



Opportunistic Enterobacteriaceae

OPPORTUNISTIC INFECTIONS OF ENTEROBACTERIACEAE

□ GRAM NEGATIVE SEPSIS

□ URINARY TRACT INFECTIONS

□ PNEUMONIA

□ ABDOMINAL SEPSIS

□ MENINGITIS

□ SPONTANEOUS BACTERIAL PERITONITIS

□ ENDOCARDITIS

OPPORTUNISTIC INFECTIONS (cont.)

GRAM NEGATIVE SEPSIS

- Life-threatening
- Usually nosocomial
- Commonly caused by *E. coli*

PATHOGENESIS:

Early Phase (REVERSIBLE)

Decreased arterial resistance; Increased cardiac output

Kinins (protein vasodilators & mediators of inflammation) in plasma due to tissue damage, endotoxin, AG-AB complexes

Second Phase (REVERSIBLE)

Increased arterial resistance; Decreased cardiac output

Third Phase (IRREVERSIBLE)

Vascular collapse with organ failure

Endotoxin induced DIC, hemorrhage and death

OPPORTUNISTIC INFECTIONS (cont.)

URINARY TRACT INFECTIONS

- Usually **ascending infection**, not hematogenous route
- Greatest incidence in **young & middle-aged females**
- Incidence increases with **age in males**
- Most commonly caused by ***E. coli***
- Diagnosis by microscopic & cultural **exam of urine**
- Obtain urine by catheter through urethra into bladder, clean catch midstream (CCMS) or suprapubic tap

PNEUMONIA

- **Nosocomial**; Spread by personnel and equipment
- Frequently caused by ***K. pneumoniae***
- Often in middle-aged males who **abuse alcohol**
- Difficult to diagnose due to **commensals in sputum**

OPPORTUNISTIC INFECTIONS (cont.)

ABDOMINAL SEPSIS

- Caused by **flora of the GI tract**
- Infections usually **polymicrobial**

MENINGITIS

- Usually **nosocomial**
- Frequently caused by ***E. coli***
- Diagnosis by microscopic & cultural **exam of CSF**

OPPORTUNISTIC INFECTIONS (cont.)

SPONTANEOUS BACTERIAL PERITONITIS

- Usually in patients with **liver ailments**
- Commonly caused by *E. coli*, but also **anaerobes & Gram-positive cocci** (*S. pneumoniae*)

ENDOCARDITIS

- **Vascular endocardial surface inflammation**
- Mostly caused by **Gram-positive cocci**, but 1-3% caused by aerobic Gram-negative rods
- Diagnosis by **blood culture**
- Difficult to treat; **Treatment is of long duration**

Virulence Factors Associated with Enterobacteriaceae

Common Virulence Factors

- Endotoxin
- Capsule
- Antigenic phase variation
- Sequestration of growth factors
- Resistance to serum killing
- Antimicrobial resistance

Factors Associated with Specific Pathogens

- Exotoxin production
- Expression of adhesion factors
- Intracellular survival and multiplication

Endotoxin-Mediated Toxicity

- **Fever**
- **Leukopenia** (reduced # of WBCs) ($<5000/\text{mm}^3$)
followed by **leukocytosis** (increased # of WBCs) ($>10-12,000/\text{mm}^3$)
- Activation of **complement**
- **Thrombocytopenia** (reduced # of platelets)
- **DIC** (Disseminated intravascular coagulation)
- **Decreased peripheral circulation and perfusion**
(blood flow) to major organs
- **Shock**
- **Death**

See Handout on
Enterobacteriaceae
General Information

Summary of *Escherichia coli* Infections

Physiology and Structure

Gram-negative bacilli.

Facultative anaerobe.

Fermenter.

Oxidase negative.

Outer membrane makes the organisms susceptible to drying.

Lipopolysaccharide consists of outer somatic O polysaccharide, core polysaccharide (common antigen), and lipid A (endotoxin).

Virulence

Refer to Boxes 29-2 and 29-3.

Endotoxin.

Permeability barrier of outer membrane.

Adhesins (e.g., colonization factor antigen, Dr adhesins).

Exotoxins (e.g., heat-stable and heat-labile enterotoxins, Shiga toxins).

Invasive capacity.

Epidemiology

Most common aerobic, gram-negative bacilli in the gastrointestinal tract.

Most infections are endogenous (patient's normal microbial flora).

Strains causing gastroenteritis are generally acquired exogenously.

Diseases

Bacteremia (most commonly isolated gram-negative bacillus).

Summary of Escherichia coli Infections (cont.)

Urinary tract infection (most common cause of bacterial UTIs; limited to bladder (cystitis) or can spread to kidneys (pyelonephritis) or prostate (prostatitis)).

At least six different pathogenic groups cause gastroenteritis (ETEC, EPEC, EIEC, EHEC, EAEC, DAEC); most cause diseases in developing countries, although EHEC is an important cause of hemorrhagic colitis (HC) and hemolytic uremic syndrome (HUS) in the United States.

Neonatal meningitis (usually with strains carrying the K1 capsular antigen).

Intra-abdominal infections (associated with intestinal perforation).

Diagnosis

Organisms grow rapidly on most culture media.

Treatment, Prevention, and Control

Treatment guided by in vitro susceptibility tests.

Infections are controlled by use of appropriate infection-control practices to reduce the risk of nosocomial infections (e.g., restricting use of antibiotics, avoiding unnecessary use of urinary tract catheters).

Maintenance of high hygienic standards to reduce the risk of exposure to gastroenteritis strains.

Proper cooking of beef products to reduce risk of EHEC infections.

Gastroenteritis Caused by *E. coli*

| Organism | Site of Action | Disease | Pathogenesis |
|---|-----------------|--|---|
| Enterotoxigenic <i>E. coli</i> (ETEC) | Small intestine | Traveler's diarrhea; infant diarrhea in underdeveloped countries; watery diarrhea, vomiting, cramps, nausea, low-grade fever | Plasmid-mediated heat-stable and/or heat-labile enterotoxins that stimulate hypersecretion of fluids and electrolytes |
| Enteropathogenic <i>E. coli</i> (EPEC) | Small intestine | Infant diarrhea in underdeveloped countries; fever, nausea, vomiting, nonbloody stools | Plasmid-mediated A/E histopathology with disruption of normal microvillus structure resulting in malabsorption and diarrhea |
| Enteroinvasive <i>E. coli</i> (EIEC) | Large intestine | Disease in underdeveloped countries; fever, cramping, watery diarrhea; may progress to dysentery with scant, bloody stools | Plasmid-mediated invasion and destruction of epithelial cells lining colon |
| Enterohemorrhagic <i>E. coli</i> (EHEC) | Large intestine | Hemorrhagic colitis (HC) with severe abdominal cramps, initial watery diarrhea, followed by grossly bloody diarrhea; little or no fever; may progress to hemolytic uremic syndrome (HUS) | Mediation by cytotoxic Shiga toxins (Stx-1, Stx-2), which disrupt protein synthesis; A/E lesions with destruction of intestinal microvillus resulting in decreased absorption |
| Enteroaggregative <i>E. coli</i> (EAEC) | Small intestine | Infant diarrhea in underdeveloped countries; persistent watery diarrhea with vomiting, dehydration, and low-grade fever | Plasmid-mediated aggregative adherence of bacilli ("stacked bricks") with shortening of microvilli, mononuclear infiltration, and hemorrhage; decreased fluid absorption |
| Diffuse aggregative <i>E. coli</i> (DAEC) | Small intestine | Watery diarrhea in infants 1 to 5 years of age | Stimulates elongation of microvilli |

Specialized Virulence Factors Associated with E. coli

Adhesins

Type 1 pili

ETEC Colonization factor antigens CFA/I, CFA/II, and CFA/III.

EAEC Aggregative adherence fimbriae AAF/I and AAF/II.

UPEC Bundle-forming protein (Bfp).

EPEC Intimin.

UPEC P pili.

EIEC Ipa protein.

UPEC Dr fimbriae.

Exotoxins

ETEC Heat-stable toxins STa and STb.

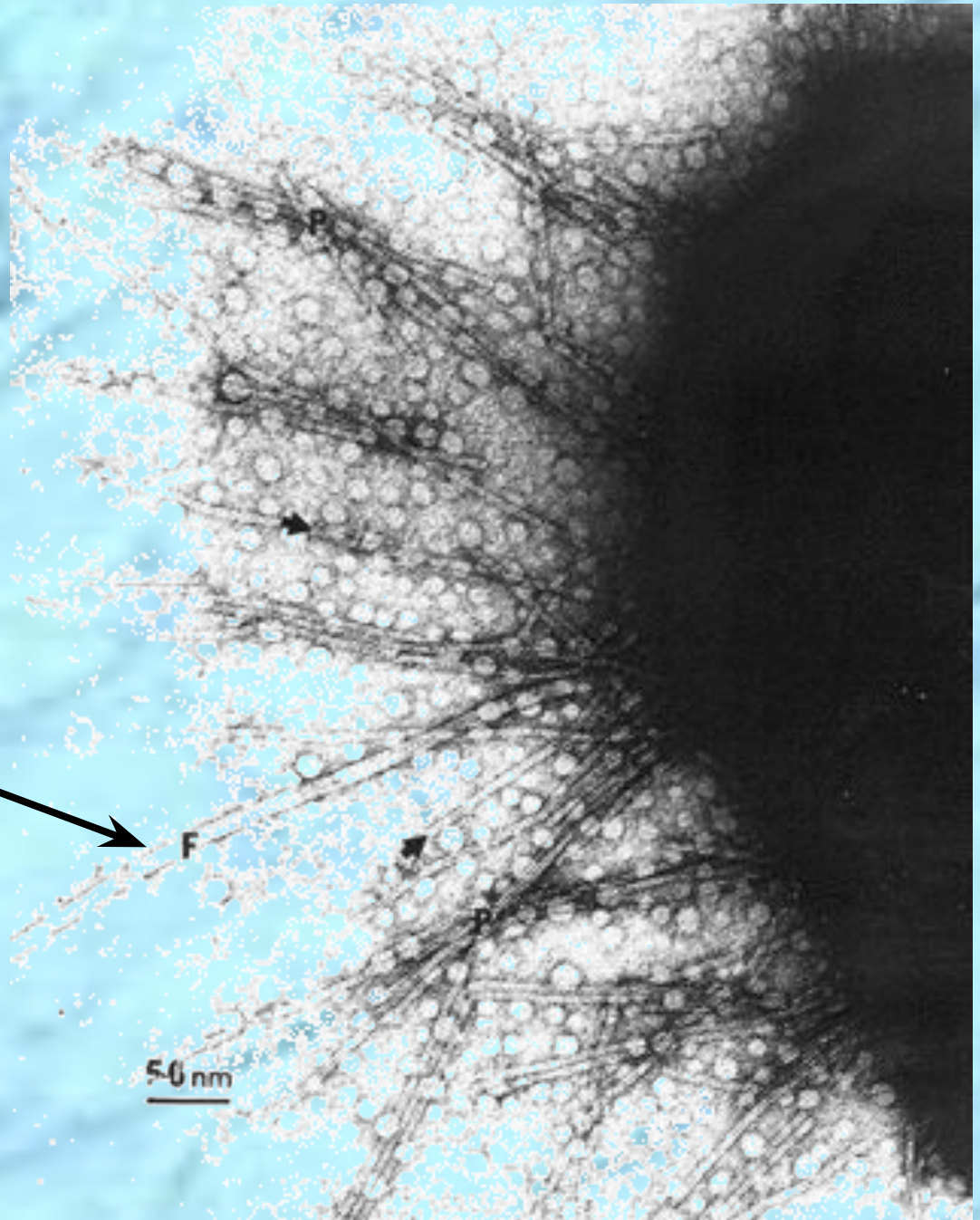
EHEC Shiga toxins Stx-1 and Stx-2.

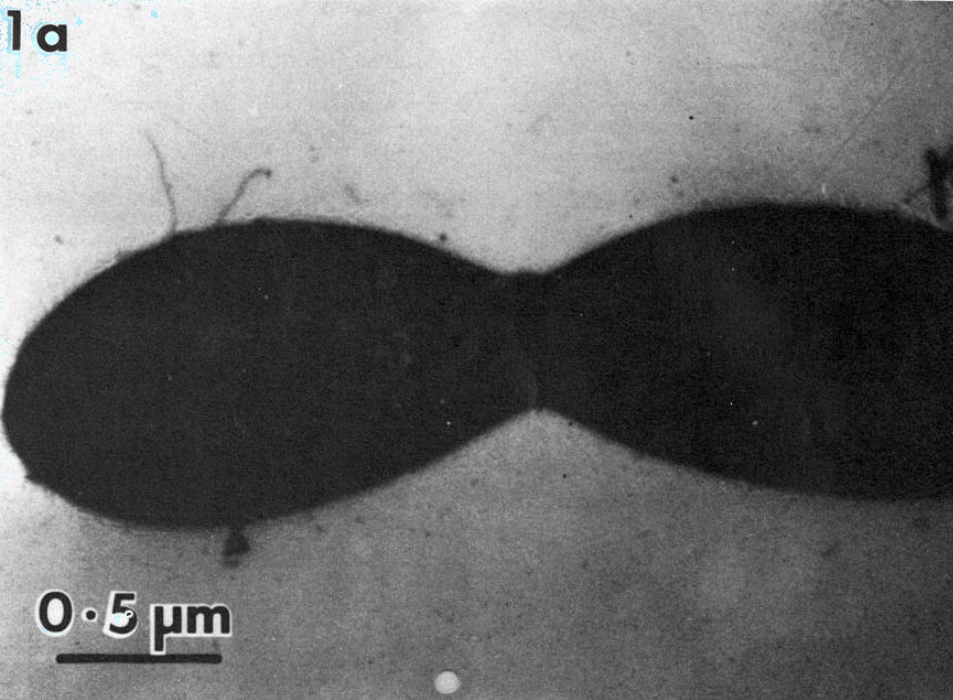
UPEC Hemolysin HlyA.

ETEC Heat-labile toxins LT-I and LT-II.

Fimbriated Bacterial Cell

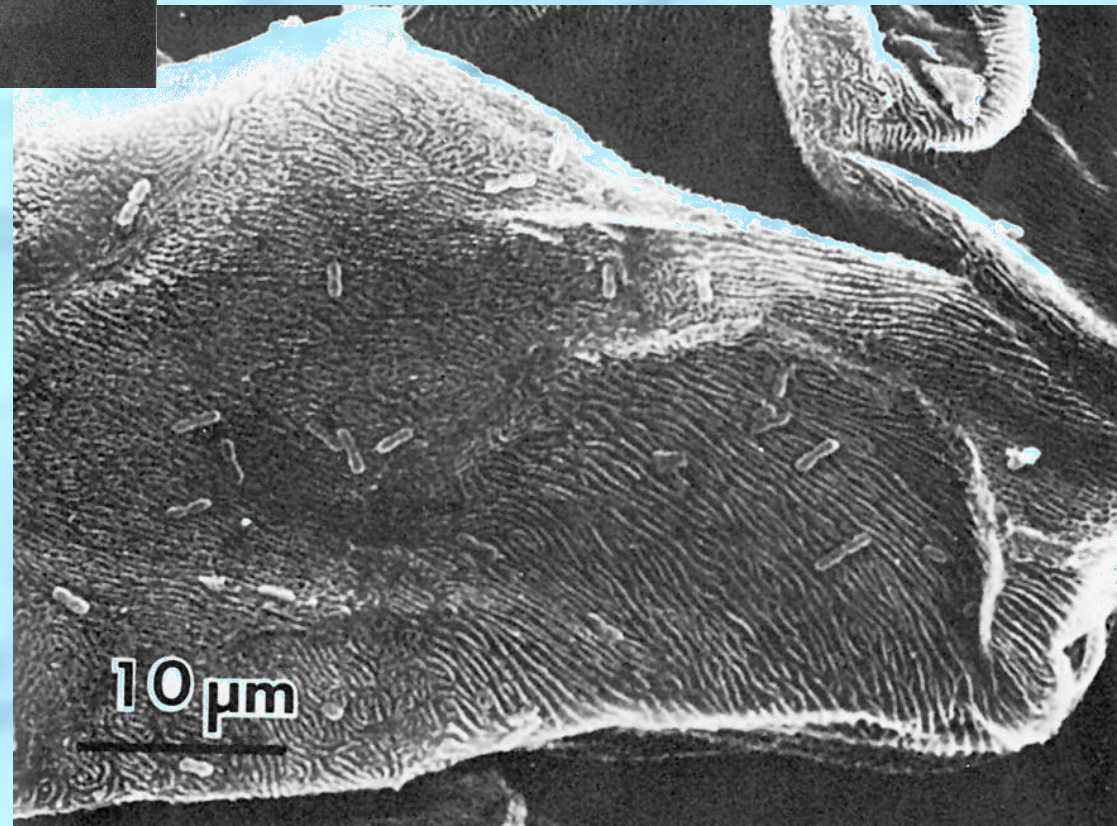
F = Flagellum
**Note: All other
appendages
are fimbriae
(a.k.a., pili)**

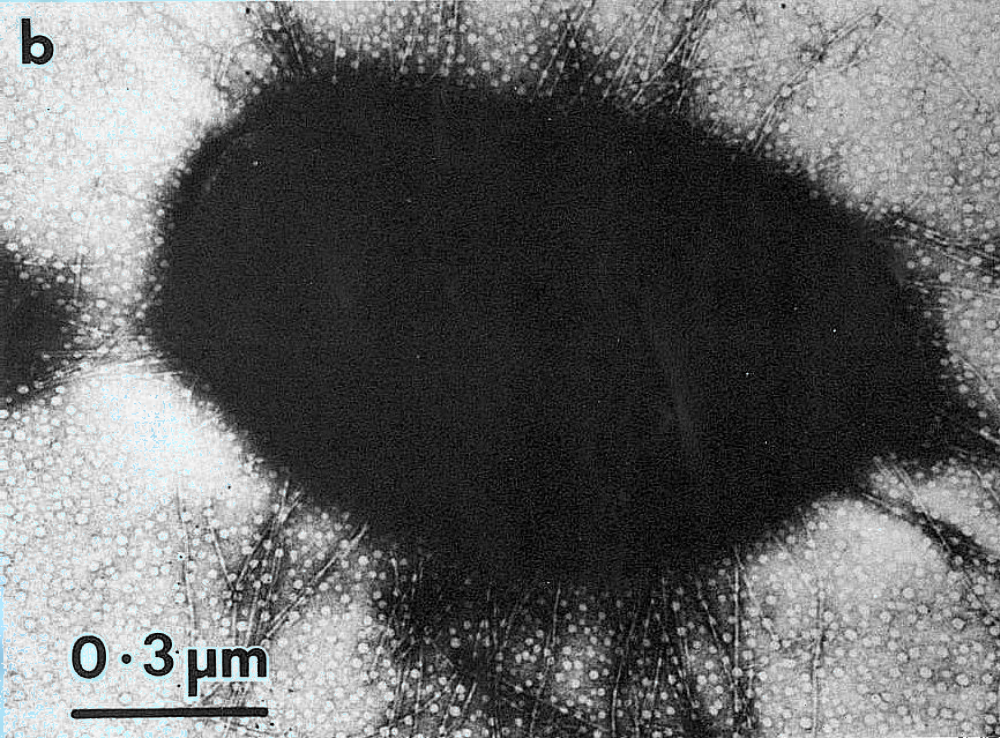




Afimbriated Bacterial Cells

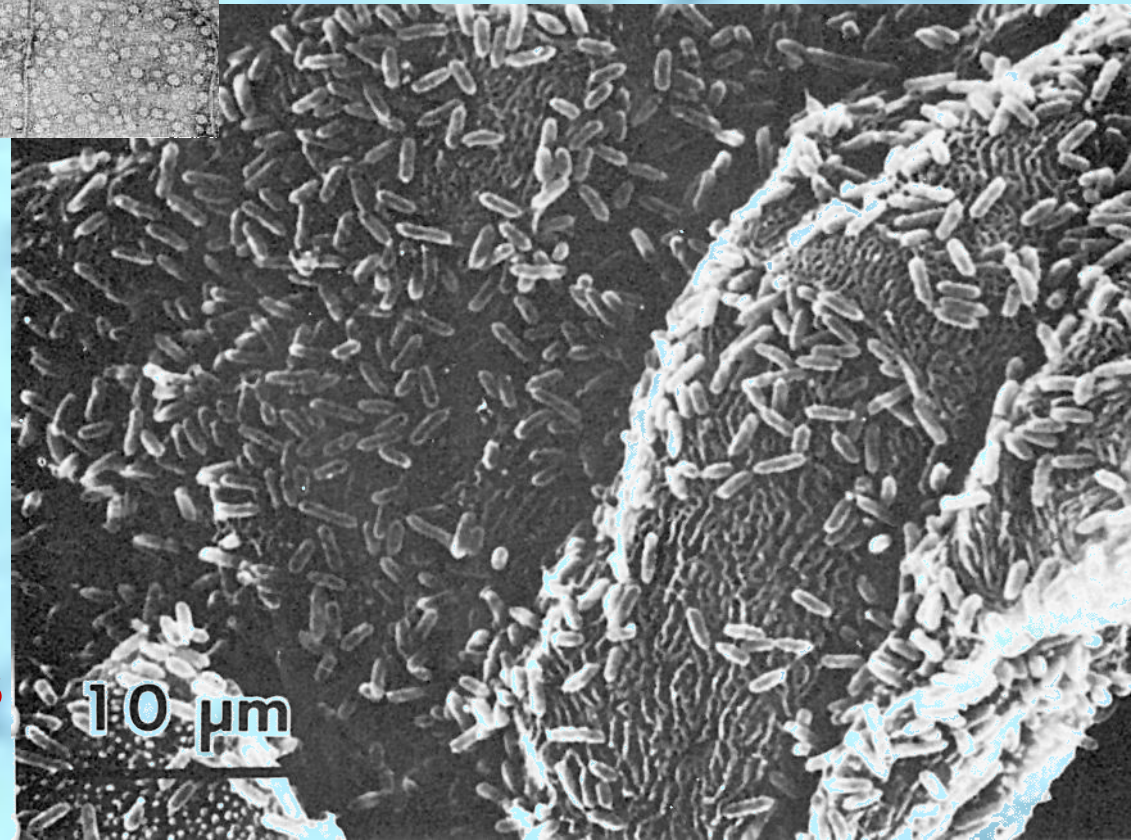
Nonadherent Afimbriated Bacterial Cells and Buccal Cells





Fimbriated Bacterial Cells

Adherent Fimbriated Bacterial Cells and Buccal Cells



MICROBIAL PATHOGEN

ADHESIN

RECEPTOR

| | | |
|---------------------------------|--|-----------------------------|
| <i>Staphylococcus aureus</i> | Lipoteichoic acid | Unknown |
| <i>Staphylococcus</i> spp. | Slime layer | Unknown |
| Group A <i>Streptococcus</i> | LTA-M protein complex | Fibronectin |
| <i>Streptococcus pneumoniae</i> | Protein | N-acetylhexosamine-gal |
| <i>Escherichia coli</i> | Type 1 fimbriae ↔ | D-Mannose |
| | CFA 1 fimbriae ↔ | GM ganglioside |
| | P fimbriae ↔ | P blood grp glycolipid |
| Other Enterobacteriaceae | Type 1 fimbriae ↔ | D-Mannose |
| <i>Neisseria gonorrhoeae</i> | Fimbriae | GD ₁ ganglioside |
| <i>Treponema pallidum</i> | P ₁ , P ₂ , P ₃ | Fibronectin |
| <i>Chlamydia</i> spp. | Cell surface lectin | N-acetylglucosamine |
| <i>Mycoplasma pneumoniae</i> | Protein P1 | Sialic acid |
| <i>Vibrio cholerae</i> | Type 4 pili | Fucose and mannose |

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> (ETEC) | Plasmid | Similar or identical to cholera toxin | Heparin-binding epidermal growth factor on heart & nerve surfaces | |
| 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> (EHEC) | 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 |



REVIEW

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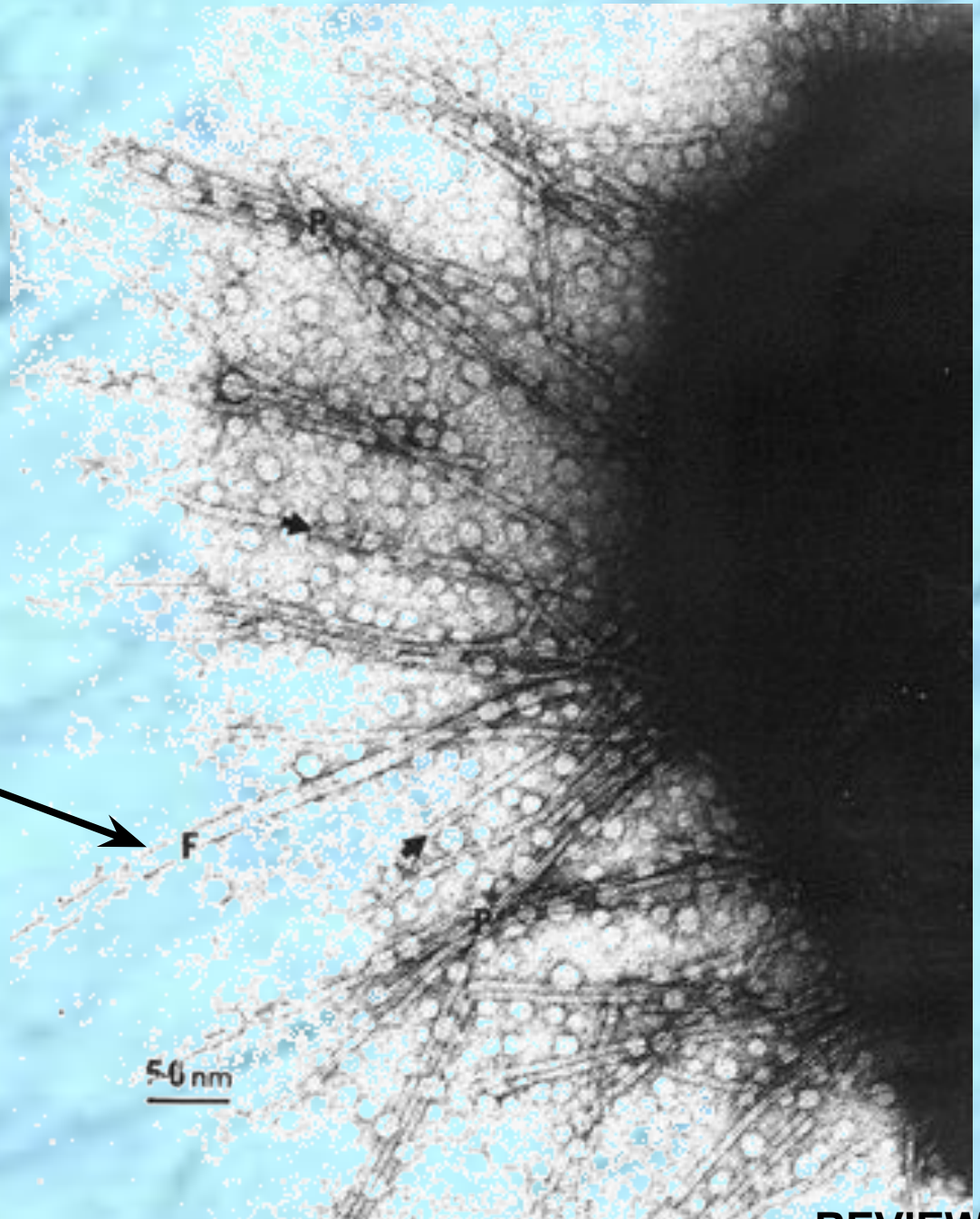
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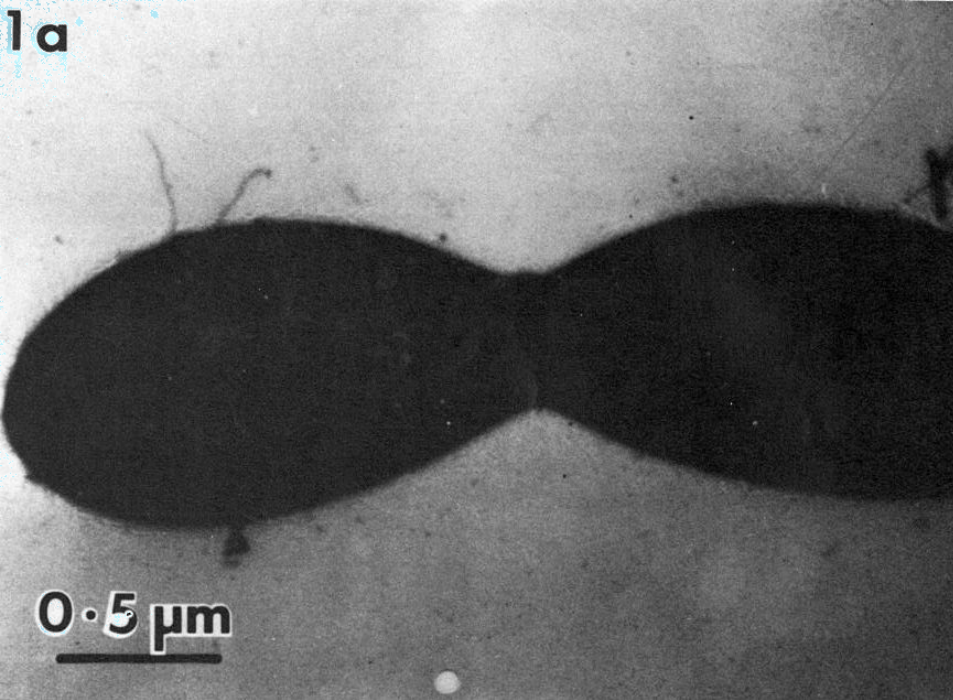
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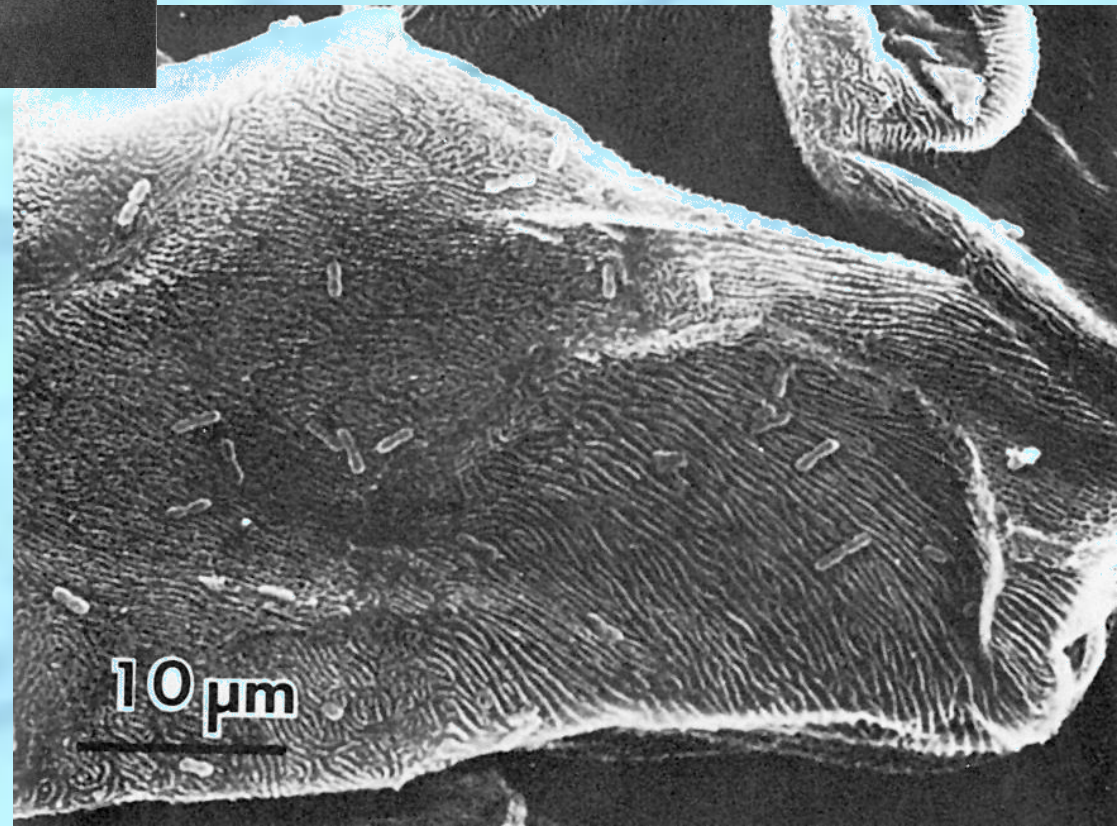
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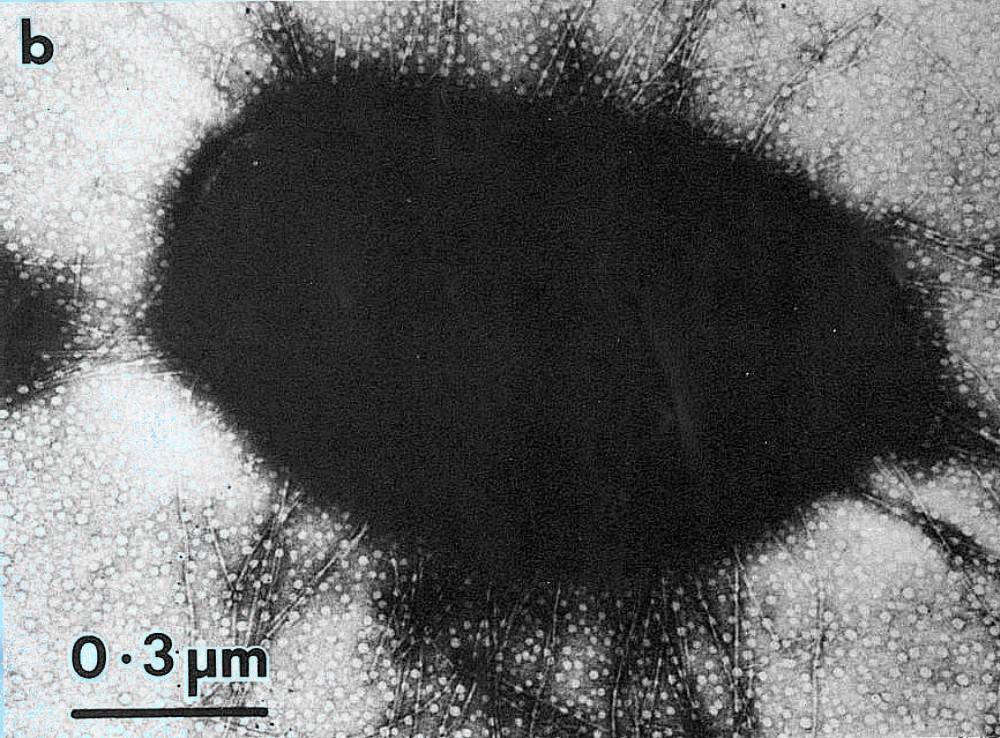




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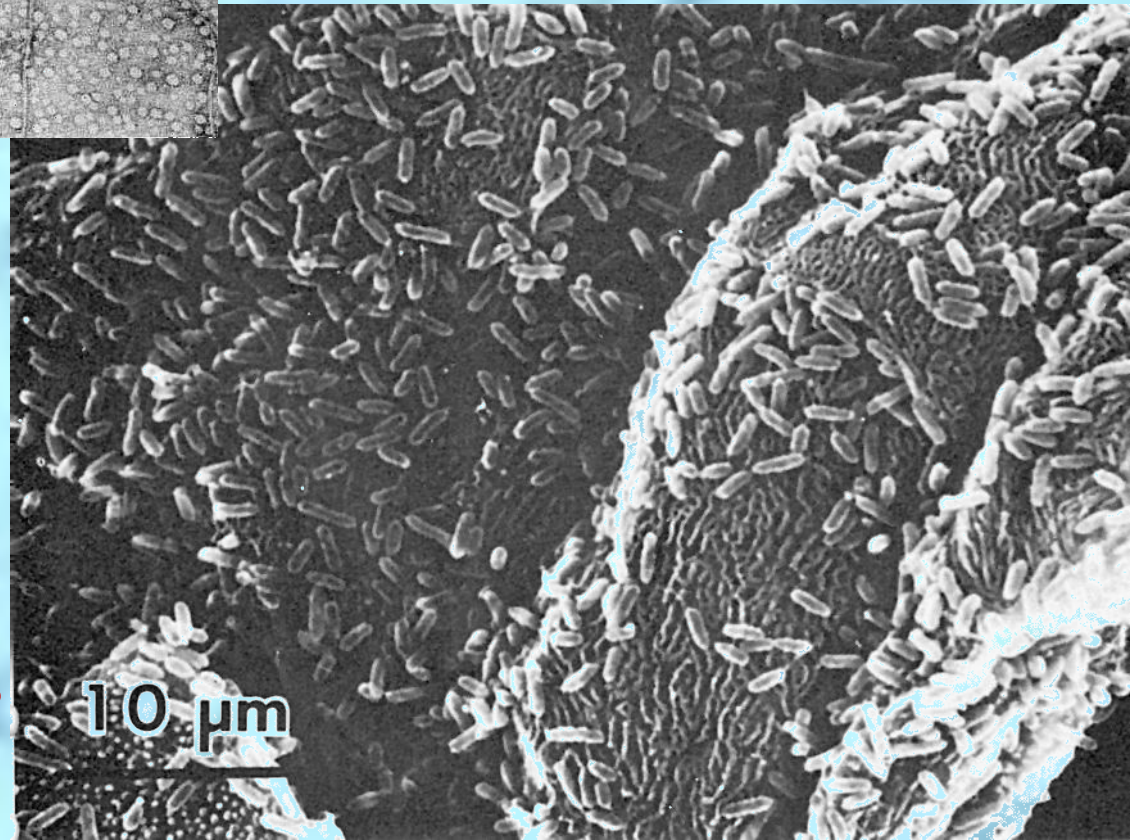
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