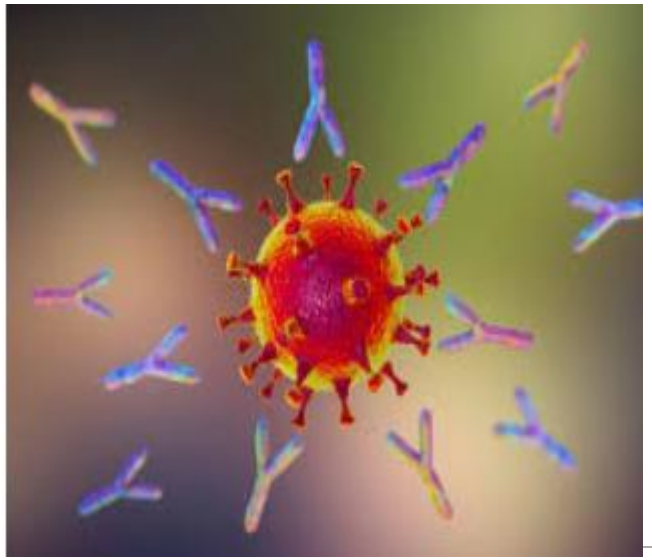
The History of Immunology





Definitions

Immunology stems from L.- *immunis* = "exempt;"
Eng. = protection from disease

Immune system = cells, tissues, and molecules that mediate resistance to infections

Immunology = study of structure and function of the immune system

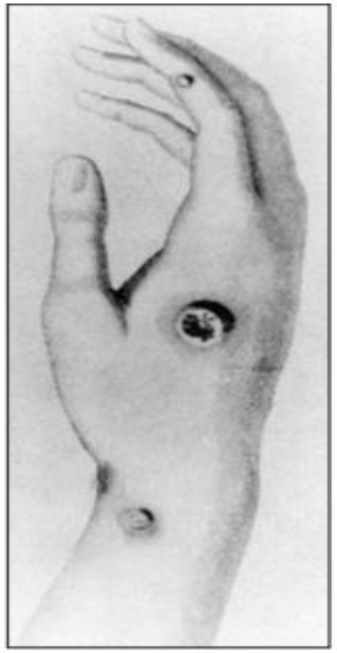
Immune response = collective and coordinated response to the introduction of foreign substances in an individual mediated by the cells and molecules of the immune system

Immunology begins with Edward Jenner's discovery that vaccination with cowpox protects against smallpox



Edward Jenner (1749–1823). Photo courtesy of the National Library of Medicine.

eight-year-old boy called James Phipps





Smallpox in India, 1970s. Photo courtesy of the World Health Organization.

Louis Pasteur



1879- discovered that aged bacterial cultures of *Pasteurella multocida* lost virulence (Pasteurelosis=**Hemorrhagic septicemia**). Referred to injection of weakened culture a "vaccine" in honor of Jenner

1881- He applied the same technique vs. anthrax

….and then rabies

Cases of selected infectious disease before and after the introduction of effective vaccines

Disease	ANNUAL CASES/YR		CASES IN 2004
	Prevaccine	Postvaccine	Reduction (%)
Smallpox	48,164	0	100
Diphtheria	175,885	0	100
Measles	503,282	37	99.99
Mumps	152,209	236	99.85
Pertussis (whooping cough)	147,271	18,957	87.13
Paralytic polio	16,316	0	100
Rubella (German measles)	47,745	12	99.97
Tetanus ("lockjaw")	1,314 (deaths)	26 (cases)	98.02
Invasive hemophilus influenzae	20,000	172	99.14

SOURCE: Adapted from W. A. Orenstein et al., 2005. *Health Affairs* 24:599.

Emil von Behring



S. Kitasato



1880's- Metchnikoff discovered phagocytic cells that ingest microbes and particles

1890- von Behring and Kitasato discovered blood sera could transfer immunity

Soluble components in the serum that are capable of killing microorganisms



Peter Alfred Gorer



Elie Metchnikoff

- 1930's: discovery of active component of blood – gamma globulin "protein"
- 1936: MHC (**Peter Alfred Gorer)**
- 1950's – discovery of T and B cells

Nobel prizes for immunologic research

Year	Recipient	Country	Research
1901	Emil von Behring	Germany	Serum antitoxins
1905	Robert Koch	Germany	Cellular immunity to tuberculosis
1908	Elie Metchnikoff Paul Ehrlich	Russia Germany	Role of phagocytosis (Metchnikoff) and antitoxins (Ehrlich) in immunity
1913	Charles Richet	France	Anaphylaxis
1919	Jules Bordet	Belgium	Complement-mediated bacteriolysis
1930	Karl Landsteiner	United States	Discovery of human blood groups
1951	Max Theiler	South Africa	Development of yellow fever vaccine
1957	Daniel Bovet	Switzerland	Antihistamines
1960	F. Macfarlane Burnet Peter Medawar	Australia Great Britain	Discovery of acquired immunological tolerance
1972	Rodney R. Porter Gerald M. Edelman	Great Britain United States	Chemical structure of antibodies
1977	Rosalyn R. Yalow	United States	Development of radioimmunoassay
1980	George Snell Jean Dausset Baruj Benacerraf	United States France United States	Major histocompatibility complex
1984	Cesar Milstein Georges E. Köhler Niels K. Jerne	Great Britain Germany Denmark	Monoclonal antibodies Immune regulatory theories
1987	Susumu Tonegawa	Japan	Gene rearrangement in antibody production
1991	E. Donnall Thomas Joseph Murray	United States United States	Transplantation immunology
1996	Peter C. Doherty Rolf M. Zinkernagel	Australia Switzerland	Role of major histocompatibility complex in antigen recognition by T cells
2002	Sydney Brenner H. Robert Horvitz J. E. Sulston	S. Africa United States Great Britain	Genetic regulation of organ development and cell death (apoptosis)

Kuby IMMUNOLOGY, Sixth Edition

Role of the immune system

- Defense against microbes
- Defense against the growth of tumor cells
  - kills the growth of tumor cells
- Homeostasis
  - destruction of abnormal or dead cells (e.g. dead red or white blood cells, antigen-antibody complex)

Immune System

Organs, Cells, Molecules

Immune System: organs

- Tonsils and adenoids
- Thymus
- Lymph nodes
- Spleen
- Payer's patches
- Lymphatic vessels
- Bone marrow

Immune system: cells

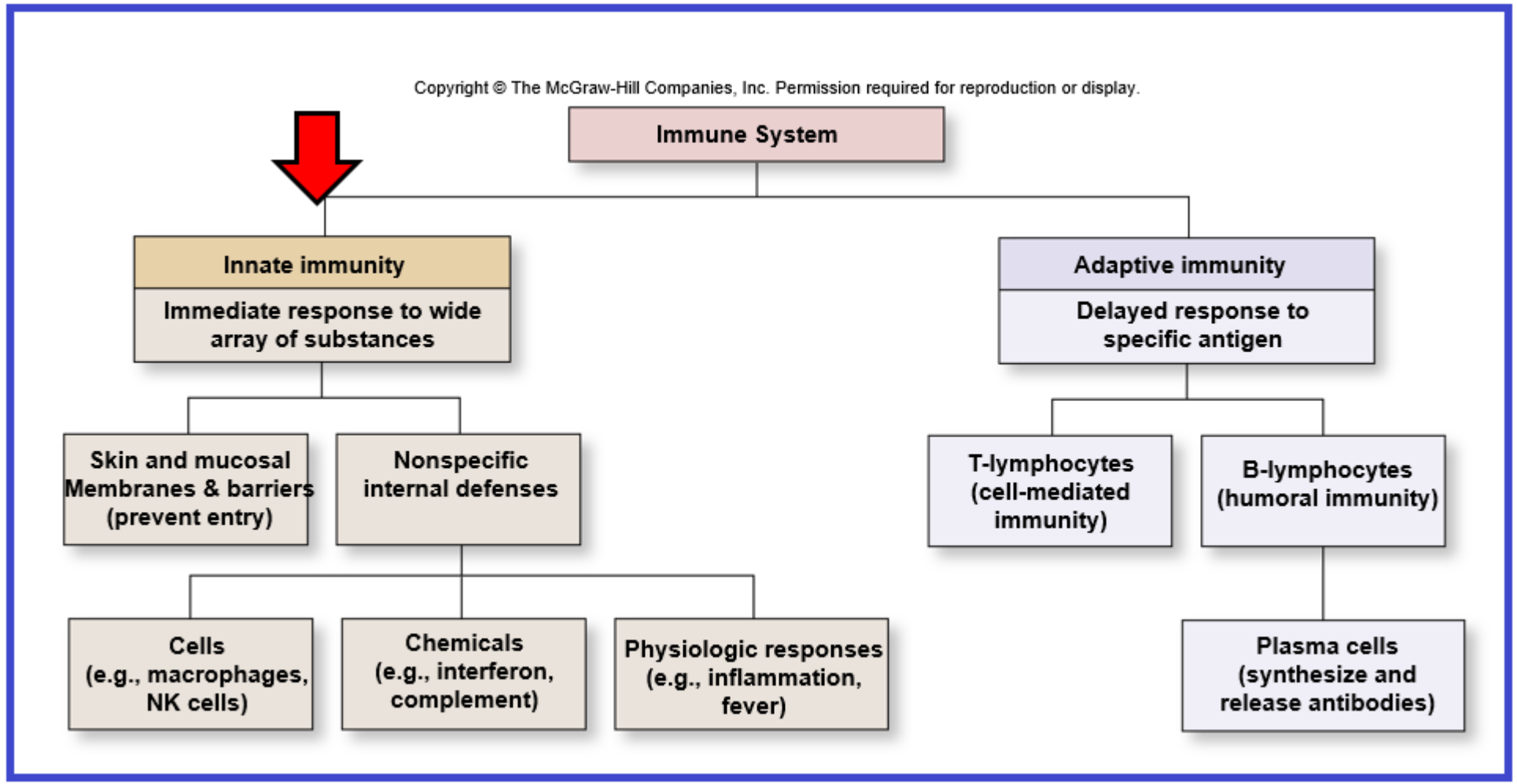
- Lymphocytes
  - T-lymphocytes
  - B-Lymphocytes, plasma cells
  - natural killer lymphocytes
- Monocytes, Macrophage
- Granulocytes
  - neutrophils
  - eosinophils
  - basophils

Immune system: molecules

- Antibodies
- Complement
- Cytokines
- Interleukines
- Interferons

Two types of immunity

1. Innate (non-adaptive)
   - ▶ first line of immune response
   - ▶ relies on mechanisms that exist before infection
2. Acquired (adaptive)
   - ▶ Second line of response (if innate fails)
   - ▶ relies on mechanisms that adapt after infection
   - ▶ handled by T- and B- lymphocytes


Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.
Immune System
Innate immunity
Immediate response to wide array of substances
Adaptive immunity
Delayed response to specific antigen
Skin and mucosal Membranes & barriers (prevent entry)
Nonspecific internal defenses
T-lymphocytes (cell-mediated immunity)
B-lymphocytes (humoral immunity)
Cells (e.g., macrophages, NK cells)
Chemicals (e.g., interferon, complement)
Physiologic responses (e.g., inflammation, fever)
Plasma cells (synthesize and release antibodies)

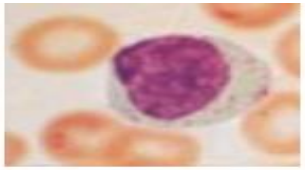
Innate - Nonspecific Defenses

1st line of defense

- *Physical barriers:* Skin and mucosal barriers - keep hazardous materials outside the body

2nd line of defense

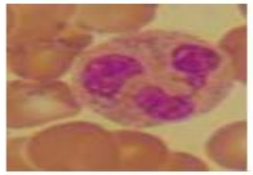
- *Phagocytes: neutrophils and macrophages: engulf pathogens and cell debris*
- *Immunological Surveillance: natural killer cells (NK cells) destroy abnormal cells.*
- *Interferons:* Chemical messengers that coordinate the defenses against viral infections. Antiviral proteins do not kill viruses but block replication in cell
- *Complement:* Complement action of antibodies to destroy pathogens
- *Inflammation:* Triggers a complex inflammatory response limiting the spread of infection
- *Fever:* A high body temperature which increases body metabolism, accelerates defenses and accelerates body defenses



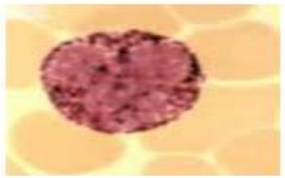
NK Cell



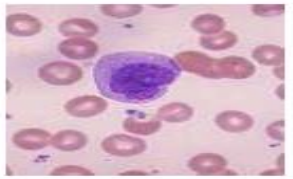
Eosinophils



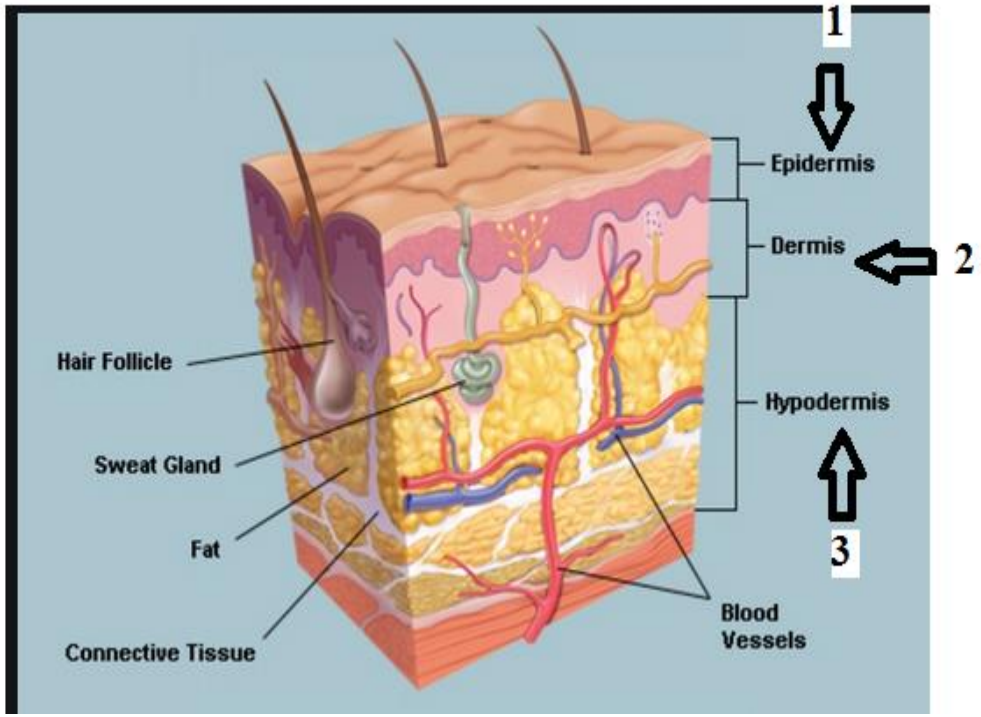
Neutrophil



Basophils & Mast cells



Monocyte Macrophage



Physical barriers

1- پوست
2- مخاط

ویژگی های پوست به عنوان سد دفاعی:

فلور طبیعی

pH 5.5

عدم رطوبت

لایه های اپیدرم و درم

پوست متشکل از سه لایه اصلی است (مساحت پوست ۲ متر مربع):

1. **اپیدرم** که شامل دو بخش سلول های کراتینوسیت (شاخی شکل) و چند لایه سلول اپی تلیال است.

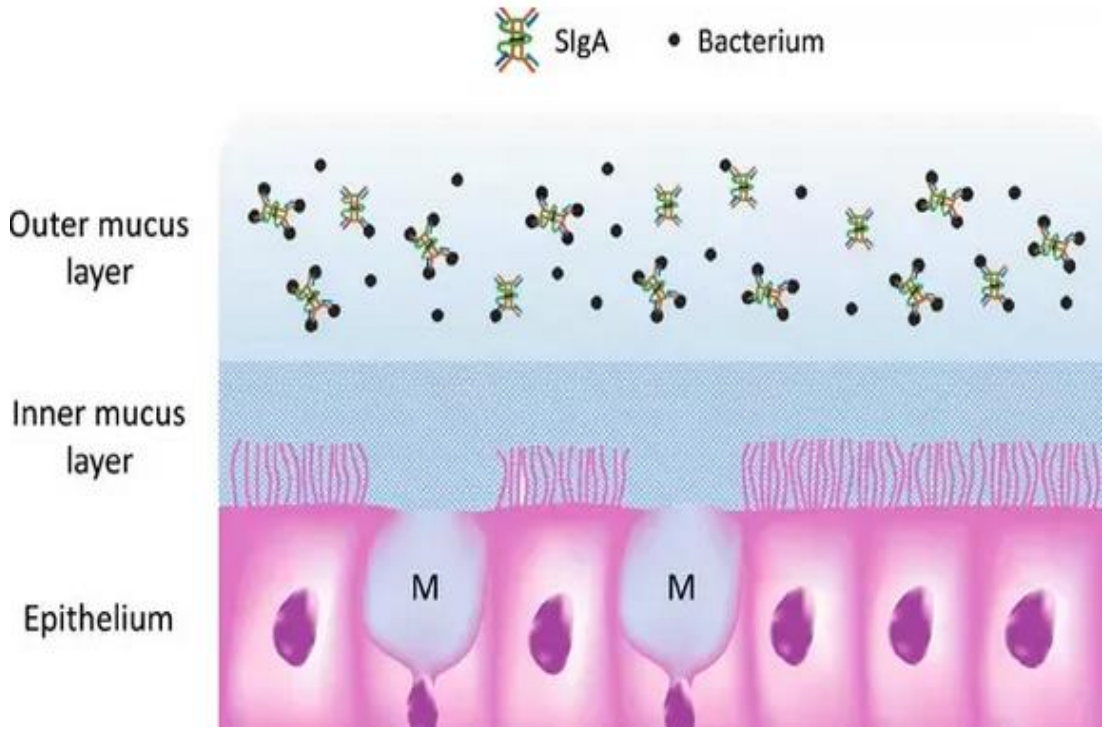
نقش کراتینوسیت: خاصیت waterproof به پوست می دهد.

نقش سلول های اپی تلیال: ترشح مواد ضد میکروبی تحت نام Defensins

در ضمن در بین سلول های اپی تلیال پوست یکسری سلول تحت نام " Intraepithelial lymphocyte" وجود دارند که مشابه لنفوسیت های T قادر به ترشح سایتوکین هستند و با توجه به داشتن رسپتور میکروارگانیسم ها را شناسایی می کنند.

2. **قسمت درم**: این ناحیه شامل sebum cells بوده که با ترشح اسیدهای چرب، پوست را چرب نگه داشته و در برابر پاتوژن ها محافظت می کنند. همچنین این ناحیه از پوست دارای غدد عرقی است (لیزوزیم و پراکسیداز)
3. **هیپودرم**: اتصال پوست به بافت های عضلانی

مخاط حدود ۴۰۰ متر مربع از بدن را پوشانده است. مژه ها سطح سلول مخاطی (سلول اپی تلیال) + ترشحات مخاطی (موسین ترشح شده) دور باکتری را گرفته و مانع اتصال می شود. از طرفی مخاط هم فلور نرمال دارد و هم بر سطح آن IgA وجود دارد.



Chemical barriers (سدهای شیمیایی)

1- pH های اسیدی (معده، پوست و مجاری ادراری)

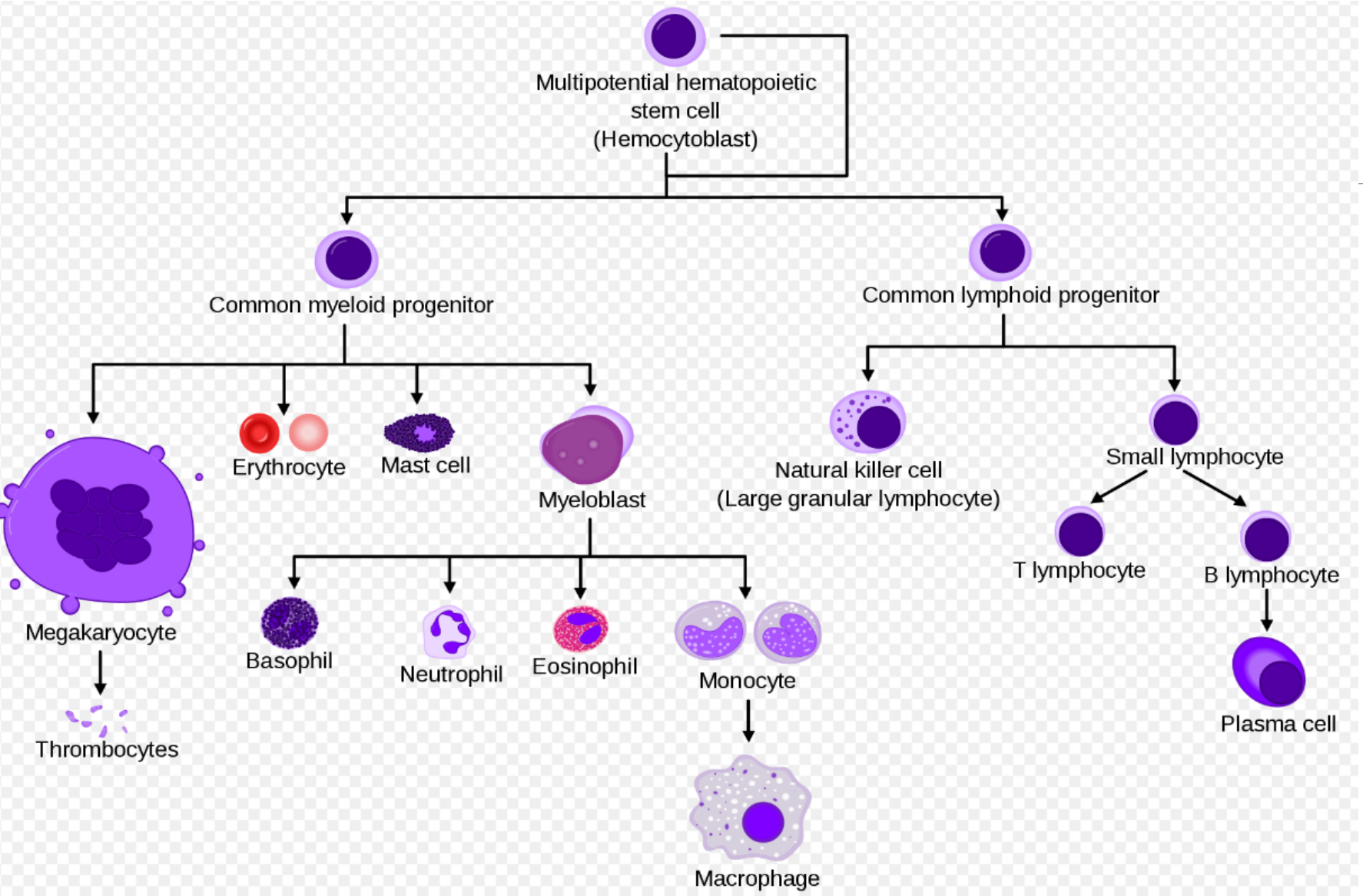
2- آنزیم های موجود در ترشحات بدن (بزاق و اشک: لیزوزیم، پراکسیداز و فسفولیپاز)، شیر (لاکتوفرین و IgA)

3- اسپرمین موجود در مایع منی

4- Surfactin در ریه ها که خاصیت اپسونیزاسیون دارد (تشدید عمل بیگانه خواری ماکروفاژهای موجود در ریه)

5- ترکیبات شیمیایی ضد میکروبی- پپتیدهای کاتیونی غنی از سیستئین موجود در اپی تلیوم و نوتروفیل ها (Defensins و Cathelicidin)

سد دوم دفاعی بدن (سلول ها و ماکروملکول های درگیر در ایمنی ذاتی)



سلول های بیگانه خوار (MQ و PMN)

سلول های کشنده طبیعی (NK cell)

سلول های دندرتیک (DC)

سایتوکین

کمپلمان