HOST-MICROBE RELATIONSHIPS AND DISEASE

PRINCY

HOST-MICROBE RELATIONSHIPS

- Microorganisms display a variety of complex relationships with other microorganisms and with larger forms of life that serve as hosts for them.

- A **host is any organism that** harbors another organism.

Symbiosis

- **Symbiosis is an association between two (or more)** species meaning “living together”. the term *symbiosis* en compasses a spectrum of relationships.

- Symbiosis can be used to describe many of the interactions between microorganisms, and also microbial interactions with higher organisms, including plants and animals.

- These interactions may be positive or negative.

- Symbiotic interactions include

1. **mutualism,**
2. **cooperation,**
3. **commensalism,**
4. **parasitism,**
5. **predation,**
6. **ammensalism, and**
7. **competition**.

- These interactions are important in natural processes and in the occurrence of disease. The interactions can vary depending on the environment and changes in the interacting organisms.

- Microorganisms, as they interact, can form complex physical assemblages that include biofilms.

- **These form on living and inert surfaces and have major impacts on microbial survival and the occurrence of disease.**

- Most microorganisms associated with the human body are bacteria; they normally colonize specific sites.

- There are both positive and negative aspects of these normal microbial associations.

- Sometimes they compete with pathogens, other times they are capable of producing opportunistic infections.

1. Mutualism [Latin *mutuus, borrowed or reciprocal*]

- ***defines the*** relationship in which some reciprocal benefit accures to both partners.

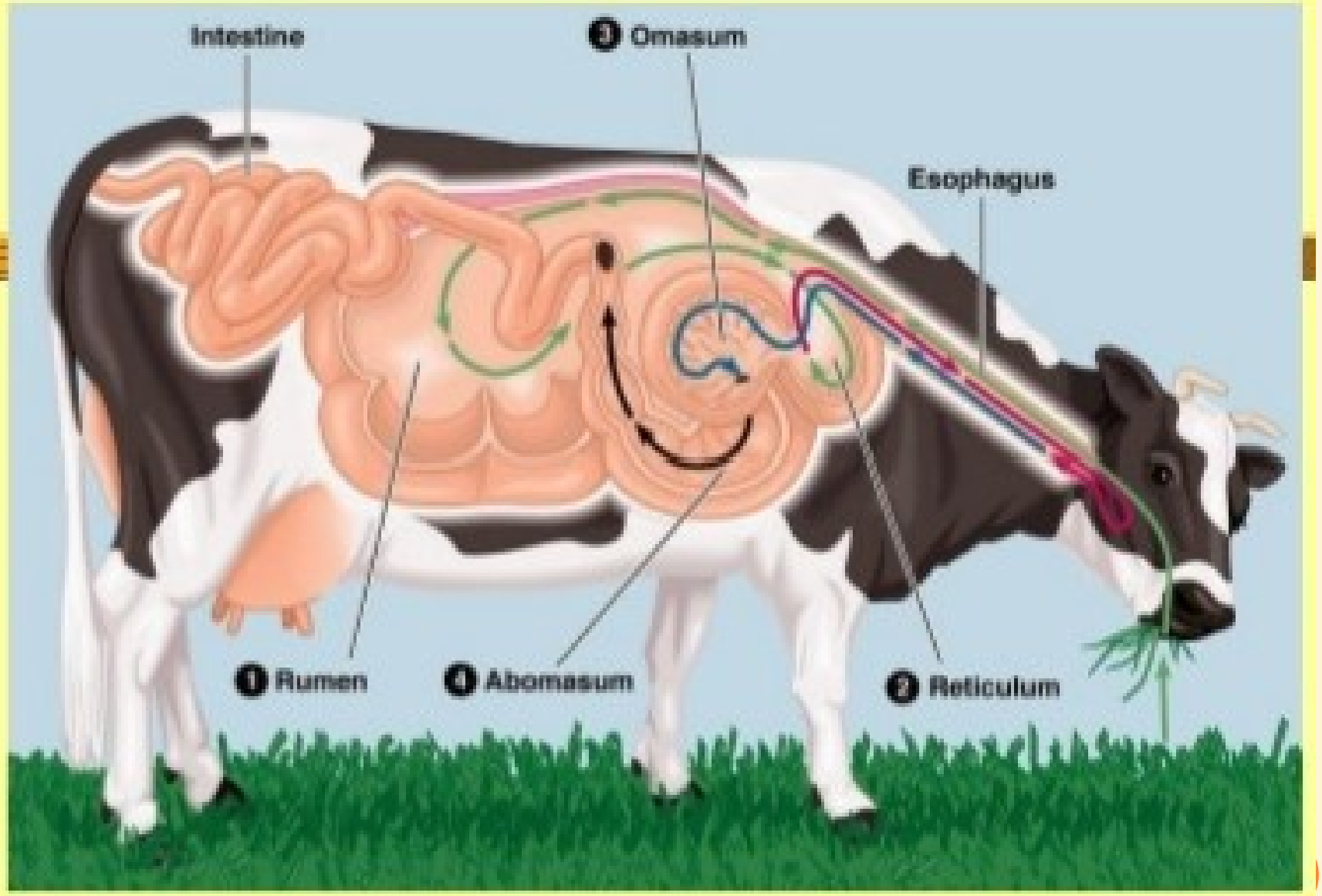
- This is an **obligatory** relationship in which the **mutualist** and the host are dependent on each other.

Examples

1. ***Microorganism-Insect Mutualisms***

- The foods used by insects often include plant sap or animal fluids lacking in essential vitamins and amino acids. The required vitamins and amino acids are provided by bacterial symbionts in exchange for a secure habitat and ample nutrients from host.

2. ***The Rumen Ecosystem***


Intestine
3 Omasum
Esophagus
1 Rumen
4 Abomasum
2 Reticulum

2. Cooperation

- Cooperation and commensalism are two positive but **not obligatory types** of symbioses found widely in the microbial world.

Examples

- Syntrophic relationships - *is an association in which* the growth of one organism either depends on or is improved by growth factors, nutrients, or substrates provided by another organism growing nearby. Sometimes both organisms benefit.

- **A cooperative** relationship is not obligatory and this nonobligatory aspect differentiates cooperation from mutualism.

3. Commensalism

- **[Latin *com, together, and mensa, table] is a *relationship*** in which one symbiont, the **commensal, benefits while** the other (sometimes called the host) is neither harmed nor helped.

- This is a unidirectional process.

- Often both the host and the commensal "**eat at the same table.**"

- **Example**
- However *S. aureus* is pathogenic, many strains of *S. aureus* are metabiotic commensals, and are present on roughly 20 to 30% of the human population as part of the skin flora.

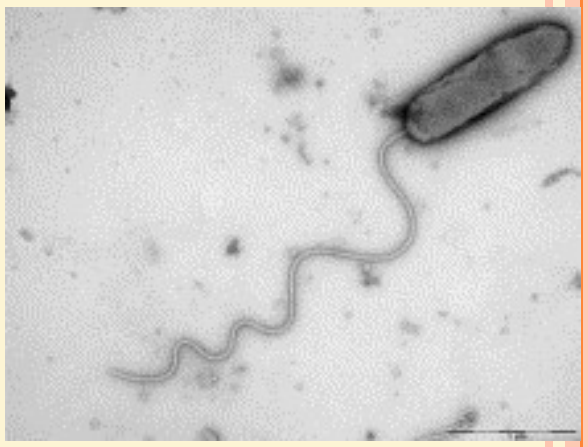
4. Predation

- As is the case with larger organisms, **predation among microbes** involves a predator species that attacks and usually kills its prey.

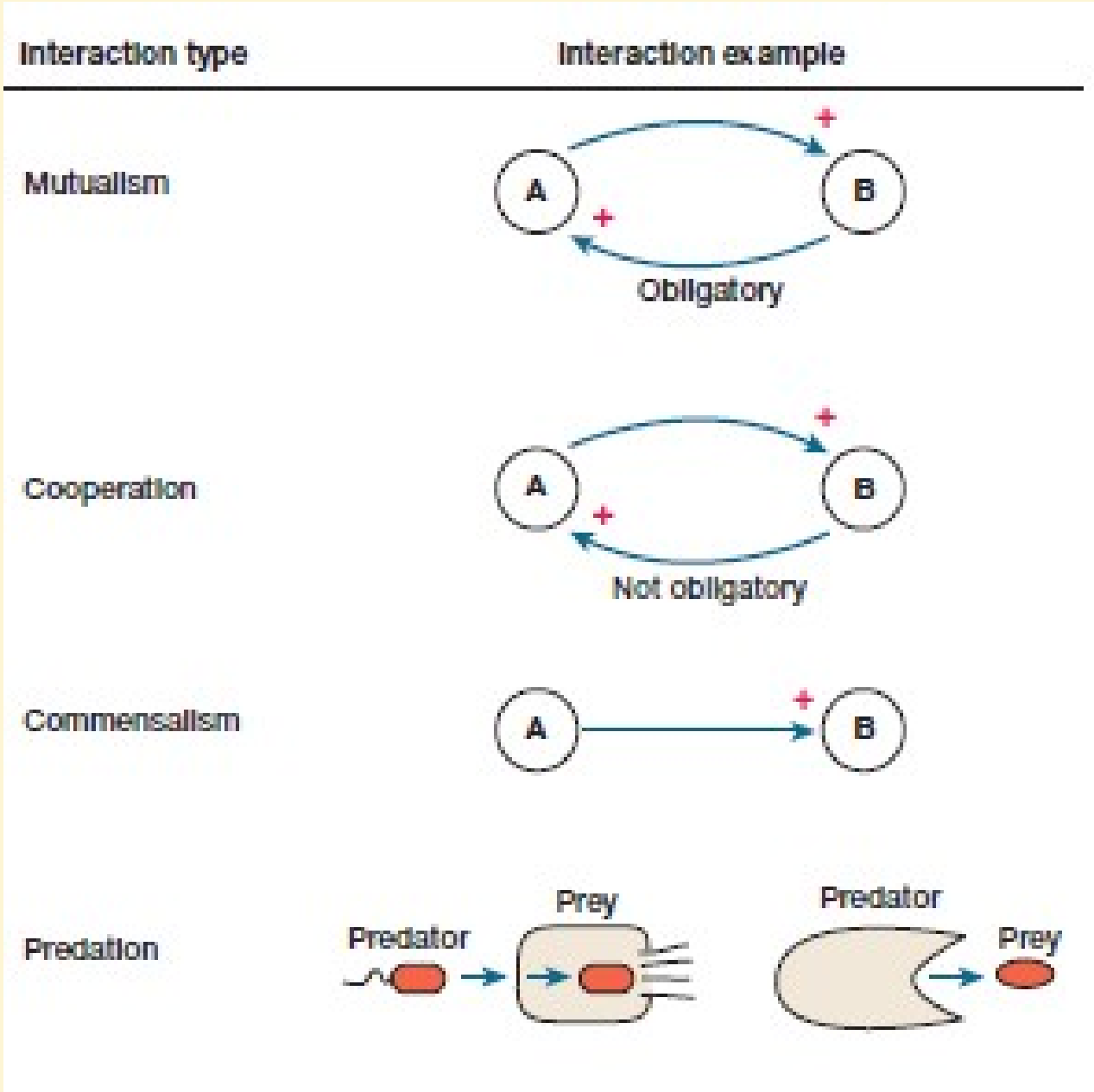
- A number of fascinating bacteria that survive by their ability to prey upon other microbes.

- One of the best example is *Bdellovibrio,*

- *Bdellovibrio is an active hunter that is vigorously motile,* swimming about looking for susceptible gram-negative bacterial prey.



MICROBIAL INTERACTIONS.



5. Amensalism

- **Amensalism (from the Latin for *not at the same table)* *describes*** the adverse effect that one organism has on another organism.

- This is a unidirectional process based on the release of a specific compound by one organism which has a negative effect on another organism.

- A classic example of ammensalism is the **production of antibiotics** that can inhibit or kill a susceptible microorganism.

6. Competition

- **Competition arises when different organisms within a population** or community **try to acquire the same resource** (physical location or a particular limiting nutrient).

- If one of the two competing organisms can dominate the environment, whether by occupying the physical habitat or by consuming a limiting nutrient, it will outgrow the other organism.

- This phenomenon was studied by E. F. Gause, who in 1934 described it as the **competitive exclusion principle.**

7. Parasitism

- **The word 'parasite' comes from the Greek *parasitos, meaning* "one who eats at another's table."**

Parasitism is one of the most complex microbial interactions.

- The line between parasitism and predation is difficult to define.
- This is a relationship between two organisms in which one benefits from the other, and the host is usually harmed.
- This can involve **nutrient acquisition and/or physical maintenance in or on the host.**

- In parasitism there is always some co-existence between host and parasite.
- Successful parasites have evolved to co-exist in equilibrium with their hosts.
- This is because a host that dies immediately after parasite invasion may prevent the microbe from reproducing to sufficient numbers to ensure colonization of a new host.

Parasitism

Amensalism

Competition

One outcompetes the other for the site's resources

Both coexist at lower levels, due to their sharing the limiting resource

Pathogens: Unsuccessful Attempts at Symbiosis

- A **pathogen** **is a** parasite capable of causing disease in a host.

Contamination, Infection, and Disease

- Contamination, infection, and disease can be viewed as a sequence of conditions in which the severity of the effects by microorganisms on their hosts increases.

- **Contamination** means that the microorganisms are present.

- Inanimate objects and the surfaces of skin and mucous membranes can be contaminated with a wide variety of microorganisms.

- Commensals do no harm, but parasites have the capacity to invade tissues.

- **Infection** refers to the multiplication of any parasitic organism within or on the host's body.

- If an infection disrupts the normal functioning of the host, disease occurs.

- **Disease** **is** a disturbance in the state of health wherein the body cannot carry out all its normal functions.

Contamination, Infection and Disease

Contamination: Microbes are present

↓

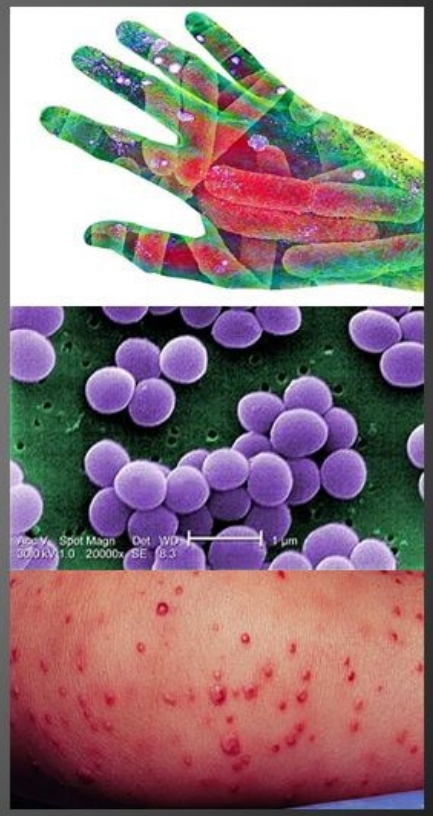
Infection (Infestation-larger parasites)

Multiplication of microbes (Microbes penetrate host defenses, enter tissue and MULTIPLY)

↓

Disease

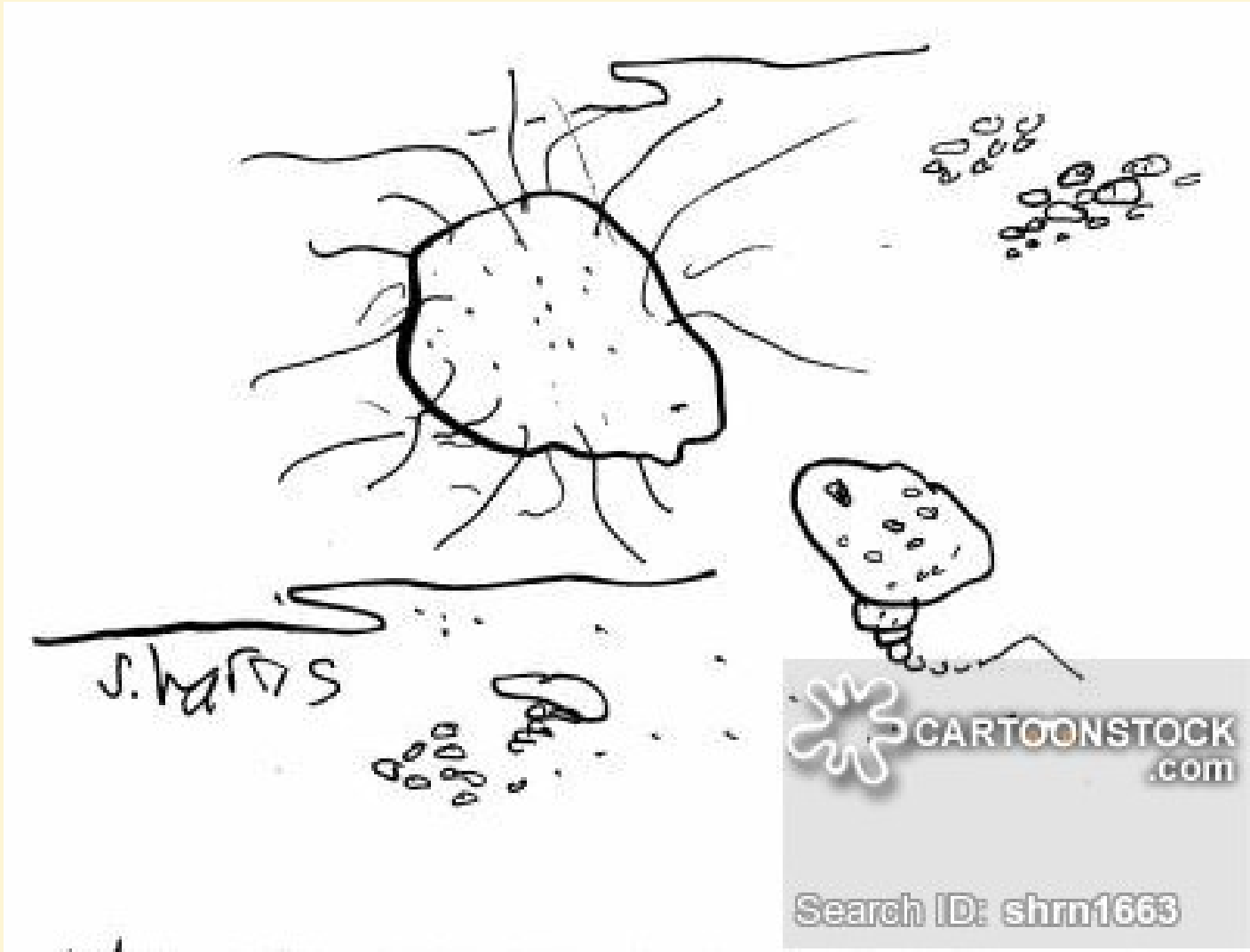
Disturbance in normal homeostasis



- **Both infection and disease result from interactions between parasites and their hosts.**

- Sometimes an infection produces no observable effect on the host even though organisms have invaded tissues.

- More often an infection produces observable disturbances in the host's state of health; that is, disease occurs.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"YOU TELL ME HOW TO GIVE THEM A FEVER, AND I'LL TELL YOU HOW TO MAKE THEM COUGH."

Pathogens, Pathogenicity, and Virulence

- Pathogens vary in their abilities to disrupt the state of an individual's health.

- **Pathogenicity is the capacity to produce disease.**

- An organism's pathogenicity depends on its ability to invade a host, multiply in the host, and avoid being damaged by the host's defenses.

- Some disease agents, such as *Mycobacterium tuberculosis, frequently cause disease* upon entering a susceptible host. Other agents, such as *Staphylococcus epidermidis, cause disease only in rare* instances and usually only in hosts with poor defenses.

- **An important factor in pathogenicity is the number of infectious organisms that enter the body**. If only a small number enter, the host's defenses may be able to eliminate the organisms before they can cause disease.

- If a large number enter, they may overwhelm the host's defenses and cause disease.

- **Virulence refers to the intensity of the disease produced by pathogens,** and it varies among different microbial species.

- Virulence also varies among members of the same species of pathogen.

- The virulence of a pathogen can be decreased by **attenuation, the weakening of the disease producing** ability of the pathogen.

Normal (Indigenous) Microflora

- Microorganisms found in various symbiotic associations with humans do not necessarily cause disease.

- An adult human body consists of approximately 10^{13} (10 trillion) eukaryotic cells. It harbors an additional 10^{14} (100 trillion) prokaryotic and eukaryotic microorganisms

- on the skin surface,
- on mucous membranes,
- and in the passage ways of the digestive, respiratory, and reproductive systems

- Organisms that live on or in the body but do not cause disease are referred to collectively as **normal microflora, or *normal microbiota*.**

- Most organisms among the normal microflora are commensals.

In skin

- *Staphylococcus aureus*
- *Lactobacillus species*

In mouth

- *Streptococcus salivarius*
- *Candida albicans (fungus)*

KINDS OF DISEASES

- Human diseases are caused by **infectious agents**, structural or functional genetic defects, environmental factors, or any combination of these causes.

Infectious and Noninfectious Diseases

- **Infectious diseases are diseases caused by infectious** agents such as bacteria, viruses, fungi, protozoa, and helminths.

- **Noninfectious diseases are caused by** any factor other than infectious organisms.

Classification of Diseases (based on root cause)

- Classification of diseases as infectious or noninfectious gives a very limited view of human disease.

- The following scheme for classifying diseases provides a more comprehensive view.

Some important types of diseases

1. ***Disease caused by infectious agents***
2. ***Inherited diseases***
3. ***Congenital diseases***
4. ***Degenerative diseases***
5. ***Nutritional deficiency diseases***
6. ***Mental disease***
7. ***Immunological diseases etc.***

2. ***Inherited diseases are caused by errors in genetic*** information.

- The resulting developmental disorders may be caused by abnormalities in the number and distribution of chromosomes or by the interaction of genetic and environmental factors.

3. ***Congenital diseases are structural and functional defects*** present at birth, caused by drugs, excessive X-ray exposure, or certain infections.

4. ***Degenerative diseases are disorders that develop in*** one or more body systems as aging occurs.

- Patients with degenerative diseases such as impaired kidney function are susceptible to infections.
- Conversely, infectious agents can cause tissue damage that leads to degenerative disease.

5. ***Nutritional deficiency diseases lower resistance to*** infectious diseases and contribute to the severity of infections.

6. ***Mental disease can be caused by a variety of factors,*** including those of an emotional, or psychogenic nature as well as certain infections.

7. ***Immunological diseases such as allergies, autoimmune*** diseases, and immunodeficiencies are caused by malfunction of the immune system.

Etc.

Communicable and Noncommunicable Diseases

- Some infectious diseases can be spread from one host to another and are said to be **communicable infectious diseases.**
- **E. g.** Rubeola (red measles)

- **Noncommunicable infectious diseases are not** spread from one host to another.
- You cannot "catch" a noncommunicable disease from another person.
- **E. g.** Tetanus

The disease process

- **How Microbes Cause Disease?**

  Microorganisms act in certain ways that allow them to cause disease. These actions include

- Gaining access to the host
- Adhering to and colonizing cell surfaces
- Invading tissues, and
- Producing toxins and other harmful metabolic products.

- However, **host defense mechanisms** tend to prevent the actions of microorganisms.

- The occurrence of a disease depends on whether the pathogen or the host wins the battle; if it is a draw, a chronic, long lasting disease may result.

How bacteria cause disease?

- Bacterial pathogens often have special structures or physiological characteristics that improve the chances of successful host invasion and infection.

- **Virulence factors are structural or physiological characteristics** that help organisms to cause infection and disease. These factors include structures such as

1. **pili** for adhesion to cells and tissues
2. **enzymes** that either help in evading host defenses or protect the organism from host defenses
3. **toxins** that can directly cause disease.

- 1. A critical point in the production of bacterial disease is the organism's **adherence, or attachment, to** a host cell's surface.

- **Adhesins are proteins or glycoproteins found on attachment** pili (fimbriae) and capsules.

- Most adhesins that have been identified permit the pathogen to adhere only to receptors on membranes of certain cells or tissues.

- E.g. an adhesin on attachment pili of certain strains of *Escherichia coli attaches to receptors on certain host* epithelial cells.

- Often the capsules and attachment pili are also antiphagocytic structures.

- It is difficult for phagocytic cells to engulf bacteria that have capsules or attachment pili, so these structures make excellent virulence factors.

- Attachment to a host cell surface is not enough to cause an infection. The microbes must also be able to colonize the cell's surface or to penetrate it.

- **2. Colonization refers** to the growth of microorganisms on epithelial surfaces, such as skin or mucous membranes or other host tissues.

- For colonization to occur after adherence, the pathogens must survive and reproduce despite host defense mechanisms (mucus, cilia, digestive enzymes etc.).

- 3. Only a few pathogens cause disease by colonizing surfaces; most have additional virulence factors that enable the pathogen to invade tissues - Digestive enzymes

- Some bacteria, such as *Pneumococci* and other *Streptococci*, release digestive enzymes that allow them to invade tissues rapidly and cause severe illnesses.

- *Streptococci* produce the enzyme **hyaluronidase**. *This enzyme digests hyaluronic acid,* a glue like substance that helps hold the cells of certain tissues together.

- **Digestion of hyaluronic acid allows** *Streptococci* to pass between epithelial cells and invade deeper tissues.

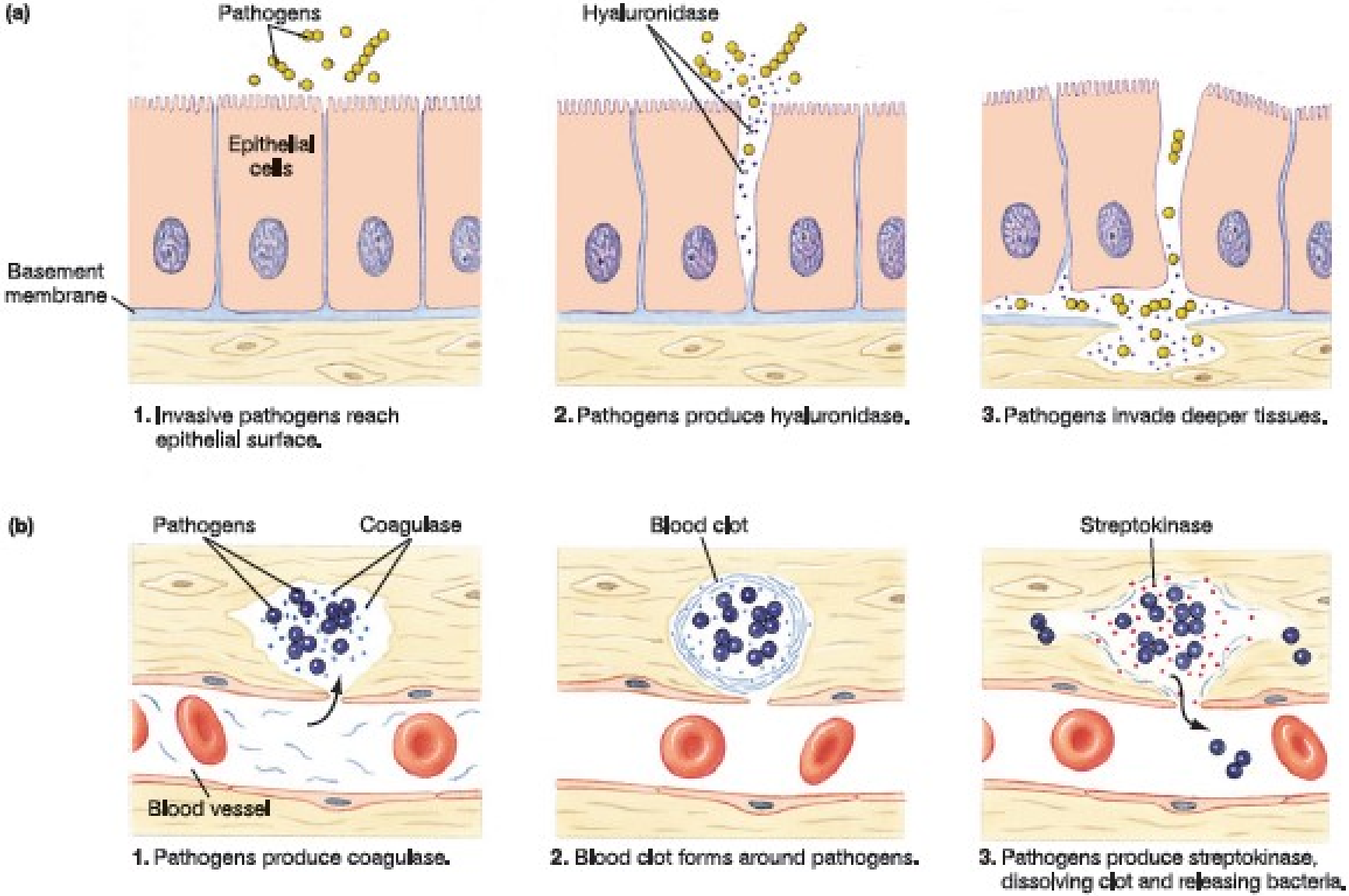


FIGURE 14.5 Enzymatic virulence factors help bacteria invade tissues and evade host defenses. (a) Hyaluronidase dissolves the "cement" that holds together the cells that line the intestinal tract. Bacteria that produce hyaluronidase can then invade deeper cells within the intestinal tissues. (b) Coagulase triggers blood plasma clotting, allowing bacteria protection from immune defenses. Streptokinase dissolves blood clots. Bacteria trapped within a clot can free themselves and spread the infection by producing streptokinase.

- 4. Most bacteria that invade tissues, damage cells and are found around cells. Thus, enzymes that contribute to tissue damage are another important virulence factor.

- **Coagulase** is a bacterial enzyme that accelerates the coagulation (clotting) of blood.

- **Coagulase is a two-edged sword:** It keeps organisms from spreading but also helps wall them off from immune defenses that might otherwise destroy them.

- Conversely, the bacterial enzyme **streptokinase dissolves** blood clots. Pathogens trapped in blood clots free themselves to spread to other tissues by secreting these virulence factors.

- **5. Bacterial toxins.**
- **A toxin is any substance that is** poisonous to other organisms.

- Some bacteria produce toxins, which are synthesized inside bacterial cells and are classified according to how they are released.

- **Exotoxin** are soluble substances secreted into host tissues.

- **Endotoxins are part of the cell wall and are released into** host tissues.

- Bacterial **endotoxins** have nonspecific effects such as fever or a sudden drop in blood pressure. They also cause **tissue damage.**

- All endotoxins consist of lipopolysaccharide (LPS) complexes.

- **Exotoxins** are **more powerful toxins** produced by several Gram-positive and a few Gram-negative bacteria.

- Most are polypeptides, which are denatured by heat, ultra violet light, and chemicals such as formaldehyde.

- Species of *Clostridium*, *Bacillus*, *Staphylococcus, Streptococcus,* and several other bacteria produce exotoxins.

Primary and secondary infection

- A **primary infection is an initial infection in a previously** healthy person.
- Most primary infections are acute (develops rapidly and runs its course quickly).

- A **secondary infection follows a primary infection,** especially in individuals weakened by the primary infection.

- A person who catches the common cold as a primary infection, for instance, might come down with a middle-ear infection as a secondary infection.

Stages of an Infectious Disease

- Most diseases caused by infectious agents have a fairly standard course, or series of stages. These stages include

1. The *incubation period*
2. *The prodromal phase*
3. *The invasive phase* (which includes the *acme),*
4. *The decline phase,* and
5. The *convalescence period*

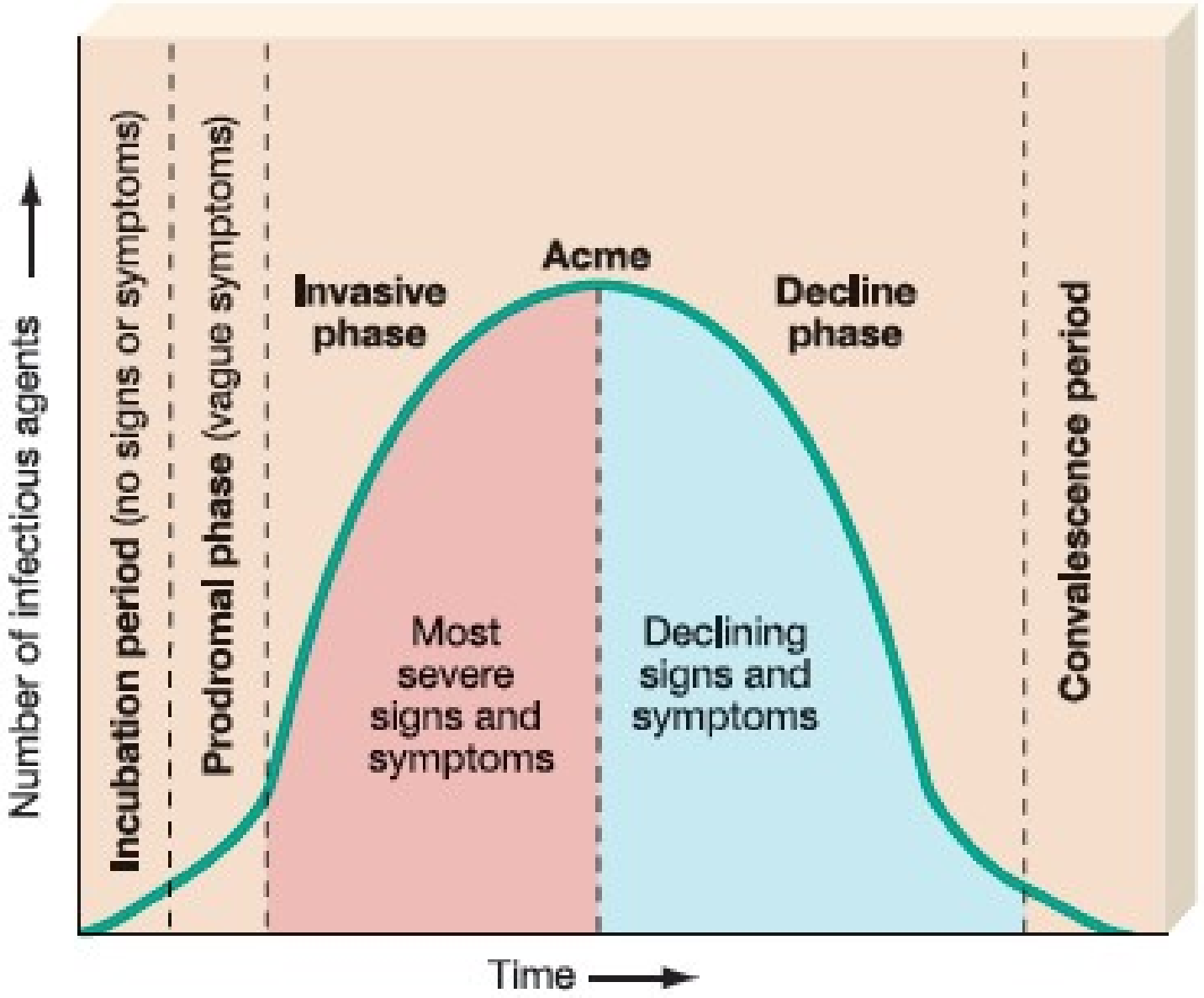


FIGURE 14.9 Stages in the course of an infectious disease.

1. The incubation period

- The **incubation period for an infectious disease is the time between infection and the appearance of signs and symptoms.**
- Each infectious disease has a typical incubation period.
- **The length of the** incubation period is determined by the properties of the pathogen and the response of the host to the organism.

2. The prodromal phase

- The **prodromal phase of disease is a short period during** which nonspecific, often mild, symptoms such as discomfort and headache sometimes appear.

- A **prodrome (*prodromos,*** Greek for "forerunner") is a symptom indicating the onset of a disease.

3. The invasive phase (which includes the acme)

- The **invasive phase is the period during which the individual** experiences the typical signs and symptoms of the disease.

- These may include fever, nausea, headache, rash, and swollen lymph nodes.

- During this phase, the time when the signs and symptoms reach their greatest intensity is known as the **acme.**

4. The decline phase

- As symptoms begin to subside, the disease enters the **decline phase—the period of illness during which host** defenses and the effects of treatment finally overcome the pathogen.

- The body's thermostat and other body activities gradually return to normal.

- Secondary infections may occur during this phase.

5. The convalescence period

- During the **convalescence period, tissues are repaired,** healing takes place, and the body regains strength and recovers.

- Individuals no longer have disease symptoms.

- Effects remaining after the disease has ended are called **sequelae** (e.g., pits and scarring following smallpox or chickenpox).

Gnotobiotic Animals

- To determine the role of the normal microorganisms associated with a host and evaluate the consequences of colonization, it is possible to deliver an animal by cesarean section and raise that animal in the absence of microorganisms—that is, germfree.

- These **microorganism- free animals** provide suitable experimental models for investigating the interactions of animals and their microorganisms.

- Gnotobiotic refers to a microbiologically monitored environment or animal that is germfree or in which the identities of all microbiota are known.

- Comparing animals possessing normal microorganisms (conventional animals) with germfree animals permits the elucidation of many complex relationships between microorganisms, hosts, and specific environments.

Koch's Postulates

- **The first direct demonstration of the role of bacteria in causing disease** came from the study of anthrax by the German physician Robert Koch (1843–1910).

- Koch used the criteria proposed by his former teacher, Jacob Henle (1809–1885), to establish the relationship between *Bacillus anthracis* and anthrax.

- Koch injected healthy mice with material from diseased animals, and the mice became ill.

- After transferring anthrax by inoculation through a series of 20 mice, he incubated a piece of spleen containing the anthrax bacillus in beef serum. The bacilli grew, reproduced, and produced endospores.

Robert Koch

- When the isolated bacilli or their spores were injected into mice, anthrax developed.
- His criteria for proving the causal relationship between a microorganism and a specific disease are known as **Koch's postulates** .
- Koch's proof that *B. anthracis* caused anthrax was independently confirmed by Pasteur and his co-workers.
- Although Koch used the general approach described in the postulates during his anthrax studies, he did not outline them fully until his work on the cause of tuberculosis.

- In 1884, he reported that this disease was caused by a rod-shaped bacterium, ***Mycobacterium tuberculosis;*** he was awarded the Nobel Prize in Physiology or Medicine in **1905** for his work.

- Koch's postulates quickly became the **cornerstone** of connecting many diseases to their causative agent. However, their use is at times not feasible.

- For instance, some organisms, like *Mycobacterium leprae,* the causative agent of leprosy, cannot be isolated in pure culture.

Table 1.1 **Koch's Application of His Postulates to Demonstrate that *Mycobacterium tuberculosis* is the Causative Agent of Tuberculosis.**

Postulate	Experimentation
1. The microorganism must be present in every case of the disease but absent from healthy organisms.	Koch developed a staining technique to examine human tissue. *M. tuberculosis* cells could be identified in diseased tissue.
2. The suspected microorganisms must be isolated and grown in a pure culture.	Koch grew *M. tuberculosis* in pure culture on coagulated blood serum.
3. The same disease must result when the isolated microorganism is inoculated into a healthy host.	Koch injected cells from the pure culture of *M. tuberculosis* into guinea pigs. The guinea pigs subsequently died of tuberculosis.
4. The same microorganism must be isolated again from the diseased host.	Koch isolated *M. tuberculosis* from the dead guinea pigs and was able to again culture the microbe in pure culture on coagulated blood serum.

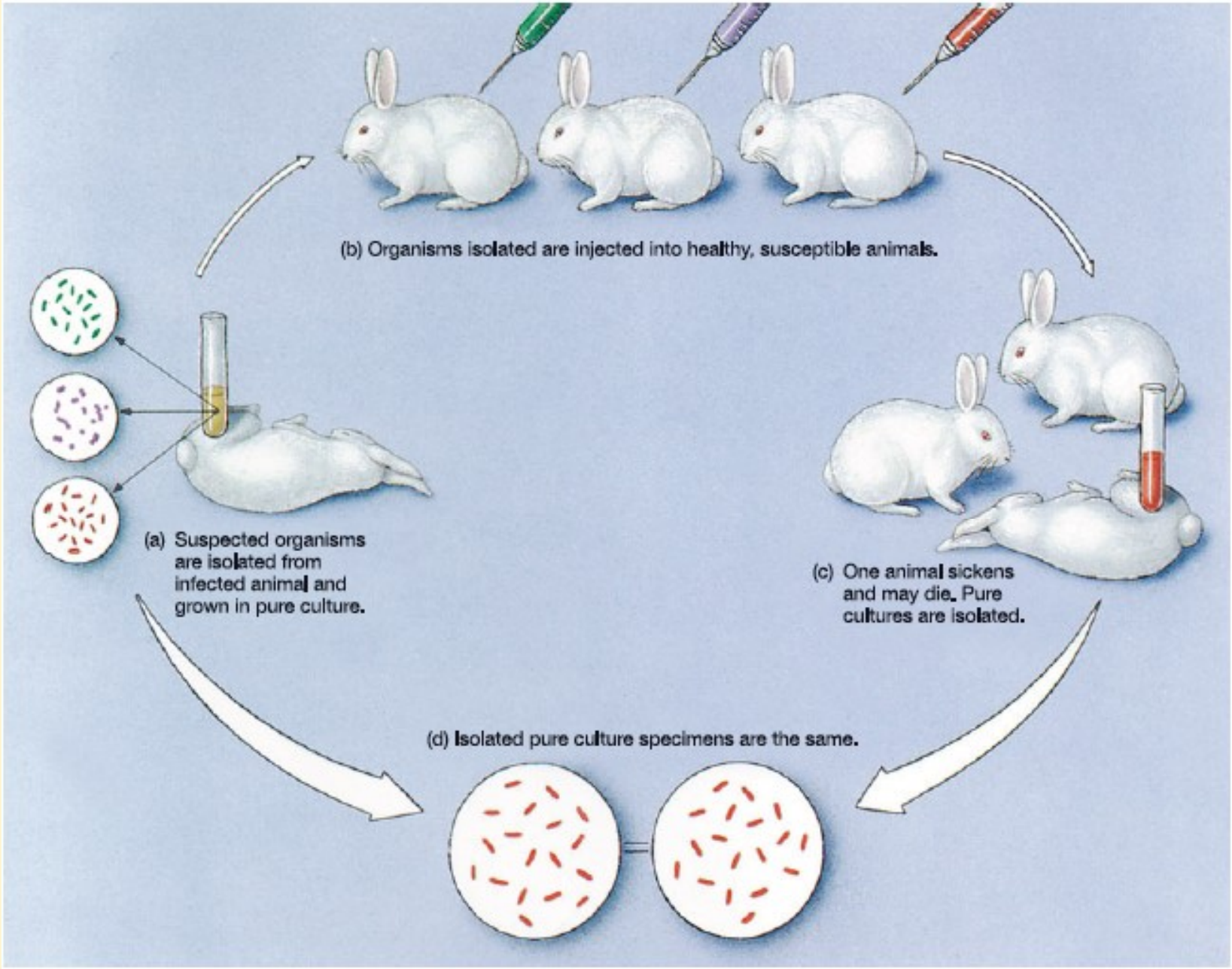


FIGURE 14.4 Demonstration that a bacterial disease satisfies Koch's Postulates.

In nutshell

- **Koch's Postulates provide a way to link a pathogen with a disease:**

1. **A specific causative agent must be observed in every case** of a disease.

2. **The agent must be isolated from a host displaying the disease** and grown in pure culture.

3. **When the agent from the pure culture is inoculated into** an experimental healthy, **susceptible host, the agent must cause the disease.**

4. **The agent must be reisolated from the inoculated, diseased experimental host** and identified as the original specific causative agent.

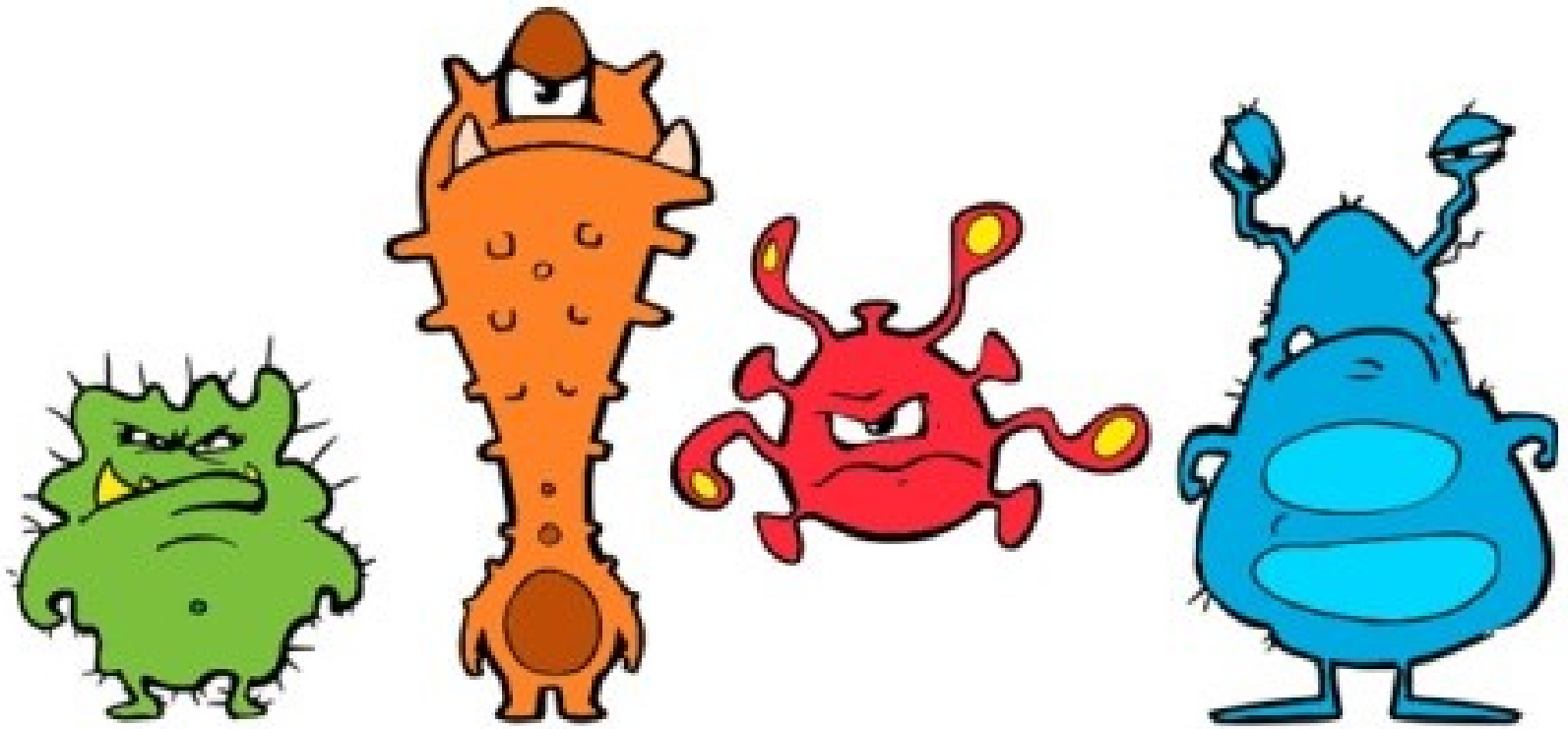
- When Koch's Postulates are met, an organism has been proved to be the causative agent of an infectious disease.

Armadillo: Culture Vessel for Leprosy

- The organism that causes Hansen's disease (leprosy) is difficult to culture.
- Many different methods had been tested and found unsatisfactory until someone tried inoculating the organism into the footpads of the nine-banded armadillo.
- There it grows very well; in fact, the organism multiplies faster there than in human tissues.

- When the organism does infect humans, it can have an incubation period of up to 30 years before disease symptoms appear.

- Before the armadillo was used to culture the organism, Koch's Postulate could not be satisfied.



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