Immune system is important!

- Infection
- Allergy
- Autoimmunity
- Transfusions/transplantation
- Cancer
- Vaccines

Extensive work still required to fully understand our immune system

Emerging Pathgons

War with Superbugs

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Obama battles 'superbugs' with national plan

By Sandee LaMotte, CNN
Updated 5:11 PM ET, Fri March 27, 2015

President Barack Obama announces a five-year plan to fight antibiotic-resistant bacteria.

Top stories


The most-visited city in the world is ...

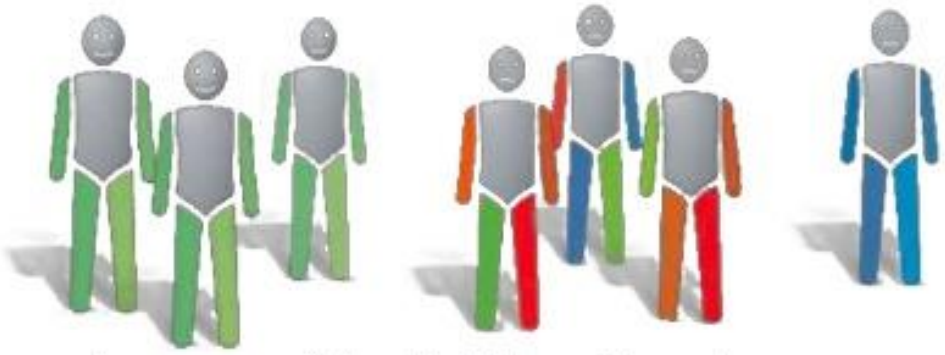

Woman learns Nazi grandpa responsible for deaths of 8,000

Personalized Medicine

Personalized Medicine

"is the tailoring of medical treatment to the individual characteristics of each patient"

The Age of Personalized Medicine



"The science of individualized prevention and therapy"

National Institute of Health

Goal of the Course

- Name and describe the principal organs, cells, and molecules of the immune system
  - understand their function
- Describe the process of immunity
- Predict the consequences of a deficiency in one particular component of the immune system
- Explain how abnormal immune function can cause disease
  - understand the regulatory controls of the immune system

Outline

- Definition of immunology and pathogen
- History of Immunology
- Branches of the immune system
- Evolution of the immune system

IMMUNOLOGY

Immunology is the study of the body's defense against infection

Most infections are cleared without noticeable symptoms.

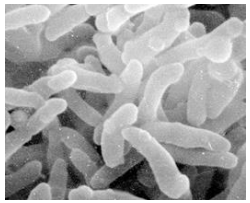
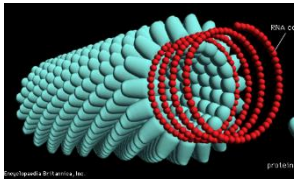
Roles of Immune System

- Maintaining homeostatic tissue functions
  - Fight pathogens
  - Repair tissue injury
  - Tolerate commensal microbiome

PATHOGEN

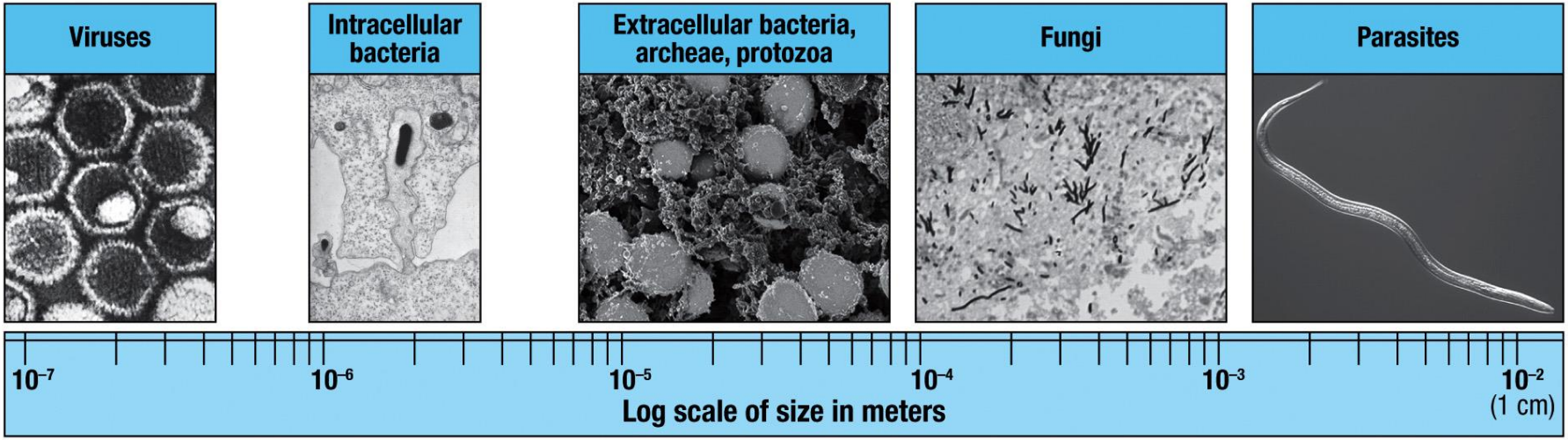
Pathogen is an organism that can induce a pathology (i.e. disease).

Examples of Pathogens

Description	Year	Pathogen	Discovered/Described	Intra/extracellular
Parasite	1500bc	Helminth worms	Ebers papyrus, Egypt	Extracellular
				
Bacteria	1676	*Bacterium*	van Leeuwenhoek	Intra/extracellular
			Father of microbiology	
Toxin	1883	Diphtheria	Roux	Intra/extracellular
				
Virus	1892	Tobacco mosaic	Ivanovsky	Intracellular
	1935	Tobacco mosaic (electron microscope)	Stanley	

Encyclopedia Britanica
http://microbewiki.kenyon.edu/index.php/Corynebacterium
Dennis Kunkel Microscopy, 2001
http://typesofparasites.com/images/parasite_helminth_worm.jpg

Scale of Pathogens



(a): CDC/Dr. Fred Murphy; Sylvia Whitfield; (b): Daniel A. Portnoy; (c): CDC; (d): CDC/Dr. Lucille Georg; (e): Courtesy of James Lok

Manifestations of Infection

- Fever
- Abscess/pus
- Rash
- Cough
- Rhinorrhea (runny nose)
- Diarrhea
- Muscle ache
- Sepsis (systemic inflammation)
- Increased leukocyte (white cell) count

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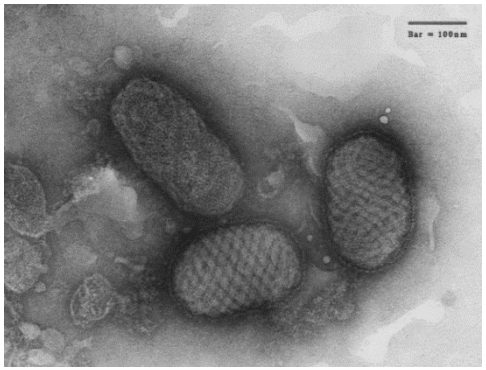
Early Immunology

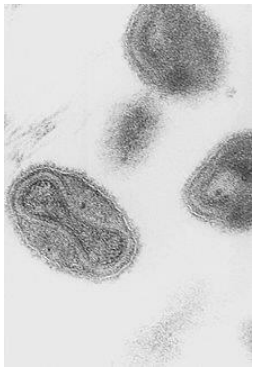
3000bc	Mesopotamia	Fever
2000bc	Egypt, China	Recognition of “adaptive” protection
400bc	Hippocrates	Anatomic identification of organs
25ad	Celsus	Four cardinal signs of inflammation (redness, swelling, heat, pain)
1000s	Sung Dynasty	“Snuff” variolation for smallpox
1600s	Fabricius	Bursa of birds described (site of hematopoiesis)
	Peyer	Lymphoid tissue identified in small intestine
1700s	Lady Montagu	Innoculation with material from smallpox lesions (based on inoculation practice in Constantinople)

Smallpox

The success story!

Smallpox *(variola major; variola minor)*



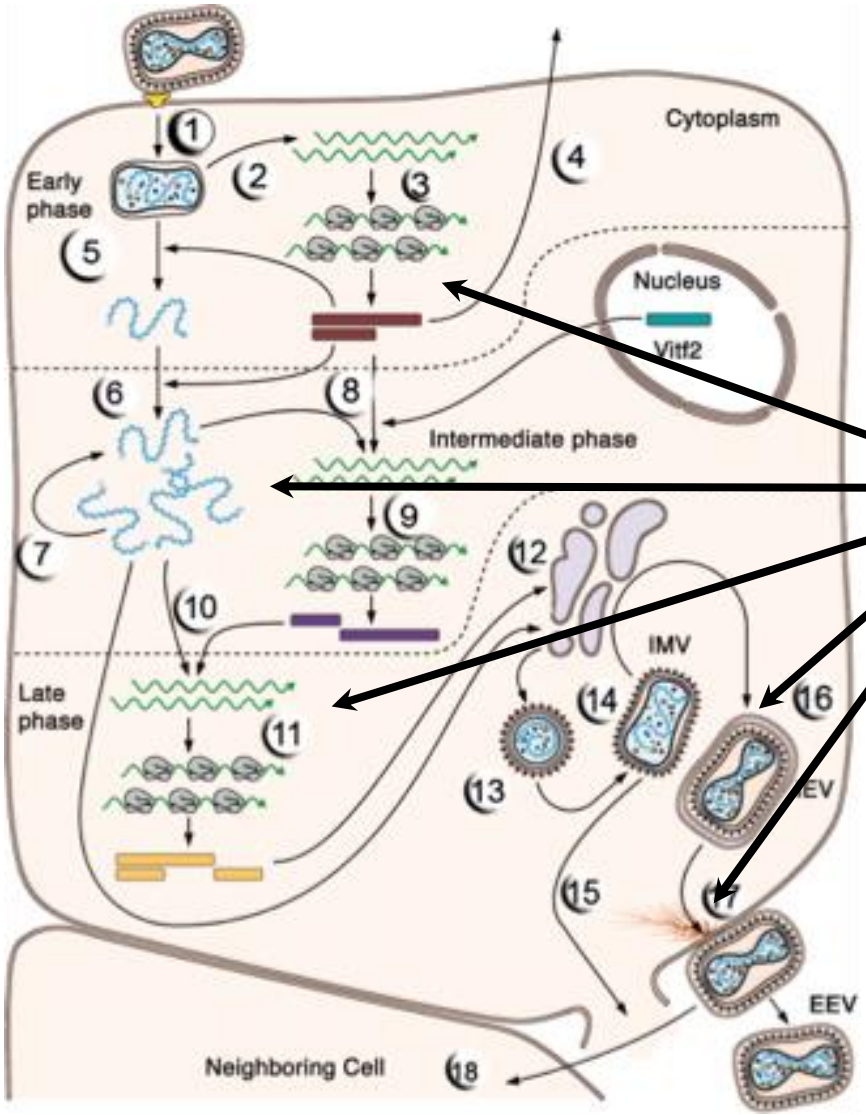


Smallpox pustule gauge, c 1920

Genome:	dsDNA
Natural host:	human (only known natural host)
Spread:	aerosols, scabs, bedding, clothing, etc.
Incubation period:	7-17 days
Symptoms:	fever, rash, vomiting, back/headache, delirium
Mortality (variola major):	30-35% [hemorrhagic smallpox (rare): 100%]
Mortality (duration):	~10-16 days post infection
Cause of death:	multi-organ involvement, severe viremia; uncontrolled immune response
Vaccination:	available; disease eradicated in 1980

https://eee.uci.edu/clients/bjbecker/PlaguesandPeople/lecture13.html

Reproductive Cycle of Pox Virus



Disruption of cellular functions

Harrison S C et al. PNAS 2004;101:11178-11192

Shitala: Hindu Goddess of Smallpox

(and its cure)

1) Broom (to sweep-up germs)

2) Fan (to collect germs)

4) Water (to purify the house)

3) Bowl (to hold germs)

****Also carries "lentils" that turned into smallpox germs**

Variolation

Dried scab inoculation-attenuated virus?
Natural course of infection
Not all always successful
2-3% mortality rate
Spread of the disease

Long long time ago

FIGURES SHOWING VACCINATION PUSTULES

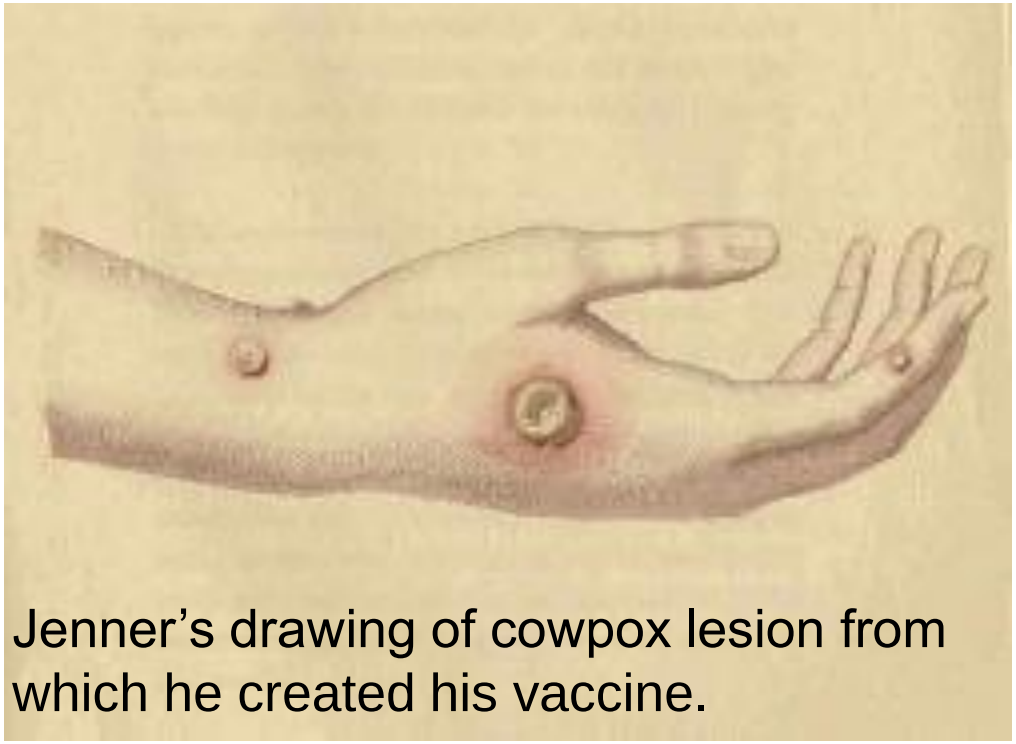
From a Chinese work on Vaccination

Lady Mary Wortley Montagu

Father of Immunology

1796 **Edward Jenner** **cowpox vaccine against smallpox**

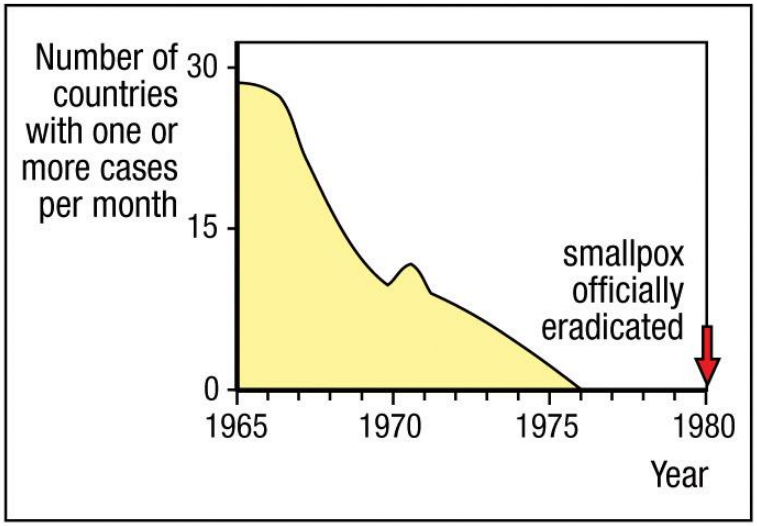
Medical Historical Library, Harvey Cushing/John Hay Whitney Medical Library, Yale University

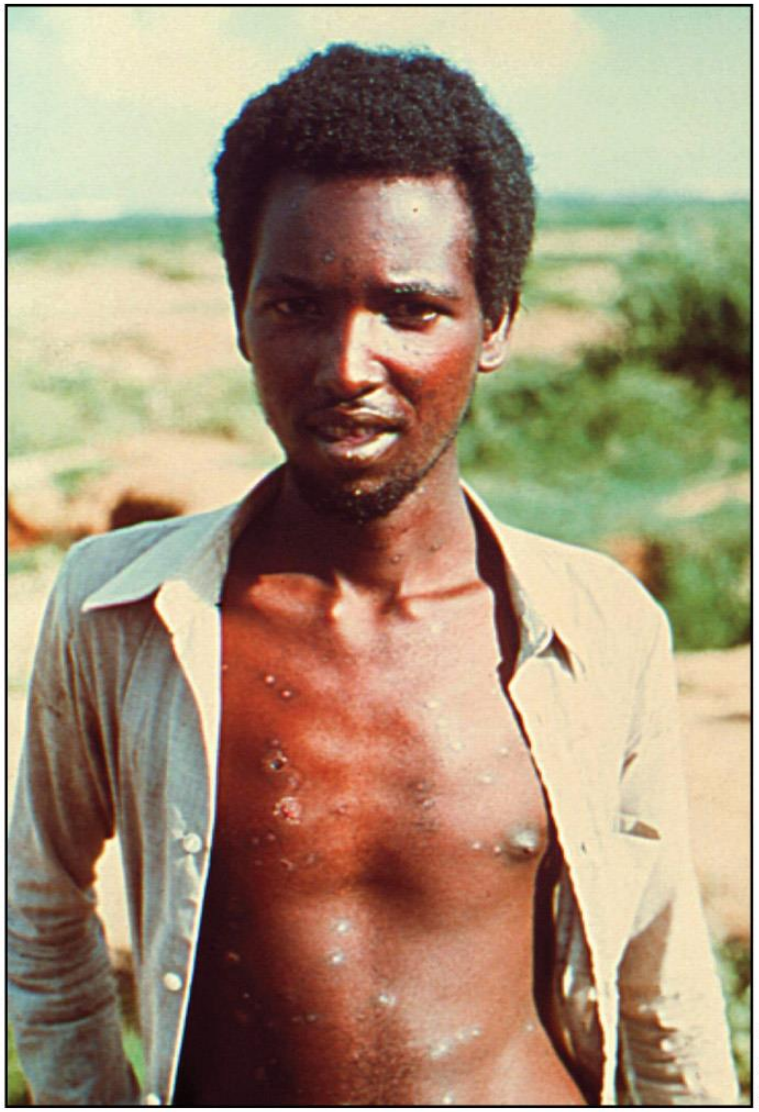


Jenner's drawing of cowpox lesion from which he created his vaccine.

Almost 100 years before the infectious theory of disease was verified by Koch (1890)

Reported Smallpox Cases (1967-1976)





Getty Images

Declaration of Smallpox Eradication (1979)

نحن أعضاء اللجنة العالمية للإشهاد الرسمى باستئصال
الجدرى نشهد بأنه قد تم إستئصال الجدرى من العالم.

WE, THE MEMBERS OF THE GLOBAL COMMISSION FOR THE CERTIFICATION OF SMALLPOX ERADICATION, CERTIFY THAT SMALLPOX HAS BEEN ERADICATED FROM THE WORLD.

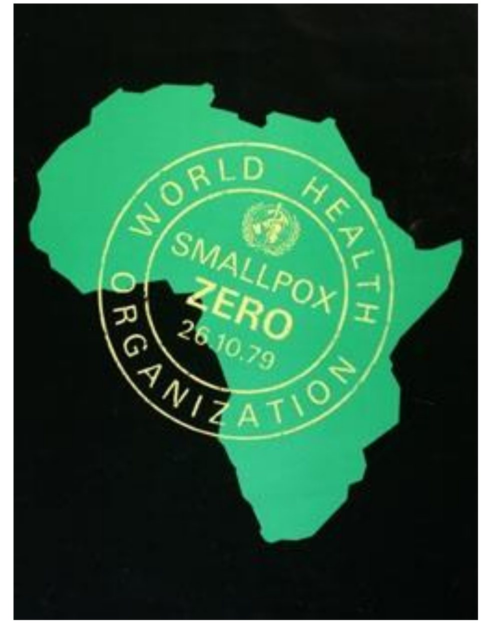
NOUS, MEMBRES DE LA COMMISSION MONDIALE POUR LA CERTIFICATION DE L'ÉRADICATION DE LA VARIOLE, CERTIFIONS QUE L'ÉRADICATION DE LA VARIOLE A ÉTÉ RÉALISÉE DANS LE MONDE ENTIER.

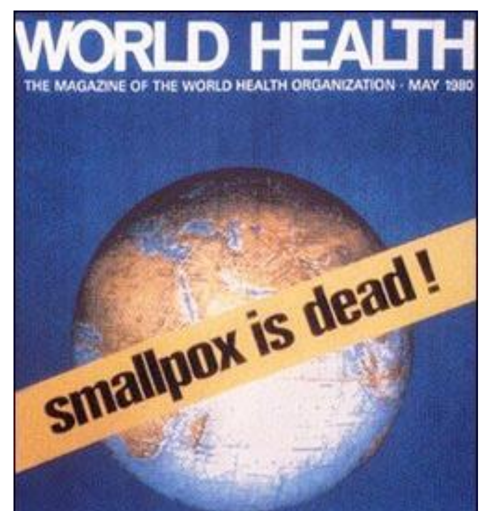
我们，全球扑灭天花证实委员会委员，
证实扑灭天花已经在全世界实现。

МЫ, ЧЛЕНЫ ГЛОБАЛЬНОЙ КОМИССИИ ПО СЕРТИФИКАЦИИ ЛИКВИДАЦИИ ОСПЫ, НАСТОЯЩИМ ПОДТВЕРЖДАЕМ, ЧТО ОСПЫ В МИРЕ БОЛЬШЕ НЕТ.

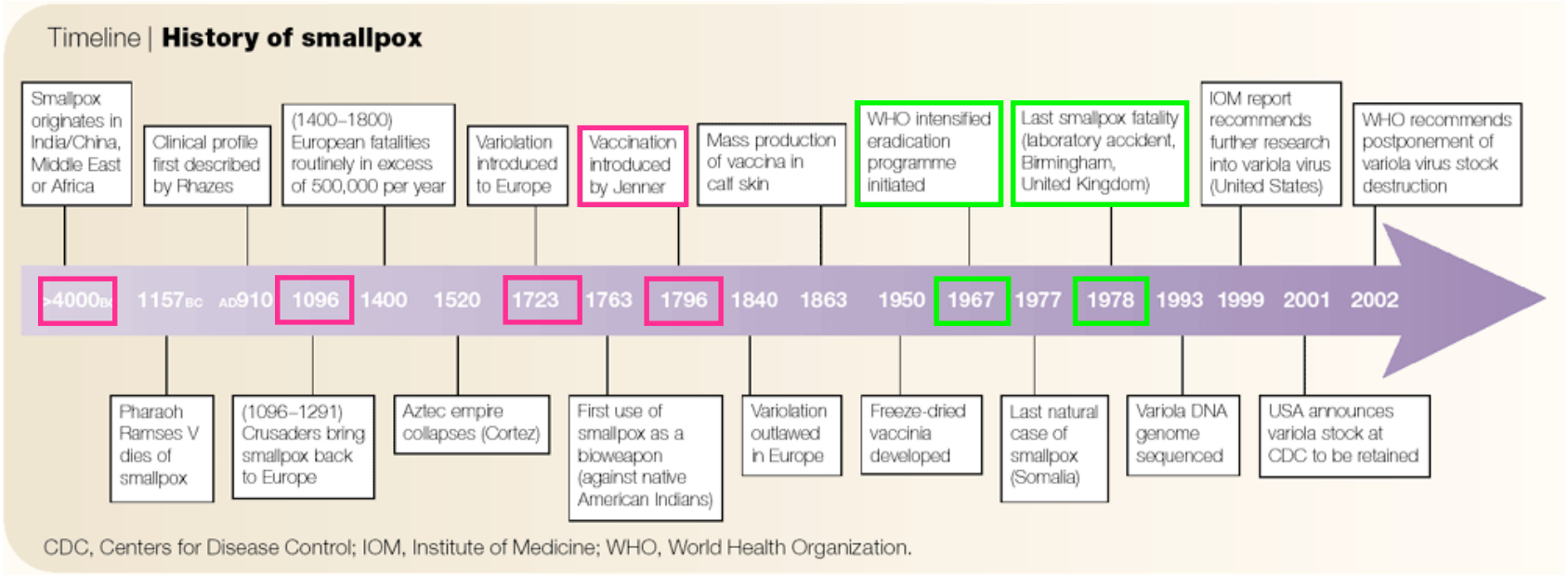
NOSOTROS, MIEMBROS DE LA COMISION MUNDIAL PARA LA CERTIFICACION DE LA ERRADICACION DE LA VIRUELA, CERTIFICAMOS QUE LA VIRUELA HA SIDO ERRADICADA EN TODO EL MUNDO.

Genève, le 9 décembre 1979





Timeline of Smallpox Eradication



Question

- Who is the father of immunology? Why?

Founders of Immunology

1880s	Pasteur	attenuated live vaccines (cholera, rabies)
	Metchnikoff	cellular theory of immunity (phagocytosis)
1890s	von Behring & Kitasato	antiserum/passive vaccination (tetanus/diphtheria antitoxin)
	Buchner, Pfeiffer, Bordet	complement (bacteriolysis and humoral immunity)
	Ehrlich	cell surface immunoglobulin (antibodies), circulatory immunoglobulin (humoral immunity) histological stains
1900s	Landsteiner	A,B & O blood groups (transfusions)
	Portier & Richet	anaphylaxis (life-threatening allergic reaction)
	von Pirquet	allergy (hypersensitivity reaction; *allos*-other, *ergon*-reaction)
	Carrel & Guthrie	first successful organ transplantation (kidney)
1920s	Fleming	penicillin

Founders of Immunology

1940s	Medawar & Fenner	immunological tolerance (organ transplantation)
1950s	Bovet	antihistamines (allergy drugs)
	Simonsen & Dempster	graft-versus-host
	Burnet	clonal selection theory of antibody production
	Isaacs & Lindemann	interferon (cytokines)
1960s	Edelman & Porter	antibody structure, cellular immunity
	Miller	role of thymus in (T cell maturation)
	Claman	bursa of Fabricius (B) and thymus (T) cells
1970s	Tonegawa & Hozumi	immunoglobulin genetics (B lymphocyte diversity)
1980s	T. Mak	T cell receptor
	Zinkernagel & Doherty	antigen recognition by T cells (MHC restriction)
	Hood	T cell receptor genes
1990s	Nomura	Toll-like receptors
2021	Kariko & Weissman	mRNA vaccine

Outline

- Definition of immunology and pathogen
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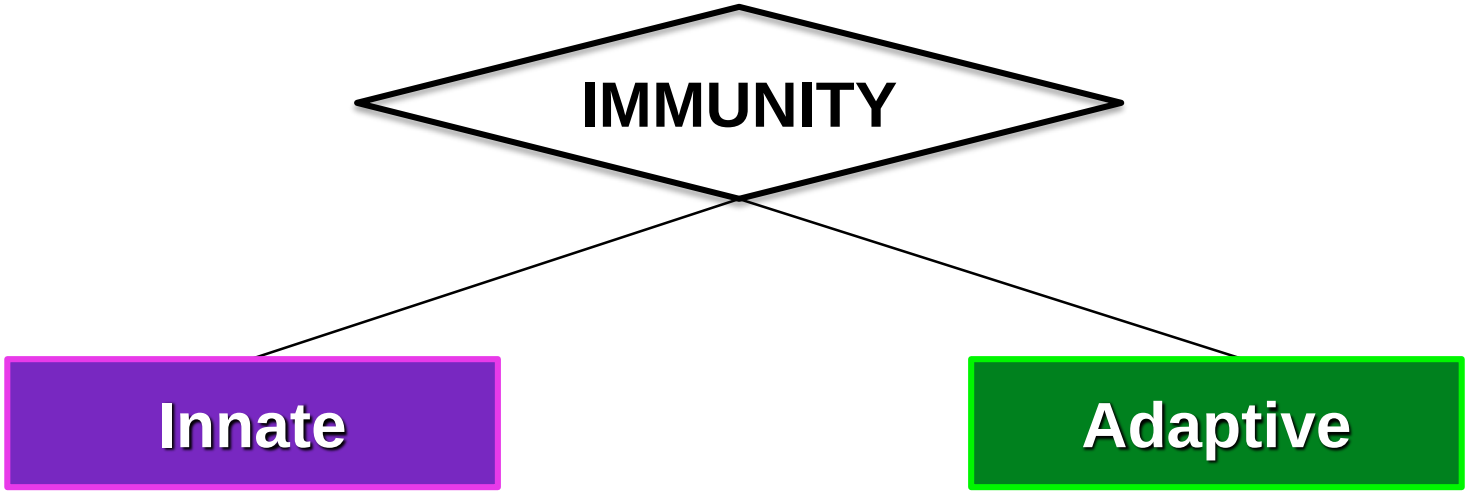
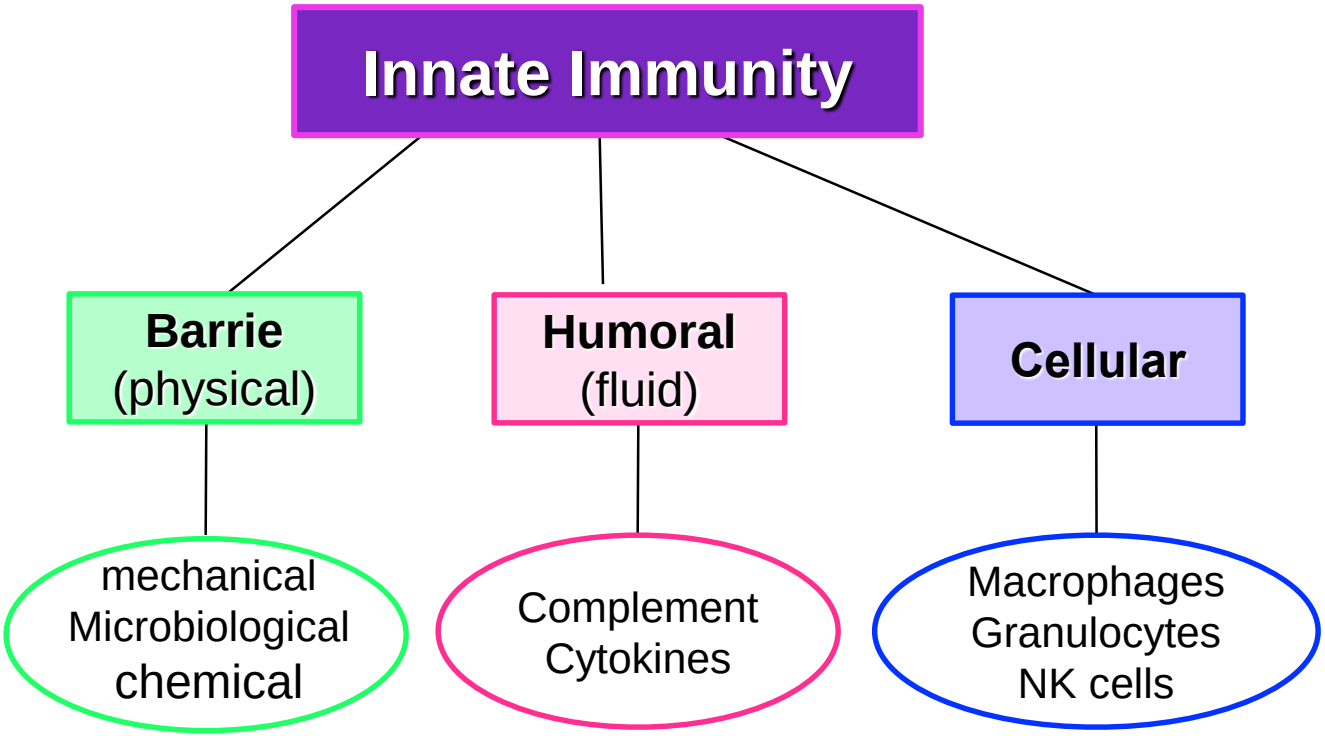
Branches of the Immune System



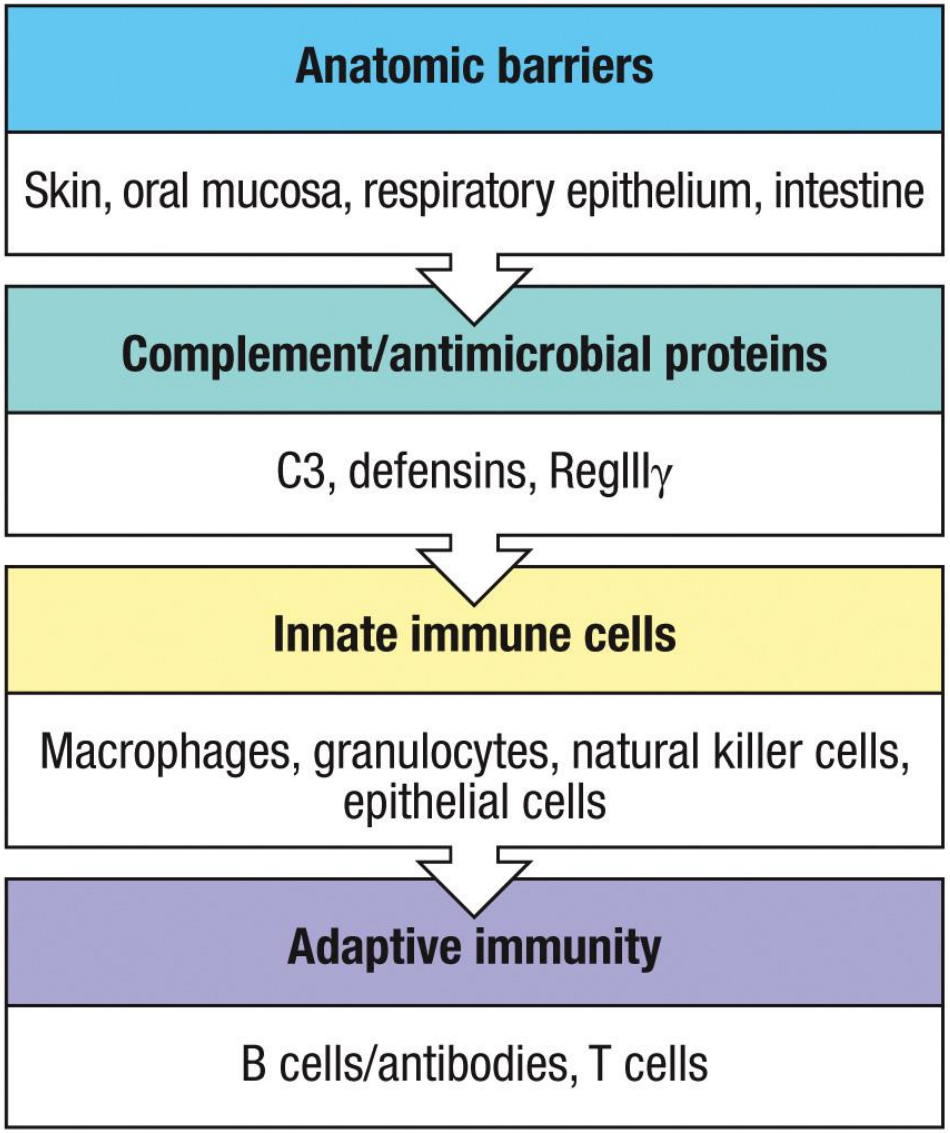
Innate immunity: nonspecific defense mechanisms that come into play immediately after a pathogen's appearance in the body.

Adaptive immunity: antigen-specific immune response

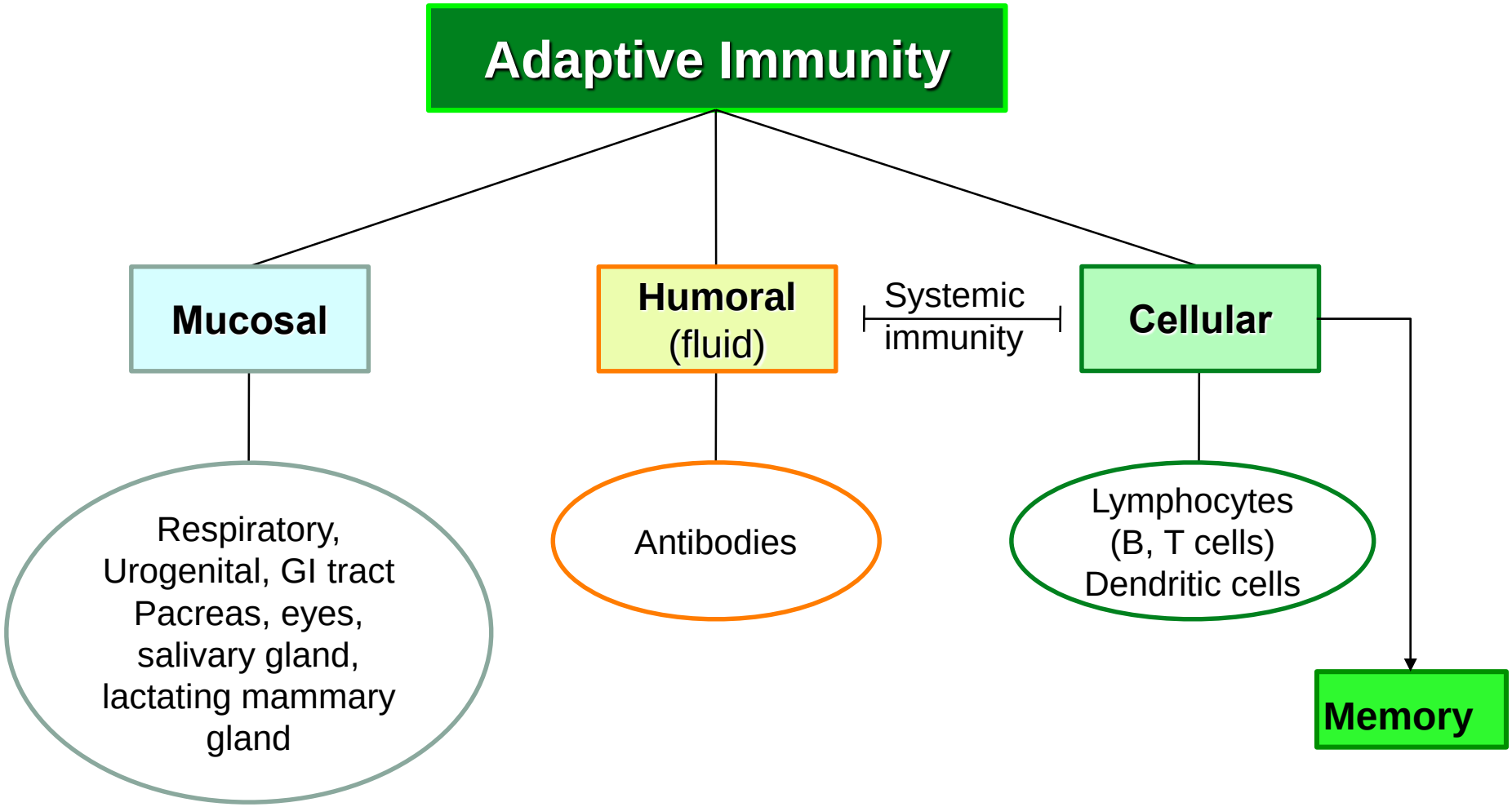
Innate Immune System



Barriers: The First Line of Defense



Adaptive Immune System



Antigen

Antigen

antibody generation

Any substance that causes an immune system to produce antibodies against it.

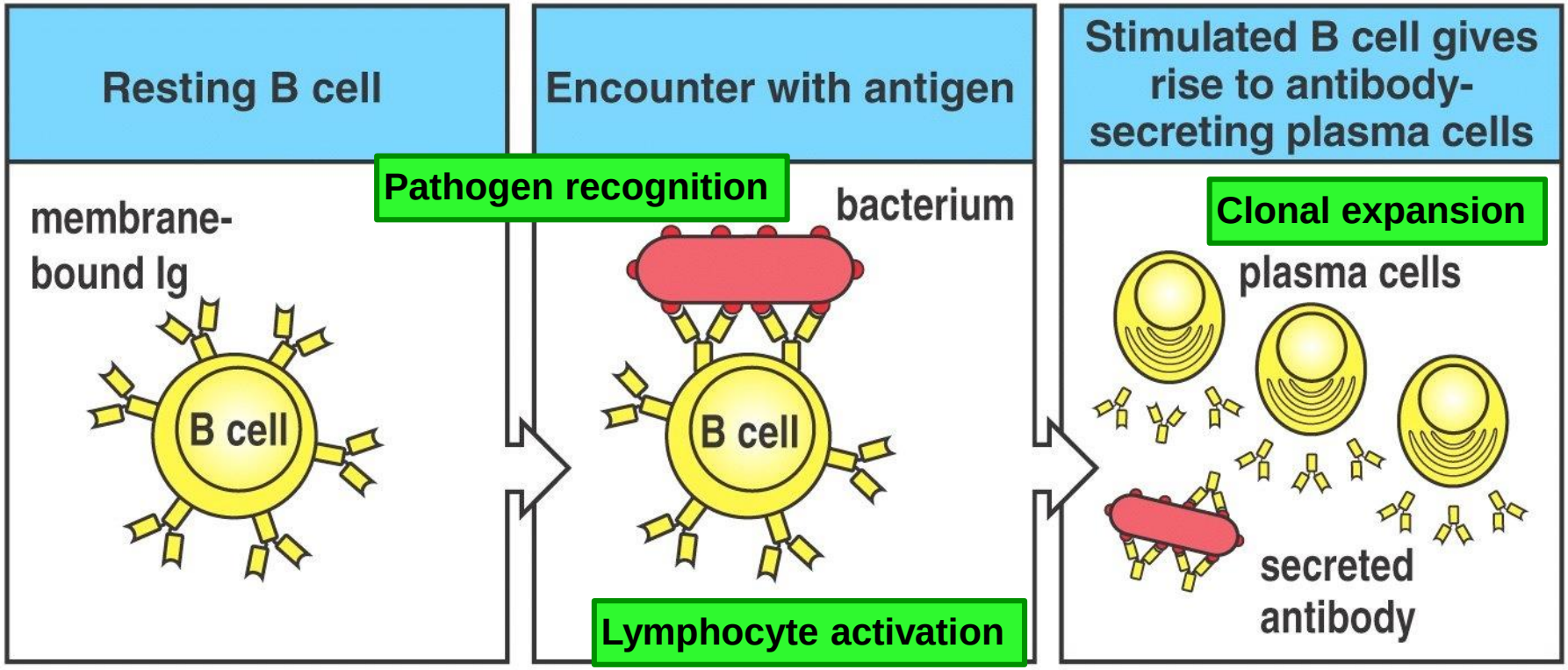
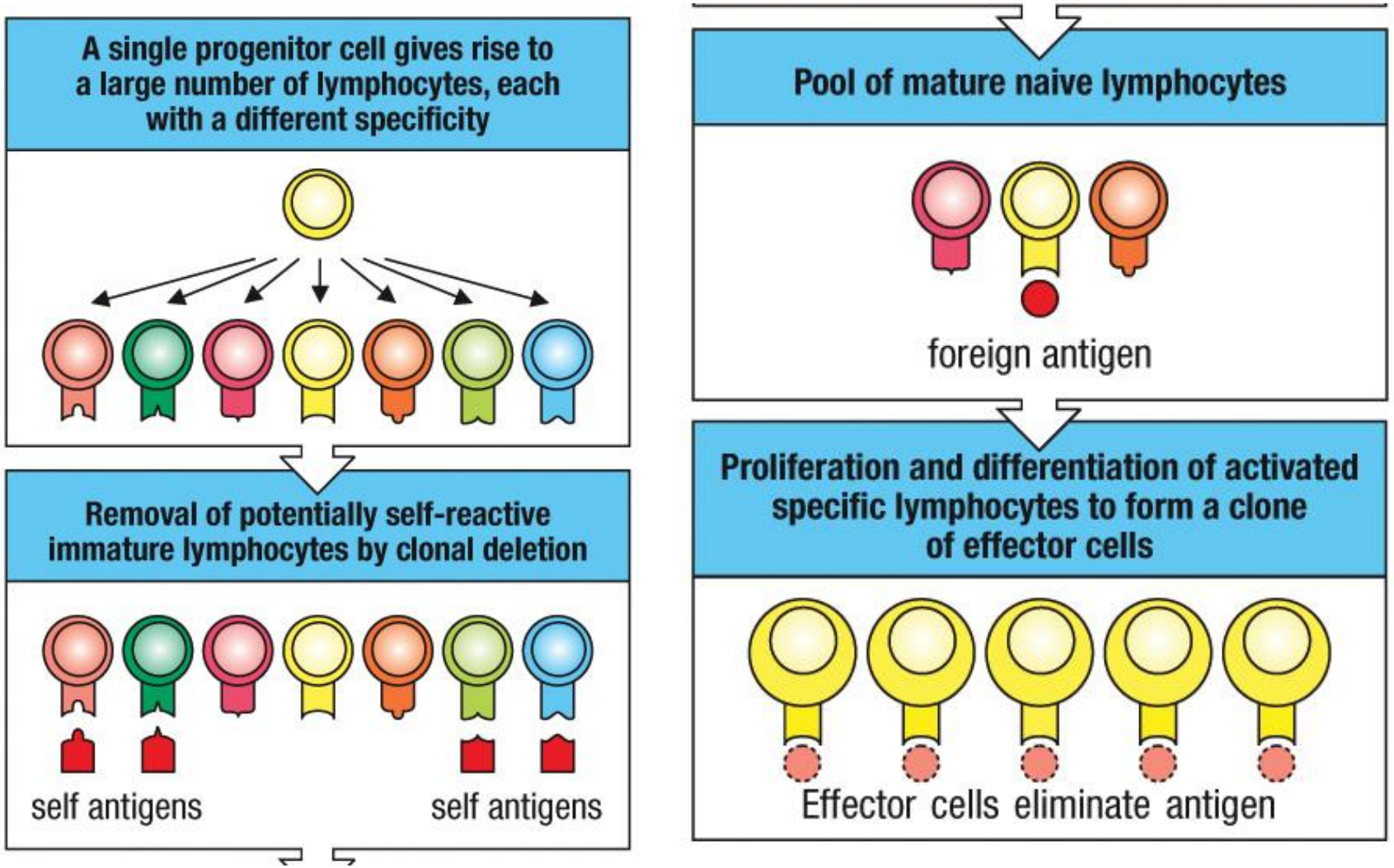


Figure 2-1 The Immune System, 2/e (© Garland Science 2005)

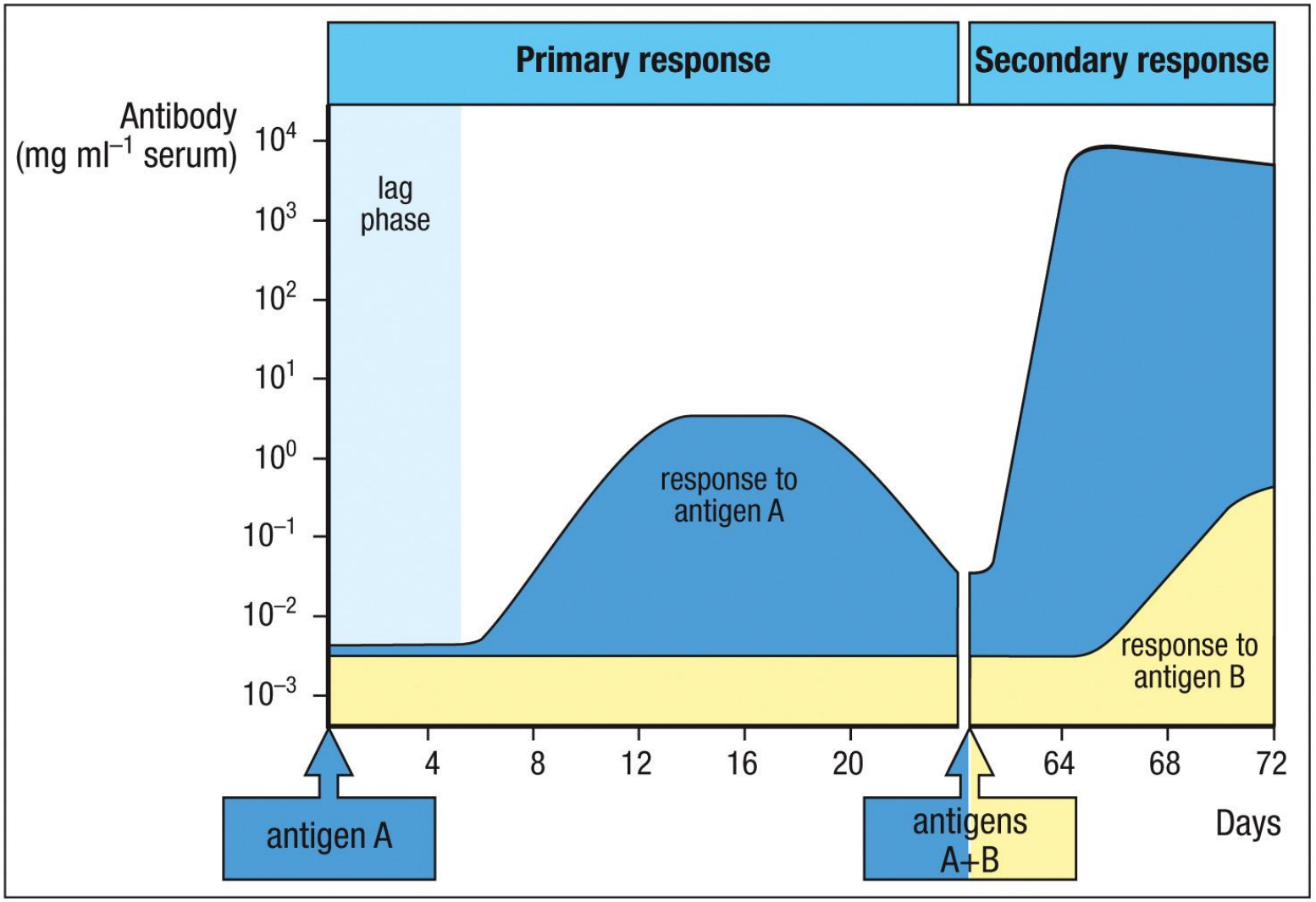
Adaptive Immunity



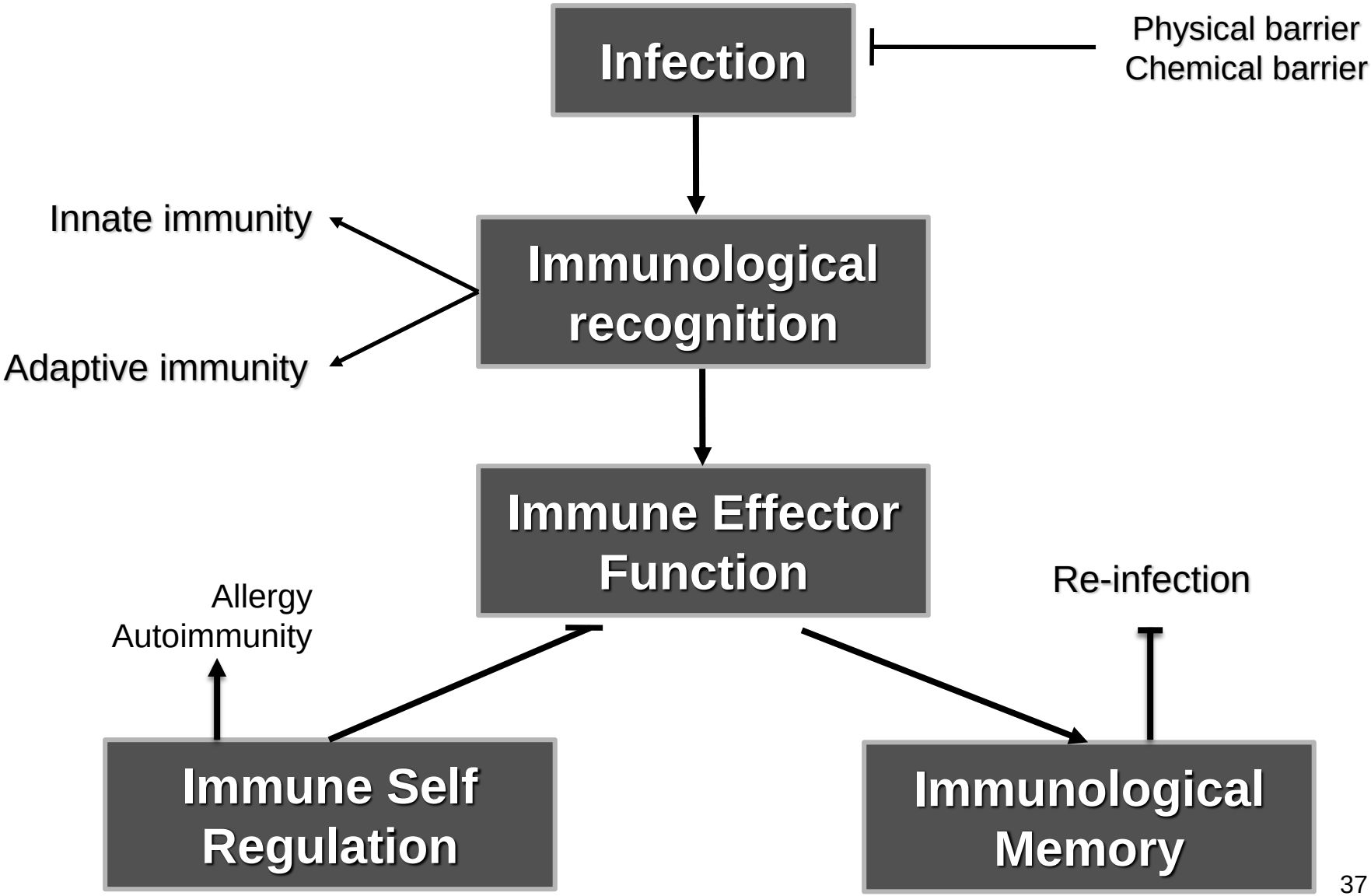
Clonal Selection: Heart of Adaptive Immunity

Postulates of the clonal selection hypothesis
Each lymphocyte bears a single type of receptor with a unique specificity
Interaction between a foreign molecule and a lymphocyte receptor capable of binding that molecule with high affinity leads to lymphocyte activation
The differentiated effector cells derived from an activated lymphocyte will bear receptors of identical specificity to those of the parental cell from which that lymphocyte was derived
Lymphocytes bearing receptors specific for ubiquitous self molecules are deleted at an early stage in lymphoid cell development and are therefore absent from the repertoire of mature lymphocytes

Immunological Memory



Stages of the Immune Response



Innate vs. Adaptive Immunity

Preformed

Developed during infection

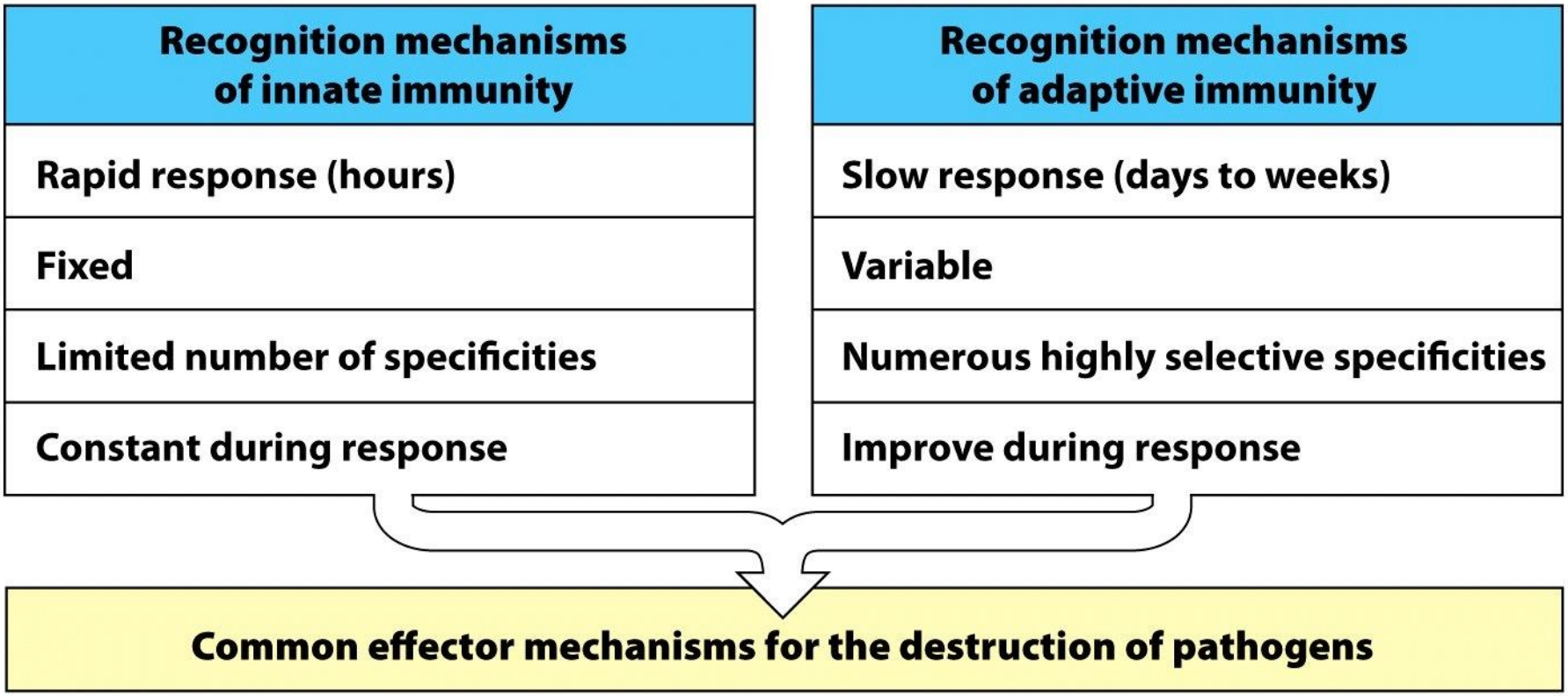


Figure 1.9 The Immune System, 3ed. (© Garland Science 2009)

Question

- What is the difference and similarity of innate and adaptive immunity?

Outline

- Definition of immunology and pathogen
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Evolution of the Immune System

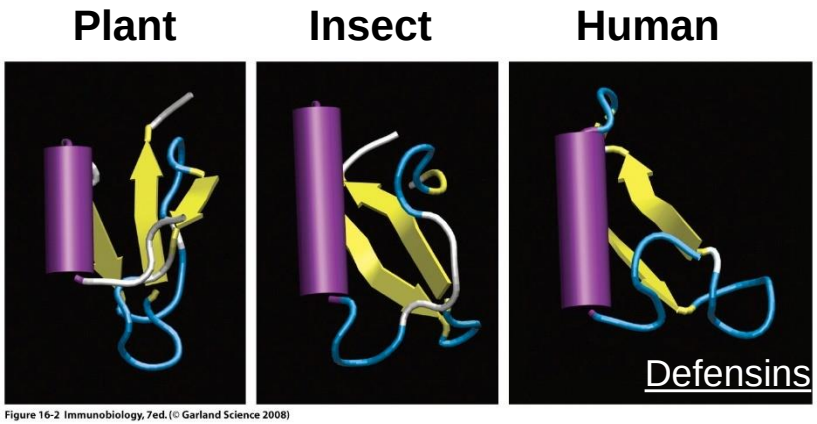

Figure 16-2 Immunobiology, 7ed. (© Garland Science 2008)

Receptor diversification

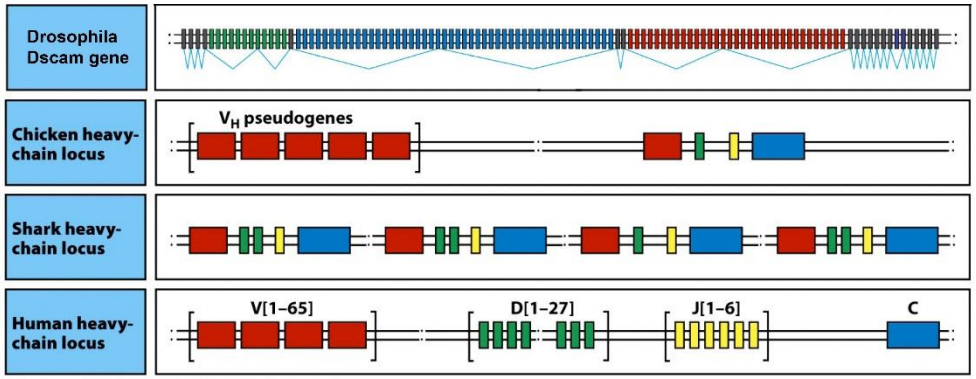

Figure 16-10 Immunobiology, 7ed. (© Garland Science 2008)
Figure 16-7 Immunobiology, 7ed. (© Garland Science 2008)

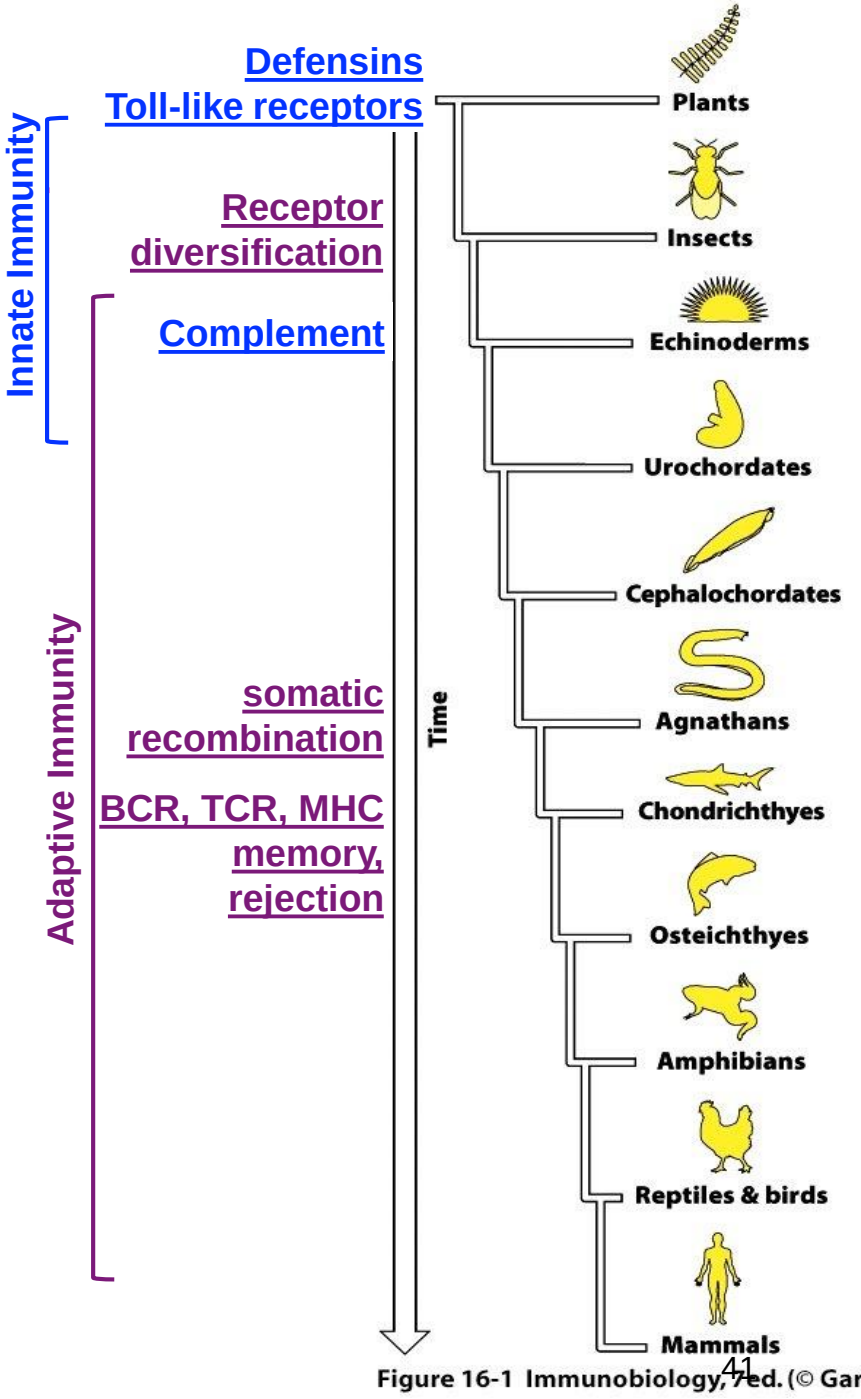

Figure 16-1 Immunobiology, 7ed. (© Gar