SPOTLIGHT ON NEONATAL ANEMIA

Essay
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By

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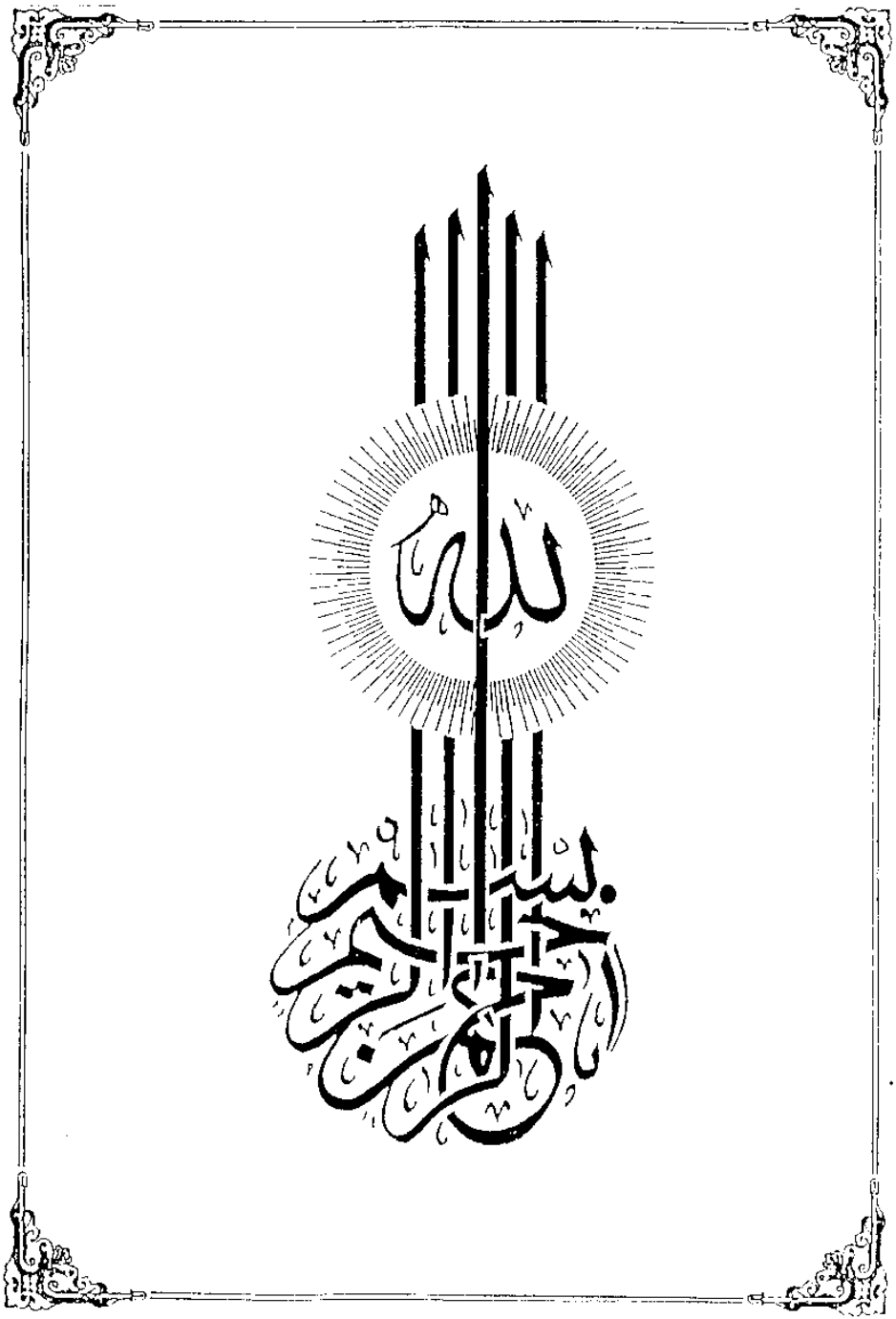
«قالوا سبحانك لا علم لنا
الا ما علمتنا انك انت
العليم الحكيم »

صدق الله العظيم

«سورة البقرة -آية ٣٢»



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I-INTRODUCTION AND AIM OF THE WORK

INTRODUCTION

It is well known that anemia is defined as a condition at which the concentration of hemoglobin or the number of red blood cell, either singly or in combination is reduced below average .The hemoglobin concentration of healthy term and premature infants undergo typical physiologic changes during the first few weeks of life ***(Miller et al;.1984)***

Anemia of the newborn is characterized by abnormally low hemoglobin concentration less than 13 gldl in cord blood at birth or less than 11 gldl in the neonatal period ***(Hoffbrand and Pettit; 1993)***.

The main causes of anemia in neonatal period are, hemorrhage, hemolysis, infection or rarely from reduced red cell production ***(Hann et al., 1991),*** while the main cause of anemia in premature babies is the decline in circulating red cell mass due to diminished erythropoietin level ***(Strauss; 1995)***.

Under ordinary circumstances, a thorough history, physical examination, basic blood studies and with a wide varieties of simple screening tests applied for " Erythropoietin deficiency disorders, hemoglobinopathies, acquired hemolytic anemias" a correct diagnosis is arrived ***(Kinney et al;1994).***

The genetic approach for diagnosis is used now obviously in the diagnosis of a varieties of anemias, notably erythroblastosis fetalis, hemoglobinopathies, and hereditary red cell membrane defects.

For establishment of the diagnosis, detailed analysis of globin DNA is highly required, or confirmation of the screening phenotype and its correlation with clinical history, physical

II- REVIEW OF LITERATURE

* Physiology of erythropoiesis and normal hematologic values.

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Erythropoiesis can be divided into Gestational and after birth erythropoiesis.

1. Gestational Erythropoiesis

Hematopoiesis in the embryo and fetus can be conceptually divided into 3 periods:- mesoblastic, hepatic and myeloid.

All blood cells are devided from the embryonic connective tissue - the mesenchyme - and erythropoiesis begins in the 19-day embryo ***(Segel; 1995)*** Isolated foci of erythropoiesis can be observed throughout the extra embryolic mesoblastic tissue in the area vasculosa of the yolk sac.

Blood islands in the yolk sac differentiate in two directions: peripheral cells in the islands form the walls of the first blood vessels, whereas the centrally located cells become the primitive blood cells or hematocytoblasts ***(Nathan and Oski; 1993)***.

The first blood cells produced by the embryo belong to the red cell series. Two distinct generations of erythrocytes can be observed in the developing embryo. Red cells arise as a result of either primitive megaloblastic erythropoiesis or definitive normoblastic erythropoiesis. Both types of cells apparently derive from Similar -appearing hematocytoblasts.

The myeloid period of hematopoiesis commences during the fourth to fifth fetal month and becomes quantitatively important by the sixth fetal month. During the last 3 months of gestation, the bone marrow is the chief site of blood cell formation. Cord blood is rich in bone marrow progenitor cells and contains multipotential (CFU-GEMM), erythroid (BFU-E), and (CFU-GM) cell lines ***(Broxmeyer et al; 1989)***.

Following birth, the amount of marrow tissue continues to grow, with no apparent increase in cellular concentration. Although the control exerted by erythropoietin during early gestation may not be important, an increasing role for erythropoietin is observed during the hepatic and myeloid phases of erythropoiesis. Erythropoietin is detectable in the cord blood of non-anemic premature infants in quantities that are comparable to or greater than that in normal adult blood ***(Hann et al;1991)***.

II.After birth erythropoiesis.

The rate of hemoglobin synthesis and production of red cells decreases dramatically during the first few days after delivery. The mechanism behind this sudden and marked decrease in red cell production is not known. It may well be initiated by the equally sudden increase in the tissue oxygen that takes place at birth. This stimulus may be transmitted to the bone marrow by the virtual disappearance of erythropoietin in the plasma ***(Nathan and Oski; 1993)***.

In the embryo and fetus, Gower1 Portland, Gower2 and HbF dominate at different stages ***(Fig.1)***.

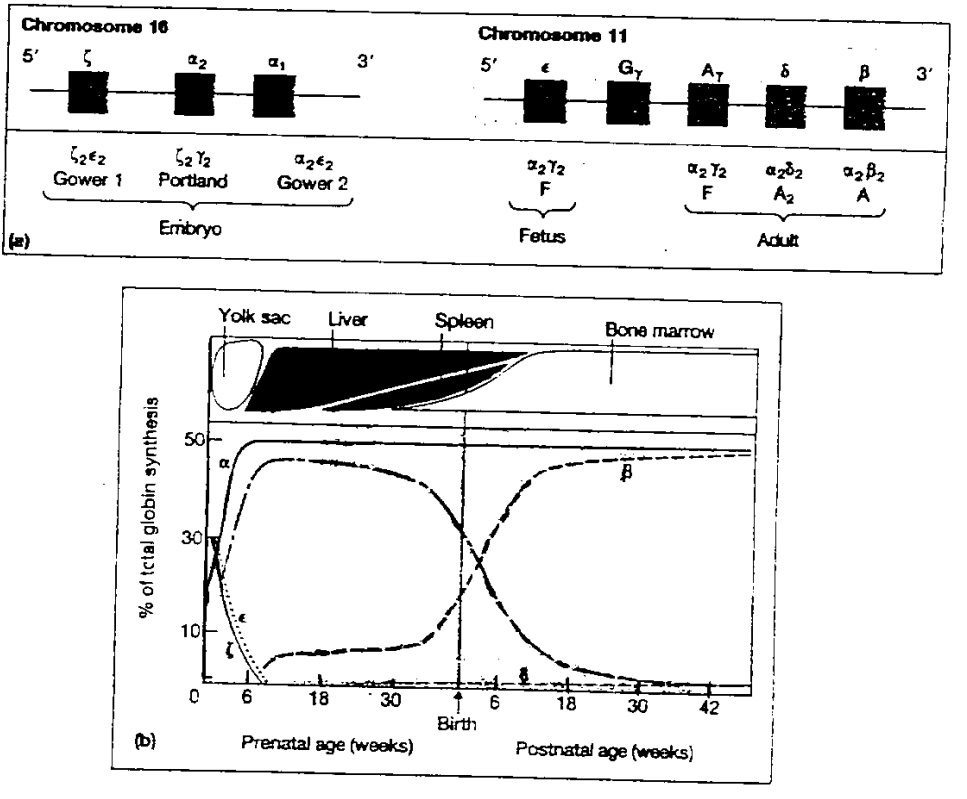

Fig.1 (a) The globin gene clusters on chromosomes 16 and 11. In embryonic, fetal and adult life different genes are activated or suppressed. The different globin chains are synthesized independently and then combine with each other to produce the different hemoglobins. The γ gene may have two sequences, differing by whether there is a glutamic acid or alanine residue at position 136 ($^{G}\gamma$ or $^{A}\gamma$, respectively). (b) Synthesis of individual globin chains in prenatal and postnatal life.

A can be demonstrated in fetuses as young as 9 weeks of gestation. ***(Segel; 1995).***

In fetuses of 9 to 21 weeks of gestation, the amount of Hb A rises from 4 to 13 % of the total Hb. After 34 to 36 weeks of gestation, the percentage of Hb A rises, while that of Hb F decreases ***(Segel;1995)***.

Types of hemoglobin at the time of birth:-

The amount of Hb F at birth varies in term infants from 53 to 95% of total hemoglobin. The Hb F concentration in blood decreases after birth by approximately 3% per week and is generally less than 2 to 3 % of the total hemoglobin by 6 months of age. This rate of decrease in Hb F production is closely related to the gestational age of the infant and is not affected by the changes in environment and oxygen tension that occur at the time of birth.

Increased proportions of Hb F at birth have been reported in infants who are small for gestational age, who have experienced chronic intrauterine hypoxia.

Fetal Hb (HbF) is the major Hb in utero, whereas Hb A is the normal Hb of extrauterine life. The relative proportion of each varies with gestational and postnatal age. One major difference between Hbs A and F is related to oxygen (O_2) transport. The transport of O_2 to peripheral tissues is regulated by several factors which include blood-O_2 capacity, cardiac output and Hb-p_2 affinity. O_2 capacity is a direct function of Hb concentration (1 g Hb combines with 1.34 ml O_2). Compensatory changes in cardiac output can maintain normal O_2 delivery under conditions in which O_2 capacity is

1- Red Cell Count:

The red cell count in cord blood varied in different stages, the mean level (5.14 ± 0.7 X 10^{12} per liter). There is a rapid rise of the order of 0.5 x 10^{12} per litre, during the first few hours of life and , at the end of the first week, the mean level is (4.86 ± 0.6 X 10^{12} per litre) ***(Hann et al; 1991)***. In premature babies with birth weight less than 1500 g in the first postnatal day of life, the mean value of RBC is (4.71 ± 0.75 X 10^{12} per litre) (***Hann et al;1991)***.

Table (2) Red cell parameters in term and premature infants during the first week of life (Glader and Naiman;1991).

Time	*Hb (gldl)*	*Hct (%)*	*Retics (%)*	*nucleated RBCs (cells/100 RBCs)*
Term				
Cord blood	(14-20)	(45- 61)	2-6	< 1.00
Day 1	18.4	58.0	< 7	< 0.40
Day 3	17.8	55.0	< 3	< 0.01
Day 7	17.0	54.0	< 1	0.
Premature < 1500g				
Cord blood	(13-18.5)	49	< 10	< 3.00
Day 7	14.8	45	< 3	< 0.01

2- Cord blood Hb :

Cord blood Hb of healthy term infants ranges between 14 and 20 gldl ***(Glader and Naiman; 1991)***. Based on this data, it is recommended that cord Hb levels less than < 13 gldl is considered abnormal ***(Hoffbrand and Pettit; 1993)***. Capillary

3- Blood Indices:

Newborn babies have large red cells, there is also a remarkable variability in size (anisocytosis), with a maximum difference between largest and smallest that is of the order of 8 μm. Special stains and microdensitometry have shown that the macrocytic cells contain significantly less Hb F than the small red cells. ***(Hann et al; 1991)***.

Mean corpuscular volume (MCV) :

Normal MCV in cord blood is 107 fl,while in the first day of life it is 108 fl, and then it falls rapidly reaching 93fl by 9 weeks (normal adult value = 82 -92 fl). Using electronic methods, values of 94 fl or less in term infants at birth have been shown to be strongly suggestive of the α - thalassemia trait or of iron-deficiency ***(Hann et al; 1991)***. In a group of premature babies with an average birth weight of 1300g, the mean MCV was 115 ± 5.0 fl on the first day of life, falling to 95 ± 4.0 by the seventh week ***(Hann et al; 1991)***.

Mean corpuscular hemoglobin (MCH) :-

MCH is also increased at birth with range of 33.5 - 41.4pg (adult range = 27 - 32 Pg). The high MCH represents the average increased quantity of Hb in individual red cells (MCH = Hb/RBC) and the decline parallels the decline in MCV ***(Hann et al; 1991)***.