

A bél normál baktérium flórája

Enterobacteriaceae

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GRAM NEGATÍV PÁLCÁK

AEROB

Bordetella

Brucella

Francisella

Pseudomonas

Acinetobacter

Legionella

FACULTATIV ANAEROB

Haemophilus

Pasteurella

Familia:

Enterobacteriaceae

Vibrionaceae

Cardiobacterium

Eikenella

Kingella

Actinobacillus

ANAEROB

Bacteroides

Prevotella

Porphyromonas

Fusobacterium

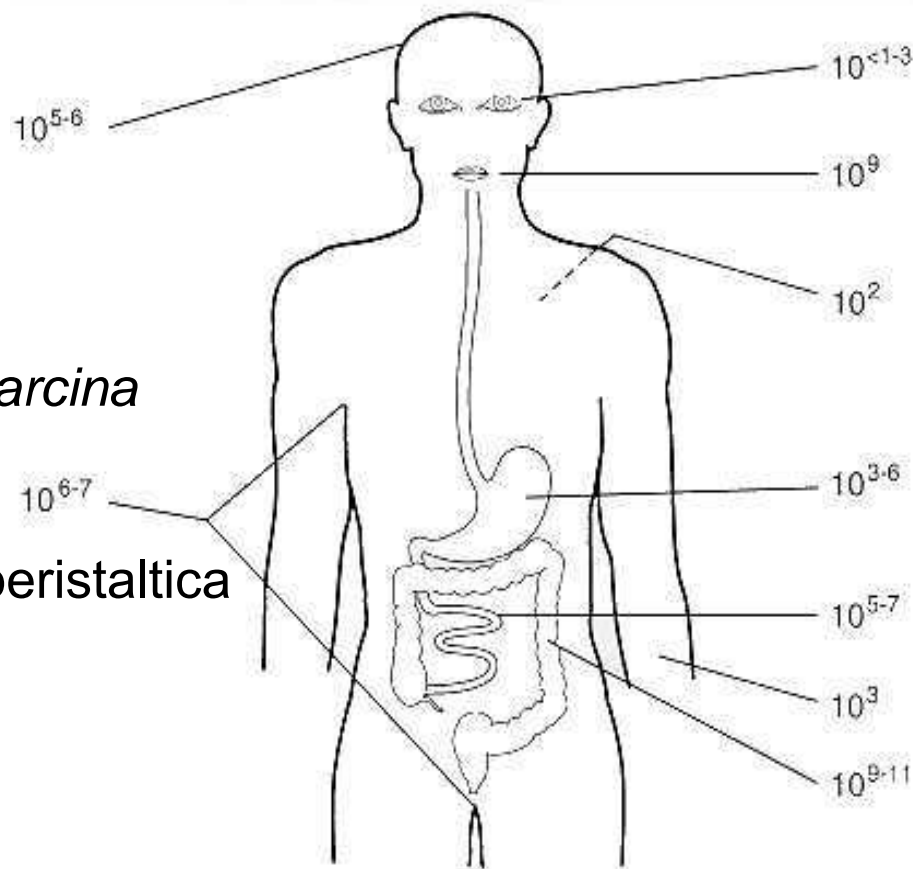
MICROAEROPHIL

Campylobacter

Helicobacter

A bél normál flórája

- **Jelentőség:**
csíramentes állat kísérletek
- **gyomor** (10^3 – 10^6 cfu/g)
 - alacsony pH
 - Residens micro flora Ø
 - Transiens flora +
 - Hypochlorhydria, stasis \Rightarrow
Lactobacillus (Boas-Oppler) & *Sarcina* spp.
- **vékonybél** (10^5 – 10^7 cfu/g)
 - emésztő enzimek & epe, gyors peristaltica
 - Residens micro flora Ø
 - Transiens flora +
- **vastagbél** (10^9 – 10^{11} cfu/g)
 - Residens micro flora



Normál baktérium flóra - vastagbél (>400 Species)

Anaerobok

A fajok 90–95%

10^{11} cfu/g faeces

Residens flóra

Bifidobacterium bifidum

Bacteroides fragilis

Eubacterium spp.

Clostridium spp.

Transiens flóra

Anaerob coccusok

Fusobakteriumok

Lactobacillusok

Facultative anaerobok

A fajok 5–10%

$\sim 10^3$ – 10^9 cfu/g faeces

Residens

Escherichia coli

Enterococcus spp.

Transiens

Klebsiella spp.

Enterobacter spp.

Proteus spp.

Providencia spp.

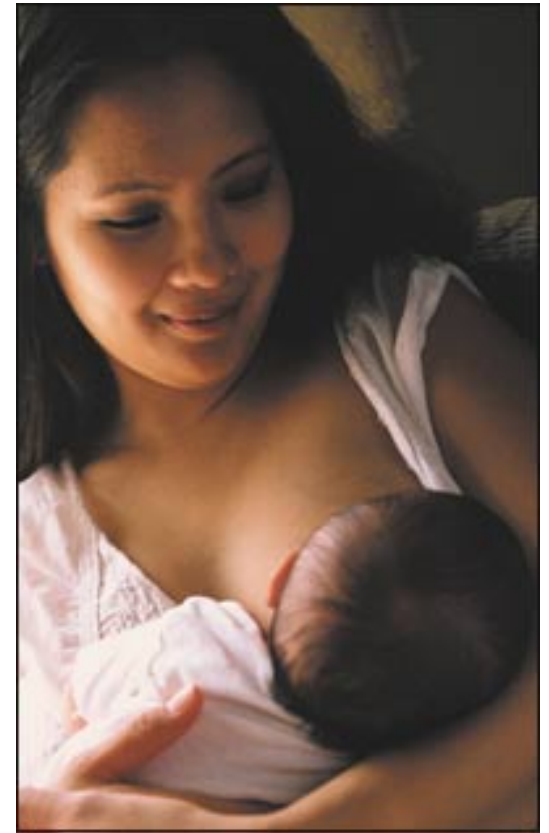
Pseudomonas spp.

Bacillus spp.

élesztőgombák, Protozoa

A vastagbél normál flórája - kialakulás

- Szoptatás, anyatej
 - Residentis
 - Bifidobacteria (pH 5,5)
 - Más fajok kolonizációja gátolt (vitamin K pótlás!)
- Normál táplálkozás
 - előbb
 - Facultative anaerobok
 - később
 - *Bacteroides fragilis*



Scanning electron micrograph of the colon mucosa of rat



Magnification: 262×



Magnification: 2.624×

| : bacterium layer, L: lumen, B: bacteria,
T: intestinal tissue

A normál vastagbél flóra szerepe, jelentősége

- Tápanyagok bontása, enterohepaticus recirculatio (epe)
- Vitamin termelés: vitamin K & B-complex
- Gáz termelés \Rightarrow distensio \Rightarrow normal peristaltica
- folyamatos fizikai & kémiai stimuláció \Rightarrow folyamatos mucosa turnover
- Biofilm formatio, epithelialis receptorok gátlása, tápanyag competitio, bacteriostaticus termékek \Rightarrow pathogen bacteriumok colonisatiojának gátlása
- Constans antigen stimulus \Rightarrow az immunrendszer extrauterin fejlődése és működése

A normál vastagbél flóra szerepe – kóros folyamatokban

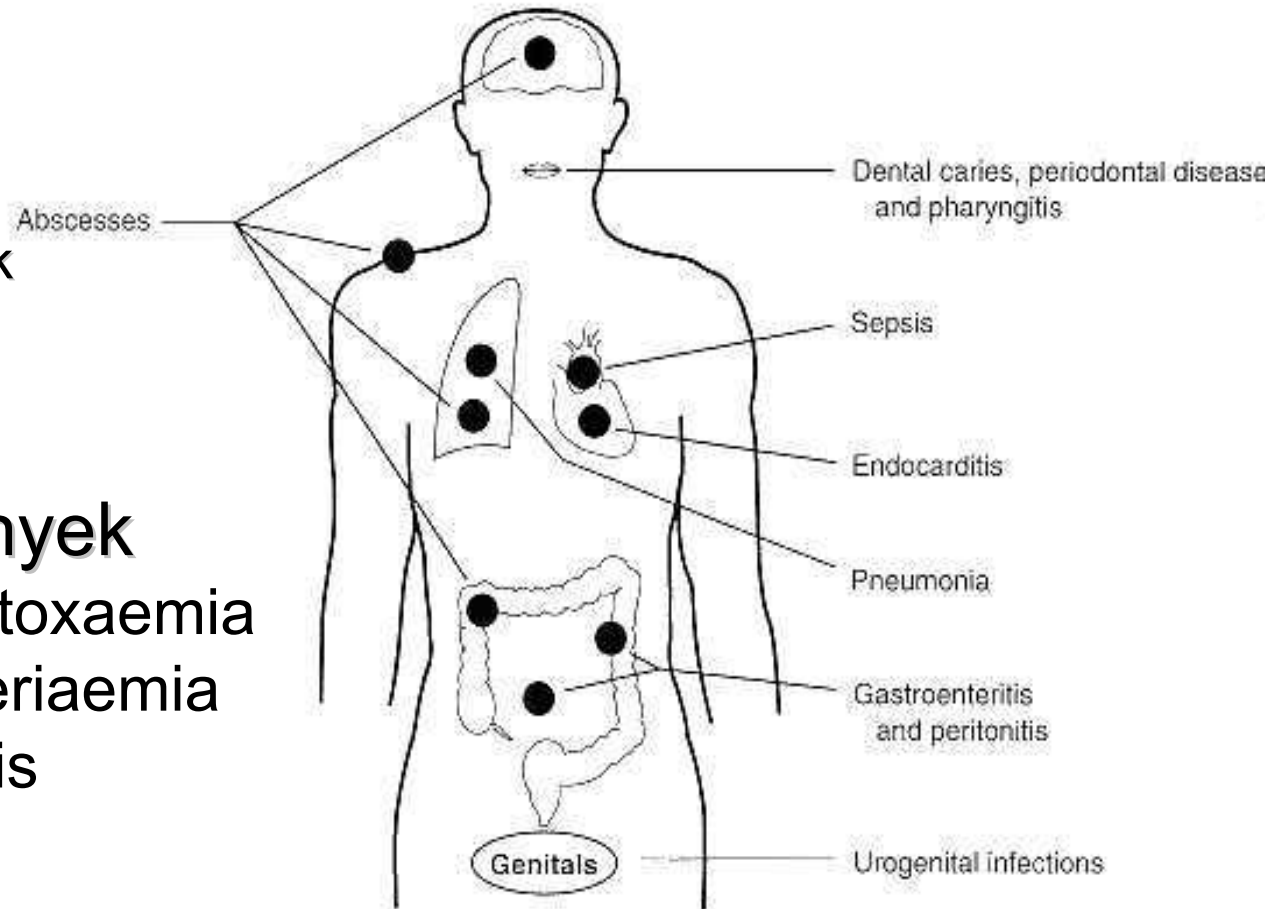
• Extra intestinalis fertőzések

• Translocatio

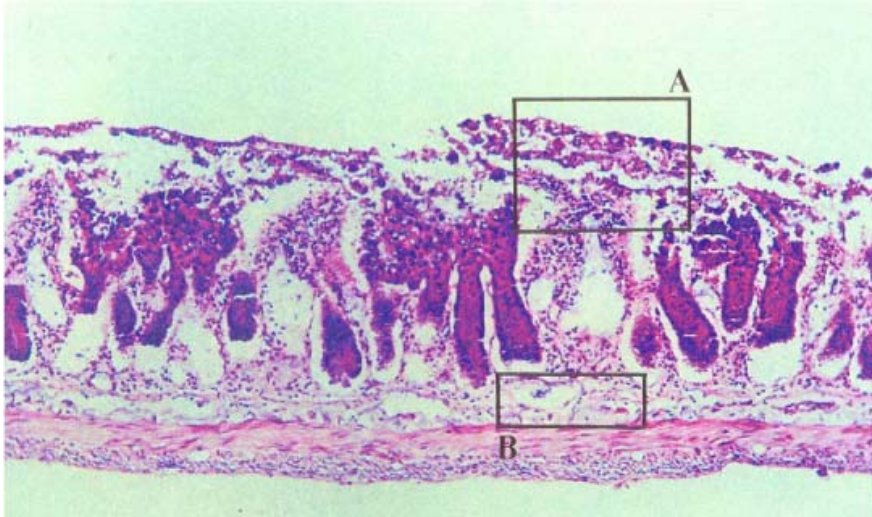
- ❖ Immune kompromittált betegek
- ❖ Obstructio
- ❖ Shock

❖ következmények

- Endotoxaemia
- Bacteraemia
- Sepsis

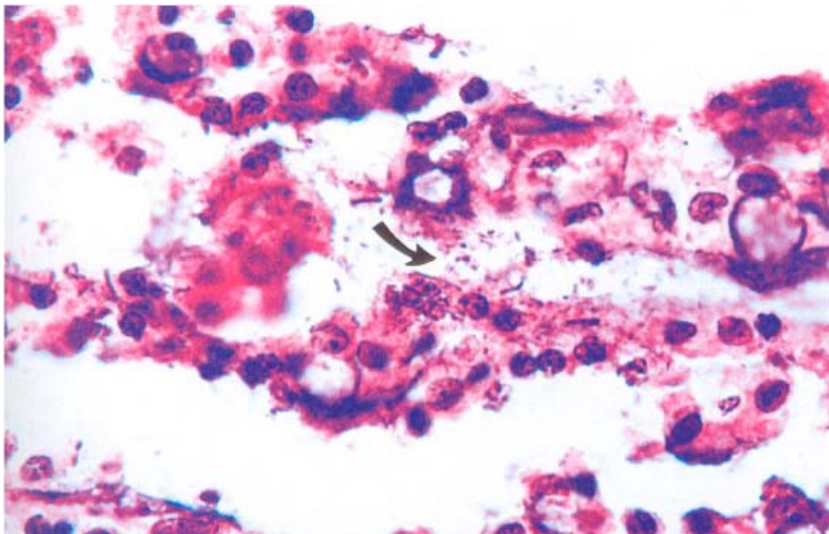


Bacterial translocation in rat after experimental intestinal obstruction

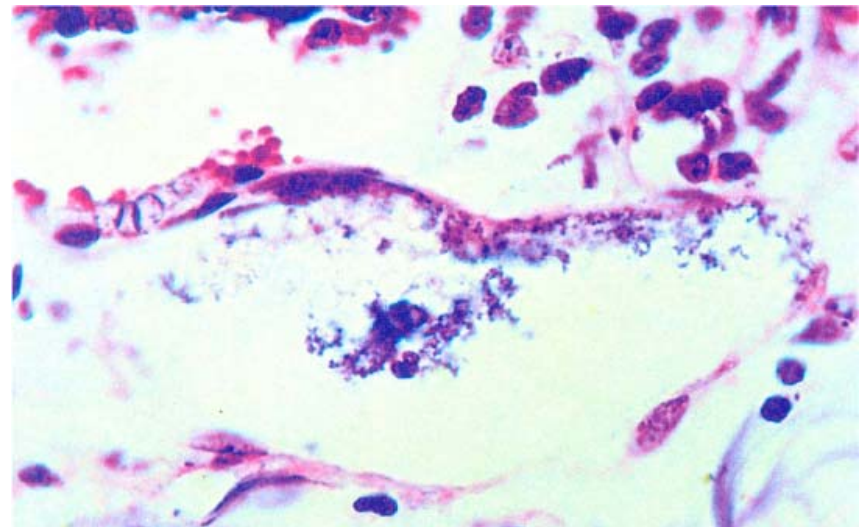


A: lifting of the epithelial cells from the lamina propria & bacterial invasion

B: cocci and rods in the submucosal lymphatic vessels



A



B

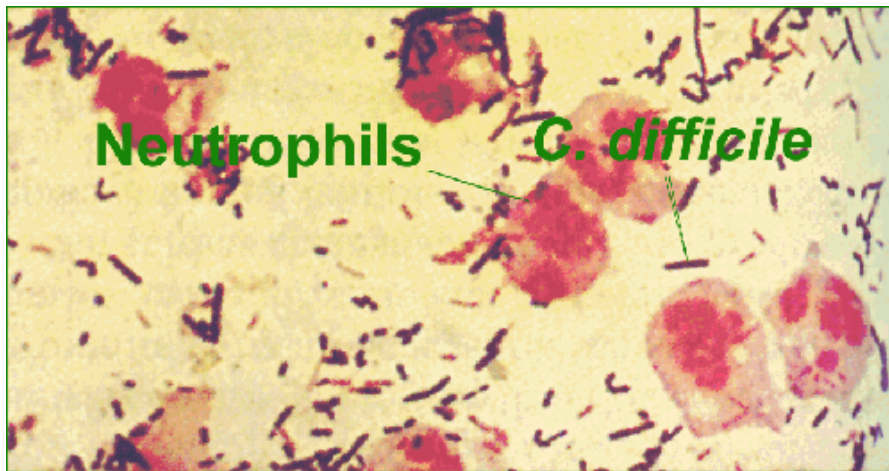
A normál vastagbél flóra egyensúlyának megváltozása

- **okai**
 - alultápláltság
 - Széles spektrumú *per os* antibiotikum terápia
- **következmények**
 - Emésztési zavar & malabsorptio, vitamin hiány
 - normal peristaltica megváltozása,
gastrointestinalisan a gáz képződés emelkedése
- **Antibioticum associált hasmenés**
 - enyhe: „közönséges” hasmenés
 - súlyos: **pseudomembranous colitis**
(*Clostridium difficile*)

Pseudomembranous colitis



Thickened wall of the colon transversum



C. difficile & neutrophils



Characteristic yellow plaques

**Gram negatív fakultatív
anaerob pálcák**

Enterobacteriaceae

Enterobacteriaceae

Morphologia: - Gram negative pálcák
- pili
(ex.: Klebsiella, Shigella)

Tenyésztés:

egyszerű (Agar, véresagar) Media

Differenciálás: pathogenic-facultative pathogenic
(biokémiai reakciók)

- a) Selective táptalajok
- b) Differential táptalajok
- c) Indicator táptalajok

Enterobacteriaceae

Antigenek és Virulencia faktorok:

O (sejtfal)

H (Flagella)

K (tok)

felszíni Proteinek

Pilusok

Exotoxin

Endotoxin

Enterobacteriaceae

Facultative pathogenek

genus

Escherichia

Klebsiella csoport

Enterobacter

Edwardsiella

Citrobacter

Proteus csoport

Serratia

Providencia

Morganella

Obligat pathogens (genera)

E. Coli

ETEC (enterotoxic)

EPEC (enteropathogen)

EIEC (enteroinvasive)

EHEC (enterohemorrhagic)

EAggEC (enteroaggregativ)

Shigella

S. dysenteriae

S. flexneri

S. boydii

S. sonnei

Salmonella

S. typhi

S. paratyphi

Yersinia

Y. pestis

Y. pseudotuberculosis

Y. enterocolitica

Enterobacteriaceae – fakultatív pathogének

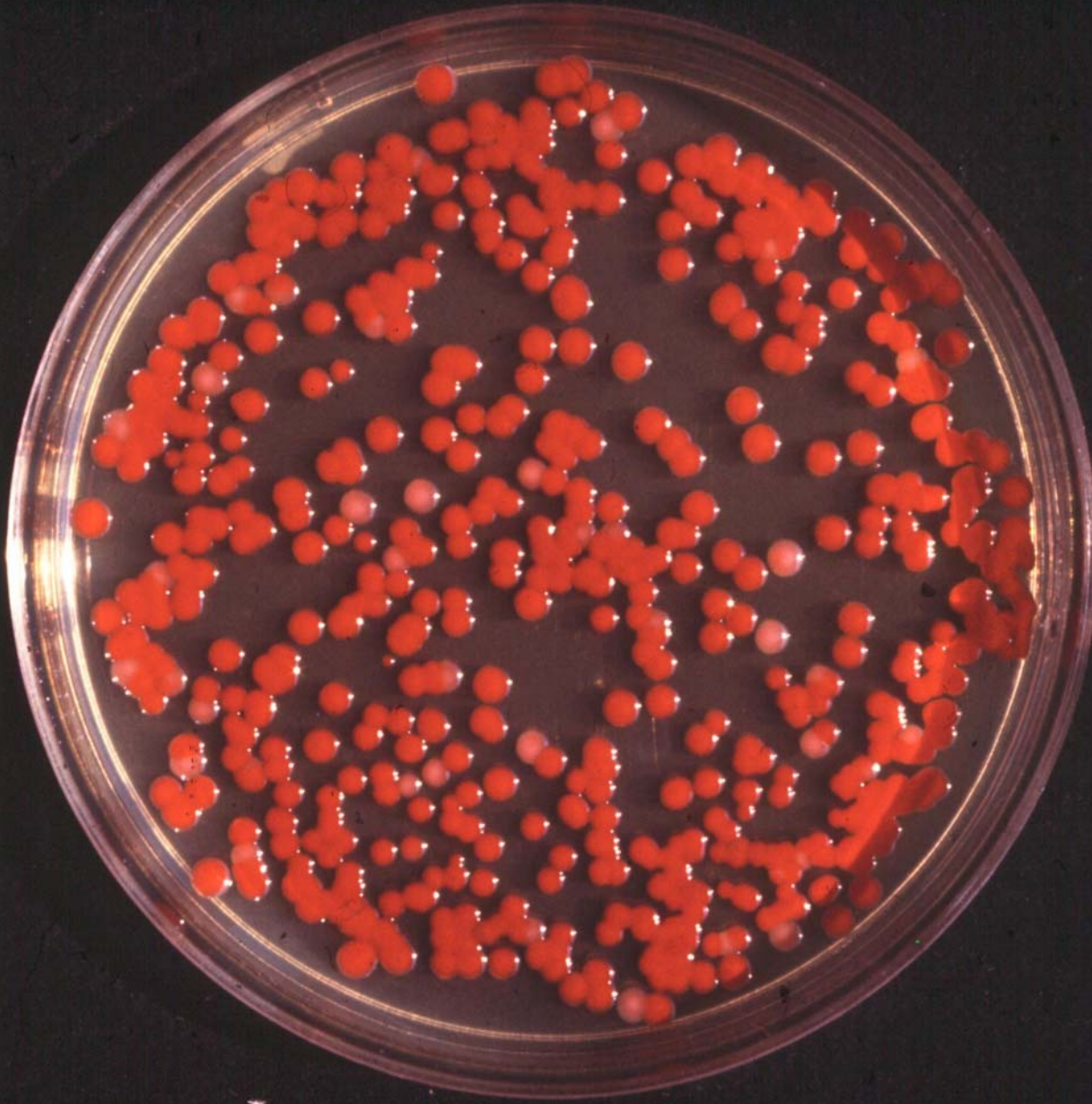
***Klebsiella, Proteus, Escherichia* etc.**

Extraintestinalis kórképek – MIND!!! gennyves gyulladás:

- a) húgyúti fertőzések
- b) cholecystitis, cholangitis
- c) peritonitis (localis, diffus)
- d) pneumonia
- e) meningitis
- f) sebfertőzések
- g) sepsis
- h) iatrogen/nosokomialis fertőzések

Diagnosis: **izolálás, identifikálás**

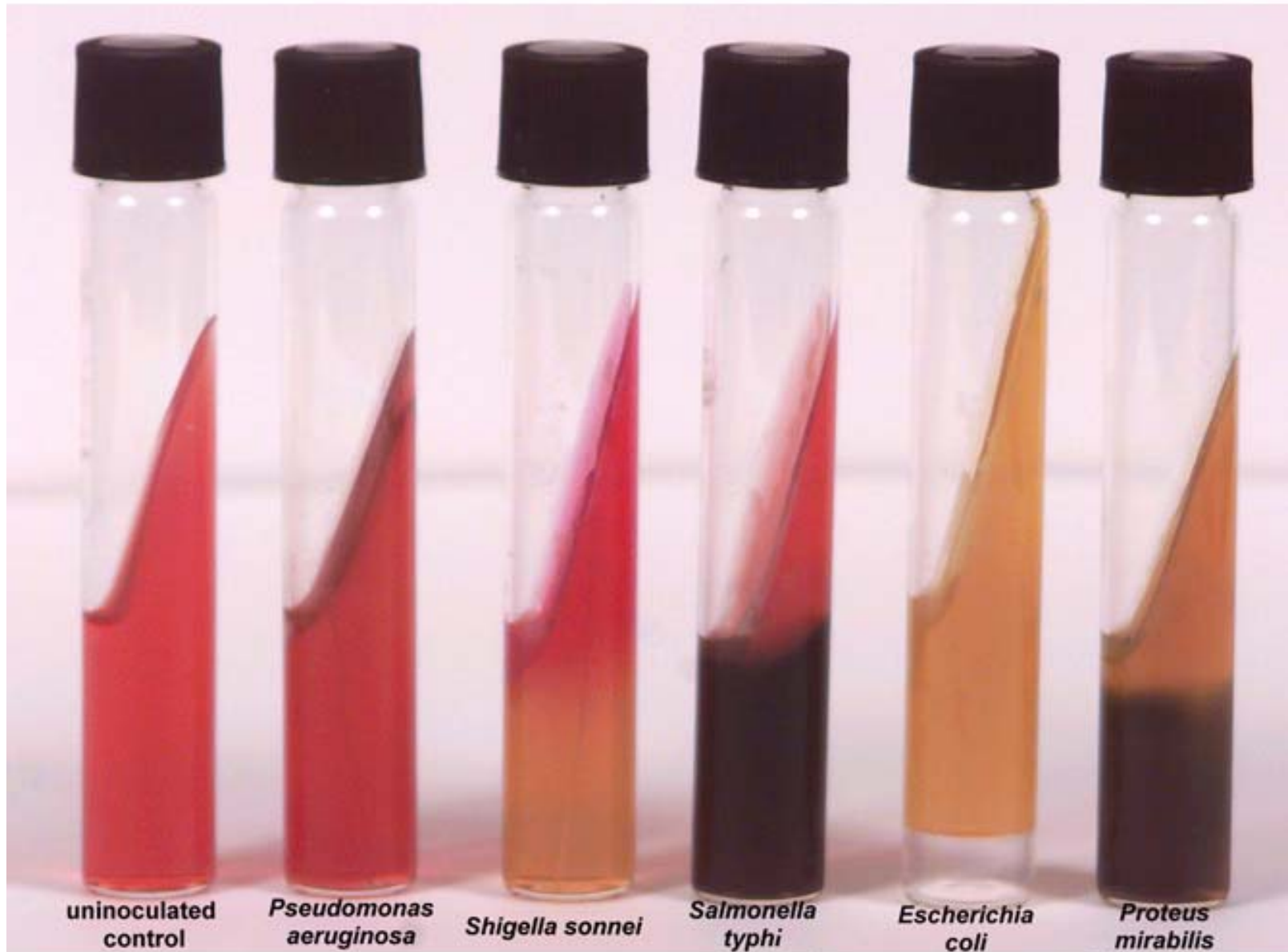
Therapia: antibiogram (ESBL)



Serratia marcescens - Serratia marcescens Durch Prodigiosin rot gefärbte Kolonien von *Serratia marcescens* auf Agargel.

TSI Medium

azonosítás



Top row, *Proteus vulgaris*; second row, unidentified enteric bacterium; third row, *Klebsiella pneumoniae*; bottom row, *Vibrio alginolyticus*.

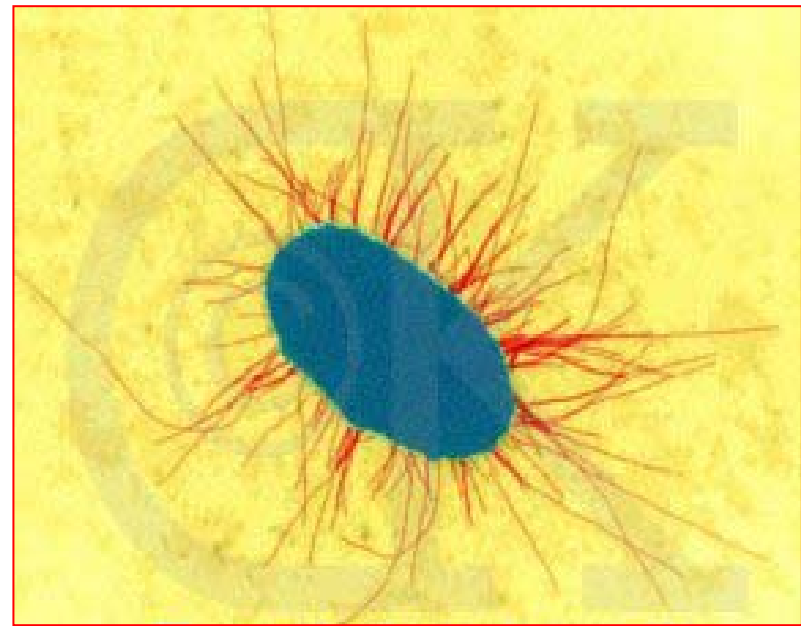


Identification

helios.bto.ed.ac.uk

Urinary tract infections (UTI) húgyúti fertőzések

- ***E. coli* (80%)**
 - Predispositio
 - Ascendáló
(ritkán haematogen)
 - Cystitis, pyelonephritis
 - **Virulencia fakotrok** (UPEC - törzsek)
 - Haemaggl. Adhesio-s fimbriae
 - Mannose resistens (MR) fimbriae (F-antigen),
P-fimbriae (vércsoport P) ⇒
pyelonephritis
 - Mannose sensitive (MS) fimbriae ⇒
cystitis
 - Haemolysinek



E. coli with Fimbriae

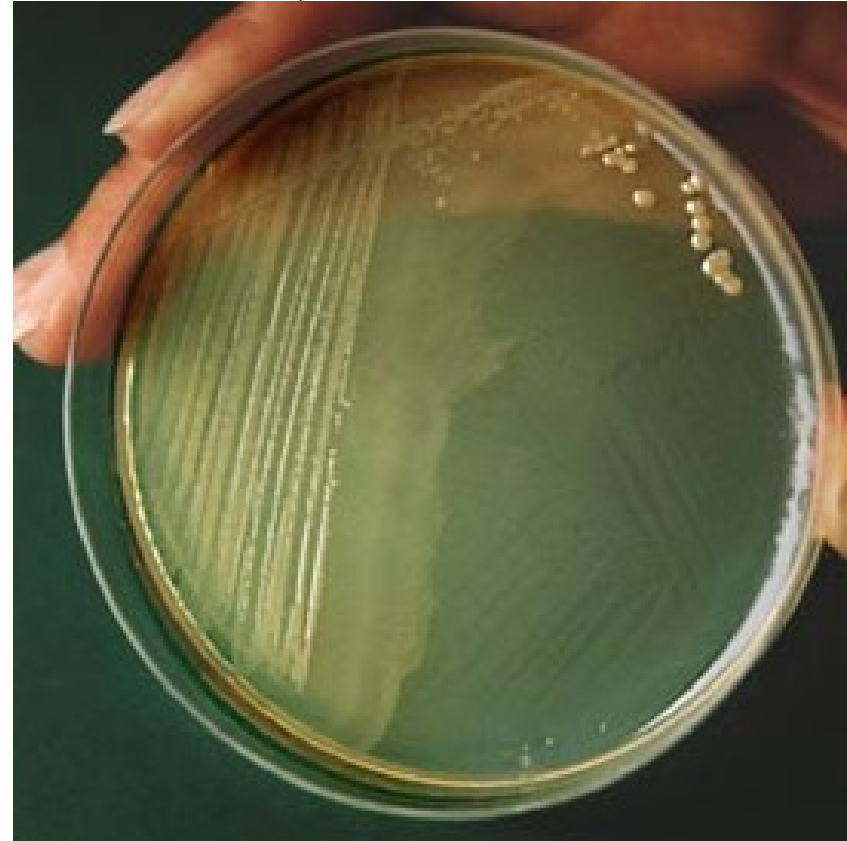


Urinary tract infections (UTI)

P. mirabilis: rajzás

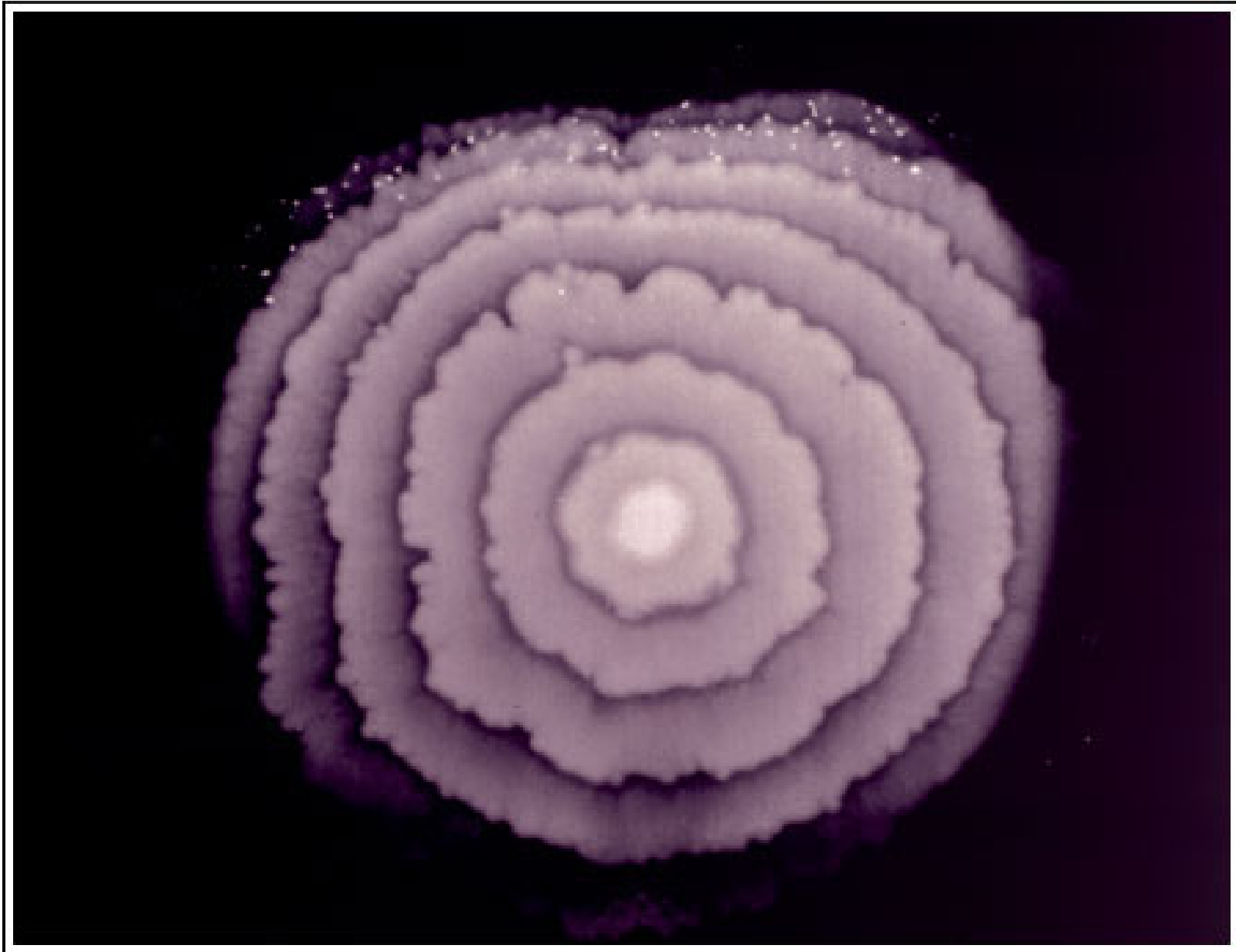
- ***P. mirabilis*, *P. vulgaris***

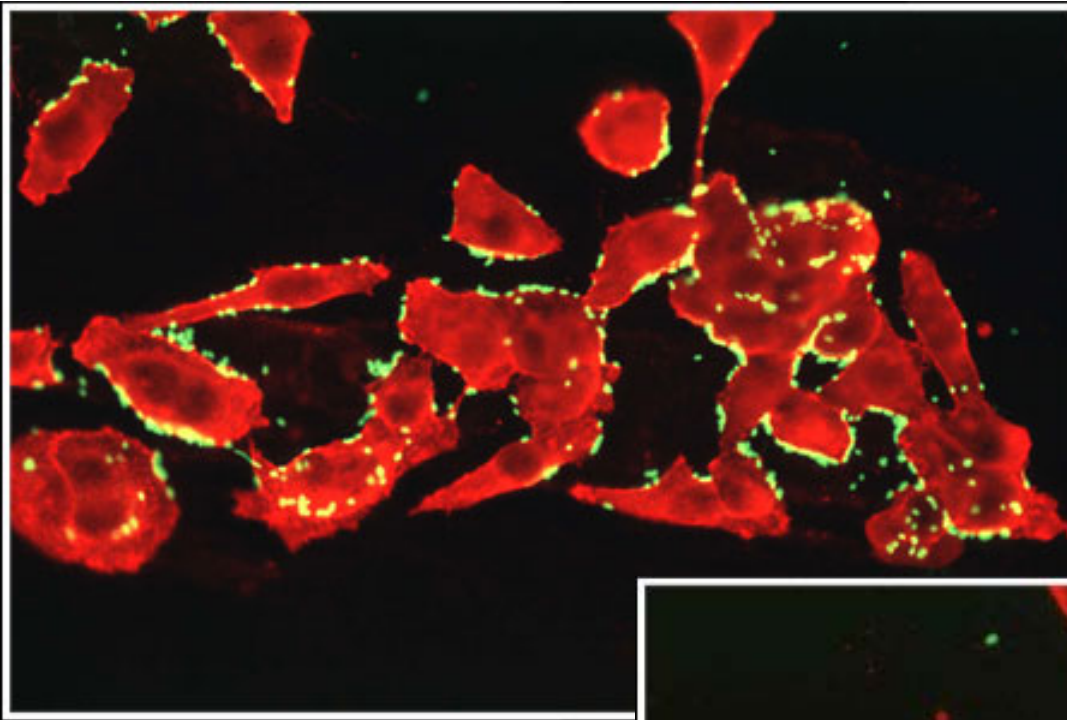
- Predispositio
- Ascendáló fertőzés
- Nosokomialis
(catheter, operatio)
- **Virulencia faktorok**
 - Flagellae:
motilitas
 - Adhesio-s fimbriae
 - Urease
(pH↑, irritatio, kőképződés)



P. mirabilis

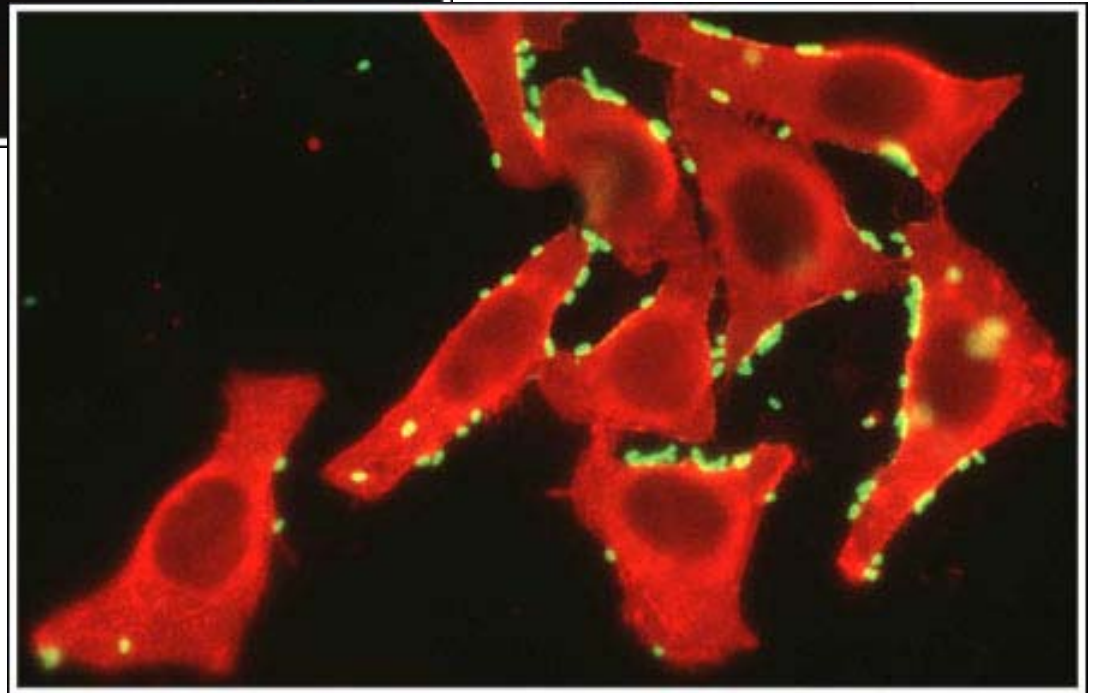
rajzás

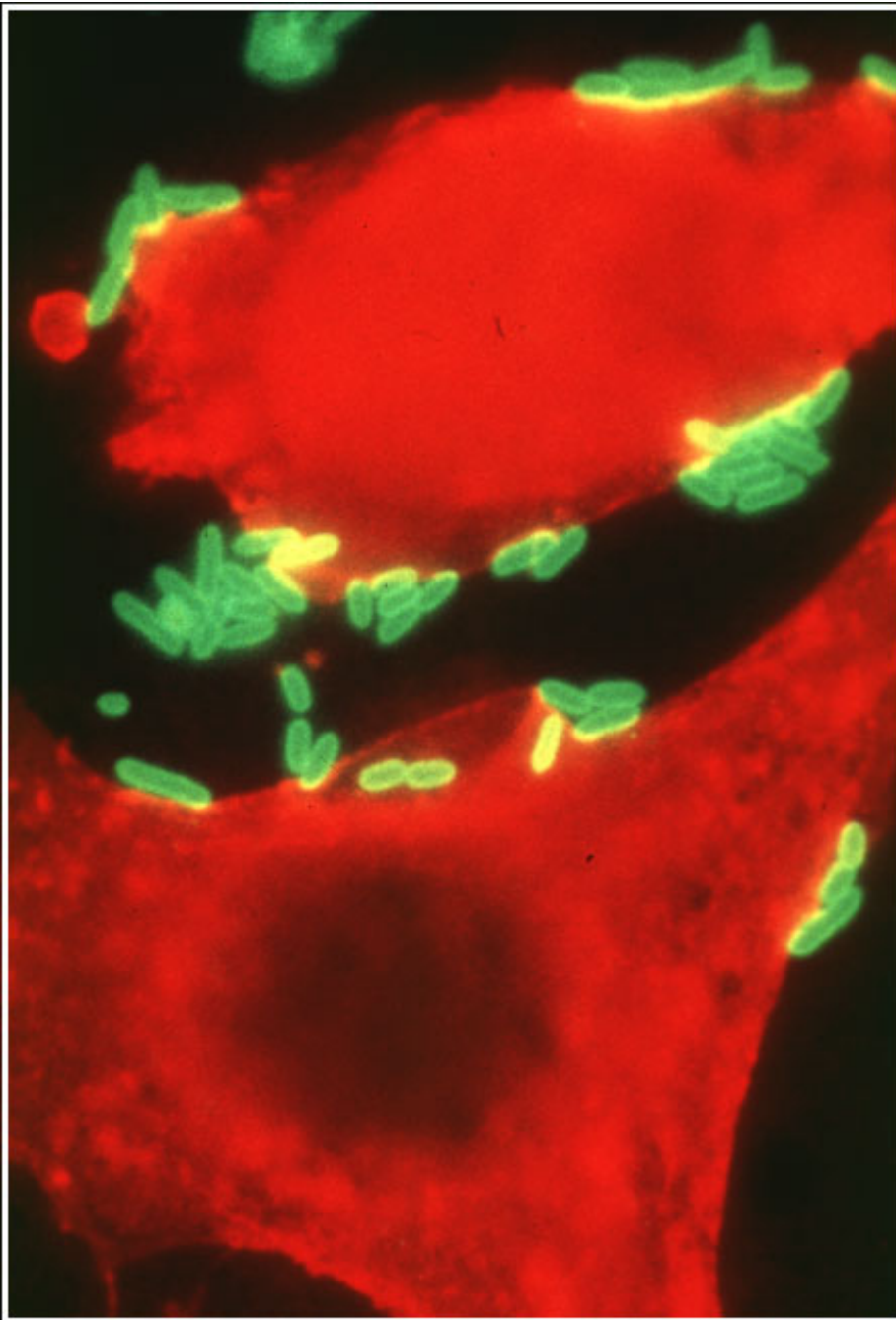




P. mirabilis

rajzás
- sejteken



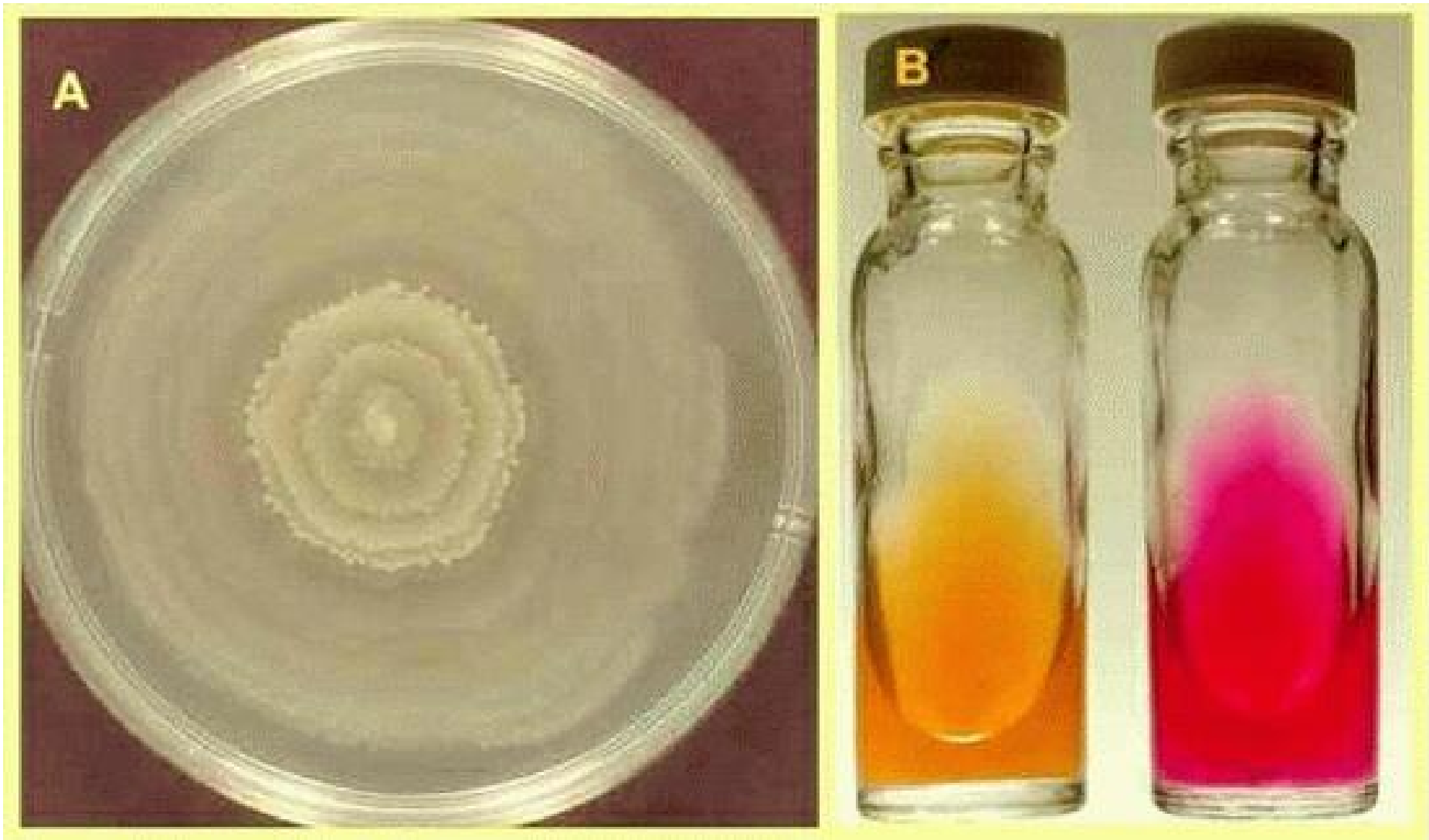


P. mirabilis

rajzás
- sejteken

Proteus vulgaris csillófestés





A: Proteus, Providentia – B: Urease Test - / +

Újszülöttkori Meningitis & Sepsis

- ***E. coli* K1**
(80–85%)
- K1-antigen
 - Azonosság
Meningococcus B-ag
 - Tolerancia ⇒
nincs ellenanyagválasz
 - Translocatio



Pneumonia

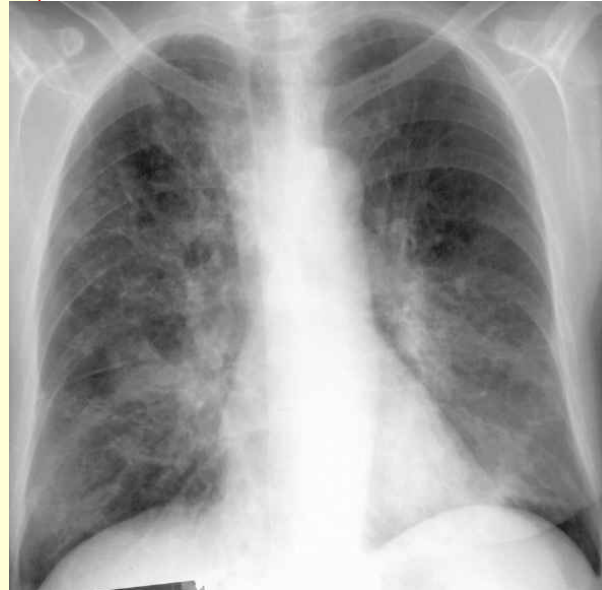
- Nosokomial
- Predispositio
- kórokozók

E. coli,

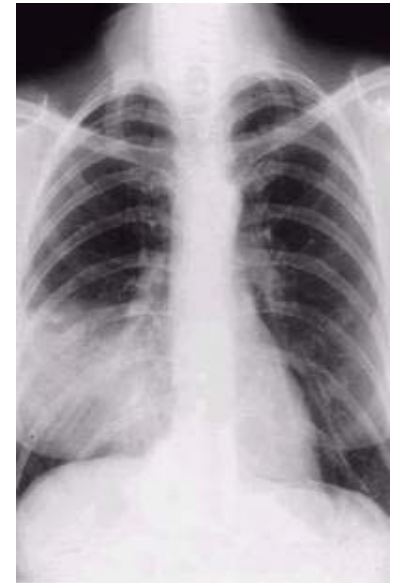
K. pneumoniae,

K. oxytoca,

Enterobacter spp.



Bronchopneumonia



Lobaris pneumonia (Friedländer)
K. pneumoniae

Klebsiella pneumoniae – Friedländer Pneumonia



Klebsiella pneumoniae



Mucoid = nyákos telepek – tok

Klebsiella pneumoniae



Klebsiella pneumoniae

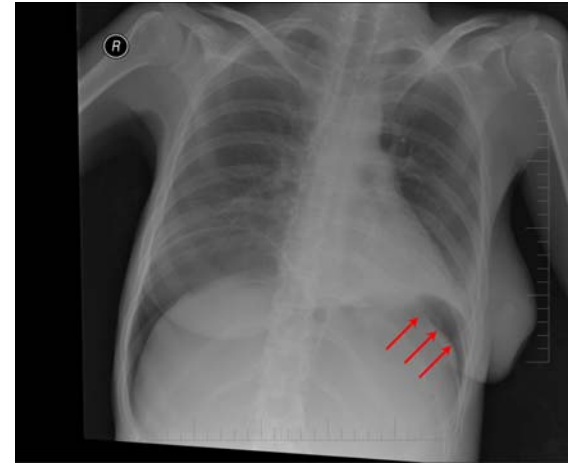
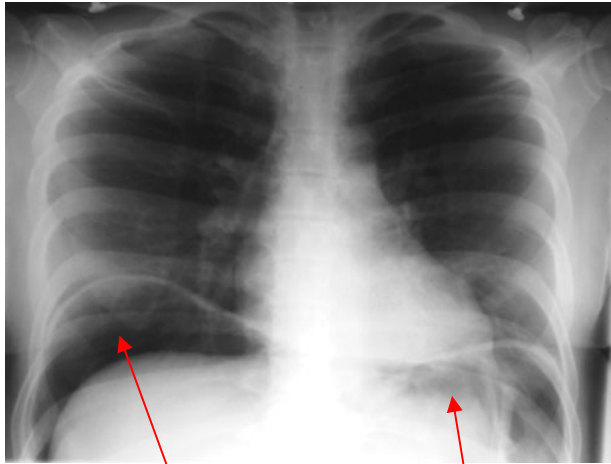




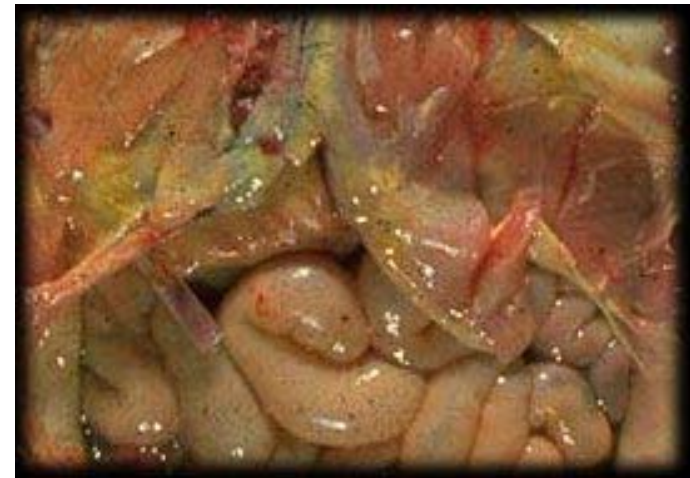
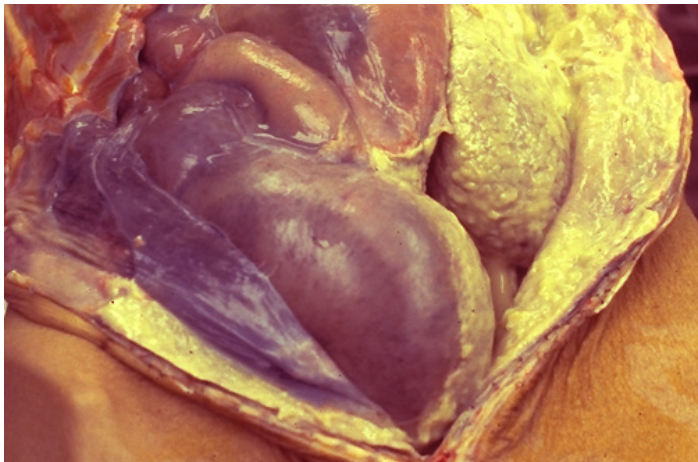
Enterobacter cloacae* *Klebsiella pneumoniae

Mucoid telepek

Intra-abdominalis fertőzések



Free abdominal air below the diaphragm: perforation ↗



Diffuse peritonitis after perforation of the colon

Enterobacteriaceae

Facultative pathogenek

genus

Escherichia

Klebsiella csoport

Enterobacter

Edwardsiella

Citrobacter

Proteus csoport

Serratia

Providentia

Morganella

Obligat pathogens (genera)

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S. sonnei

Salmonella

S. typhi

S. paratyphi

Yersinia

Y. pestis

Y. pseudotuberculosis

Y. enterocolitica

FIGURE 25-1 Virulence mechanisms of E coli.

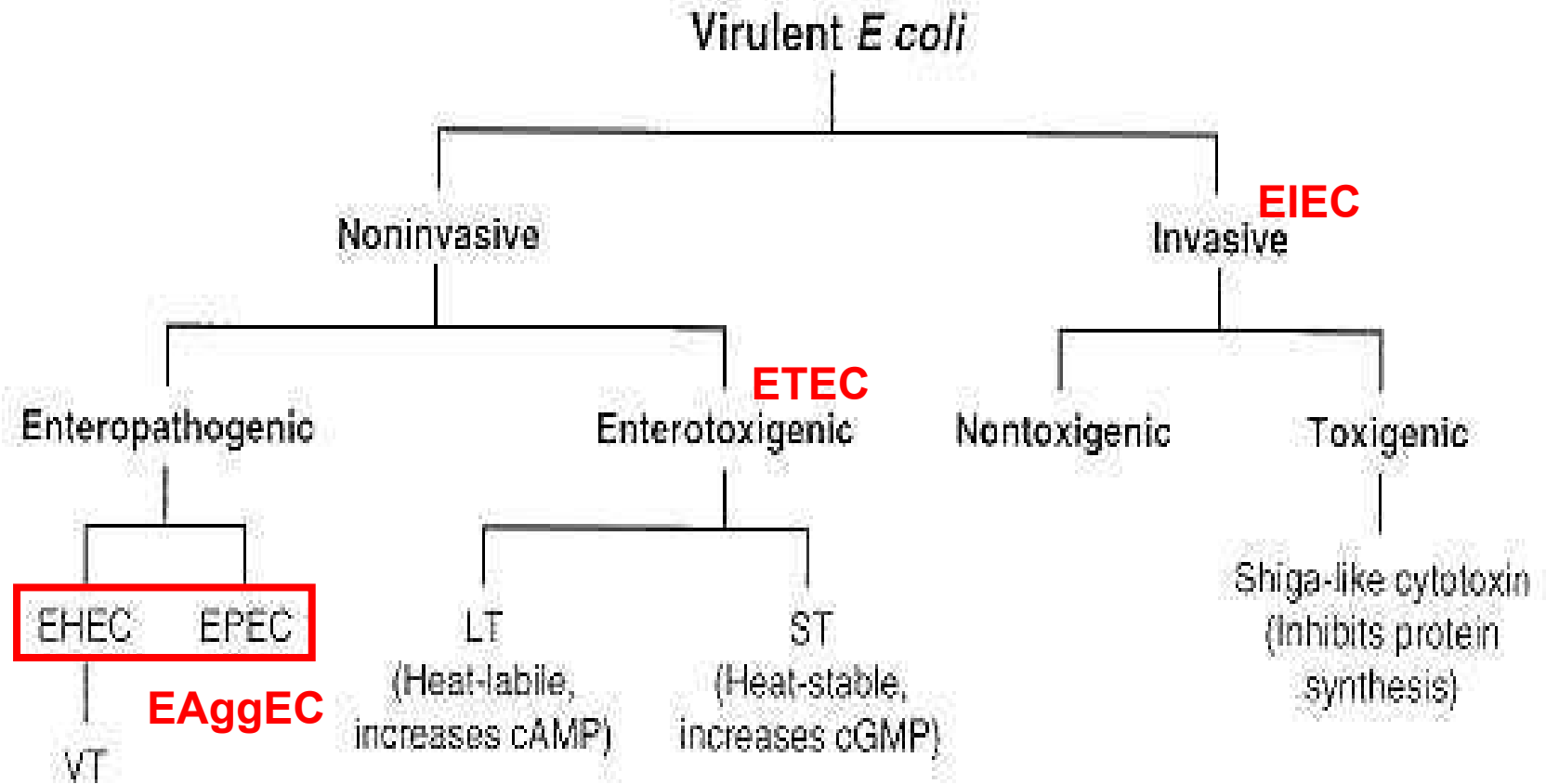
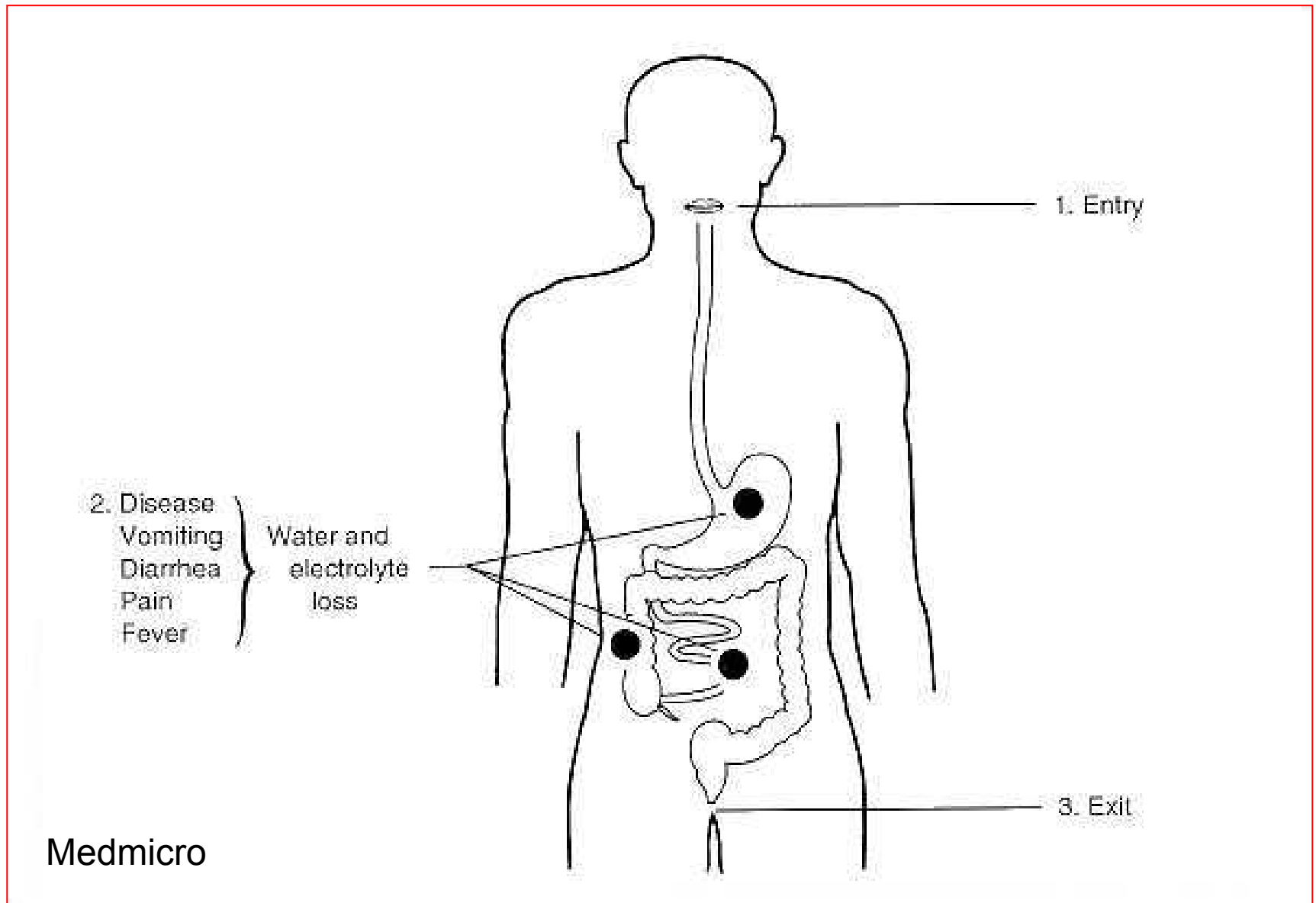


FIGURE 25-2 Pathogenesis of E. coli diarrheal disease.



Pathogen (enterovirulens) *E. coli* - 1

ETEC (entertoxicus)

LT (hő-labilis) ST (hő-stabil)

ST hatásmechanizmus (hyperactivatio):

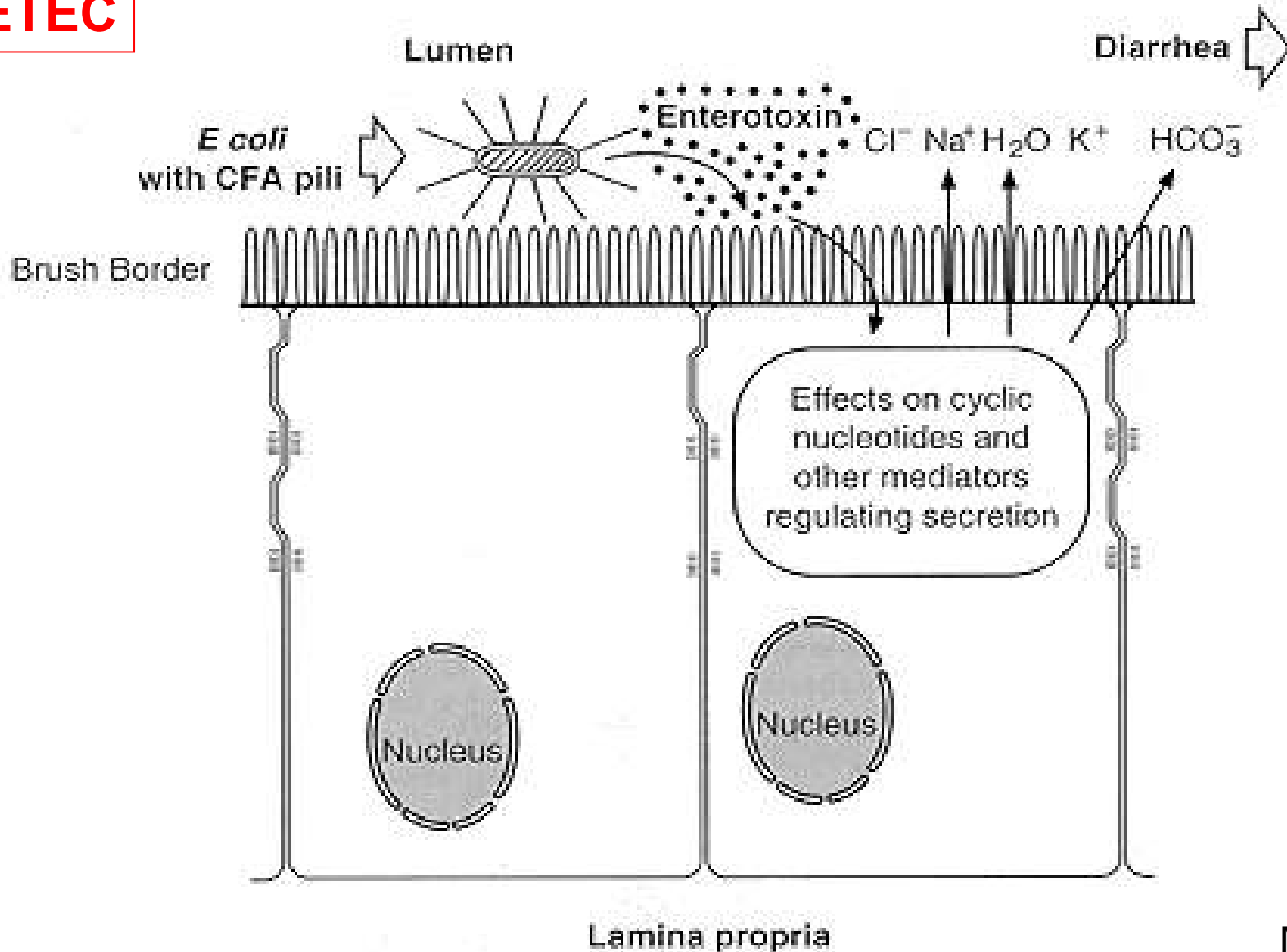
ADP-Rybosilatio Guanilcyclase →

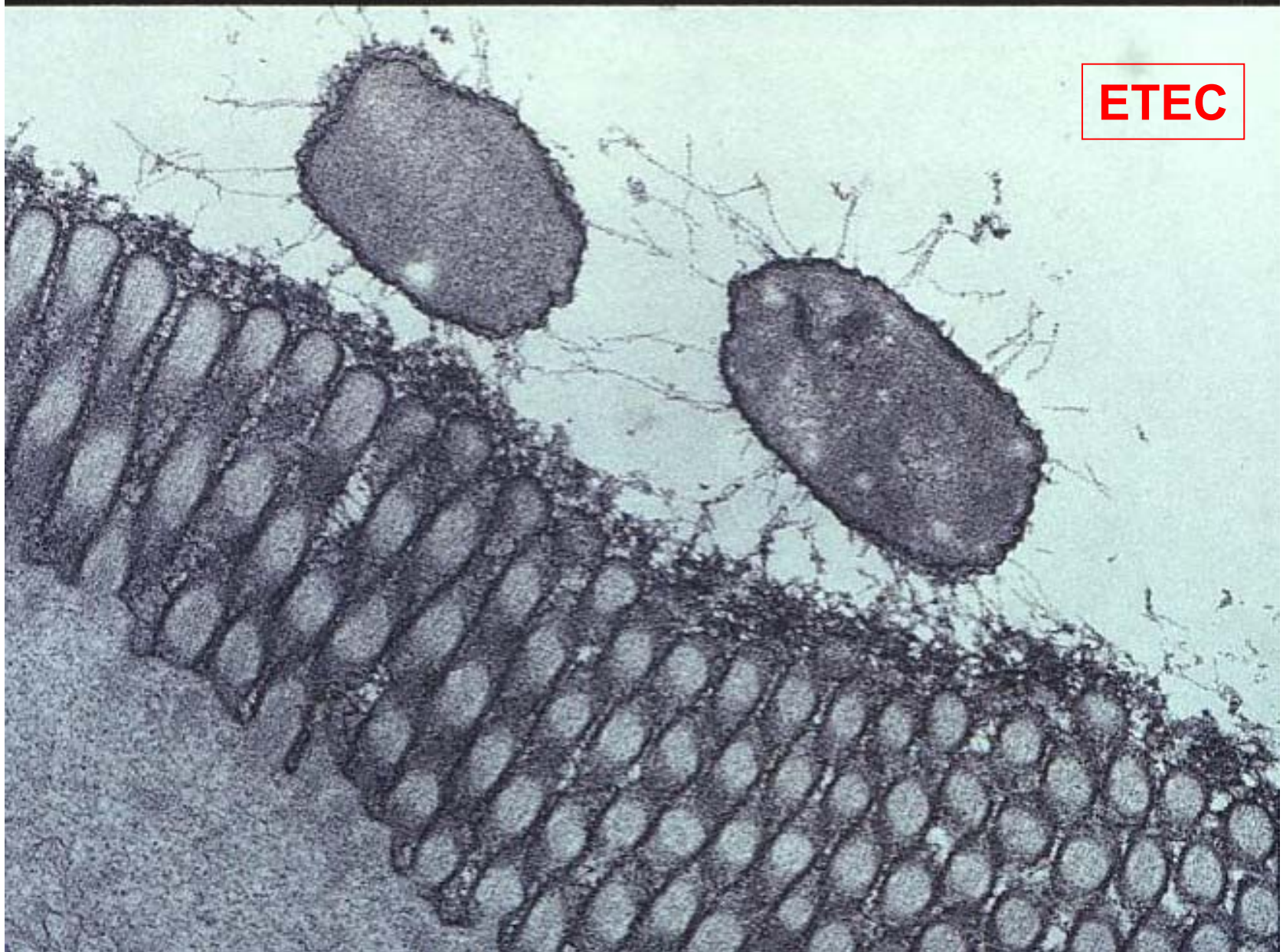
cGMP ↑ ⇨ víz- és folyadék veszteség

Fimbriae (CFA = **c**olonisation **f**actor **a**ntigens)

FIGURE 25-3 Cellular pathogenesis of E coli having CFA pili.

ETEC

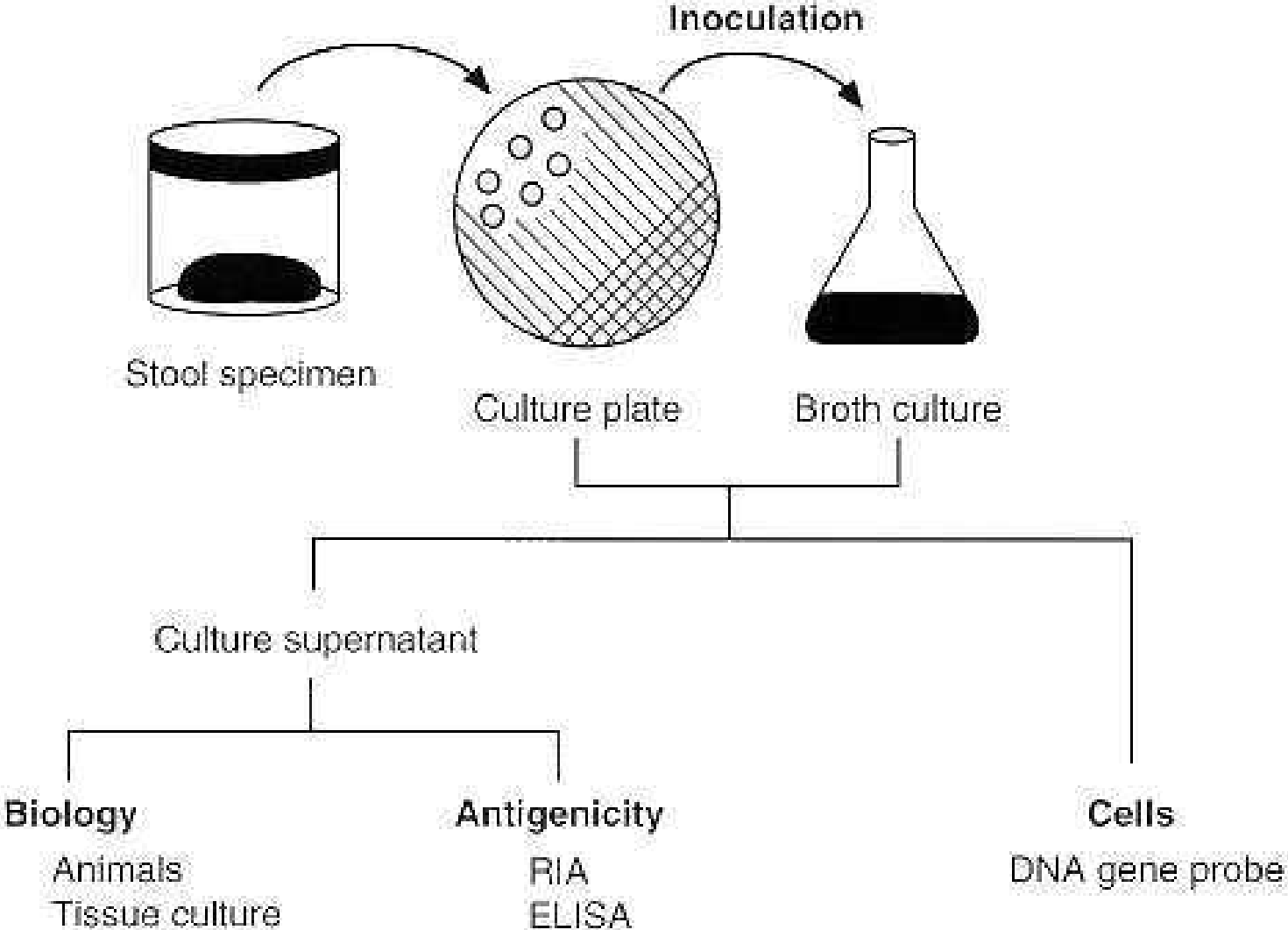




ETEC

Fig.4.26 Enterotoxigenic E. coli infection. Transmission electron micrograph showing bacteria adhering to the brush-border of human intestinal mucosal cells. By courtesy of Dr. S. Knutton

FIGURE 25-4 Laboratory methods for isolation and identification of ETEC.



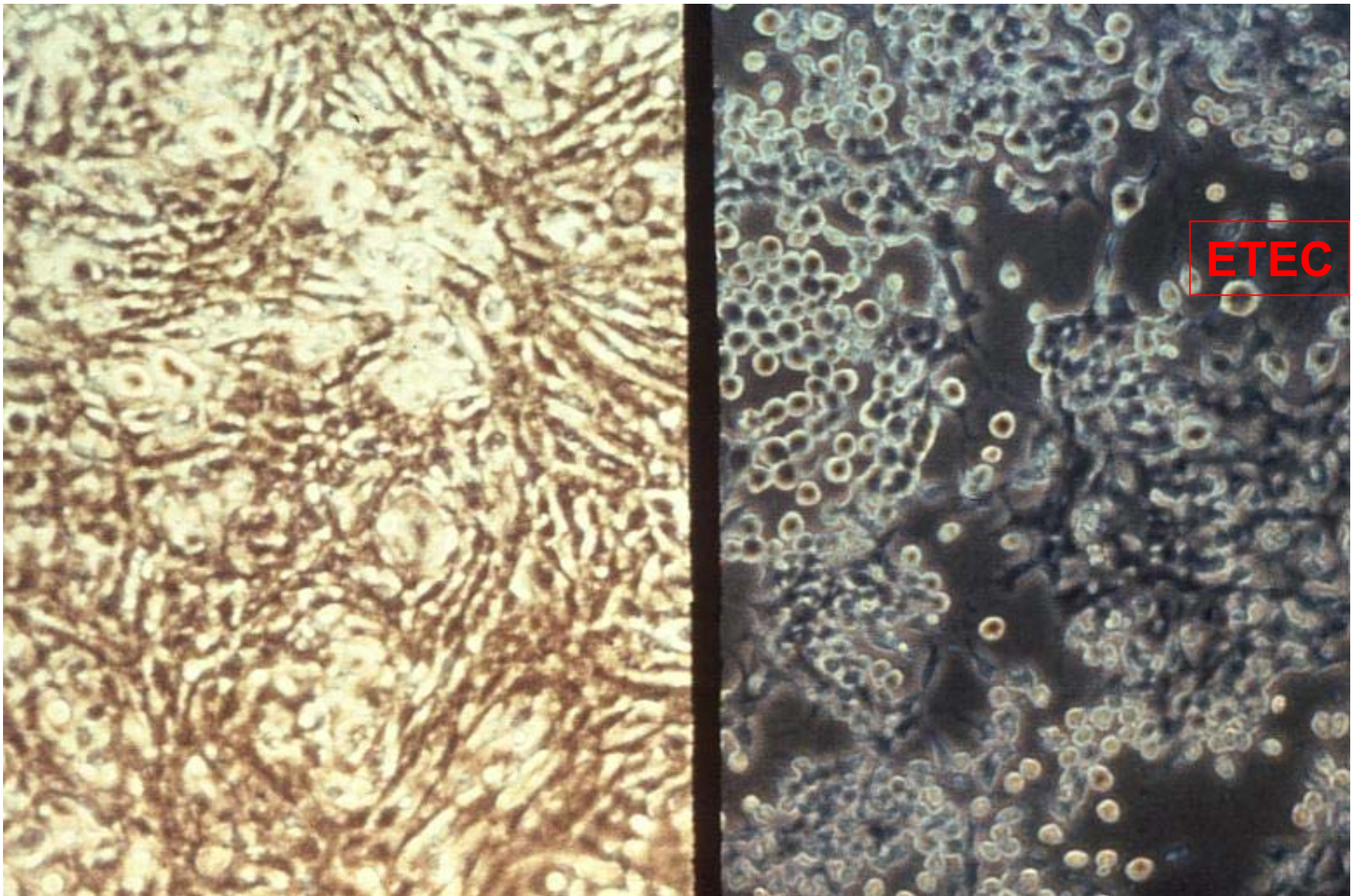


Fig. 4.14 Bacterial diarrhea. Y1 adrenal cell assay for E. coli LT enterotoxin, showing normal cells (left) and cells after exposure to LT toxin (right). Note disruption of monolayer and rounding up cells. By courtesy of Dr. H.L. DuPont.

Pathogen *E. coli* -2-3

EPEC (enteropathogen) O26; O55; O111;
O126...

Adhaesio: Adherencia Factor (EAF)

Bundle Forming Pilus (BFP)

Type III. Secretion-system*:

Protein filaments (EspA)

Tir (translocated intimin receptor)

Intimin (*eae**) → Actin; kefeszegély eltűnik →
sejthalál

* Chromosome coded

EAggEC (enteroaggregativ)

Fimbriae, ST-like, Haemolysin-like Toxin

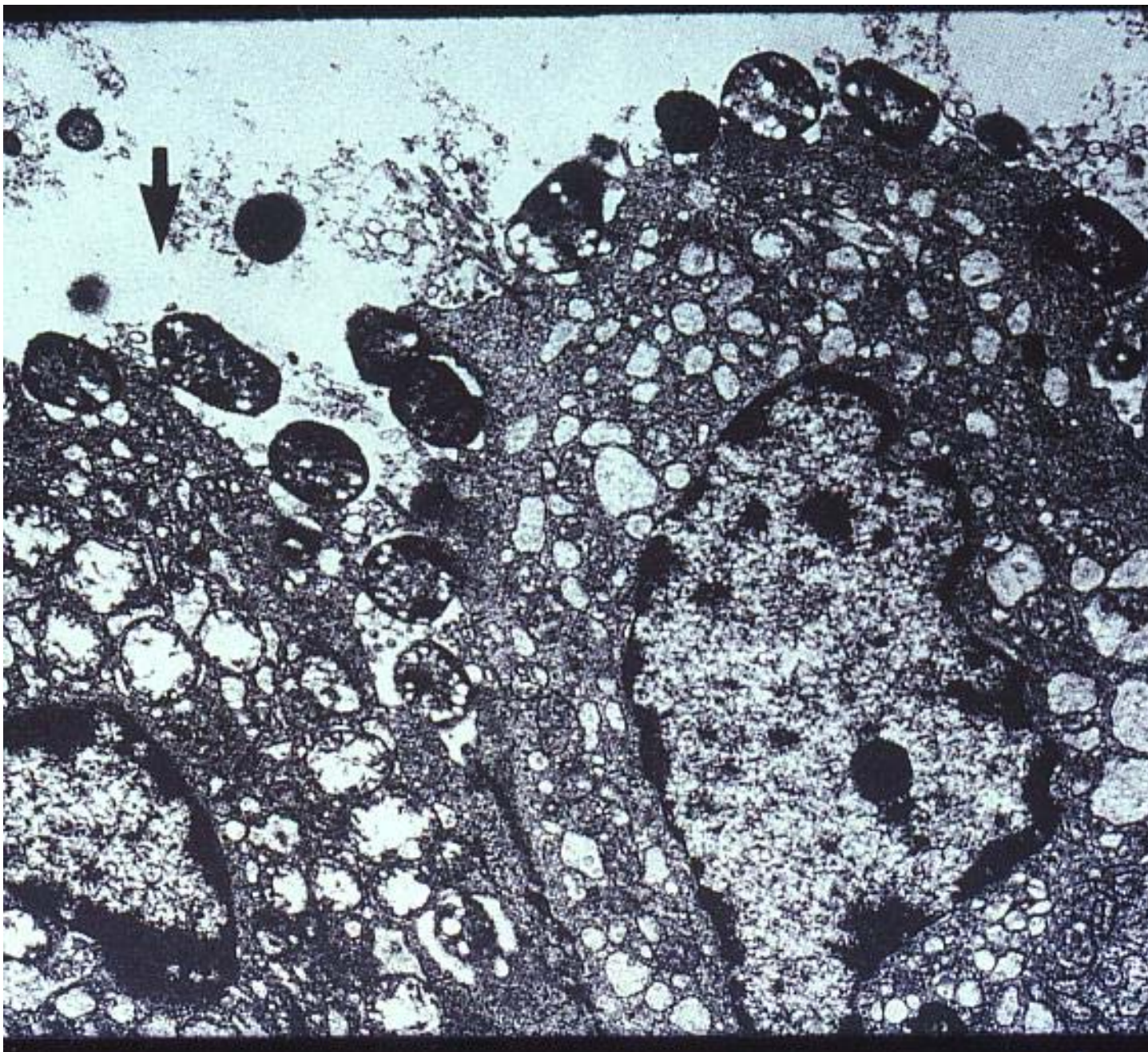


Fig.4.19 E. coli diarrhea. Electron micrograph of enteropathogenic E. coli (arrowed) attached to mucosal epithelial cells of ileum. The microvillus border of the epithelial cells has been largely destroyed by bacteria and the cells show signs of degeneration. X3000 By courtesy of Dr. J.R. Cantey

EPEC



Fig.4.27 Enteropathogenic E. coli infection. Electron micrograph showing close, localized adherence of bacteria to human intestinal mucosal cells and localized destruction of microvilli. By courtesy of Dr. S. Knutton

EPEC

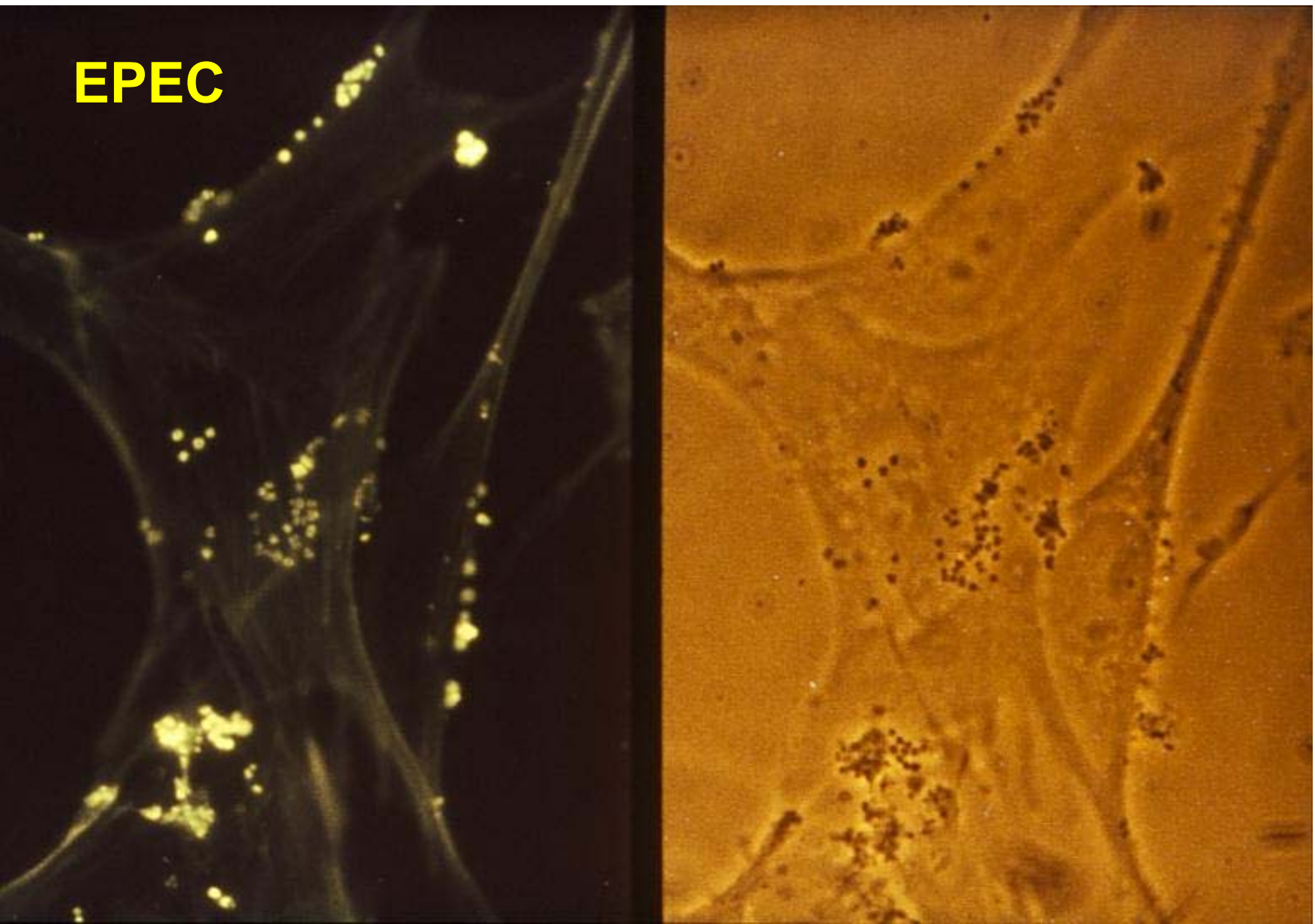


Fig. 4.28 Enteropathogenic E. coli infection. Fluorescent actin test specific for EPEC organisms. Left: fluorescent microscopy showing aggregated actin. Right: phase contrast microscopy showing location of bacteria. By courtesy of dr. S. Knutton

Pathogen *E. coli* - 4

EIEC (enteroinvasive)

O28; O32; O112; O115; O124, O136; O143, O144 u.a.

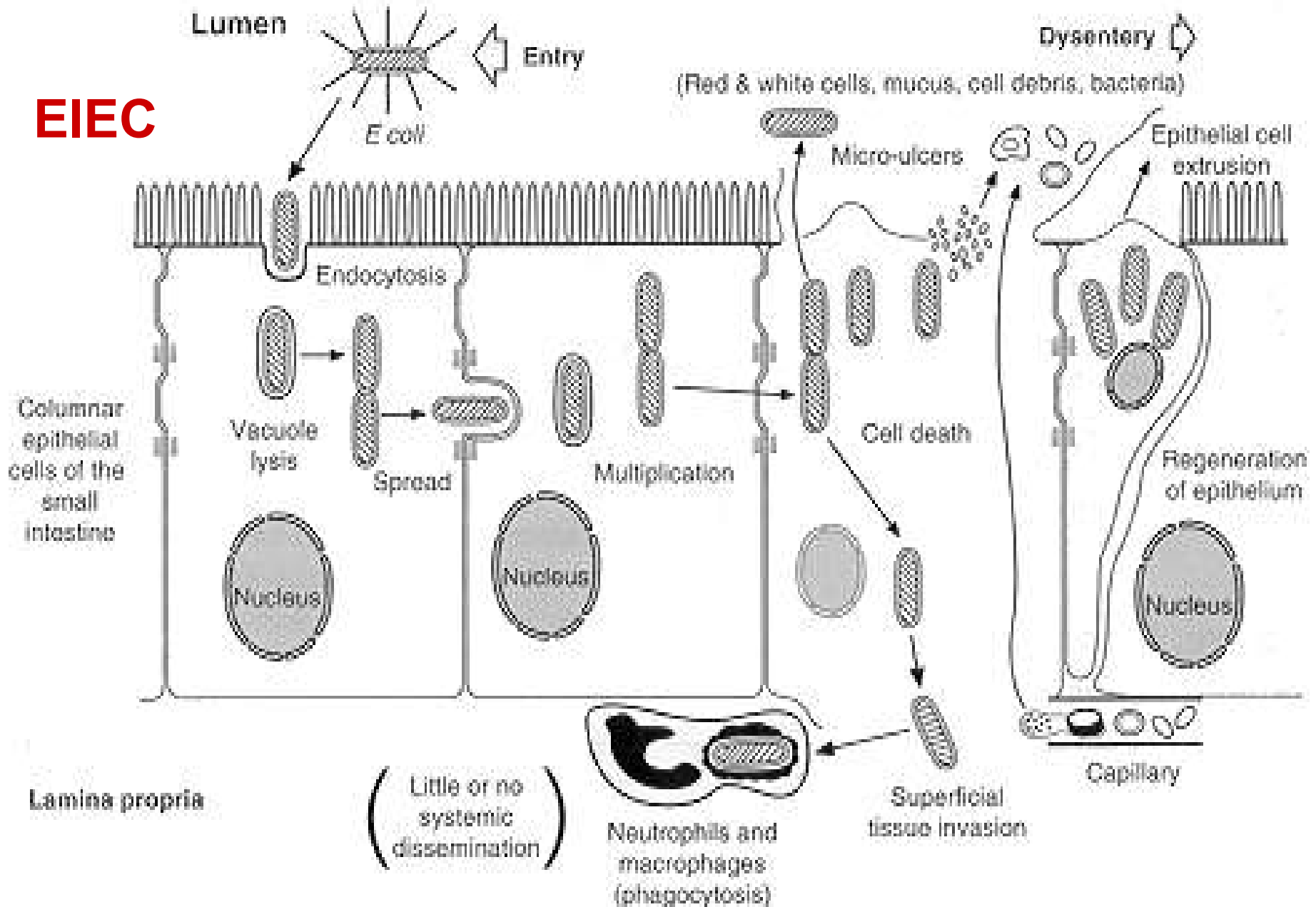
Pathogenesis:

Shigella szerű

Type III. Secretion-system

FIGURE 25-5 Cellular pathogenesis of invasive E coli

EIEC



EIEC

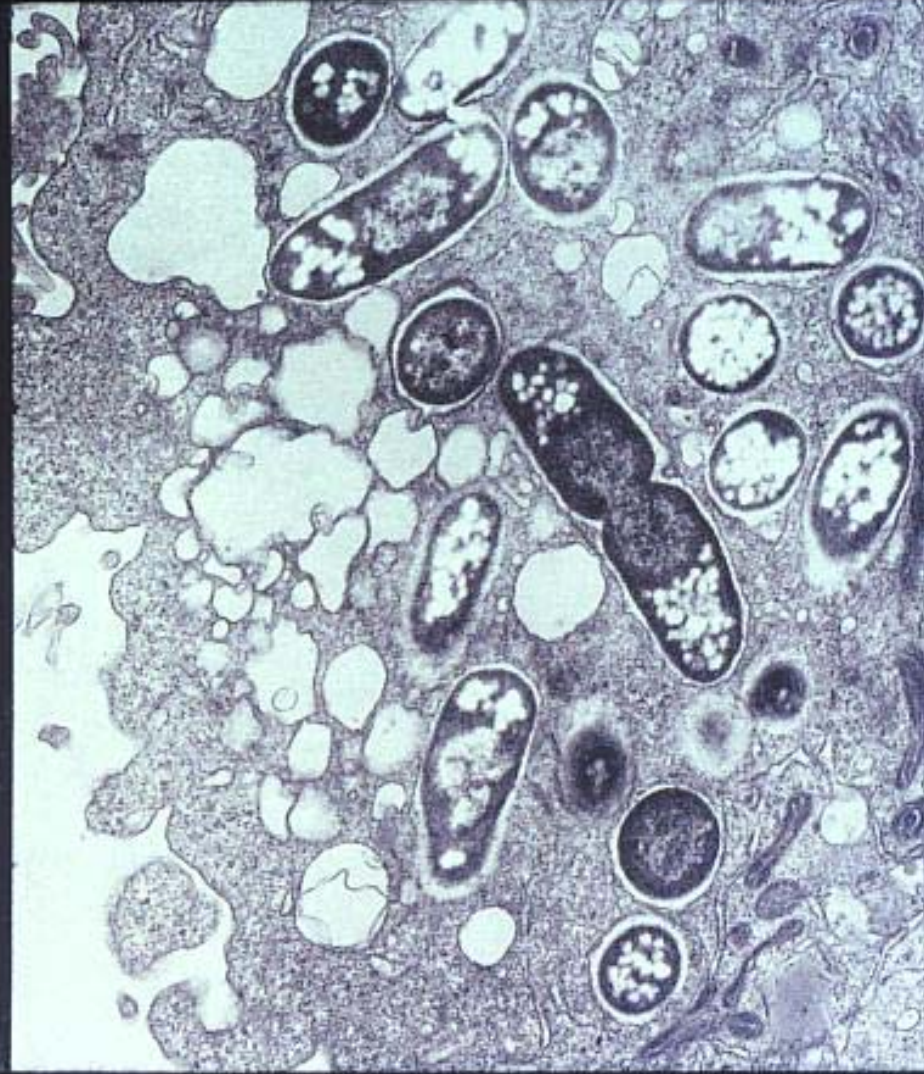
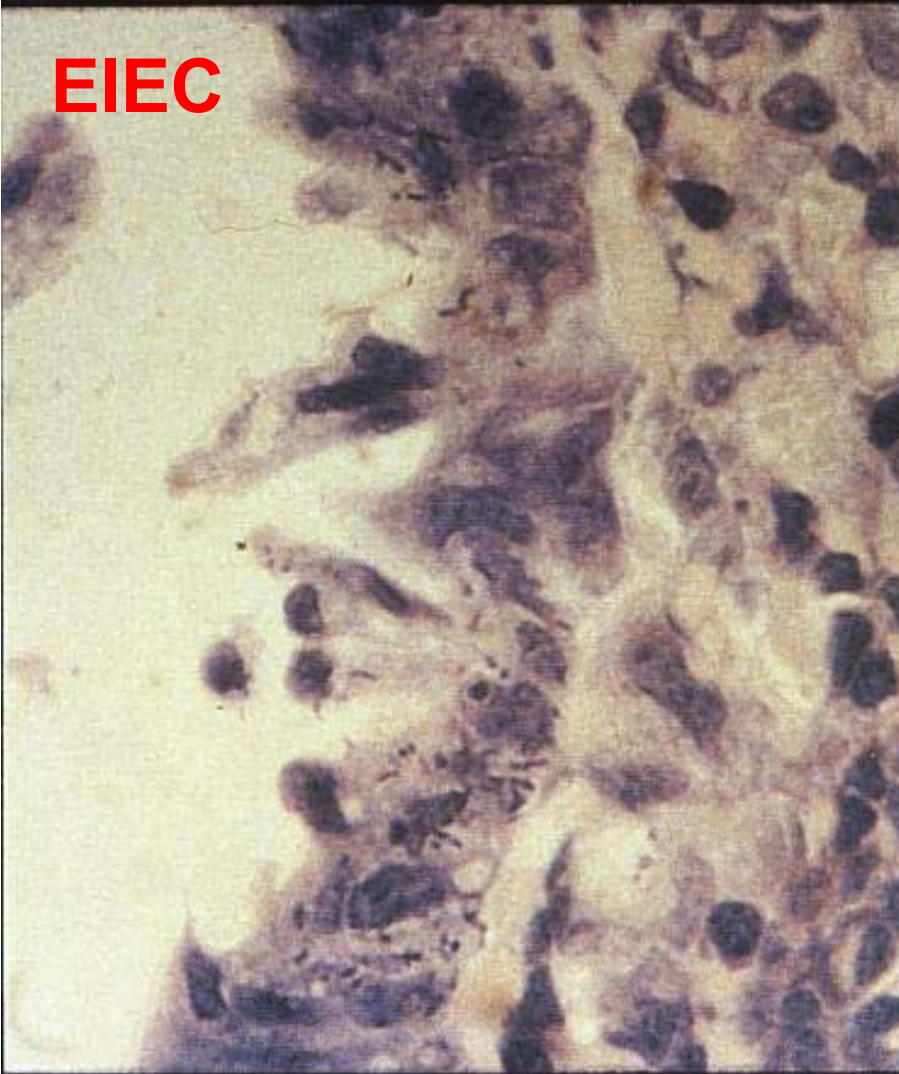
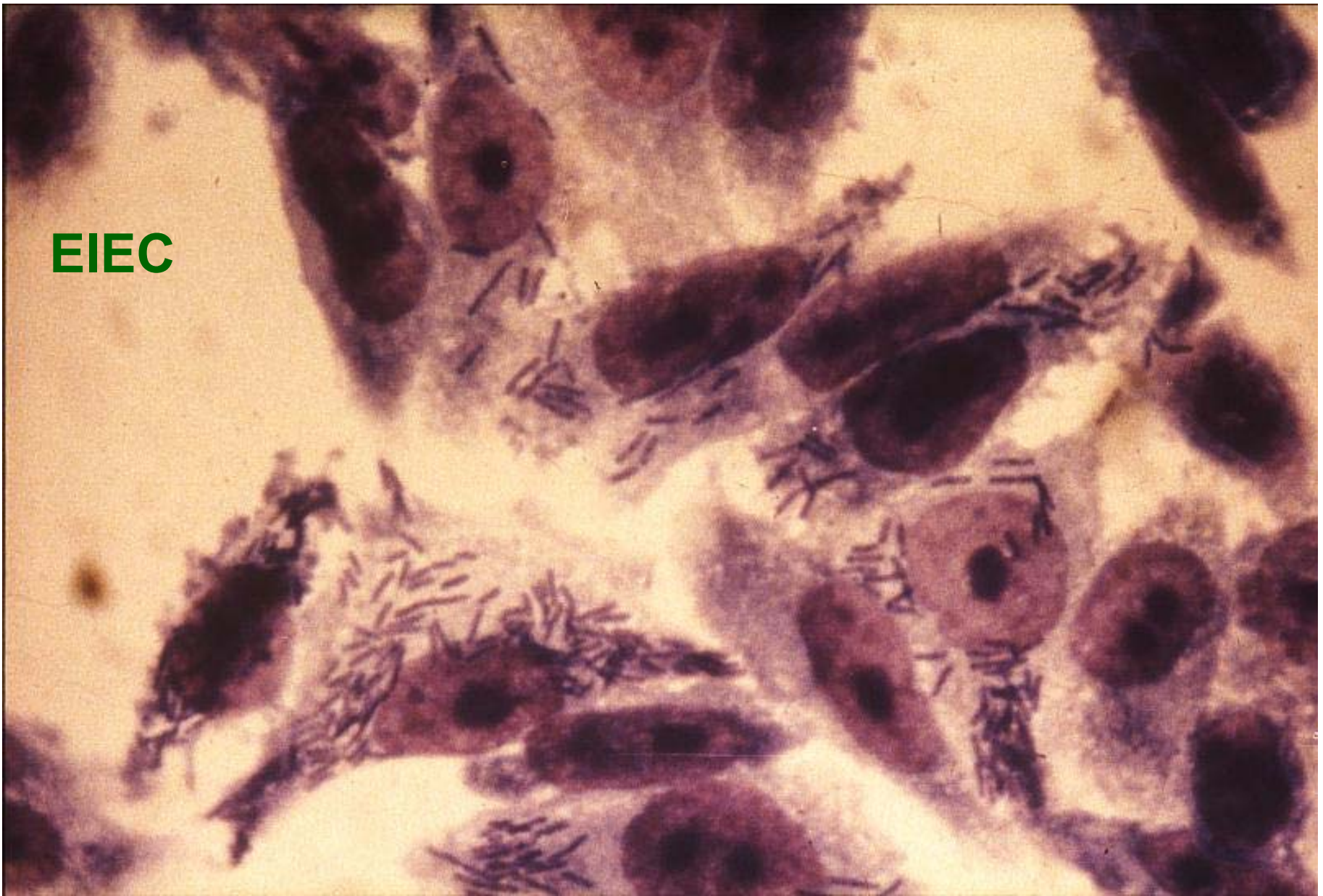


Fig. 4.17 Enteroinvasive E. coli infection. Invasion of mucosal layer of the intestine by E. coli organisms. There is necrosis of the mucosal layer at the site of invasion (left). Transmission electron micrograph showing enteroinvasive E. coli organisms within HEp-2 cell (right). By courtesy of Dr. S. Knutton.



EIEC

Fig. 4.31 Enteroinvasive E. coli infection. EIEC organisms invading HeLa cells in vitro. By courtesy of Dr. S. Knutton.

Pathogen *E. coli* - 5

EHEC (enterohemorrhagic) = VTEC O157:H7

SLT = Verotoxin = Shiga Toxin (stx1, 2, 2c)
hatásmechanizmus: fehérje szintézis gátlása →
cytotoxicus Haemolysin

Klinikai kép:

HUS (haemolyticus uraemiás syndroma)

Haemolyticus Anaemia

Trombocytopenia

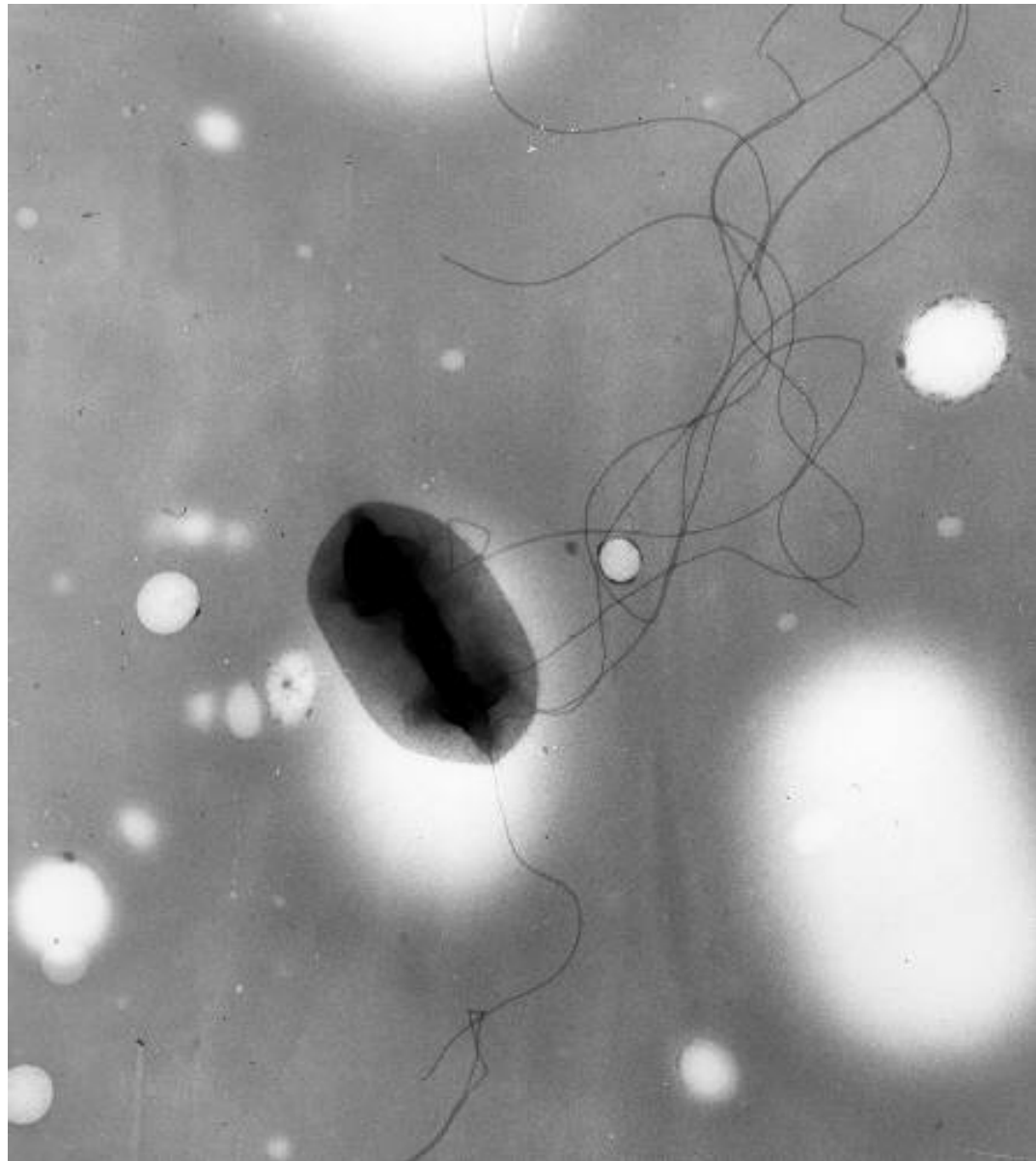
acut vese elégtelenség

Haemorrhagiás colitis

Pathogen *E. coli* törzsek

EHEC
(enterohaemorrhagiás)
= VTEC O157:H7

Transmission electron
micrograph of
Escherichia coli
O157:H7



EHEC (enterohemorrhagisch) = VTEC O157:H7



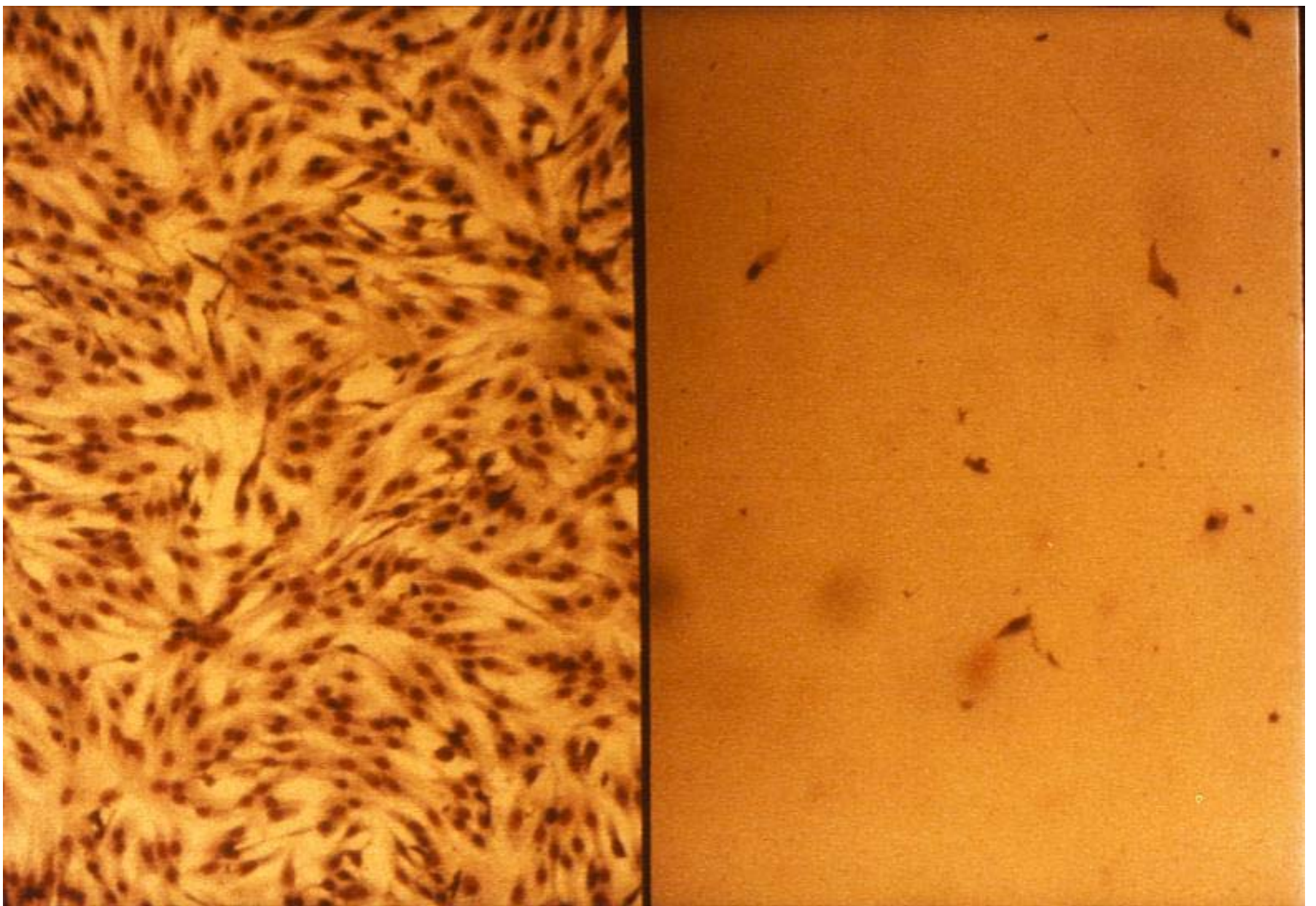


Fig. 4.29 Enterohaemorrhagic *E. coli* infection. Assay for Shiga-like toxin (Verotoxin) produced by EHEC (Serotype O157). Left: Normal monolayer of Vero cells. Right: Destruction of Vero cells by the toxin. By courtesy of Dr. S. Knutton

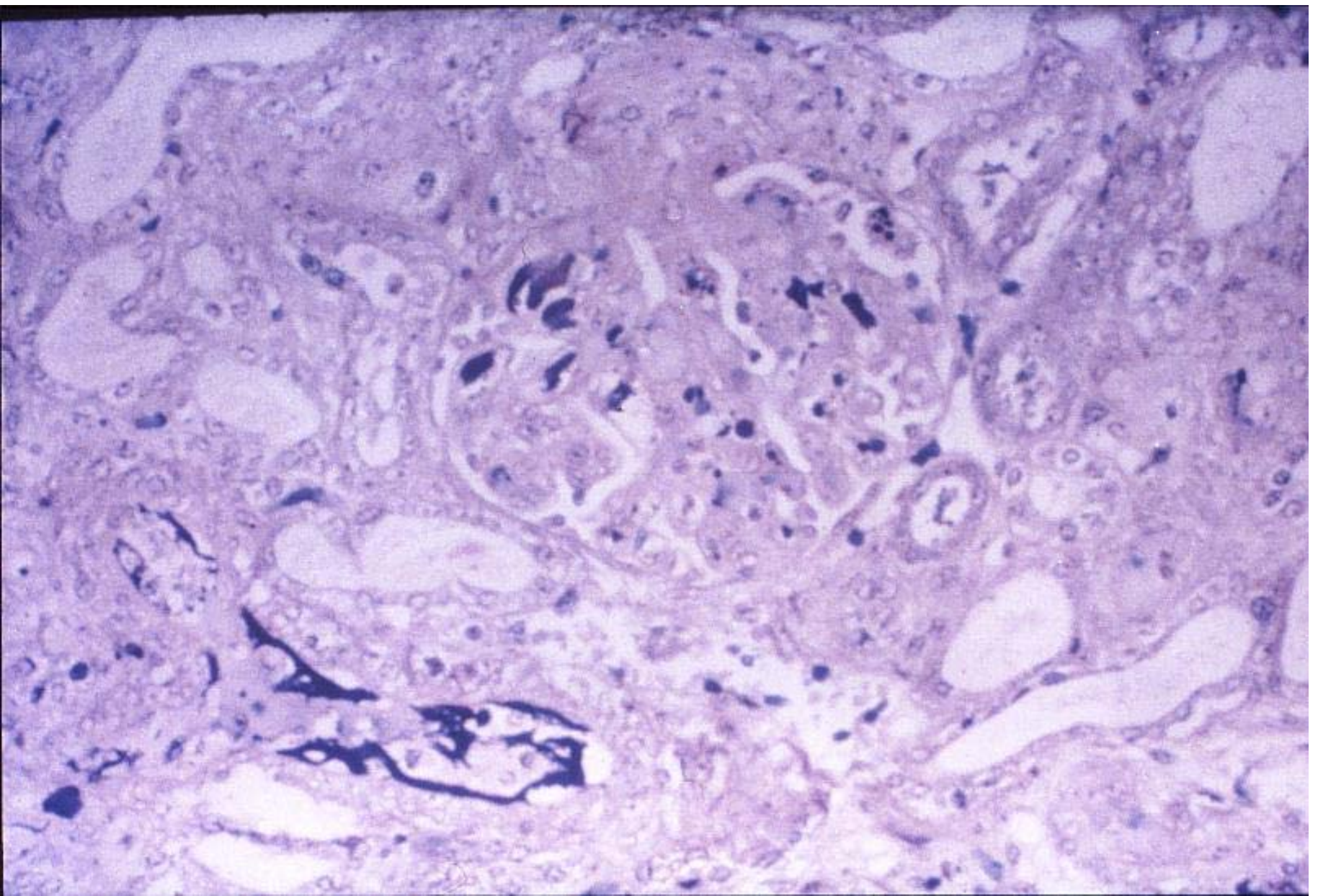


Fig. 4.30 Enterohaemorrhagic *E. coli* infection. Weigert stain showing fibrin 'thrombi' in glomerular capillaries in haemolytic uraemic syndrome. By courtesy of Dr. H.R. Powell

Pathogen *E. coli* törzsek

Diagnosis

Direct kimutatás

Szerotipizálás

Virulencia faktorok kimutatása!

Prophylaxis

Expositio prophylaxis

Therapia

Víz- és folyadékpótlás

Antibiogram

**Gram negatív fakultatív
anaerob pálcák**

Vibrionaceae

GRAM NEGATÍV PÁLCÁK

AEROB

Bordetella

Brucella

Francisella

Pseudomonas

Acinetobacter

Legionella

FACULTATIV ANAEROB

Haemophilus

Pasteurella

Familia:

Enterobacteriaceae

Vibrionaceae

Cardiobacterium

Eikenella

Kingella

Actinobacillus

ANAEROB

Bacteroides

Prevotella

Porphyromonas

Fusobacterium

MICROAEROPHIL

Campylobacter

Helicobacter

BACTERIALIS BÉLFERTZŐZÉSEK

I. Typus

Enterotoxin

Hypersecretio
vékonybél

vizes hasmenés

Vibrio cholerae
Escherichia coli
(ETEC)

II. Typus

Inflammatio

Invasio a mucosaba
Vastagbél

gennyes, véres, nyákos
hasmenés

Shigella
E. coli (EIEC) (EPEC, EHEC)
Salmonella
Yersinia enterocolitica
Campylobacter jejuni
Aeromonas sp.
Vibrio parahaemolyticus

III. Typus

Penetratio, Generalisatio

Intracellularis kórokozó
Ileum

Typhus, Sepsis

Salmonella typhi
S. paratyphi A, B
Yersinia enterocolitica
Y. pseudotuberculosis
Campylobacter fetus

Exogen, bejutás: per os, faeco–oralis transmissio; hygiene!

Clostridium difficile
Clostridium perfringens

**Gram negatív facultative anaerob pálcák
(Positiv Glucose fermentatio)**

Oxidase positive

Oxidase negative

Vibrionaceae

Aeromonadaceae

Enterobacteriaceae

Vibrio

Plesiomonas

Aeromonas

Facultative
pathogenic

Obligate
pathogenic

P. shigelloides

A. hydrophila

***V. cholerae*
V. parahaemolyticus
*V. vulnificus***

Escherichia
Klebsiella
Enterobacter
Proteus
Serratia
Providencia
Morganella
Edwardsiella
Citrobacter
Hafnia

Salmonella
Shigella
Yersinia

Vibrionaceae

Species	kórkép
<i>V. cholerae</i> O1 klasszikus & El Tor	Cholera
<i>V. cholerae</i> O139	Cholera
<i>V. parahaemolyticus</i>	Gastroenteritis
<i>V. vulnificus</i>	sebfertőzés, sepsis
Non-agglutinable (NAG) vibrios	Gastroenteritis (ritkán)

Vibrio cholerae

R. Koch, 1883

Morphologia

- Gr–, hajlott pálca
- Facultative anaerob

Biokémiai reakciók

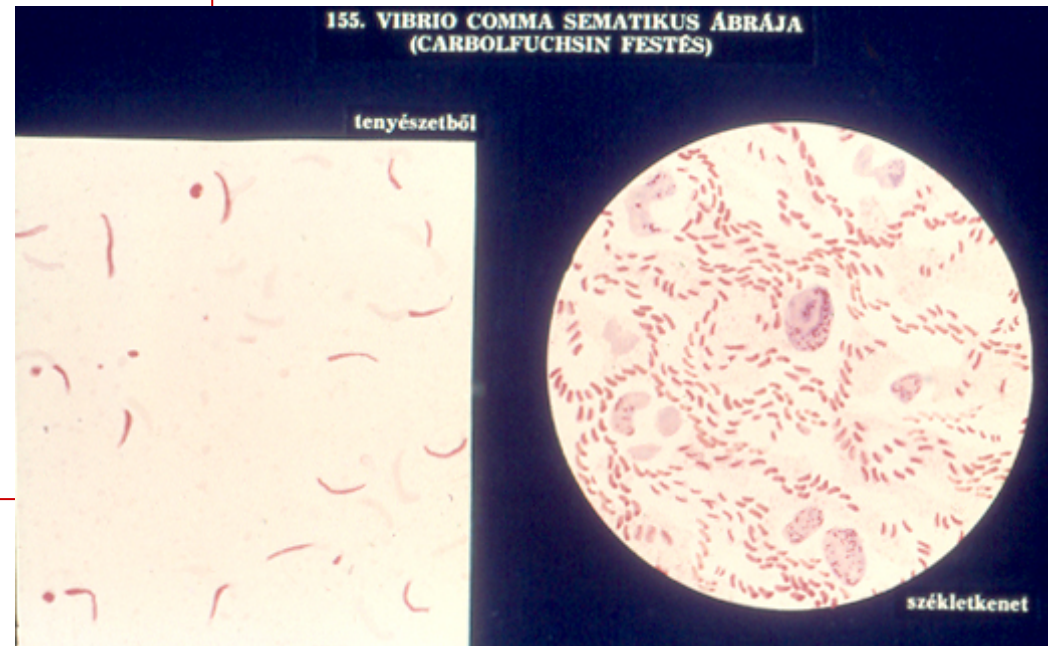
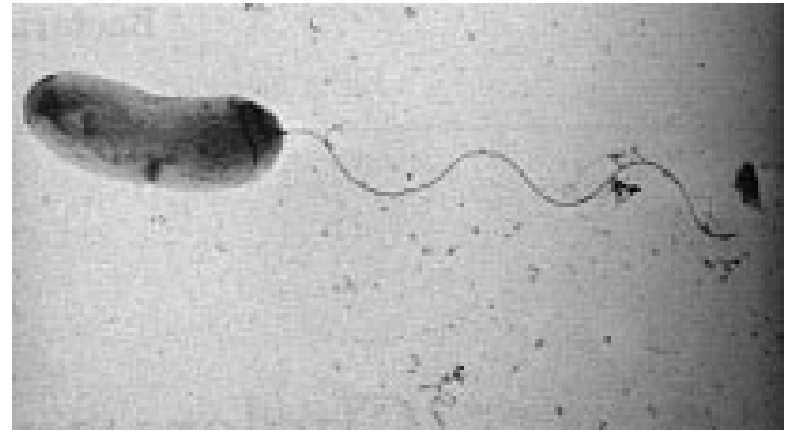
Glukose OF ‡

Motilitas +

Catalase +

Oxidase +

Nitrate Reductio +

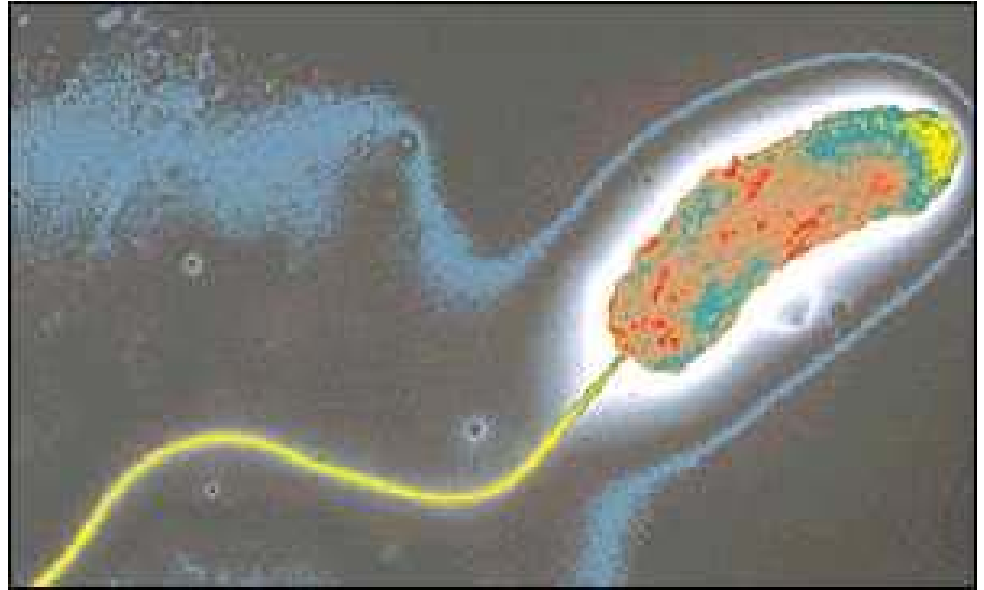


V. cholerae



38

V. cholerae



Antigen szerkezet, virulencia faktorok

O (sejtfal) - 138

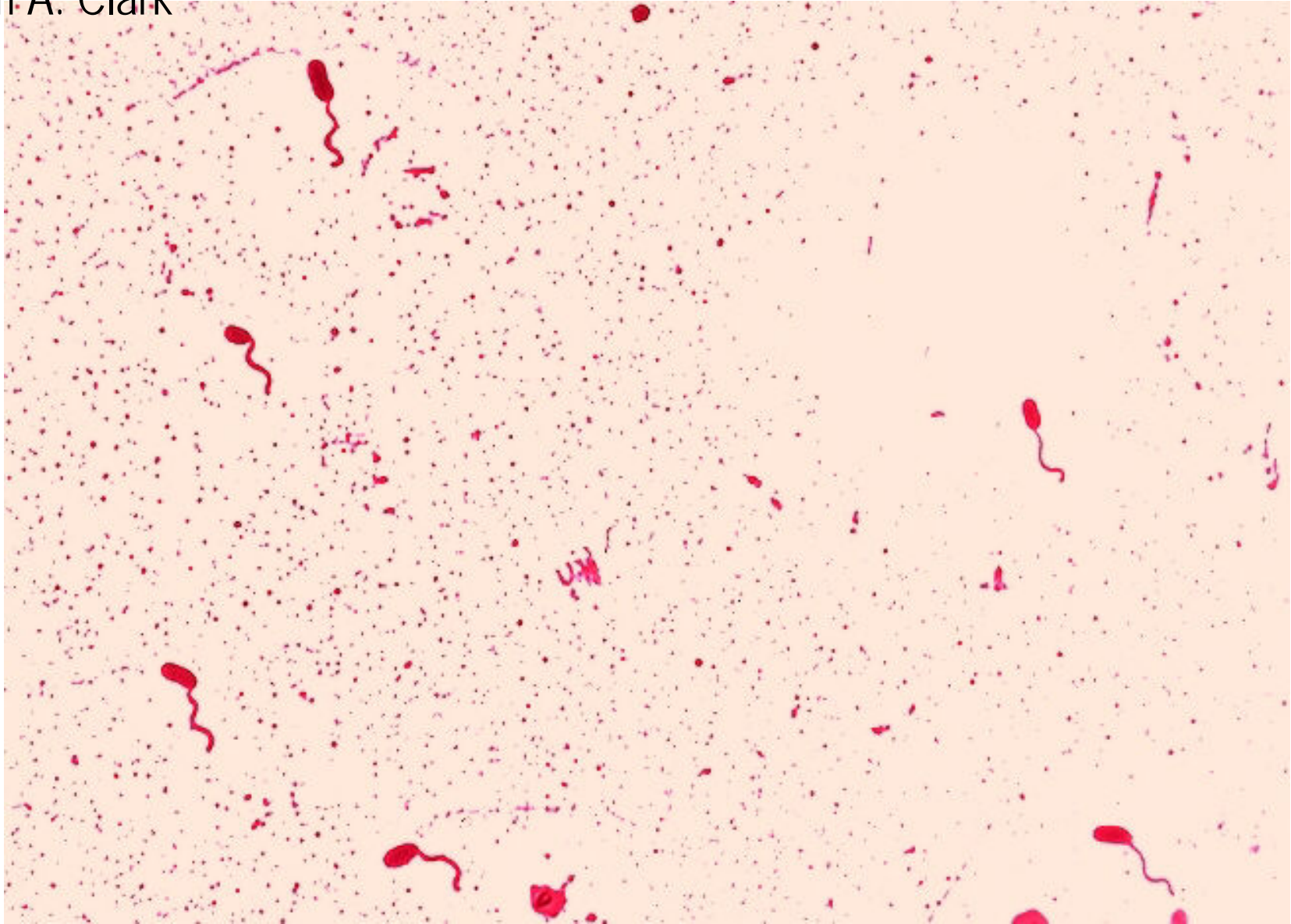
O1 & O139

H flagellaris (közös)

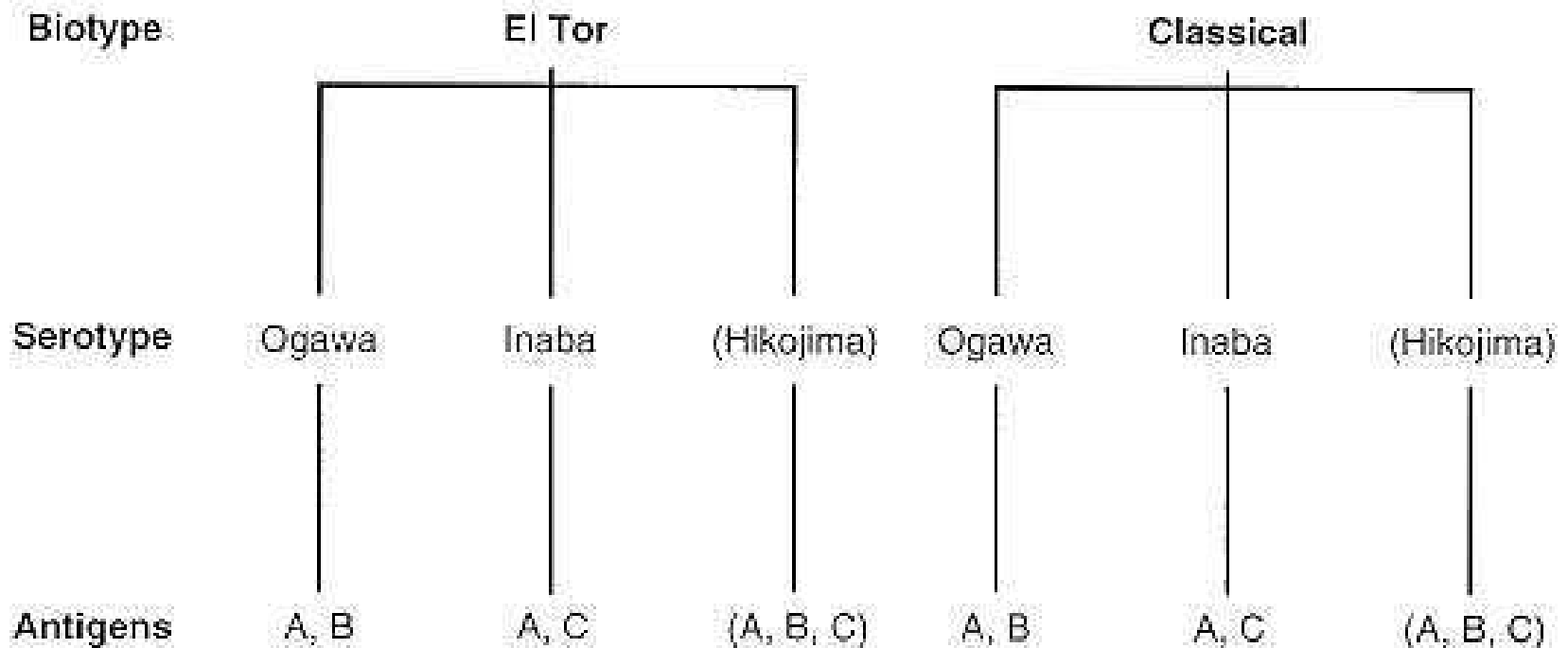
Fimbriae: A, B, C

O1: Bio és szerotípusok

Vibrio cholerae. Leifson flagella stain (digitally colorized). CDC/Dr. William A. Clark



V. cholerae O1 Bio- & Serotypusok



Virulencia faktorok

Virulencia faktor	Biologiai hatás
Cholera toxin	Folyadék & electrolyt veszteség hypersecretio
Fimbriae	Adhesio - mucus membrane
Accessory colonisation factor	Adhesio - mucus membrane
Haemagglutination protease (mucinase)	Bélben gyulladás degradatio (tight junctions)
Siderophorok	vas sequestratio
Neuraminidase	Toxin receptor up-regulatio

V. cholerae

Pathogenesis – Obligat human pathogen

Fertőzés forrása: **1. emberek (beteg); hordozó** (incubatio, constans hordozó és reconvalescens ürítő – székletszóródás! – legyek!)

2. kontaminálódott élelmiszer (tengeri halak, herkentyűk!)
és **ivóvíz**

Reservoir: algák, kagylók, Planktonok

Transmissio: Peroralis

behatolás: GI

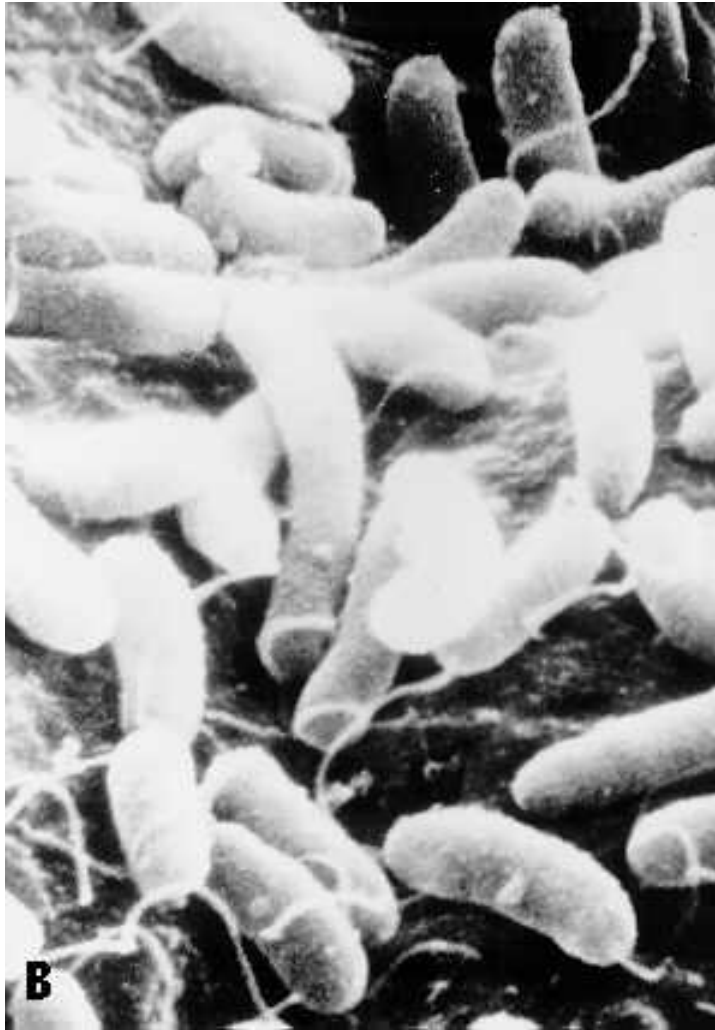
Toxin termelődés a vékonybélben

NINCS DISSEMINATIO!

Kórkép: Cholera –Cholera toxin miatt

Immunitas: localis IgA (IgG vérben!)

Adhaesion of *V. cholerae* to intestinal epithelium

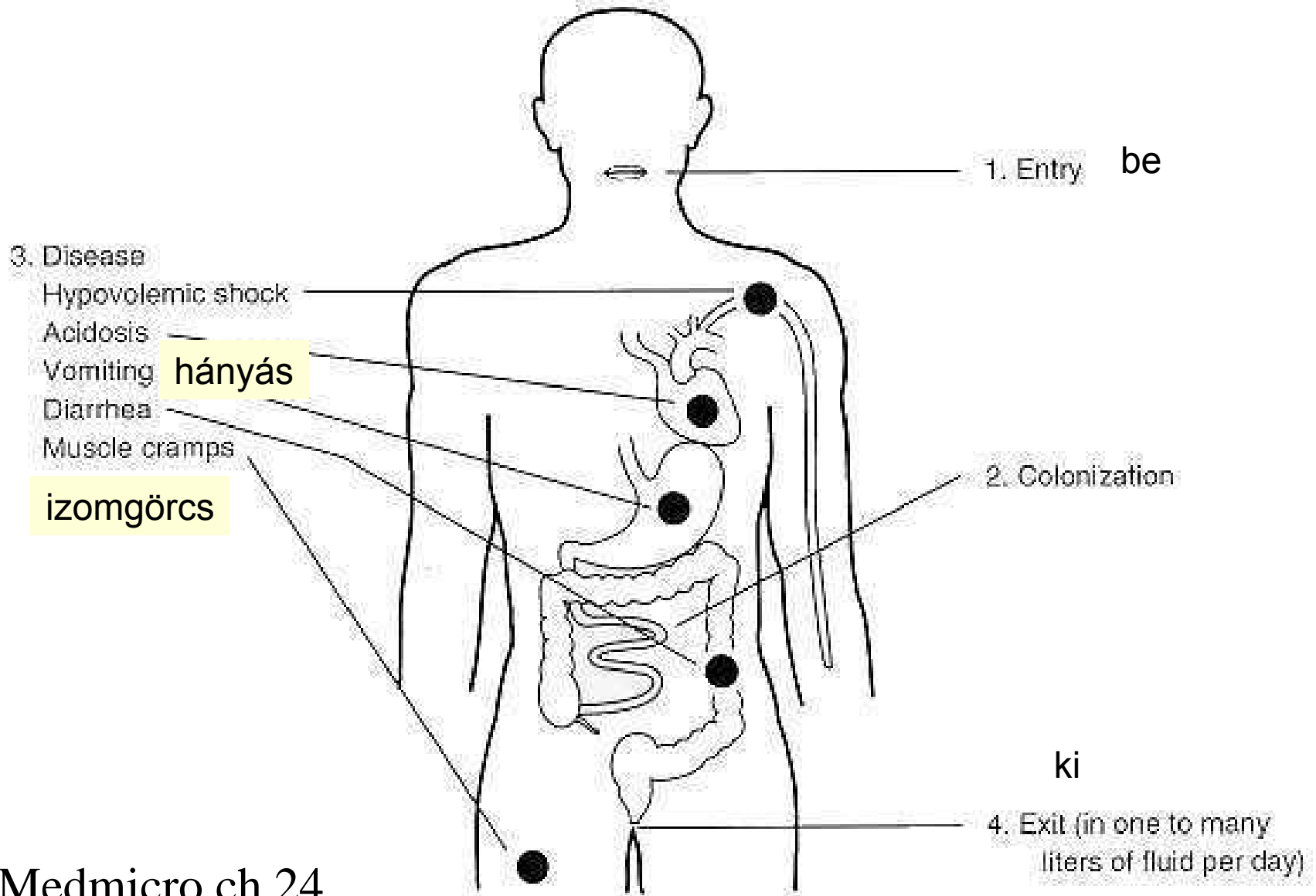


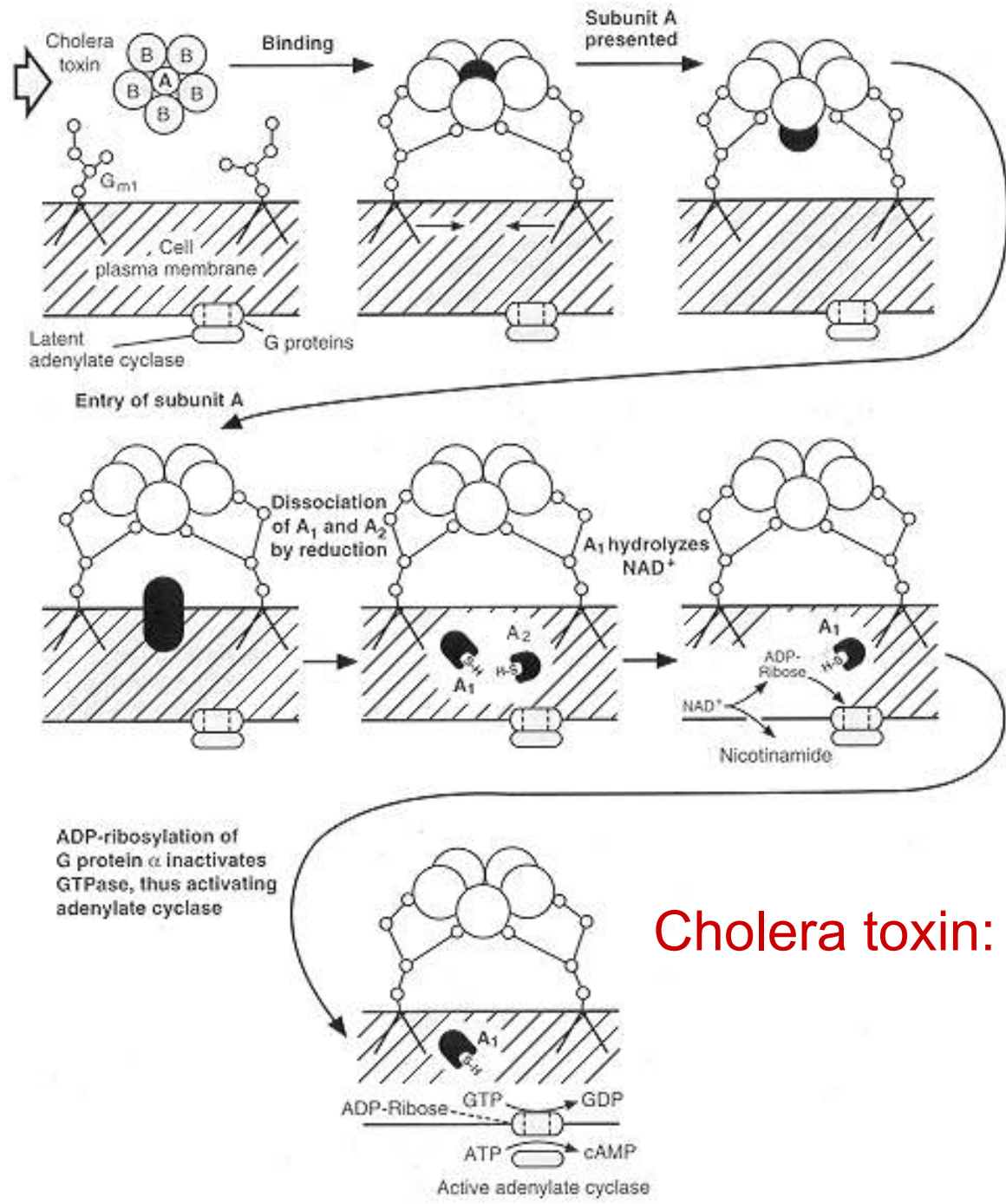
SEM, $\times 4.000$



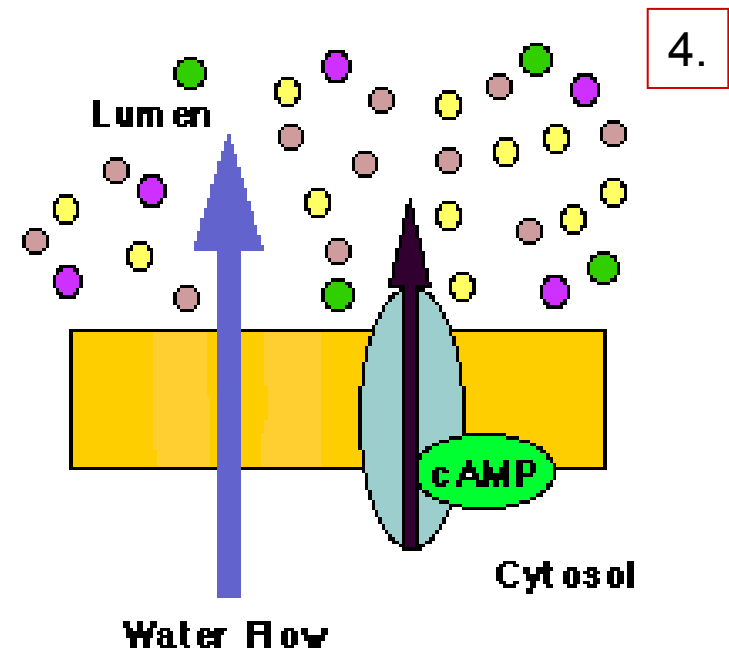
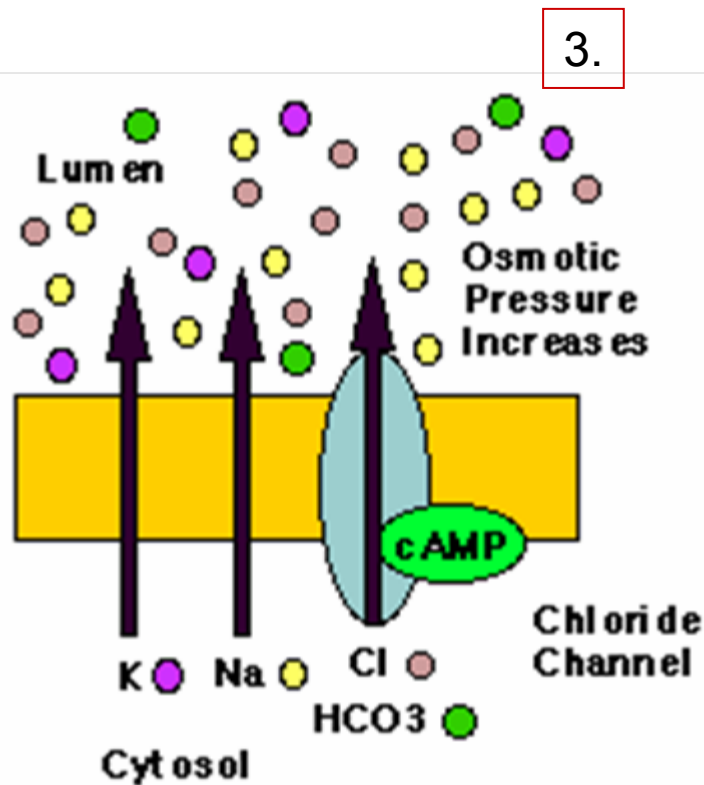
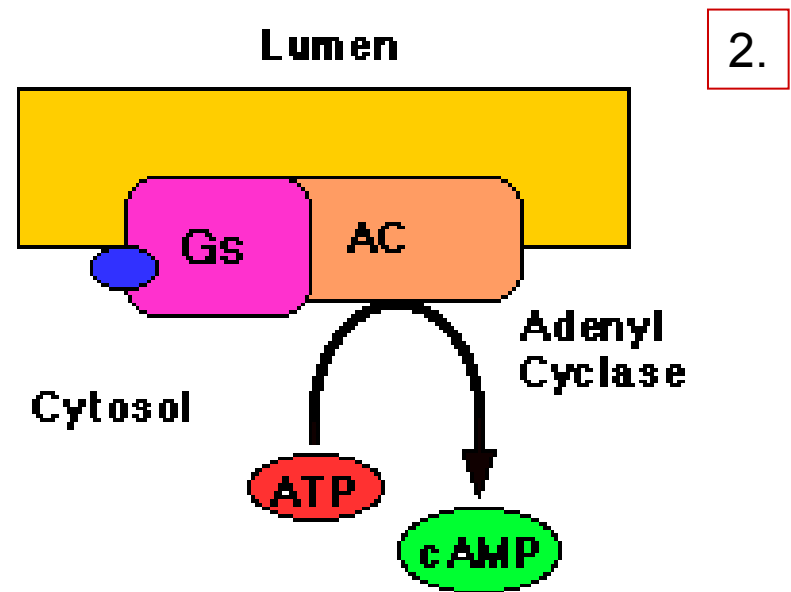
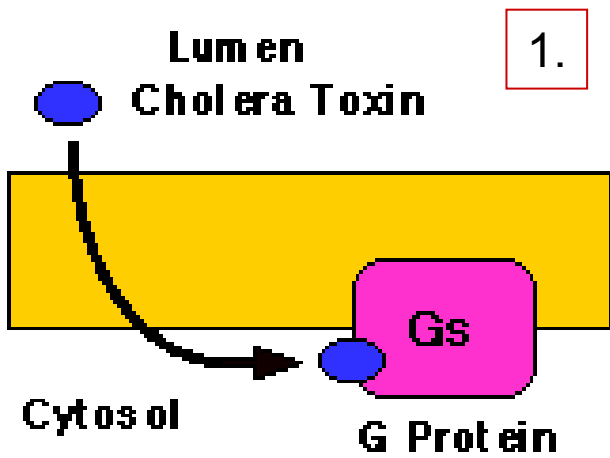
TEM, $\times 16.000$

FIGURE 24-1 Pathophysiology of cholera.

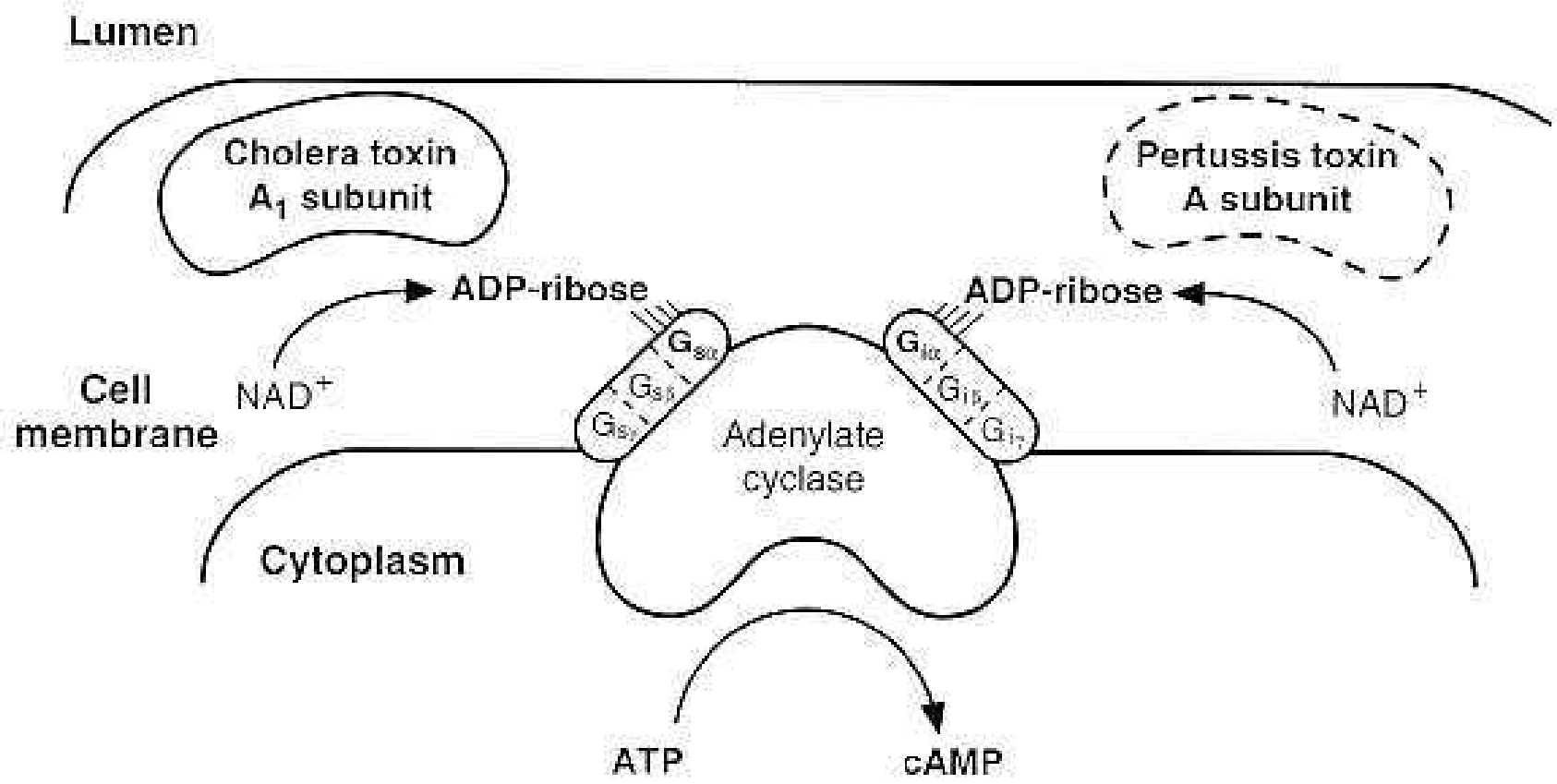




Cholera toxin: hatásmechanizmus



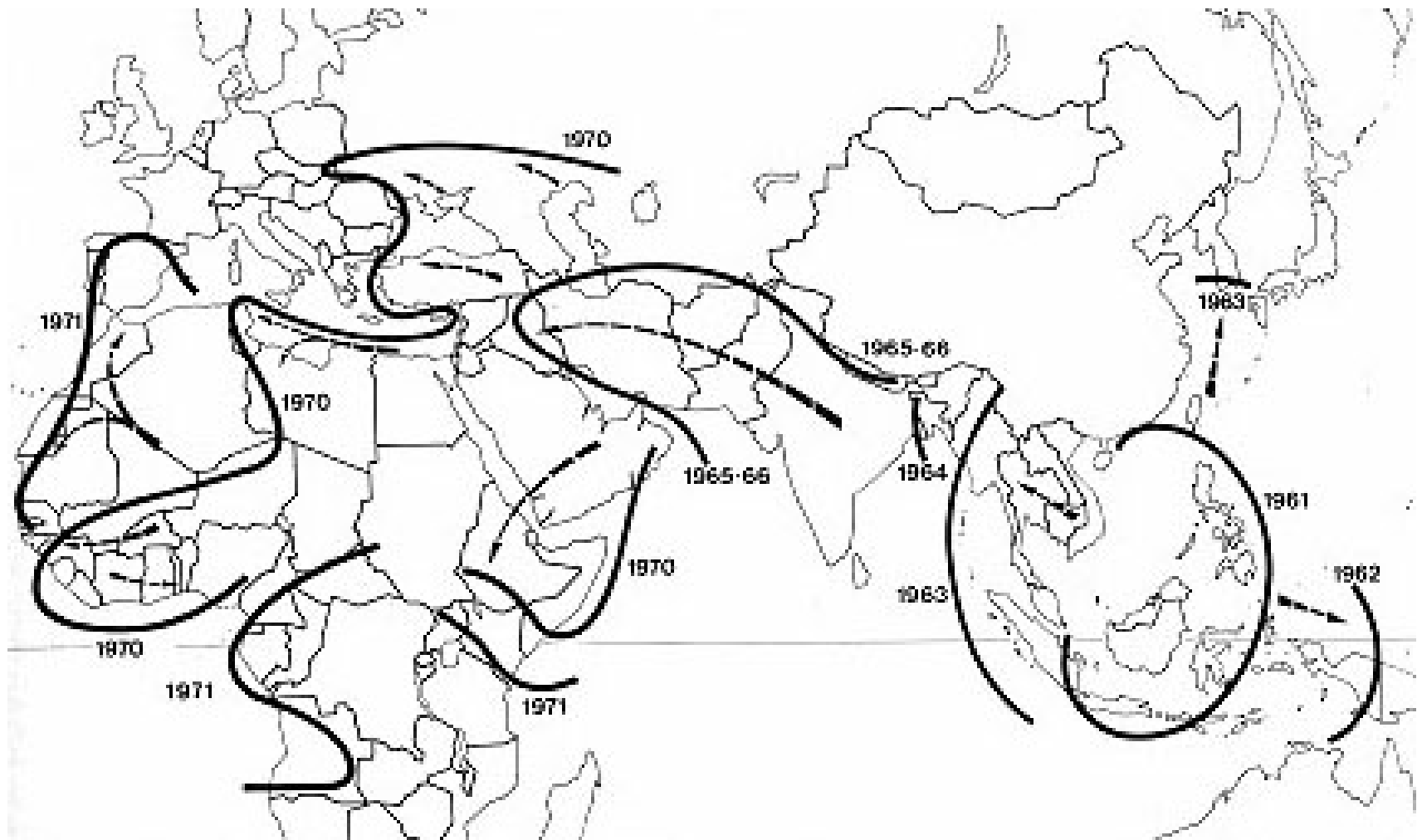
Cholera Toxin és Pertussis Toxin



Cholera Pandemia

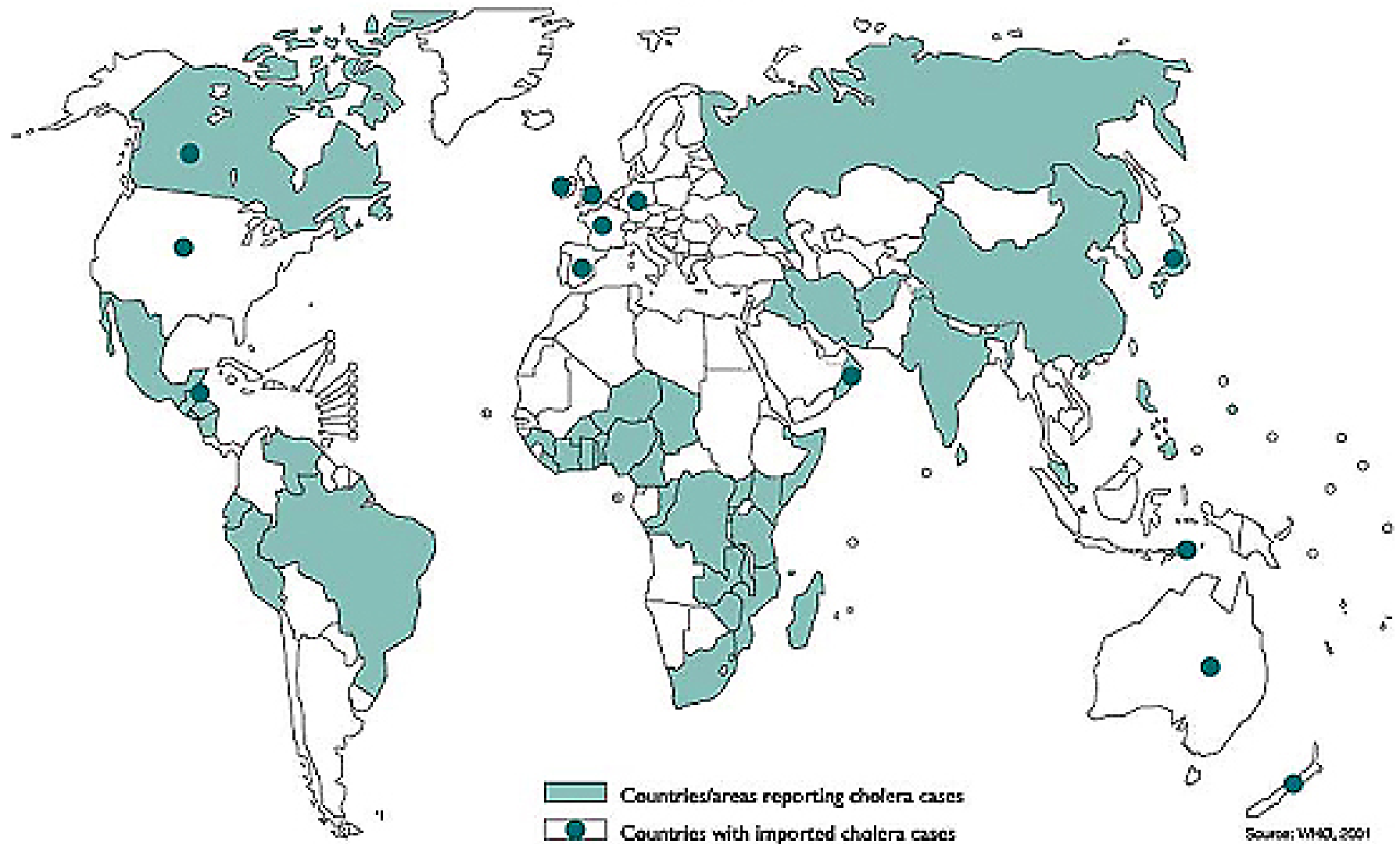
- **India, Ganges**
- **Intercontinentalis utazás, kereskedelem, háborúk ⇒ 7 pandemia 1817 óta**
- **jelenleg: 7. pandemia, V. El Tor**
 - 1961: Asia
 - 70's–80's: Africa, Europa, Oceania
 - 1991: dél-America
- **1992 : *V. cholerae* O139 „Bengal”**
 - Gyors terjedés (Asia, Europa, USA)
 - Nincs keresztimmunitás az O1-törzsekkel
 - 8. pandemia?

7th Cholera Pandemia 1961



Cholera esetek, WHO: 2000–2001

Cholera, 2000–2001

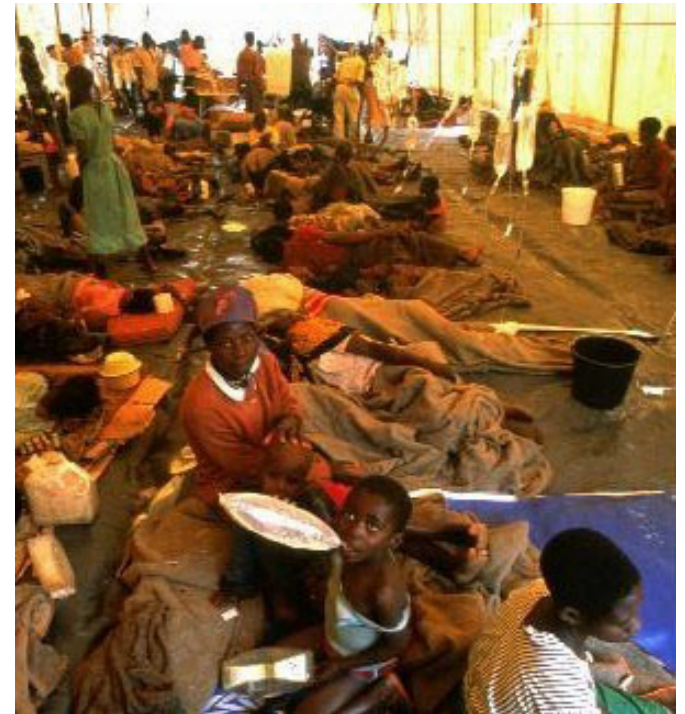


Source: WHO, 2001

Cholera járvány kitörése



Cholera camp in Mozambique



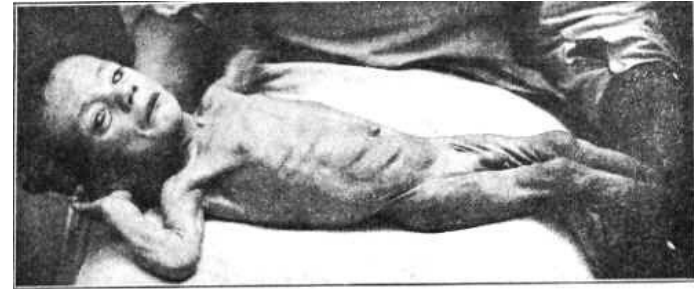
Cholera clinic in Mozambique

Cholera: klinikai kép

- Rizslé szerű diarrhoea (25 L/nap)
- Dehydratio
- Haemoconcentratio
- vér pH ↓
- Serum K^+ ↓, Na^+ ↓
- Serum Glucose ↑
- Shock
- Letalitás
 - kezeletlen
 - Classical: 60%
 - El Tor: 15–30%
 - kezelt: 1%

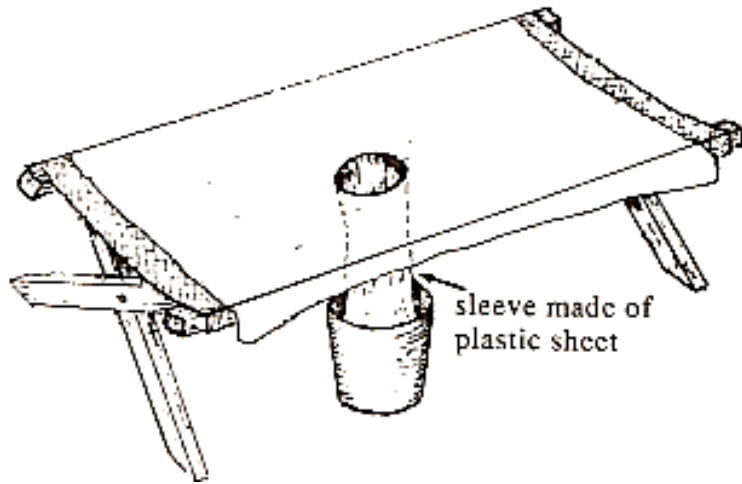


Rizslé szerű széklet



Rehydratio előtt és után

Cholera ágyak



Diagnosis

- anamnézis!
- minta: széklet
- Direct microscopos vizsgálat: sötét látótér

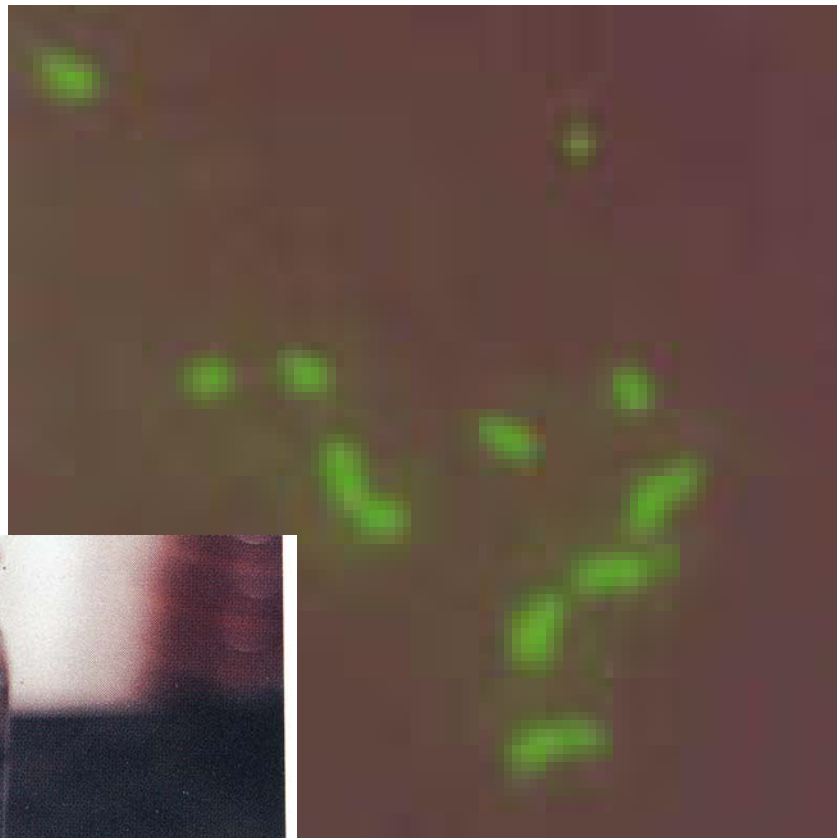
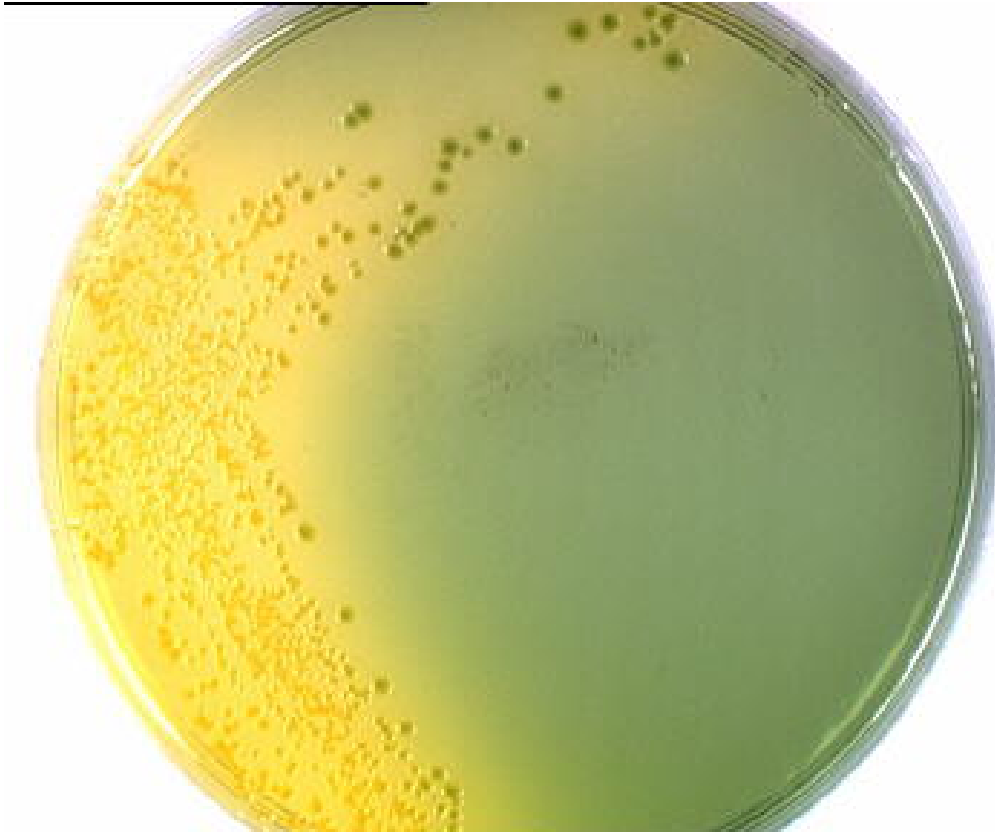
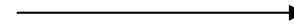


Fig. 50 Rice water stool in cholera. The voluminous watery stool excreted at the height of the illness is nearly colourless and contains flecks of mucus. Effects of the disease can be reversed by replacement of water and electrolyte losses. Courtesy of Dr A. M. Geddes.

Diagnosis

Transport: alkalikus peptonvíz
tenyésztés: TCBS táptalaj



Diagnosis



identifikálás

Biokémiai reakciók

szerotipizálás (O1, O139)

Antibiogram



V. cholerae

Prophylaxis

Expositio prophylaxis

Tiszta ivóvíz! – élelmiszer higiénie,
szennyvízhálózat, csatornázás – ivóvíz hálózat
védelme a szennyeződéstől!

Tömegtájékoztatás, nevelés, higiénés
szabályok betartása, betartatása

Isolatio; Quarantine

kezelés, fertőtlenítés, vízforralás

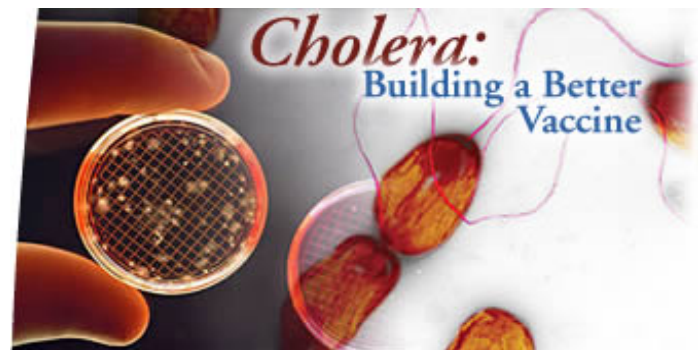
Hordozók követése, felkutatása, kezelése

Bejelenteni! (helyi hatóságok, WHO)

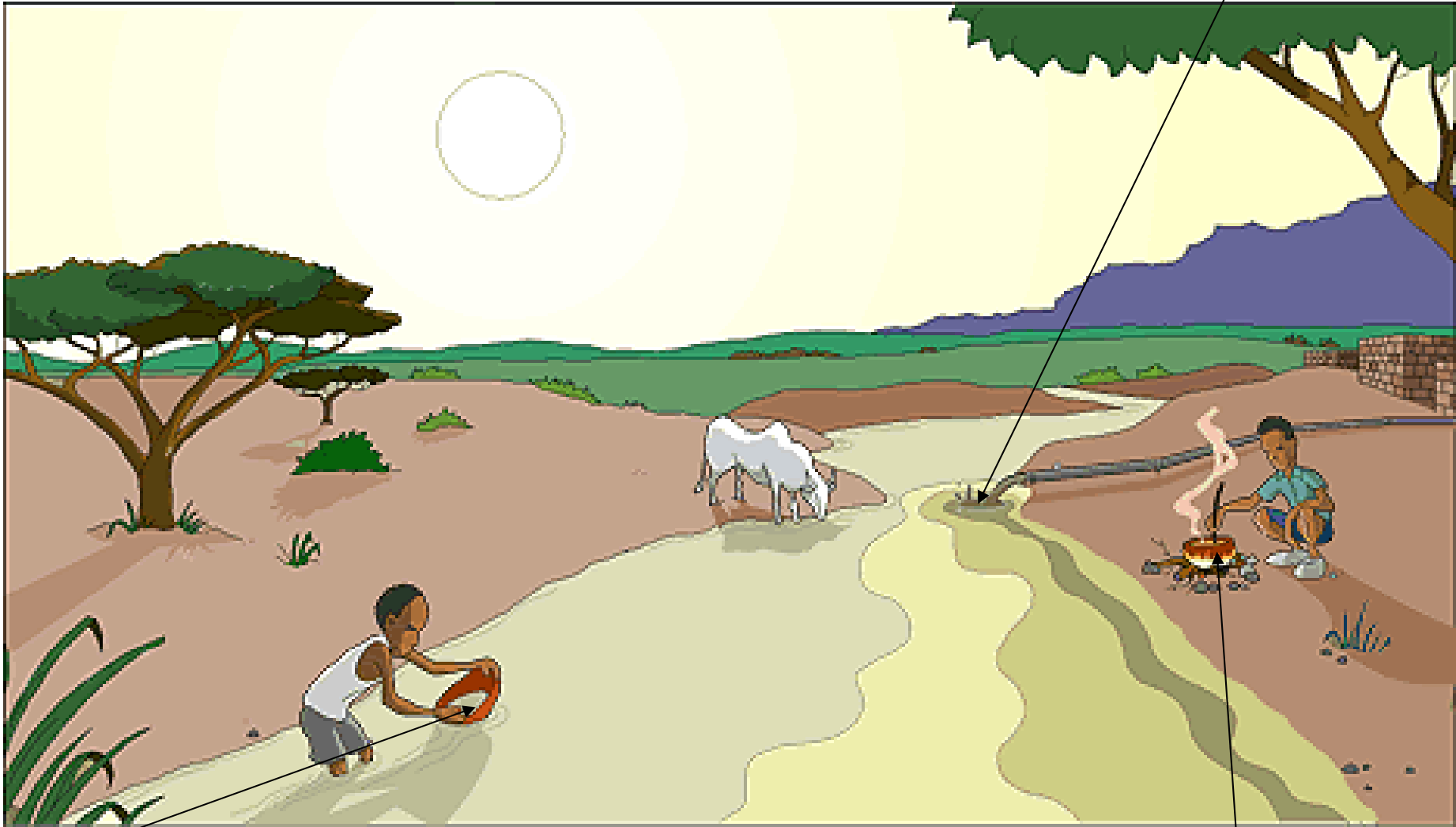
• Immune prophylaxis

Vaccinatio

- Vaccina (csak O1 ellen!)
 - **Elölt bacterium, parenteralis**
 - elölt bacterium + B-alegység Toxoid *per os*
 - Gén manipulált, attenuált *V. cholerae per os*
- Védelem: 3–6 hónapig tart, 50–60%-os
- Endémiás területre utazók
- WHO: hamis biztonságérzet (!)



Prevention of cholera: mass education of hygienic rules



Cholera Therapia



Salt-sticks



Coke

Cholera Therapia

- **Folyadék és electrolyte pótlás**

- Intravénás
- Per os Oral Rehydration Fluid
ORF

- Glucose 20g/l
- NaHCO_3 : 2,5 g/l
- NaCl: 3,5 g/l
- KCl: 1,5 g/l

- **Antibioticum**

- Ciprofloxacin
- Doxycycline

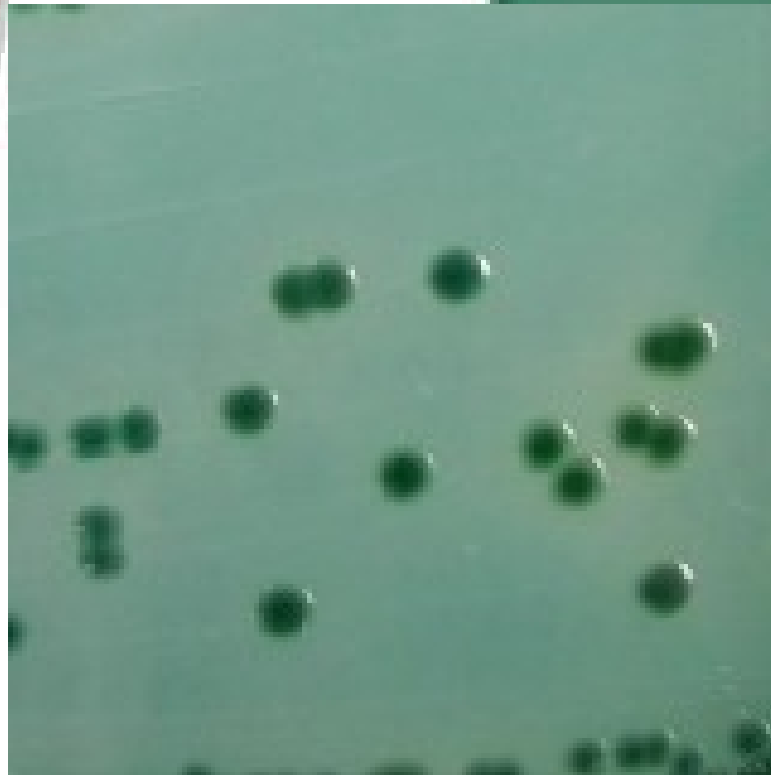
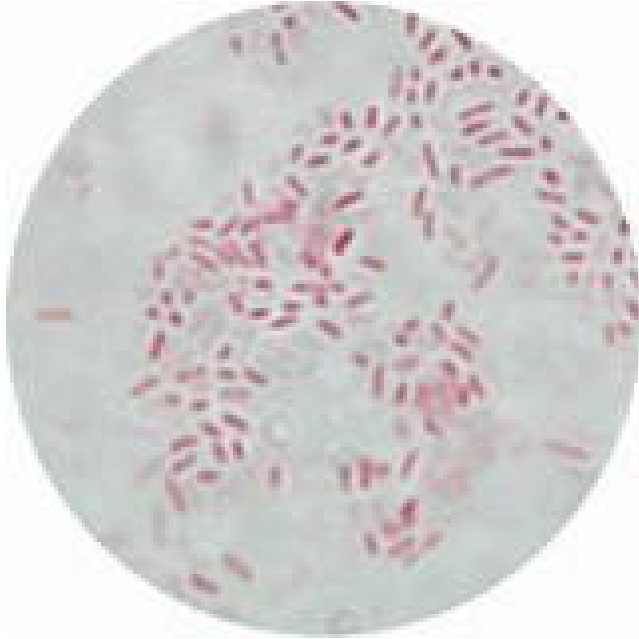


Peru



Bangladesh

Vibrio parahaemolyticus



"Vibrio Parahaemolyticus"

Food Poisoning



Gastroenteritis



V. vulnificus

Fig. 10.20 Cellulitis. Severe infection with bullous lesions due to *V. vulnificus* infection following immersion of leg in brackish water.

A clinical photograph showing the patient's arm with a large, dark, bullous lesion characteristic of Vibrio vulnificus cellulitis. The lesion is dark purple to black, indicating hemorrhage, and is surrounded by a lighter, erythematous, and edematous area. The patient's arm is positioned vertically, and the lesion is located on the upper arm. The background is a light blue clinical drape.

V. vulnificus

**Fig. 10.21 Vibrio
cellulitis. Haemorrhagic,
bullous lesions of V.
vulnificus sepsis. By
courtesy of Dr. J.R.
Cantey**

A. hydrophila



A. hydrophila infectio halban



Natural water sources

P. shigelloides



Sea food



Cellulitis

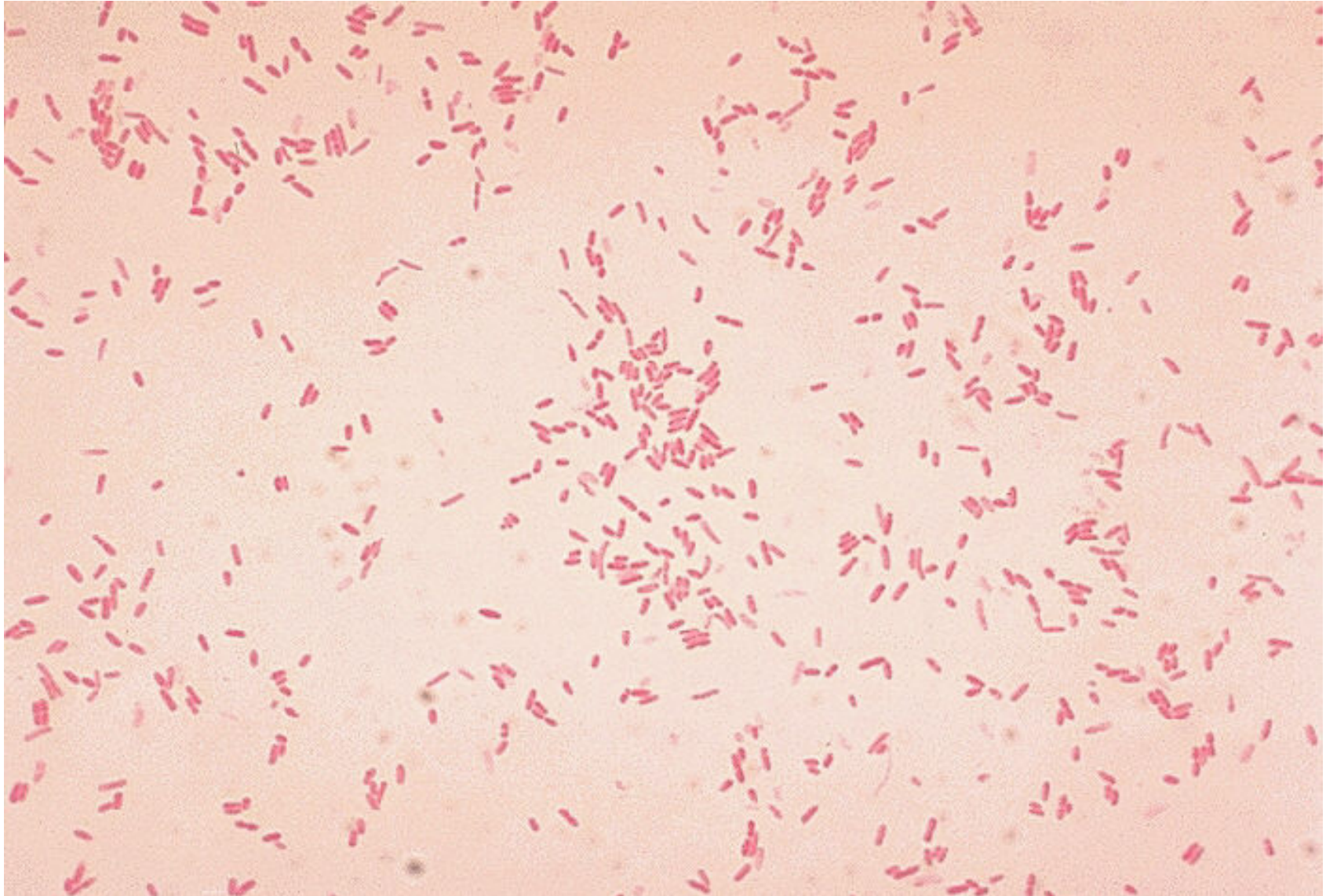


Myonecrosis

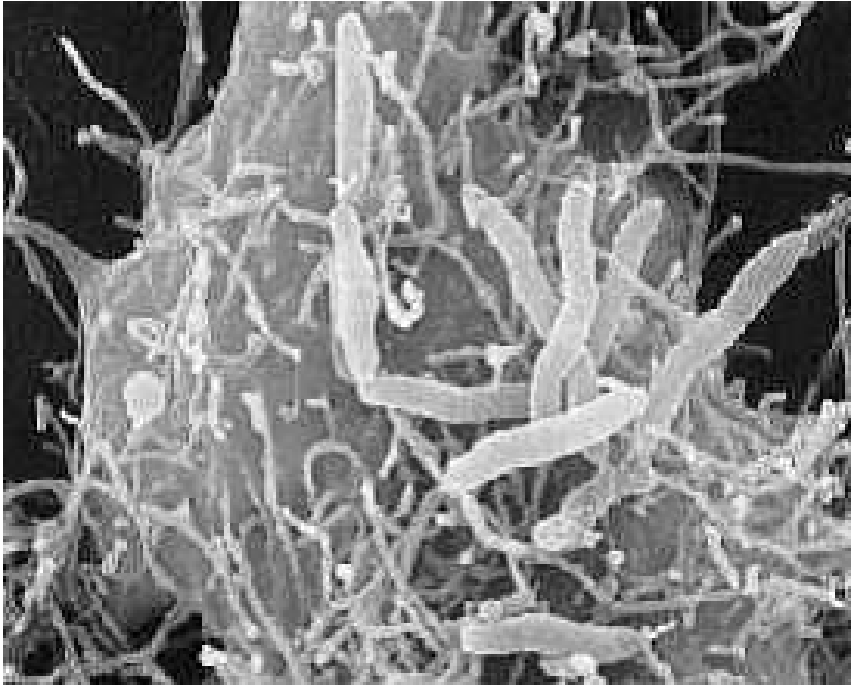
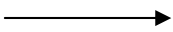


Gastroenteritis

Aeromonas hydrophi 1a



Aeromonas hydrophi 1 a



Plesiomonas shigelloides

<http://www.vetmed.wisc.edu>

web.umn.edu

www.buddycom.com

Aeromonas hydrophila a



Aeromonas hydrophila



Zakynthos, 2004

Folyt. Köv. ...

