Functional Disorders of Neutrophils

An Essay

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ABSTRACT

white blood Although neutrophils are the most abundant type of , quantitative immune system and form an essential part of the cells abnormalities tack most of researchers work, so it was a deemed of interest to review qualitative abnormalities.This review of disorders of neutrophil number and function will discuss and classification, clinical presentation, important research advances in the field and then provide a clinical diagnostic approach for these category of diseases, and new advances in therapy, prognosis and response.

Key words : neutrophils - Functional disorders of neutrophils

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*HIES: Hyperimmunoglbulin E syndrome, *AR: Autosomal dominant

List of Abbreviations

AGEs	Advanced glycation (glycosylation or glycoxidation) end products
AML	Acute myeloid leukemia
ATP	Adenosine triphosphate
BPI	Bacterial permeability-increasing protein
C/EBP	CCAAT\enhancer-binding protein epsilon
C3e	The third component of complement
C5a	The fifth component of complement
CB	Cytochalasin B
CFU-GM	Granulocyte Monocyte-Colony Forming Unit
CGD	Chronic Granulomatous Diseas
cGMP	Cyclic guanosin monophosphate
CHD	Coronary heart disease
CHS	Chédiak-Higashi syndrome
CML	Chronic myeloid leukemia
CT cell	Cytotoxic T-cells
$DF^{32}P$	Di-isopropyl flurophosphatase
DHR	Dihydrorhodamine 123
E-64-d	A thiol proteinase inhibitor
EPO	Eosinophilic peroxidase
FMF	Familial Mediterranean fever
FMLP	Formyl methionyl-leucyl phenylalanine
G6PD	Glucose-6-phosphate dehydrogenase
G-CSF	Granulocyte colony-stimulating factor
GDP	Glucose diphosphate
GEF	Guanine exchange factor
GFR	Glomerular filtration rate
GM-CSF	Granulocyte-macrophage colony-stimulating factor
GPCRs	G protein–coupled receptors
GS	Griscelli syndrome
GVHD	Grafts versus host disease
H_2O_2	Hydrogen peroxide
HD	Haemodialysis
HIES	Hyperimmunoglobulin E syndrome
HIV	Human immunodeficiency virus
HLH	Hemophagocytic lymphohistiocytosis
HOCl	Hypochlorous acid
HSCT	Histocompatable stem cell transplantation
IAV	Influenza A virus

IBD	Inflammatory bowel disease
ICAMS	Intercellular Adhesion Molecules
IFN-α	Interferon-α
IFN-γ	Interferon γ
IL-3	Interleukin-3
ITAMs	Immunoreceptor tyrosine-based activation motifs
IVIG	Intravenous Ig infusion therapy.
LAD	Leukocyte adhesion deficiency
LFA-1	Leukocyte factor antigen-1
LJP	Localized juvenile periodontitis
LLS	lazy leucocyte syndrome
LPS	Lipopolysaccharides
Mac-1	Macrophage antigen-1
LSP-1	Lymphocyte-specific protein-1
LTB4	Leukotriene B_4
LYST gene	Lysosomal trafficking regulator gene
MDS	Myelodysplastic syndrome
MPO	Myeloperoxidase
MRSA	Methicillin-resistant S aureus
MYH9	Non-muscle myosin heavy chain IIA gene
NADPH	Nicotinamide adenine dinucleotide phosphate
NBT	Nitroblue tetrazolium test.
NK	Natural killer cell
NOS	Nitric oxide synthetase
OCA	Oculocutaneous albinism
PAF	Platelet-activating factor
6PGD	6 phosphogluconate dehydrogenase
PMN	Polymorphnuclear leukocyte
PS	Phosphatidylserine
RER	Rough endoplasmic reticulum
ROS	Reactive oxygen species
SAA	Serum amyloid A
SCD	Sickle cell disease
SGD	Specific granule deficiency
SMCE	Store-mediated calcium entry
SOD	Superoxide dismutase
TH2	T helper cells
TLR	Toll-like receptor
TNF- α	Tumor necrosis factor- α
Tyk2	Tyrosine kinase 2
VCAM-1	Vascular cell adhesion molecule-1
XLP	X-linked lymphoproliferative syndrome

Introduction

Neutrophils are the predominant white blood cells involved in phagocytic killing of micro-organisms like bacteria and fungi. They are also referred to as polymorphonuclear or segmented, owing to their characteristic lobulated nucleus. They are at the end stage of maturation **(Ravandi et al., 2005).**

Neutrophils play a critical role in host defense by phagocytizing and digesting microorganisms, and inappropriate activation of neutrophils may result in damage to normal host tissues. In the resting uninfected host, the production and elimination of neutrophils are balanced, resulting in a fairly constant concentration of neutrophils in peripheral blood (**Baehner, 2005).**

This chapter reviews the morphology, structure, development, kinetics, and function of normal neutrophils.

Morphology

Ehrlich (1880) introduced techniques for staining blood cells that provided a means to identify and classify white corpuscles. He divided blood cells into lymphocytes, large mononuclear cells with indented nuclei (later called monocytes), and polymorphous nucleated cells with granules staining neutrophilic, acidophilic, or basophilic (**Baehner, 2005).**

In the normal adult human, the life of neutrophils is spent in three environments: marrow, blood, and tissues. Marrow is the site of differentiation of hematopoietic stem cells into neutrophil progenitors and of proliferation and terminal maturation of neutrophilic granulocytes (myeloblast to segmented neutrophils) (**Dorothy et al., 2007).**

Myeloblast

The word myeloblast describes an immature cell, typically found in the bone marrow and not in the blood **(Skubtiz, 2004)**. The myeloblast is the youngest myeloid precursor recognizable in the bone marrow smear employing Wright-Giemsa polychrome stain. Because they are in the process of growth and division, myeloblasts vary considerably in size from 10 to 20 μm in diameter. The nucleus is large and round, with finely granular chromatin and one or two pale blue nucleoli, granules are absent, and the cytoplasm is scanty (Figure 1) (**Baehner, 2005).**

In wet films, myeloblasts appear immobile with thin, tenacious borders. The cytoplasm is hazy and usually contains no stainable substance other than mitochondria. Leukemic myeloblasts that contain no perceptible granules often are identified by special stains that demonstrate the presence of Myel-

operoxidase (MPO) or esterase, thus providing early evidence of differentiation. Particularly in patients with acute leukemia, the nucleus may show several wide and deep indentations, suggesting lobulation. Such myeloblasts suggest more rapid maturation on the part of the nucleus than of the cytoplasm (asynchronism of Di Guglielmo). Also in association with leukemia, Auer bodies are evident in the cytoplasm of cells **(Skubtiz, 2004).**

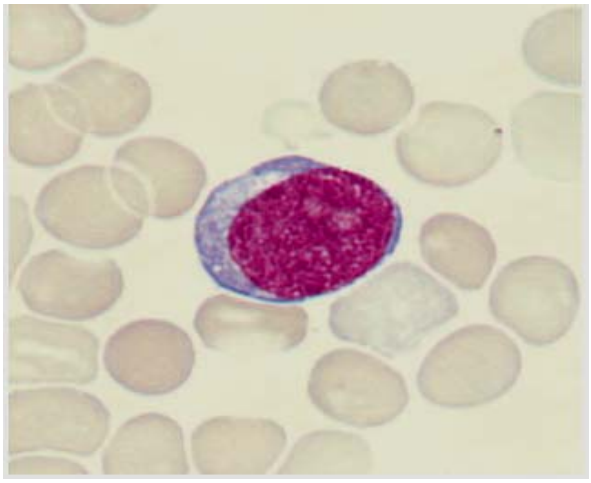

Figure 1: Myeloblast **(Lichman et al., 2007).**

Promyelocytes

The promyelocyte is larger than the myeloblast and the myelocyte, being greater than 20 μm in diameter. The nucleus, nuclear chromatin, and nucleoli resemble those of the myeloblast, but the differentiating feature is the presence of many violet granules (Figure 2a). These so-called azurophilic or primary granules are homogeneous, dense, and round to ovoid and are bounded by a unit membrane (Figure 2b) (**Baehner, 2005).**