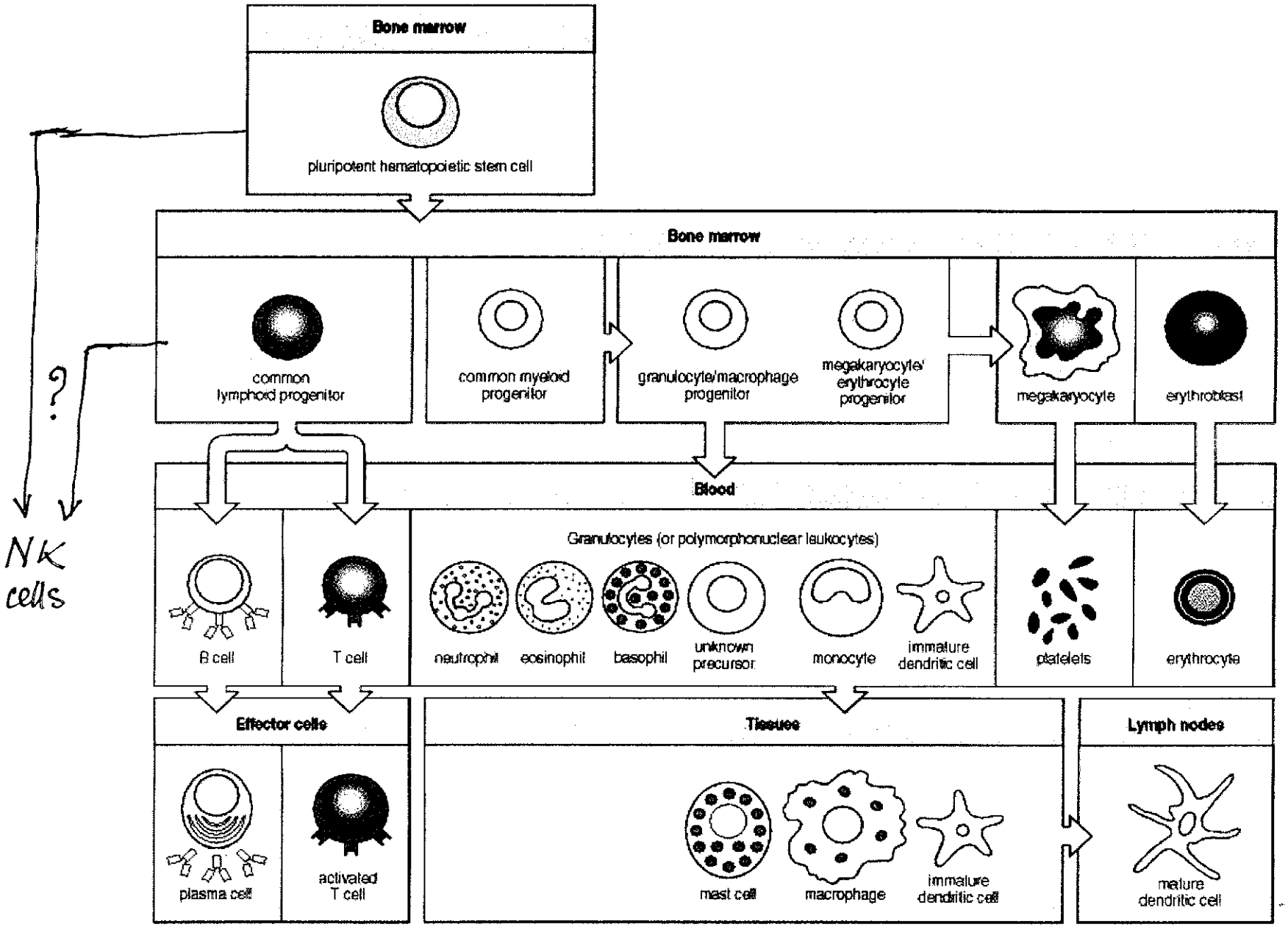
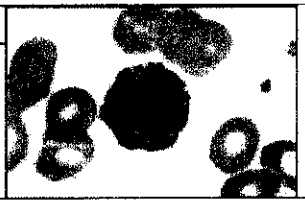
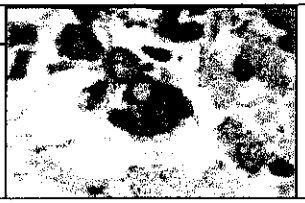
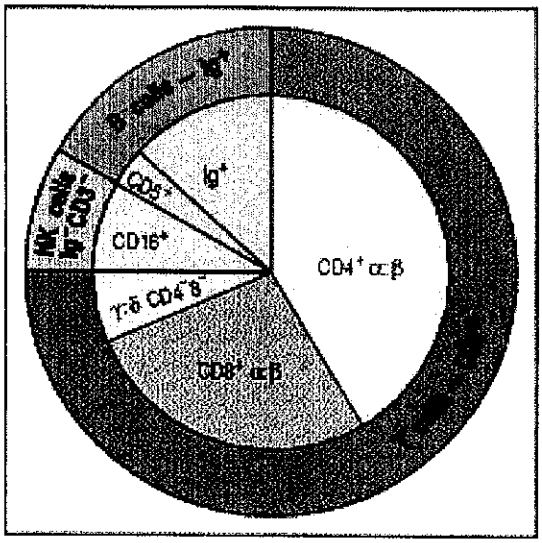

Bone marrow
pluripotent hematopoietic stem cell
Bone marrow
common lymphoid progenitor
common myeloid progenitor
granulocyte/macrophage progenitor
megakaryocyte/ erythrocyte progenitor
megakaryocyte
erythroblast
?
NK cells
Blood
Granulocytes (or polymorphonuclear leukocytes)
B cell
T cell
neutrophil
eosinophil
basophil
unknown precursor
monocyte
immature dendritic cell
platelets
erythrocyte
Effector cells
Tissues
Lymph nodes
plasma cell
activated T cell
mast cell
macrophage
immature dendritic cell
mature dendritic cell

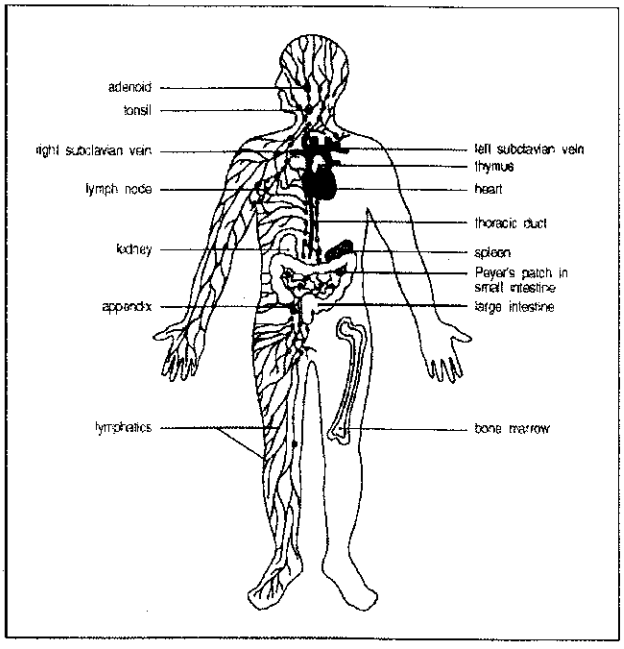
Cell		Activated function
Macrophage		Phagocytosis and activation of bactericidal mechanisms Antigen presentation
Dendritic cell		Antigen uptake in peripheral sites Antigen presentation in lymph nodes
Neutrophil		Phagocytosis and activation of bactericidal mechanisms
Eosinophil		Killing of antibody-coated parasites
Basophil		Unknown
Mast cell		Release of granules containing histamine and other active agents

	Evaluation of the cellular components of the human immune system		
	B cells	**T cells**	**Phagocytes**
Normal numbers ($x10^9$ per liter of blood)	Approximately 0.3	Total 1.0–2.5 CD4 0.5–1.6 CD8 0.3–0.9	Monocytes 0.15–0.6 Polymorphonuclear leukocytes Neutrophils 3.00–5.5 Eosinophils 0.05–0.25 Basophils 0.02
Measurement of function *in vivo*	Serum Ig levels Specific antibody levels	Skin test	—
Measurement of function *in vitro*	Induced antibody production in response to pokeweed mitogen	T-cell proliferation in response to phytohemagglutinin or to tetanus toxoid	Phagocytosis Nitro blue tetrazolium uptake Intracellular killing of bacteria

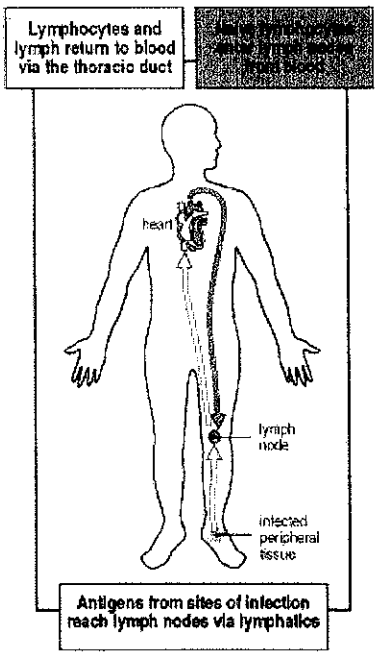
	Evaluation of the humoral components of the human immune system				
	Immunoglobulins				**Complement**
Component	IgG	IgM	IgA	IgE	
Normal levels in adults	600–1400 mg dl^{-1}	40–345 mg dl^{-1}	60–380 mg dl^{-1}	0–200 IU ml^{-1}	CH_{50} of 125–300 IU ml^{-1}


CD5+
Ig+
CD16+
CD4+ αβ
γδ CD4-8-
CD8+ αβ

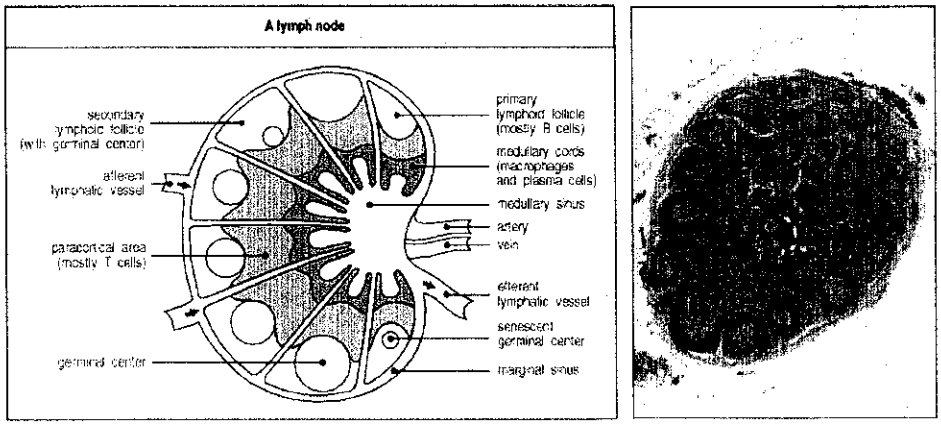
4


adenoid
tonsil
right subclavian vein
lymph node
kidney
appendix
lymphatics
left subclavian vein
thymus
heart
thoracic duct
spleen
Peyer's patch in small intestine
large intestine
bone marrow

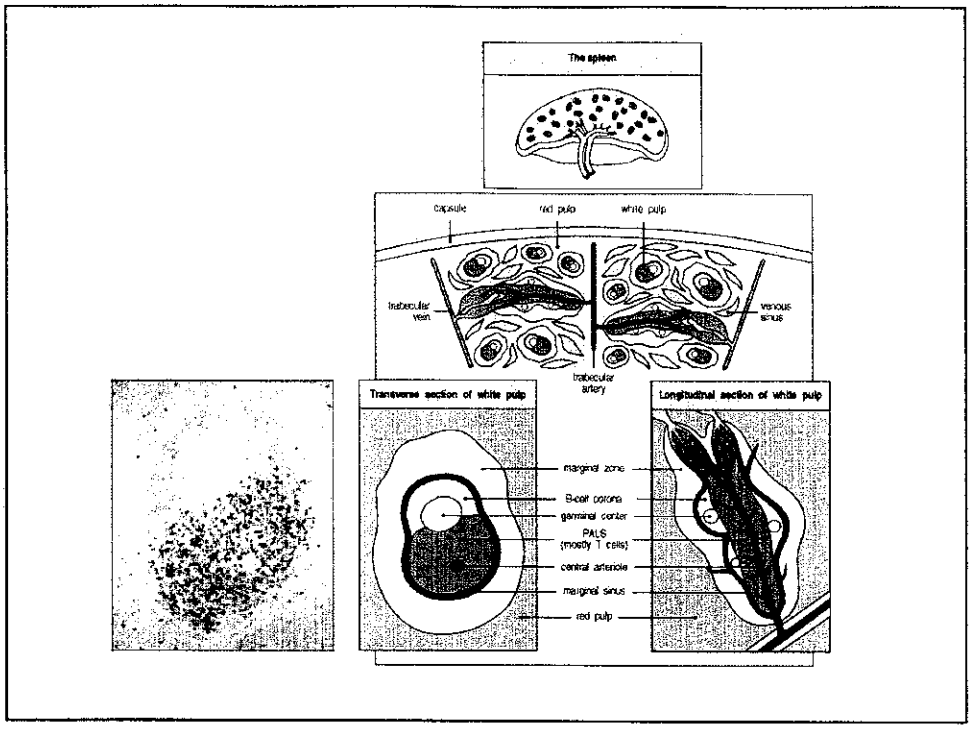
5


Lymphocytes and lymph return to blood via the thoracic duct
heart
lymph node
infected peripheral tissue
Antigens from sites of infection reach lymph nodes via lymphatics

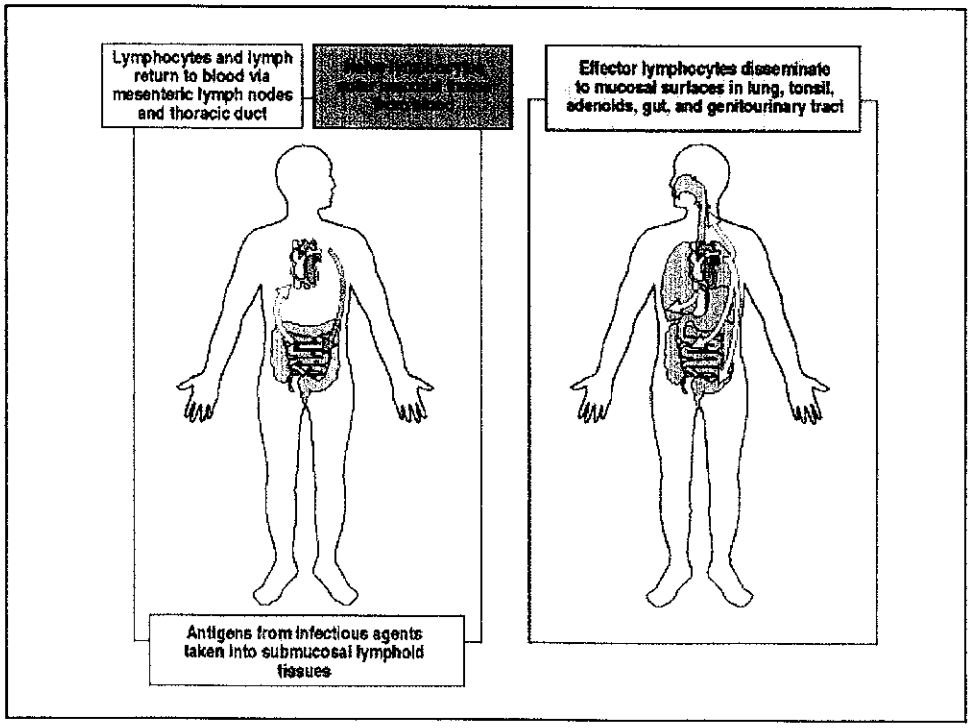
6


A lymph node
secondary lymphoid follicle (with germinal center)
afferent lymphatic vessel
paracortical area (mostly T cells)
germinal center
primary lymphoid follicle (mostly B cells)
medullary cords (macrophages and plasma cells)
medullary sinus
artery
vein
efferent lymphatic vessel
senescent germinal center
marginal sinus

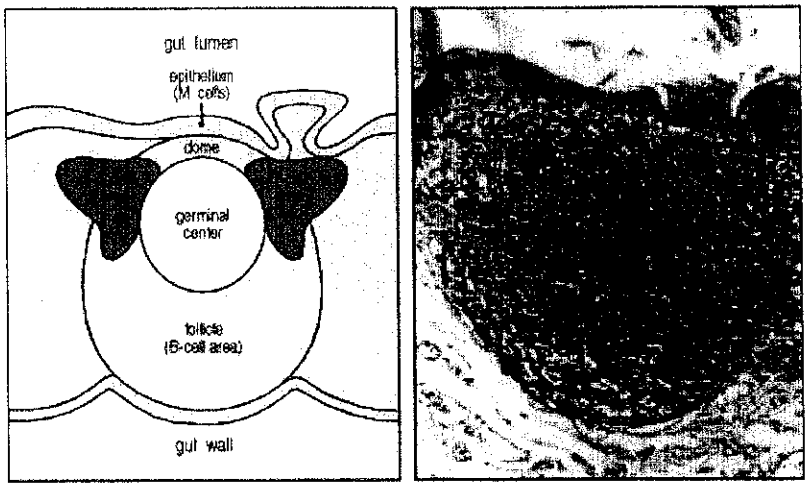
7


The spleen
capsule
red pulp
white pulp
trabecular vein
venous sinus
trabecular artery
Transverse section of white pulp
Longitudinal section of white pulp
marginal zone
B-cell corona
germinal center
PALS (mostly T cells)
central arteriole
marginal sinus
red pulp

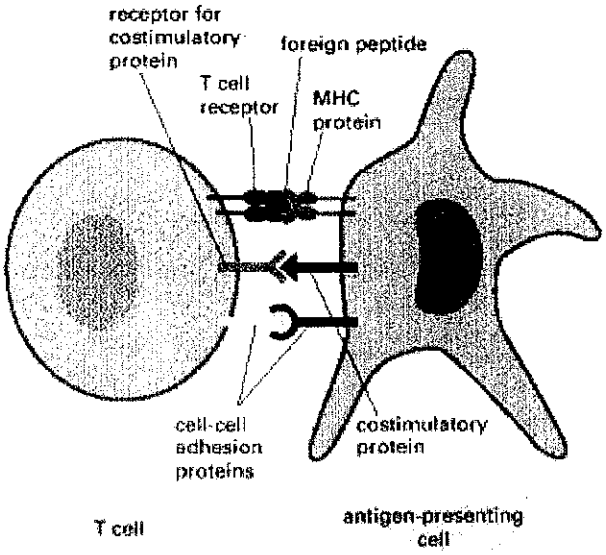
8


Lymphocytes and lymph return to blood via mesenteric lymph nodes and thoracic duct
Effector lymphocytes disseminate to mucosal surfaces in lung, tonsil, adenoids, gut, and genitourinary tract
Antigens from infectious agents taken into submucosal lymphoid tissues

9


gut lumen
epithelium
(M cells)
dome
germinal
center
follicle
(B-cell area)
gut wall

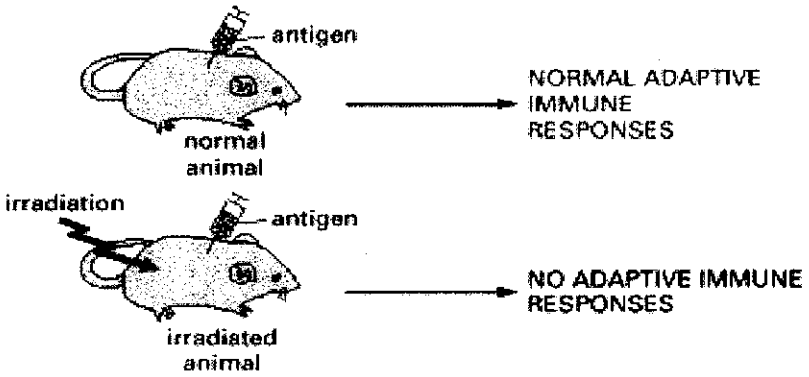
10


receptor for
costimulatory
protein
foreign peptide
T cell
receptor
MHC
protein
cell-cell
adhesion
proteins
costimulatory
protein
T cell
antigen-presenting
cell

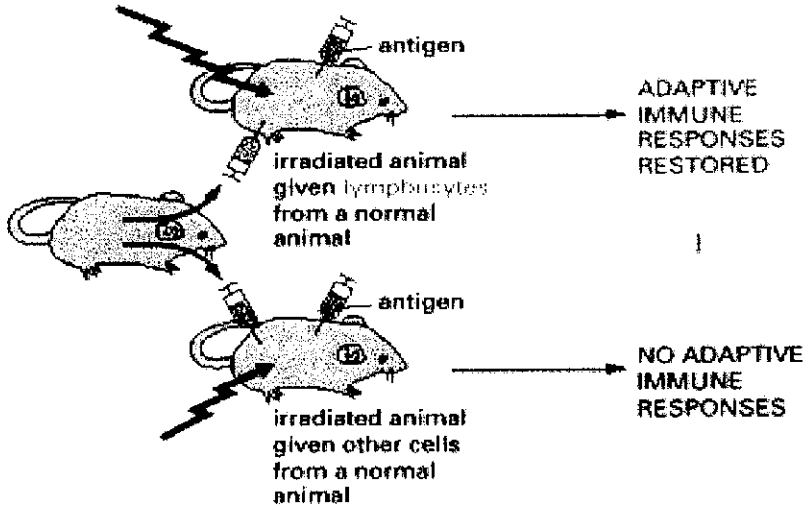
11

Antigen	Effect of response to antigen	
	Normal response	Deficient response
Infectious agent	Protective immunity	Persistent infection
Innocuous substance	Allergy	No response
Grafted organ	Rejection	Acceptance
Self organ	Autoimmunity	Self tolerance
Tumor	Tumor immunity	Cancer

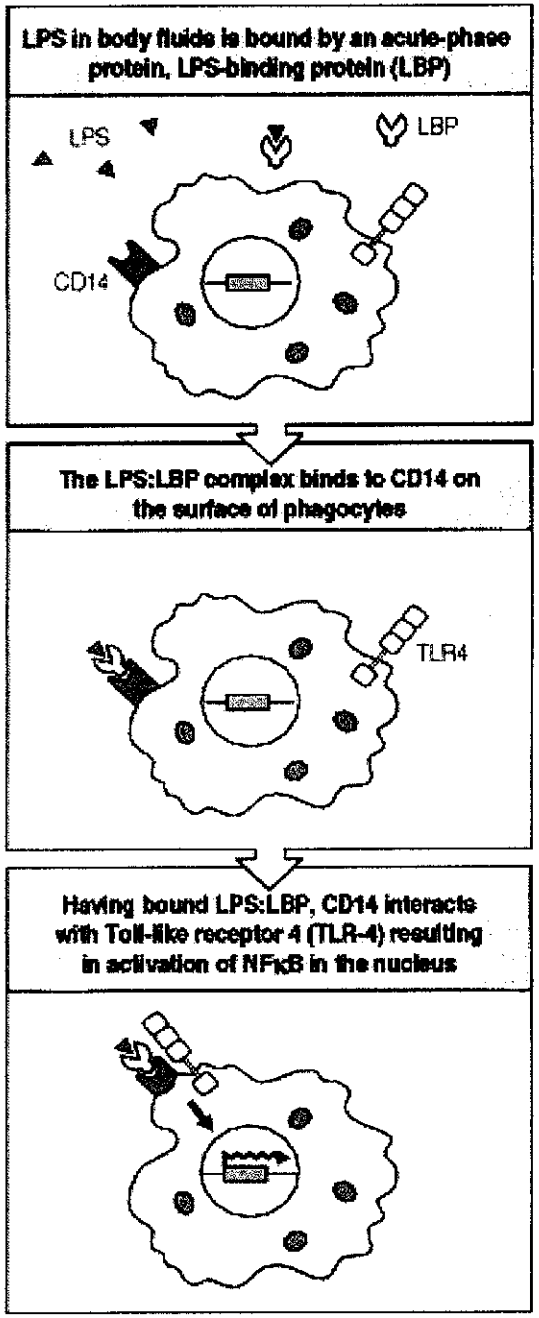
12



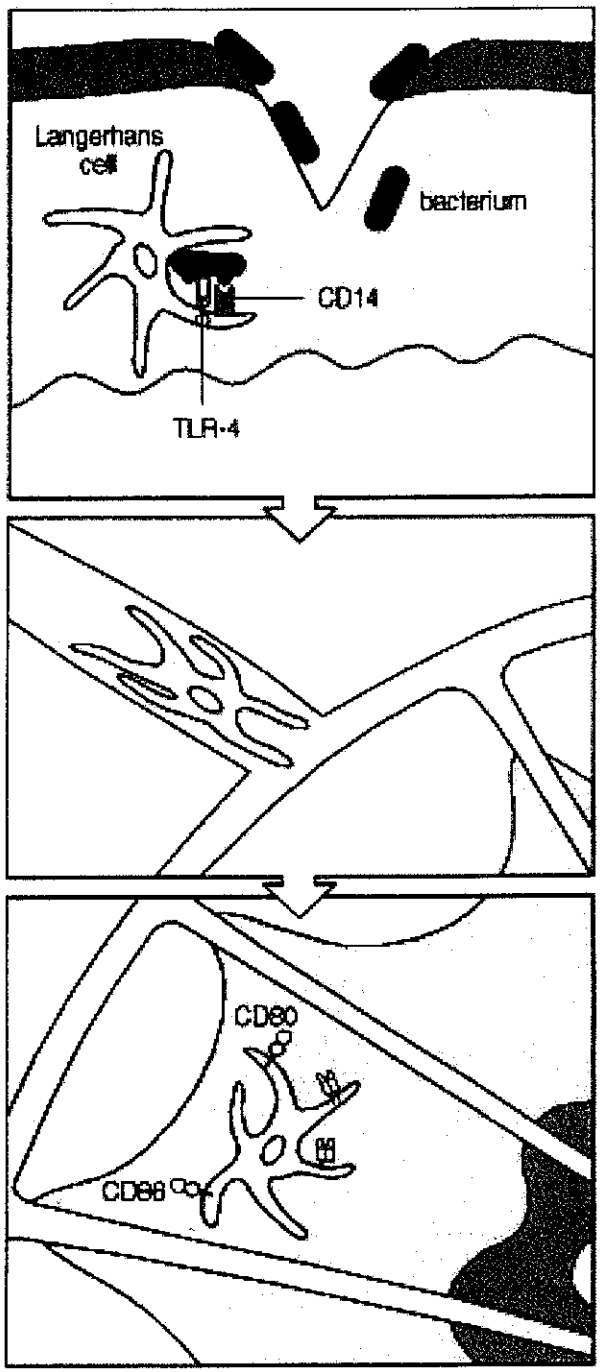
CONTROL



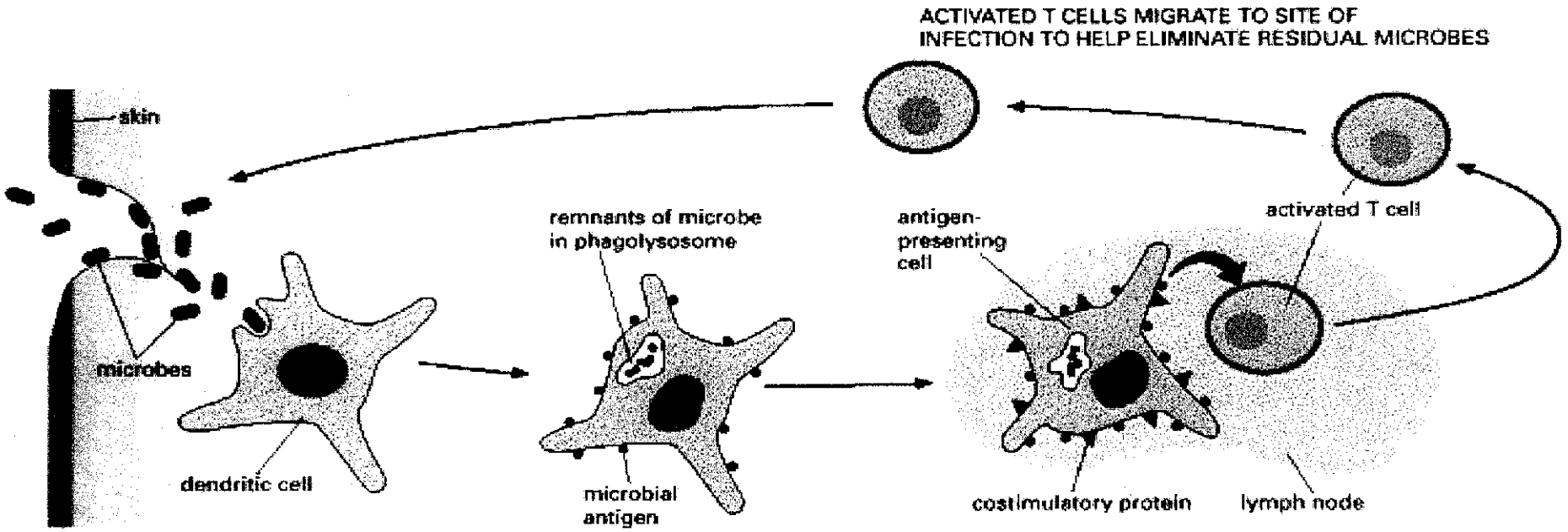
EXPERIMENT

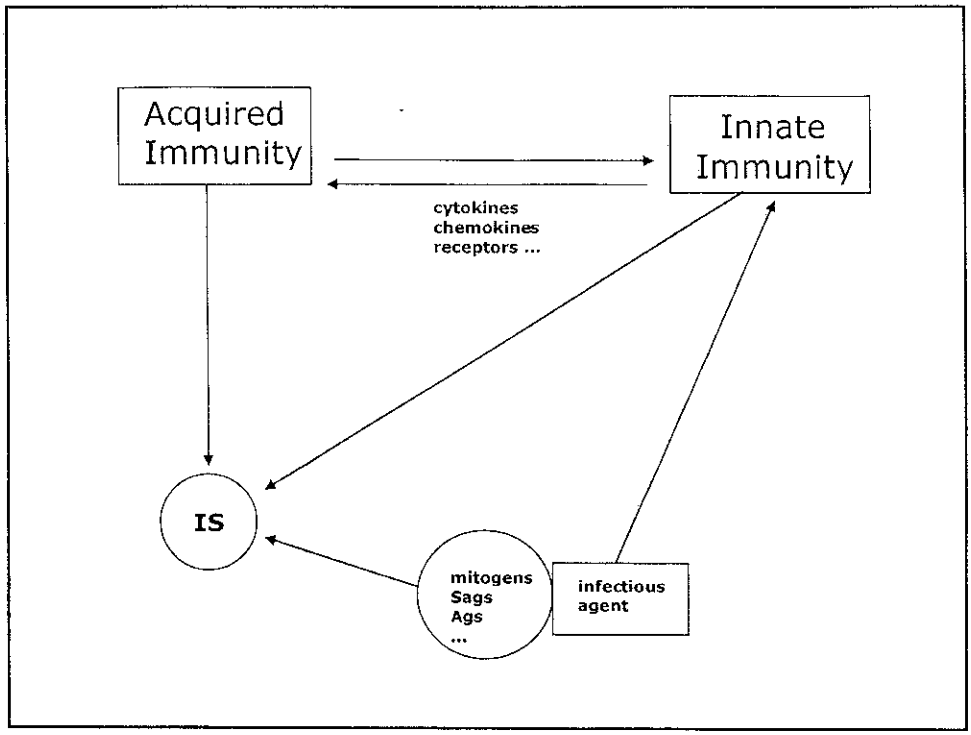

LPS in body fluids is bound by an acute-phase protein, LPS-binding protein (LBP)
LPS
LBP
CD14
The LPS:LBP complex binds to CD14 on the surface of phagocytes
TLR4
Having bound LPS:LBP, CD14 interacts with Toll-like receptor 4 (TLR-4) resulting in activation of NFκB in the nucleus

14


Langerhans cell
bacterium
CD14
TLR-4
CD80
CD86

15

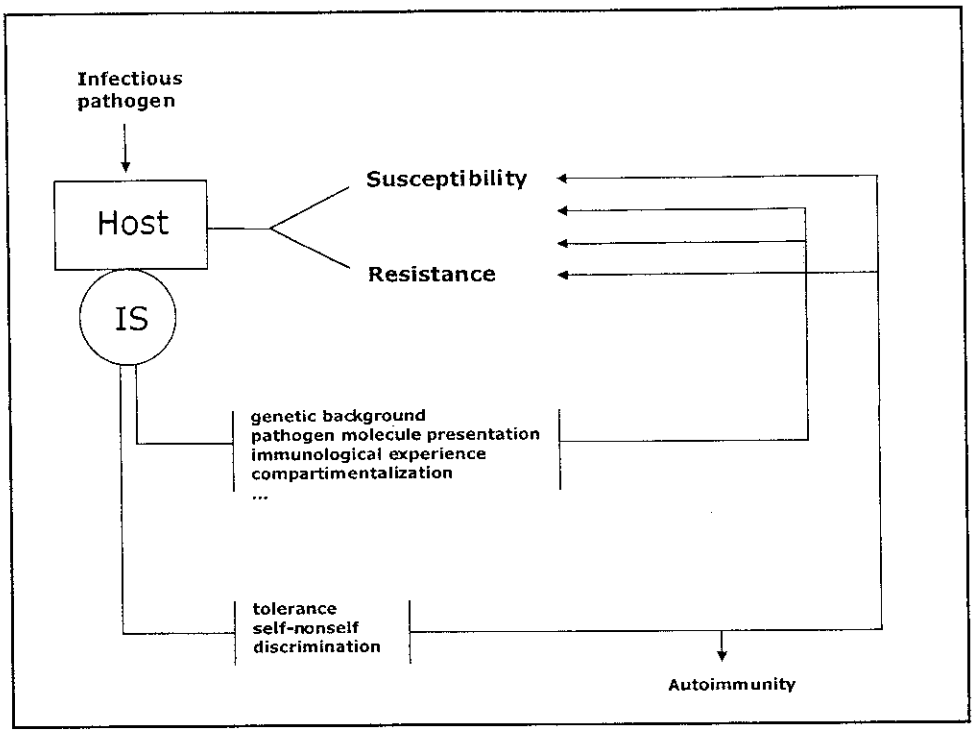

ACTIVATED T CELLS MIGRATE TO SITE OF INFECTION TO HELP ELIMINATE RESIDUAL MICROBES
skin
microbes
dendritic cell
remnants of microbe in phagolysosome
microbial antigen
antigen-presenting cell
activated T cell
costimulatory protein
lymph node
MICROBES ENTER THROUGH BREAK IN SKIN AND ARE PHAGOCYTOSED BY DENDRITIC CELL
DENDRITIC CELL MATURES AND CARRIES MICROBIAL ANTIGENS TO LOCAL LYMPH NODE TO BECOME AN ANTIGEN-PRESENTING CELL
ANTIGEN-PRESENTING CELL ACTIVATES T CELLS TO RESPOND TO MICROBIAL ANTIGENS
INNATE IMMUNE RESPONSE
ADAPTIVE IMMUNE RESPONSE



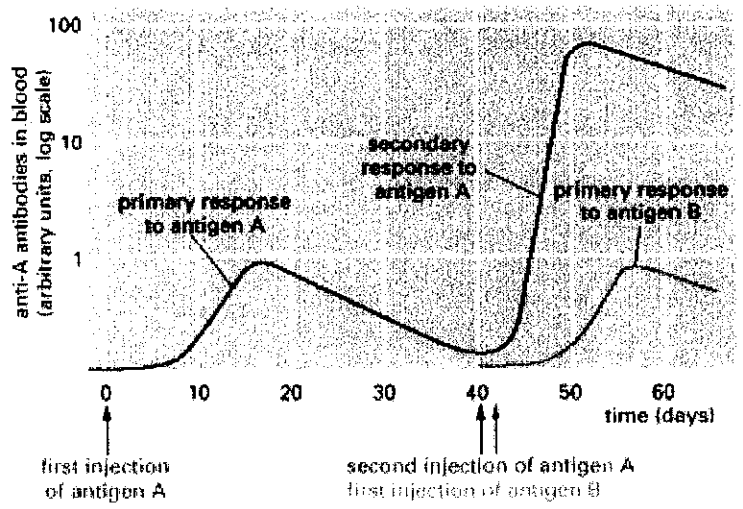
17

Receptor characteristic	Innate immunity	Adaptive immunity
Specificity inherited in the genome	Yes	No
Expressed by all cells of a particular type (e.g., macrophages)	Yes	No
Trigger immediate response	Yes	No
Recognize broad classes of pathogen	Yes	No
Encoded in multiple gene segments	No	Yes
Require gene rearrangement	No	Yes
Clonal distribution	No	Yes
Able to recognize a wide variety of molecular structures	No	Yes

18


Infectious pathogen
Host
IS
Susceptibility
Resistance
genetic background
pathogen molecule presentation
immunological experience
compartimentalization
...
tolerance
self-nonself
discrimination
Autoimmunity

19


100
10
1
anti-A antibodies in blood (arbitrary units, log scale)
primary response to antigen A
secondary response to antigen A
primary response to antigen B
0
10
20
30
40
50
60
time (days)
first injection of antigen A
second injection of antigen A
first injection of antigen B

20