Corynebacterium
Erysipelothrix
& Listeria

Pathogenic Anaerobic Gram-Positive Bacilli

Corynebacterium diphtheriae	Diphtheria
C. jeikeium (CDC group JK)	Opportunistic infections
C. urealyticum (Coryneform group D-2)	Urinary tract infections
C. pseudodiphtheriticum	Endocarditis; lower respiratory tract infections
C. minutissimum	Skin infections (erythrasma); systemic infections
C. ulcerans	Pharyngitis (mild to diphtheria-like)
C. xerosis	Opportunistic infections
Arcanobacterium (Corynebacterium) haemolyticum	Pharyngitis
Actinomyces (Corynebacterium) pyogenes	Granulomatous ulcerative infections
Rhodococcus (Corynebacterium) equi	Suppurative pneumonia; opportunistic infections
Listeria monocytogenes	Meningitis; septicemia; granulomatosis infantiseptica; endocarditis
Erysipelothrix rhusiopathiae	Erysipeloid; septicemia; endocarditis
Gardnerella vaginalis	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

	Corynebacterium	Mycobacterium	Nocardia
CELL WALL:			
DL-DAP	+	+	+
LL-DAP	-	-	-
gly		-	-
Ara	+	+	+
gal	+	+	+
Acid-fast	-	+	±
Catalase			+
Serological Cross-reactivity	+	+	+
Cell Surface K-Ag	+	-	-
Mycolic Acids	C_{32} - C_{36} Corynemycolic (C_{32}) Corynemycolenic (C_{32})	C_{50} - C_{90} Mycolic	C_{50} Tetrahydronucardic (C_{50})
Adjuvant activity	+	+	-
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*

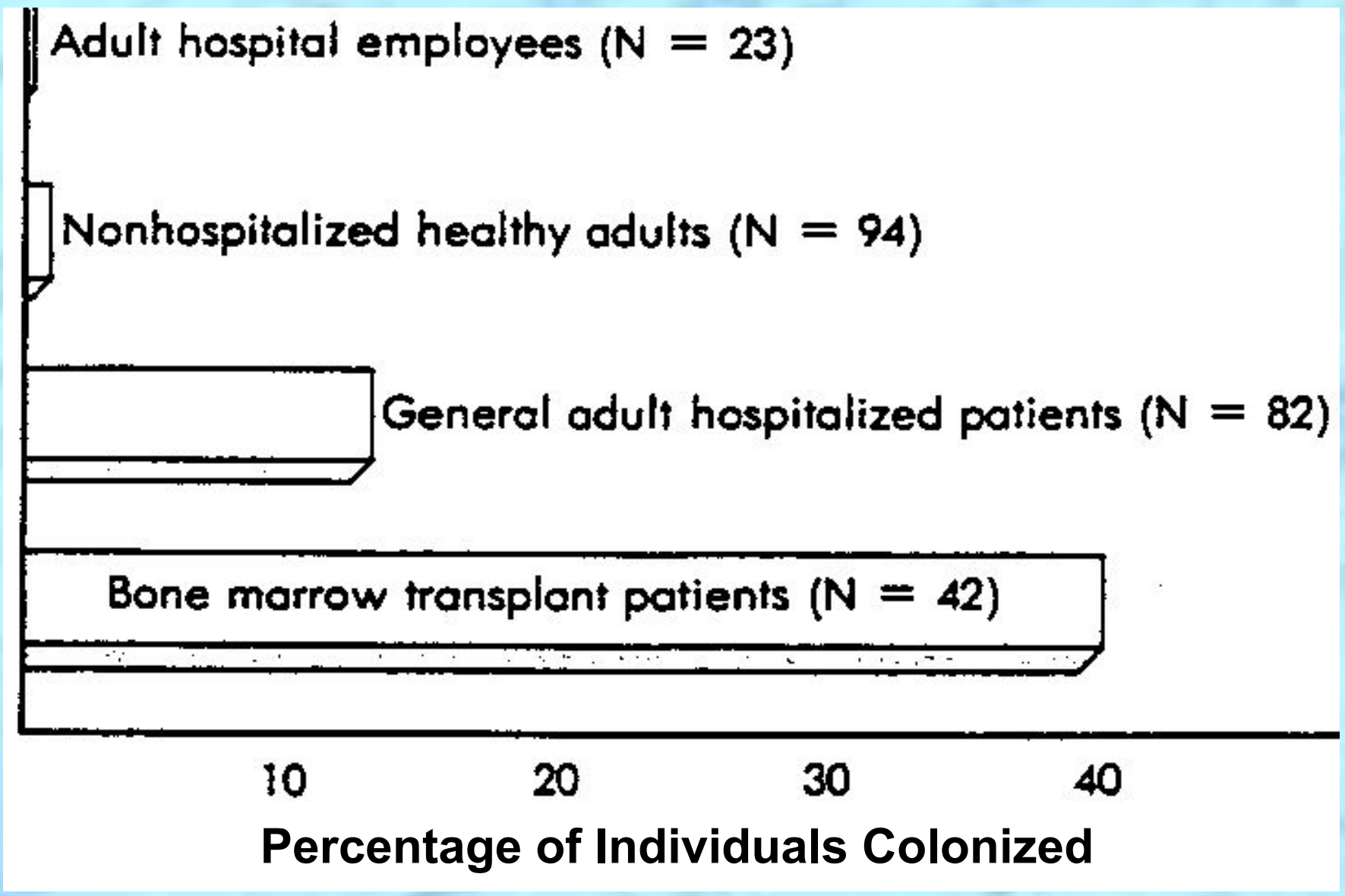
Corynebacterium urealyticum

- **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

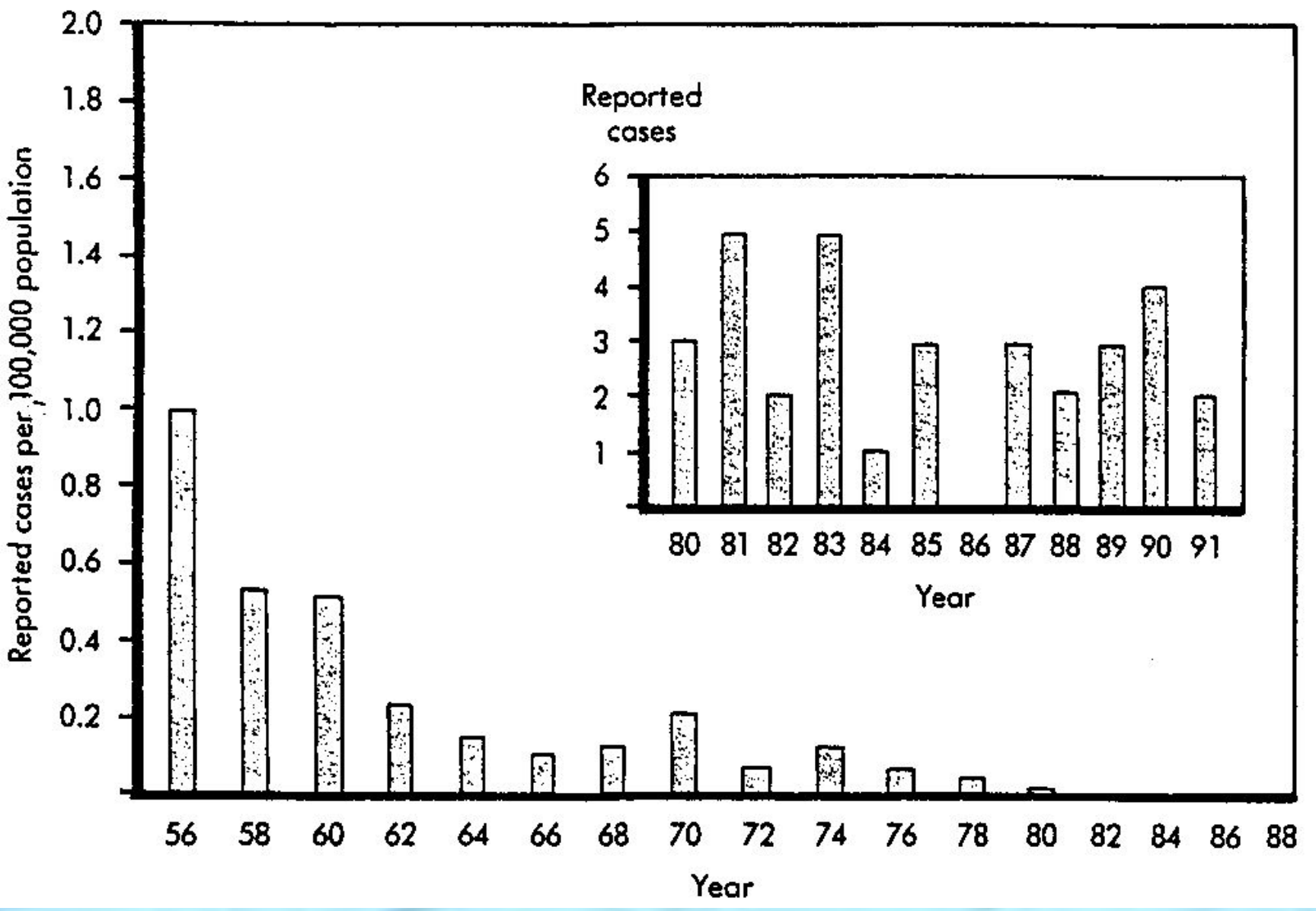
Early use of diphtheria antitoxin to neutralize exotoxin

Penicillin or erythromycin effective for infected patients and asymptomatic carriers

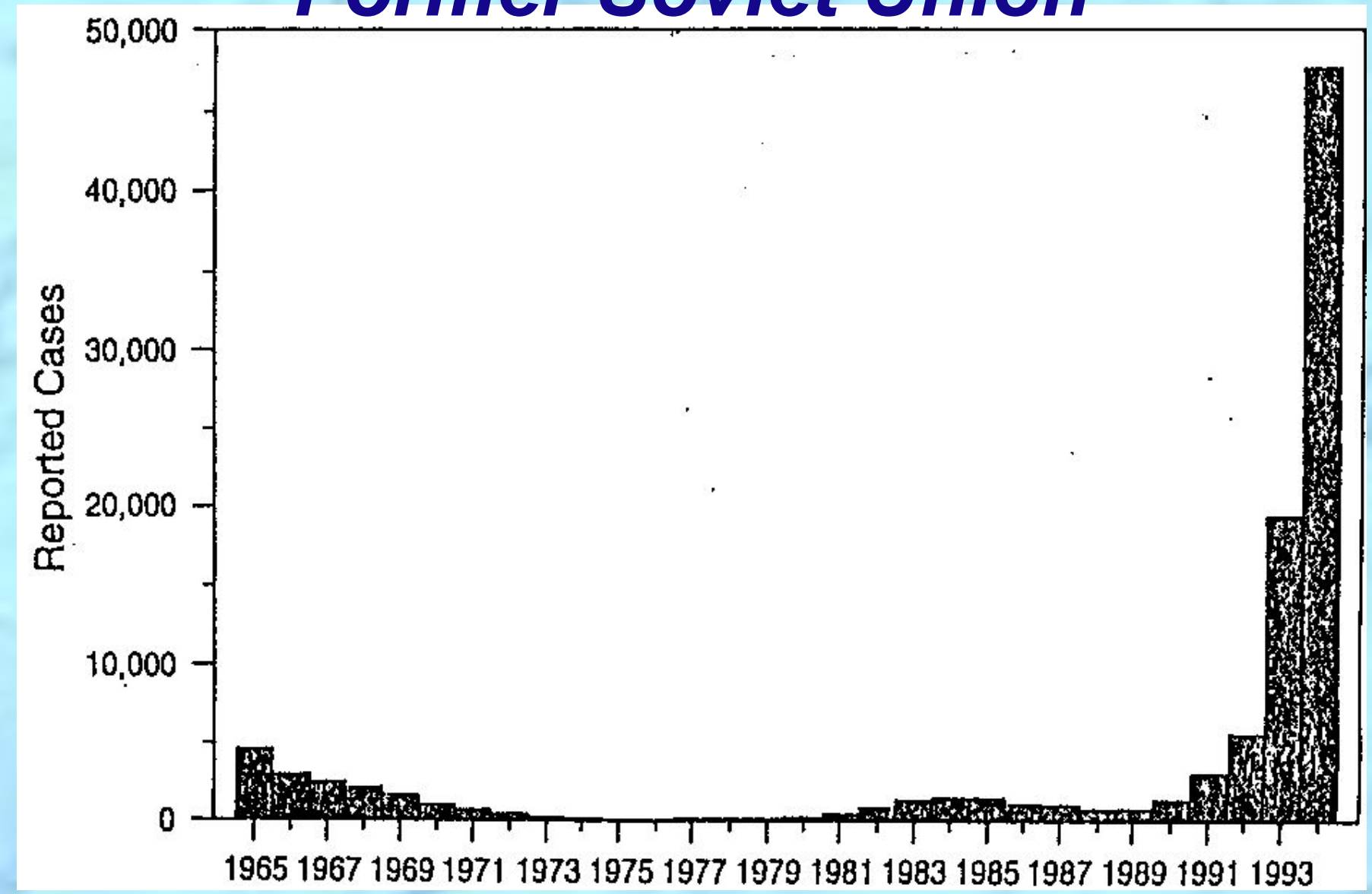
Active immunization with diphtheria toxoid during childhood (DPT vaccine), then booster shots every 10 years for life

Antimicrobial prophylaxis for close contacts of patients with diphtheria

Incidence of Diphtheria in the USA



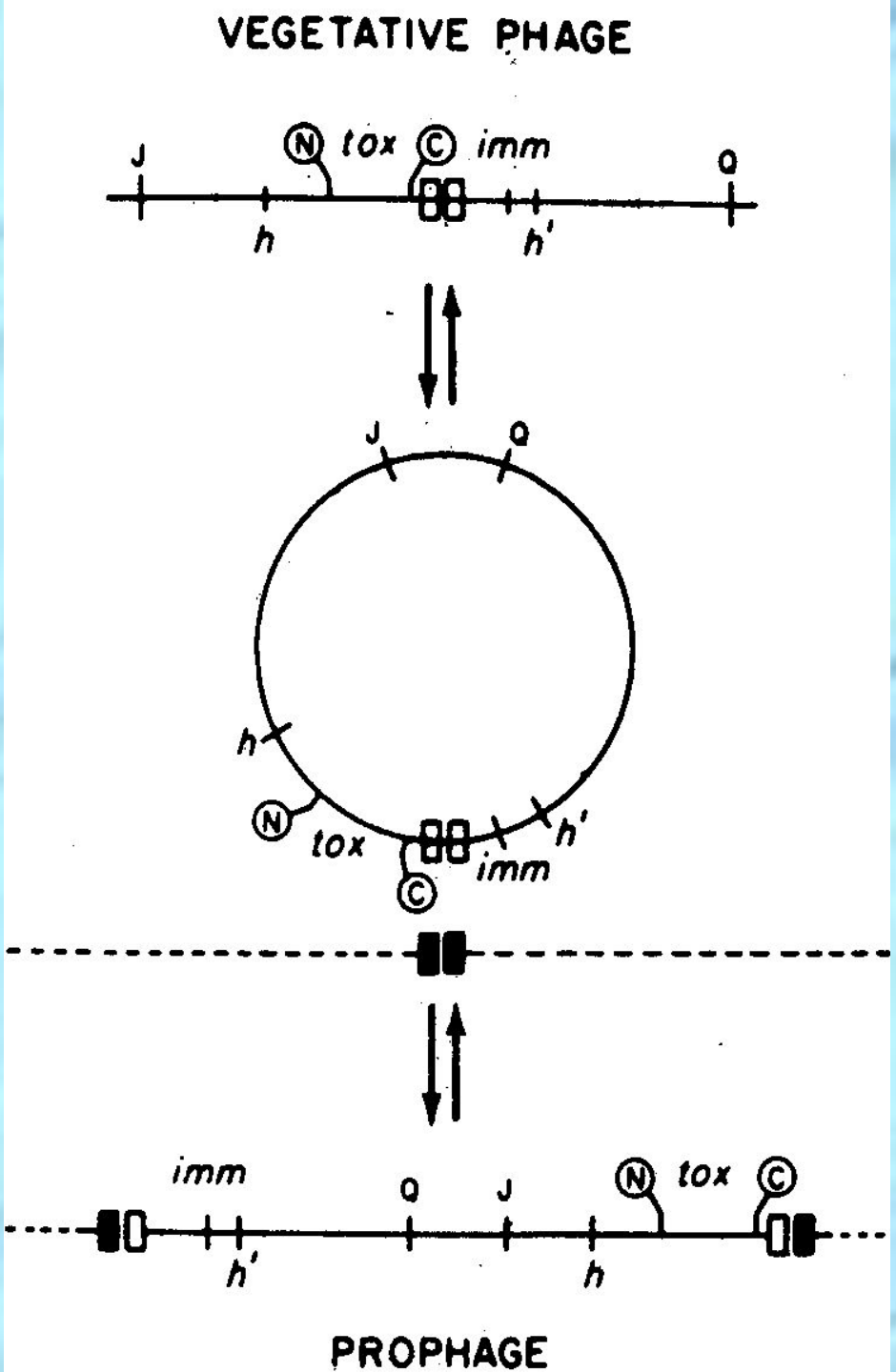
Incidence of Diphtheria in Former Soviet Union



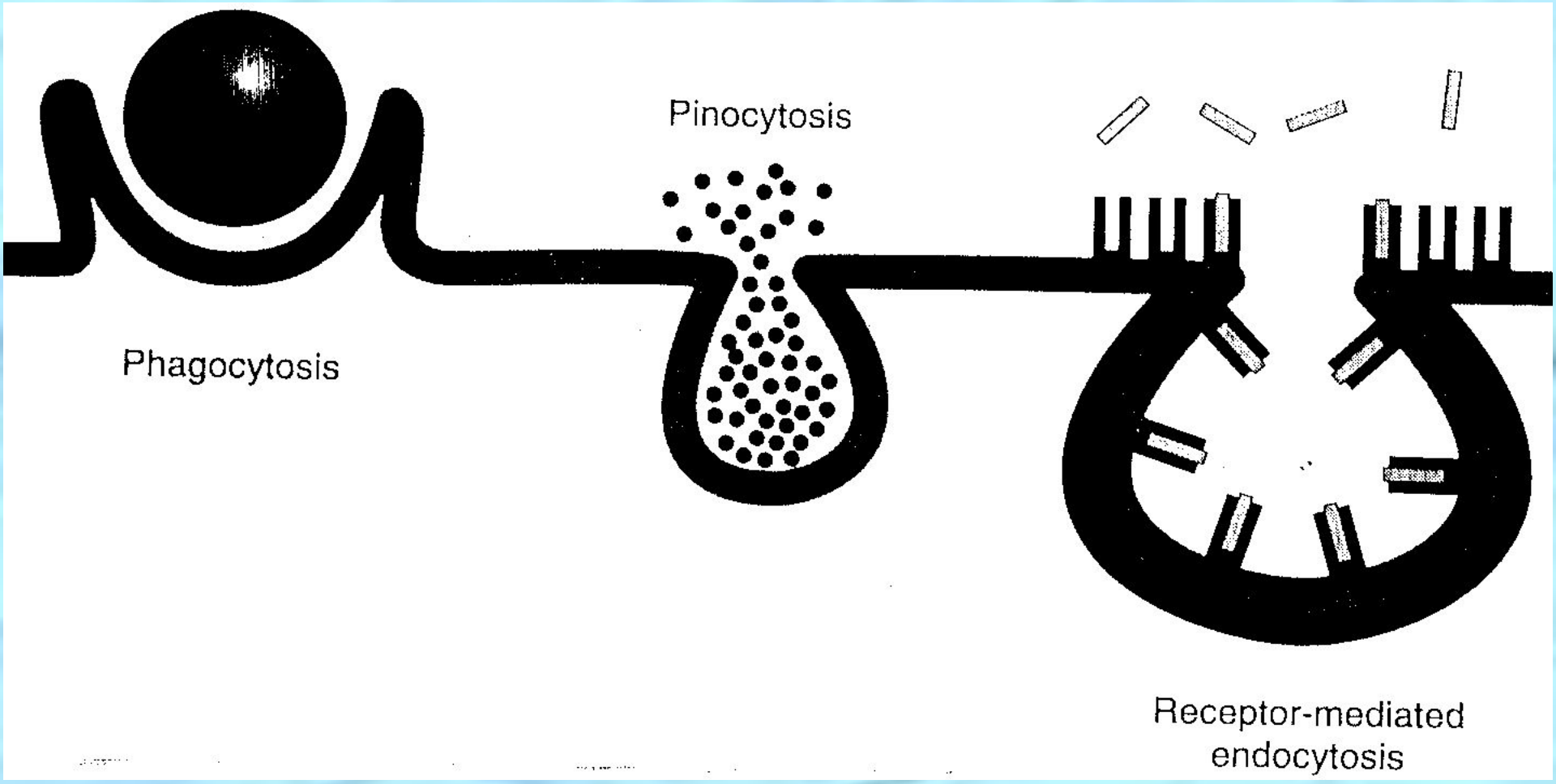
Virulence Factors in Corynebacterium Species

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

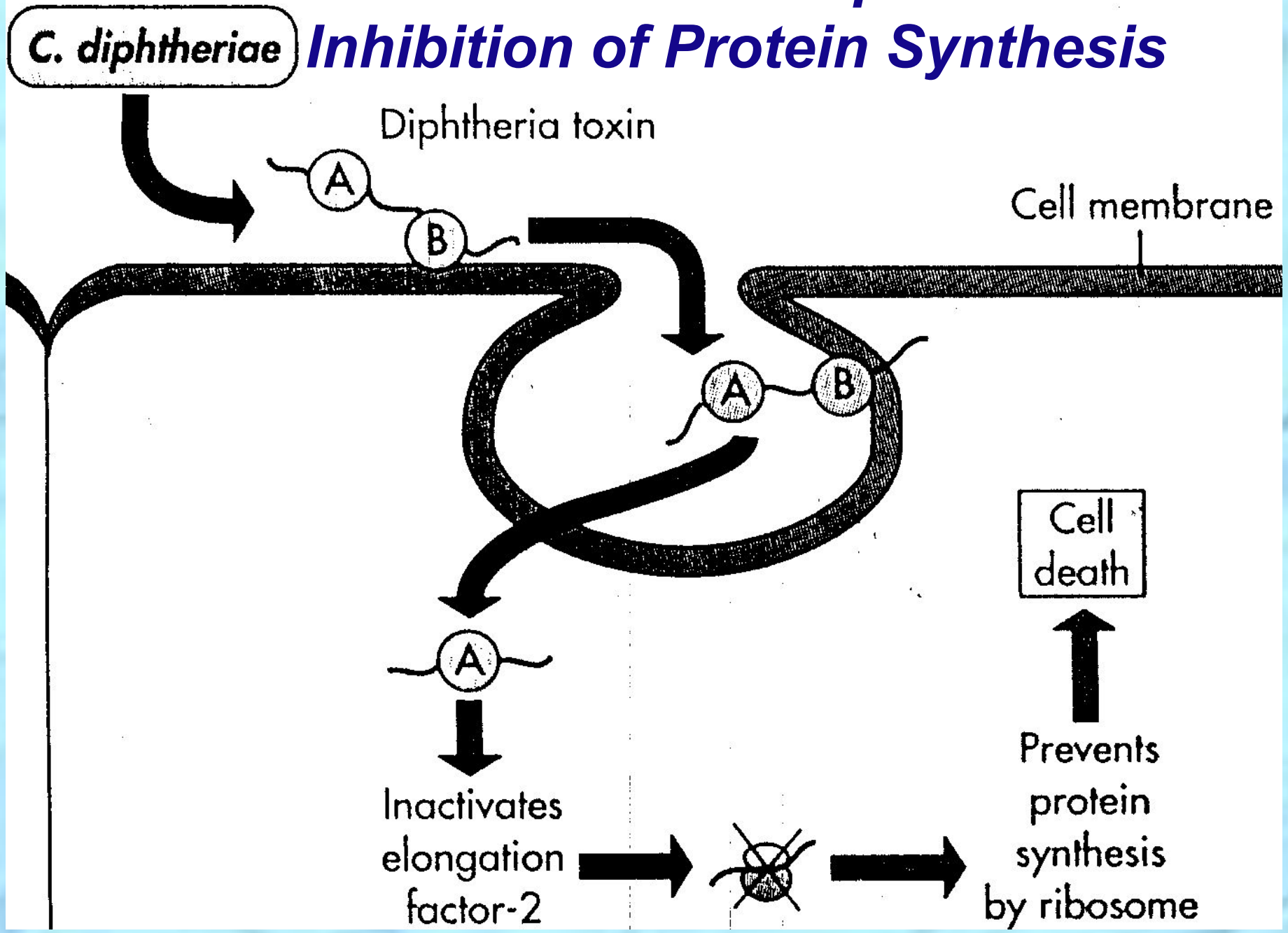
Diphtheria tox Gene in Beta Bacteriophage and Prophage



See Handout on Exotoxins


Pinocytosis
Phagocytosis
Receptor-mediated
endocytosis

Mechanism of Action of Diphtheria Toxin: Inhibition of Protein Synthesis



Molecular Structure of Diphtheria Toxin

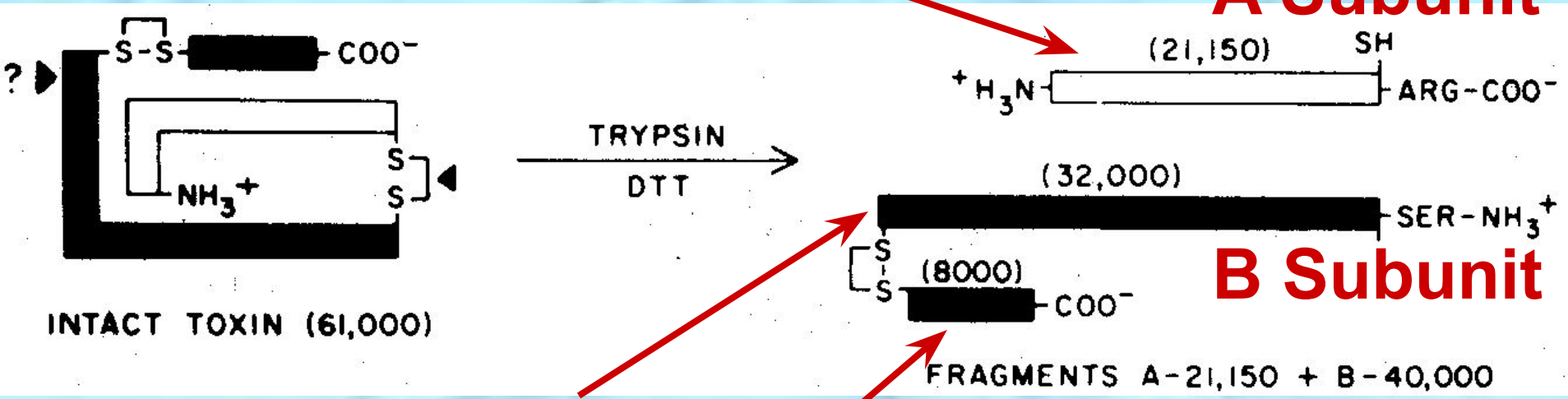


TABLE 19-3 Properties of A-B Type Bacterial Toxins

TOXIN	ORGANISM	GENETIC CONTROL	SUBUNIT STRUCTURE	TARGET CELL RECEPTOR	BIOLOGICAL EFFECTS
Anthrax toxins	*Bacillus anthracis*	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
Bordetella adenylate cyclase toxin	*Bordetella* species	Chromosomal	A-B	Unknown, probably glycolipid	Increase in target cell cAMP level, modified cell function or cell death
Botulinum toxin	*C. botulinum*	Phage	A-B	Possibly ganglioside (GD_{1b})	Decrease in peripheral, presynaptic acetylcholine release, flaccid paralysis
Cholera toxin	*V. cholerae*	Chromosomal	A-5B	Ganglioside (GM_1)	Activation of adenylate cyclase, increase in cAMP level, secretory diarrhea
Diphtheria toxin	*C. diphtheriae*	Phage	A-B	Probably glycoprotein	Inhibition of protein synthesis, cell death
Heat-labile enterotoxins	*E. coli*	Plasmid	Similar or identical to cholera toxin		
Pertussis toxin	*B. pertussis*	Chromosomal	A-5B	Unknown, probably glycoprotein	Block of signal transduction mediated by target G proteins
Pseudomonas exotoxin A	*P. aeruginosa*	Chromosomal	A-B	Unknown, but different from diphtheria toxin	Similar or identical to diphtheria toxin
Shiga toxin	*Shigella dysenteriae*	Chromosomal	A-5B	Glycoprotein or glycolipid	Inhibition of protein synthesis, cell death
Shiga-like toxins	*Shigella* species, *E. coli*	Phage	Similar or identical to Shiga toxin		
Tetanus toxin	*C. tetani*	Plasmid	A-B	Ganglioside (GT_1) and/or GD_{1b}	Decrease in neurotransmitter release from inhibitory neurons, spastic paralysis

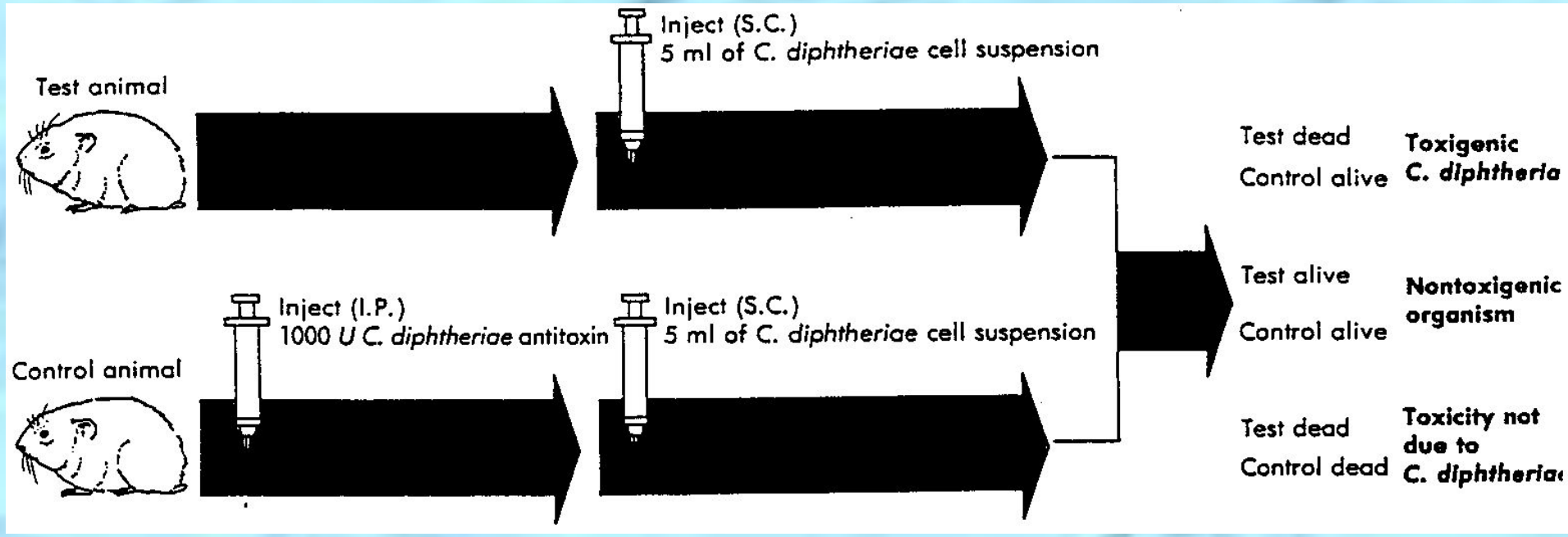
Heparin-binding epidermal growth factor on heart & nerve surfaces

Diagnostic Schick Skin Test

Immune Status to C. diphtheriae and Sensitivity to Diphtheria Toxoid

	TOXIN		TOXOID		
	36 h	120 h	36 h	120 h	Interpretation
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

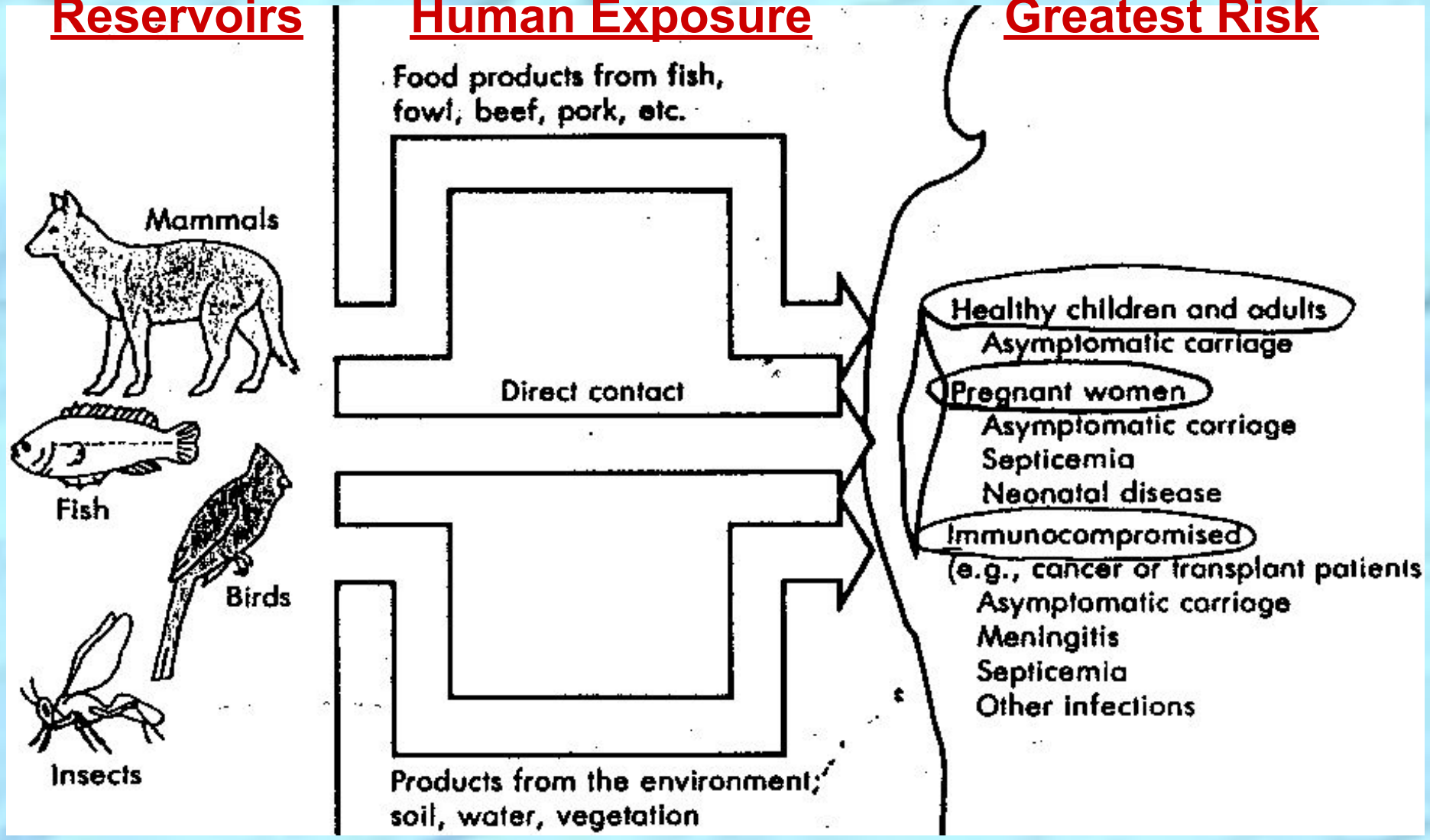
GEOGRAPHY/SEASON

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



Listeriosis

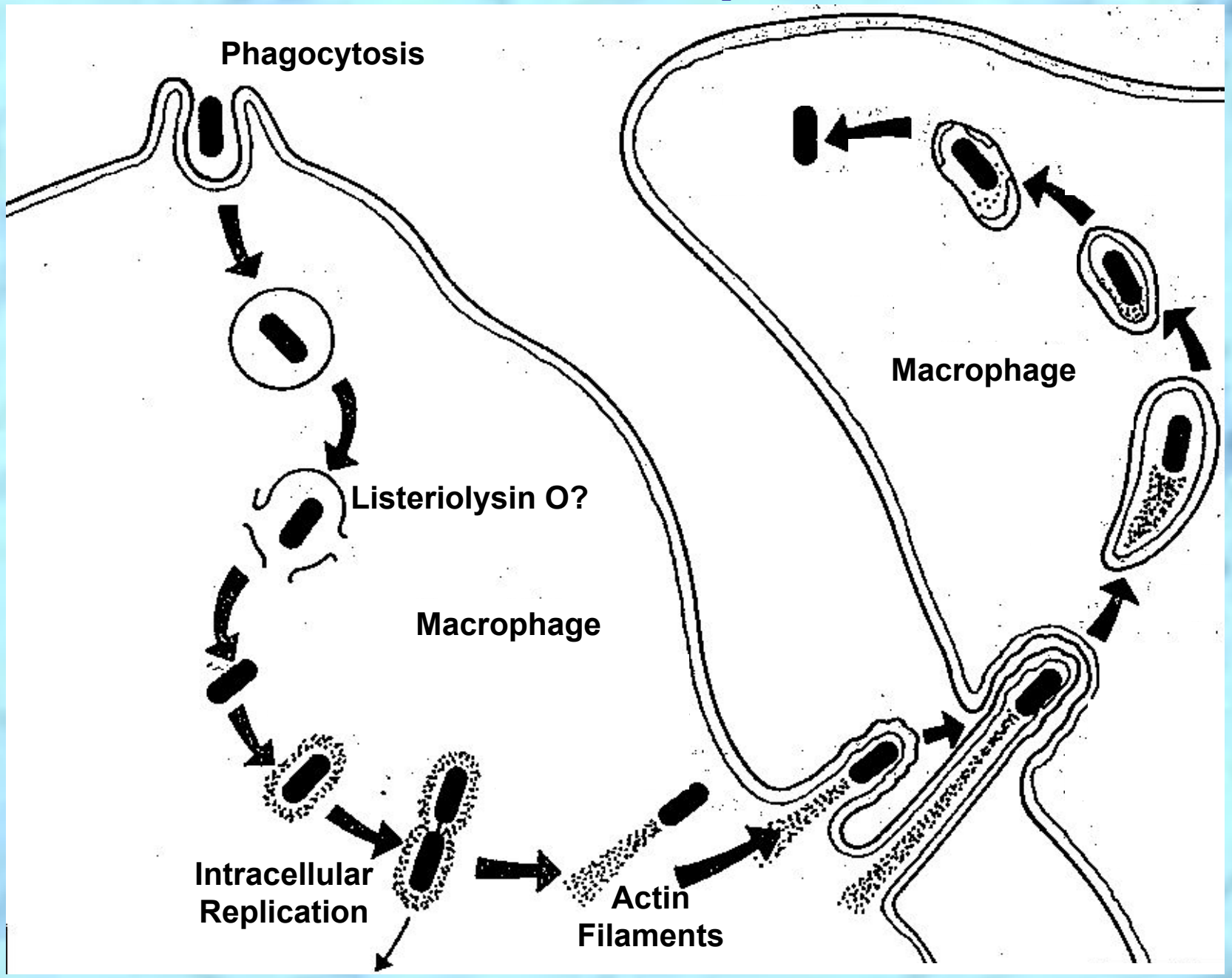
- **Neonates, elderly & immunocompromised**
- **Granulomatosis infantiseptica**
  - Transmitted to fetus **transplacentally**
  - **Early septicemic form:** 1-5 days post-partum
  - **Delayed meningitic form:** 10-20 days following birth
- **Intracellular** pathogen
  - Cell-mediated and humoral immunity 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

REVIEW

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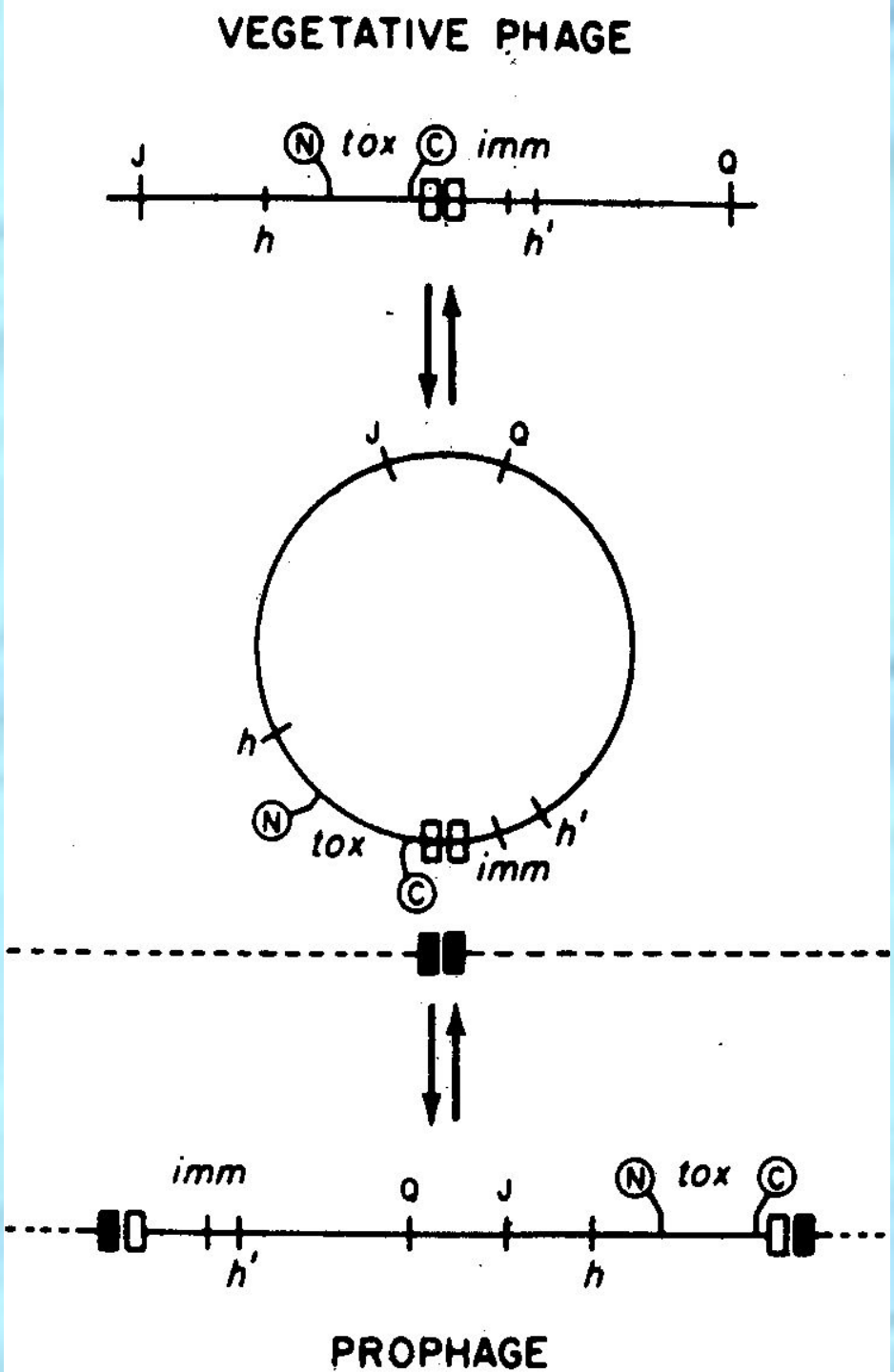

REVIEW

See Handout on Exotoxins

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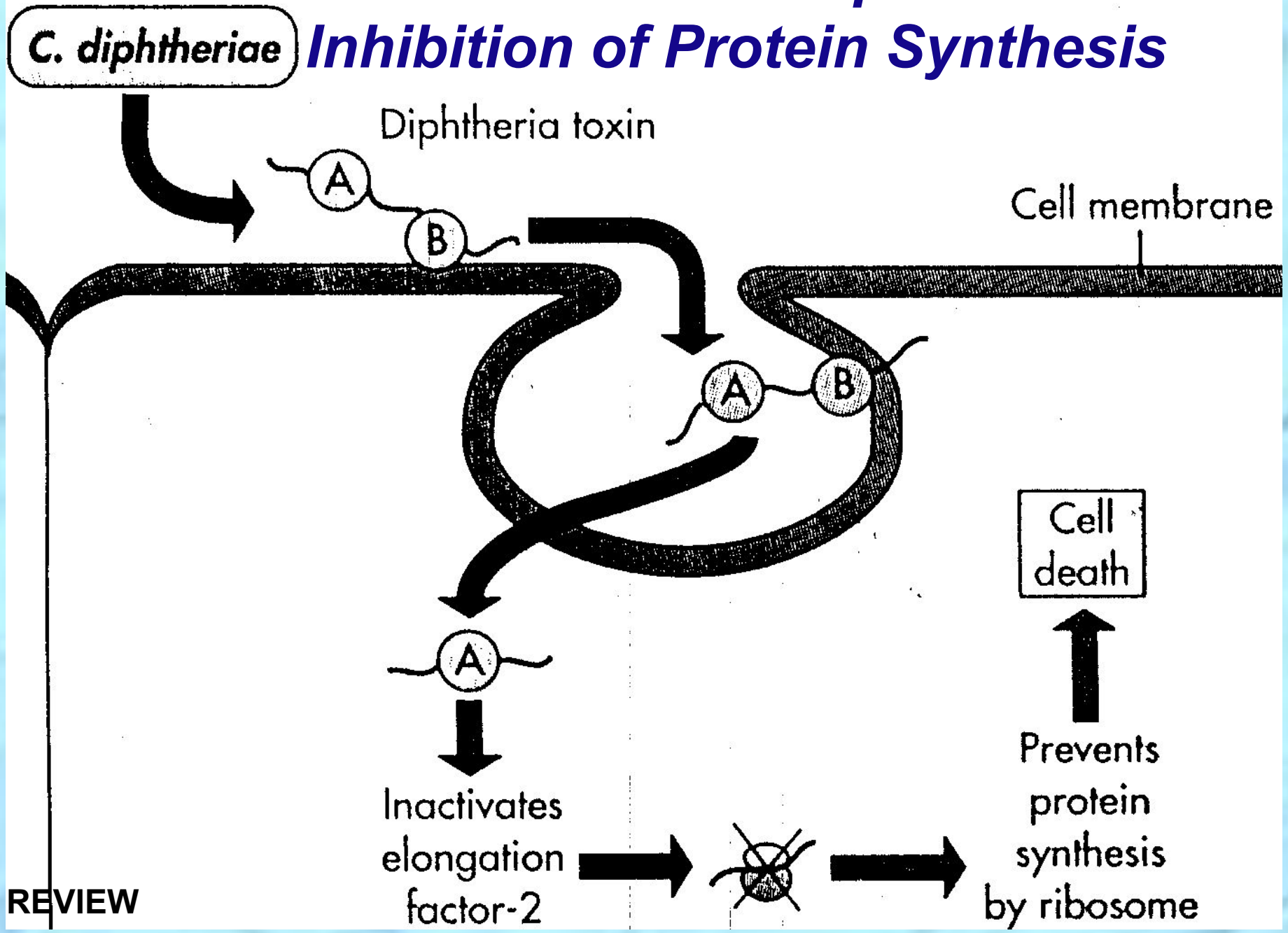

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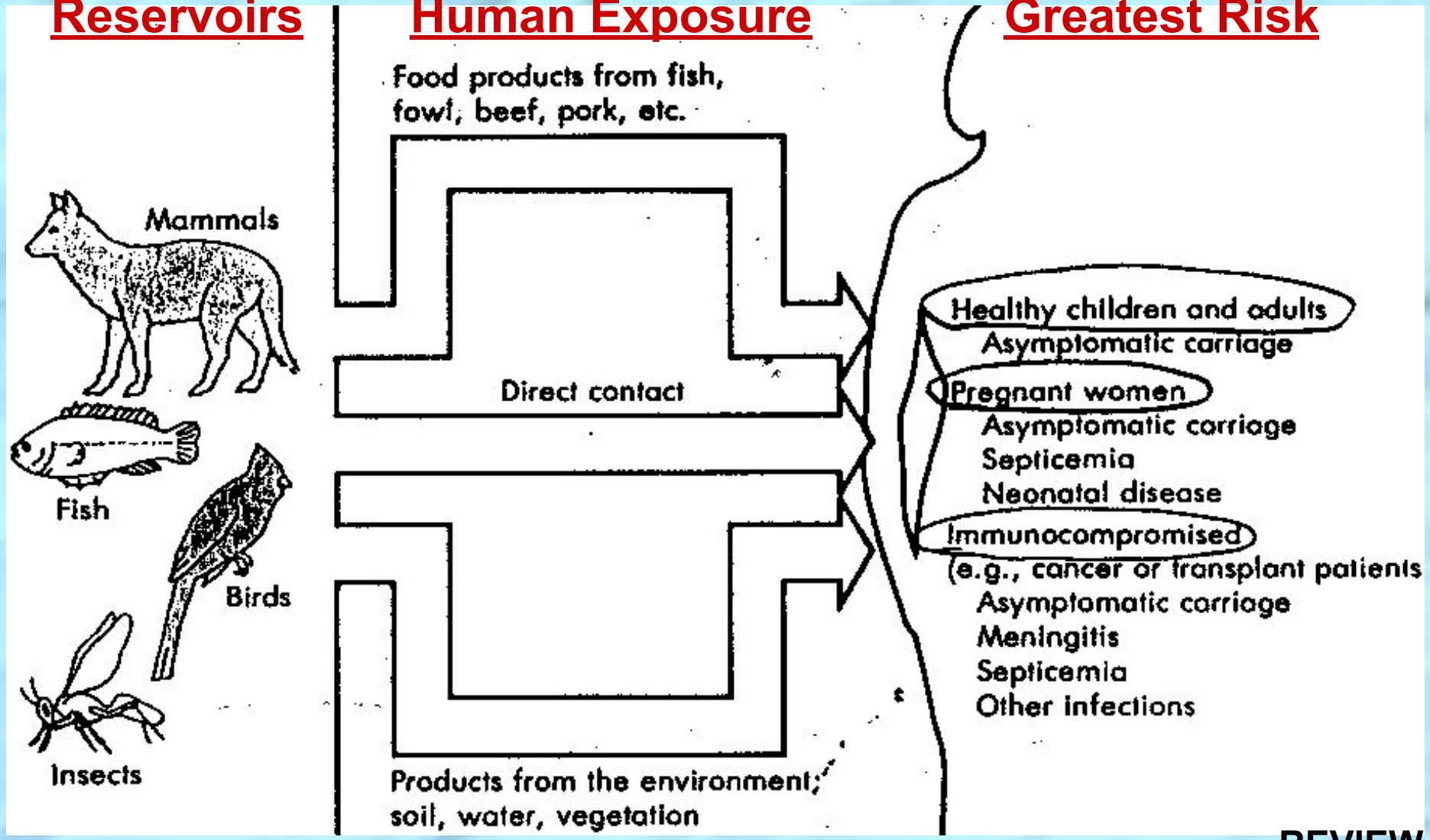

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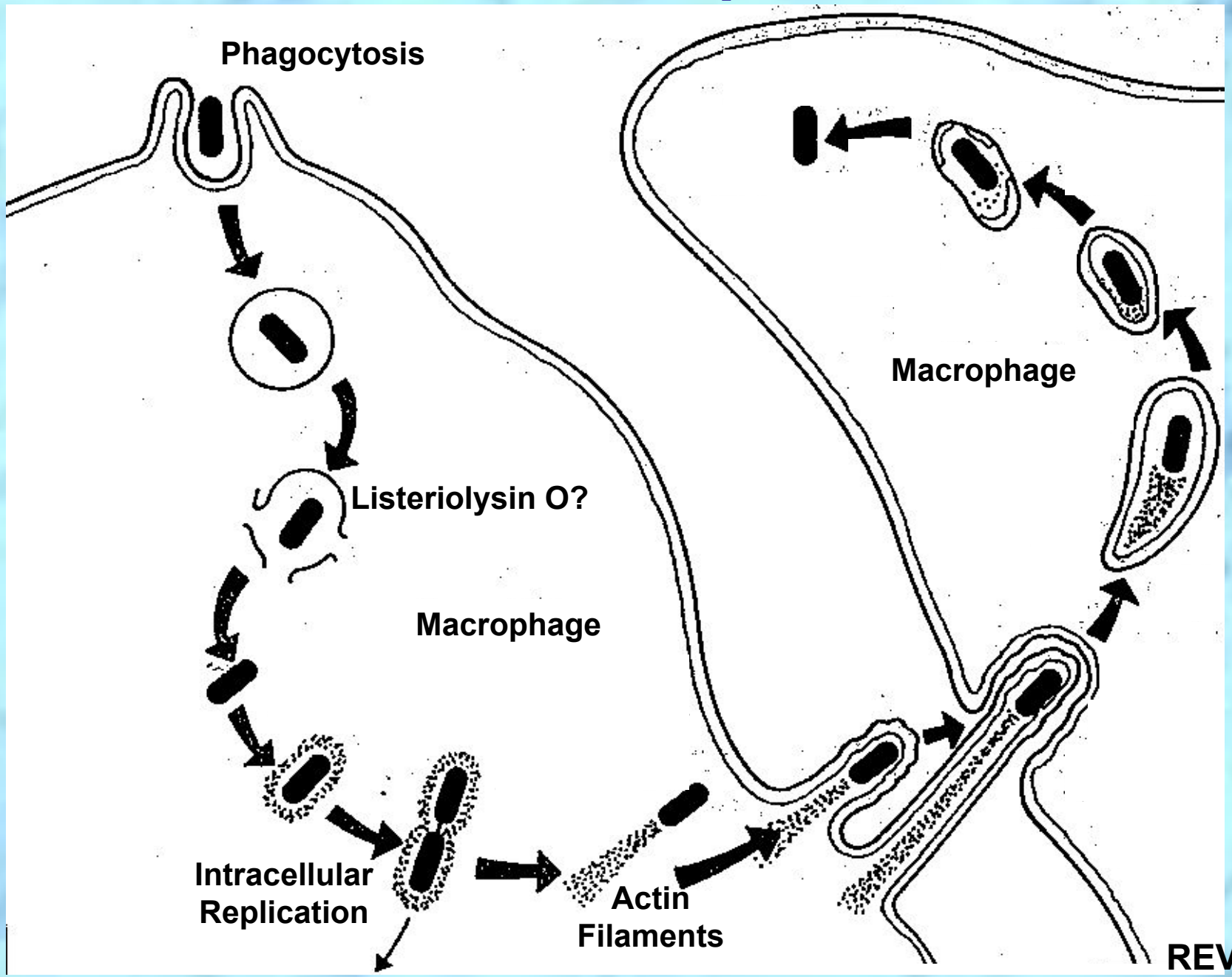

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