



Corynebacterium
Erysipelothrix
& Listeria

Pathogenic Anaerobic Gram-Positive Bacilli

Corynebacterium diphtheriae
C. jeikeium (CDC group JK)
C. urealyticum (Coryneform group D-2)
C. pseudodiphtheriticum

C. minutissimum

C. ulcerans

C. xerosis

Arcanobacterium
(*Corynebacterium*)
haemolyticum

Actinomyces (*Corynebacterium*)
pyogenes

Rhodococcus (*Corynebacterium*)
equi

Listeria monocytogenes

Erysipelothrix
rhusiopathiae

Gardnerella vaginalis

Diphtheria

Opportunistic infections
Urinary tract infections

Endocarditis; lower
respiratory tract
infections

Skin infections
(erythrasma); systemic
infections

Pharyngitis (mild to
diphtheria-like)

Opportunistic infections
Pharyngitis

Granulomatous ulcerative
infections

Suppurative pneumonia;
opportunistic infections

Meningitis; septicemia;
granulomatosis
infantiseptica; endo-
carditis

Erysipeloid; septicemia;
endocarditis

Bacterial vaginosis

Corynebacteria (Genus *Corynebacterium*)

- Aerobic or facultatively anaerobic
- Small, **pleomorphic** (club-shaped), gram-positive bacilli that appear in short chains (“V” or “Y” configurations) or in clumps resembling “**Chinese letters**”
- Cells contain **metachromatic granules** (visualize with methylene blue stain)
- **Lipid-rich cell wall** contains meso-diaminopimelic acid, arabino-galactan polymers, and short-chain **mycolic acids**
- **Lysogenic bacteriophage** encodes for potent exotoxin in virulent strains

Distinguishing Features of CMN Group

CELL WALL:	<u>Corynebacterium</u>	<u>Mycobacterium</u>	<u>Nocardia</u>
<input type="checkbox"/> DL-DAP	+	+	+
LL-DAP	-	-	-
gly		-	-
Ara	+	+	+
gal	+	+	+
Acid-fast	-	+	±
Catalase			+
<input type="checkbox"/> Serological Cross-reactivity	+	+	+
Cell Surface K-Ag	+	-	-
<input type="checkbox"/> Mycolic Acids	C ₃₂ - C ₃₆ Corynemycolic (C ₃₂) Corynemycolenic (C ₃₂)	C ₅₀ - C ₉₀ Mycolic	C ₅₀ Tetrahydronocardic (C ₅₀)
Adjuvant activity	+	+	-
<input type="checkbox"/> Cord factor	+	+	+
Sulfolipids	-	+	-
IRON-CHELATING COMPOUNDS	-	+	+
POLYPHOSPHATE	+	+	+
PERCENT G + C	55-58	64-69	62-68

Pathogenic Corynebacterial Species

□Corynebacterium diphtheriae

□Corynebacterium jeikeium

□Corynebacterium urealyticum

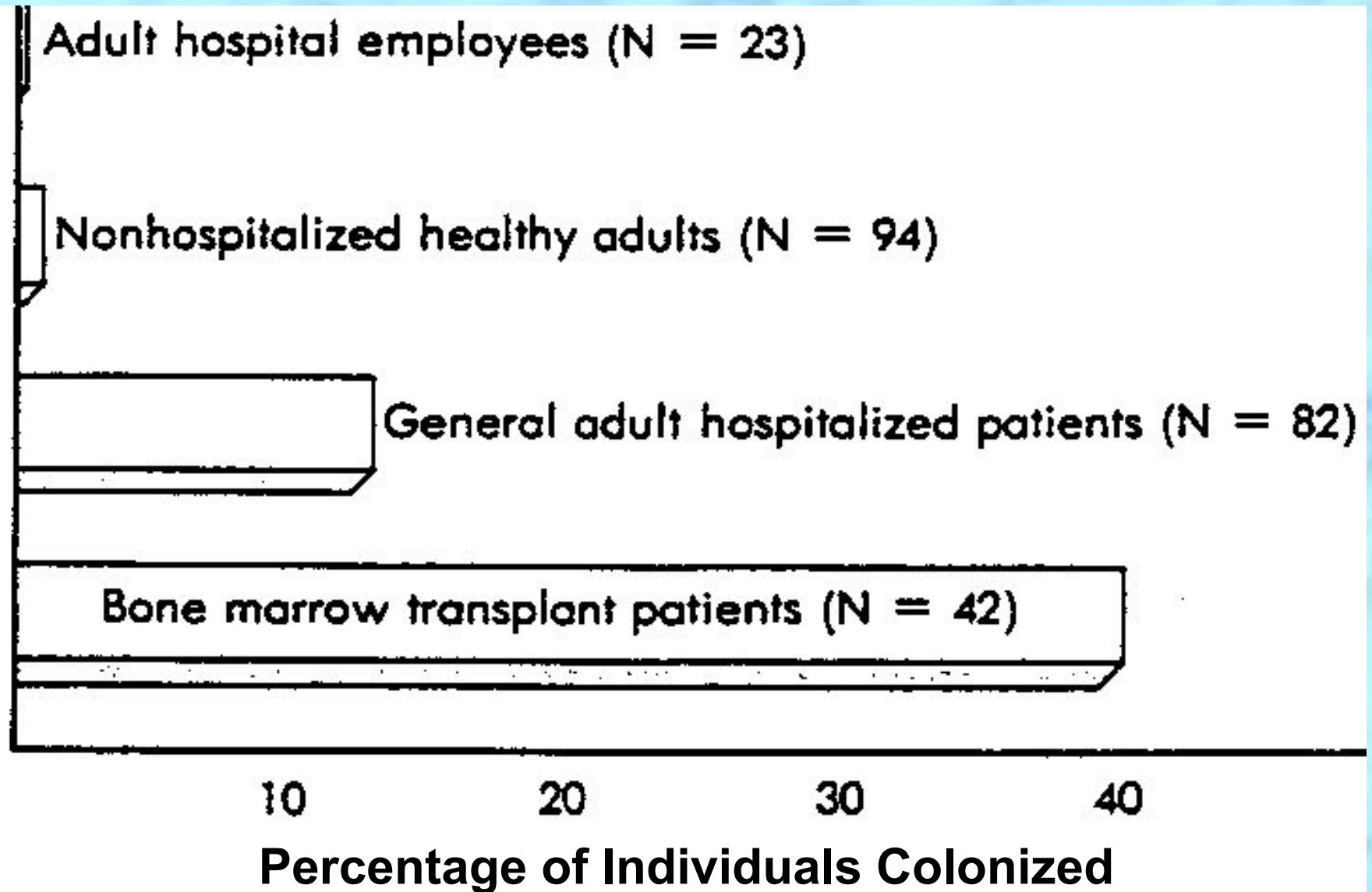
Corynebacterium urealyticum

- **Urinary tract infections** (UTI's); rare but important
- **Urease** hydrolyzes urea; release of NH_4^+ , increase in pH, alkaline urine, renal stones

Corynebacterium jeikeium

- **Opportunistic** infections in **immunocompromised** (e.g., patients with blood disorders, bone marrow transplants, intravenous catheters)
- **Multiple antibiotic resistance** common (**MDR**)
- **Carriage on skin** of up to 40% of hospitalized patients (e.g., marrow t-plants)

Corynebacterium jeikeium Carriers



Corynebacterium diphtheriae

- **Respiratory diphtheria** (pseudomembrane on pharynx) and **cutaneous diphtheria**
- Prototype A-B exotoxin acts systemically
 - **Toxoid** in DPT and TD vaccines
- **Diphtheria toxin** encoded by tox gene introduced by lysogenic bacteriophage (prophage)
- **Selective media:** cysteine-tellurite; serum tellurite; Loeffler's
- Gravis, intermedius, and mitis colonial morphology

Epidemiology of Diphtheria

DISEASE/BACTERIAL FACTORS

Diphtheria exotoxin disrupts peptide formation in ribosomes

Phospholipase D increases vascular permeability and promotes spread of organism

TRANSMISSION

Person to person by inhalation or skin contact

Asymptomatic carriage maintains bacteria in population

WHO IS AT RISK?

Unvaccinated people

People in crowded, poor urban areas

Children

GEOGRAPHY/SEASON

Worldwide, where vaccination programs are not in place

No seasonal incidence

MODES OF CONTROL

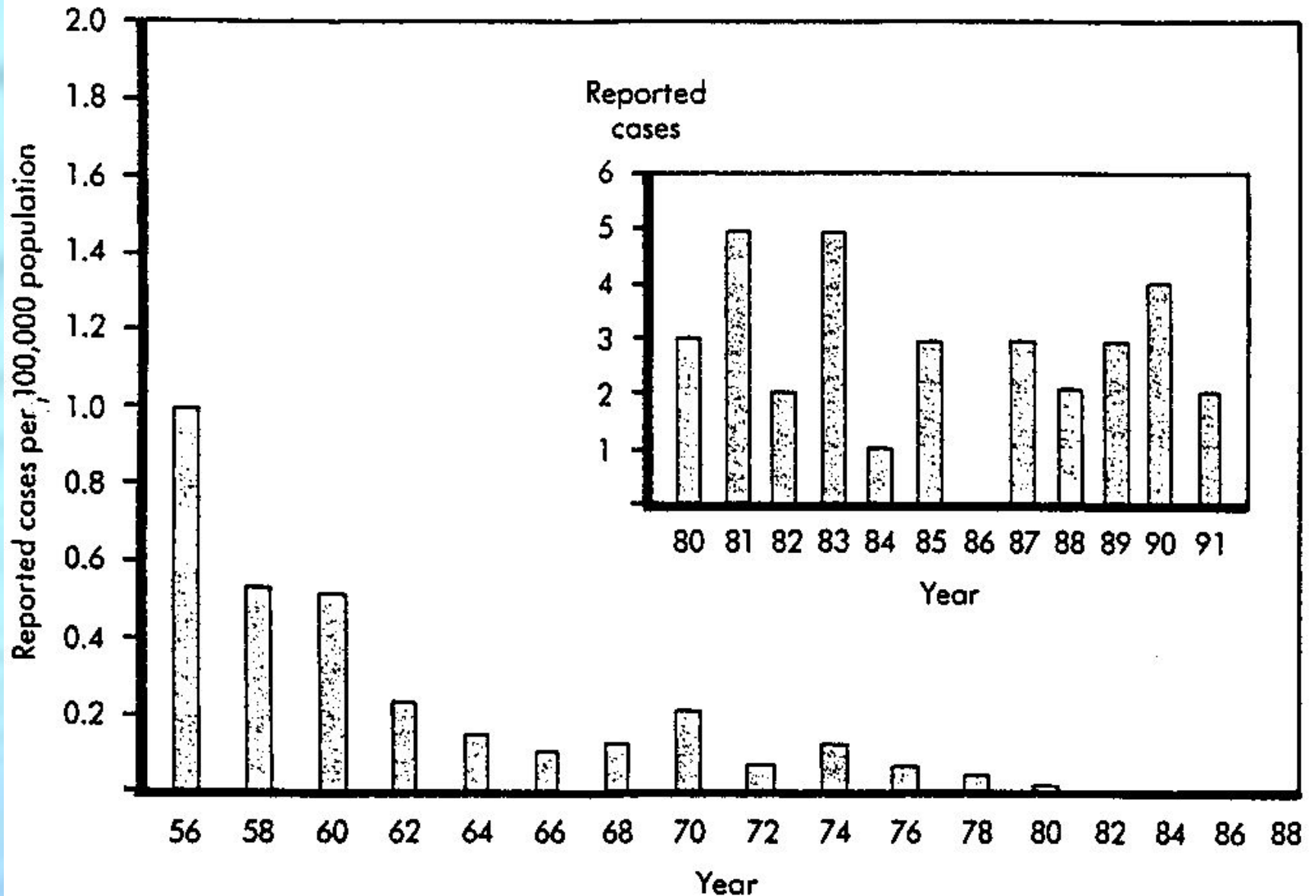
Early use of diphtheria antitoxin to neutralize exotoxin

Penicillin or erythromycin effective for infected patients and asymptomatic carriers

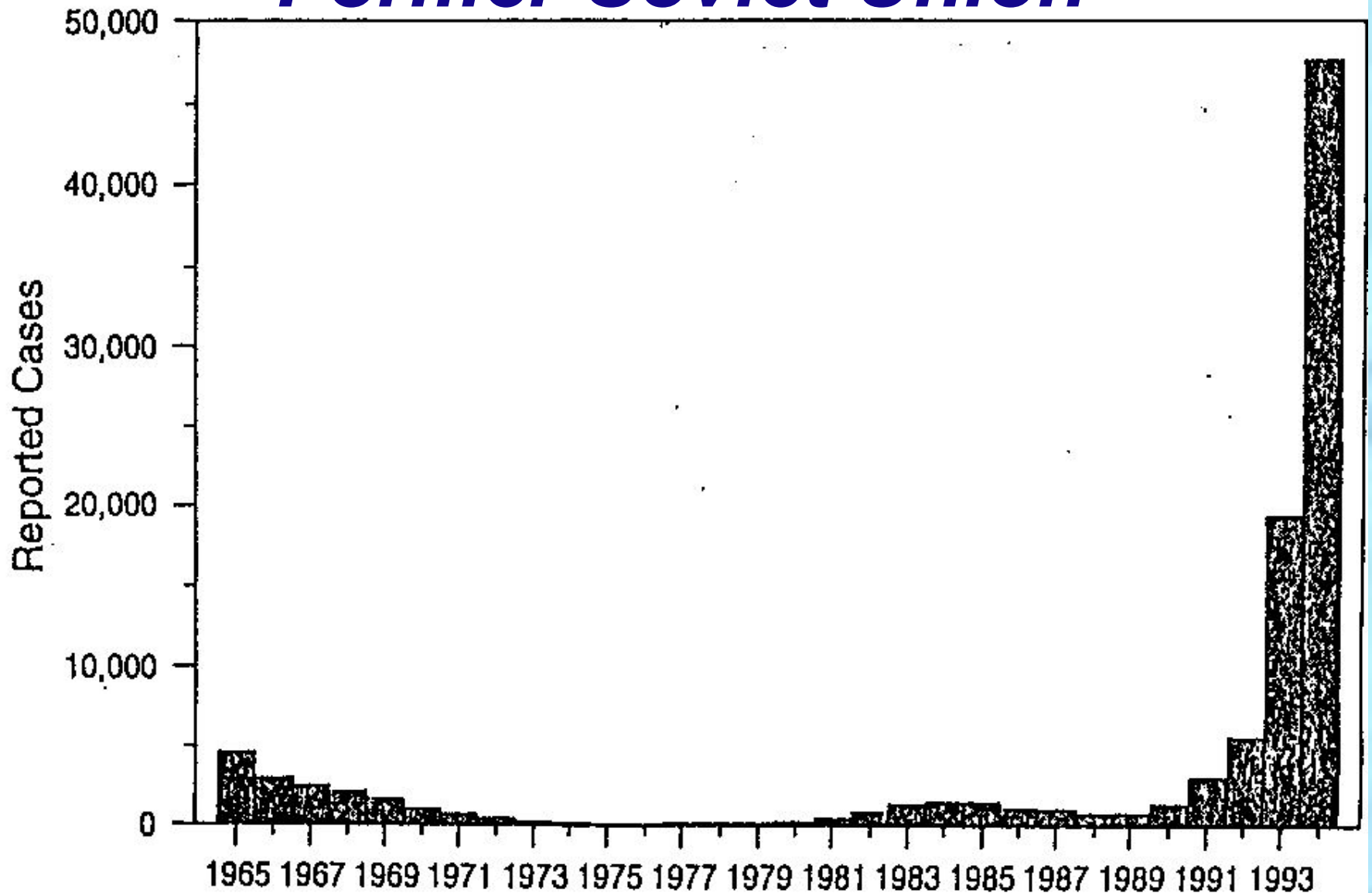
Active immunization with diphtheria toxoid during childhood (DPT vaccine), then booster shots every 10 years for life

Antimicrobial prophylaxis for close contacts of patients with diphtheria

Incidence of Diphtheria in the USA



Incidence of Diphtheria in Former Soviet Union



Virulence Factors in *Corynebacterium* Species

C. diphtheriae

Diphtheria exotoxin

C. jeikeium

Antibiotic resistance

C. urealyticum

Antibiotic resistance; urease
production

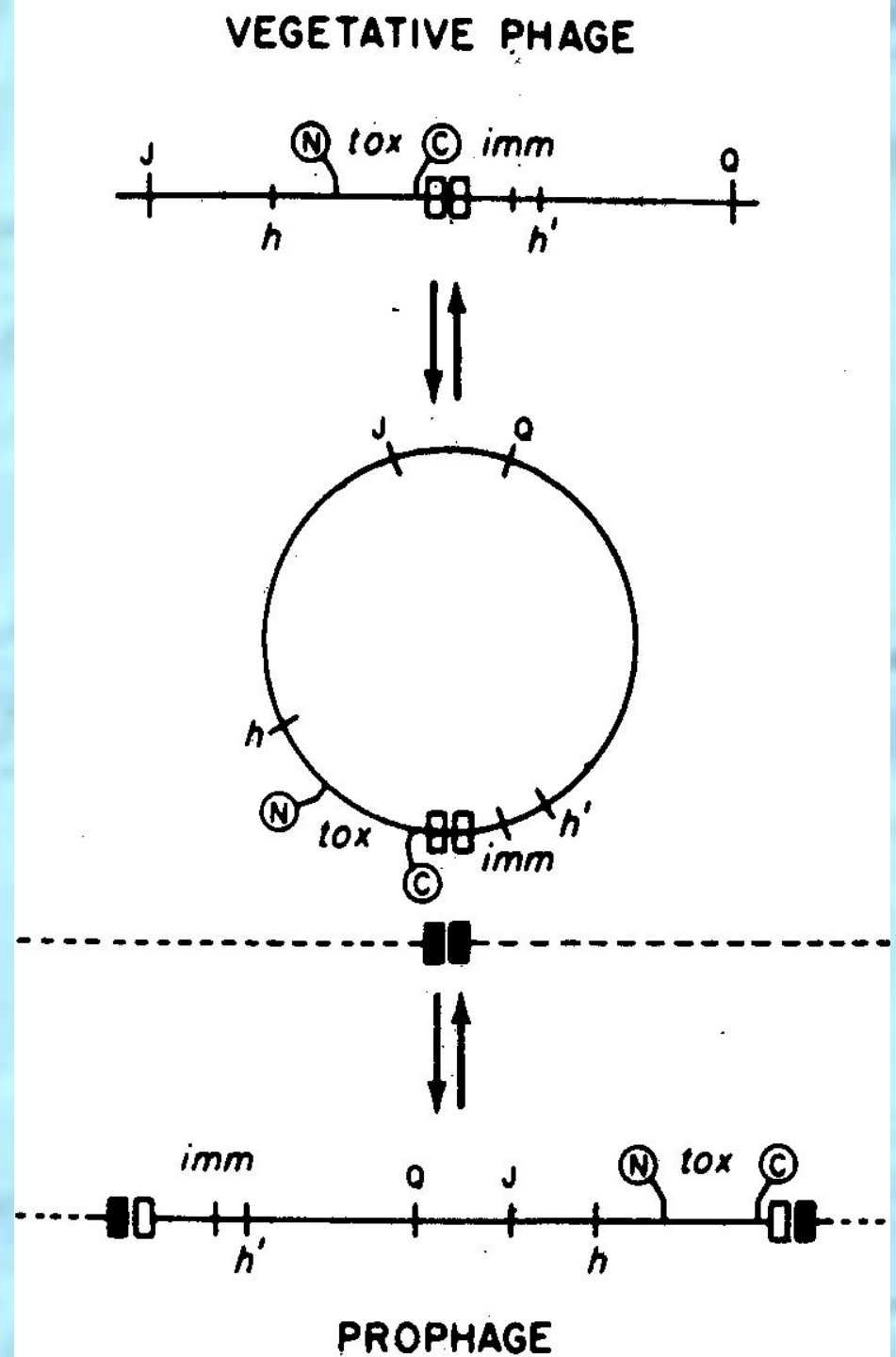
C. pseudotuberculosis

Diphtheria exotoxin;
phospholipase D

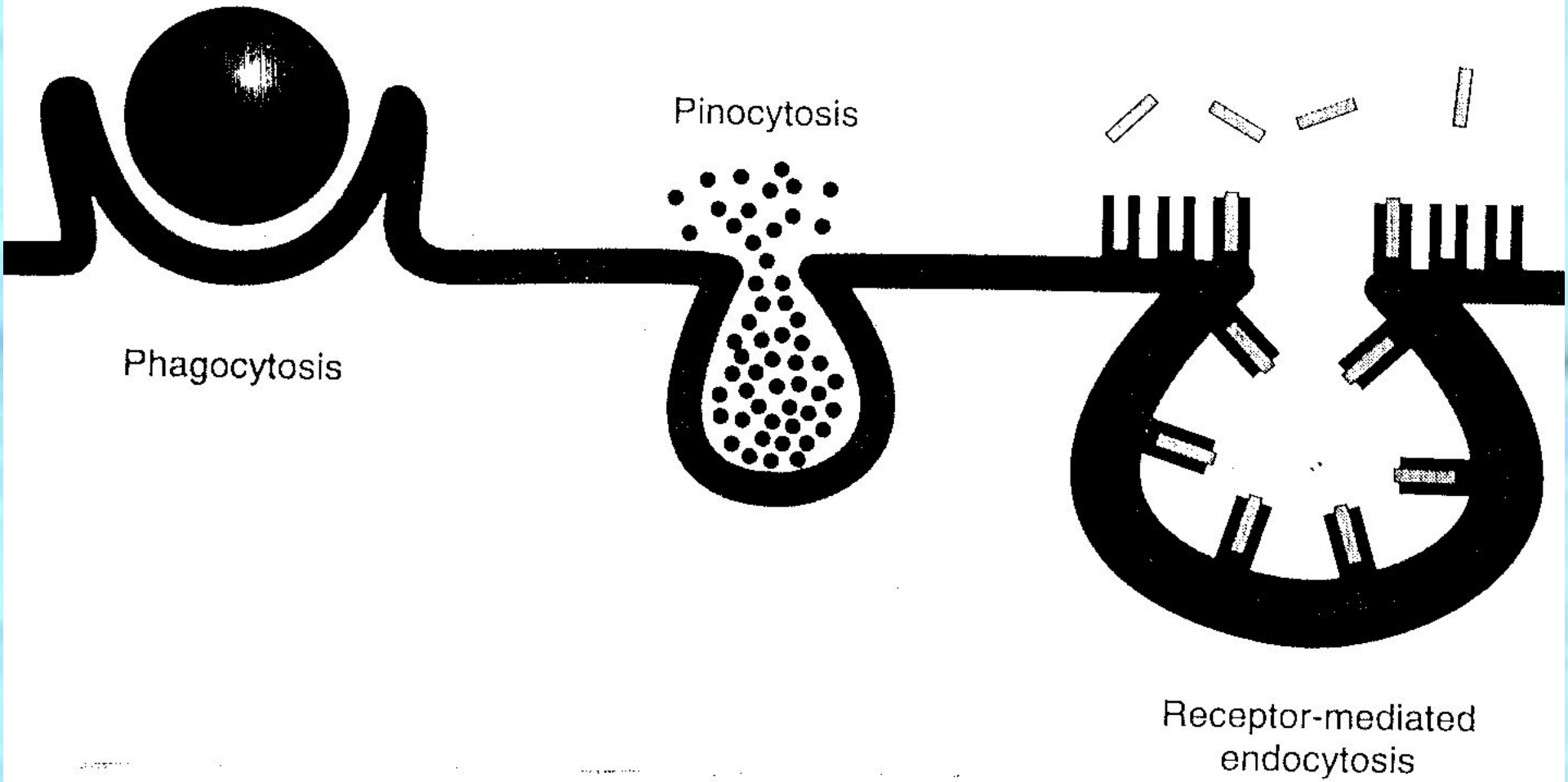
C. ulcerans

Diphtheria exotoxin;
phospholipase D

Diphtheria tox Gene in Beta Bacteriophage and Prophage

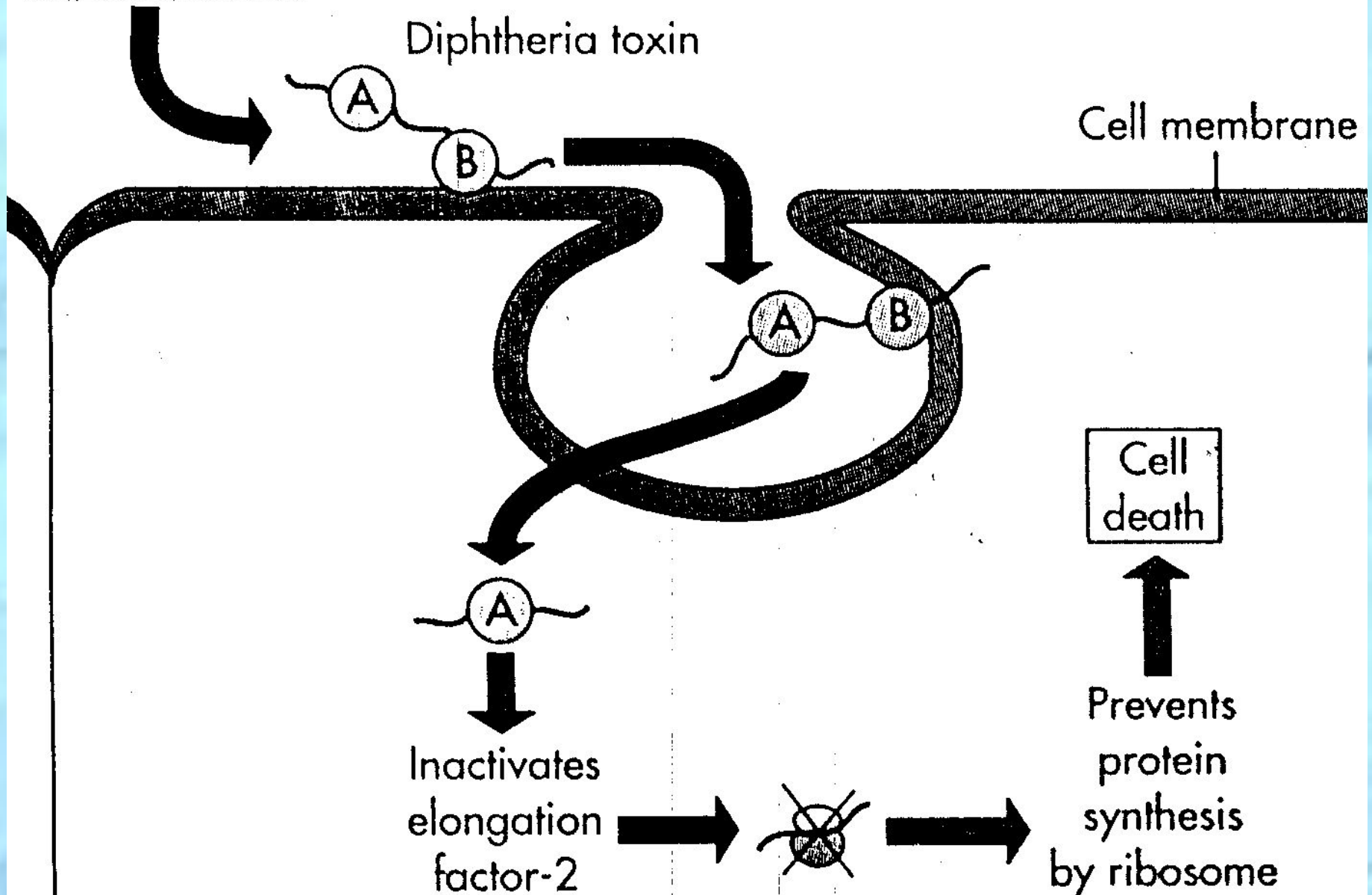


See Handout on Exotoxins

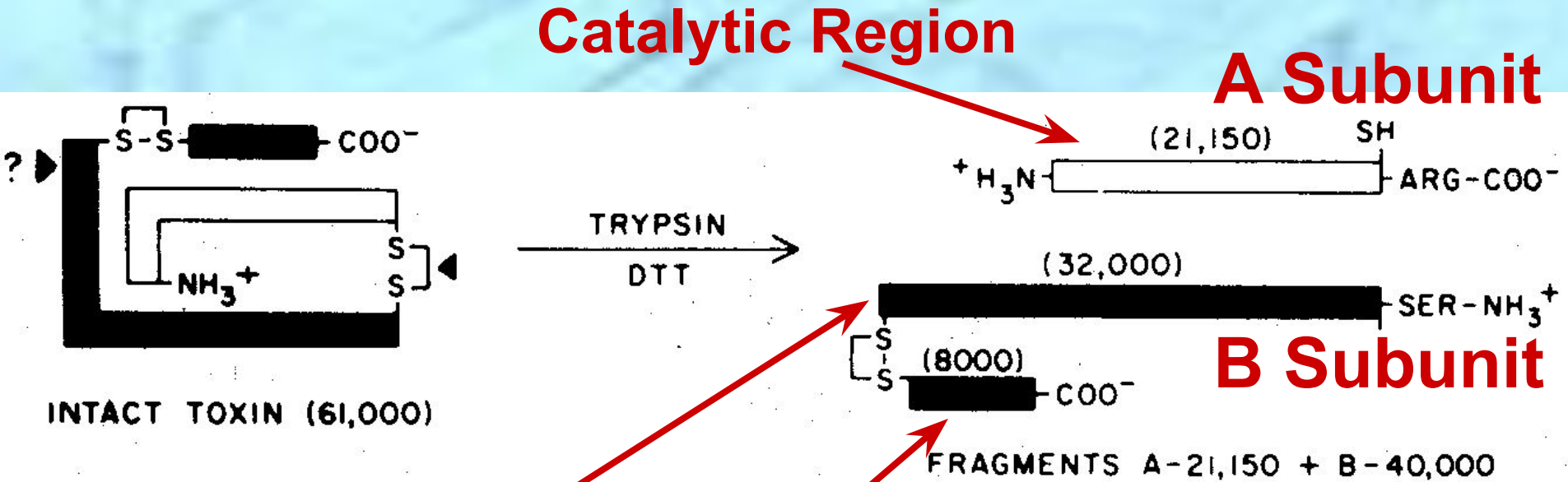


Mechanism of Action of Diphtheria Toxin:

C. diphtheriae Inhibition of Protein Synthesis



Molecular Structure of Diphtheria Toxin



Translocation Region
Receptor-Binding Region

TABLE 19-3

Properties of A-B Type Bacterial Toxins

TOXIN	ORGANISM	GENETIC CONTROL	SUBUNIT STRUCTURE	TARGET CELL RECEPTOR	BIOLOGICAL EFFECTS
Anthrax toxins	<i>Bacillus anthracis</i>	Plasmid	Three separate proteins (EF, LF, PA)	Unknown, probably glycoprotein	EF + PA: increase in target-cell cAMP level, localized edema; LF + PA: death of target cells and experimental animals
<i>Bordetella</i> adenylate cyclase toxin	<i>Bordetella</i> species	Chromosomal	A-B	Unknown, probably glycolipid	Increase in target cell cAMP level, modified cell function or cell death
<i>Botulinum</i> toxin	<i>C. botulinum</i>	Phage	A-B	Possibly ganglioside (GD _{1b})	Decrease in peripheral, presynaptic acetylcholine release, flaccid paralysis
<i>Cholera</i> toxin	<i>V. cholerae</i>	Chromosomal	A-5B	Ganglioside (GM ₁)	Activation of adenylate cyclase, increase in cAMP level, secretory diarrhea
Diphtheria toxin	<i>C. diphtheriae</i>	Phage	A-B	Probably glycoprotein	Inhibition of protein synthesis, cell death
Heat-labile enterotoxins	<i>E. coli</i>	Plasmid	Similar or identical to cholera toxin		
Pertussis toxin	<i>B. pertussis</i>	Chromosomal	A-5B	Unknown, probably glycoprotein	Block of signal transduction mediated by target G proteins
<i>Pseudomonas</i> exotoxin A	<i>P. aeruginosa</i>	Chromosomal	A-B	Unknown, but different from diphtheria toxin	Similar or identical to diphtheria toxin
Shiga toxin	<i>Shigella dysenteriae</i>	Chromosomal	A-5B	Glycoprotein or glycolipid	Inhibition of protein synthesis, cell death
Shiga-like toxins	<i>Shigella</i> species, <i>E. coli</i>	Phage	Similar or identical to Shiga toxin		
Tetanus toxin	<i>C. tetani</i>	Plasmid	A-B	Ganglioside (GT ₁) and/or GD _{1b}	Decrease in neurotransmitter release from inhibitory neurons, spastic paralysis

Heparin-binding epidermal growth factor on heart & nerve surfaces

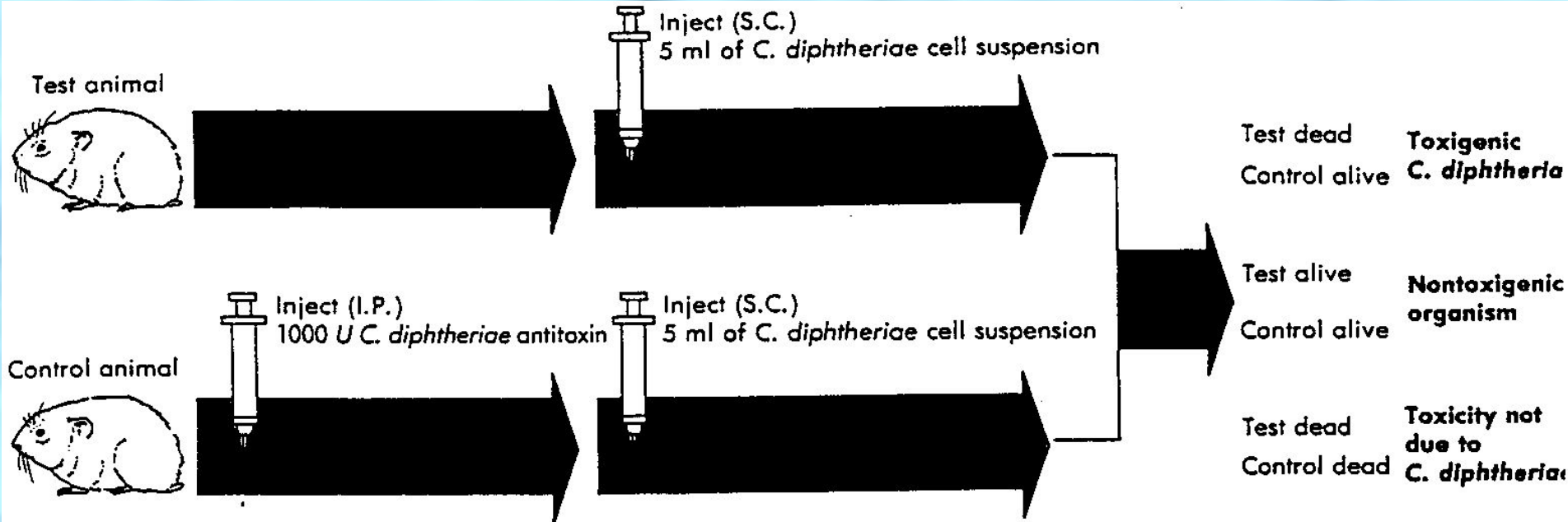


Diagnostic Schick Skin Test

Immune Status to C. diphtheriae and Sensitivity to Diphtheria Toxoid

	<u>TOXIN</u>		<u>TOXOID</u>		Interpretation
	36 h	120 h	36 h	120 h	
POSITIVE REACTION	-	+	-	-	Nonimmune, Nonsensitive
NEGATIVE REACTION	-	-	-	-	Immune, Nonsensitive
PSEUDO REACTION	+	-	+	-	Immune, Sensitive
COMBINED REACTION	+	+	+	-	Nonimmune, Sensitive

In vivo Detection of Diphtheria Exotoxin





Listeria monocytogenes

- Gram-positive beta-hemolytic bacillus
- **Multiply at refrigerator temperatures (4°C)**
- **Tumbling motility** at room temperature
- **CAMP Test positive** (like Group B *Streptococcus*)

Where do we find Listeria?

- Intestinal tract of mammals & birds (especially chickens)
- Persists in soil
- **Soft cheeses & unwashed raw vegetables**
- Raw or undercooked food of animal origin
 - Luncheon meats
 - Hot dogs
- **Large scale food recalls** have become common

Epidemiology of Listeriosis

DISEASE/BACTERIAL FACTORS

Organism can grow in macrophages and epithelial cells
Asymptomatic carriage is possible
Virulent strains produce listeriolysin O
Can grow in cold temperatures (refrigerators)

TRANSMISSION

Ingestion of contaminated food products
Transplacental

WHO IS AT RISK?

Neonates
Elderly
Pregnant women
Immunocompromised patients

GEOGRAPHY/SEASON

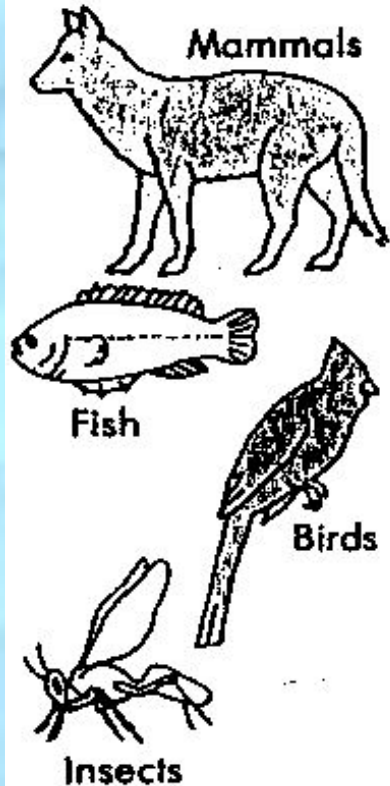
Ubiquitous and worldwide
Sporadic, with peak occurrence in the warmer months

MODES OF CONTROL

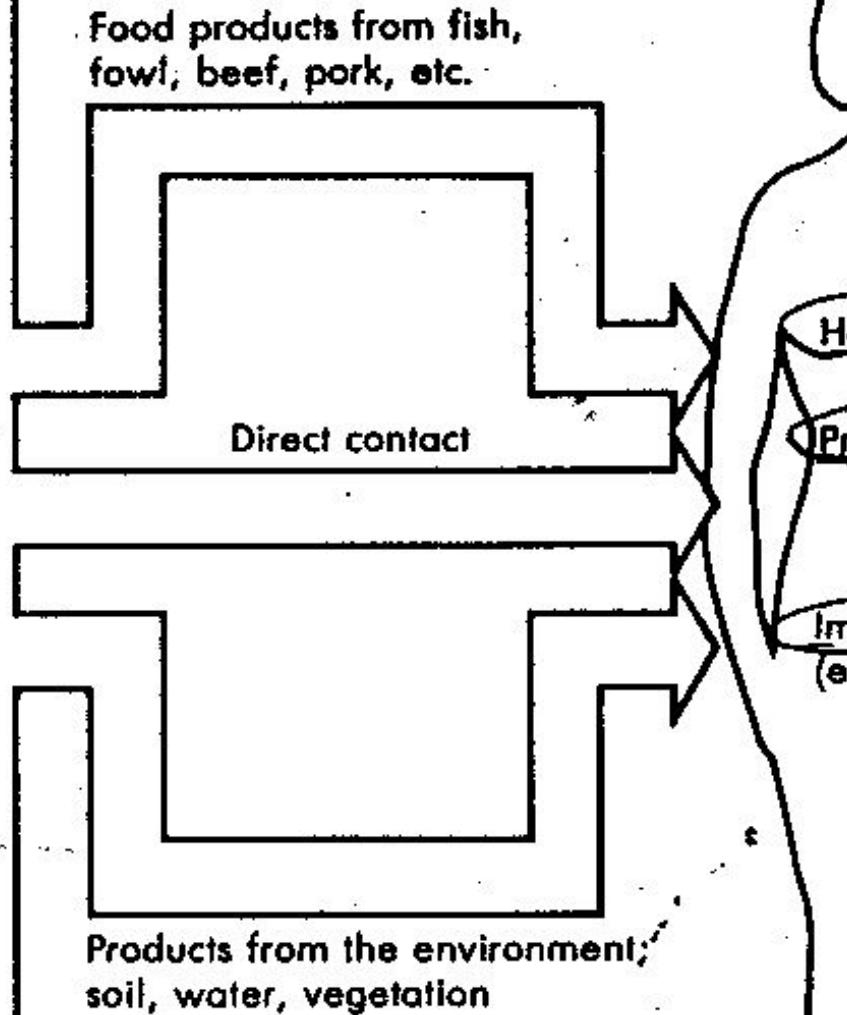
Penicillin or ampicillin, alone or in combination with an aminoglycoside
People at high risk should avoid eating raw or partially cooked food of animal origin, soft cheeses, and unwashed raw vegetables

Epidemiology of Listeria Infections

Natural Reservoirs



Common Routes for Human Exposure



Population at Greatest Risk

Healthy children and adults
Asymptomatic carriage

Pregnant women
Asymptomatic carriage
Septicemia
Neonatal disease

Immunocompromised
(e.g., cancer or transplant patients)
Asymptomatic carriage
Meningitis
Septicemia
Other infections

Listeriosis

□ Neonates, elderly & immunocompromised

□ Granulomatosis infantiseptica

- Transmitted to fetus **transplacentally**
- **Early septicemic form:** 1-5 days post-partum
- **Delayed meningitic form:** 10-20 days following birth

□ Intracellular pathogen

- Cell-mediated and humoral immunity develop
- Only **cell-mediated immunity is protective**

Methods That Circumvent Phagocytic Killing

METHOD

EXAMPLE

Inhibition of phagolysosome infusion

Legionella species, *Mycobacterium tuberculosis*, *Chlamydia* species

Resistance to lysosomal enzymes

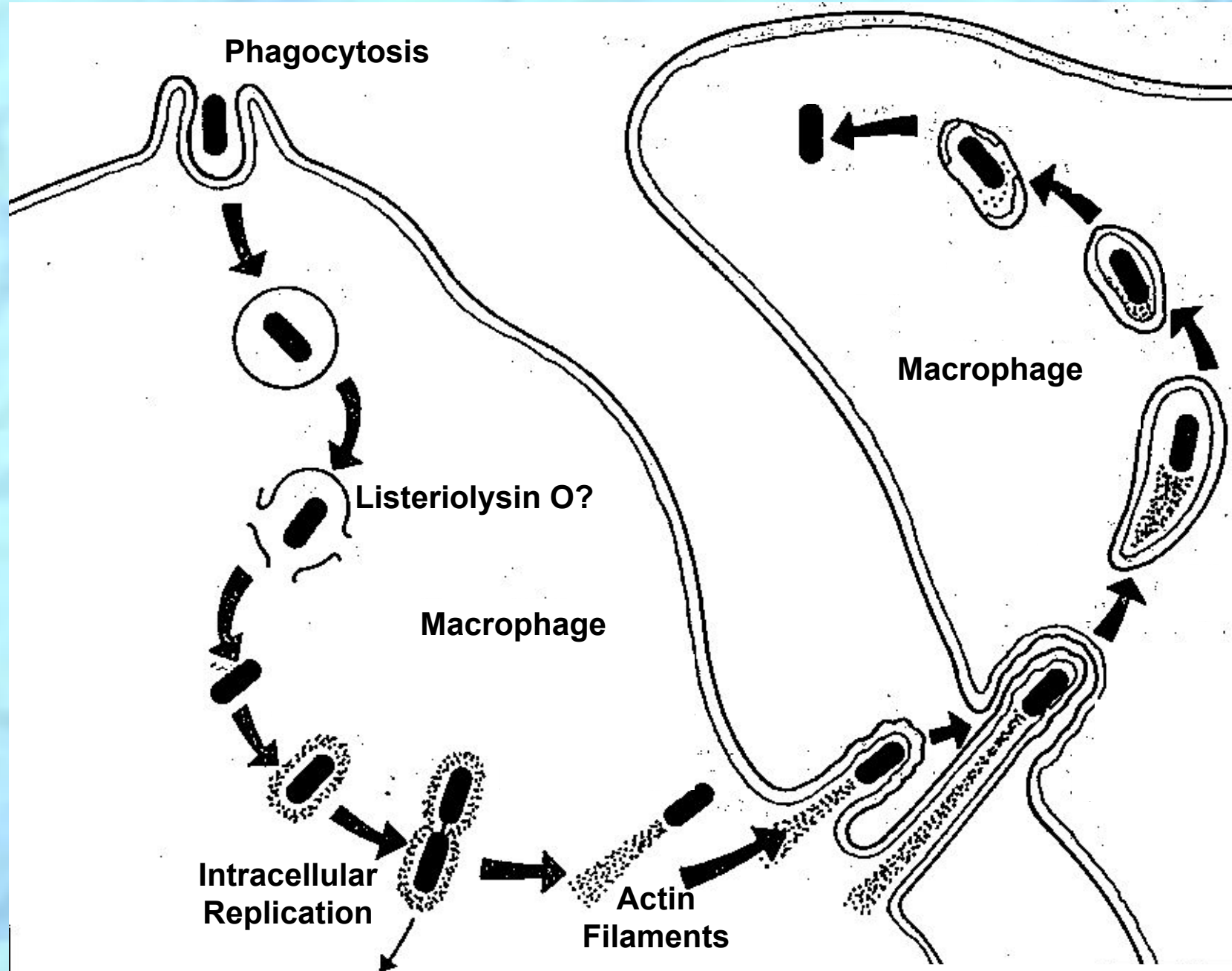
Salmonella typhimurium, *Coxiella* species, *Ehrlichia* species, *Mycobacterium leprae*, *Leishmania* species

Adaptation to cytoplasmic replication

★ *Listeria* species, *Francisella* species, *Rickettsia* species

See Chpt. 19

Intracellular Survival & Replication of Listeria





Erysipelothrix rhusopathiae

- Gram-positive non-motile bacillus; forms filaments
- **Occupational disease** of meat and fish handlers, hunters, veterinarians
 - **Preventable** with protective gloves & clothing
- **Erysipeloid** in humans; erysipelas in swine & turkeys
 - Organisms enter through **break in skin**
 - Nonsuppurative, **self-limiting skin lesions** with **erythema and eruption**
 - **Peripheral spread** may lead to generalized infection, septicemia and/or endocarditis
 - Organisms can be isolated from skin biopsy

Epidemiology of Erysipelothrix Infection

DISEASE/BACTERIAL FACTORS

Disease is common in swine but rare in humans
Organism is ubiquitous

TRANSMISSION

Inoculation through abrasion or wound

WHO IS AT RISK?

Those who occupationally handle meat (butchers), poultry, fish, or animals (farmers, veterinarians)

GEOGRAPHY/SEASON

Worldwide distribution in animals

MODES OF CONTROL

Penicillin is very effective

Organism is resistant to the sulfonamides, aminoglycosides, and vancomycin

Covering of exposed skin surfaces when exposed occupationally to animals

No vaccine available



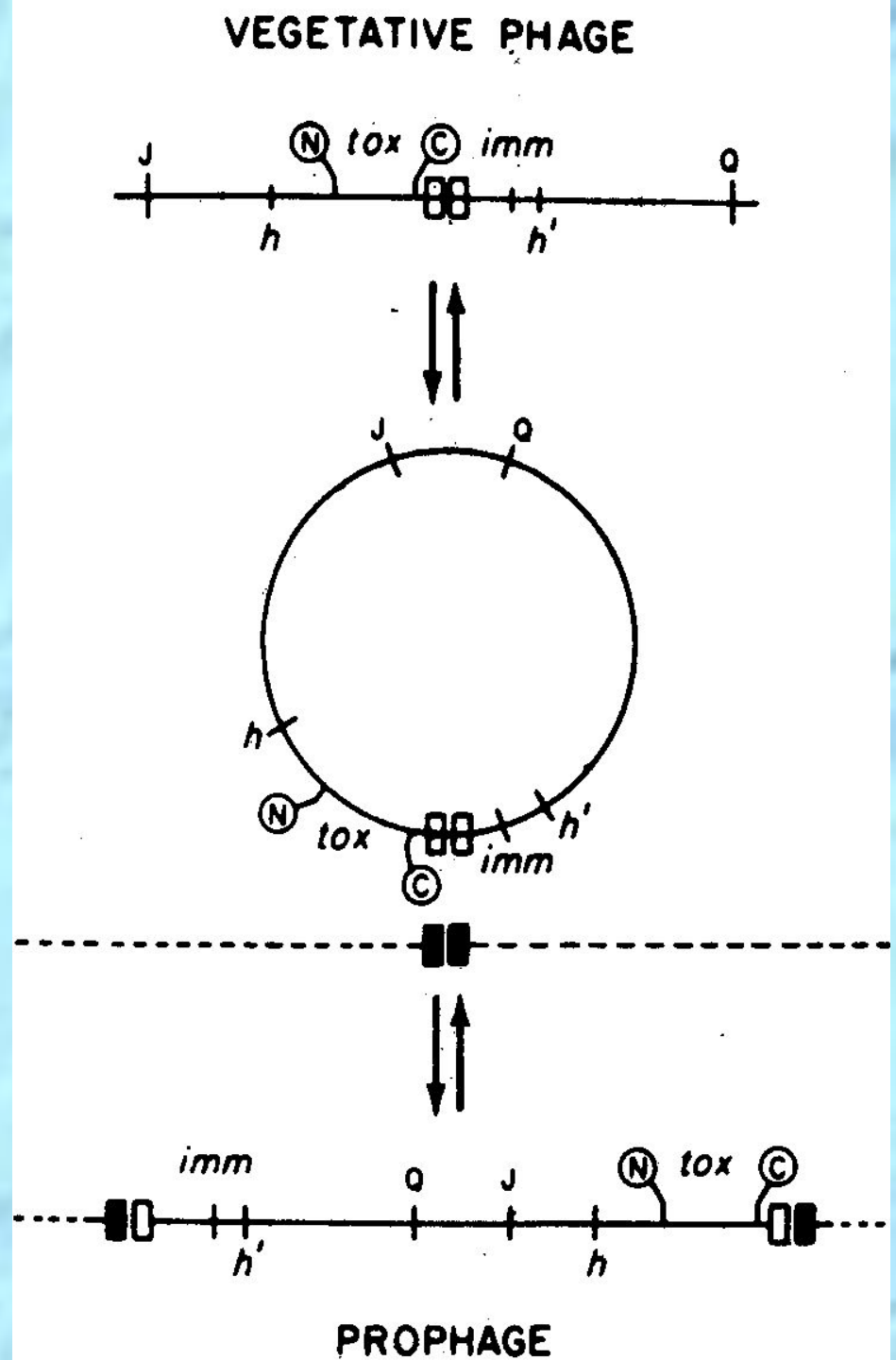
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Diphtheria tox Gene in Beta Bacteriophage and Prophage

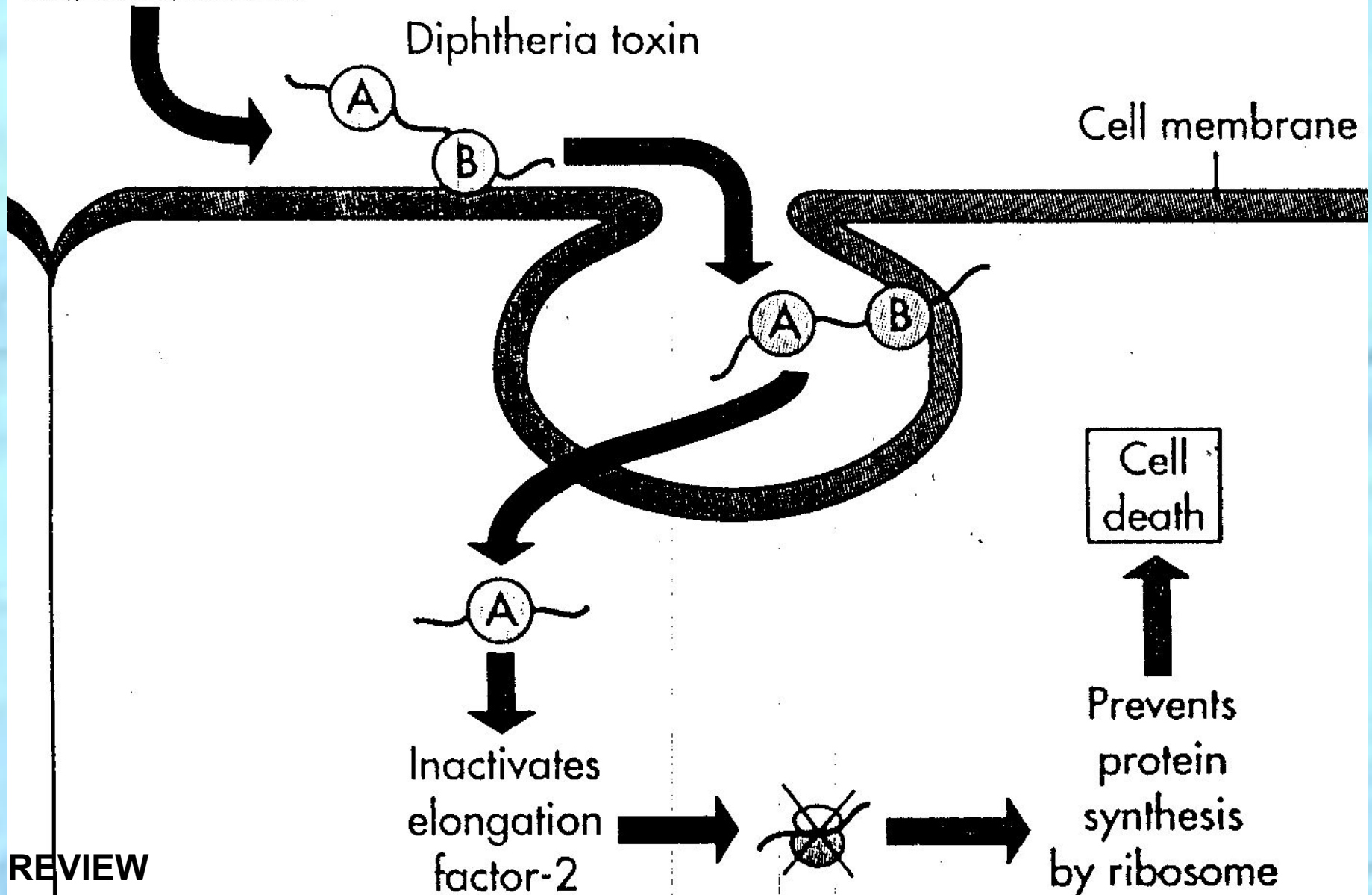
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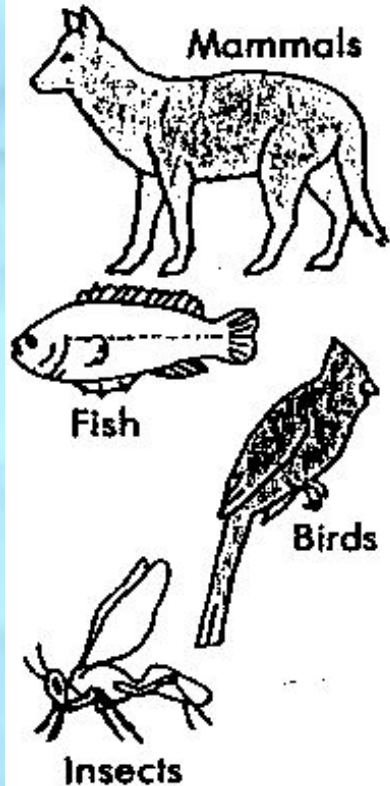
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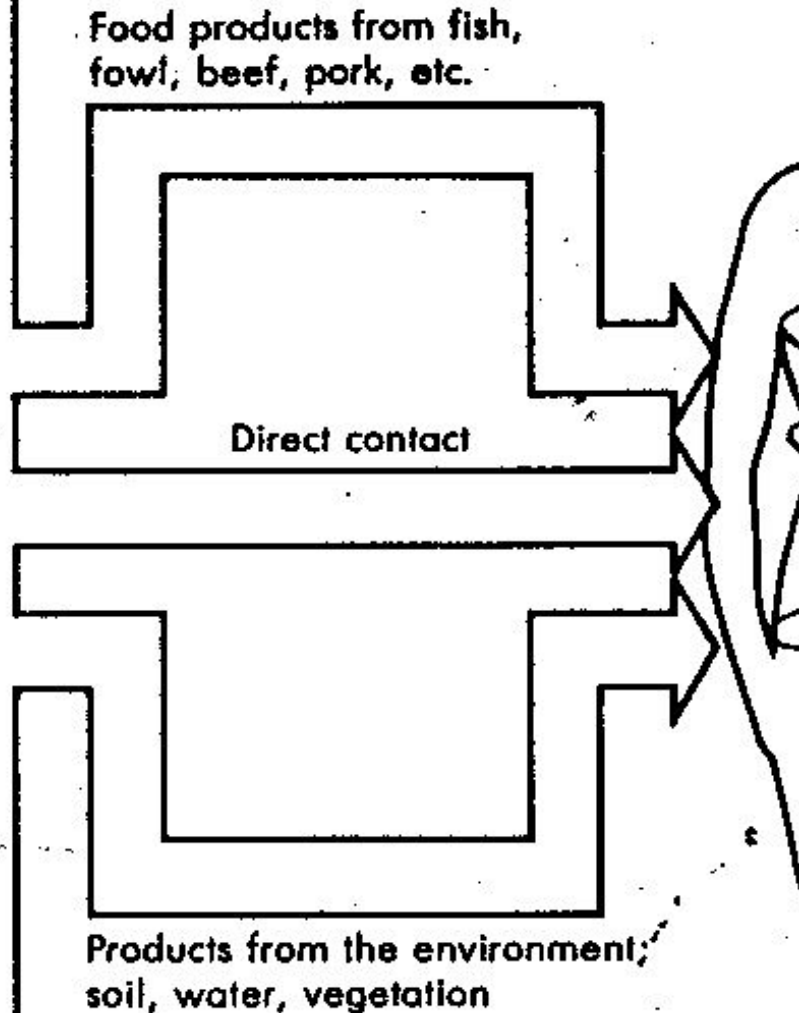
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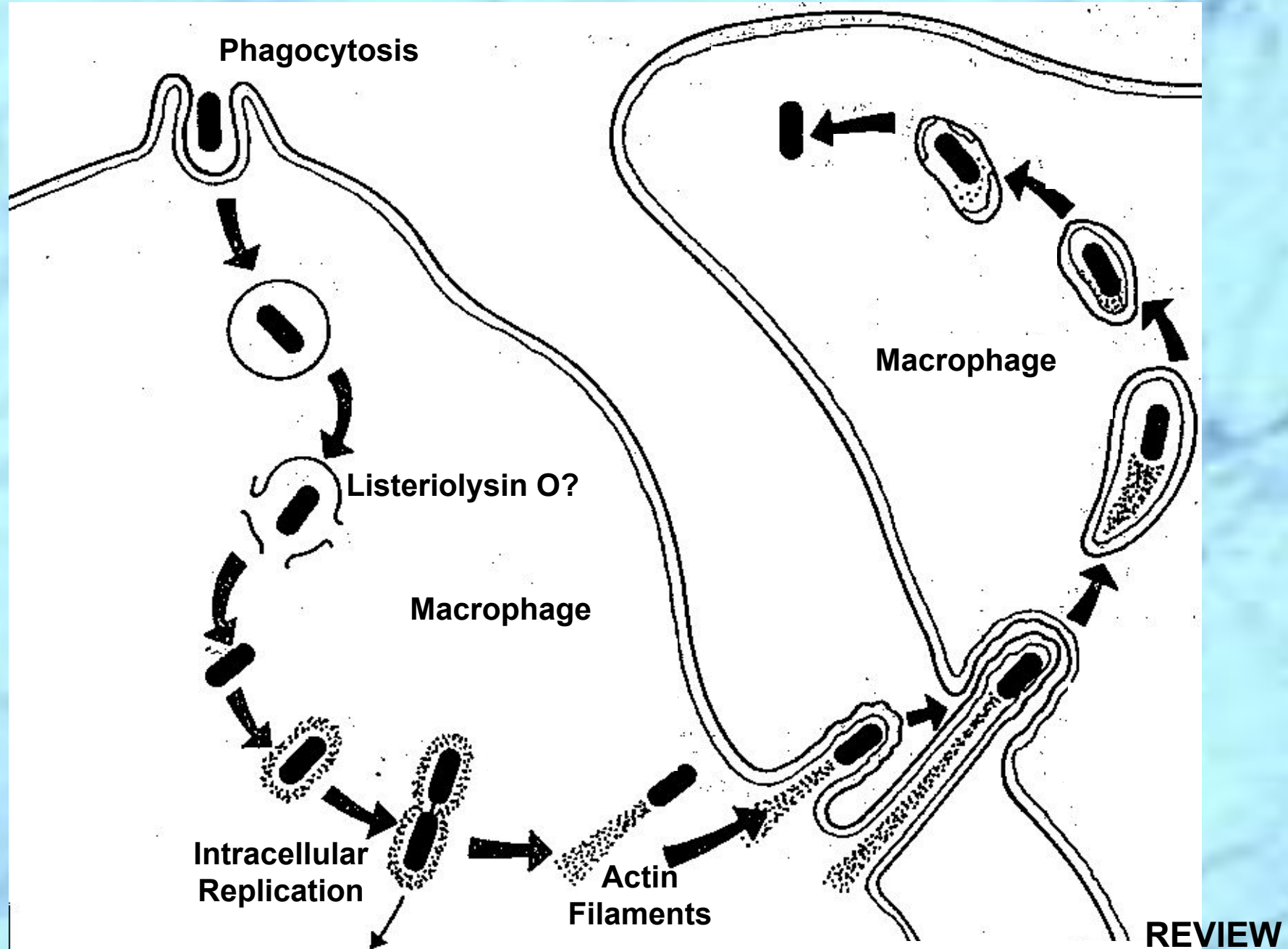
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