4B – Adaptive Immunity
…the end…☹

Adaptive (specific) Immunity

- The general idea:
  - body can recognize specific invader and act to destroy that specific invader.
  - Adaptive immunity develops during an individual's lifetime.
- Result of processes that are:
  - highly specific against one pathogen, often even against one strain of a pathogen
  - NOT inherent, innate or inborn, but only developing after exposure to the pathogen

Dual Nature of Adaptive Immunity

B cells and T cells

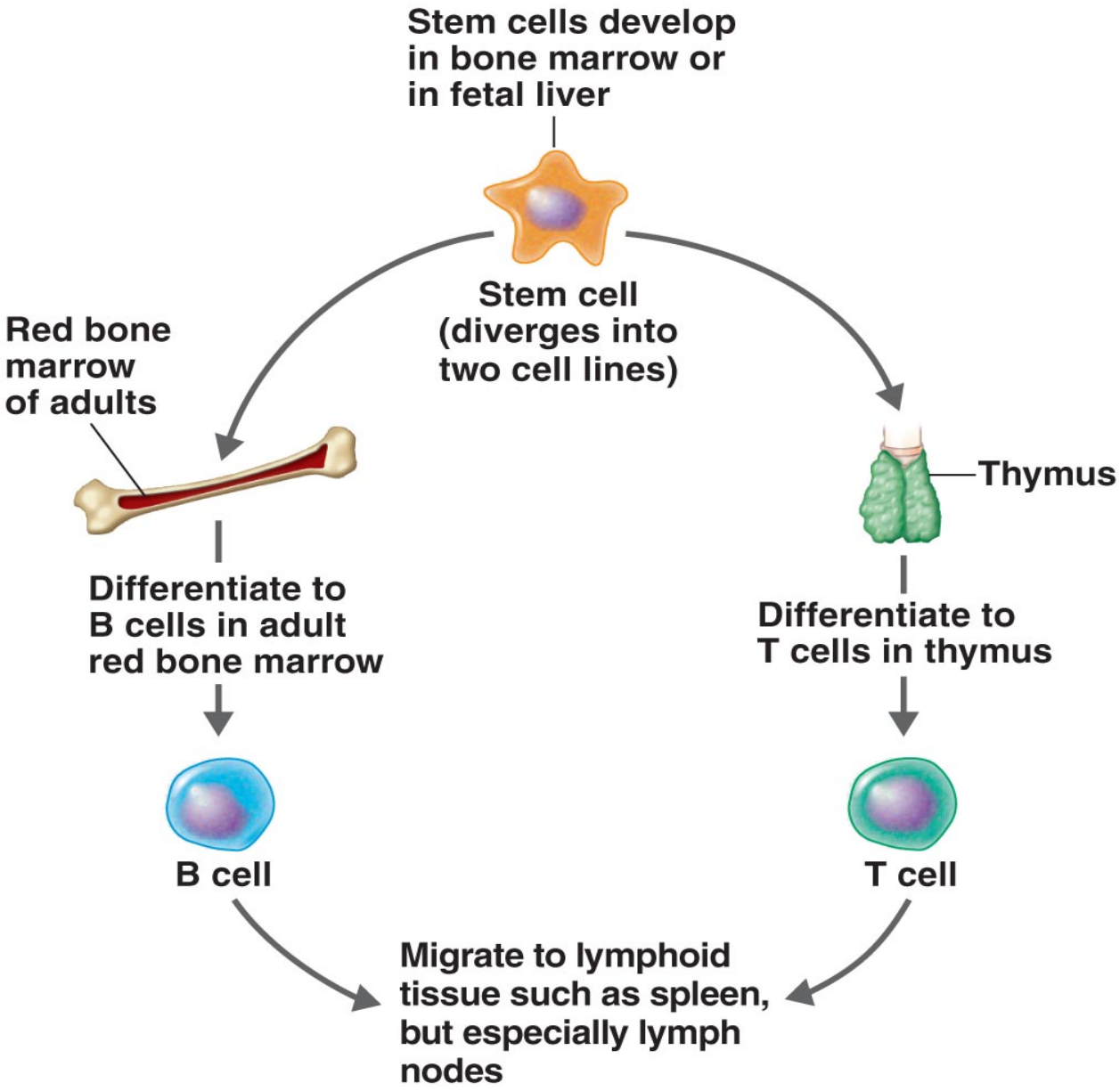


Figure 17.8

Dual Nature of Adaptive Immunity

- T and B cells develop from stem cells in bone marrow
- Humoral immunity(B – cells)
  - B cells mature in the bone marrow
  - Due to antibodies
- Cellular immunity
  - Due to T cells
  - T cells mature in the thymus

- Antigen (Ag): A substance that causes the body to produce specific antibodies or sensitized T cells.

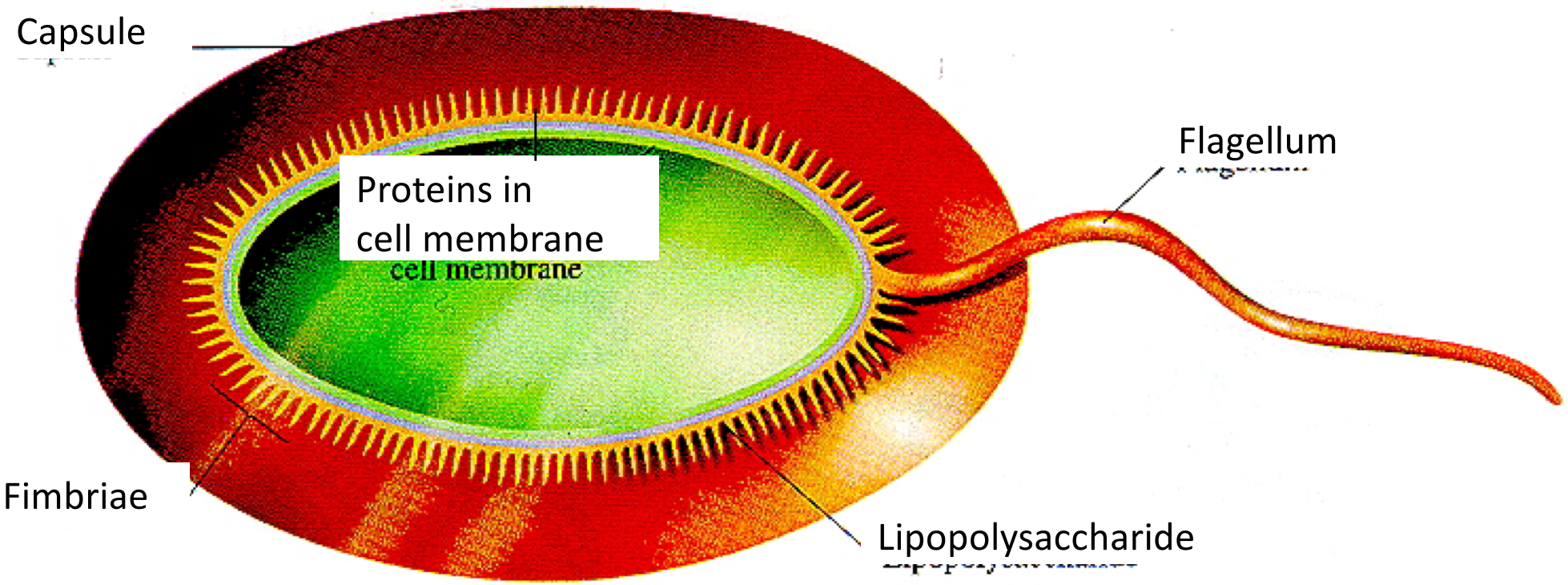
- Antibodies (Ab): Proteins made in response to an Ag; can combine with that Ag.

•Antigens (Ag)

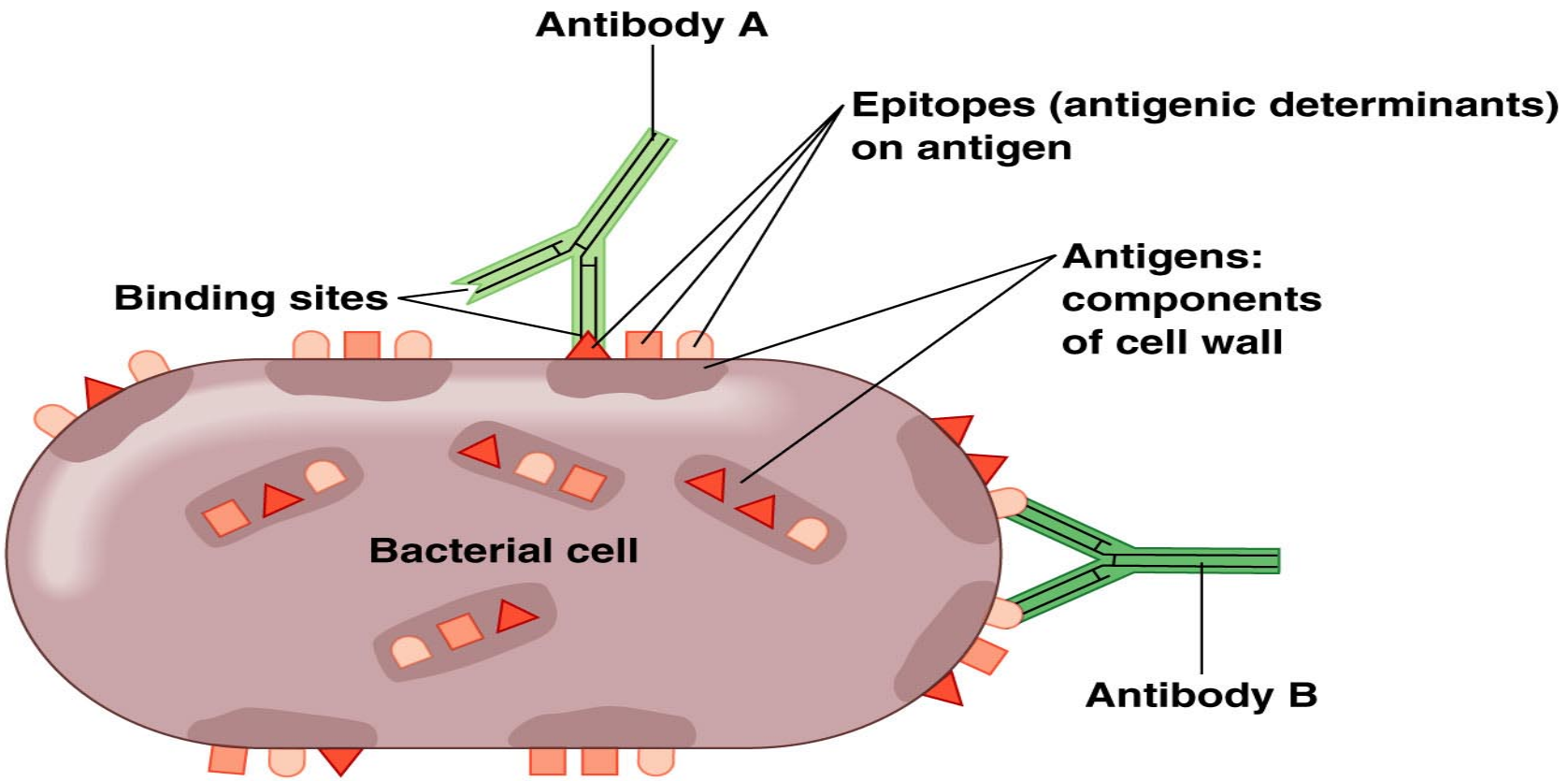
- Antigens : substances that elicit (stimulate) an immune response
- Antigens are usually foreign macromolecules such as proteins or large polysaccharides

•Antigens

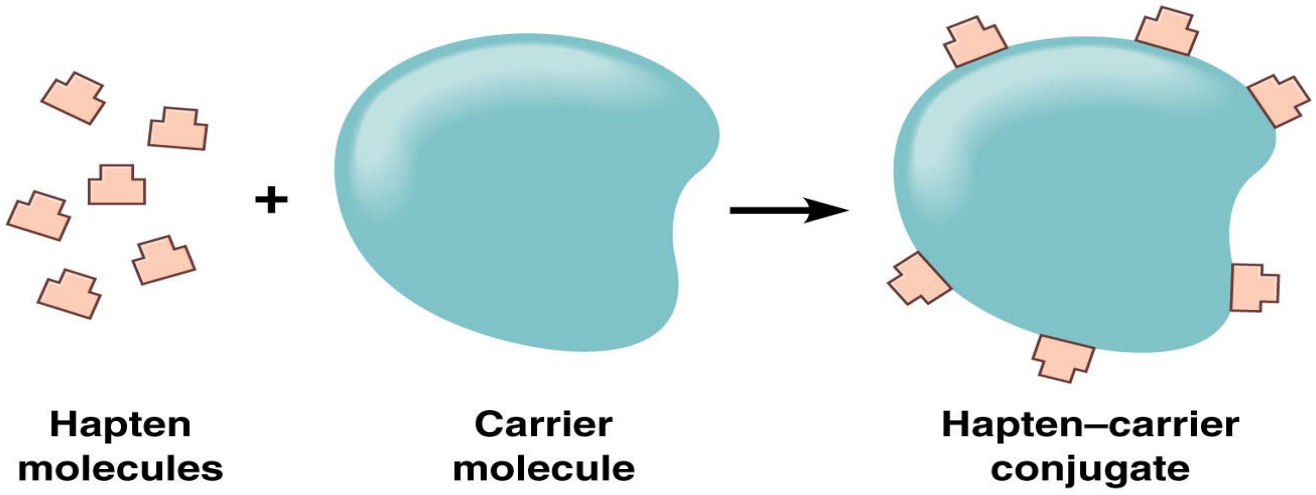
- antigens occur as:
  - *parts* of pathogens, such as viral protein or bacterial capsule



- Epitopes (or antigenic determinants): the specific places on the surface of antigens where antibodies bond:



- Haptens: Small molecules not antigenic by themselves, but forming antigens when bonded with blood proteins such as albumin. Become the determinant sites.
- Penicillin is a good example of a hapten



Antigens occur as:

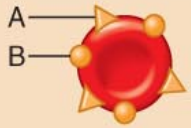
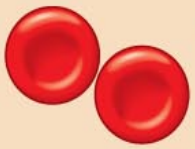
- *products* of pathogens, such as bacterial exotoxins
- vaccines (preparations of one or more antigens administered to confer immunity)

  - Attenuated whole-agent vaccines
    - Living but weakened
  - Inactivated whole-agent vaccines
    - Microbes killed usually by formalin or phenol
  - Toxoids
    - Inactivated toxins
  - Subunit vaccines
    - Use only antigenic fragments
    - Recombinant vaccines created (genetically modified yeast against Hepatitis B viral protein coat)

antigens occur as:

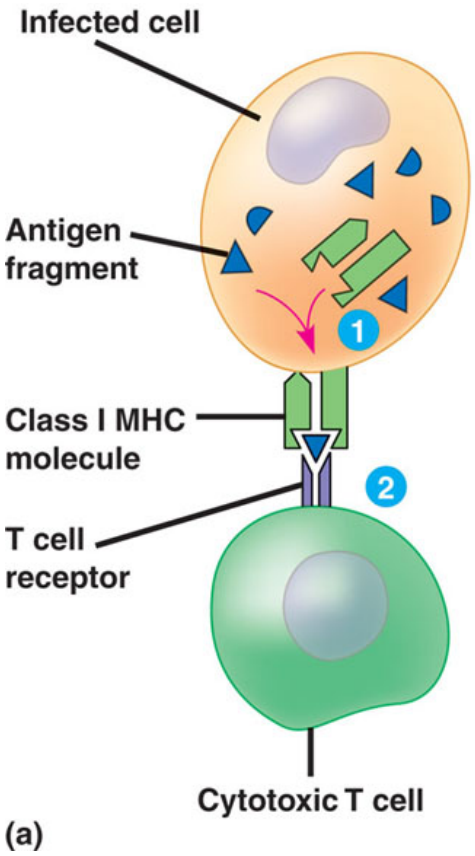
- substances causing allergies (allergens)
- chemicals on the surface of all tissues (tissue antigens or MHC — major histocompatibility complex—antigens)
  - ABO blood group system as example
    - RBC (red blood cell) antigens

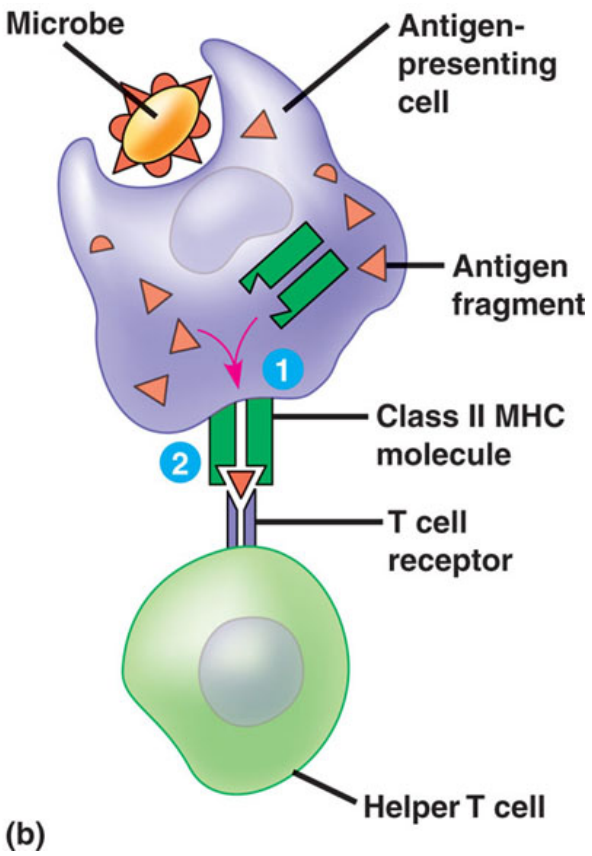
Table 19.2 The ABO Blood Group System

Blood Group	Erythrocyte or Red Blood Cell Antigens	Illustration	Plasma Antibodies	Blood That Can Be Received	Frequency (% U.S. Population)		
					White	Black	Asian
AB	A and B		Neither anti-A nor anti-B antibodies	A, B, AB, O	3	4	5
B	B		Anti-A	B, O	9	20	27
A	A		Anti-B	A, O	41	27	28
O	Neither A nor B		Anti-A and Anti-B	O	47	49	40

"Self " antigens and Major Histocompatibility Complex (MHC)

- Class 1 MHC molecules
  - Found on all nucleated cells
  - Activate Natural Killer Cells if missing or changed
- Class 2 MHC molecules
  - Work with both Cytotoxic T Cells Helper T cells
  - Derived from foreign materials that have been internalized

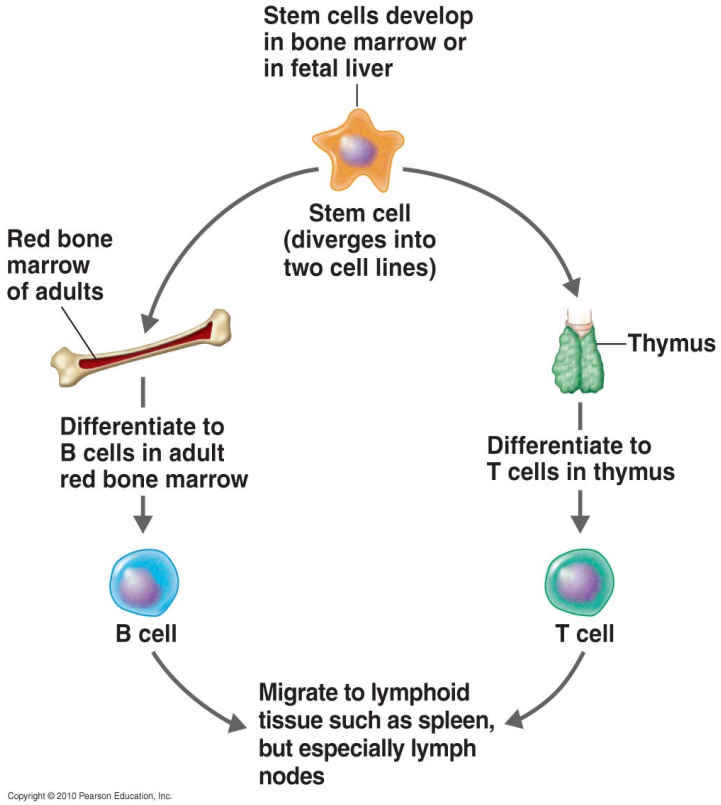




- Self-Tolerance
  - Body should not make Ab against self.
  - Autoimmunity
    - Diseases produced by failure in the immune system to recognize and tolerate self-antigens
      - » Lupus
      - » Rheumatoid arthritis
      - » Multiple sclerosis
      - » See pp. 532-533 (more than 40 autoimmune diseases!)

•Development of Immune System

- Some immature lymphocytes (80%) are processed by thymus to become T cells (T lymphocytes)
- Other immature lymphocytes are processed by bone marrow to become B cells (B lymphocytes)
- T cells produce
  Cell Mediated (Cellular) Immunity
- B cells produce
  Humoral (Antibody-Mediated) Immunity



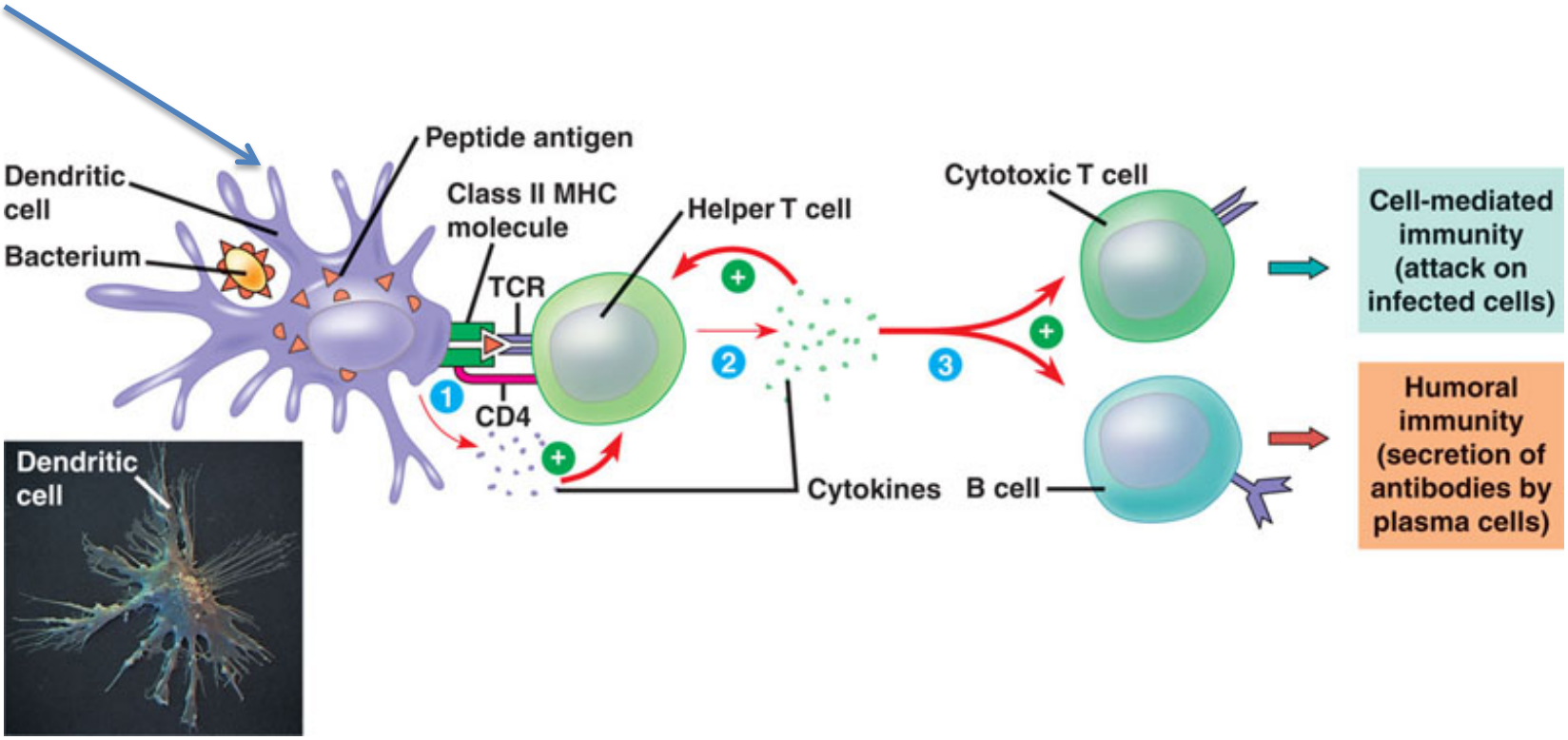
Immune Responses

- Humoral Immunity
  - Involves B cells
  - produces antibodies that circulate in the blood, plasma and lymph
  - cells do not have to be next to antigen to attack
- Cell-mediated Immunity
  - Involves T cells
  - cells must be next to antigens to attack

Example (a response to nearly all Antigens)

- Helper T cells
  - attach to macrophage that has attacked an antigen
    - often uses CD4 receptors (binds to class 2 MHC)
  - Releases interleukin (a Cytokine)
  - activates Cytotoxic T cells and Plasma B cells

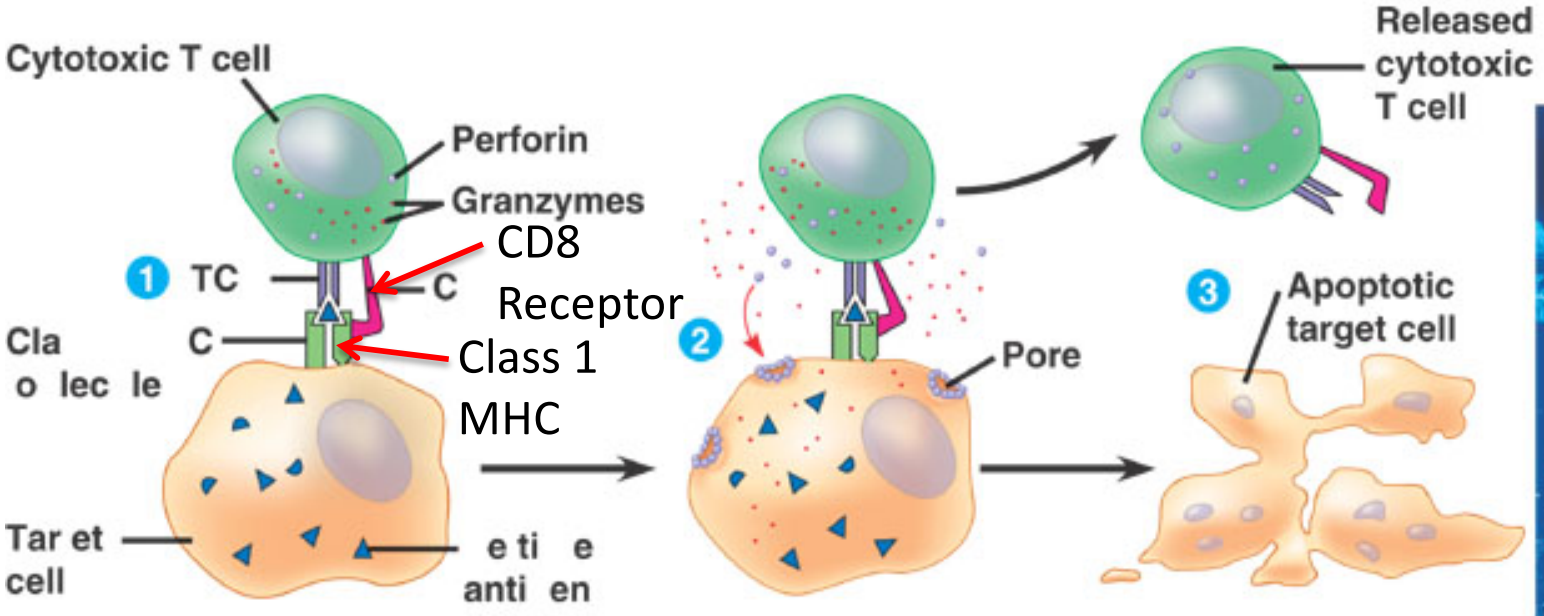
An Antigen Presenting Cell



Example of a Cell-mediated Response

- Cytotoxic T cells
  - attach to infected cells / Cancer Cells
  - Usually uses a CD8 receptor (binds to class 1 MHC)
  - perforin (protein) makes a pore in membrane
  - ions and water enters pores
  - infected cell lyses

Remember, involved with "self"



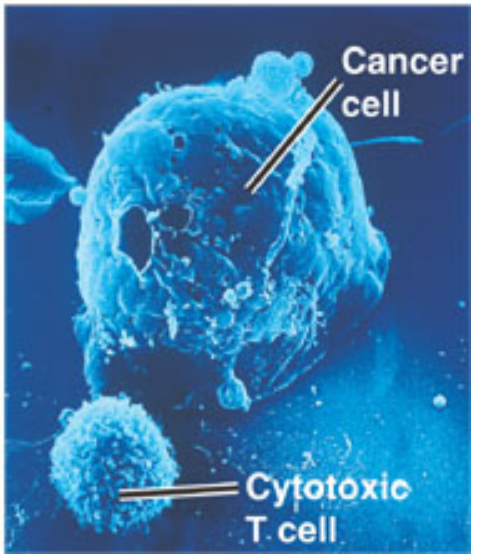
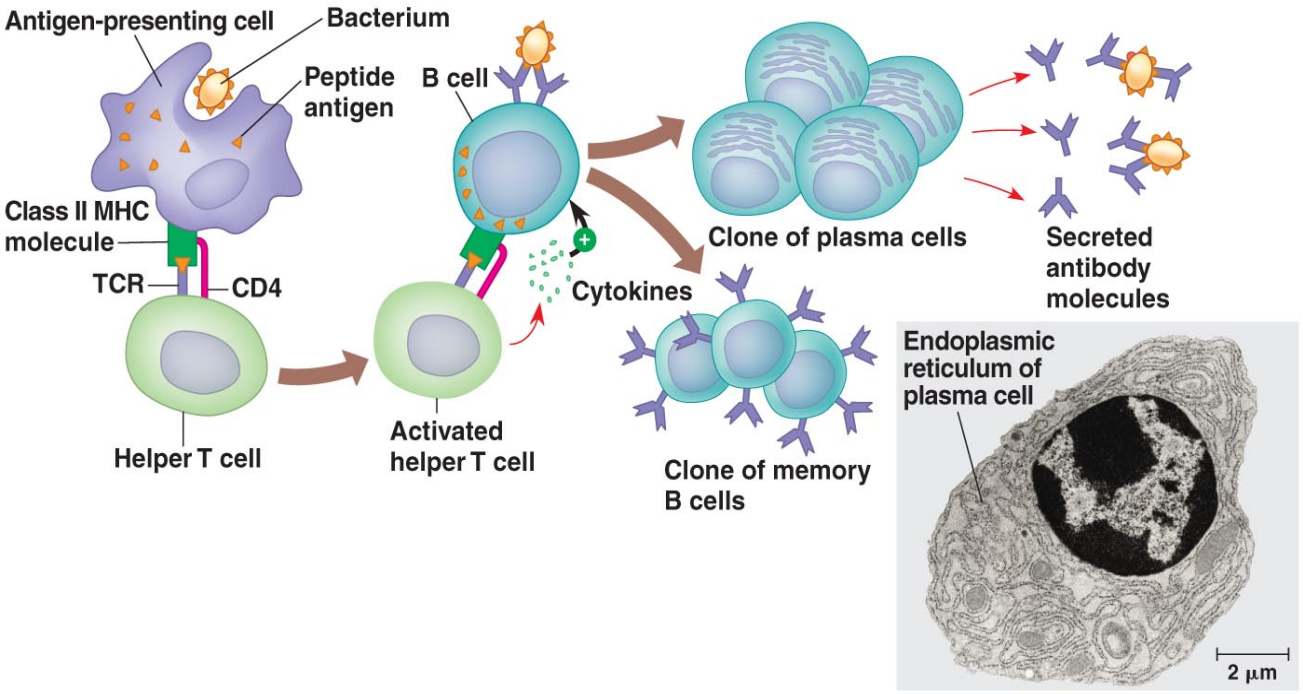


Table 17.2 Principal Cells That Function in Cell-Mediated Immunity

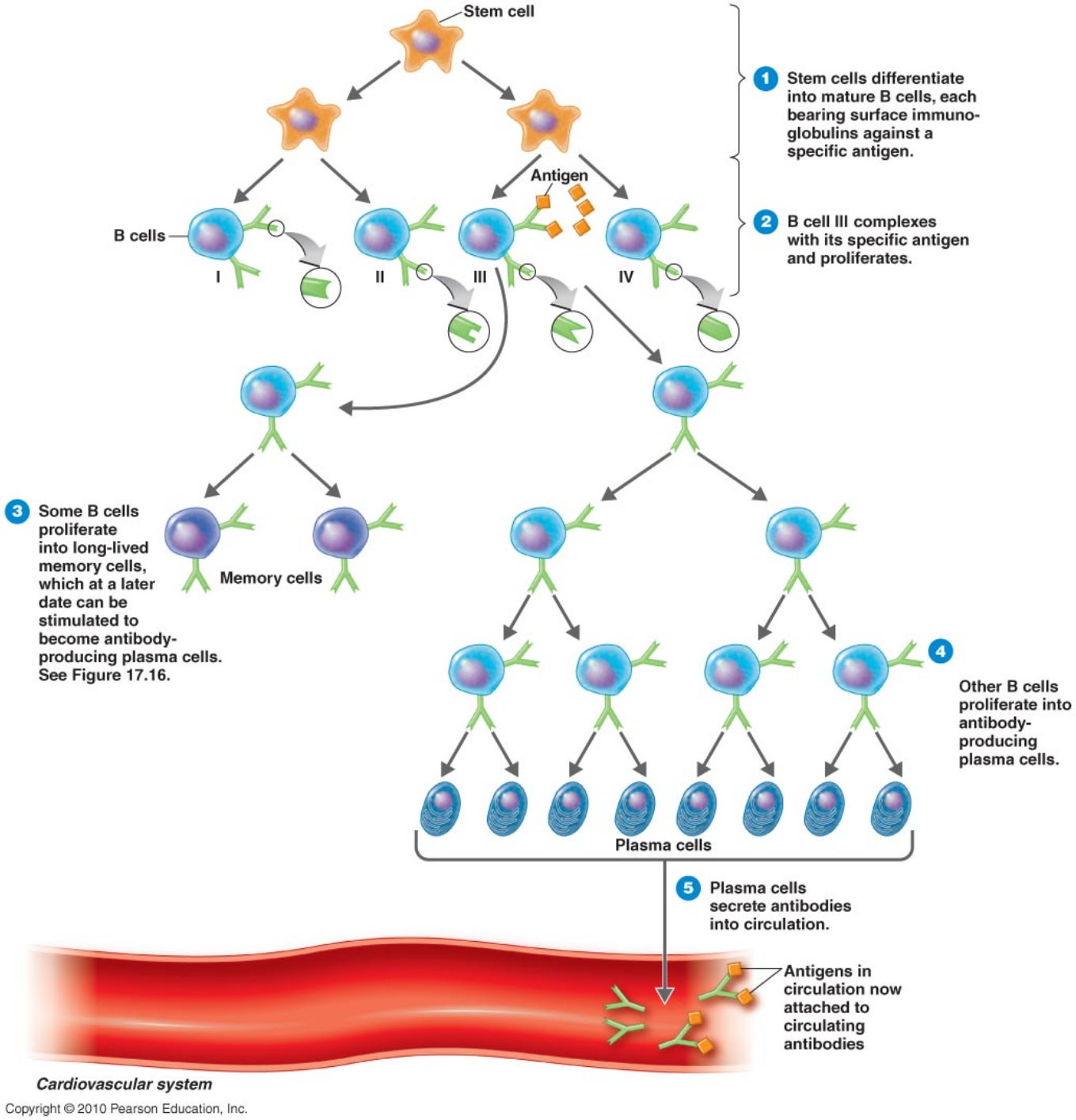
Cell	Function
T Helper (T_H1) Cell	Activates cells related to cell-mediated immunity: macrophages, T_C cells, and natural killer cells
T Helper (T_H2) Cell	Stimulates production of eosinophils, IgM, and IgE
Cytotoxic T Lymphocyte (CTL)	Destroys target cells on contact; generated from T cytotoxic (T_C) cell
T Regulatory (T_{reg}) cell	Regulates immune response and helps maintain tolerance
Activated Macrophage	Enhanced phagocytic activity; attacks cancer cells
Natural Killer (NK) Cell	Attacks and destroys target cells; participates in antibody-dependent cell-mediated cytotoxicity

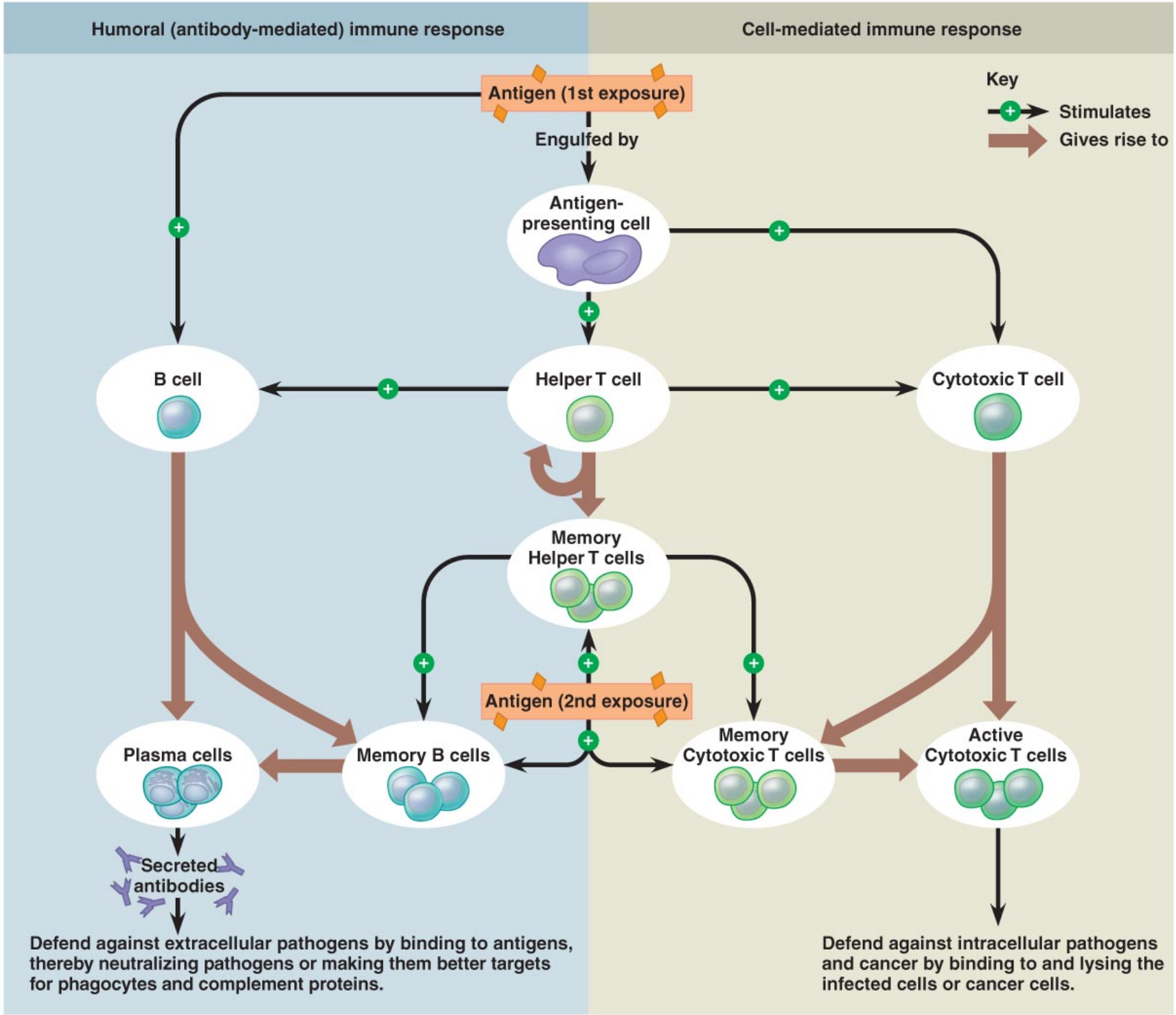
Example of a B-cell (humoral immunity) Response to Extracellular Pathogens



- extracellular pathogens
- Plasma B cells produce antibodies
- Memory B cells live a long time and can help produce other B cells quickly when re-infected by the same antigen

- Clonal selection and differentiation of B cells





Cytokines

- generic term for protein "messenger" chemicals that allow one cell to communicate with another. There are *many (more than 200?)*:
  - Interleukins (at least 29 kinds): communicate between white blood cells
  - interferons: from virus-infected cells
  - histamine: causes inflammation and allergy

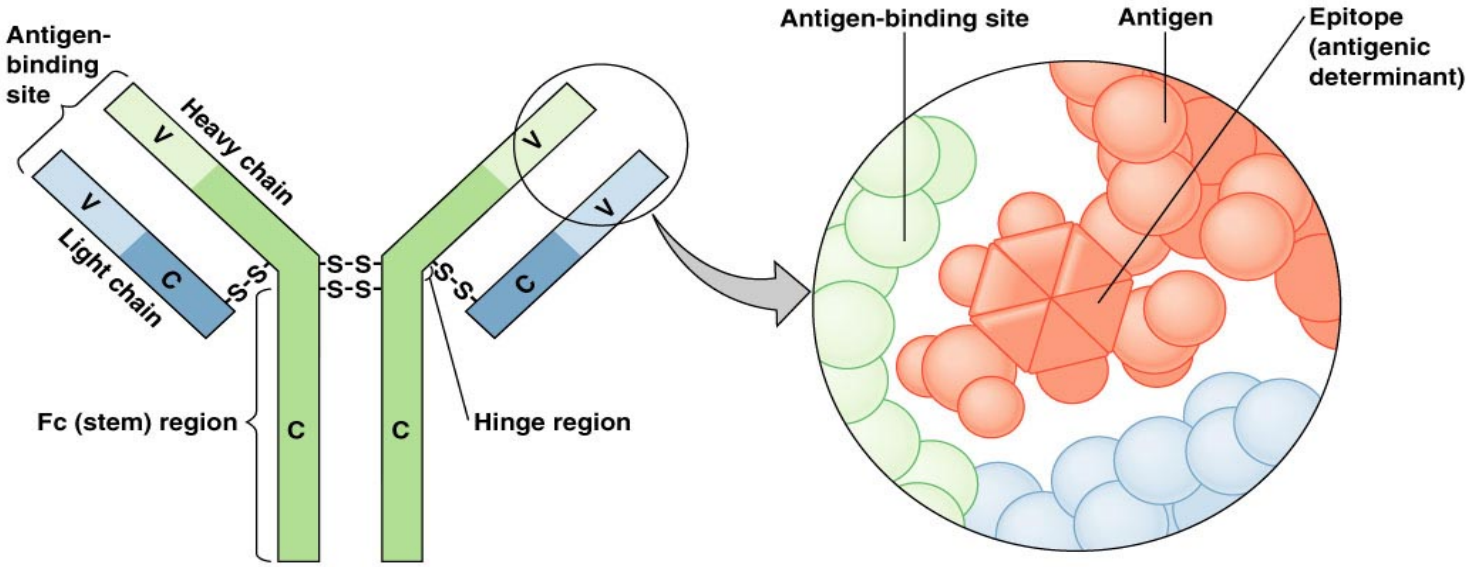
Cells Communicate via Cytokines

Cytokine	**Representative Activity**
Interleukin-1 (IL-1)	Stimulates T_H cells in presence of antigens; attracts phagocytes
Interleukin-2 (IL-2)	Proliferation of antigen-stimulated $CD4^+$ T helper cells, proliferation and differentiation of B cells; activation of $CD8^+$ T cells and NK cells
Interleukin-12 (IL-12)	Inhibits humoral immunity; activates T_H1 cellular immunity

Cells Communicate via Cytokines

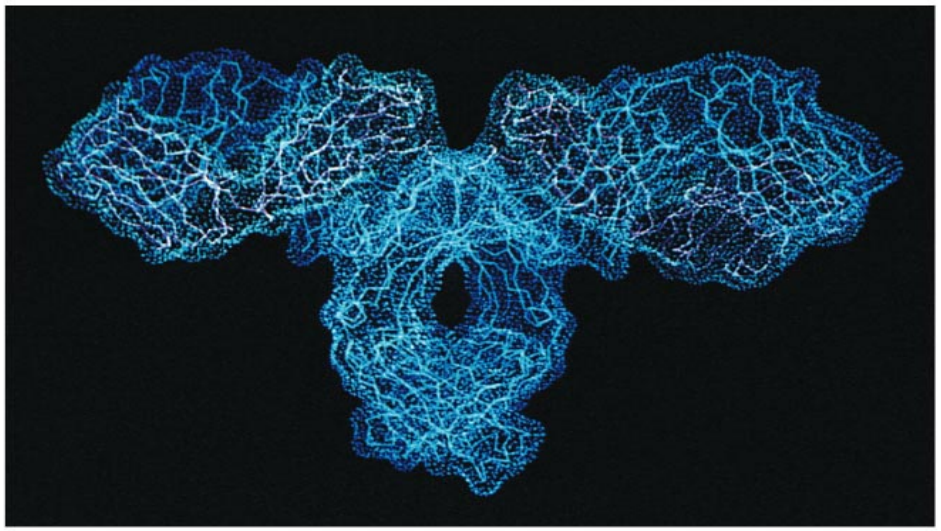
Cytokine	**Representative Activity**
Chemokines	Induce the migration of leukocytes
TNF-α	Promotes inflammation
Hematopoietic cytokines	Influence differentiation of blood stem cells
IFN-α and IFN-β	Response to viral infection; interfere with protein synthesis
IFN-γ	Stimulates macrophage activity

Antibody Structure



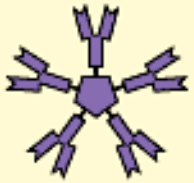
(a) Antibody molecule

(b) Enlarged antigen-binding site bound to an epitope



(c) Computer graphic model of an antibody molecule

Table 43.1 The Five Classes of Immunoglobulins

IgM (pentamer) 	IgMs are the first circulating antibodies to appear in response to an initial exposure to an antigen; their concentration in the blood then declines rapidly. Thus the presence of IgM usually indicates a current infection. IgM consists of five Y-shaped monomers arranged in a pentagonal structure. The numerous antigen-binding sites make it very effective in agglutinating antigens and in reactions involving complement. IgM is too large to cross the placenta and does not confer maternal immunity.
IgG (monomer) 	IgG is the most abundant of the circulating antibodies. It readily crosses the walls of blood vessels and enters tissue fluids. IgG also crosses the placenta and confers passive immunity on the fetus. IgG protects against bacteria, viruses, and toxins in the blood and lymph, and triggers action of the complement system.
IgA (dimer) 	IgA is produced by cells in mucous membranes. The main function of IgA is to prevent the attachment of viruses and bacteria to epithelial surfaces. IgA is also found in many body secretions, such as saliva, perspiration, and tears. Its presence in the first milk produced helps protect the infant from gastrointestinal infections.
IgD (monomer) 	IgD antibodies do not activate the complement system and cannot cross the placenta. They are mostly found on the surfaces of B cells, probably functioning as antigen receptors that help initiate the differentiation of B cells into plasma cells and memory B cells.
IgE (monomer) 	IgE molecules are slightly larger than IgG and represent only a small fraction of the antibodies in the blood. The tails attach to mast cells and basophils and, when triggered by an antigen, cause the cells to release histamine and other chemicals that cause an allergic reaction.

IgM - First to appear, numerous binding sites make them effective at agglutinating antigens.

IgG – Most abundant, crosses placenta

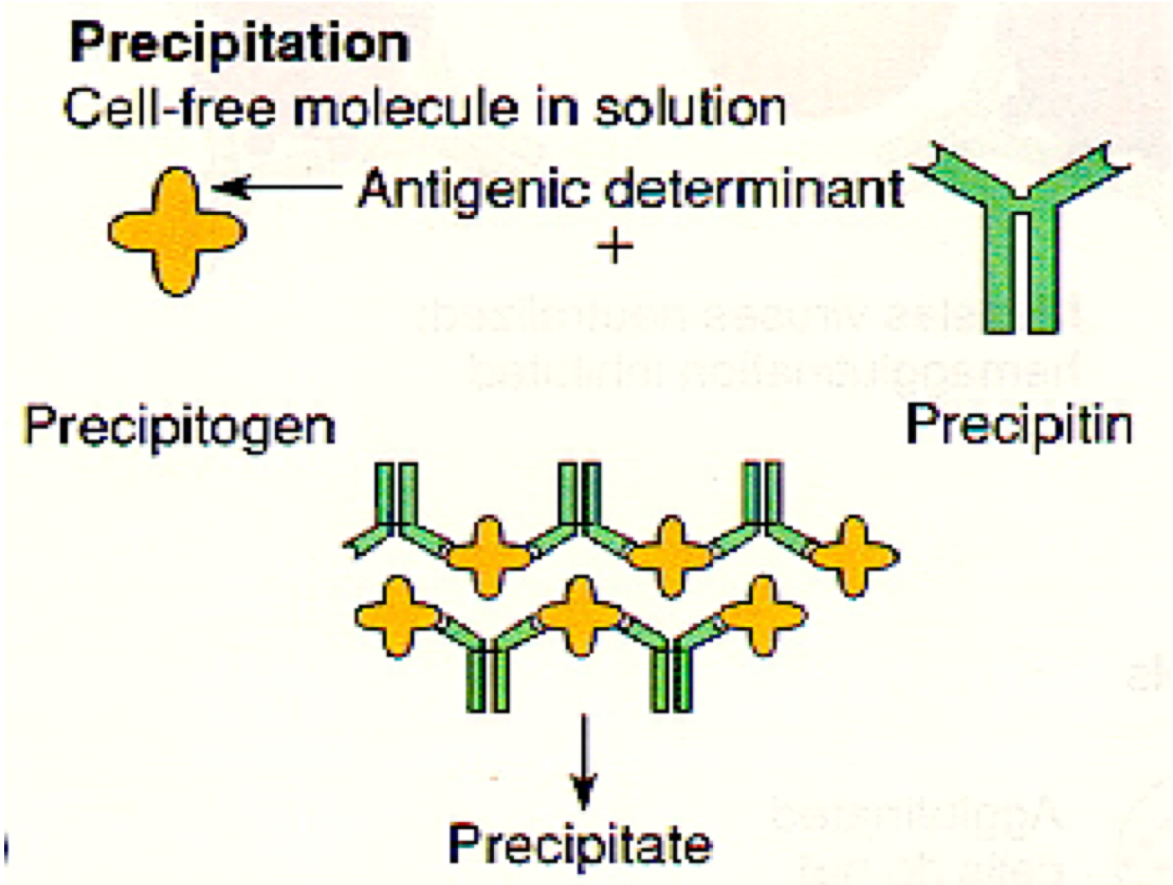
IgA – produced in mucous membranes, prevent virus/bacteria attachment to epithelial cells; present in “first milk” – protects infants from GI infections.

IgD – Mostly found on B cells as antigen receptors

IgE – Involved with allergic reactions; cause release of histamine

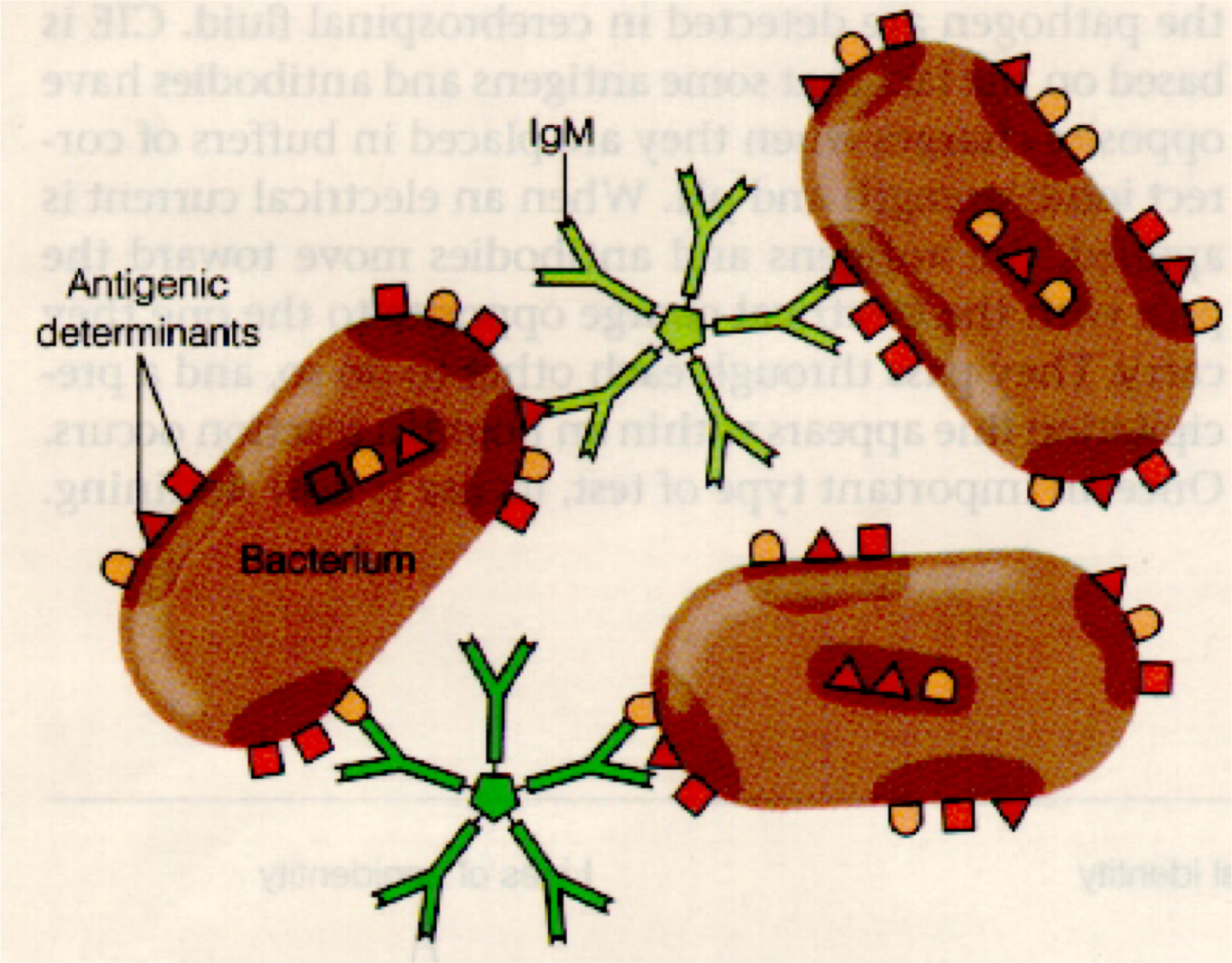
Acquired Immunity: Things Abs can do

- 1. Precipitation: soluble Ag becomes insoluble, forms precipitate

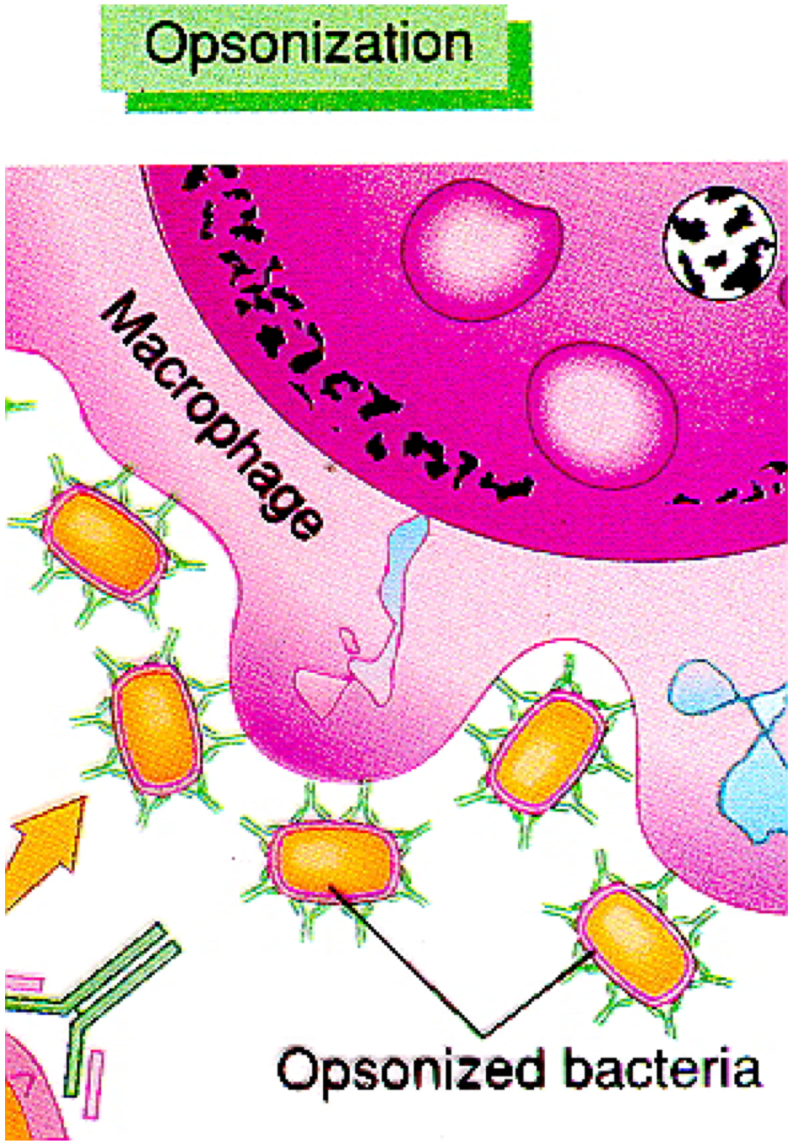


Essay!

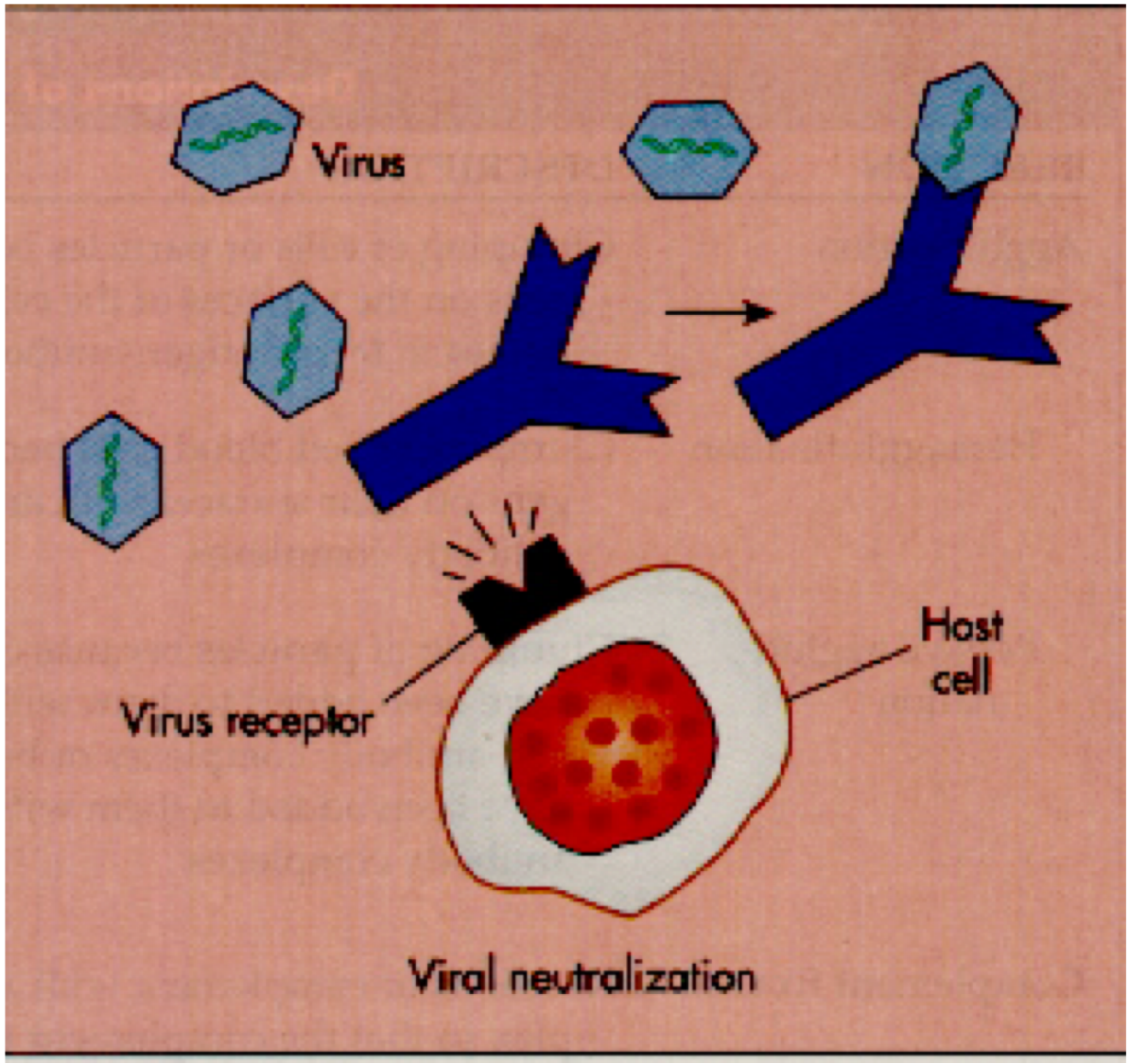
- 2. Agglutination: particles, such as bacteria, are clumped together



- 3. Opsonization: pathogens prepared for phagocytosis

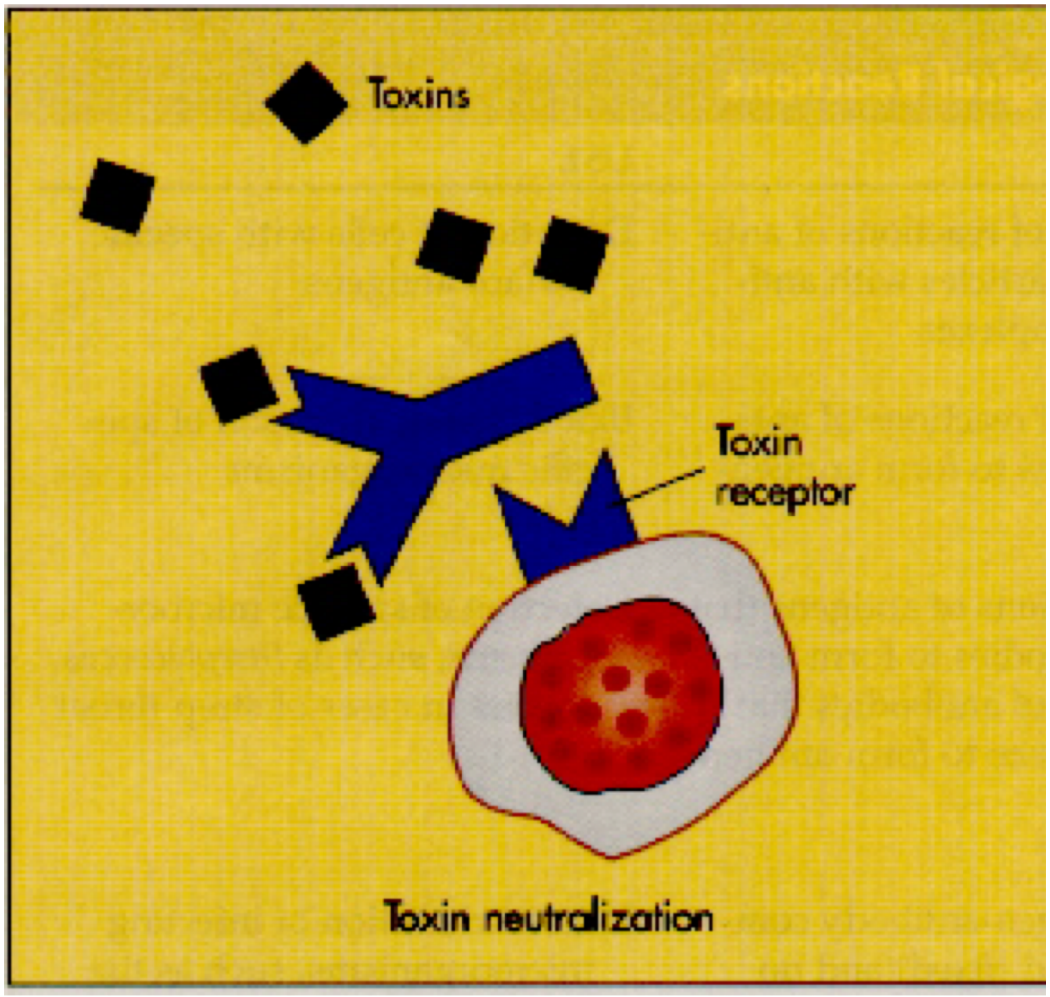


- 4. Viral neutralization:
  Abs bond to virus,
  block attachment to
  host cell



things antibodies can do

- 5. Toxin neutralization: Abs bond to toxin; inactivate it (antitoxins: Abs that neutralize toxins)

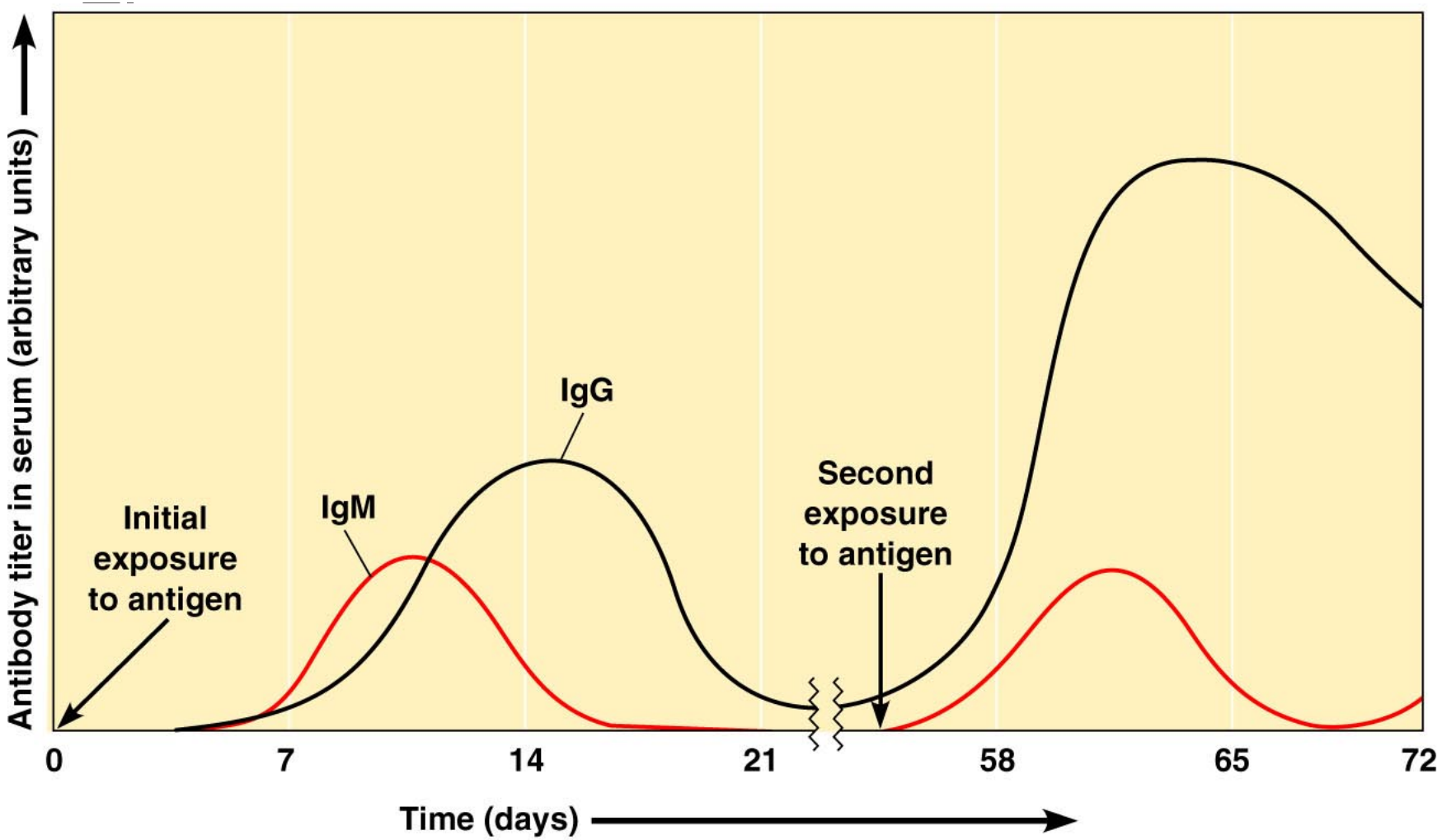


More terms….

- Serology: The study of reactions between antibodies and antigens.
- Antiserum: The generic term for serum because it contains Ab.
- Globulins: Serum proteins
- Immunoglobulins: Antibodies

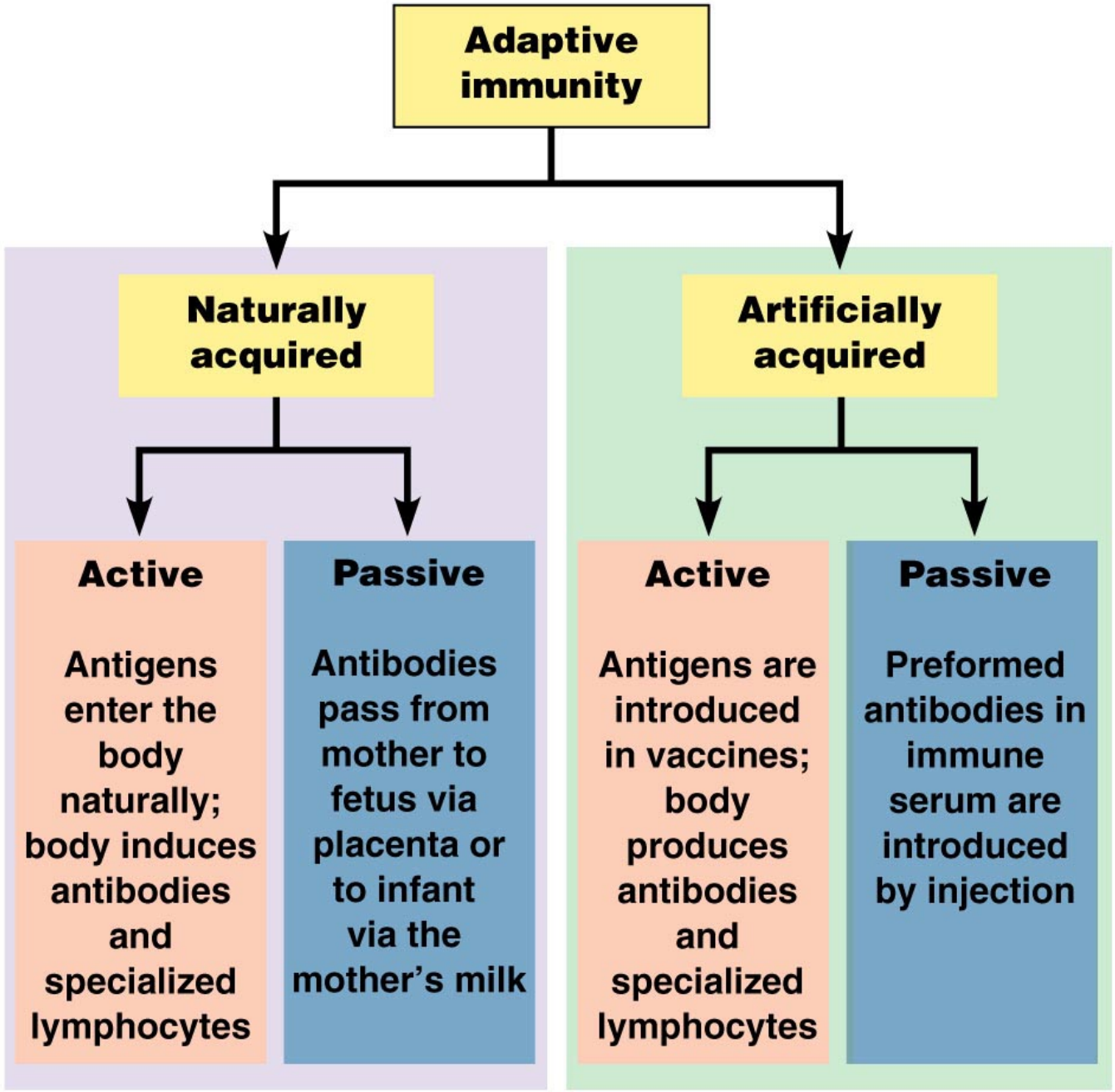
Immunological Memory

- Titer = level of antibodies in blood



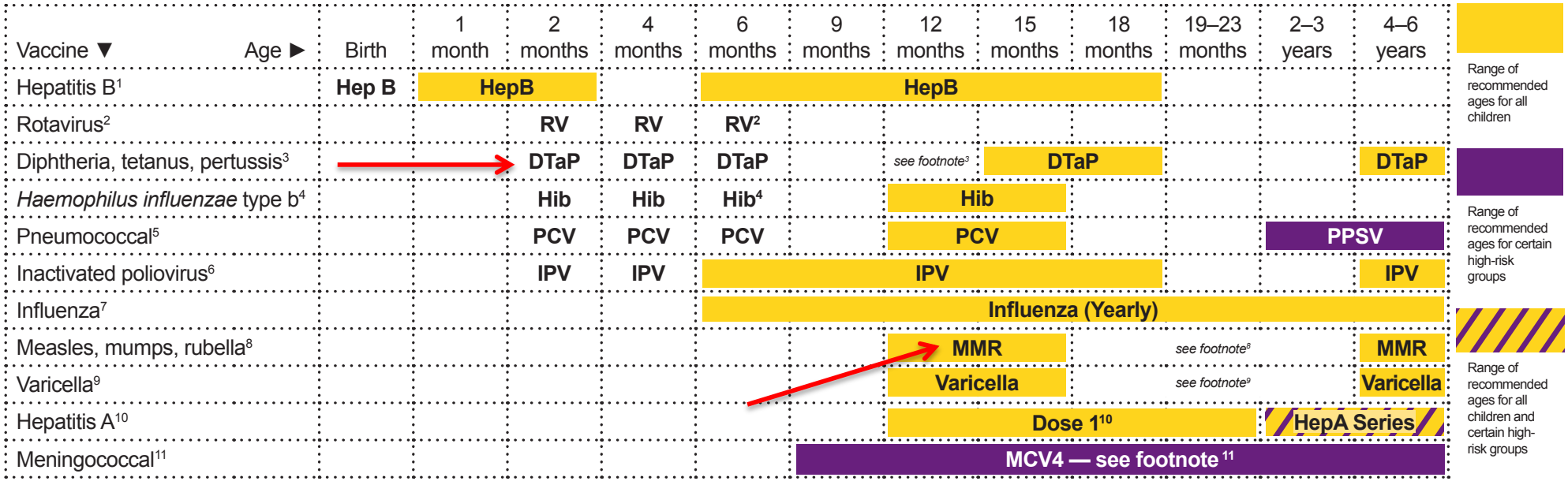
immune memory

- Upon subsequent exposure to same Ag, the immune response is rapid and strong: will prevent infection
  - humoral: minutes to hours
  - CMI: 1–2 days
- Memory is stored in “trained” B or T cells (B or T memory cells) that form clones in lymph nodes and other lymphatic tissues; may remain for life
- Memory cells rapidly activate upon new exposure to Ag and produce immune response

- 

Another great possible Essay! 4 types of adaptive immunity

FIGURE 1: Recommended immunization schedule for persons aged 0 through 6 years—United States, 2012 (for those who fall behind or start late, see the catch-up schedule [Figure 3])



This schedule includes recommendations in effect as of December 23, 2011. Any dose not administered at the recommended age should be administered at a subsequent visit, when indicated and feasible. The use of a combination vaccine generally is preferred over separate injections of its equivalent component vaccines. Vaccination providers should consult the relevant Advisory Committee on Immunization Practices (ACIP) statement for detailed recommendations, available online at http://www.cdc.gov/vaccines/pubs/acip-list.htm. Clinically significant adverse events that follow vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS) online (http://www.vaers.hhs.gov) or by telephone (800-822-7967).

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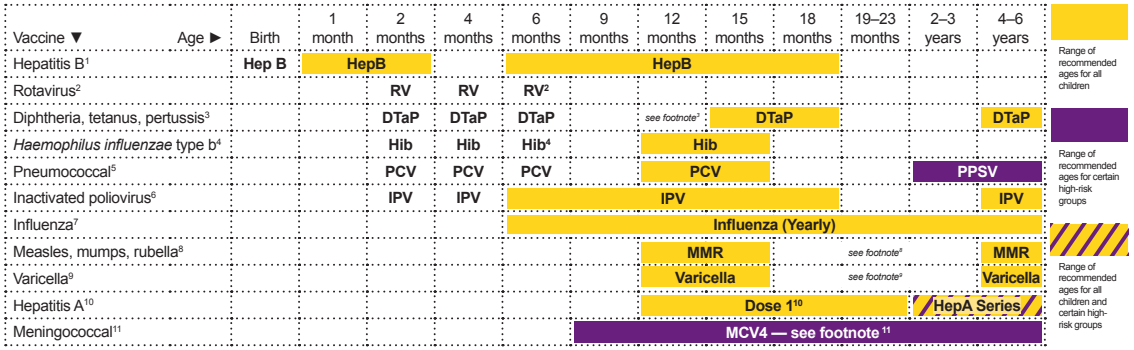

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1. **Hepatitis B (HepB) vaccine.** (Minimum age: birth)
   At birth:
   - Administer monovalent HepB vaccine to all newborns before hospital discharge.
   - For infants born to hepatitis B surface antigen (HBsAg)–positive mothers, administer HepB vaccine and 0.5 mL of hepatitis B immune globulin (HBIG) within 12 hours of birth. These infants should be tested for HBsAg and antibody to HBsAg (anti-HBs) 1 to 2 months after receiving the last dose of the series.
   - If mother's HBsAg status is unknown, within 12 hours of birth administer HepB vaccine for infants weighing ≥2,000 grams, and HepB vaccine plus HBIG for infants weighing <2,000 grams. Determine mother's HBsAg status as soon as possible and, if she is HBsAg-positive, administer HBIG for infants weighing ≥2,000 grams (no later than age 1 week).

   Doses after the birth dose:
   - The second dose should be administered at age 1 to 2 months. Monovalent HepB vaccine should be used for doses administered before age 6 weeks.
   - Administration of a total of 4 doses of HepB vaccine is permissible when a combination vaccine containing HepB is administered after the birth dose.
   - Infants who did not receive a birth dose should receive 3 doses of a HepB-containing vaccine starting as soon as feasible (Figure 3).
   - The minimum interval between dose 1 and dose 2 is 4 weeks, and between dose 2 and 3 is 8 weeks. The final (third or fourth) dose in the HepB vaccine series should be administered no earlier than age 24 weeks and at least 16 weeks after the first dose.
2. **Rotavirus (RV) vaccines.** (Minimum age: 6 weeks for both RV-1 [Rotarix] and RV-5 [Rota Teq])
   - The maximum age for the first dose in the series is 14 weeks, 6 days; and 8 months, 0 days for the final dose in the series. Vaccination should not be initiated for infants aged 15 weeks, 0 days or older.
   - If RV-1 (Rotarix) is administered at ages 2 and 4 months, a dose at 6 months is not indicated.
3. **Diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine.** (Minimum age: 6 weeks)
   - The fourth dose may be administered as early as age 12 months, provided at least 6 months have elapsed since the third dose.
4. ***Haemophilus influenzae* type b (Hib) conjugate vaccine.** (Minimum age: 6 weeks)
   - If PRP-OMP (PedvaxHIB or Comvax [HepB-Hib]) is administered at ages 2 and 4 months, a dose at age 6 months is not indicated.
   - Hiberix should only be used for the booster (final) dose in children aged 12 months through 4 years.
5. **Pneumococcal vaccines.** (Minimum age: 6 weeks for pneumococcal conjugate vaccine [PCV]; 2 years for pneumococcal polysaccharide vaccine [PPSV])
   - Administer 1 dose of PCV to all healthy children aged 24 through 59 months who are not completely vaccinated for their age.
   - For children who have received an age-appropriate series of 7-valent PCV (PCV7), a single supplemental dose of 13-valent PCV (PCV13) is recommended for:
     — All children aged 14 through 59 months
     — Children aged 60 through 71 months with underlying medical conditions.
   - Administer PPSV at least 8 weeks after last dose of PCV to children aged 2 years or older with certain underlying medical conditions, including a cochlear implant. See *MMWR* 2010:59(No. RR-11), available at http://www.cdc.gov/mmwr/pdf/rr/rr5911.pdf.
6. **Inactivated poliovirus vaccine (IPV).** (Minimum age: 6 weeks)
   - If 4 or more doses are administered before age 4 years, an additional dose should be administered at age 4 through 6 years.
   - The final dose in the series should be administered on or after the fourth birthday and at least 6 months after the previous dose.
7. **Influenza vaccines.** (Minimum age: 6 months for trivalent inactivated influenza vaccine [TIV]; 2 years for live, attenuated influenza vaccine [LAIV])
   - For most healthy children aged 2 years and older, either LAIV or TIV may be used. However, LAIV should not be administered to some children, including 1) children with asthma, 2) children 2 through 4 years who had wheezing in the past 12 months, or 3) children who have any other underlying medical conditions that predispose them to influenza complications. For all other contraindications to use of LAIV, see *MMWR* 2010;59(No. RR-8), available at http://www.cdc.gov/mmwr/pdf/rr/rr5908.pdf.
   - For children aged 6 months through 8 years:
     — For the 2011–12 season, administer 2 doses (separated by at least 4 weeks) to those who did not receive at least 1 dose of the 2010–11 vaccine. Those who received at least 1 dose of the 2010–11 vaccine require 1 dose for the 2011–12 season.
     — For the 2012–13 season, follow dosing guidelines in the 2012 ACIP influenza vaccine recommendations.
8. **Measles, mumps, and rubella (MMR) vaccine.** (Minimum age: 12 months)
   - The second dose may be administered before age 4 years, provided at least 4 weeks have elapsed since the first dose.
   - Administer MMR vaccine to infants aged 6 through 11 months who are traveling internationally. These children should be revaccinated with 2 doses of MMR vaccine, the first at ages 12 through 15 months and at least 4 weeks after the previous dose, and the second at ages 4 through 6 years.
9. **Varicella (VAR) vaccine.** (Minimum age: 12 months)
   - The second dose may be administered before age 4 years, provided at least 3 months have elapsed since the first dose.
   - For children aged 12 months through 12 years, the recommended minimum interval between doses is 3 months. However, if the second dose was administered at least 4 weeks after the first dose, it can be accepted as valid.
10. **Hepatitis A (HepA) vaccine.** (Minimum age: 12 months)
    - Administer the second (final) dose 6 to18 months after the first.
    - Unvaccinated children 24 months and older at high risk should be vaccinated. See *MMWR* 2006;55(No. RR-7), available at http://www.cdc.gov/mmwr/pdf/rr/rr5507.pdf.
    - A 2-dose HepA vaccine series is recommended for anyone aged 24 months and older, previously unvaccinated, for whom immunity against hepatitis A virus infection is desired.
11. **Meningococcal conjugate vaccines, quadrivalent (MCV4).** (Minimum age: 9 months for Menactra [MCV4-D], 2 years for Menveo [MCV4-CRM])
    - For children aged 9 through 23 months 1) with persistent complement component deficiency; 2) who are residents of or travelers to countries with hyperendemic or epidemic disease; or 3) who are present during outbreaks caused by a vaccine serogroup, administer 2 primary doses of MCV4-D, ideally at ages 9 months and 12 months or at least 8 weeks apart.
    - For children aged 24 months and older with 1) persistent complement component deficiency who have not been previously vaccinated; or 2) anatomic/functional asplenia, administer 2 primary doses of either MCV4 at least 8 weeks apart.
    - For children with anatomic/functional asplenia, if MCV4-D (Menactra) is used, administer at a minimum age of 2 years and at least 4 weeks after completion of all PCV oses.
    - See *MMWR* 2011;60:72–6, available at http://www.cdc.gov/mmwr/pdf/wk/mm6003. pdf, and Vaccines for Children Program resolution No. 6/11-1, available at http://www. cdc.gov/vaccines/programs/vfc/downloads/resolutions/06-11mening-mcv.pdf, and *MMWR* 2011;60:1391–2, available at http://www.cdc.gov/mmwr/pdf/wk/mm6040. pdf, for further guidance, including revaccination guidelines.

This schedule is approved by the Advisory Committee on Immunization Practices (http://www.cdc.gov/vaccines/recs/acip), the American Academy of Pediatrics (http://www.aap.org), and the American Academy of Family Physicians (http://www.aafp.org).
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