BIOL 4323 General Immunology

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

*Protective adaptations in higher organisms to rid the body of foreign particles (microbial and otherwise) and abnormal cells

Our Immune system involves the **interplay** between our **Non-specific** and our **Specific** Immune responses

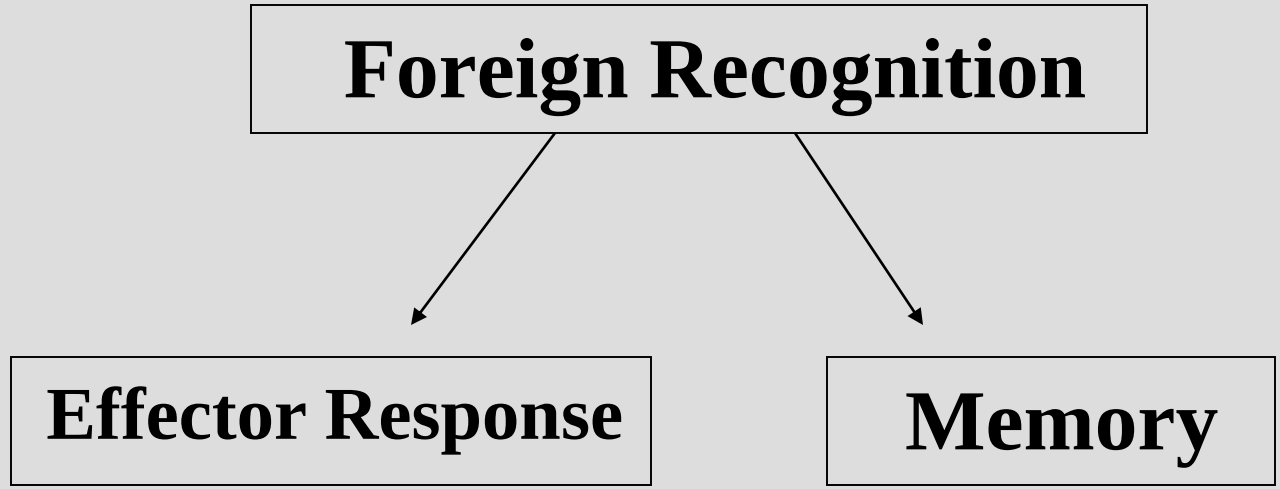
Non-specific immunities collectively referred to as our **Innate** immunity

Specific immunities are referred to as our **Adaptive** immunity for which there are 2 branches:

Humoral immunity

Cell-mediated immunity

Our immune systems generate an almost infinite variety of cells and substances

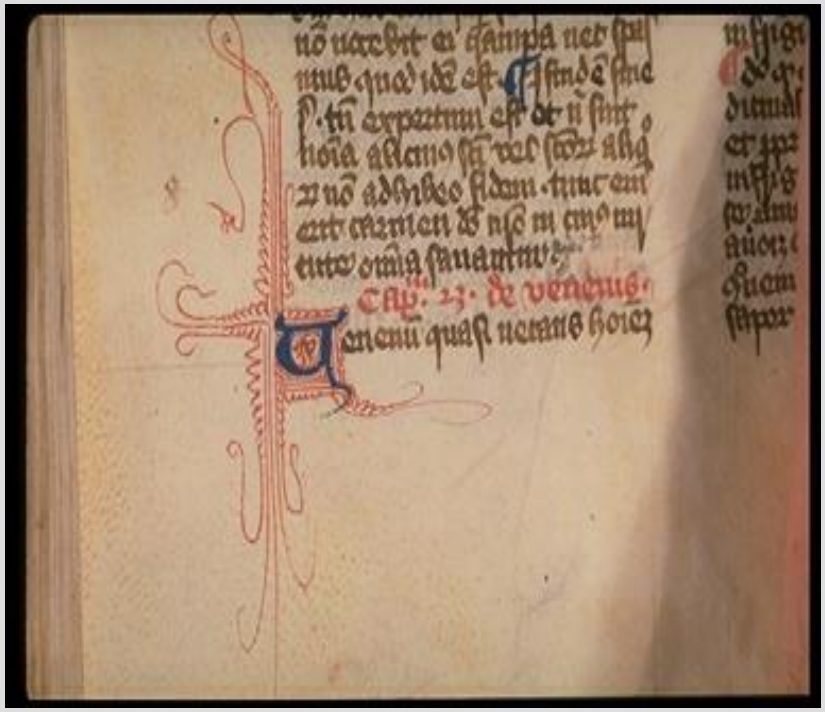


To eliminate or neutralize particle

Upon 2° exposure produces enhanced response

*In some cases, the IR fails to function; at other times, the IR can turn on its host

First, a brief immunological history…



Rare medical manuscript from ~1361 –
Rosa medicinae

400 B.C. – philosophers noted resistance to plague by those who recovered

-houses were fumigated with sulfur vapors after illnesses

50 B.C. – Lucretius suggested disease was caused by invisible living creatures

10th Cent – Turks inoc children with particles from smallpox blisters

towards modern times…

Lady Mary Wortley Montague
(1689-1762)

War on smallpox…

1718- **Lady Montague** became aware of a practice, called **variolation** or inoculation, and introduced it to Britain after first having her own children treated.

1774 – Benjamin Jesty

1796- Edward Jenner

1798 –Edward Jenner noticed immunity bestowed to milkmaids – injected fluid from cowpox blister into skin of patient (orphan or prisoner)

1989- WHO announced smallpox was eradicated from the world

Louie Louie…

Pasteur inoculating sheep at Msr. Rossignol's farm – May, 1881

Louis Pasteur

1879- discovered that aged bacterial cultures of *Pasteurella* lost virulence. Referred to injection of weakened culture a "vaccine" in honor of Jenner

1881- He applied the same technique vs. anthrax

….and then rabies

Louis Pasteur watching as Joseph Meister receives attenuated rabies vaccine (1885)

Figure 1-2
Kuby IMMUNOLOGY, Sixth Edition

TABLE 1-1 Cases of selected infectious disease before and after the introduction of effective vaccines

	ANNUAL CASES/YR		CASES IN 2004
Disease	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.

Table 1-1
Kuby IMMUNOLOGY, Sixth Edition

First insights into mechanics of immunity…

Emil von Behring

S. Kitasato

Elie Metchnikoff

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

∴ cells conferred immunity

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

∴ liquid of blood conferred immunity

Q: Which confers immunity… cells or serum?

A: *Both cells and serum contribute to immunity*!

- 1930's – early techniques made it easier to study **humoral** elements [than cellular ones].

  -discovery of active component of blood – gamma globulin "protein"

- 1950's – discovery of T and B cells

  Later discoveries linked lymphocytes to both cellular and humoral immunity

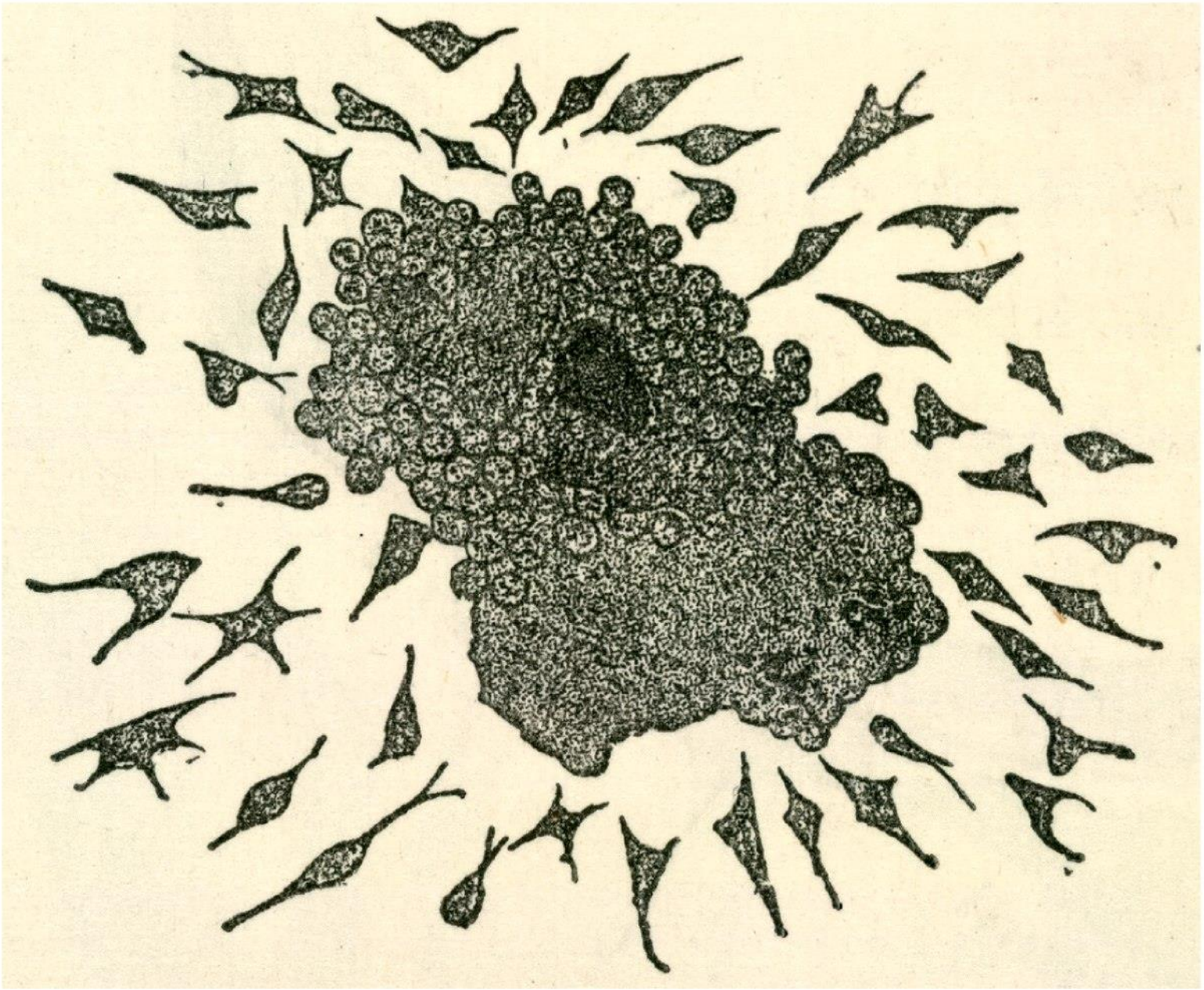
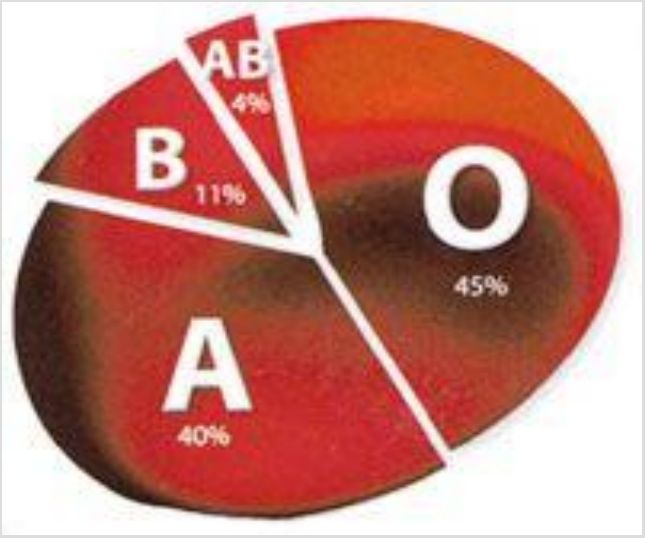


Figure 1-3
Kuby IMMUNOLOGY, Sixth Edition

Understanding specificity of antibody for antigen took years

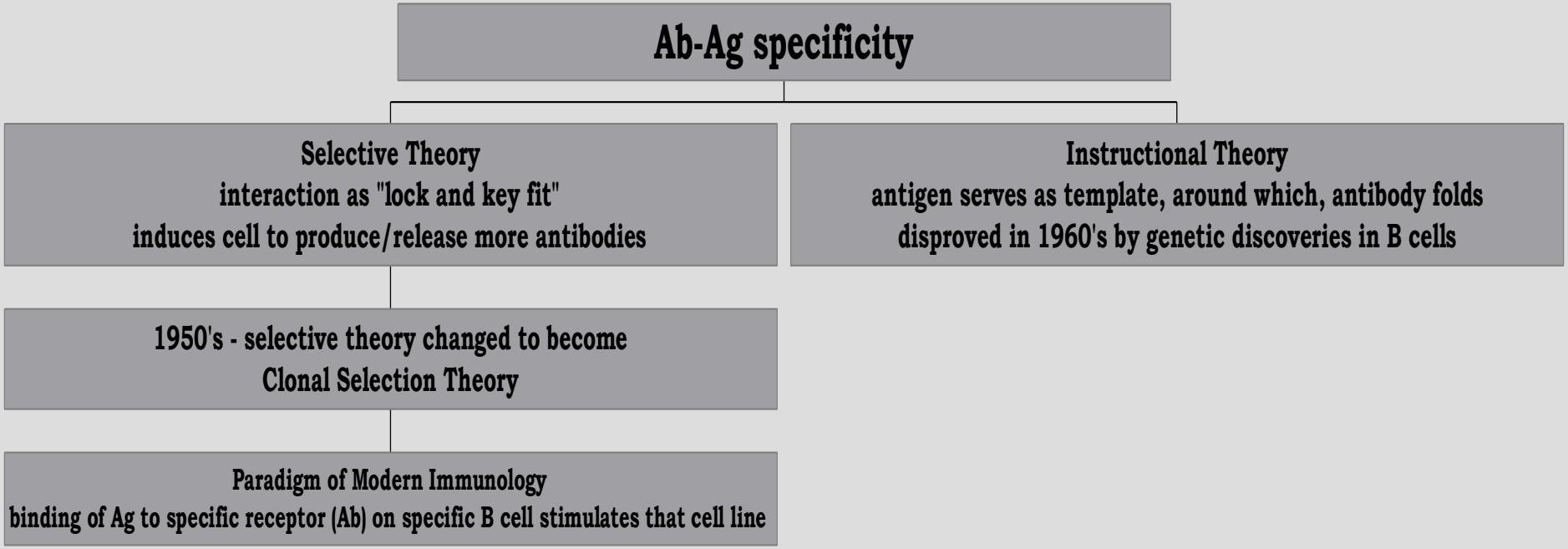
Karl Landsteiner



- **Early 1900's-** Landsteiner revealed antibody could be produced vs. most any organic compound

- **Last 20 yrs-** Antibody specificity reveals unlimited range of reactivity – also to newly synthesized chemicals!

2 competing theories for antibody-antigen specificity



Paul Erlich's side chain hypothesis for antibody formation (1900)

- Pluripotent blood cells with variety of receptor "side chains"
- Contact with foreign molecules (antigen) stimulated increased receptor production
- Specific receptors produced on cells prior to contact with antigen

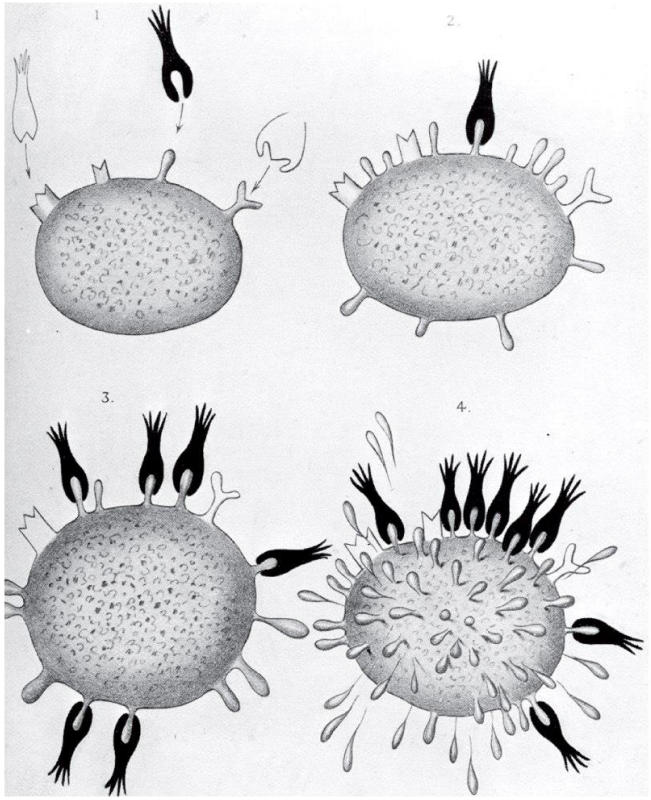


Figure 1-4
Kuby IMMUNOLOGY, Sixth Edition

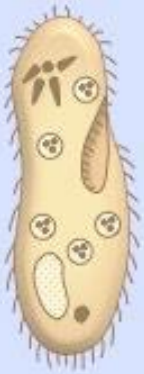
Foundation of selective theory

TABLE 1-2 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)

Table 1-2
Kuby IMMUNOLOGY, Sixth Edition

Pathogens

CELLULAR (LIVING)				ACELLULAR (NON-LIVING)	
					
Parasites *(e.g. helminthes)* ⇒ Tapeworm	**Protozoa** *(e.g. plasmodia)* ⇒ Malaria	**Fungi** *(e.g. tinea)* ⇒ Athlete's foot	**Prokaryote** *(i.e. bacteria)* ⇒ Leprosy	**Virus** *(e.g. HIV)* ⇒ AIDS	**Prion** ⇒ CJD

1st Anatomical barriers in innate immunity

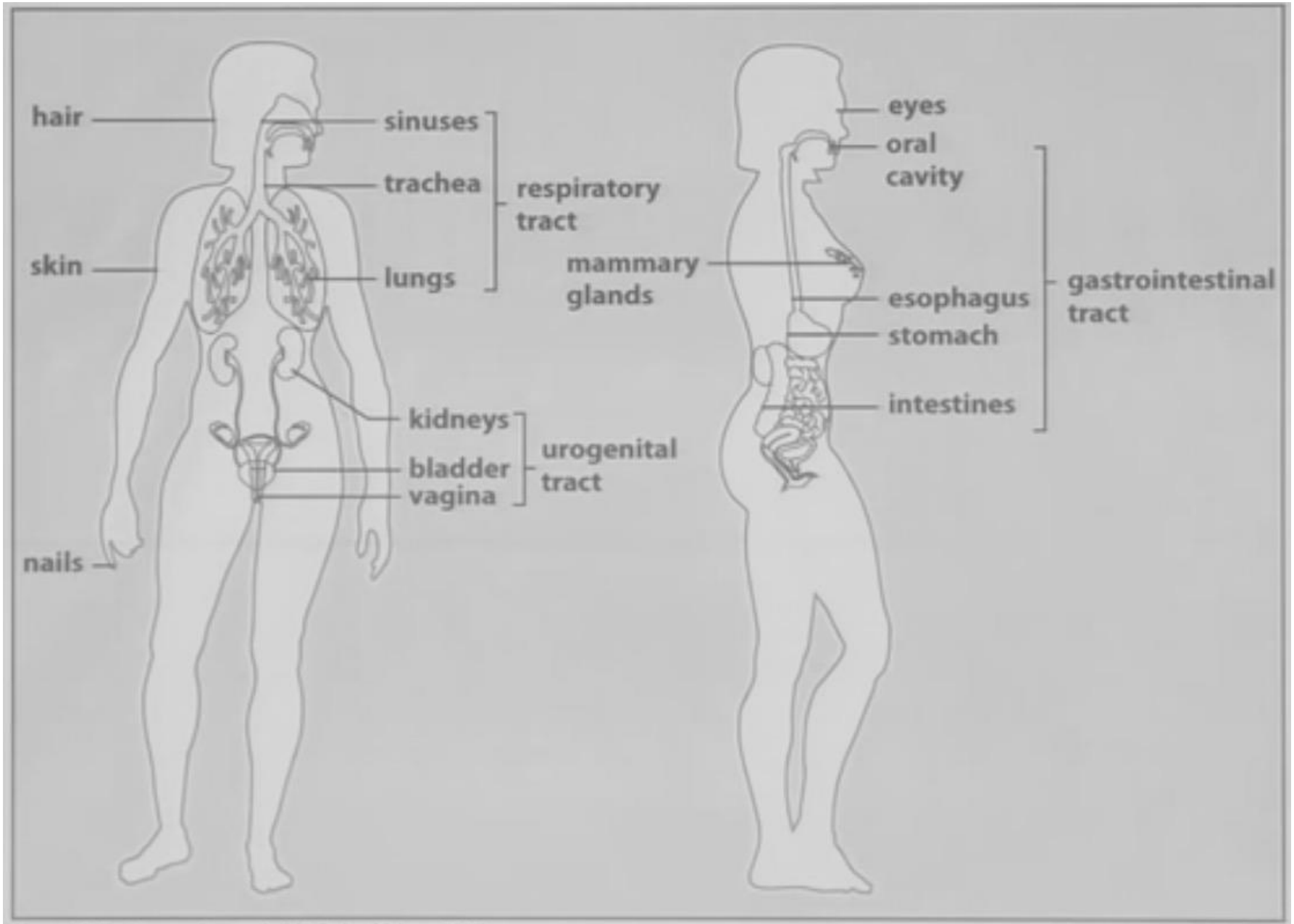


Figure 1.5 The Immune System, 3ed. (© Garland Science 2009)

1st Anatomical barriers in innate immunity

	Skin	Gastrointestinal tract	Respiratory tract	Urogenital tract	Eyes
Mechanical	Epithelial cells joined by tight junctions				
	Flow of fluid, perspiration, sloughing off of skin	Flow of fluid, mucus, food, and saliva	Flow of fluid and mucus, e.g., by cilia Air flow	Flow of fluid, urine, mucus, sperm	Flow of fluid, tears
Chemical	Sebum (fatty acids, lactic acid, lysozyme)	Acidity, enzymes (proteases)	Lysozyme in nasal secretions	Acidity in vaginal secretions Spermine and zinc in semen	Lysozyme in tears
	Antimicrobial peptides (defensins)				
Microbiological	Normal flora of the skin	Normal flora of the gastrointestinal tract	Normal flora of the respiratory tract	Normal flora of the urogenital tract	Normal flora of the eyes

Figure 1.6 The Immune System, 3ed. (© Garland Science 2009)

Inflammation

Fig 1.6 (2nd Ed) Fig 1.8 (3rd Ed)

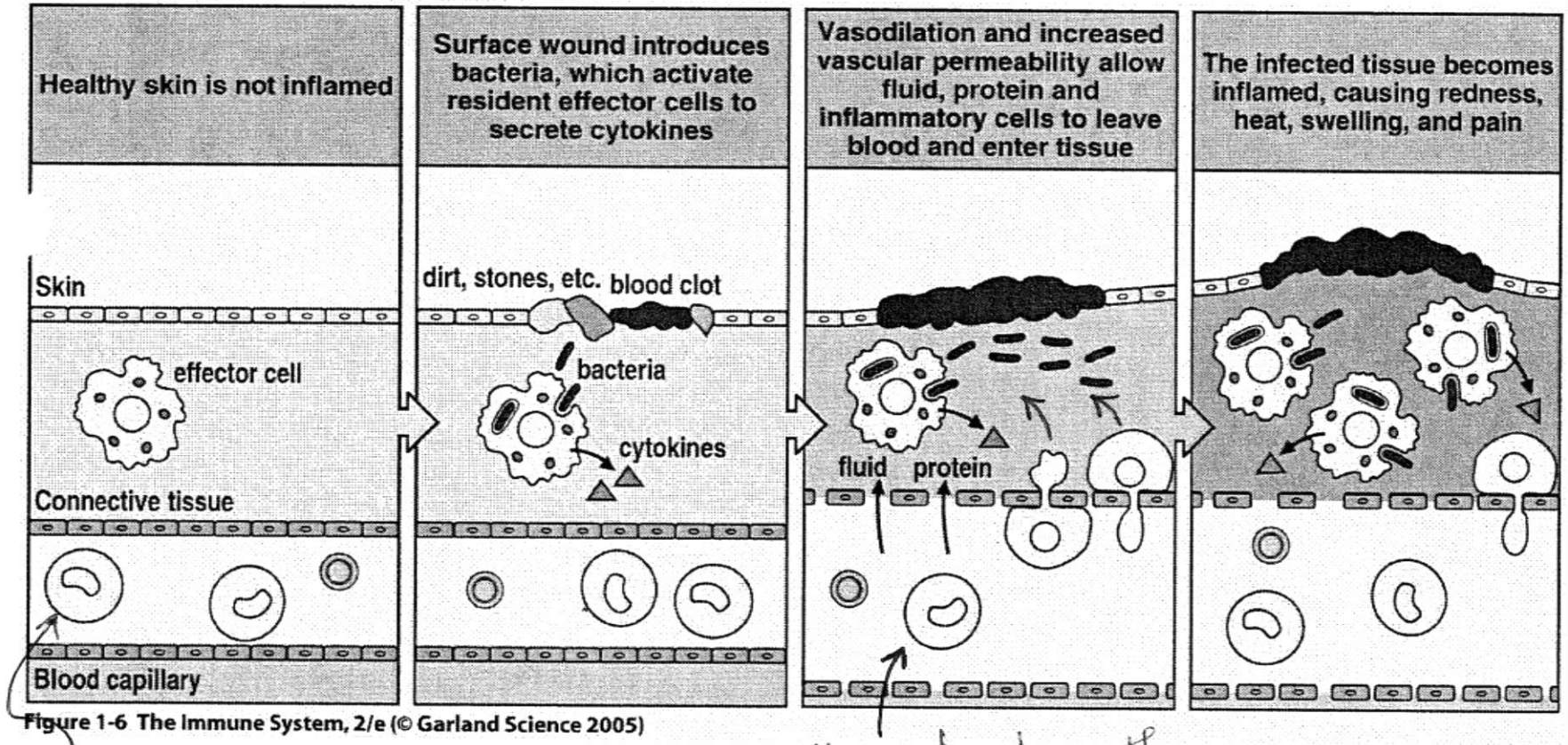


Figure 1-6 The Immune System, 2/e (© Garland Science 2005)

Monocyte

Monocytes leave the blood vessels and then differentiate into macrophages at

Innate immune recognition

Fig 1.5 (2nd Ed.) Fig 1.7, 3rd Ed.

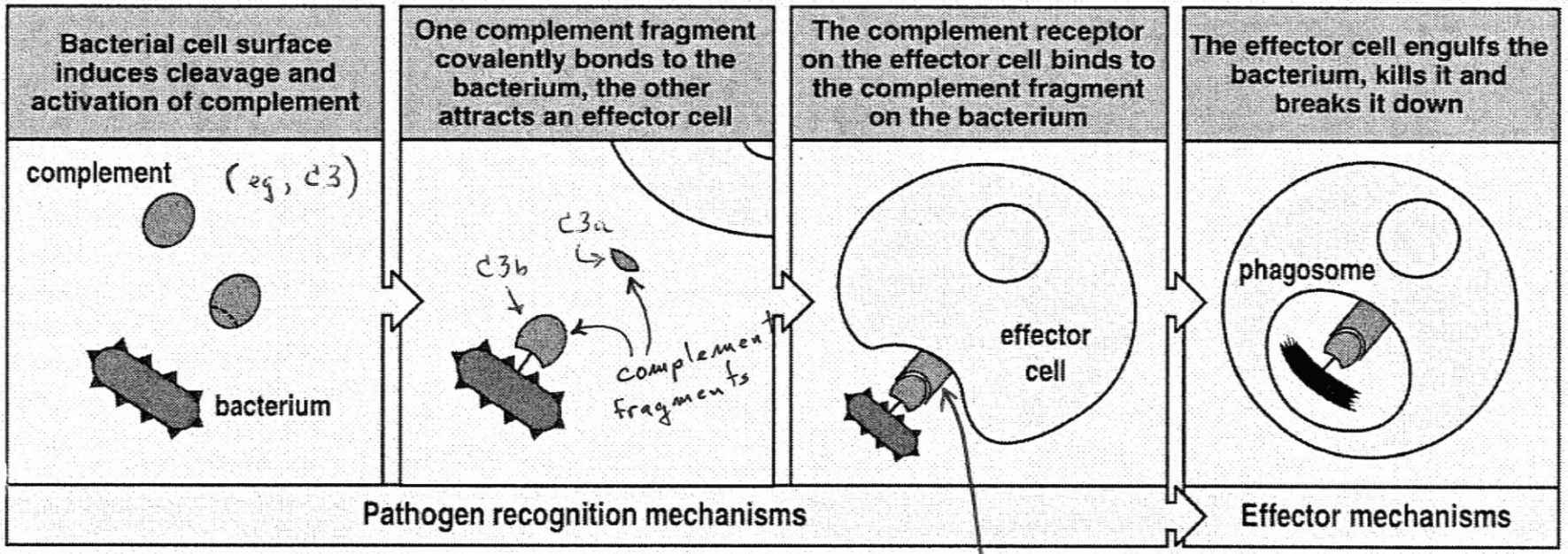
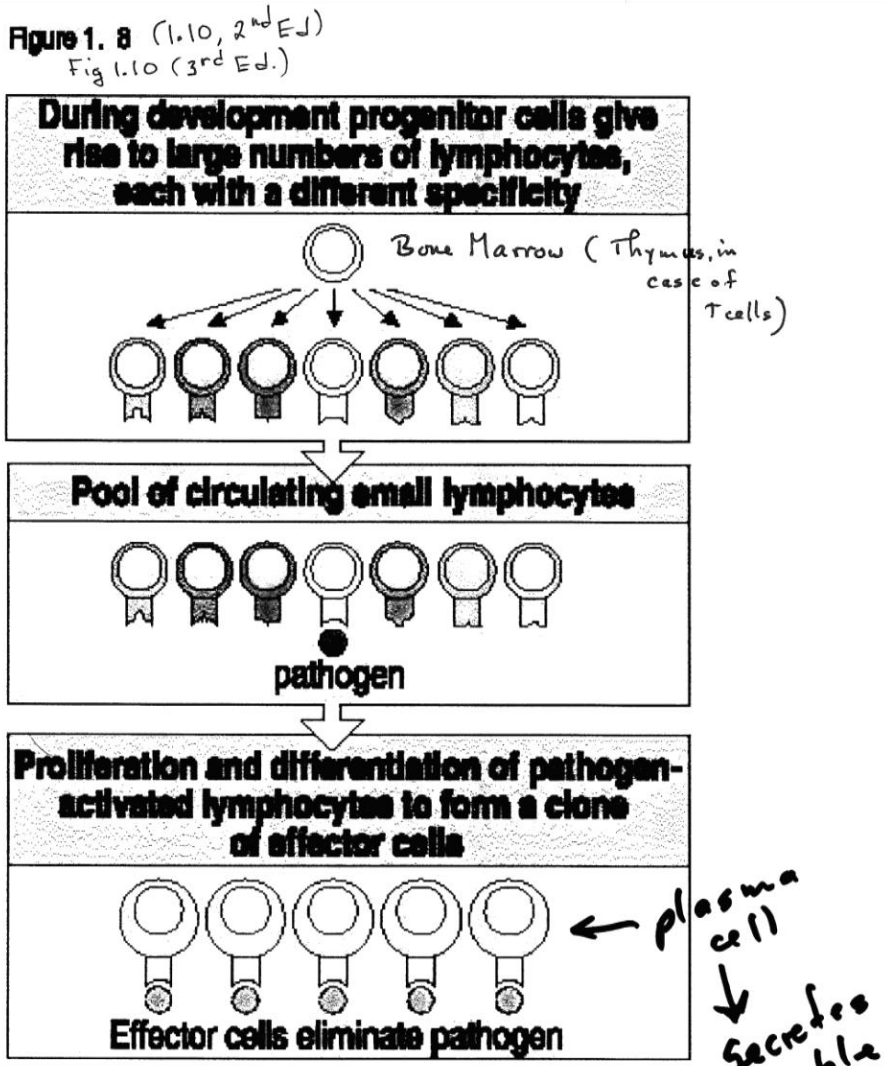


Figure 1-5 The Immune System, 2/e (© Garland Science 2005)

Complement Receptor (Binding to complement fragment initiates phagocytosis.)

Adaptive Immunity



Adaptive Immunity & Clonal Selection

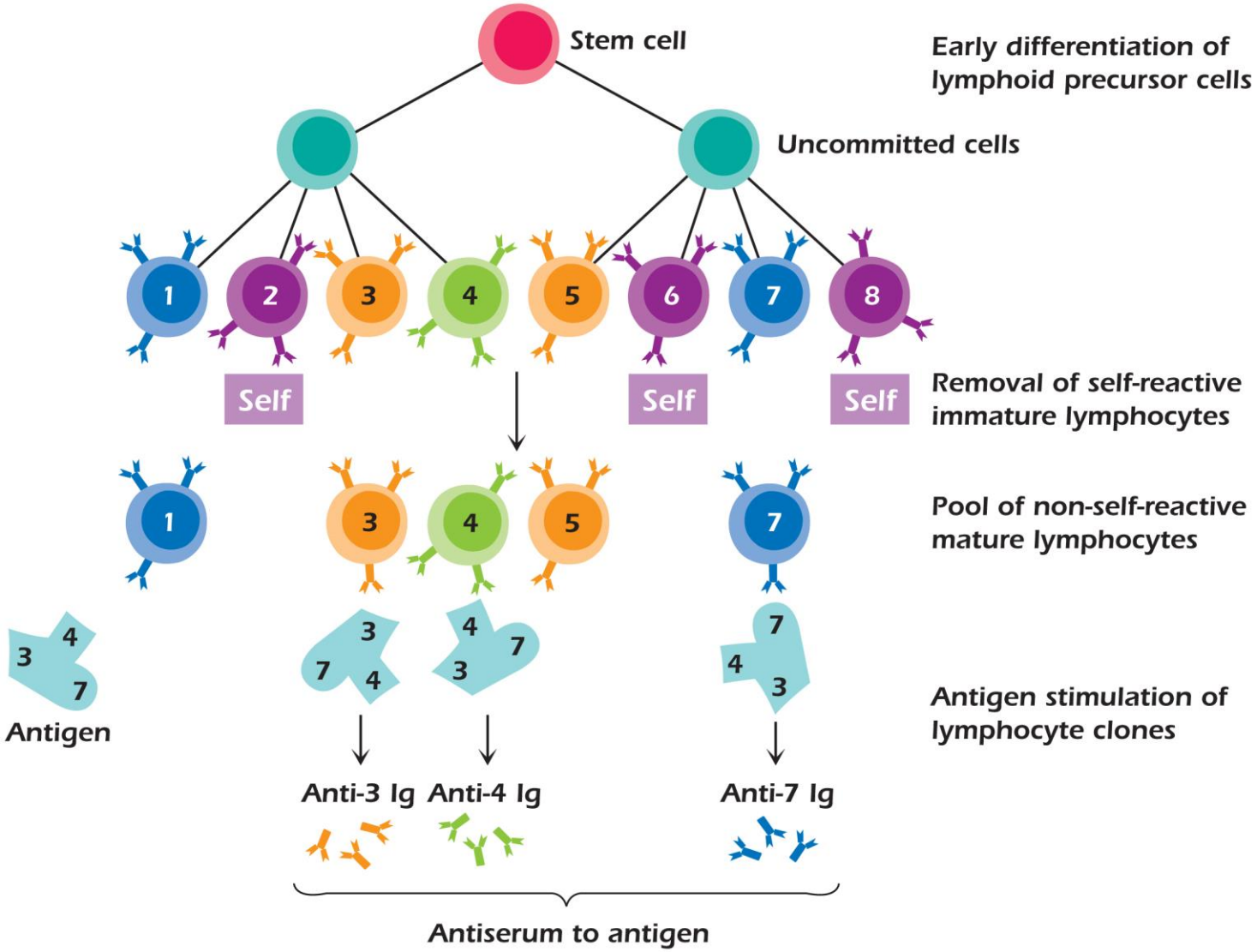
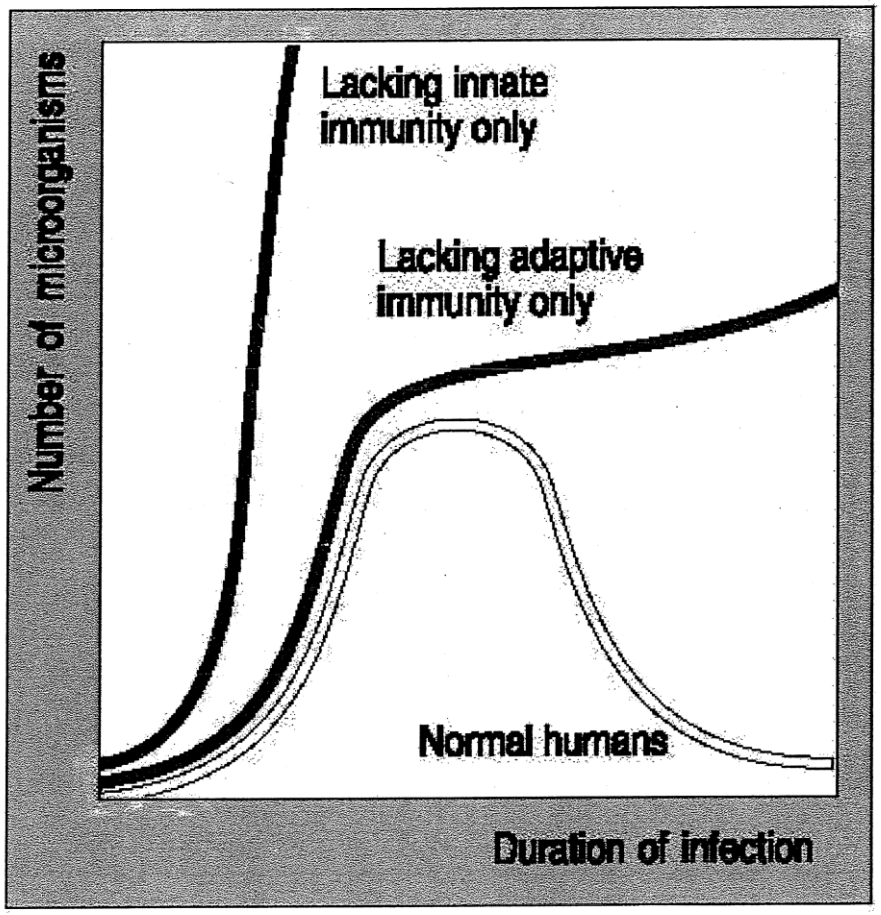


FIGURE 1.1. Clonal selection theory of B cells leading to antibody production

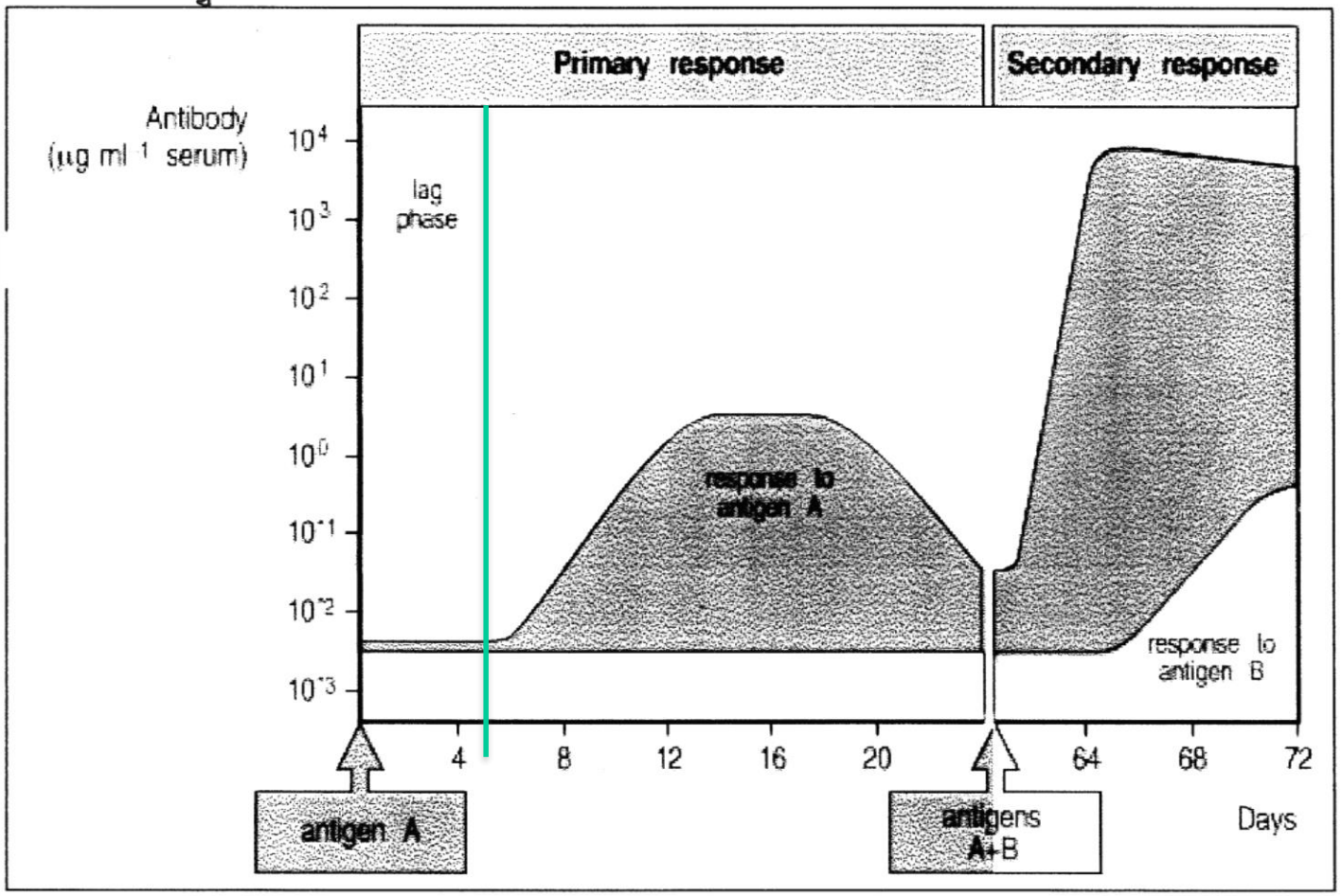
Innate *vs* adaptive immunity

	innate	adaptive
self / non-self discrimination	present, reaction is against foreign	present, reaction is against foreign
lag phase	absent, reponse is immediate	present, response takes at least a few days
specificity	limited, the same response is mounted to a wide variety of agents	high, the response is directed only to the agents that initiated it.
diversity	limited, hence limited specificity	extensive, and resulting in a wide range of antigen receptors.
memory	absent, subsequent exposures to agent generate the same response	present, subsequent exposures to the same agent induce amplified reponses



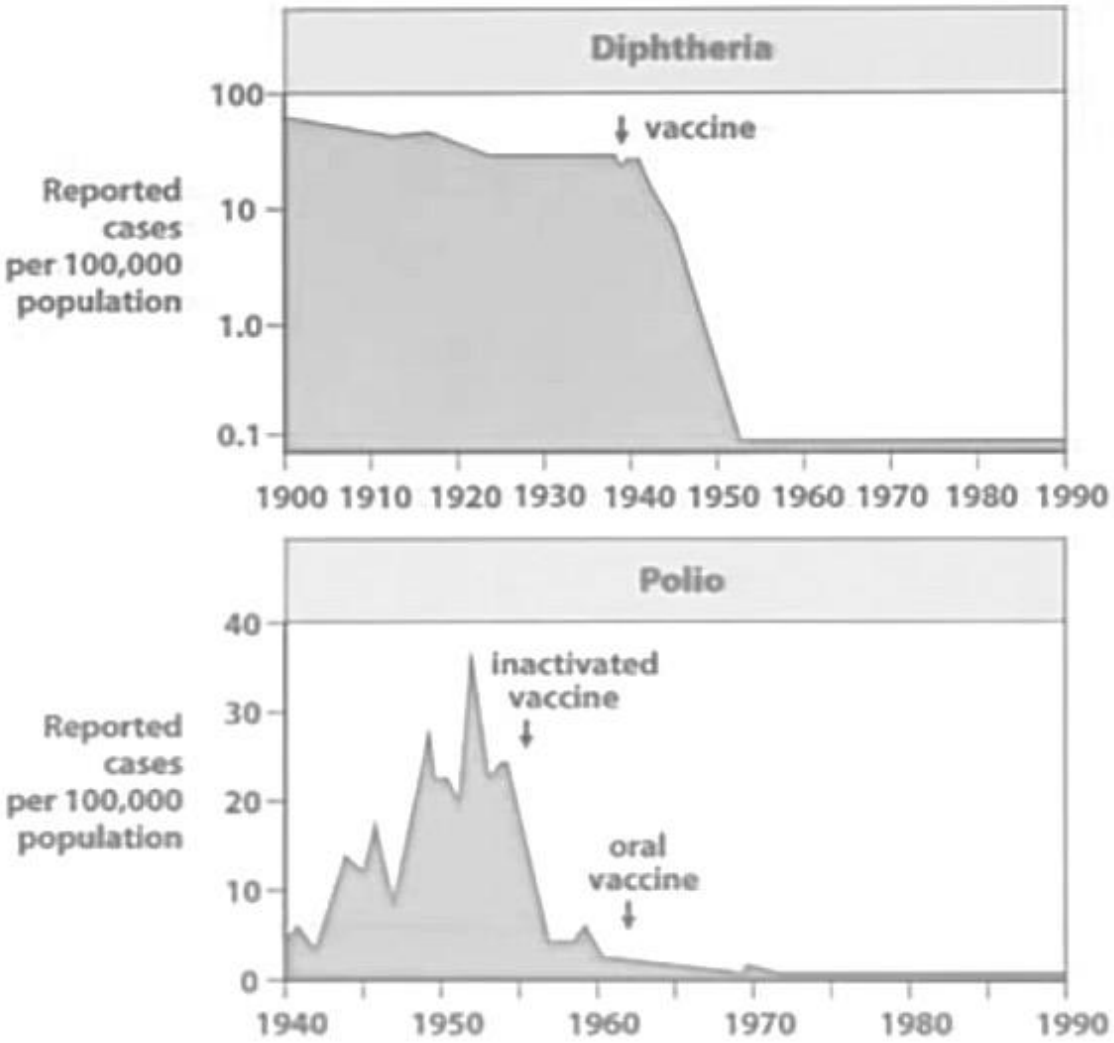
Immunological Memory

3rd Ed. Fig 1.26



(Janeway, Fig 1.19)

Vaccines


Diphtheria
Reported cases per 100,000 population
100
10
1.0
0.1
vaccine
1900 1910 1920 1930 1940 1950 1960 1970 1980 1990
Polio
Reported cases per 100,000 population
40
30
20
10
0
inactivated vaccine
oral vaccine
1940 1950 1960 1970 1980 1990