Assessment of Neutrophilic Function in Infants of Diabetic Mother

Thesis

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By

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﴿وأنزل الله عليك الكتاب
والحكمة وعلّمك ما لم تكن تعلم
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Hayam Mohamed Saied Soliman

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List of Abbreviations

ANC	Absolute neutrophil count
CBC	Complete blood count
CFU-G	Colony- forming unit- granulocyte
CFU-GM	Colony-forming unit- granulocyte macrophage
Cyto	Cytoplasmic tail
EGF	Epidermal- growth- factor- like
FCR	FC receptors
GBS	Group B staphylococci
G-CSF	Granulocyte colony-stimulating factor
Glut 1	Glucose transporter-1
GM-CSF	Granulocyte-macrophage colony-stimulating factor
GP	Glycoprotein
hCS	Human chorionic somato-mammatropin
HLA-DR	Human lecukocyte antigen DR
hPL	Human placental lactogen
ICAM-1	Inter cellular adhesion molecule-1
IDDM	Insulin dependent diabetes
IDMS	Infant of diabetic mother
Ig	Immunoglobulins
IL-1	Interleukin-1
IL-8	Interleukin 8
ILCS	Innate lymphoid cells
LFA-1	Leukocyte functional antigen-1
LPS	Lipopolysaccharide
MCP-1	Monocyte chemotactic protein-1
MHC	Major histocompatibility complex
NADPH	Nicotinamide adenine dinucleotide phosphate
PB	Peripheral blood
PICD	Phagocytosis induced cell
PMNS	Polymorphonuclear cells
PMNS	Polymorphonuclear leukocyte
PNAD	Peripheral node addressin
PNL	Polymorphnouclear leukocyte
PSGL-1	p-selectin glycoprotein ligand-1
ROS	Reactive oxygen species
TLR	Toll-like-receptors
TM	Transmembrane domain
TNF-1	Tumor necrosis factor 1
VCAM-1	Vascular cell adhesion molecule-1
WBC	White blood cells
WHVP	Wedged hepatic venous pressure
α1-AT	Alpha 1-antitrypsin

Introduction

Three to ten percent of pregnancies are affected by abnormal glucose regulation, 80-88% of which are related to abnormal glucose control of pregnancy or gestational diabetes mellitus of mothers. Infant born to mothers with glucose intolerance are at an increased risk of respiratory distress, growth abnormalities (either large for gestational age or small for gestational age), hyperviscosity secondary to polycythemia, hypoglycemia, congenital malformations, hypocalcemia, hypomagnesemia and iron abnormalities ***(Barnes, 2007).***

Added to the previously mentioned complications, few studies have shown that infants of diabetic mothers have impaired neutrophil motility & phagocytic capacity ***(Metha and Petrova, 2005).*** Furthermore, neutrophil migration (chemotaxsis) was found to be abnormal at birth in both term and preterm infants born to diabetic mothers ***(Stoll, 2003).***

However, maternal gestational diabetes leads to impairment of cord blood neutrophil motility and phagocytic bactericidal capacity independently from the insulin requirement for the maintenance of normoglycemia during pregnancy ***(Metha and Petrova, 2005).***

Aim of the Work

Assessment of neutrophils in infants of diabetic mother; number, neutrophils killing and chemotaxsis and correlating this to the prognosis of the patient.

The Immune System

Introduction:

The immune system is designed to protect the body from pathogens. It begins to develop in the embryo and starts with hematopoietic stem cells which differentiate into granulocytes, monocytes, and lymphocytes. These stems cells also differentiate into erythrocytes and megakaryocytes and continue to be produced and differentiate throughout the lifetime ***(Muller et al., 2002).***

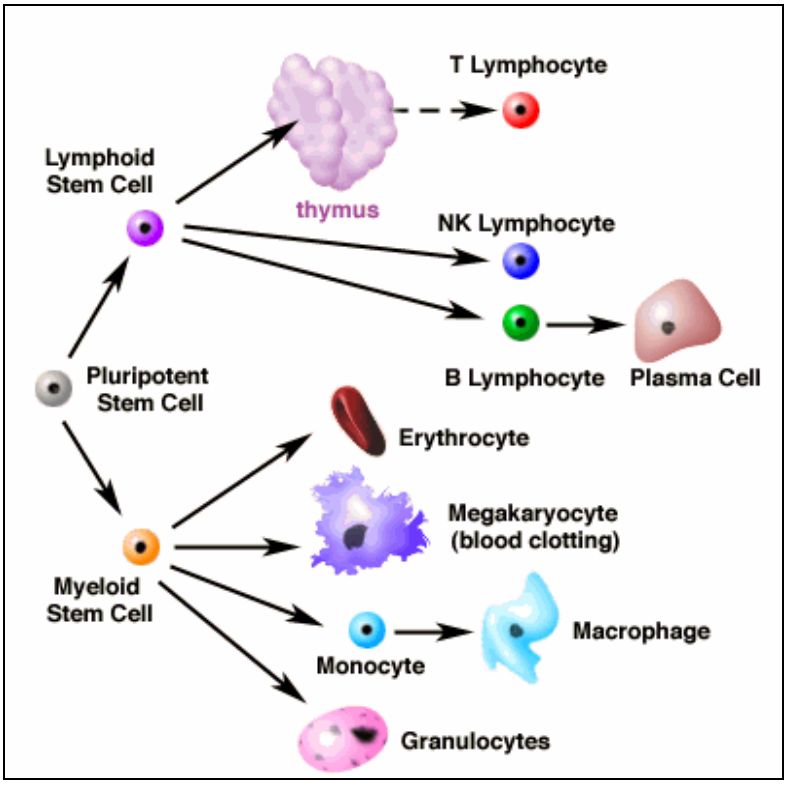

Figure (1): Stem cell differentiation

The immune system is an organization of cells and molecules with specialized roles in defending against infection. It has fundamentally different types of responses to invading microbes ***(Devles and Roitt, 2000).***

The immune system is divided into two categories:

- Innate
- Adaptive.

Innate immunity: nonspecific defense mechanisms that come into play immediately or within hours of an antigen's appearance in the body ***(Litman et al., 2005)***.

Innate immunity includes:

- Anatomic (skin, mucous membrane)
- Physiologic (Temperature, PH)
- Cells: mast cells, phagocytes (monocyte, neutrophil and macrophages), basophils and eoisinophils, natural killer cells.
- Complement system and inflammatory mediators.

(Rus et al., 2005)

Innate immune responses

Cellular components of innate responses:

The innate immune system consists of all the immune defenses that lack immunologic memory ***(Peter et al., 2000).***

Innate immunity is nonspecific and noneducable. It is the body's first line of defense against many bacterial pathogens. Innate immunity resides in the skin, the mucous membranes, the polymorphonuclear cells (PMNs), and the complement system ***(Hagey et al., 2002).***

Innate immune recognition is mediated by germ-line-encoded receptors, which means that the specificity of each receptor is genetically predetermined. One advantage of these germ-line-encoded receptors is that they evolved by natural selection to have defined specificities for infectious microorganisms ***(Ruslan Medzhitov et al., 2000).***

Adaptive immunity: refers to antigen-specific immune response. The antigen first must be processed and recognized, the adaptive immune system creates an army of immune cells specifically designed to attack that antigen. It includes a "memory" that makes future responses against a specific antigen more efficient ***(Pancer and Cooper 2006).***