CAMPBELL BIOLOGY: CONCEPTS & CONNECTIONS,
NINTH EDITION, GLOBAL EDITION
PowerPoint Lectures

Chapter 24
The Immune System

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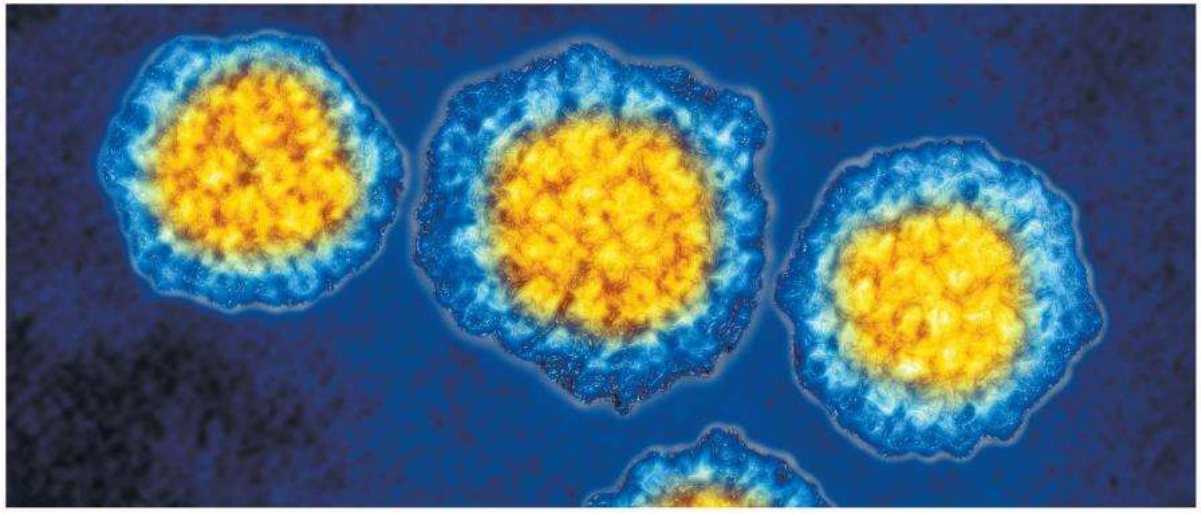
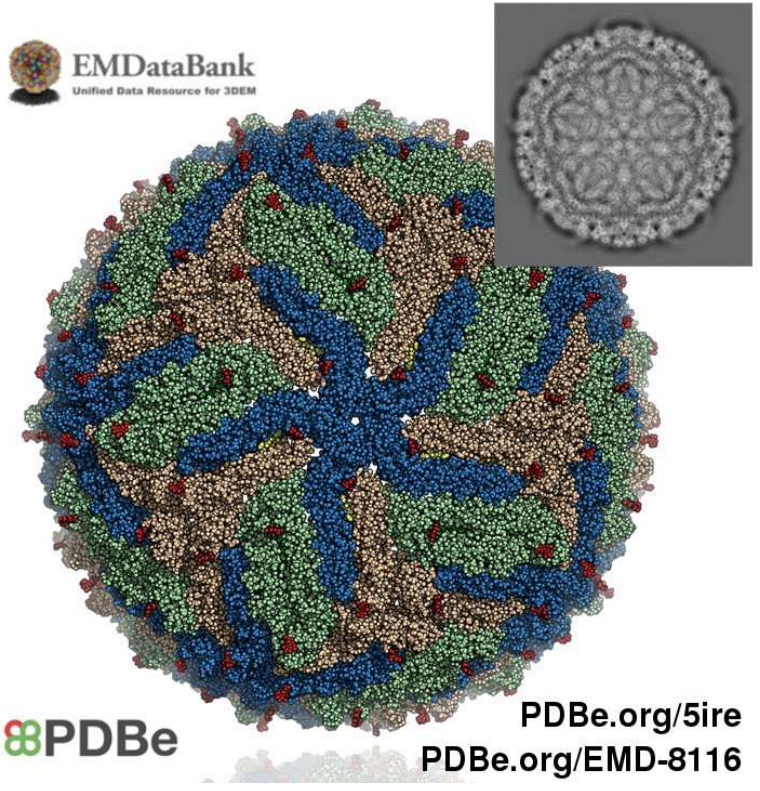
Introduction

- Viruses can cause cancers.
- In the 1980s, scientists discovered that the sexually transmitted human papillomavirus (HPV) caused
  - essentially all cervical cancers and
  - most cases of anal cancers.
- In the last several years two HPV vaccines have been developed:

  Gardasil (2006) and Cervarix (2009)



http://www.ebi.ac.uk/pdbe/about/news/structure-zika-virus-revealed



- Experts believe that for an HPV vaccine to significantly reduce the incidence of cancer it must provide long-term immunity (protection), ideally for three to four decades.
  - Without long-term protection, it might simply postpone susceptibility to the infection.
- How long does immunity from HPV last with Gardasil and Cervarix vaccination?
  - The short answer is we do not know yet.
  - The decades worth of data on the long-term effects of the vaccines are not available.

Safety?

口服輪狀病毒疫苗新北補助低收戶約1千人可受惠
udn 聯合新聞網 - 2019年5月28日
民進黨新北市議員張志豪昨指出，台北、桃園等縣市都已經補助輪狀病毒疫苗，家長帶著孩子到台北市診所詢問輪狀病毒疫苗，都會被問是否為台北 ...

〈台北都會〉嬰幼兒輪狀病毒疫苗新北將補助中低收
當地來源 - 自由時報電子報 - 2019年5月28日

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大腸直腸癌疫苗，第一階段臨床試驗成功
科技新報 TechNews - 2019年5月25日
令人聞之色變的大腸癌是否能有疫苗問世？根據一項最新癌疫苗在第一階段試驗證實安全，且會刺激免疫系統活化

抗癌新突破！大腸直腸癌疫苗第一階段臨床試驗成功
自由時報電子報 - 2019年5月26日

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New Maine Law Ends Non-Medical Excuses for Avoiding Vaccination
Gizmodo - 2019年5月27日
A woman holds her daughter with other mothers in a hallway, Thursday, May 2, 2019, at the Statehouse in Augusta, Maine, where the Senate ...

Maine Ends Religious And Philosophical Exemptions For Vaccinations
IFLScience - 2019年5月27日

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澎湖B型流感流行衛生局掌握通報施打疫苗
芋傳媒 TaroNews (新聞發布) - 2019年5月28日
澎湖近期出現B 型流感群聚環境小規模流行，公私醫療院縣政府衛生局表示，提供克流感疫苗接種有163 人，並無

抗夏季流感加強教育增購疫苗

Experiment Reveals How to Make Nearly 70% of Vaccine-Hesitant ...
ScienceAlert - 2019年5月21日
A new study has shown it's possible to persuade members of our community who oppose vaccines to change their opinion by confronting them ...

Vaccine Expert: False Information on Web Must Be Stopped
Voice of America - 2019年5月22日

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水痘、麻疹來勢洶洶你家孩子接種的疫苗還有效嗎
Heho健康 (新聞發布) - 2019年5月25日
台北榮民總醫院副院長、家醫科醫師黃信彰表示，水痘、打疫苗，目前水痘、麻疹均有相對的公費疫苗提供兒童施

醫療中心涉違規供應疫苗更揭雪櫃同時存放食物
評論 - on.cc東網 - 2019年5月24日

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獨家／台首件HPV疫苗受害救濟案衛福部決定上訴
中央社即時新聞 - 2019年5月13日
中央社記者陳偉婷台北14日電）一名女孩接種HPV疫苗後決認定無法排除與疫苗的關聯性，衛福部應補償。衛福部

HPV疫苗荒家計會暫停收新症
評論 - on.cc東網 - 2019年5月15日

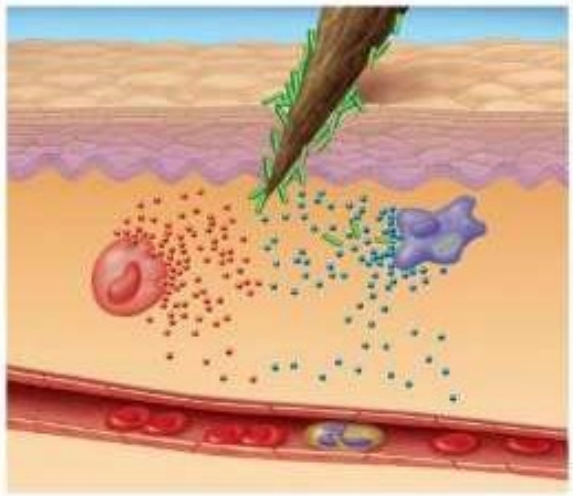
查看全部

Why vaccine hesitancy is a giant threat to global health and the ...
New Statesman - 11 小時前
Even Donald Trump, no stranger to half-assed anti-vaccine messaging, has said that children “have to get their shots”. The world's leading ...

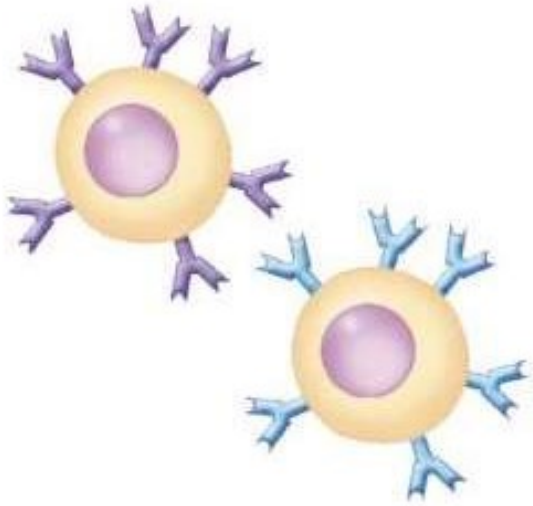
麻疹今年病例近百部分青壯族群疫苗保護力低
新頭殼 - 2019年5月28日
疾管署今（28）日公佈新確診1例國內感染麻疹病例，為北部20多歲男性，專家提醒，麻疹傳染力強，且部分年輕人的疫苗保護力可能已衰退。 疾病管制 ...

Figure 24.0_1

Chapter 24: Big Ideas



Innate Immunity
24.1-24.2



Adaptive Immunity
24.3-24.16

Disorders of the Immune System
24.17-24.18

INNATE IMMUNITY

24.1 All animals have innate immunity 先天性免疫力

- Nearly everything in the environment teems with **pathogens**, agents that cause disease.
- The immune system is the body's system of defenses against agents that cause disease.
- **Innate immunity** is a series of defenses that
  - act immediately upon infection and
  - are the same whether or not the pathogen has been encountered before.
- Invertebrates rely solely on innate immunity, which may consist of
  - an exoskeleton, low pH, the enzyme lysozyme, and
  - immune cells capable of phagocytosis, cellular ingestion and digestion of foreign substances. Antimicrobial peptide 抗菌胜肽
- Vertebrates have innate and adaptive immunity.

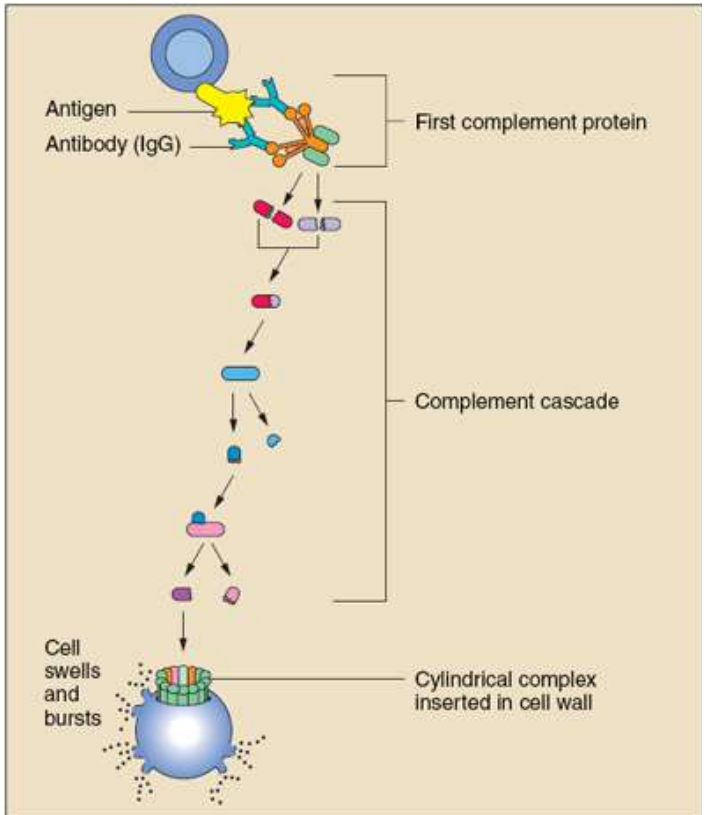
Innate external barriers
skin/exoskeleton, acidic environment, secretions, mucous membranes, hairs, cilia

if external barriers breached

Innate internal defenses
phagocytic cells, natural killer cells, defensive proteins, inflammatory response

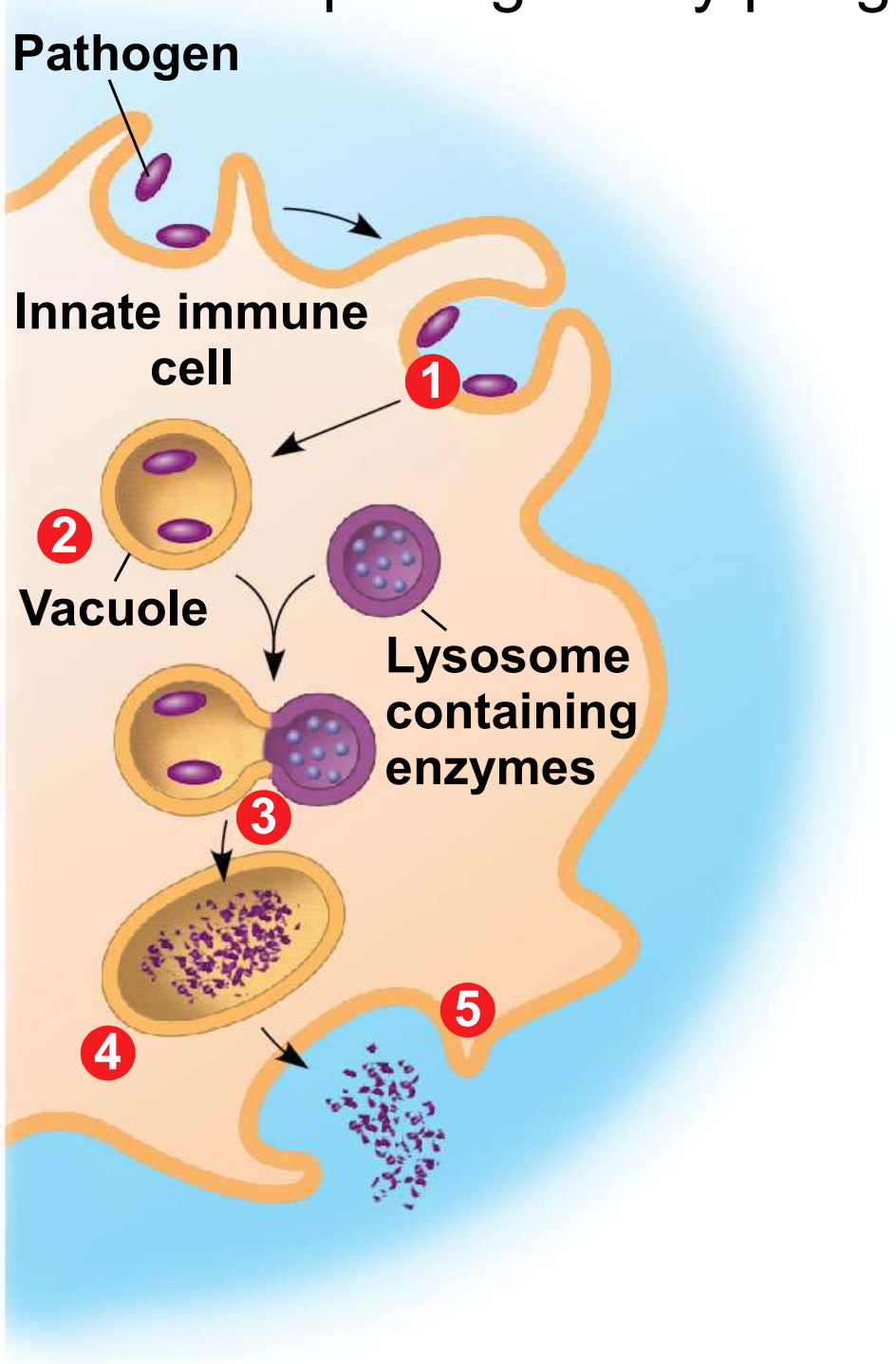
24.1 All animals have innate immunity

- Vertebrate innate immunity includes
  - barriers such as skin and mucous membranes, 干擾素
  - **interferons**, proteins produced by virus-infected cells, that help to limit the cell-to-cell spread of viruses,
  - **neutrophils** (phagocytic cells), (blood)
  - **macrophages**, large phagocytic cells that wander through the interstitial fluid,
  - **natural killer** cells that attack cancer cells and virus-infected cells, and
  - a **complement system**, a group of about 30 kinds of proteins that can act with other defense mechanisms.



http://flipper.diff.org/app/items/6795

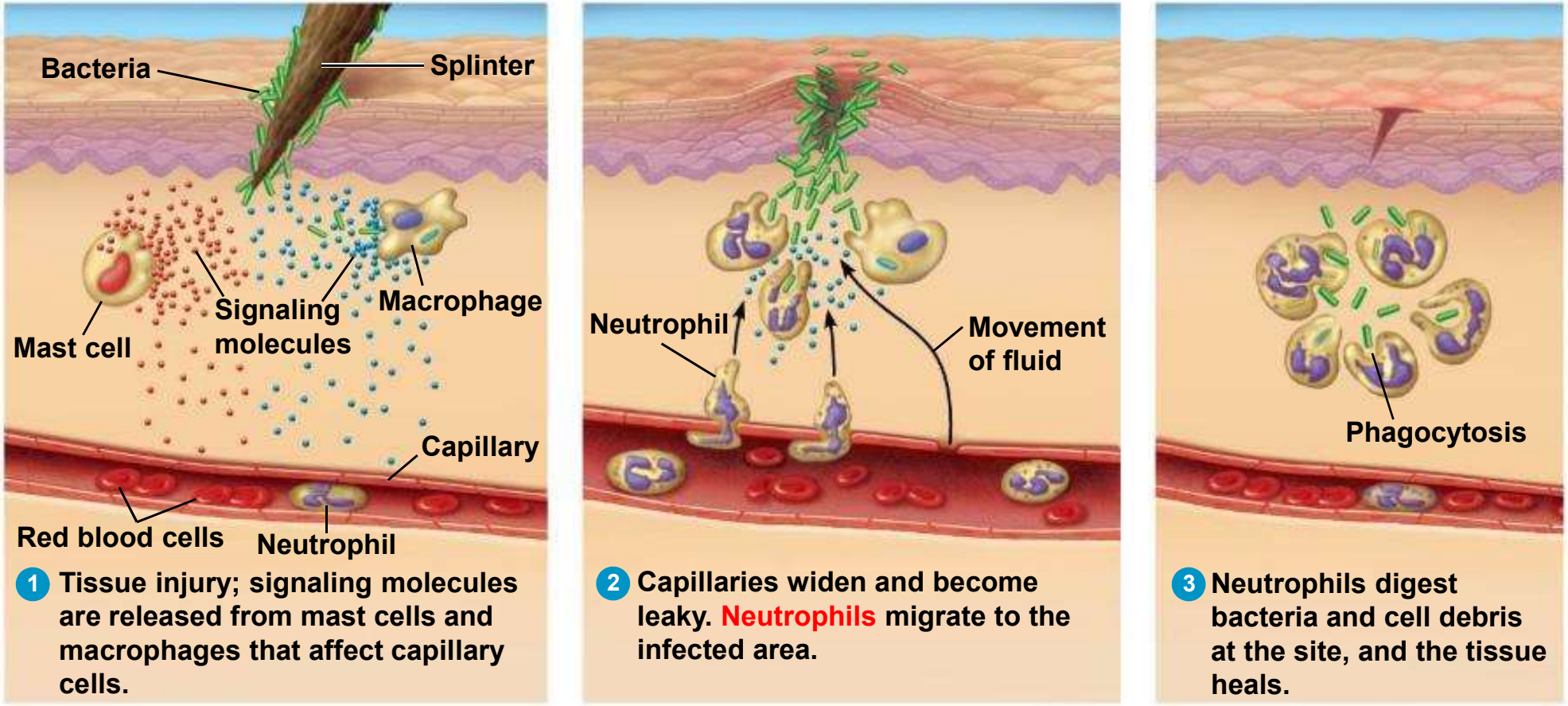
Figure 24.1b Destruction of pathogens by phagocytosis



24.2 Inflammation mobilizes the innate immune response

- Tissue damage triggers the inflammatory response, a major component of our innate immunity, which can
  - disinfect and clean infected tissues and
  - limit the spread of infection to surrounding tissues.
- Figure 24.2 shows the chain of events that occurs when a splinter has broken the skin, allowing infection by bacteria.
- Inflammation may be localized or widespread (systemic).
- Sometimes microorganisms get into the blood or release toxins that are carried throughout the body in the bloodstream.
- Bacterial infections can bring about an overwhelming systemic inflammatory response leading to septic shock, characterized by very high fever and low blood pressure. 敗血性休克

紅、腫、熱、痛



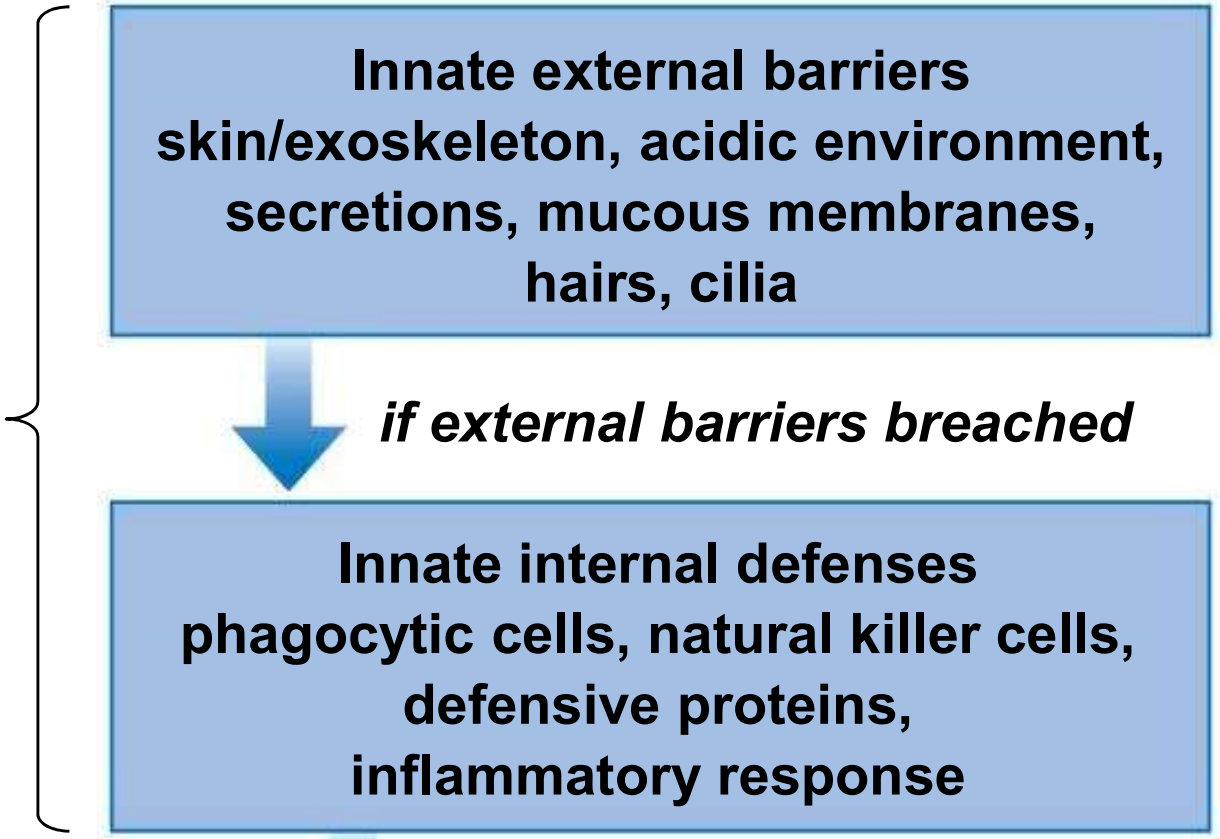
1. Tissue injury; signaling molecules are released from mast cells and macrophages that affect capillary cells.
2. Capillaries widen and become leaky. Neutrophils migrate to the infected area.
3. Neutrophils digest bacteria and cell debris at the site, and the tissue heals.

ADAPTIVE IMMUNITY

24.3 The adaptive immune response counters specific invaders

- Adaptive immunity, also called acquired immunity, is a set of defenses, found only in vertebrates, that is activated only after exposure to specific pathogens.
- Unlike innate immunity, adaptive immunity differs from individual to individual, depending on what pathogens they have been previously exposed to.
- Antigens are
  - any molecule that elicits an adaptive immune response,
  - nonself molecules that protrude from pathogens or other particles, such as viruses, bacteria, mold spores, pollen, house dust, or the cell surfaces of transplanted organs.
- When the immune system detects an antigen, it responds with an increase in the number of cells that either attack the invader directly or produce immune proteins called antibodies.

- Rapid response
- Recognize broad ranges of pathogens
- No “memory”



- Slower response
- Recognize specific pathogens
- Have “memory”

24.3 The adaptive immune response counters specific invaders

- Antibodies are proteins found in blood plasma that attach to one particular kind of antigen and help counter its effects.
- Adaptive immunity has a remarkable "memory."
  - It can "remember" antigens it has encountered before, sometimes even many decades earlier, and react against them more quickly and vigorously on subsequent exposures.
- Lymphocytes
  - are white blood cells that spend most of their time in the blood and the tissues and organs of the lymphatic system,
  - are responsible for adaptive immunity, and
  - provide specialized defenses that act on pathogens located in either the body fluids or inside cells.

24.3 The adaptive immune response counters specific invaders

- Adaptive immunity is usually obtained by natural exposure to antigens, but it can also be achieved by vaccination, also known as immunization, in which the immune system is confronted with a vaccine, composed of a harmless variant or part of a disease-causing microbe, such as an inactivated bacterial toxin, a dead or weakened virus, or a piece of a virus.
- Whether antigens enter the body naturally (if you catch the flu) or artificially (if you get a flu vaccine), the resulting immunity is called active immunity, because the person's own immune system actively produces antibodies.
- It is also possible to acquire passive immunity by receiving premade antibodies.

抗蛇毒血清：健保資料統計，每年約有一千多人遭毒蛇咬傷。一劑抗蛇毒血清售價為新台幣七千九百元 http://www.rhythmsmonthly.com/?p=12222

製造蛇毒血清十年 三匹血清馬正式退休 (Total 53) http://pansci.asia/archives/flash/104728 2016/8

我國現行兒童預防接種時程

106 年 4 月修編

接種年齡 / 疫苗	24hr 內儘速	1 month	2 months	4 months	5 months	6 months	12 months	15 months	18 months	24 months	27 months	30 months	滿 5 歲至入國小前	國小學童
B 型肝炎疫苗(HepB)	第一劑	第二劑				第三劑[7]								
卡介苗(BCG)[1]					一劑									
白喉破傷風非細胞性百日咳、b 型嗜血桿菌及不活化小兒麻痺五合一疫苗(DTaP-Hib-IPV)			第一劑	第二劑		第三劑[7]			第四劑[6]					
結合型肺炎鏈球菌疫苗(PCV13)[2]			第一劑	第二劑			第三劑							
水痘疫苗(Varicella)							一劑							
麻疹腮腺炎德國麻疹混合疫苗(MMR)							第一劑						第二劑	
日本腦炎疫苗(JE)[3]								第一劑 第二劑			第三劑		第四劑	
流感疫苗(Influenza)[4]						← 初次接種二劑，之後每年一劑 →								
A 型肝炎疫苗(HepA)[5]							第一劑		第二劑					
減量破傷風白喉非細胞性百日咳及不活化小兒麻痺混合疫苗(Tdap-IPV)													一劑	

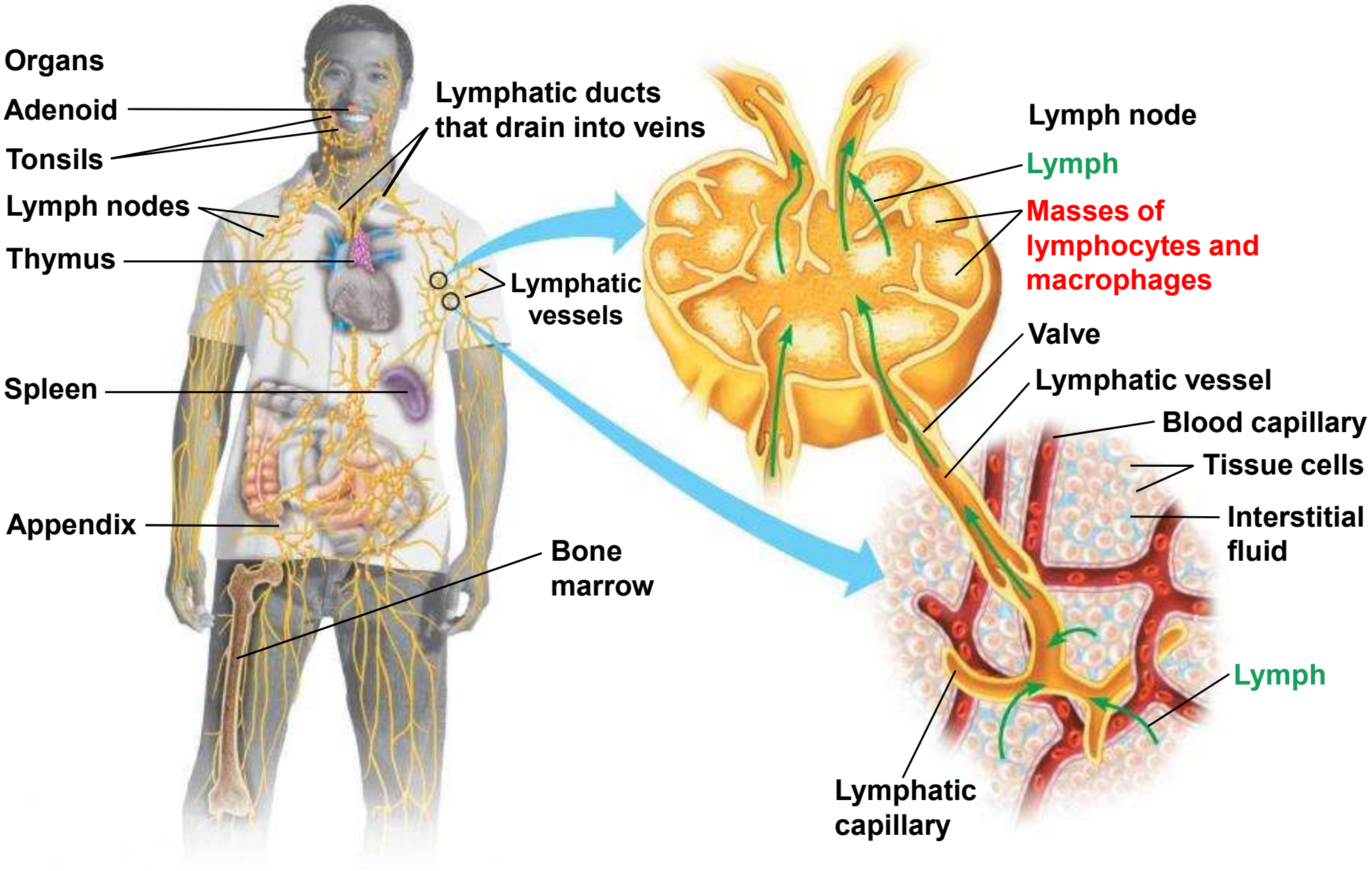
1. 105年起，卡介苗接種時程由出生滿24小時後，調整為出生滿5個月(建議接種時間為出生滿5-8個月)。
2. 104年起，結合型肺炎鏈球菌疫苗(PCV13)納入幼兒常規接種項目。第一劑與第二劑接種至少間隔8週。
3. 日本腦炎疫苗出生滿15個月接種第1劑;間隔2週接種第2劑。
4. 8歲(含)以下兒童，初次接種流感疫苗應接種2劑，2劑間隔4週。
5. A型肝炎疫苗免費接種之實施對象為設籍於30個山地鄉、9個鄰近山地鄉之平地鄉鎮及金門、連江兩縣之兒童，接種時程為出生滿1歲接種第1劑，間隔6-12個月接種第2劑。
6. 106年5月1日起，五合一疫苗第四劑接種年齡由出生滿27個月，調整回出生滿18個月接種。
7. 106年5月1日起，以六合一疫苗暫用以取代嬰幼兒應接種之第3劑B型肝炎疫苗及五合一疫苗。

24.4 The lymphatic system becomes a crucial battleground during infection

- The lymphatic system is
  - involved in innate and adaptive immunity and
  - consists of a network of
    - lymphatic vessels, lymph nodes, and lymph.
    - lymph, which is similar to the interstitial fluid that surrounds body cells but contains less oxygen and fewer nutrients.
- Lymphatic vessels
  - collect fluid from body tissues and return it as lymph to the blood.
- The lymphatic system thus has two main functions:
  - to return tissue fluid back to the circulatory system and
  - to fight infection.

- Lymph organs
  - include the spleen and lymph nodes and
  - are packed with white blood cells that fight infections.
- As lymph circulates through lymphatic organs it
  - Collects microbes, parts of microbes, and microbial toxins,
  - transports them to lymphatic organs where
    - macrophages in lymphatic organs engulf the invaders and
    - lymphocytes may mount an adaptive immune response.

Figure 24.4

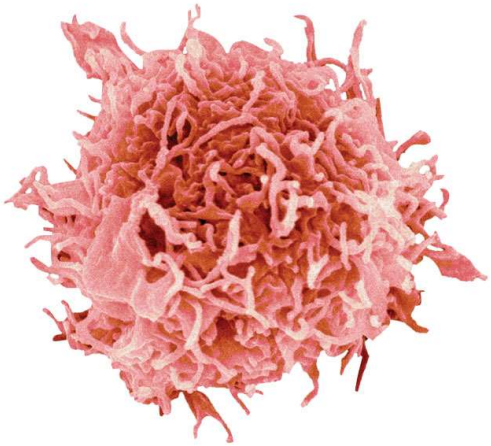

Organs
Adenoid
Tonsils
Lymph nodes
Thymus
Spleen
Appendix
Bone marrow
Lymphatic ducts that drain into veins
Lymphatic vessels
Lymph node
Lymph
Masses of lymphocytes and macrophages
Valve
Lymphatic vessel
Blood capillary
Tissue cells
Interstitial fluid
Lymph
Lymphatic capillary

24.5 Lymphocytes mount a dual defense

- Lymphocytes
  - are white blood cells that spend most of their time in the tissues and organs of the lymphatic system,
  - are responsible for adaptive immunity, and
  - originate from stem cells in the bone marrow.
    - B lymphocytes or B cells continue developing in bone marrow.
    - T lymphocytes or T cells develop further in the thymus.
- By mounting a dual defense, B and T cells defend against infections in body fluids and those inside cells.

- B cells 體液
  - participate in the humoral immune response,
  - defend primarily against bacteria and viruses present in body fluids, and
  - secrete antibodies into the blood and lymph.
- T cells
  - participate in the cell-mediated immune response,
  - defend against infections inside body cells,
  - attack cells infected with bacteria or viruses, and
  - promote phagocytosis by other white blood cells and by stimulating B cells to produce antibodies.
  - Thus, some T cells play a part in both the cell-mediated and humoral immune responses.

Millions of kinds of B and T cells each with different **antigen receptors,** capable of binding one specific type of antigen, wait in the lymphatic system, where they may respond to invaders. A tiny fraction of lymphocytes will be ever used



B Cell

T Cell

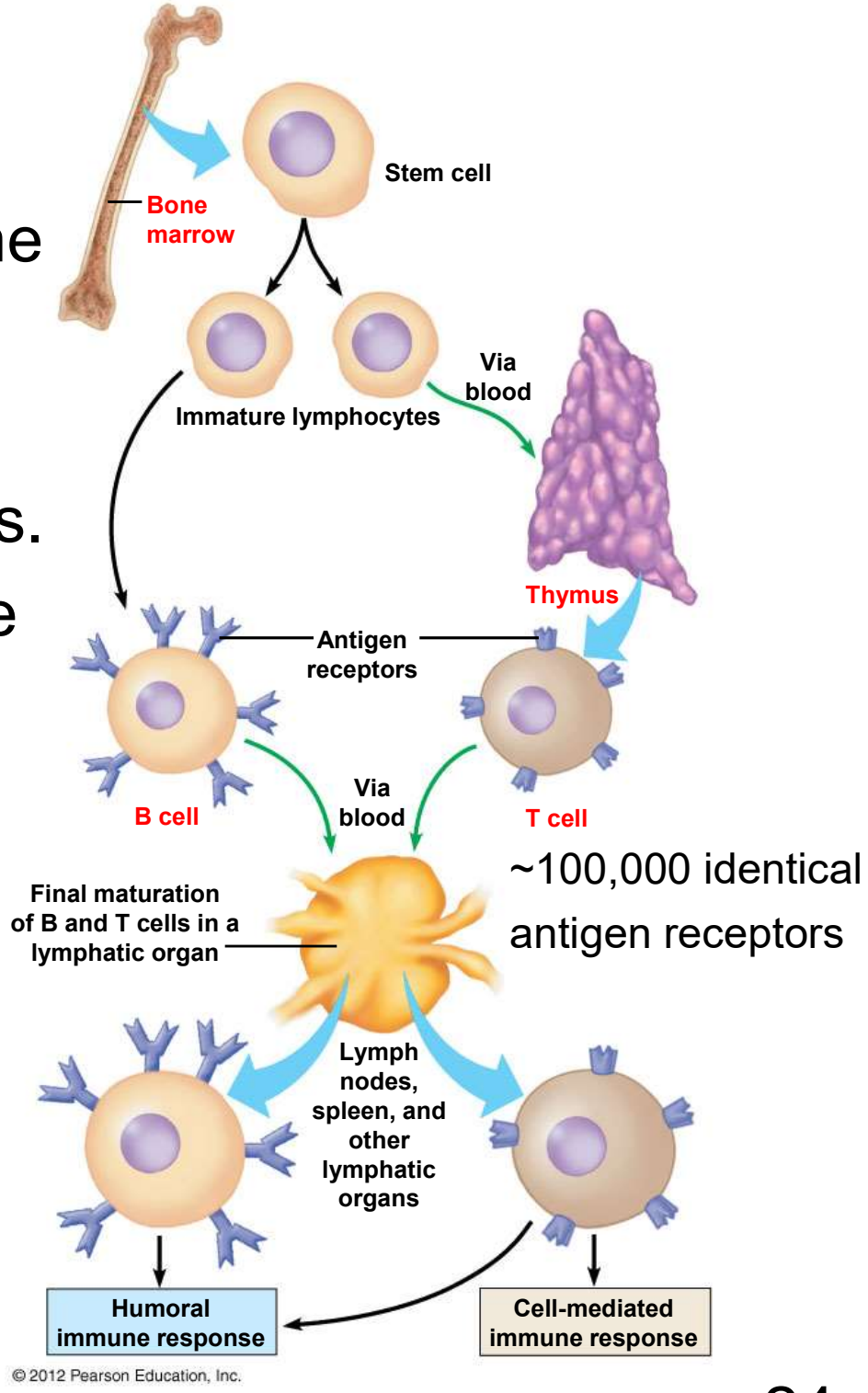
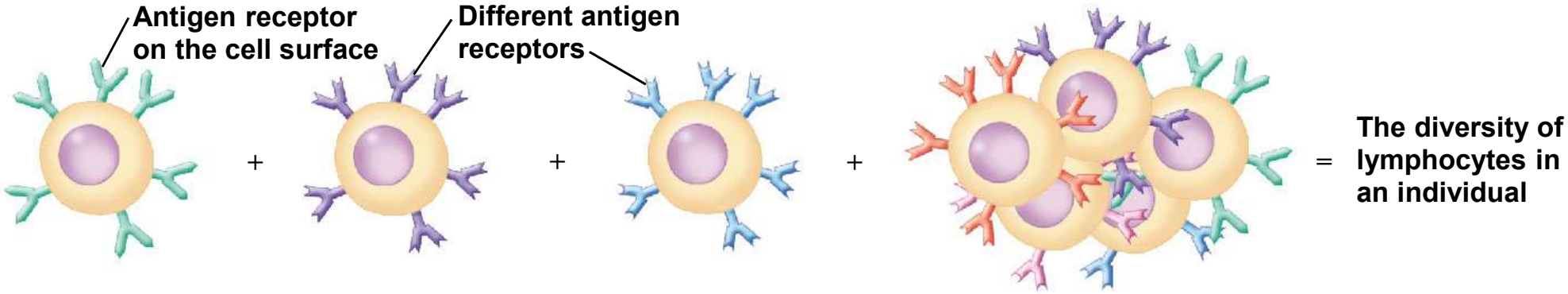


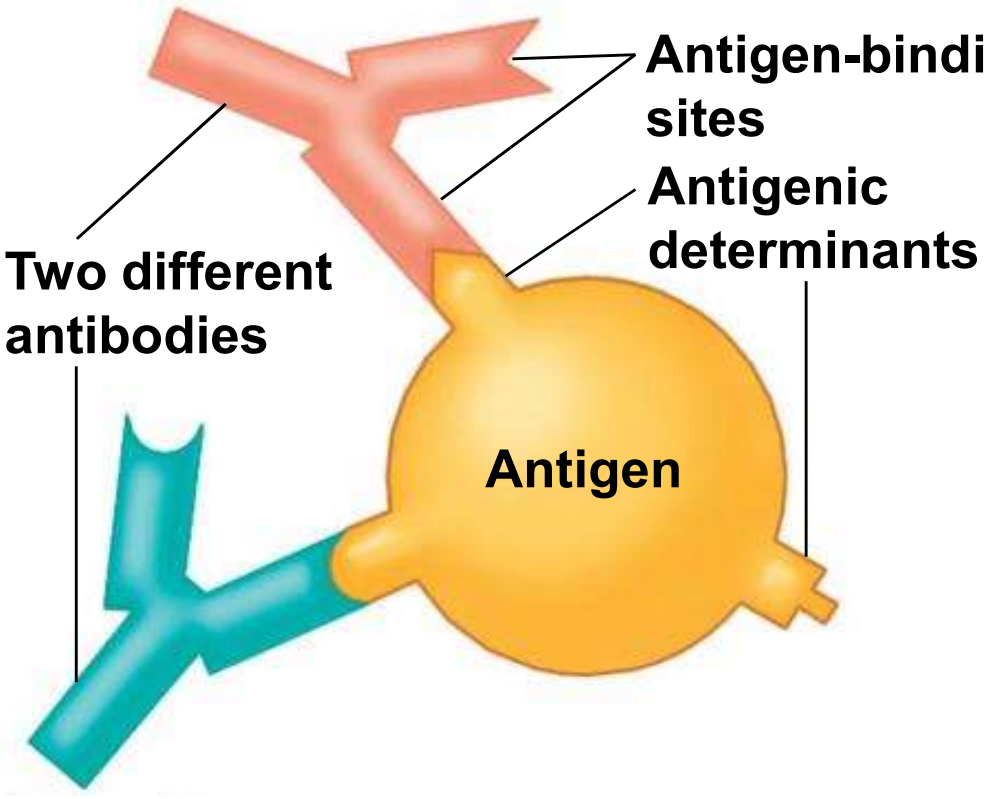
Figure 24.5b The diversity of lymphocytes in an individual



24.6 Antigen receptors and antibodies bind to specific regions on an antigen

- Both the humoral and cell-mediated immune responses are initiated when lymphocytes recognize antigens.
  - B cells bind antigens directly.
  - T cells require an additional step for recognition.
- Antigens usually do not belong to the host animal.
- Most antigens are proteins or large polysaccharides that protrude from the **surfaces** of viruses or foreign cells.
- Common examples are
  - protein-coat molecules of viruses,
  - parts of the capsules and cell walls of bacteria, and
  - macromolecules on the surface cells of other kinds of organisms, such as protozoans and parasitic worms.

- Antigenic determinants are
  - specific regions on an antigen where antibodies bind and
  - sometimes called epitopes.
- Antigen receptors on B cells, as well as antibodies, recognize and bind to the antigenic determinant.
- The specific region of an antigen receptor or antibody that recognizes an antigenic determinant is the antigen-binding site.



The binding site and antigenic determinant have shapes like a lock and key.

An antigen usually has several different determinants.

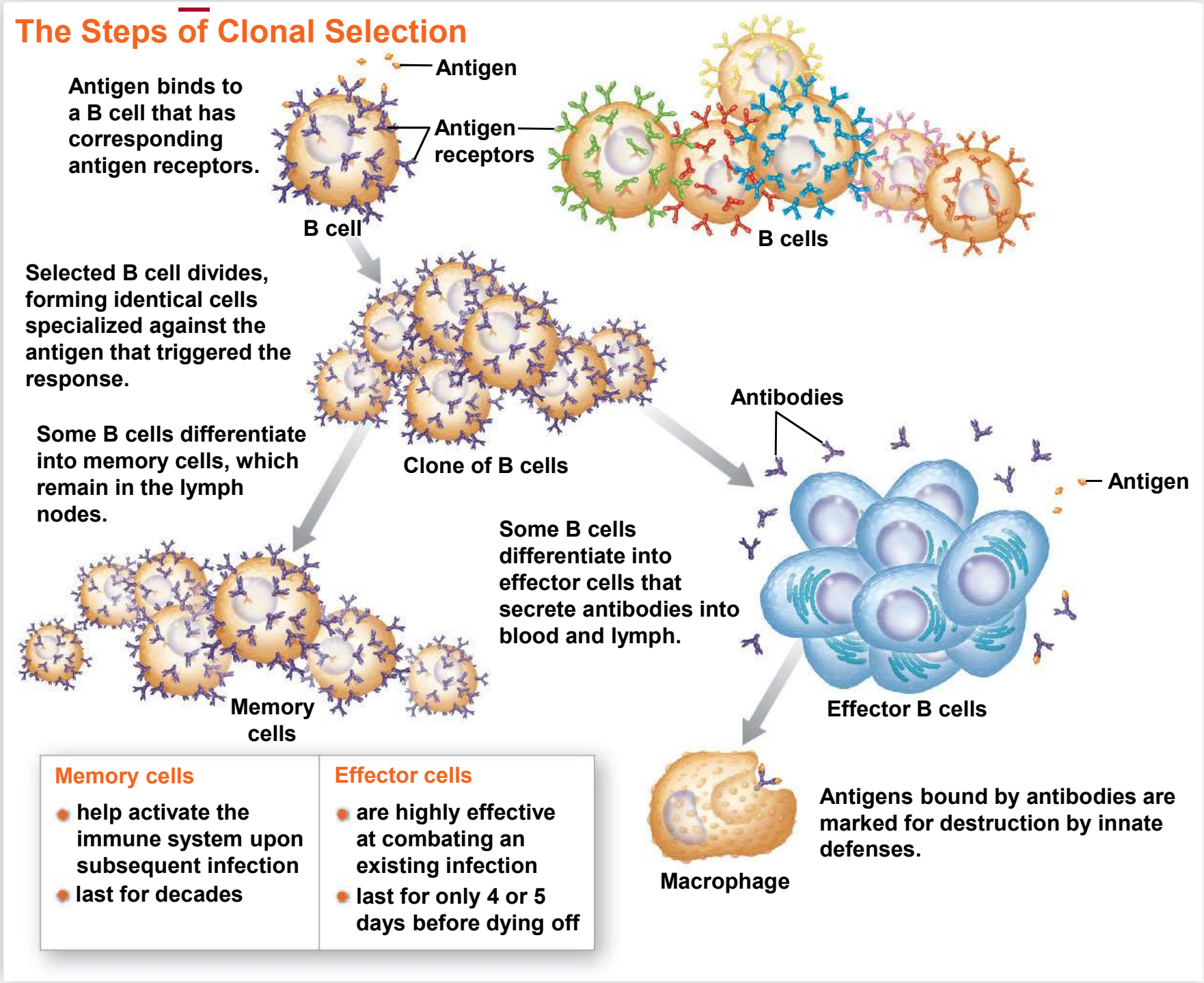
In Figure 24.6, two different antibodies are shown binding to the same antigen, which in this case has three determinants.

24.7 Clonal selection mobilizes defensive forces against specific antigens

- The humoral and cell-mediated immune responses both defend against a wide variety of antigens through a process known as **clonal selection**.
- Inside the body, an antigen encounters a diverse pool of B and T lymphocytes. However, one particular antigen interacts only with a fraction of lymphocytes, those bearing receptors that are specific to that antigen.
- Once activated by the antigen, the lymphocytes proliferate, forming a clone of thousands of cells "selected" to recognize and respond to the antigen.
  - Some of these cells, called effector cells, act immediately to combat infection.

- Others known as memory cells lie in wait to help activate the immune system upon subsequent exposure to the antigen.
- When an antigen enters the body it activates only a small subset of lymphocytes that have complementary receptors.
- In clonal selection, the selected lymphocyte cells
  - multiply into clones of short-lived effector cells, specialized for defending against the antigen that triggered the response, and
  - multiply into memory cells, which confer long-term immunity.
  - Plasma cells are the effector cells produced during clonal selection of B cells.

Figure 24.7_5


The Steps of Clonal Selection
Antigen binds to a B cell that has corresponding antigen receptors.
Antigen
Antigen receptors
B cell
B cells
Selected B cell divides, forming identical cells specialized against the antigen that triggered the response.
Clone of B cells
Some B cells differentiate into memory cells, which remain in the lymph nodes.
Some B cells differentiate into effector cells that secrete antibodies into blood and lymph.
Antibodies
Antigen
Memory cells
Effector B cells
Macrophage
Antigens bound by antibodies are marked for destruction by innate defenses.
Memory cells
help activate the immune system upon subsequent infection
last for decades
Effector cells
are highly effective at combating an existing infection
last for only 4 or 5 days before dying off

24.8 The primary and secondary responses differ in speed, strength, and duration

- The clonal selection of B cells occurs in two responses.
  - In the primary immune response, clonal selection produces
    - effector cells and
    - memory cells that may confer lifelong immunity.
  - In the secondary immune response, memory cells are activated by a second exposure to the same antigen.
- Primary vs. secondary immune responses
  - The primary immune response
    - occurs upon first exposure to an antigen and
    - is slower than the secondary immune response.
  - The secondary immune response
    - occurs upon second exposure to an antigen and
    - is faster and stronger than the primary immune response.

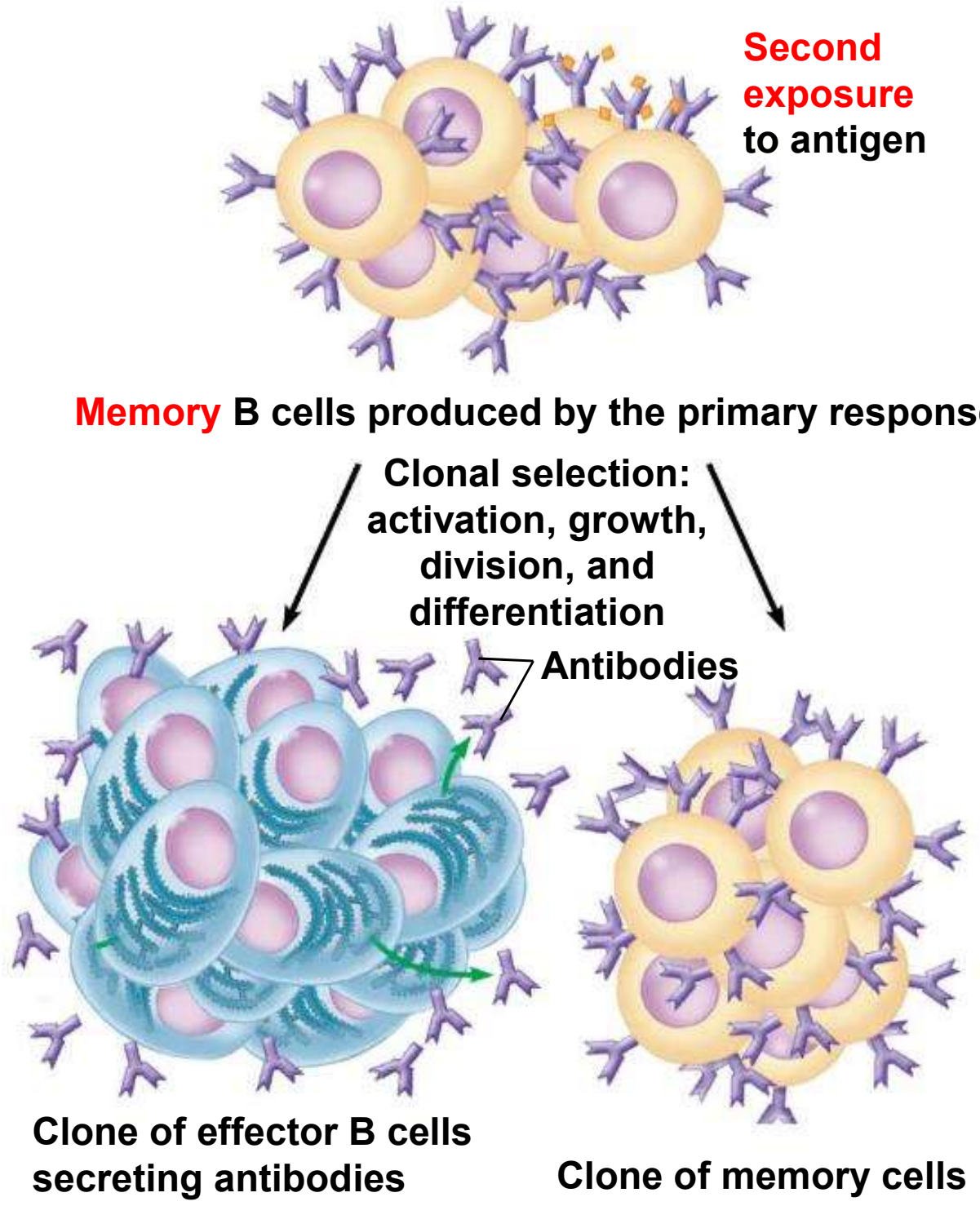
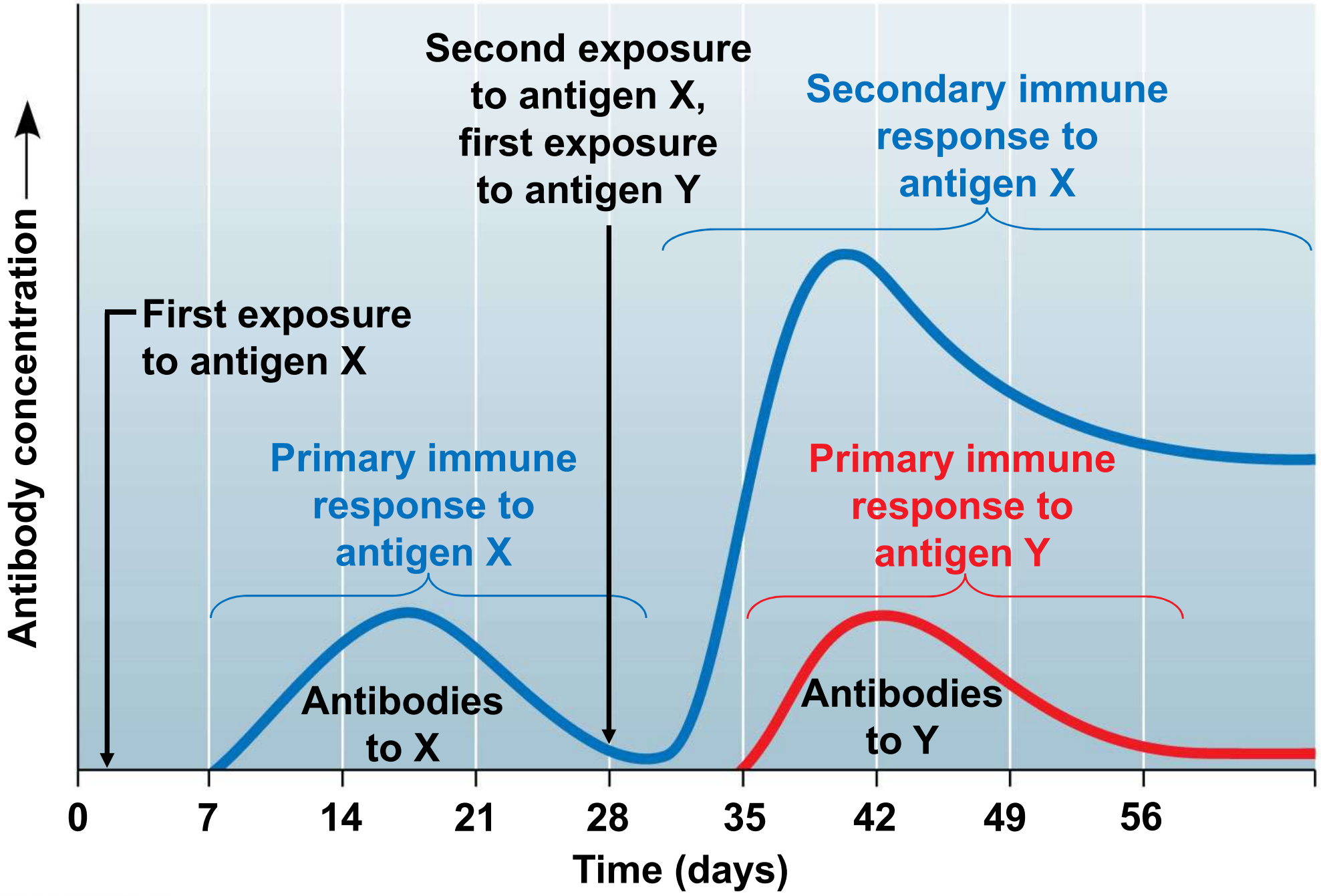
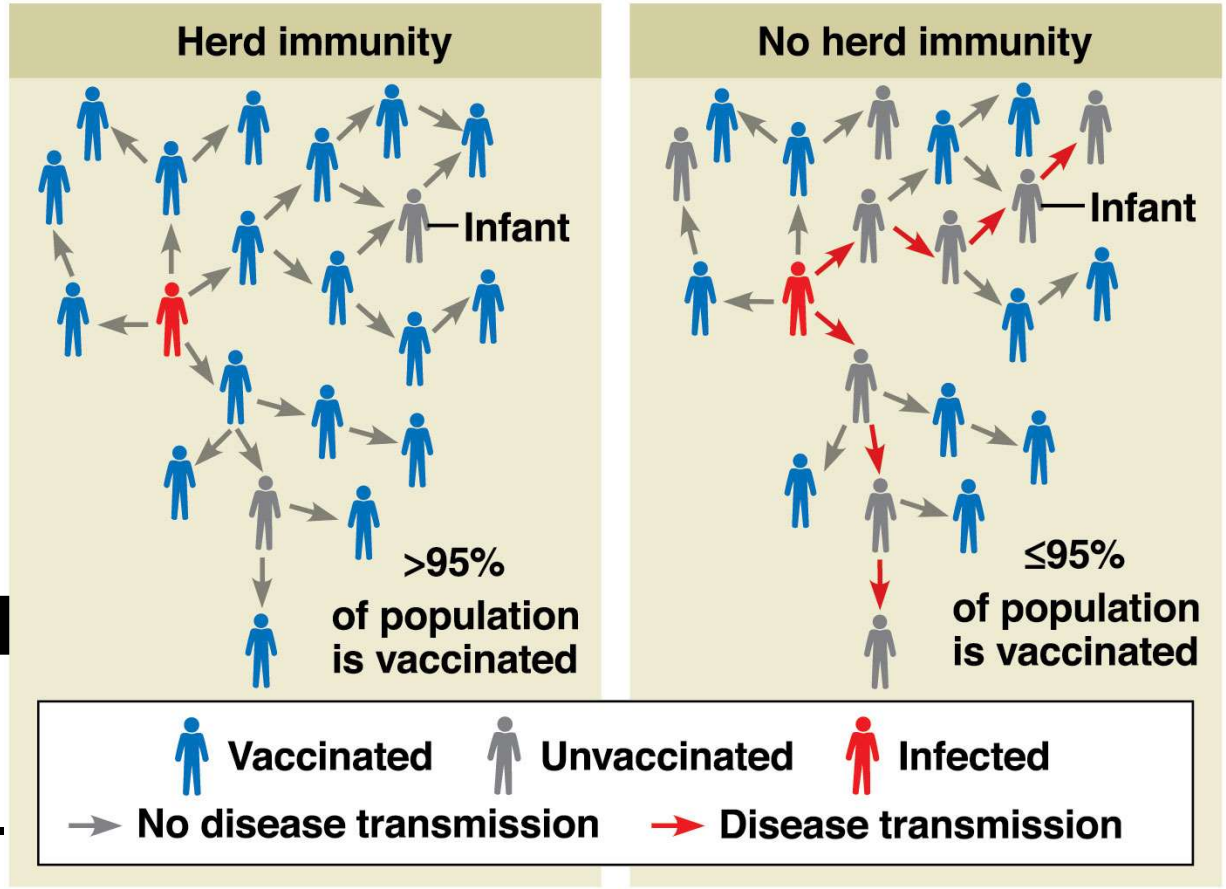

Second exposure to antigen
Memory B cells produced by the primary response
Clonal selection: activation, growth, division, and differentiation
Antibodies
Clone of effector B cells secreting antibodies
Clone of memory cells

Figure 24.7B



24.9 CONNECTION: Herd immunity prevents the outbreak of infectious disease

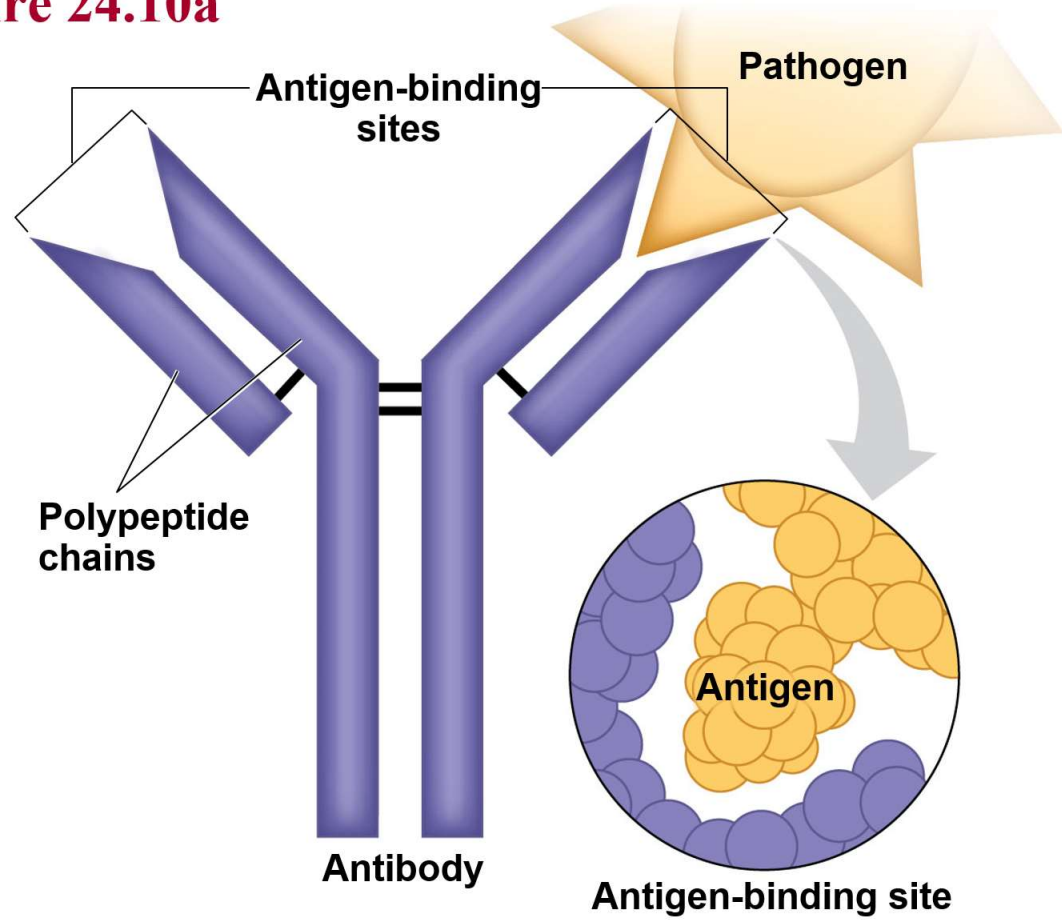
- When most people in a population are vaccinated, a disease cannot spread.
- This community protection, called **herd immunity**, is the rationale behind state-mandated vaccinations for children in public schools.



24.10 The structure of an antibody matches its function

- Antibodies do not kill pathogens.
- An antibody has two related functions in the humoral immune response:
  - to recognize and bind to a certain antigen and
  - to assist in eliminating that antigen.

Figure 24.10a



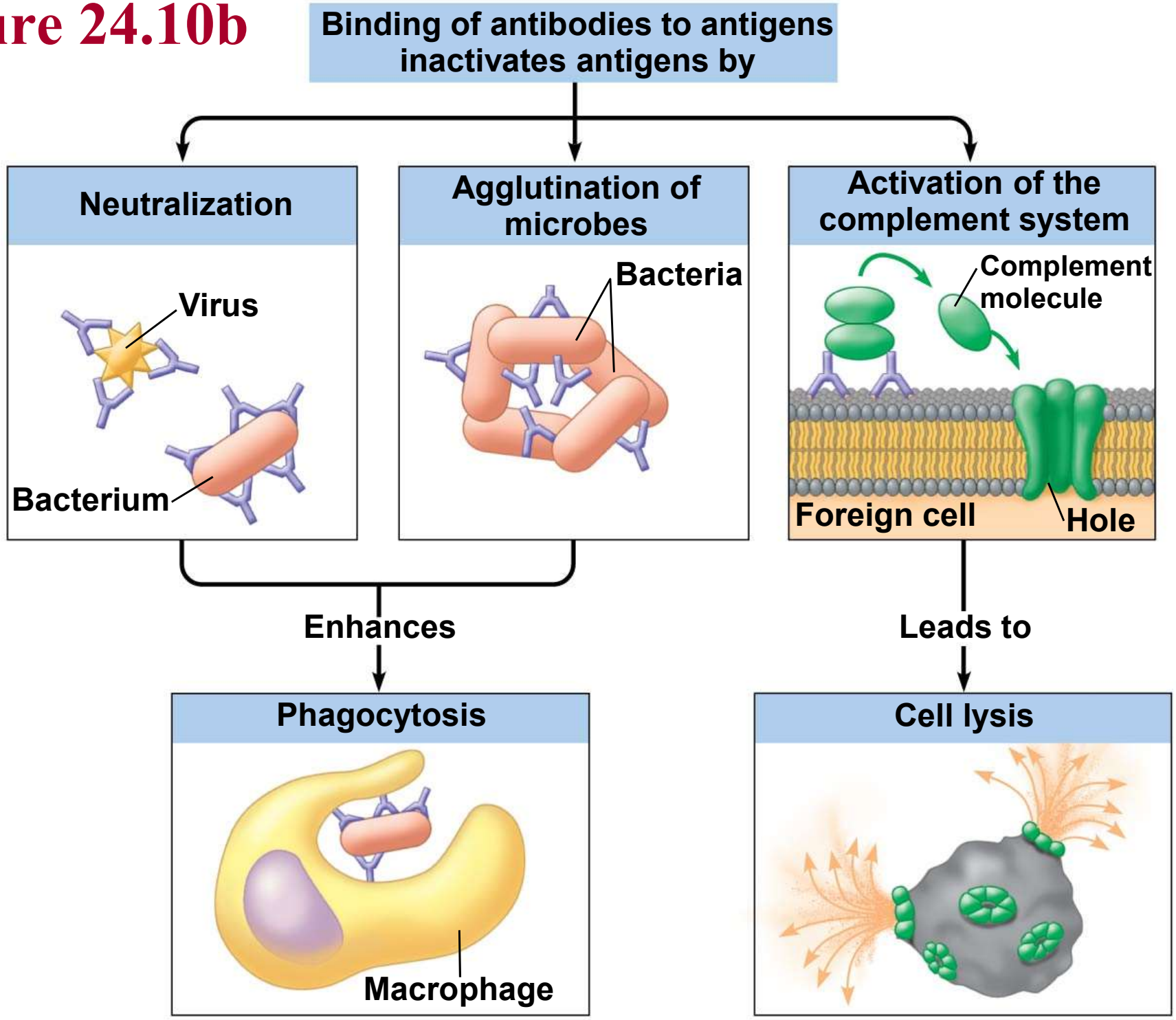
- The structure of an antibody allows it to perform both of these functions.
- A computer-generated rendering of an antibody molecule illustrates the Y shape of antibodies.

24.9 The structure of an antibody matches its function

- Each antibody molecule consists of four polypeptide chains bonded together to form a Y shape.
- The tip of each arm of the Y forms an antigen-binding site, a region of the molecule responsible for the antibody's recognition-and-binding function.
- A huge variety in the three-dimensional shapes of the binding sites of different antibodies
  - accounts for the diversity of lymphocytes and
  - gives the humoral immune response the ability to react to virtually any kind of antigen.
- All antibody mechanisms involve a specific recognition-and-attack phase followed by a nonspecific destruction phase.

- Thus, the antibodies of the adaptive humoral immune response, which identify and bind to foreign invaders, must work with the components of innate immunity.
- The antigen-antibody complex boosts the function of phagocytic cells of innate immunity in 2 ways:
  - neutralization, binding to surface proteins on a virus or bacterium; blocking its ability to infect a host cell and presenting an easily recognized structure to macrophage
  - agglutination, using both binding sites of an antibody to join invading cells together into a clump, and
- In addition to phagocytosis, the antigen-antibody complex promotes activation of another innate immune response, the complement system.
- Activated complement proteins can attach to a foreign cell.

Figure 24.10b



Antibodies are powerful tools in the lab and clinic

- Antibodies are widely used in
  - laboratory research and
  - the treatment of disease.

Western blot
Immunostaining
ELISA …

- Toxin-linked antibodies carry out a precise search-and-destroy mission, selectively attaching to and killing tumor cells.
- Monoclonal antibodies (mAb) are
  - identical antibodies
  - produced by cells that are all descendants of a single, hybrid cell.

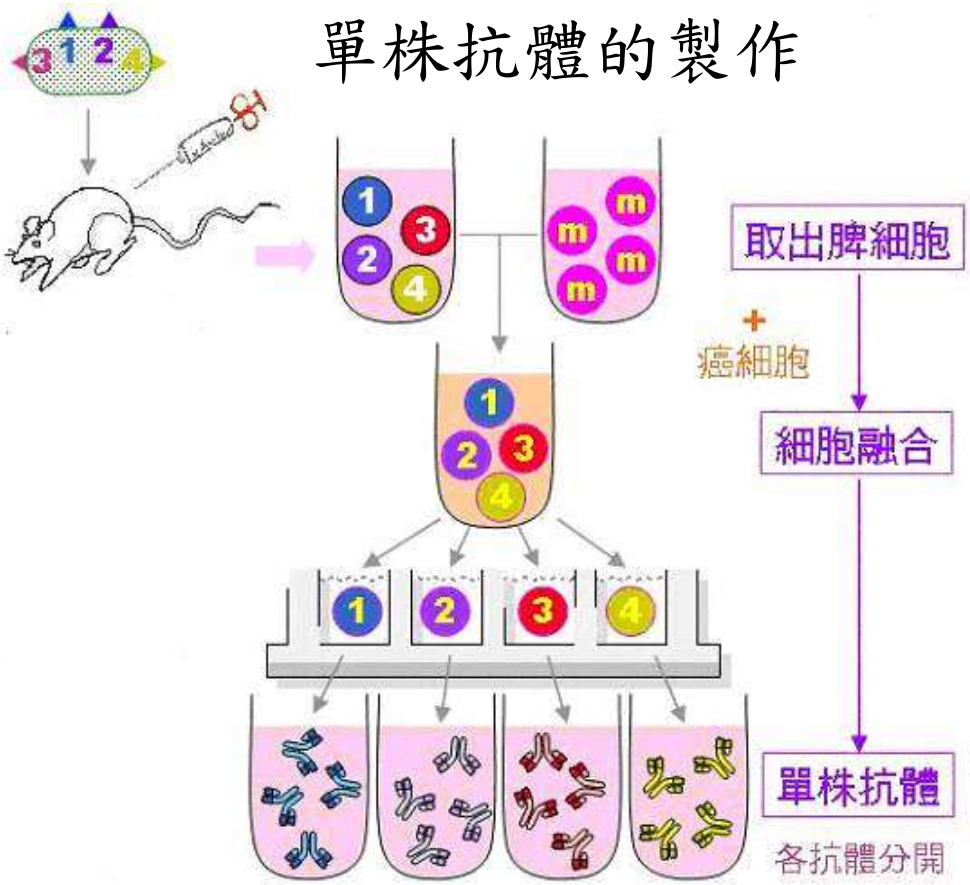
單株抗體

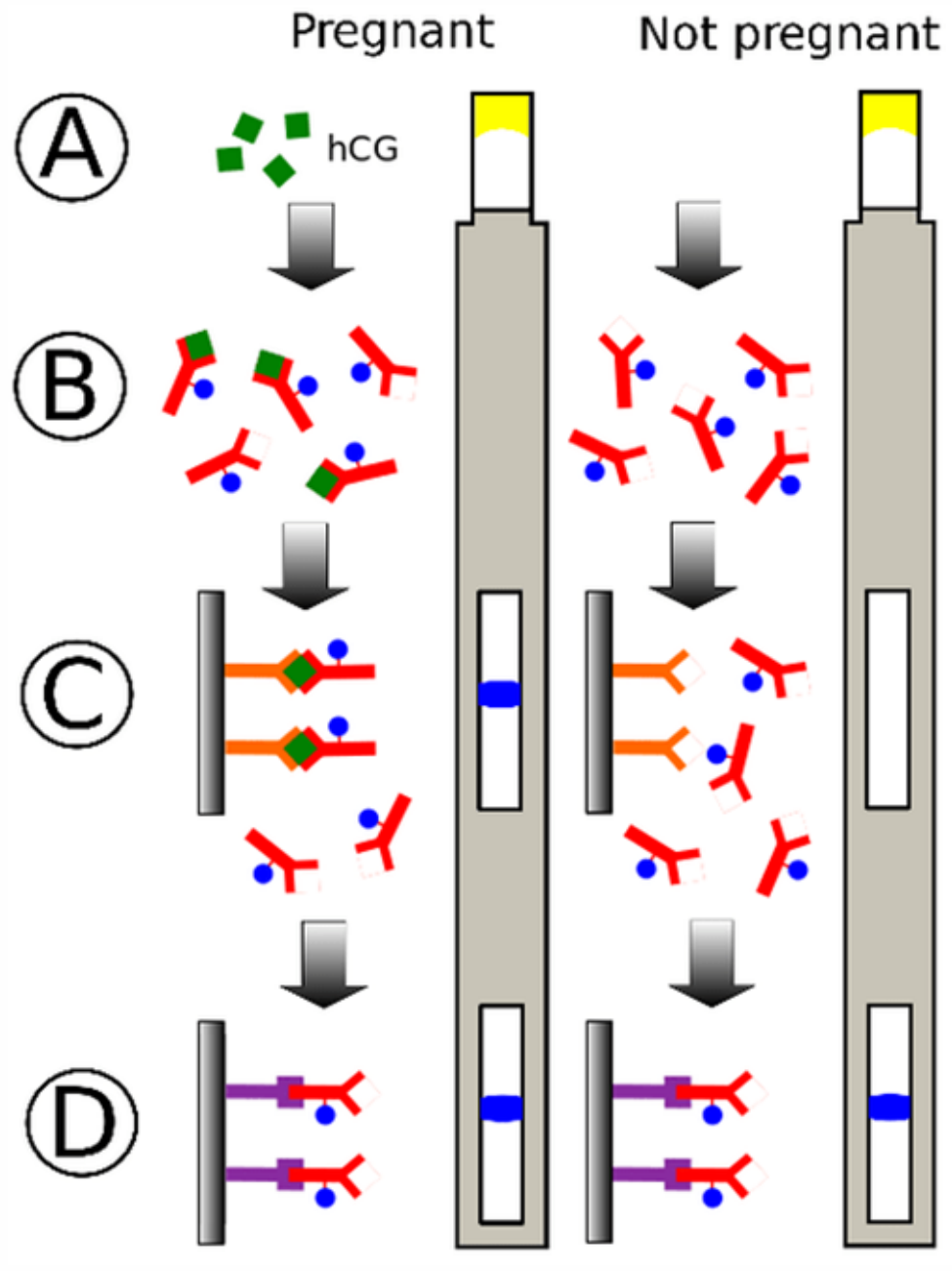
- The most popular type of pregnancy test uses an antibody to detect a hormone called human chorionic gonadotropin (hCG), which is present in the urine of pregnant women.

人類絨毛膜促性腺激素

Pregnancy Test

http://www.sumanasinc.com/webcontent/animations/content/pregtest.html





http://life.nthu.edu.tw/~lseduip/U-BET/ubet/F4/group4/monoab/mono.htm

https://autumnleaves.embraced.co/2014/08/%E6%88%91%E8%A6%81%E7%95%B6%E7%88%B8%E7%88%B8%E4%BA%86%E3%80%82/

24.11 SCIENTIFIC THINKING: Scientists measure antibody levels to look for waning immunity after HPV vaccination

- Active adaptive immunity to a specific pathogen can be gained through
  - a natural infection or vaccination.
- With human papilloma virus (HPV), infections are common. Approximately 50% of all sexually active adults become infected by the virus.
  - Usually there are no noticeable symptoms.
  - The immune system usually clears HPV infection within two years.
- In some infected individuals, HPV
  - escapes the immune system for many more years and
  - interferes with the regulation of cell growth in the infected epithelial cells.

24.11 SCIENTIFIC THINKING: Scientists measure antibody levels to look for waning immunity after HPV vaccination

- This increases the likelihood that mutations will accumulate and result in cervical and anal cancers.
- Two vaccines made with HPV antigens (in this case, proteins from the viral surface) were developed to promote artificial immunity before individuals come into contact with cancer-causing viral strains.
  - In 2006, the HPV vaccine Gardasil was approved in the United States. 加衛苗
  - A second vaccine, Cervarix, was approved in 2009. 卉妍康

HPV 子宮頸癌疫苗之分別?
http://www.hchealth.hk/vaccine-sub9.html

- Scientists are collecting data to determine how effective Gardasil and Cervarix are so far.
  - Individuals being studied were among the first to be vaccinated, in clinical trials that began as early as 1998.
  - The study participants were either vaccinated against specific strains of HPV or injected with a placebo.
  - Both vaccines have been between 93 and 100% effective in preventing precancerous cervical lesions.
  - That is good news, but it does not tell us how long that effectiveness will last.
- Can we predict if or when the HPV vaccine's effectiveness will decrease?
  - Not exactly.
  - But we can get an idea of how long the HPV vaccination lasts by measuring the level of antibodies being produced against HPV years after vaccination.

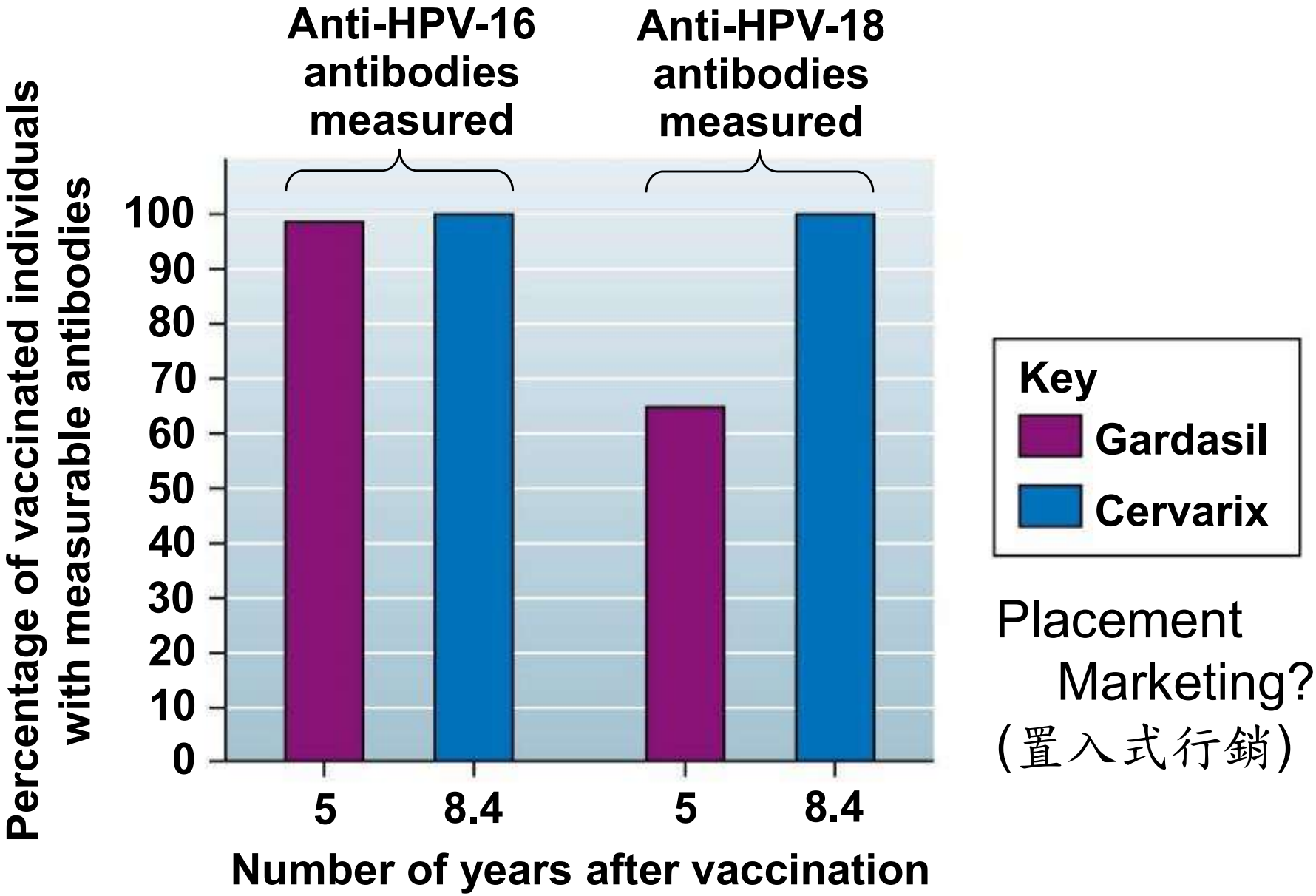
- HPV vaccination induces long-term, continual production of antibodies.
  - How the immune system produces antibodies for long periods against some antigens is unclear.
  - There is evidence that some plasma cells migrate from the lymph nodes to the bone marrow where they live and produce antibodies for years.
  - Another hypothesis is that memory cells are continually activated and therefore continually differentiating into plasma cells.

跨國追蹤：HPV疫苗政策下的黑布 (2018.11起國一女生全部免費接種)
https://www.twreporter.org/topics/hpv-vaccine

日本在2013年，決定「不建議施打」，也成為世界第一個從公費施打轉為「不建議施打」的國家。(Note: HPV並不會大規模流行)

各國皆通報嚴重不良事件

	台灣	英國	日本	美國
不良事件通報數	115	8835	3130	44902
嚴重事件（包含住院或延長住院）	46	3038	1784	3836



Placement Marketing?
(置入式行銷)

Data from S-E. Olsson et al., Induction of immune memory following administration of a prophylactic quadrivalent human papillomavirus (HPV) types 6/11/16/18 L1 virus-like particle (VLP) vaccine, *Vaccine* 25: 3931–4939 (2007); C. M. Roteli-Martin et al., Sustained immunogenicity and efficacy of the HPV16/18 AS04-adjuvanted vaccine up to 8.4 years of follow-up, *Landes Bioscience* 8:3 (2012).

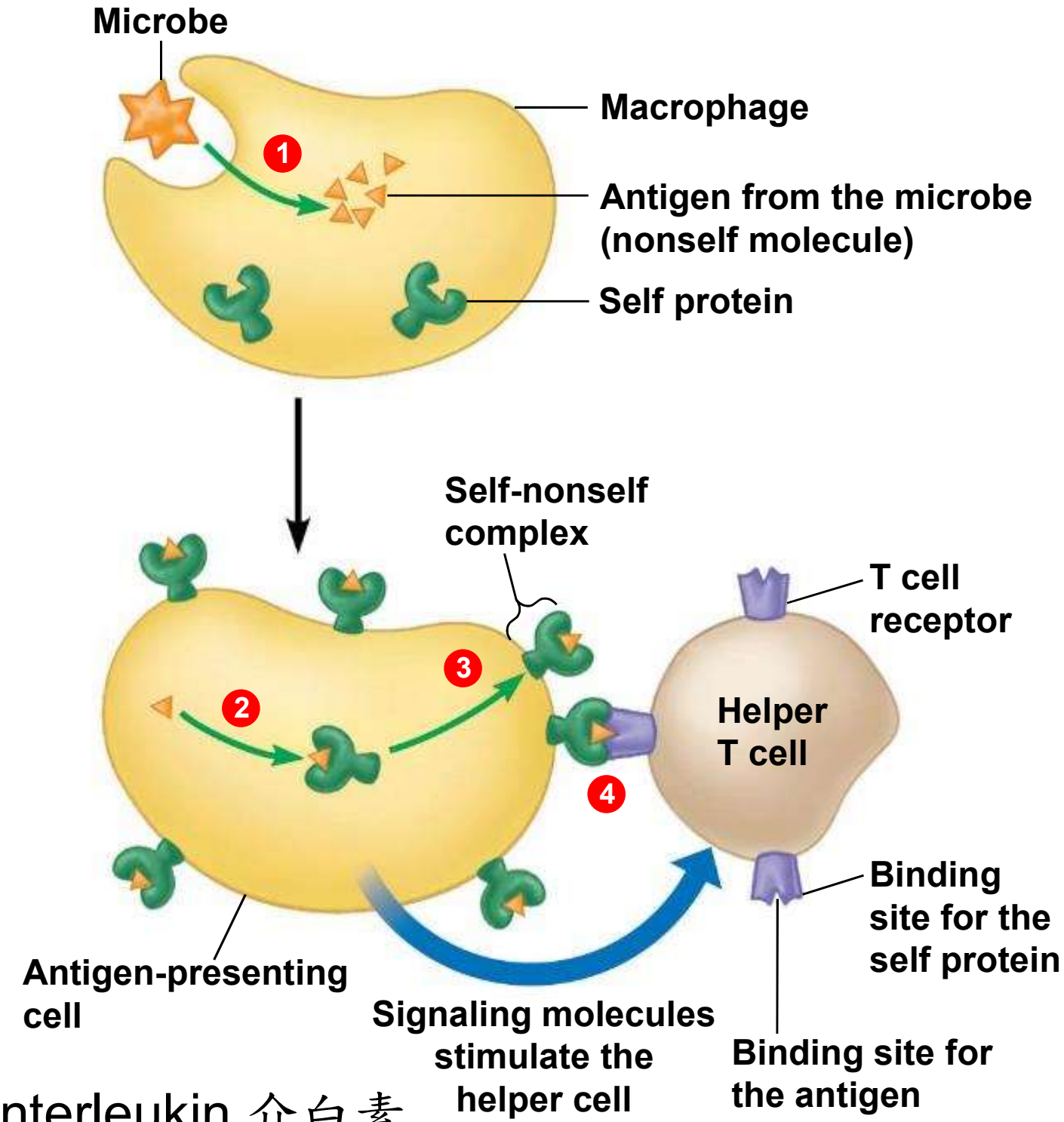
24.12 Helper T cells stimulate the humoral and cell-mediated immune responses

- The cell-mediated immune response
  - is produced by cytotoxic T cells and
  - battles pathogens that have already entered body cells.
- A type of T cell called a helper T cell triggers both the humoral and cell-mediated immune responses.
- Signals from helper T cells
  - initiate production of antibodies that neutralize pathogens and
  - activate cytotoxic T cells that kill infected cells.
- Two requirements must be met for a helper T cell to activate adaptive immune responses.
  - A foreign molecule must be present that can bind specifically to the antigen receptor.

- This antigen must be displayed on the surface of an antigen-presenting cell. (Macrophages and B cells are two types of antigen-presenting cells.)

- Consider a typical antigen-presenting cell, a macrophage, as shown in Figure 24.12A.
  - The macrophage ingests a microbe or other foreign particle and breaks it into fragments—foreign antigens.
  - Then molecules of a special protein belonging to the macrophage, a self protein, bind the foreign antigens—nonself molecules.
  - They then display them on the cell's surface.
  - Helper T cells recognize and bind to the combination of a self protein and a foreign antigen, called a self-nonself complex.

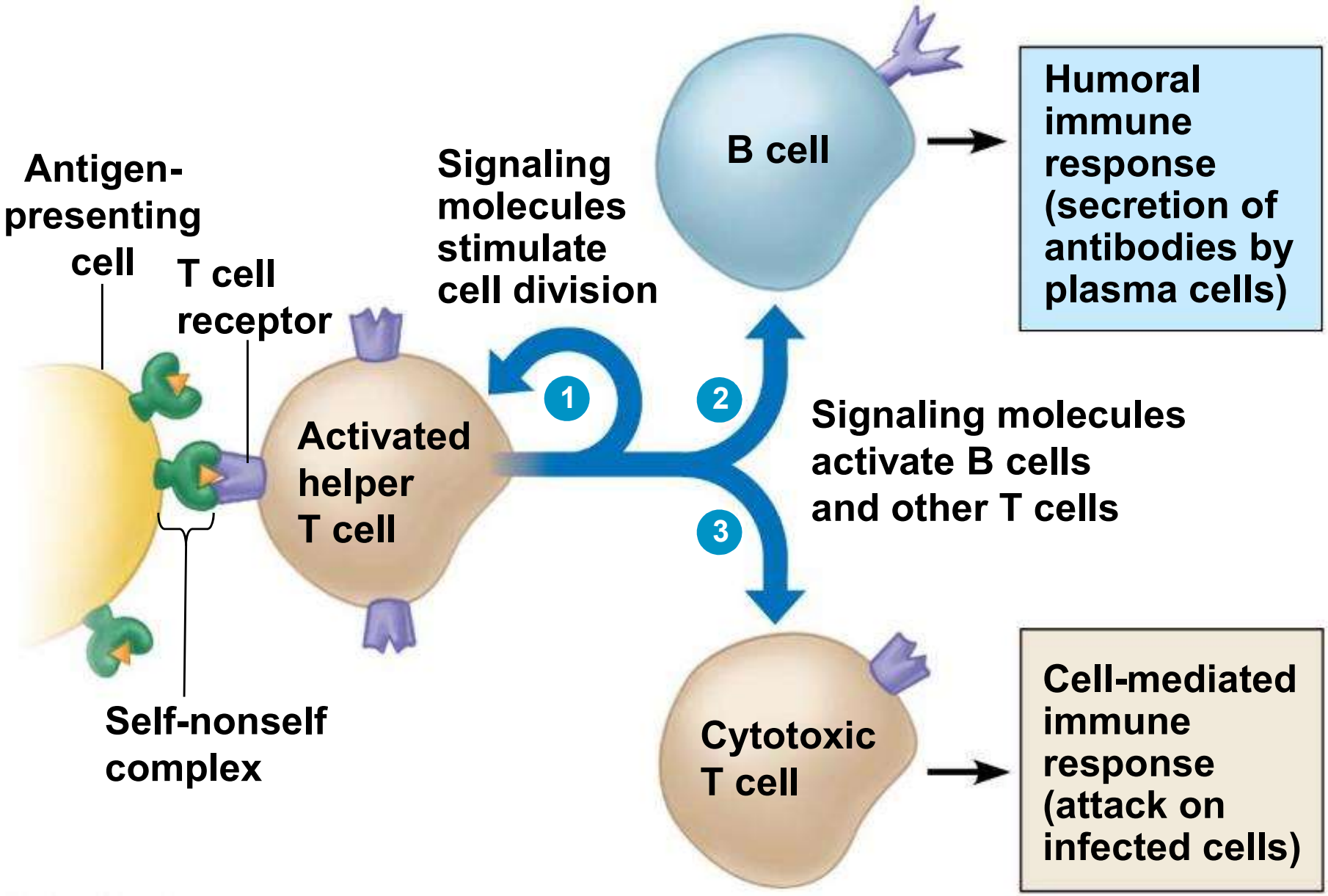
主要組織相容性複合物
Major Histocompatibility Complex, MHC



Interleukin 介白素

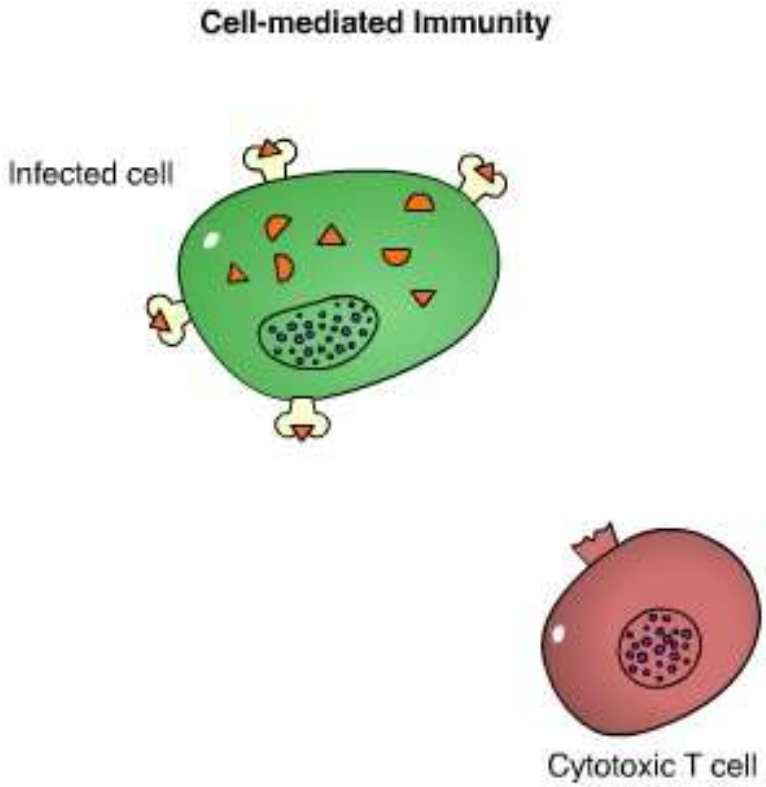
24.12 Helper T cells stimulate the humoral and cell-mediated immune responses

- Activated helper T cells promote the immune response, with a major mechanism being the secretion of additional stimulating proteins. These signaling molecules have three major effects.
  - They stimulate clonal selection of the helper T cell, producing **memory cells and more effector helper T cells**.
  - They help activate B cells, thus stimulating the humoral immune response.
  - They stimulate the activity of cytotoxic T cells of the cell-mediated immune response, our next topic.


Antigen-presenting cell
T cell receptor
Self-nonself complex
Activated helper T cell
Signaling molecules stimulate cell division
1
2
3
B cell
Humoral immune response (secretion of antibodies by plasma cells)
Signaling molecules activate B cells and other T cells
Cytotoxic T cell
Cell-mediated immune response (attack on infected cells)

24.12 Cytotoxic T cells destroy infected body cells

- Cytotoxic T cells are the only T cells that kill infected cells. Once activated,
  - clonal selection ensues, and
  - effector cytotoxic T cells identify infected cells through a self-nonself complex.
- An infected cell has foreign antigens, molecules belonging to the viruses or bacteria infecting it, attached to self proteins on its surface.

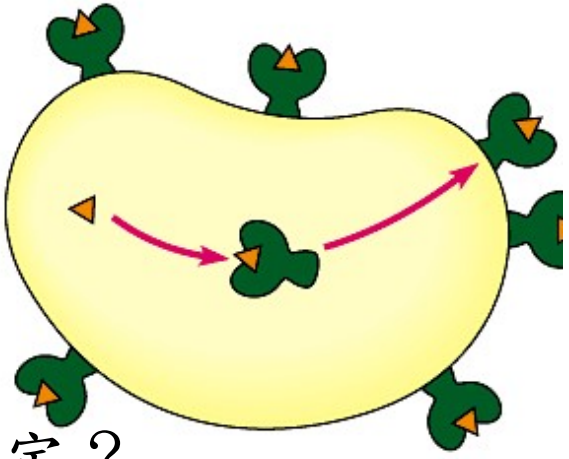


細胞膜上的MHC一般可分做兩類：

第一類MHC：在所有有核的細胞上都可發現，主要功能是將抗原呈現在細胞膜上，以供T細胞辨識。

第二類MHC：主要表現在抗原呈現細胞（antigen presenting cell）如巨噬細胞、B細胞等，以呈現抗原，而得與輔助T細胞結合，啟動專一性免疫機制。

6 loci, 12 genes, hundreds of alleles



MHC and sexual selection: 命中注定 or 基因決定？

Prefer mates with different MHC type?

Influence of HLA on human partnership and sexual satisfaction

Scientific Reports (2016) **6**: 32550

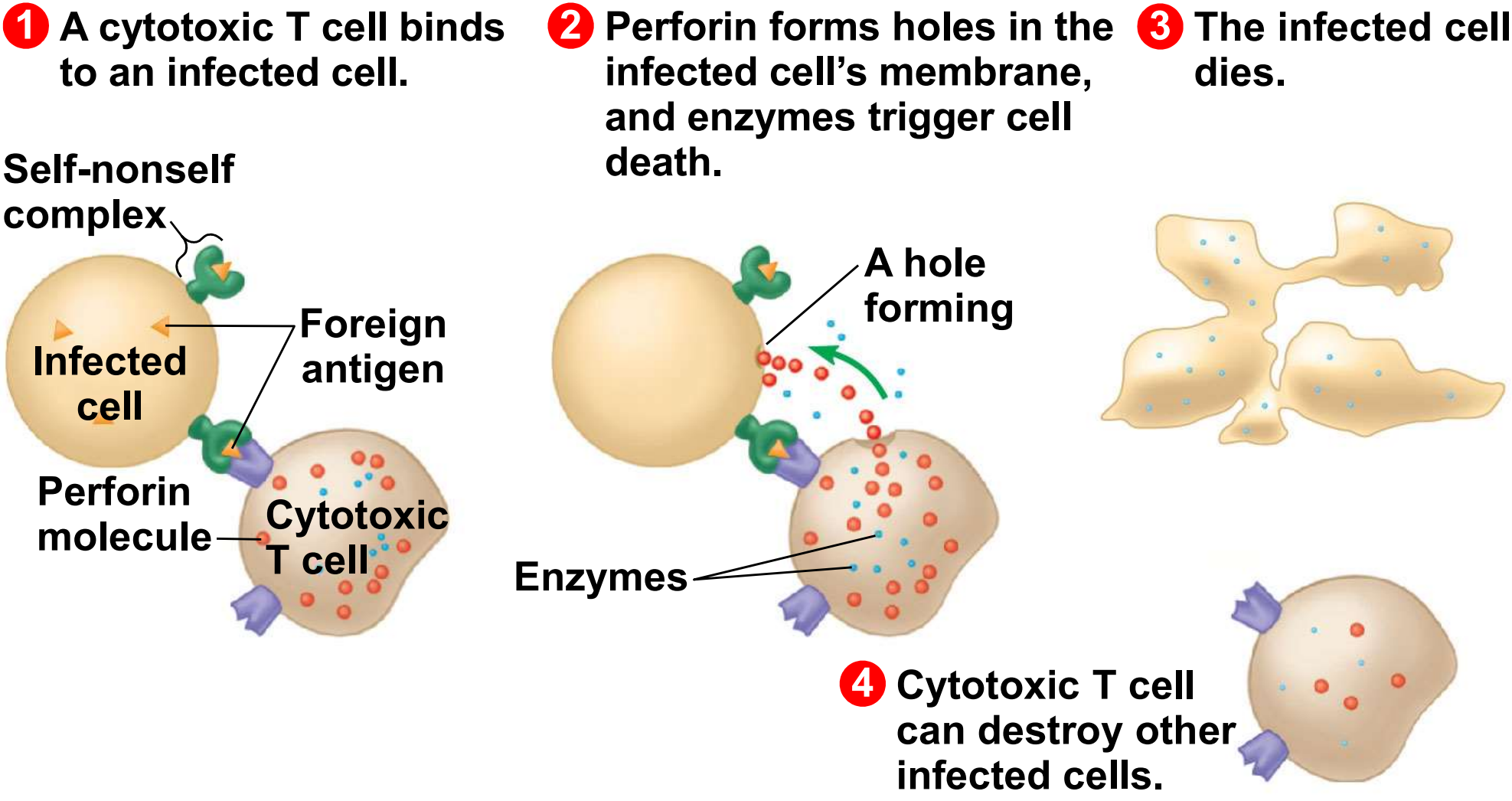
HLA dissimilarity correlates with partnership, sexuality and enhances the desire to procreate. We conclude that HLA mediates mate behaviour in humans.

HLA (Human leukocyte antigen) = MHC

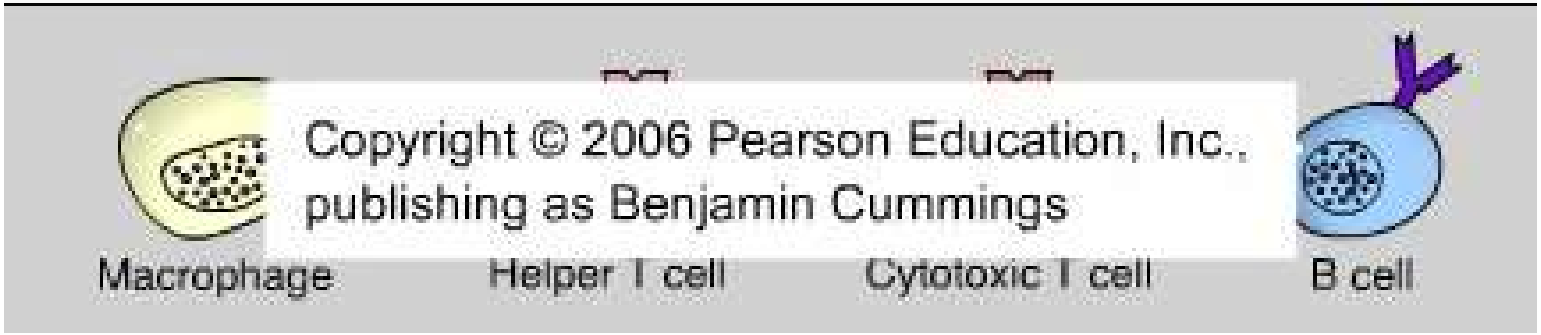
24.13 Cytotoxic T cells destroy infected body cells

- The self-nonself complex on an infected body cell is like a red flag to cytotoxic T cells that have matching receptors.
  - A cytotoxic T cell binds to the infected cell, which activates the T cell, to synthesize several toxic proteins, including one called perforin.
  - Perforin is discharged from the cytotoxic T cell and attaches to the infected cell's plasma membrane, making holes in it. T cell enzymes then enter the infected cell and promote its death by a process called apoptosis.
  - The infected cell is destroyed, and the cytotoxic T cell may move on to destroy other cells infected with the same pathogen.

Figure 24.13_4



Animation: Helper T Cells



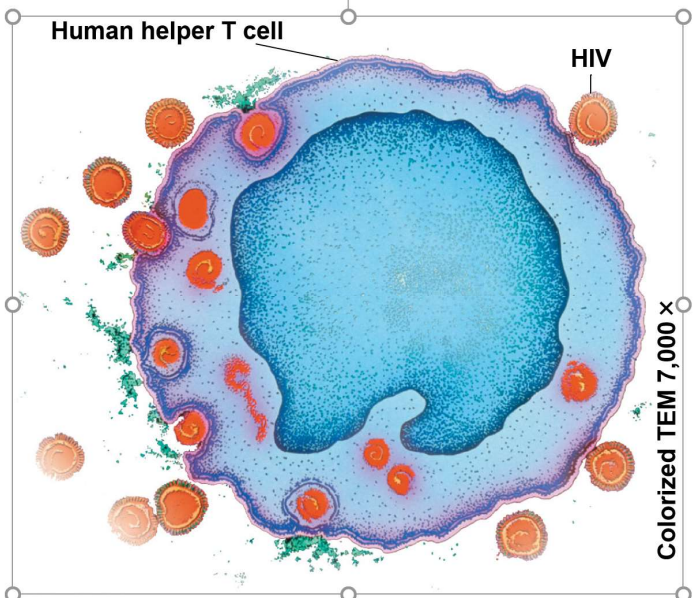
(内容重複1’30”即可)

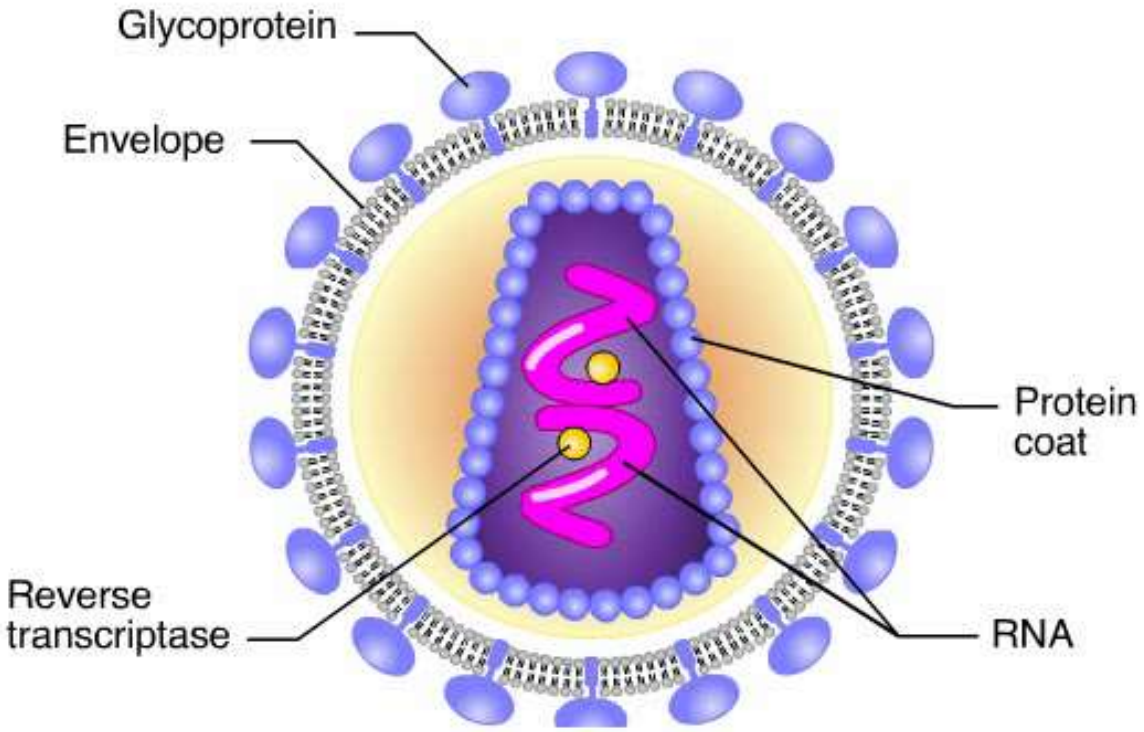
- Cytotoxic T cells also play a role in protecting the body against the spread of some cancers.
- About 15-20% of human cancers worldwide are caused by viruses, including
  - human papillomavirus virus (HPV)
  - hepatitis B virus, which can trigger liver cancer, and
  - Epstein-Barr virus, which can cause lymphomas, cancer of the lymphocytes.

24.14 CONNECTION: HIV destroys helper T cells, compromising the body's defenses

- AIDS (acquired immunodeficiency syndrome), results from infection by HIV, the human immunodeficiency virus.
  - Since 1981 AIDS has killed more than 39 million people, and more than 35 million people live today with HIV.
  - In 2010,
    - 2.7 million people were newly infected with HIV, and
    - over 1.8 million died of AIDS.
  - Most HIV infections and AIDS deaths occur in nonindustrialized nations of southern Asia and sub-Saharan Africa.
- The AIDS virus usually attacks helper T cells, impairing the cell-mediated immune response and humoral immune response, and opening the way for opportunistic infections.

Animation: HIV Reproductive Cycle

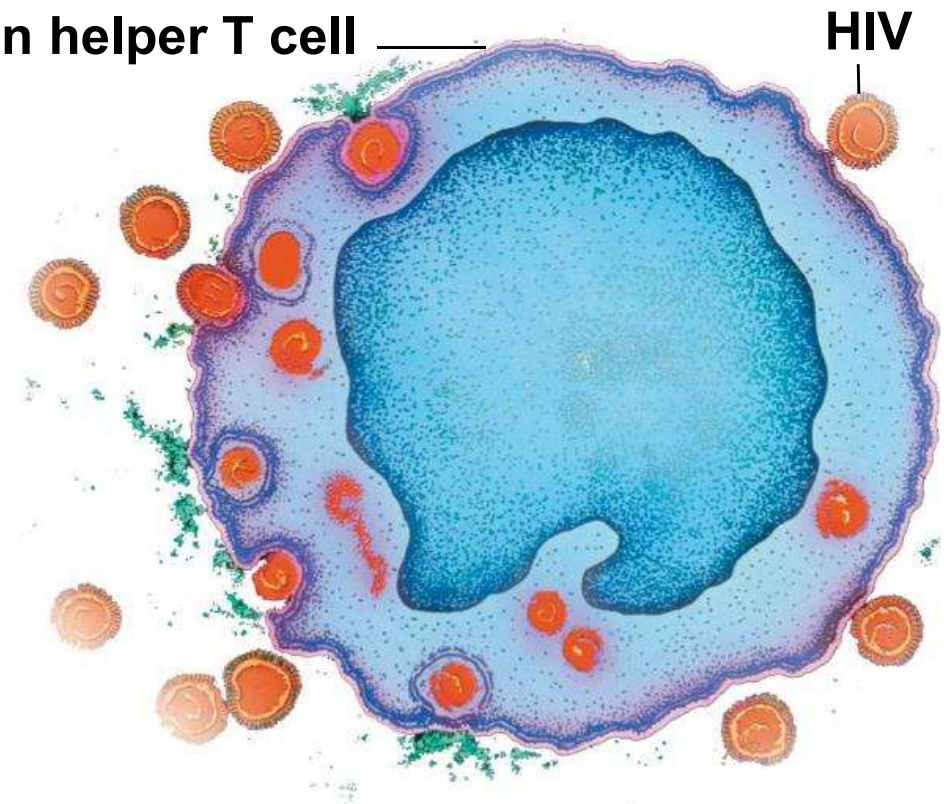




Although AIDS is currently incurable, anti-HIV drugs can slow HIV reproduction and the progress of AIDS for years, allowing most patients to lead normal lives.

2012: FDA approved the 1st HIV prevention pill, for people who have a high risk of infection

- AIDS is currently incurable, although drugs can slow HIV reproduction and the progress of AIDS.
- Drugs, vaccines, and education are areas of focus for prevention of HIV infection.
- HIV mutates at a very high rate during replication because reverse transcriptase does not have an editing function to correct mistakes as DNA polymerase does.
- At one time, there was great hope that a “cocktail” of three anti-AIDS drugs could eliminate the virus in an infected person.
- The continual use of anti-AIDS drugs has led to the spread of drug-resistant HIV strains.



- AIDS patients typically die from
  - opportunistic infections and cancers
  - that would normally be resisted by a person with a healthy immune system.
- Until there is a vaccine or a cure, the best way to stop AIDS is to educate people about how the virus is transmitted.

HIV positive & AIDS; From 600 to 200 $T_h/\mu L$

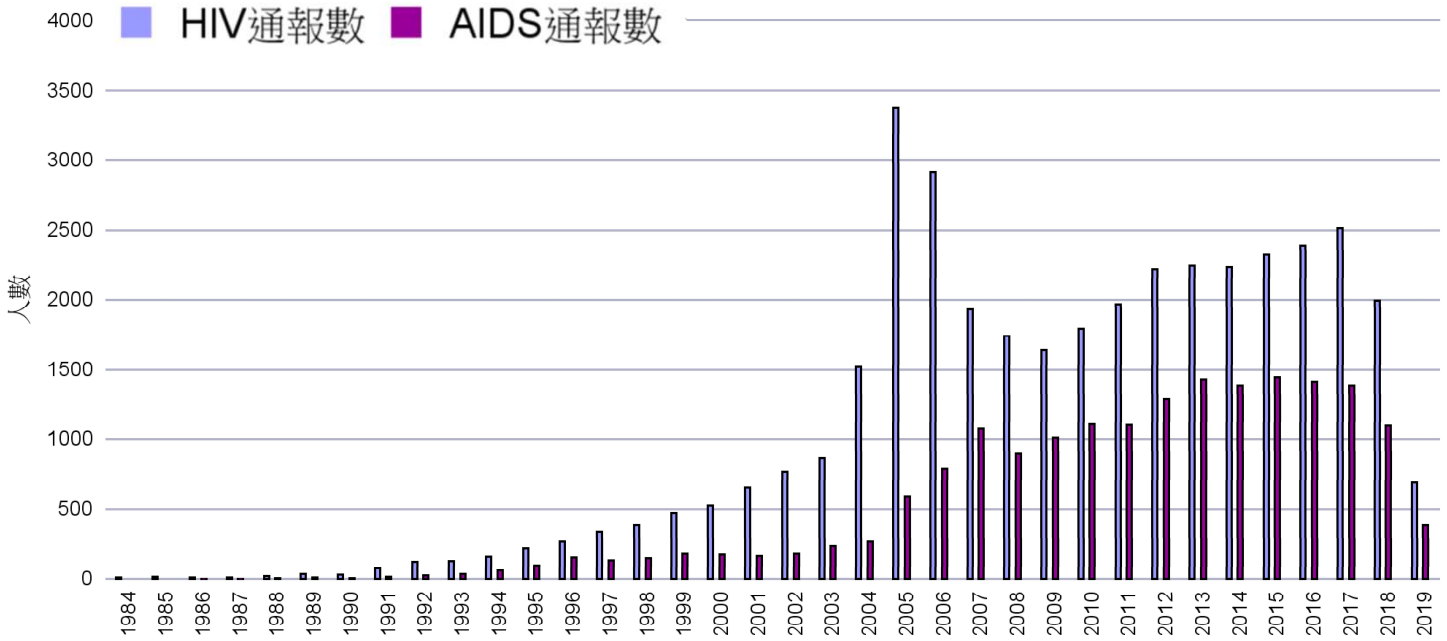
HIV/AIDS統計月報表

【西元2019年4月份】(依診斷日分析)
【西元2019年1月1日累積至2019年4月30日】(依診斷日分析)
【西元2016年、2017年、2018年】(依診斷日分析)
【西元1984年累積至2019年4月30日】(依診斷日分析)

※自2005年起AIDS通報定義除出現伺機性感染和有關AIDS 的腫瘤外，新增CD4小於200cells/mm3

通報時國籍別	感染者數 ※1			發病者數		
	本月通報數(%)	本年個案數(%)	累積個案數(%)	本月通報數(%)	本年個案數(%)	累積個案數(%)
本國籍	168 (96.55%)	686 (96.89%)	38,603 (96.95%)	102 (99.03%)	389 (98.48%)	18,291 (98.94%)
外國籍	6 (3.45%)	22 (3.11%)	1,214 (3.05%)	1 (0.97%)	6 (1.52%)	196 (1.06%)
總計	174 (100%)	708 (100%)	39,817 (100%)	103 (100%)	395 (100%)	18,487 (100%)

本國籍感染人類免疫缺乏病毒者趨勢圖
1984年至2019年4月(依診斷日分析)



2018年總感染數1992人，依危險因素分析，性行為佔96%（男男間性行為佔86%、異性戀佔11%）、靜脈毒癮佔2%。感染者年齡25-34歲最多，佔44%，其次為15-24(26%)、35-49(24%)。

衛福部愛滋病統計資料
https://www.cdc.gov.tw/Category/Page/rCV9N1rGUz9wNr8lggsh2Q

24.15 EVOLUTION CONNECTION: The rapid evolution of HIV complicates AIDS treatment

- As HIV reproduces, mutations occur, some of which can generate new strains of the virus.
  - The virus mutates at a very high rate during replication because reverse transcriptase does not have an editing function to correct mistakes.
  - Some of these mutated viruses are less susceptible to destruction by the immune system and survive, proliferate, and mutate further.
  - Skipping doses of medication allows HIV to replicate, increasing the risk that virus will mutate
  - Multidrug regimens
  - Control use of anti-HIV drug: the timing for drug application to avoid drug-resistance or let the virus mutate until it become susceptible to the drugs again

24.16 The immune system depends on our molecular fingerprints

- The ability of lymphocytes to recognize the body's own molecules to distinguish self from nonself enables our adaptive immune response to battle foreign invaders without harming healthy body cells.
- The key to this ability is that each person's cells have a unique collection of self proteins on the surface that provide molecular "fingerprints" recognized by the immune system.
- Genes at multiple chromosomal loci code for major histocompatibility complex (MHC) molecules, the main self proteins.
- When a person receives an organ transplant or tissue graft, the person's T cells recognize the MHC markers on the donor's cells as foreign.
- Donors are used that most closely match the patient's tissues.
- Transplants between identical twins do not typically have this problem.

DISORDERS OF THE IMMUNE SYSTEM

24.17 CONNECTION: Immune system disorders result from self-directed or underactive responses

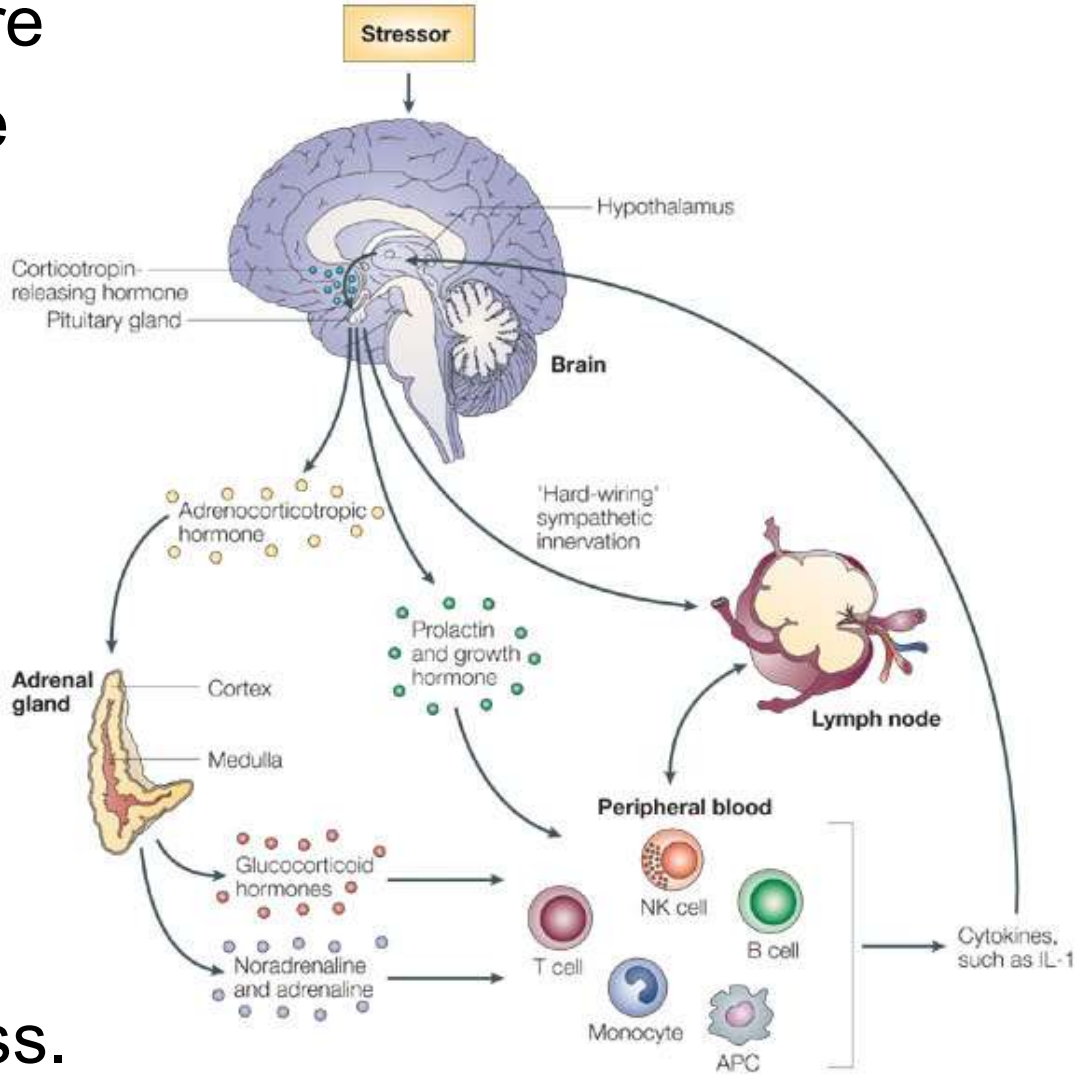
- Autoimmune diseases occur when the immune system turns against the body's own molecules.

自體免疫疾病以及它們影響的組織		
疾病名稱	影響的組織	症狀
紅斑狼瘡症(Systemic lupus erythematosus)	全身的結締組織 (B cell make Ab against self molecules)	臉部發疹、關節疼痛、發燒、疲累、腎臟問題、體重減輕
第一型糖尿病 (Type I diabetes)	胰臟中製造胰島素的細胞 (targeted by cyototoxic T cell)	多尿、視力模糊、體重減輕、疲勞、易怒
葛瑞夫氏症（Graves' disease）	甲狀腺（造成機能亢進）	脆弱、易怒、畏熱、易流汗、體重減輕、失眠
風濕性關節炎（Rheumatoid arthritis）	關節 (cartilage & bone of joints)	疼痛且具損傷性的關節發炎
多發性硬化症（Multiple sclerosis）	神經系統 (mylein sheath attacked by T cells)	失去對肌肉的控制、記憶力減退
Crohn's disease	Against intestine normal flora	chronic digestive tract inflammation

- Immunodeficiency diseases are under reactions of the immune system, in which an immune response is either defective or absent.

SCID: severe combined immunodeficiency

- The immune system may also be suppressed by
  - cancer of the lymphatic system,
  - radiation, and
  - physical or emotional stress.

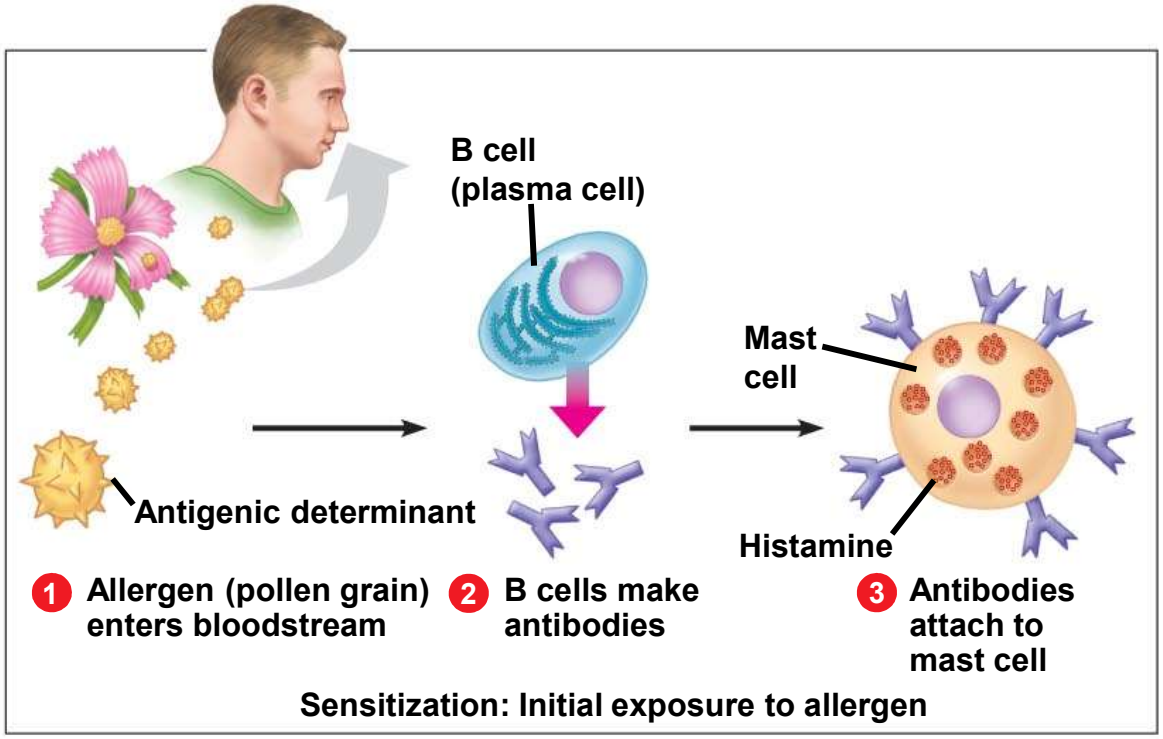


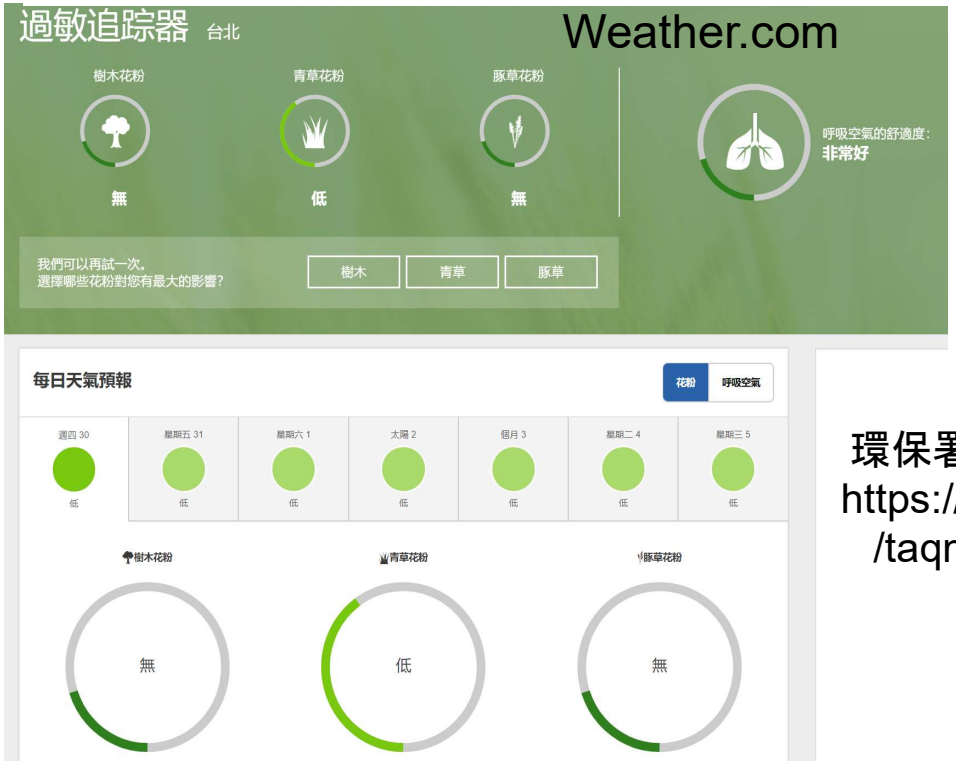
http://www.nature.com/nri/journal/v5/n3/fig_tab/nri1571_F1.html

24.18 CONNECTION: Allergies are overreactions to certain environmental antigens

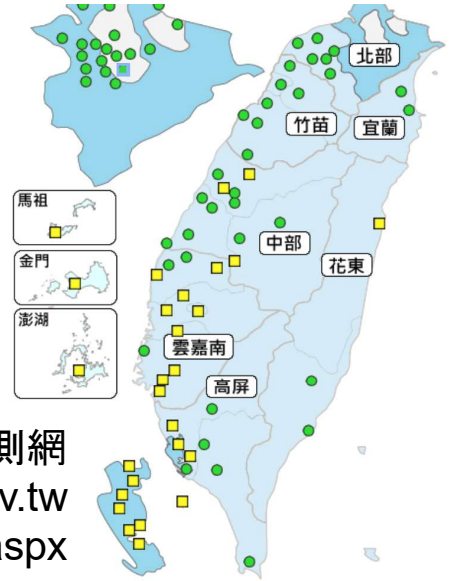
- Allergies are hypersensitive (exaggerated) responses to otherwise harmless antigens in our surroundings.
- Antigens that cause allergies are called allergens.
- Allergic reactions typically occur
  - very rapidly and in response to tiny amounts of an allergen.
- Allergic reactions can occur in many parts of the body, including
  - nasal passages, bronchi, and skin.
- The symptoms of an allergy result from a two-stage reaction.
  - The first stage, called sensitization, occurs when a person is first exposed to an allergen.
  - The second stage begins when the person is exposed to the same allergen later.
    - The allergen binds to mast cells.
    - Mast cells release histamine, causing irritation, itchy skin, and tears.

- Antihistamines 抗組織胺
  - interfere with histamine's action, provide temporary relief, but often make people drowsy.
- Anaphylactic shock 過敏性休克
  - is a dangerous allergic reaction,
  - may occur in people who are extremely sensitive to certain allergens, such as bee venom, penicillin, or allergens in peanuts or shellfish, and
  - can be treated with injections of epinephrine.





環保署空氣品質監測網
https://taqm.epa.gov.tw
/taqm/tw/default.aspx



對健康影響	良好	普通	對敏感族群不健康	對所有族群不健康	非常不健康	危害
空氣品質指標(AQI)	0~50	51~100	101~150	151~200	201~300	301~500
狀態色塊	●	■	▲	⬢	◆	✸
站數	53	28	0	0	0	0

有效數據不足：0站。
係指設備維護、儀器校正、儀器異常、傳輸異常、電力異常或有效數據不足等需查修維護情形，以致資料暫時中斷服務。

古亭 (一般站) (分鐘值)

AQI 空氣品質指標		45 良好
O_3 (ppb) 臭氧	8小時移動平均	49
	小時濃度	39
$PM_{2.5}$ ($\mu g/m^3$) 細懸浮微粒	移動平均	11
	小時濃度	19
PM_{10} ($\mu g/m^3$) 懸浮微粒	移動平均	22
	小時濃度	29
CO (ppm) 一氧化碳	8小時移動平均	0.30
	小時濃度	0.52
SO_2(ppb) 二氧化硫	小時濃度	2.6
NO_2(ppb) 二氧化氮	小時濃度	24

單位 ： 1.μg/m³，微克/立方公尺
2.ppb，十億分之一
3.ppm，百萬分之一

You should now be able to

1. Describe the risks and prevention of HPV infections.
2. Describe the nature of innate defenses in invertebrates and vertebrates.
3. Describe the steps of the inflammatory response and explain how they help to prevent the spread of disease.
4. Describe the specific nature of adaptive immune system responses.
5. Describe the structure and functions of the lymphatic system.
10. Describe four effector mechanisms of the humoral immune system.
11. Describe the uses of antibodies in medicine.
12. Describe the research testing the effectiveness of vaccines against HPV.
13. Describe the specific functions of helper T cells and how they interact with other cells.
14. Explain how cytotoxic T cells destroy infected body cells.
15. Explain how HIV infects cells, multiplies, and causes disease.
16. Explain why it has been difficult to develop a successful treatment for AIDS.
17. Explain how the immune system identifies the body's own molecules and how this system complicates organ transplantations.
18. Describe how the malfunction or failure of the immune system can cause disease.
19. Explain why allergies occur and what causes anaphylactic shock.