THE CLINICAL SIGNIFICANCE OF C-REACTIVE PROTEIN DETERMINATION IN DIFFERENTIATING BACTERIAL AND ASEPTIC MENINGITIS SYNDROMES IN EGYPTIAN INFANTS AND CHILDREN

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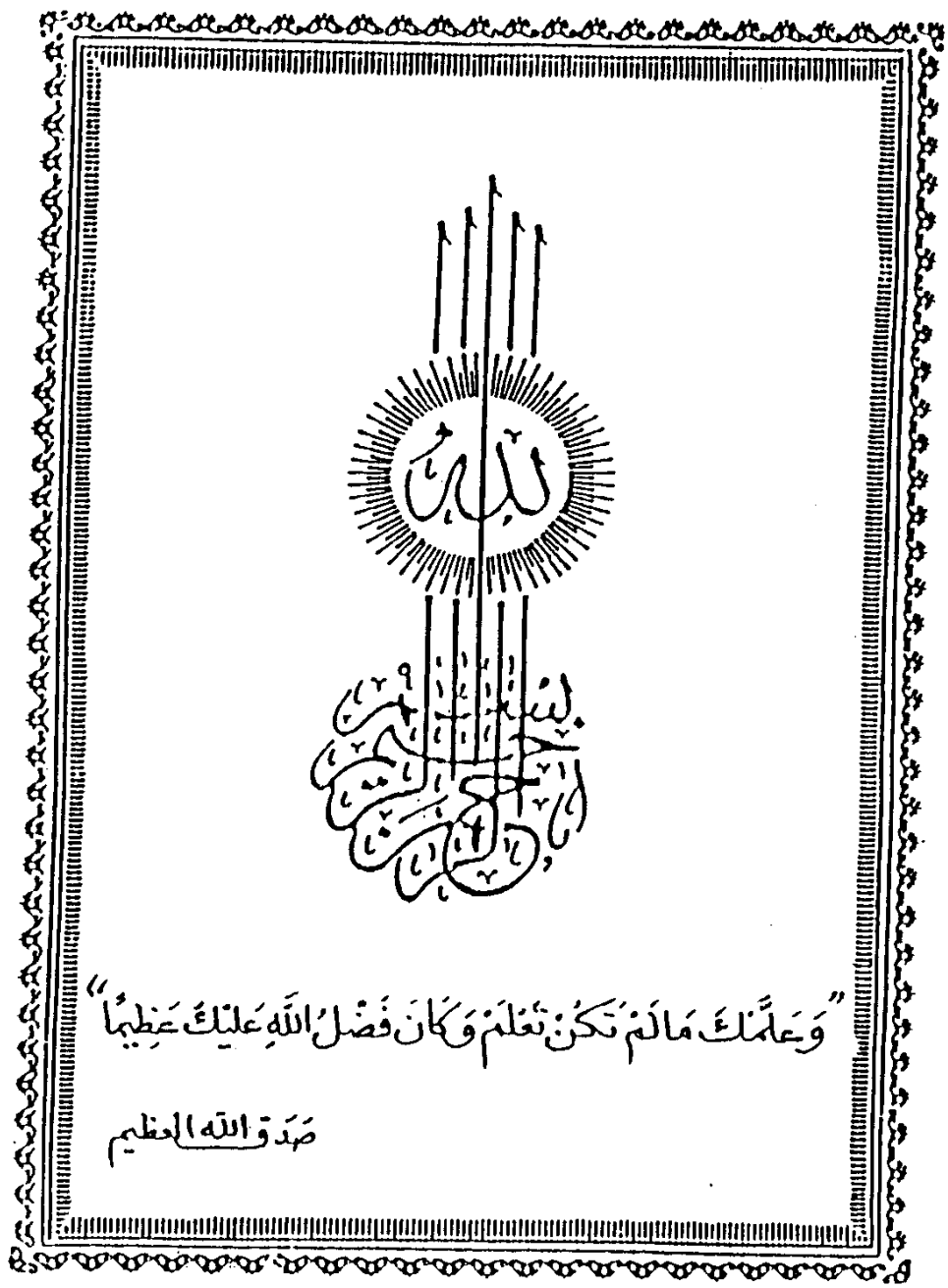

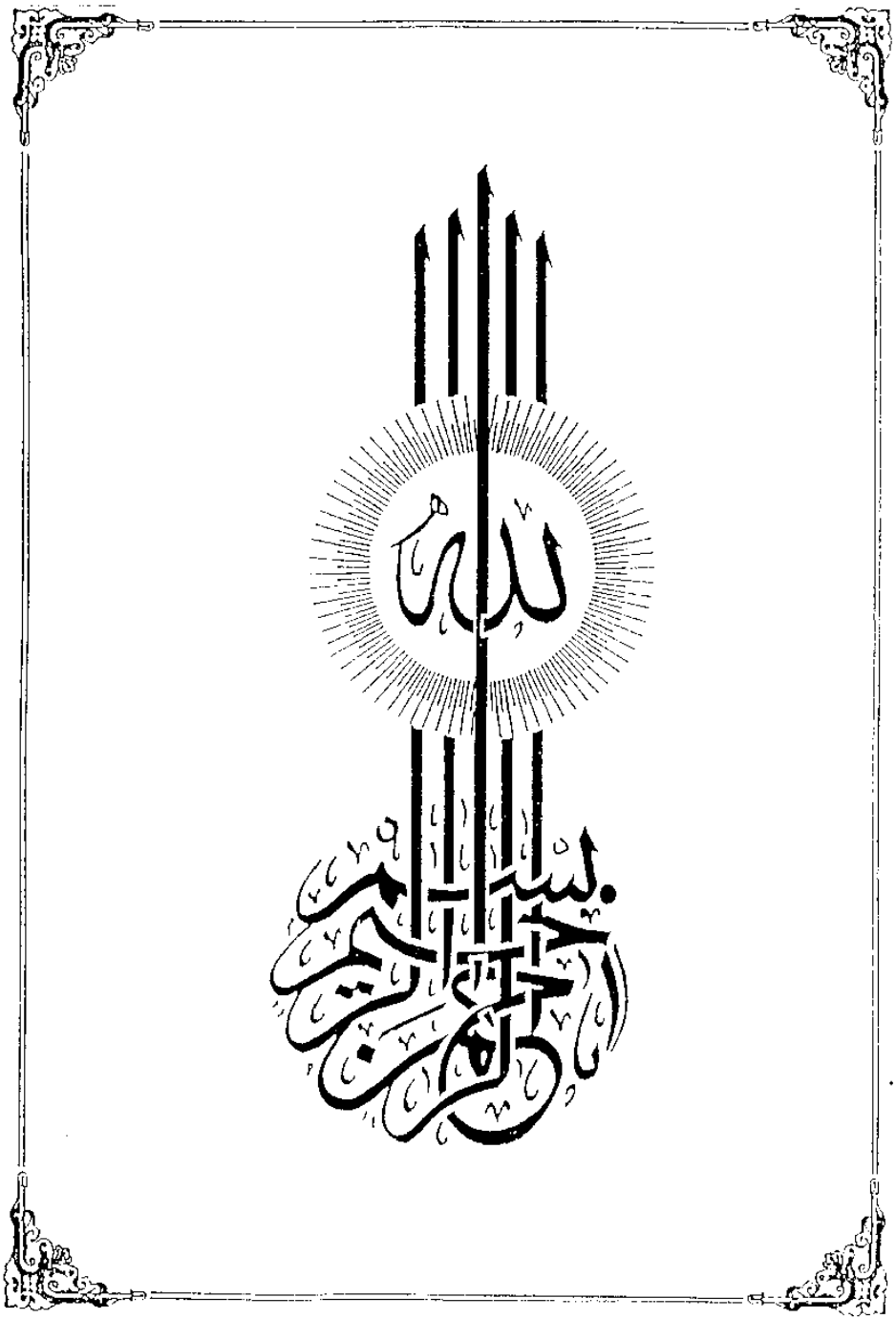

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ERRATA

Page	Line	Fault	Correction
1	Last line	10 years interval	10 year intervals
38	25th line	sinuses, leakage of a brain abscess	sinuses or leakage of a brain abscess
40		Bell and McCormic, 1981)	Bell and McCormick, 1981).
42	3rd line	present	presents.
67	9th line	sequetially.	sequentially.
72	16th line	to us	Girgis et al., (1986. b)
83	11th line	therapeutic levels between	therapeutic levels are kept between.
85	11th line	organsim	Organism.
87	22nd line	routes of administration	routes of ampicillin administration.
96	20th line	detemining	determining
102	17th line	conuvlsions	convulsions.
107		Hoeprch	Hoeprich
109		menifestation	manifestation
119	1st line	a streile	a sterile
126	9th line	aggultination	agglutination
127	5th line	Organsim	organism.
144	5th line	similar	similar
145	1st line	beacuase	because
146	5th line	Turberculous	Tuberculous
148		prodominance	predominance

INTRODUCTION AND AIM OF THE WORK

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Bacterial meningitis is endemic in Egypt and has been a reportable disease since 1912 (EL-AKKAD. 1969). Sporadic cases are seen allover the year but it increases more in winter (Girgis et al., 1986).

The main causative organisms are: Neisseria meningitidis (56%), Streptococcus pneumoniae (8%) and Haemophilus influenzae (3%) and in the remaining (33%) no organisms could be isolated from the cerebrospinal fluid (CSF) probably due to previous antibiotic therapy and / or lack of proper diagnostic techniques (Miner and Edman, 1978).

Meningococcal meningitis occurs with epidemic waves at approximately 10 years interval and lasts for a 2 to 3 years period (EL-AKKAD 1969; Girgis et al., 1986).

Attention was recently drawn to the value of serum and CSF C-reactive protein measurements in differentiating bacterial and viral meningitis in developed west countries (Corrall et al., 1981; Peltola et al., 1984; Abramson et al., 1985).

In this study we will try to evaluate the level of C-reactive protein in the CSF and in the serum of infants and children suffering from bacterial and aseptic meningitis as a diagnostic tool, and to determine if either or both measurements are of clinical significance in the differentiation of bacterial from aseptic meningitis.

ACUTE PHASE REACTANTS

ACUTE PHASE REACTANTS (A.P.R.)

Definition:

The term "acute phase reactants" is generally considered to refer to protein components of plasma whose concentration change in response to tissue damage. This increase is attributed to their enhanced synthesis and catabolism (Gewurz et al., 1982). Tissue damage may be induced by a wide variety of stimuli including tissue injury, acute and chronic inflammation, connective tissue disease and neoplasia (Cooper and Ward, 1979).

Acute phase reactants show at least two common features. The first feature is that, they almost all contain significant amounts of carbohydrates. The second feature is that they all are synthesized in liver parenchymal cells and more precisely by hepatocytes. Hence, acute phase reactants may be defined as, trauma-inducible, liver-produced, plasma glycoproteins (Koj, 1974).

CLASSIFICATION OF A.P.R. RESPONSE FOLLOWING EXPOSURE TO STIMULI

1) Concentrations of which may increase by about 50%:
   * Ceruloplasmin.
   * C_3.
2) Concentrations of which may increase 2 to 3 folds:
   * Alpha -1- Acid glycoprotein.
   * Alpha -1- antitrypsin.
   * Alpha -1- antichymotrypsin.
   * Haptoglobin.
   * Fibrinogin.
3) Concentrations of which may increase up to 1000 folds:
   * C- reactive protein.
   * Serum amyloid A.

   As shown above, the acute phase proteins differ markedly in the magnitude of their rise after stimulus.

4) Other acute phase proteins:
   * Alpha -2- macroglobulin.
   * Kininogen.
   * Kininogenase.
   * Angiotensinogen (Kushner et al., 1981).

C-REACTIVE PROTEIN

C- REACTIVE PROTEIN (C-RP)

Definition:

C-RP, is an acute phase protein normally present in the serum in trace amounts, whose concentration rises rapidly and markedly during reaction to tissue injury, inflammation and infection (Kushner and Feldmann, 1978).

Synthesis of C-RP:

The liver is known to be the site of synthesis of C-RP (Koj, 1974). Immunoenzymatic techniques were utilized to visualize C-RP synthesizing cells in rabbit's liver, at intervals after intramuscular injection of turpentine. C-RP was detected only in hepatocytes and not in other types of hepatic cells.

It was suggested that a mediator which acted initially in the portal zones was responsible for induction of C-RP synthesis, yet the nature of this mediator is unknown (Kushner et al., 1981). But Pepys (1982), Trienekens and Willems (1985), Considered interleukin 1 "IL.1"-which is a macrophage derived factor [also was known as lymphocyte activating factor (LAF)] - as an important trigger molecule, capable of stimulating hepatocytes to secrete acute phase proteins such as C-RP.

Serum C-RP becomes readily detectable 6 to 12 hours after tissue injury, or onset of infection probably under the

influence of humoral mediators such as leukocyte endogenous mediator (endogenous pyrogen) and prostaglandin PGE_1 (Klerk and Anderson, 1982).

Normal Levels Of C-RP:

The serum concentrations of C-RP in newborns is not different from those of adults and in both it is a trace only (Bienvenu et al., 1984).

Kindmark (1972) found that normal serum concentrations are 0.6 microgram/ml for healthy newborns, 3.2 microgram/ml at the age of 1 day, and 1.6 microgram/ml at the age of 1 week to 1 month.

Saxtad et al., (1970) found C-RP values ranging from 0.5 microgram/ml to 6 microgram/ml in 16% of healthy infants 1-15 months of age, but the technique used by Saxtad, et al., was less sensitive than the technique used by Kindmark (Sabel and Hanson, 1974).

Peltola (1982) showed that a C-RP serum level of 19 mg/l or less is considered normal but because a limit of 10 mg/l has been proposed, only measurements below this value were regarded as indisputably negative.

The normal level of C-RP in cerebrospinal fluid (CSF) of normal neonates ranged from 0.1 - 0.6 mg/dl and it falls within the same range in older infants and children (Philip, and Baker, 1983). C-RP in CSF diffuses from serum to CSF without any evidence of being formed in central nervous system (Pepys, 1982; Trienekens and Willems, 1985).

Serum C-RP In Human Diseases:

Elevated levels of C-RP in serum have been found in virtually all diseases associated with active inflammation, necrosis or tissue destruction (Trieneken's and Willems 1985). Elevated levels are also seen in patients with rheumatoid diseases, acute infectious processes, postmyocardial infarctions, surgery, advanced and widespread malignancy and chronic infections (Gewurz et al., 1982).

CLINICAL SIGNIFICANCE OF SERUM C-RP:

As increased hepatic production of C-RP is a very early and sensitive response to most forms of microbial infections, the value of its measurement -in serum- in the diagnosis and management of various infective conditions has been established (De Beer et al., 1984; Trienekens and Willems, 1985).

Its measurement provides a simple screening test for organic diseases (Klerk and Anderson, 1982).

Serum levels of C-RP increase rapidly up to 1000 fold within 1-2 days, reaching concentrations as high as 300-500 microgram/ml during intense inflammatory reactions, then these levels fall rapidly after withdrawal of the provoking stimulus.