

Immunological changes in different intensive Care Unit patients

Essay

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List of Abbreviations

Abb.	Meaning
ACLF	Acute on chronic liver failure
ADP	Adenosine Di-phosphate
APCs	Antigen presenting cells
APCs	Antigen presenting cells PEW
ARDs	Adult respiratory distress syndrome
ATP	Adenosine Tri phosphate
BBB	Blood brain barrier
bDNA	Bacterial DNA
BT	Bacterial translocation
C3b	Complement 3b
C4	Complement factor 4
CARS	Compensatory anti-inflammatory response syndrome
CD	Cluster of differentiation
CKD	Chronic kidney disease
CL	Chemilumine scence
CR	Complement receptor
CR1	Complement receptor type 1
CRP	C-Reactive protein
CTP	Child turcotte Pugh score
CVD	Cardiovascular disease
DAMPs	Danger (or) Damage associated molecule patterns
DM	Diabetes mellitus

Abb.	Meaning
ELAM	Endothelial cell leucocyte adhesion molecule
ESRD	End stage renal disease
HbA1c	Haemoglobin A1c
HD	Haemodialysis
HLA	Human leucocytic antigen
HRS	Hepatorenal syndrome
IAP	Inhibitor of apoptosis protein
IBO	Intestinal bacterial growth
ICAM	Intracellular adhesion molecule
IFN	Interferon
Ig	Immunoglobulin
IL	Inter leukin
LBP	Lipopolysaccharide binding protein
LBP	Lipopoly saccharide protein
LPs	Lipopoly saccharides
MD	Mystery domain
MODs	Multi organ dysfunction syndrome
N.F	Nuclear factor
NAD	Nicotinamide adenine dinucleotide
NADPH	Nicotinamide adenine dinucleotide phosphate
NK cells	Natural killer cells
NO	Nitric oxide
Ox LDL	Oxidized low density lipoprotein
PAF	Platelet activating factor
PAMPs	Pathogen associated molecular patterns
PD	Peritoneal dialysis

Abb.	Meaning
PEW	Protein energy wasting
PMNs	Polymorph nuclear cells
RES	Reticulo endothelial system
SAA	Serum amyloid A protein
SBP	Spontaneous bacterial peritonitis
SDD	Selective digestive tract decontamination
SIRS	Systemic inflammatory response syndrome
SR	Scavenger receptor
TAX₂	Thromboxane A ₂
TCR	T.cell receptor
TGFb	Transforming growth factor b
TH cells	T. helper cells
TLR	Toll like receptor
TNF	Tumor necrosis factor
TRLs	Toll like receptors
UTI	Urinary tract infection
VCAM	Vascular cell adhesion molecule

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Introduction

The immune system has evolved to protect the host from a universe of pathogenic microbes that are themselves constantly evolving. The immune system also helps the host eliminate toxic or allergenic substances that enter through mucosal surfaces.⁽¹⁾

The immune system includes physical barriers to prevent tissue invasion, an innate response which is rapid, nonspecific and serves as an immediate first line of defense against an infection; and the adaptive immune response, which develops over a matter of days, is specific for the foreign antigen, and results in long-term immune memory.

The normal function of each of these elements is altered in the critically ill patient, rendering the patient vulnerable both to infection and to the systemic consequences of a dysfunctional defense response⁽²⁾.

Aim of the Work

Study different immunological changes and its effects in different ICU patients and ways to protect and manage different possible complications.

Chapter (1):

Basic Immunology

Multicellular creatures face a daunting series of challenges if they are to survive and persist on this planet. They must feed, grow, and reproduce processes that mandate an interaction with the surrounding world and, in particular, with other living organisms. At the same time, they must protect themselves from becoming food for others, or more generally, from the adverse consequences of this interaction with the living world. This task falls to a remarkably sophisticated network of humoral and cellular elements collectively known as the immune system.

The immune system includes physical barriers to tissue invasion, an innate response system that can be mobilized within minutes of a new threat, and an adaptive component that requires more time for its initial activation but that, once activated, is characterized by both specificity and memory. The normal function of each of these elements is altered in the critically ill patient, rendering the patient vulnerable both to infection and to the systemic consequences of a dysfunctional defense response.⁽²⁾

The immune system: an evolutionary and conceptual overview

An effective immune system has evolved over more than a billion years in response to the fundamental evolutionary imperative: living organisms that are unable to survive long enough to replicate are lost forever from the tree of life. Reproductive survival is more than simply withstanding threats arising from the microbial world. Contrary to earlier theories of the role of the adaptive immune response, the ability to discriminate self from non-self has minimal, if any, utility in promoting reproductive success (although it is the contemporary bane of the transplant surgeon). A more relevant model of immunity stemming from the work of immunologists such as Janeway and Matzinger ⁽³⁾ is that the primary force driving the evolution of immunity is the need to recognize and respond to danger.

Danger takes many forms. It may be invasion of tissue by bacteria, fungi, or viruses, but it also may be the invasion of tissue through traumatic injury the bite of a predator or the prick of a thorn or the transformation of normally growing tissues into a cancer. The immune system faces no evolutionary pressure to determine the nature of the threat, only to recognize that a threat is present. Thus the mechanisms of immunity that

have evolved do not differ fundamentally in their responses to injured tissue or bacteria. The microbial world has presented humans with the most diverse group of antigenic stimuli, so responses to bacteria are the most complex and numerous in our immunologic repertoire, but they are neither exclusive nor unique. In fact, because bacteria and viruses are also living organisms, their interaction with the eukaryotic world has been particularly complex and, over time, mutually beneficial.

The immune system can be thought of as comprising three elements that arose at differing times during the evolution of life (Fig. 1). Physical barriers the bacterial cell wall or the epithelial barriers of the skin and mucous membranes are the most primitive form of defense, dating back to the initial evolution of unicellular organisms. As multicellular organisms appeared about 1 billion years ago, new systems to recognize and avert danger the coagulation and complement cascades, danger receptors, and phagocytic cells evolved and collectively comprised the innate immune response. With the evolution of bony fishes some 600 million years ago, a third component of immunity emerged, carried out by lymphocytes and known as the “adaptive immune response.” These three arms of the immune system support and interact with one other, although it is convenient to consider them separately here.

Physical barriers to microbial invasion

The physical barriers to invasion by pathogenic micro-organisms include both cells of the host and a complex indigenous microbial flora that exists in symbiosis with the host.

The Endogenous Microbial Flora as a Component of Normal Host Defenses.

A normal, healthy human being is made up of approximately 10^{13} mammalian cells and about 250 different types of cells. This same healthy individual harbors 10^{14} microbial cells on mucosal surfaces, representing at least 500 to 1000 different species of organisms and at least two to three times the number of genes expressed in a human being.⁽⁴⁾

The normal human is seen quite appropriately as an eukaryotic scaffold for a larger, and genetically more diverse, aggregation of prokaryotic life.⁽⁵⁾ The interaction between the micro-organism and the host has defined the evolution of the human innate response to danger. Multicellular organisms have developed complex and highly effective mechanisms to identify and respond to threats from the microbial world. The endogenous bacterial flora, however, also plays multiple key roles in the normal defenses of the mammalian host. The mucosal surfaces of the healthy individual are carpeted with a

complex, indigenous microbial flora. The presence of this flora restricts access to potential mucosal binding sites for exogenous pathogens and so plays a key role in preventing infection with organisms such as *Salmonella*⁽⁶⁾ conversely, when the indigenous flora is disrupted by antibiotics, the host becomes more susceptible to infection with antibiotic-resistant organisms such as *Candida*.⁷ Members of the indigenous flora produce a variety of antimicrobial substances that inhibit the growth of other gut organisms and so stabilize patterns of normal flora. They also promote the development and maintenance of the normal intestinal epithelium⁽⁸⁾ and of a normal systemic inflammatory response to injury.⁽⁹⁾

Symbiotic host–microbial interactions also occur at the level of the gene. For example, the baculoviral protein p35 can inhibit the programmed cell death, or apoptosis, of virally infected cells and so promotes viral persistence by blocking a key component of normal host defenses. Orthologues of the p35 gene, however, probably reflecting the incorporation of viral DNA into the mammalian genome, are present in human and other cells as members of a family of proteins known as the inhibitor of apoptosis protein (IAP) family. IAPs inhibit apoptosis, and their expression in inflammatory neutrophils

enables the neutrophil to survive longer during an acute inflammatory response.⁽¹⁰⁾

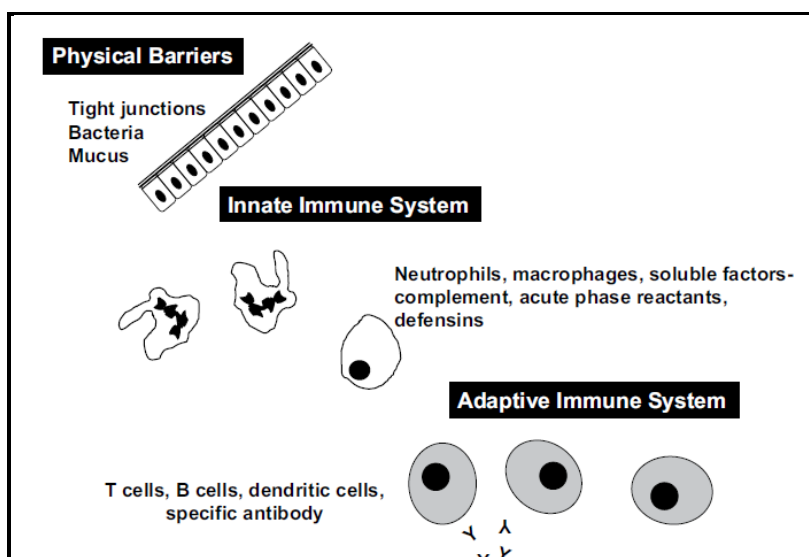


Fig. (1): The immune system can be conceptualized as comprising three main components: the mucocutaneous barriers that separate the internal organs from the external environment, an innate immune system that responds aggressively but nonspecifically to an acute threat, and an adaptive immune system that is delayed in its expression but demonstrates exquisite specificity for its targets and thus results in minimal collateral damage to the host.

Similarly, Nampt, a bacterial protein that enables the micro-organism to synthesize nicotinamide adenine dinucleotide (NAD), has become incorporated into the eukaryotic genome both as an enzyme in a pathway of NAD synthesis and as an anti-apoptotic factor for a variety of cell types.⁽¹¹⁾

Perhaps the most remarkable example of the complex and mutually beneficial symbiotic relationships that have arisen