM), and adenovirus infections (*Johnson, 1982*).

The California virus, which is an arthropod borne virus (arbo virus), is responsible for a small number of cases (*Beghi et al., 1984*).

All these viral infections, together with leptospirosis, comprise about 95% of cases of aseptic meningitis (*Adams and Victor, 1989*).

Rarely, the icteric phase of infectious hepatitis is preceded by mild meningitis, and infectious mononucleosis and Mycoplasma pneumoniae rarely cause what appears to be a primary meningitis (*Johnson, 1982*).

Recently it has been recognized that infection with human immunodeficiency virus (HIV) may present as an acute, self-limited aseptic meningitis with an infectious mononucleosis like picture . HIV has been obtained from the CSF in the acute phase, *(Gray et al., 1988).*

Also recently, herpes simplex virus type I has been isolated from the CSF of a patient with so-called mollaret meningitis *(Steele et al., 1982).*

III- Fungal Meningitis:

Cryptococcosis:

Cryptococcosis, caused by the capsulate yeast Cryptococcus neoformans, present in the excereta of wild and domestic birds is most frequently recognized as a disease of the central nervous system, although the primary site of infection is the lungs occurring sporadically throughout the world but it is now seen most often in patients with AIDS *(Evans, 1992).*

Pathogenesis:

Infection follows inhalation of the cells of C. neoformans which, in nature, are thought to be small, allowing the organism to enter deep into the lung *(Evans, 1992)*.

Pulmonary infection has a tendency toward spontaneous resolution and is frequently asymptomatic but Silent hematogenous spread to the brain leads to clusters of cryptococci in the perivascular areas of cortical gray matter, basal ganglia and other areas of the CNS giving the picture of meningoencephalitis which is fatal without appropriate therapy *(Bennett, 1987)*.

IV- Carcinomatous Meningitis:

It is a common form of CNS invasion in malignancy that does not cause a myelopathy unless there is extensive subpial infiltration from adjacent roots causing nodules with secondary compression or infiltration of the cord *(Ropper and Martin, 1994)*.

Headache is common, and repeated CSF examination eventually reveals malignant cells, an elevated protein, and in some cases, reduced CSF glucose concentration *(Ropper and Martin, 1994)*.

Leukemias and lymphomas are the most common sources of meningeal reactions in meningeal carcinomatosis (from lung, breast or other source) great numbers of neoplastic cells may extend through the leptomeninges involving cranial and spinal nerve roots, and produce a picture of meningitis with normal or low CSF glucose values *(Beghi et al., 1984)*.

V- Chemical meningitis:

Acute meningitis following a diagnostic lumber puncture or spinal anesthesia may be due to bacterial or chemical contamination of the equipment or anesthesia agent *(Hyslop and Montgomery, 1982)*.

Reactions to certain medications can cause a clinical picture and CSF profile similar to that of meningitis *(Scheld, 1994)*.

VI- Diseases of obscure origin:

In a number of chronic acutely recurring diseases of obscure origin, the CSF formula corresponds to that of aseptic meningitis:

1- The Vogt Koyanagi-Harada syndrome, characterized by iridocyclitis, depigmentation of hair and skin, loss of eyelashes and deafness.

2- Allergic hypersensitivity meningitis, occurring in the course of serum sickness and connective tissue diseases such as lupus erythematosus.

3- Behcet disease distinguished by relapsing iridocyclitis, meningitis and ulcers of mouth and genitalia *(Adams and Victor, 1989).*

Bacteriology

Bacteriology

Characters of the Most Common Causative Organisms of Bacterial Meningitis

I- Neisseria meningitidis:

A- Description of the organism:

They are Gram- negative oval cocci occurring in pairs with the opposed surfaces flat or even slightly concave characteristically found inside the polymorphonuclear cells of the inflammatory exudate.

Extracellular cocci also occur and there may be considerable variation in their size and intensity of staining *(fallon and slack, 1992)*.

They are non - sporing and non - motile but capsules are present on most freshly isolated strains *(Fallon and Young, 1989)*.

B- Cultural Characters:

They are aerobic but grow better in an atmosphere containing 5-10 % CO_2 with optimum temperature 35-37^{0}C and optimum pH 7.0-7.7 *(Fallon and Young,1989)*.

They are non haemolytic on blood agar and produce gray, glistening, slightly convex colonies of 0.5-1.0 mm in diameter within 8-24h, but incubation should be continued for another 24h, when the colonies become 2-3 mm with an opaque raised center and thin transparent margins which may be crenated (*Fallon and Slack, 1992*).

C- Biochemical reactions:

The meningococci produce acid from glucose and maltose. They also are quickly positive in oxidase reaction *(Fallon and Young, 1989)*.

D-Serologic classification:

The serogroups of meningococci of pathologic importance whose polysaccharide antigen structure has been determined are: A,B,C,X,Y,Z, 29E and W 135 *(Frasch et al., 1985)*.

Meningococci of groups A and C are those principally associated with epidemics while group B meningococci are common inter-epidemic strains *(Achtman, 1990)*.

Outer membrane protein and lipoprotein serotypes occur within groups B,C,Y and W 135 and may be identified by reference laboratories for epidemiologic purposes *(Frasch et al., 1985)*.

E-Habitat:

The natural habitat of meningococcus is the human nasopharynx; around 5-10% of normal populations are carriers. A sharp increase in the carrier rate precedes the occurrence of clinical cases *(Broome, 1986)*.

II-Haemophilus influenzae:

A-Description of the organism:

Haemophili are pleomorphic Gram-negative rods that may show filamentous or spherical forms especially in old cultures *(Howard, 1992)*.

They are non-motile and non-sporing, and most strains are non-encapsulated, but a few more virulent forms are encapsulated: they are demonstrable by thin India ink wet films and by their swelling reaction with type-specific antiserum *(Duguid, 1989)*.

Under suitable cultural conditions, some strains form fimbriae, which enable them to haemagglutinate human, guinea-pig and other animal red cells at 4°C *(Scott and Old, 1981)*.

B-Cultural Characters:

They grow aerobically, and only poorly anaerobic-ally with the optimum pH 35-37° C, and a few strains require CO_2 concentration 5-10% *(Duguid, 1989)*.

The dependence on blood for growth on culture media is based on a requirement of both X factor (haemin), and V factor (NAD) needed for the synthesis of the iron-containing respiratory enzymes, and for the oxidation-reduction process respectively *(Howard, 1992)*.

The amount of V factor in ordinary blood agar is usually suboptimal, so that colonies are very small, except if the medium is supplemented with NAD or if an organism excreting excess of NAD (e.g. Staph. aureus) is streaked across the surface of the agar with the result of growth stimulation in its vicinity (Satellitism) or if blood agar is heated for a few minutes at 75-100° C *(Duguid, 1989)*.

Selective media, such as Fildes agar, are helpful in cases where specimens containing often commensals that can mask the Haemophili are dealt with *Duguid, 1989)*.

C-Biochemical reactions:

Haemophilus influenzae is catalase-positive, oxidase positive and ferments glucose and galactose producing acid but not gas *(Howard, 1992)*.

Kilian (1976) has divided strains of Haemophilus influenzae into six biovar by their indole, urease and ornithine decarboxylase reactions. The biovar of any strain appears to be stable enough to be a clone marker in epidemiological studies.

D-Antigenic characters:

While non-capsulate strains are antigenically very heterogeneous, Capsulate ones are divided into six serotypes labeled a-f, identified by precipitation, swelling or agglutination with type-specific antisera *(Zinnemann, 1960)*.

The capsules are polysaccharide in composition and the most important of these is type b which is a polymer of ribosyl ribitol phosphate, since strains of this type, mostly in biovar I, are responsible for most cases of Haemophilus meningitis *(Howard, 1992)*.

E-Habitat:

H. influenzae is exclusively a human parasite which resides principally in the upper respiratory tract. Non capsulate strains are present in 25-80%

of healthy people, and capsulate strains in 5-10% of which capsular type b strains are found in 1-5% *(Sell, 1982)*.

III-Streptococcus pneumoniae:

A-Description of the organism:

It is a Gram-positive, non-motile, non sporing encapsulated lanceolate coccus approximately 1 micrometer in diameter, with a tendency to occur in pairs with the broader ends opposed *(Finch, 1992)*.

B-Cultural characters:

The pneumococcus is aerobic and facultatively anaerobic growing best in air or hydrogen with 5-10% CO_2 and pH 7-7.8 at optimum temperature of 37°C *(Duguid and Ross, 1989)*.

It can grow on ordinary media, but better in media with 5-10% serum, blood or heated blood, which supplies nutrients, pH buffers and catalase *(Duguid and Ross, 1989)*.

Overnight growth on blood agar produces 1 mm colonies which are round, domed and surrounded by a zone of α-haemolysis. With more prolonged incubation, autolysis results in subsidence of the center to create the typical draughtsman appearance *(Finch, 1992)*.

Some strains e.g. of stereotype 3 and 7 produce larger mucked colonies which may remain convex from excessive capsular polysaccharide formation *(Duguid and Ross, 1989)*.

The pneumococcus is soluble in bile and this distinguishes it from other haemolytic streptococci, which are also resistant to optochin unlike the pneumococcus *(Cowan, 1974)*.

A culture of pneumococci contains a few mutant organisms that are unable to produce capsules giving rise to rough colonies instead of smooth colonies produced by capsulate pneumococci with loss of virulence of these rough colonies *(Duguid and Ross, 1989)*.

C-Biochemical reactions:

The pneumococci are catalase negative and oxidase negative and form cid only from glucose, lactose and sucrose, and many strains also from nulin *(Duguid and Ross, 1989).*

D-Antigenic characters:

Some 83 serotypes of pneumococcus are distinguished by differences n the nature of the polysaccharide antigen that composes their capsules and is partly secreted into the culture medium in the form of a loose slime, or specific soluble substance (SSS), the type of which is determined by its reaction with type-specific antisera, tested first in pools and then singly *(Whitby et al., 1985).*

This may be done by agglutination or precipitation, but most simply by swelling reaction wherein the homologous specific antiserum coats and outlines with antibody the margin of the hitherto invisible capsule and so makes the cocci appear enlarged *(Duguid and Ross, 1989).*

Pneumococci of some 23 serotypes cause approximately 90% of cases of bacteremic pneumococcal pneumonia and meningitis *(Smart et al., 1987).*

E-Habitat:

Streptococcus pneumoniae is a member of the normal resident oropharyngeal flora of 5-7% of the population mostly isolated in winter *(Finch,1992).*

Epidemiology