RHEOLOGIC PROPERTIES OF BLOOD IN NORMAL PREGNANCY AND EPH - GESTOSIS

THESIS

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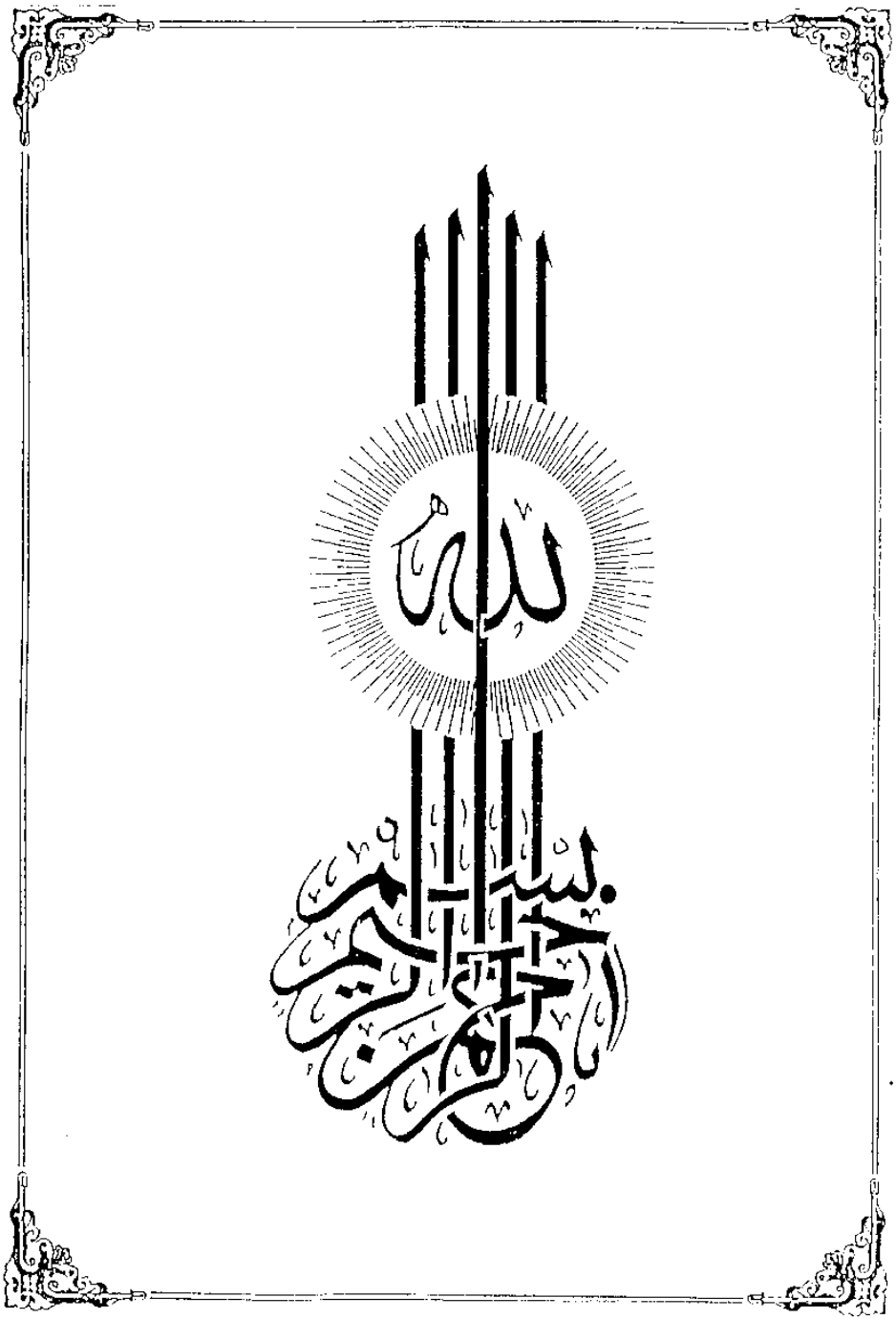
Sawsan Said Hafez



The result of these are of great importance for the therapy of they allow in the future a more planned and better controllable medical treatment.

INTRODUCTION

Yet the end of all this, is the production of a perfectly healthy baby by a contended, healthy mother.

There is now evidence that pregnancy creates its own homeostatic laws (Frank E. Hytten and Tom Lind, 1973). Normal measurements can be defined only as those occuring in normal pregnancy i.e., in manifestly healthy women who have trouble-free pregnancy, resulting in healthy well-grown infant. (Treloar et al., 1967).

Ideally, therefore, a normal range of values should refer to measurements made under standard conditions and by reliable techniques on young healthy, well-nourished pregnant women. It need hardly be said that such information is rarely available, so we should take care to distinguish maternal physiological adjustments from true pathology. (Guerrero and Florez, 1969).

NOMENCLATURE AND DEFINITION

For many decades, nomenclature of E P H - Gestotsis was highly confused. Besides toxaemia, pre-eclampsia and hypertensive disorders of pregnancy, bizarre combinations of names and words have been suggested. (Organisation Gestosis - Press 1975).

With its different aspects, the problem Gestosis touches a whole number of special fields of medicine besides obstetricians and pediatricians, scientists, trained in small, highly specialised sectors, are called for research on cause and sequelae of the E P H - Gestosis (E P H - Gestosis symposium, 1969).

NOMENCLATURE

E P H - GESTOSIS :

Pregnancy = Gestatio

Complicated = ... osis

... by

E = Edema

P = Proteinuria

H = Hypertension

E P H - Gestosis

DEFINITIONS

E = Edema ..... Excessive (inadequate) increase of body weight during pregnancy, usually due to fluid retention, i.e., more than

500 g/week

2000 g/month average

13 kg/entire pregnancy

Demonstrable pretibial edema are of gestosis origin, if they are still present after a night's bedrest.

P = *Proteinuria* ..... *Protein in the 24 hours - urine specimen, more than 0.5% Esbach/ or similar quantitative test, like paper stick) is pathological.*

H = *Hypertension* ..... *Last normal reading 135/85 mm Hg. First pathological reading 140/90 mm Hg.*

CLASSIFICATION

Symptomatic Classification

1) Monosymptomatic E P H - Gestosis

E = Edema

P = Proteinuria

H = Hypertension

2) Polysymptomatic E P H - Gestosis

Combination of two of all three symptoms

3) Imminent (impending) Eclampsia = EI

Objective and Subjective symptoms

: Objective = *Hyperreflexia, motoric excitation, impared conciousness, sudden deterioration, cyanosis.*

: Subjective= *Headaches, visual disturbances, acute symptomes of the upper abdomen.*

4) Eclampsia

Convulsive eclampsia.

Pathogenetic Classification

1) Superimposed Gestosis.

a. pre-existing vascular disease.

b. pre-existing renal disease.

2) Transient (essential) Gestosis

no sign and symptomes after puerperium.

3. Concomitant Diseases

   a. Pre-existing disease, presenting E P H - Symptomes, not changing during pregnancy.

   b. Concomitant disease and E P H - Gestosis, e.g. chronic hyper-tensive-vascular disease (without E P H - Gestosis).

4. Unclassified Gestosis.

POSTULATED MECHANISMS OF TOXEMIA

Although the cause of toxemia remains unkown, recent advances in our understanding of the physiology of pregnancy, particularly in relation to regulation of uterine blood flow, have resulted in findings which might have importance in the understanding of this challenging disease. There is a clinical evidence for suggesting that reduction in uteroplacental blood flow is the setting in which toxemia occurs. The higher incidence of the disease in primiparous women may be related to the less developed uterine vasculature. Anatomic confirmation in women has demonstrated the caliber of the uterine arteries in multiparous women to be greater than in the primigravid state (Beker, 1948) Uteroplacental ischemia was postulated as a cause of toxemia by Yound as early as 1914; and Page and Ogden in 1939).

In 1960, Hunter and Howard reported the isolation of a pressor substance they named "*hysterotonin*" from the amniotic fluid and decidua of patients with toxemia. Subsequently, Brown et al. (1965) reported the presence of a high concentration of renin in human amniotic fluid from normal pregnancy. Toxemia can be associated with high plasma renin (Tapia et al., 1972; Weir et al., 1973) and angiotensin (Massani et al., 1967).

In one study of plasma renin activity in normal pregnant women and toxemic women there was no significant difference in the levels in the two groups (Tapia et al., 1972). Since it is known that in toxemia there is increased sensitivity to angiotensin, interpretation of a given level of plasma renin activity is difficult. Similarly, if arteriolar responsiveness to angiotensin in pregnancy is dependent upon concomitant presence of a vasodilator mateial, reduction in uteroplacental blood flow may diminish prostaglandin release. Since synthesis of prostaglandin is dependent upon substrate concentration, a reduction in uterine blood flow could reduce delivery of arachidonic acid to the uterus. It has been recently demonstrated that pregnant rabbits have elevated peripheral PGE Levels (Venuto et al., 1975). Thus, one can look upon reduction in uteroplacental blood flow as either increasing renin secretion or potentiating the effect of circulating angiotensin by a concomitant reduction in prostaglandin synthesis. More work is necessary in this area to determine the sequence of events occurring with the development of hypertension in toxemia.

There is an increase in clotting factors in normal pregnancy (Bonnar et al., 1969; Todd et al., 1965) and pregnancy is associated with a mild activation of the clotting mechanism (Hyde et al., 1973).

Of interest in this regard is the finding that normal pregnant women who have had renal biopsies demonstrate on immunofluorescent staining slight deposits of fibrin in glomeruli (Morris et al., 1964).

Toxemia consistently exhibet one coagulation abnormality; increased amounts of cryofibrinogen in the blood (Mokav and Covey, 1964; Wardle et al, 1969; Galton et., 1971). The presence of cryofibrinogen in toxemia indicates that a fibrin monomer is present and since fibrinolysis is depressed in pregnancy, circulating fibrin deposited in the glomerulus might not be lysed (Henderson et al., 1970). Evidence of platelet damage in toxemia is the demonstration by Mckay (1964) that platelet adhesiveness is increased compared to normal pregnancy. The increase in acid phosphatase found in some toxemic patients is thought to represent acid phosphatase liberated from platelets during intravascular destruction.

Thus, there is evidence of a mild intravascular coagulation with toxemia, and the disappearance of fibrin deposists in glomeruli following cessation of pregnancy indicated removal of glomerular fibrin probably through intra and extracellular proteolysis.

Patients with severe toxemia may develop a hemolytic-uremic syndrome which may be transitory or prolonged (Brain et al., 1967). Marked fragmentation of red blood cells is seen on smear and may be associated with the development of renal cortical necrosis. The cause of the intravascular coagulation is thought to be liberation of trophoblastic material from the placenta.

In addition to elevated plasma renin and renin substrate concentration in pregnancy, plasma angiotensinase activity is similarly increased (Tapia et al., 1972). Some studies suggest that angiotensinase activity is decreased in toxemia and that decreased inactivation of angiotensin II plays a role in the pathogenesis of hypertension. However, others (Landesman et al., 1963; Hickler et al., 1963), have reported increased plasma angiotensinase activity in pre-eclampsia.

Plasma renin activity is elevated throughout pregnancy, being highest at the end of the second trimester and returning to normal within 1 week after delivery. Although low plasma renin activity has been found in toxemia by Helmer and Judson (1967) and by Brown et al., (1965), others (Tapia et al., 1972; Cordon et al., 1973) have found levels similar to those of normal pregnancy.