Samedi 21 et dimanche 22 novembre 1987

TRIBUNE DE GENEVE

INTERDIT PAR LE CONSEIL D'ÉTAT VAUDOIS

MORT AU VACHERIN

Nouveau coup dur pour le vacherin Mont-d'Or: ce fromage fabriqué dans le Jura vaudois doit être immédiatement retiré du marché et ne plus être exporté parce que sa croûte peut être infectée par une bactérie responsable de la listériose. Ainsi en a décidé vendredi l'Office fédéral de la santé publique (OFSP). Le Conseil d'Etat vaudois quant à lui a interdit avec effet immédiat la fabrication et la commercialisation du Mont-d'Or après avoir constaté une recrudescence de cas de listériose humaine dans le canton. Cette maladie provoque le décès de plusieurs personnes chaque année en Suisse depuis 1983. Dix cas, dont trois mortels, ont été recensés dans le canton de Vaud depuis la mi-octobre, date à laquelle une nouvelle épidémie s'est propagée.

page 3

Pommersche Gutsleberwurst
fein und grob, je 100 g

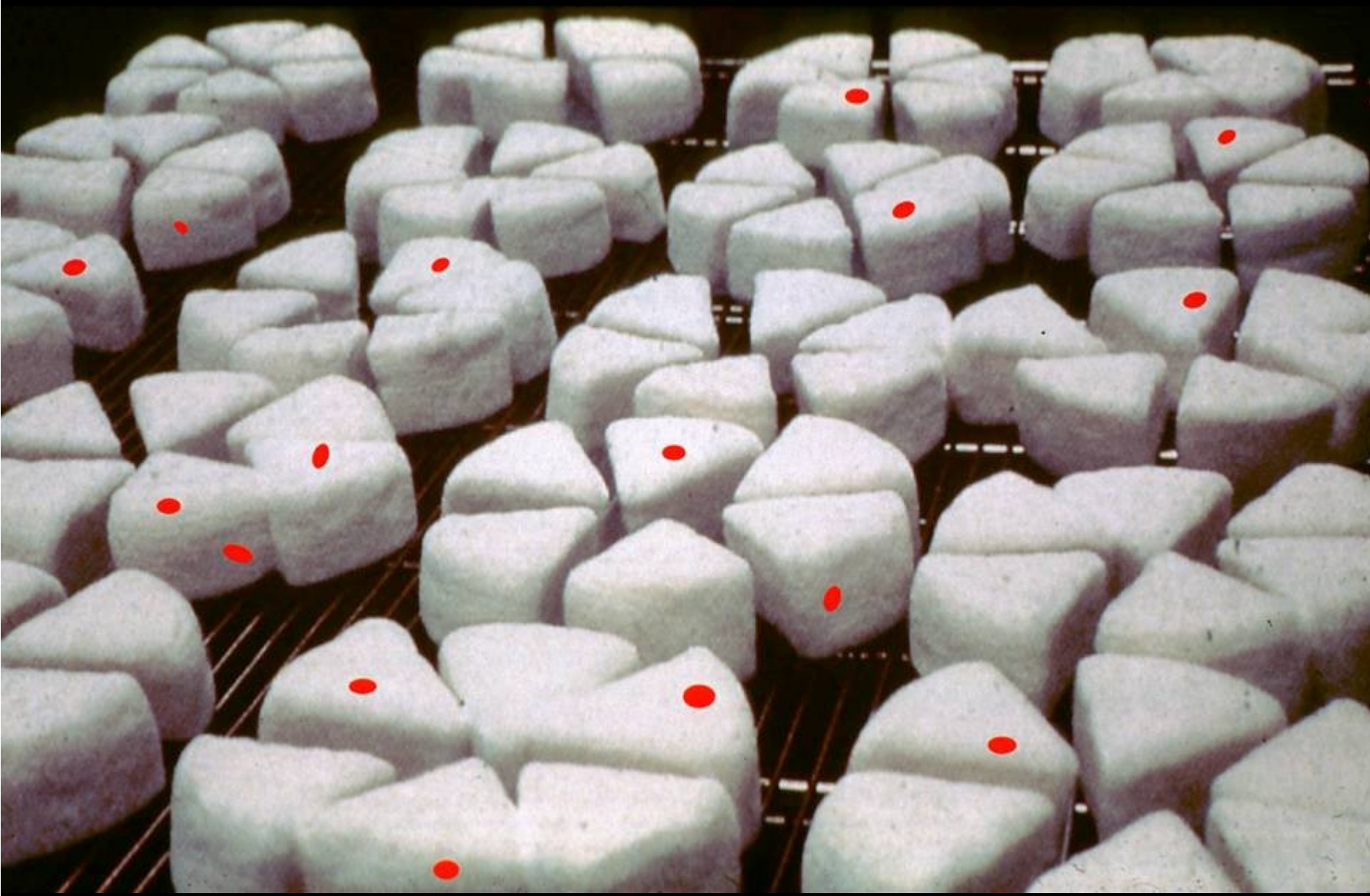
2,28
€ 1,17

Bauernsalami "Hausmacherqualität"
1-kg-SB-Packung

9,98
€ 5,10

Frisches Lachsfilet
Eine Spezialität zum Braten oder Pochieren, 100 g

1,98
€ 1,01

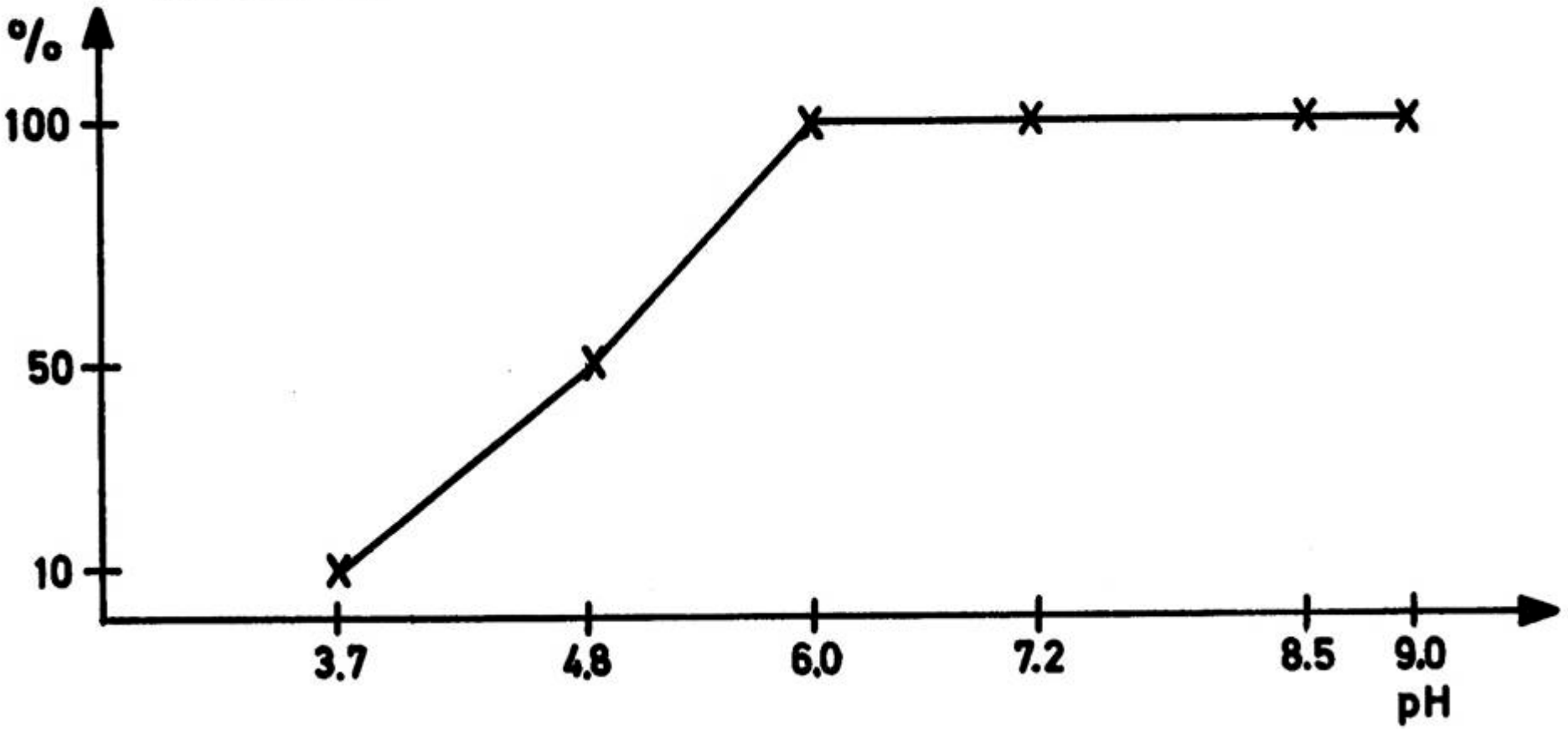


Frequency of contamination with *Listeria* of various food items (not all isolates belong to pathogenic species)[a]

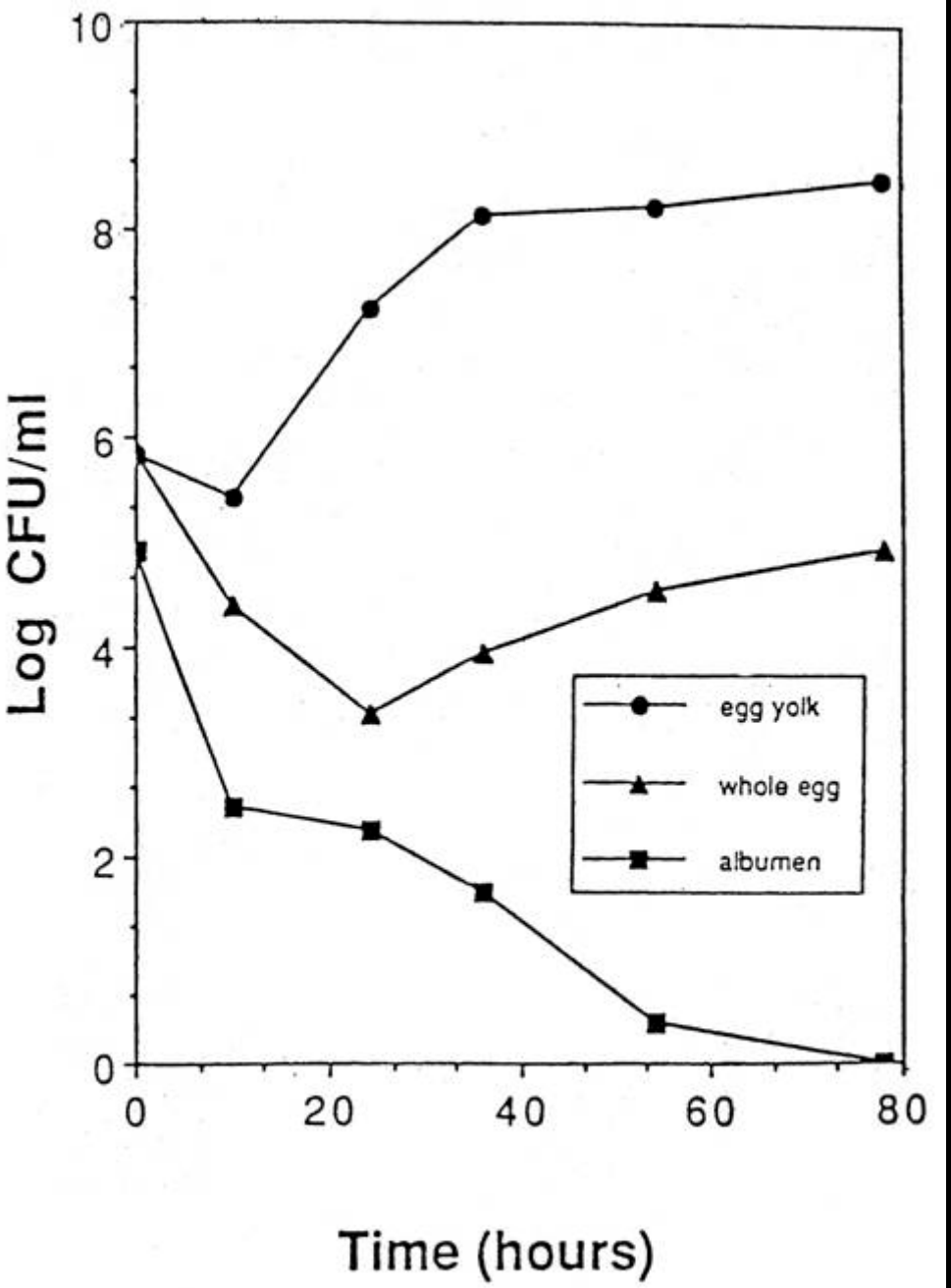
Specimen	Frequency
Raw milk	1–5%
Cheese (soft)	10–20%
Meat (beef, pork): raw	≤50%
ready to eat	1–3%
Sausage (salami, mettwurst)	≤80%
Pâté	≤50%
Poultry	≤60%
Seafood	≤20%
Mushroom	10%
Lettuce	10–20%
Radish	20–30%
Carrot	0%
Tomato	0%

[a]Data taken from Ref. 4

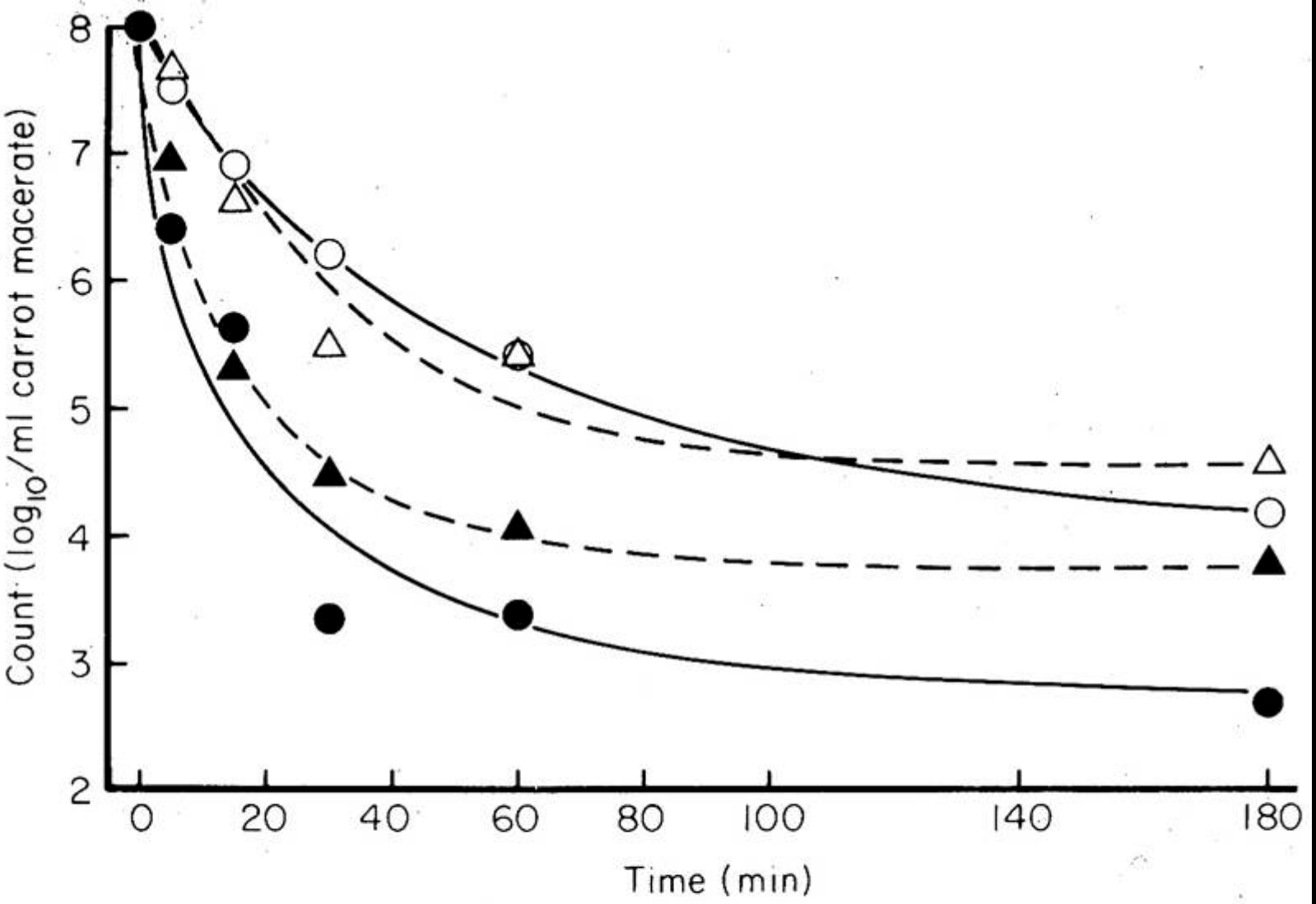
pH-stability of L. monocytogenes.
Survival rate 1 hour after inoculation of Na-barbital acetate buffer




Rama



Behavior of L. monocytogenes *Brie-1 in raw whole egg, albumen, and egg yolk at 20°C*



The survival of *Listeria monocytogenes* strain LM 82 in a carrot macerate at 4°C (●, ○, ———) or 30°C (▲, △, – – – –). Numbers of listerias were determined on Oxford agar (closed symbols) and on tryptose agar + streptomycin (open symbols)

Food safety

List of food items which may contain *L. monocytogenes*

- Sausages (Salami, Paté)
- Raw meat, in particular turkey and chicken
- Sandwiches
- Lettuce, raw mushrooms
- Raw milk and products made from this material (i.e. mayonnaise)
- Soft cheese (Munster, Roquefort, Camembert, Brie)
- Fresh cheese (ricotta, feta)
- Sea food (mussels, salmon)
- All kind of meals which are conserved after having been heated

List of food items which in general are free of Listeriae

- all kinds of food immediately after heating
- pasteurized milk, yoghurt (industrial products!)
- hard cheese
- chocolate, marmalade, cookies
- raw carrots
- raw apples
- raw tomatoes

Dietary Recommendations for Preventing Food-Borne Listeriosis

For all persons:

- Thoroughly cook raw food from animal sources (e.g., beef, pork, and poultry).
- Thoroughly wash raw vegetables before eating.
- Keep uncooked meats separate from vegetables, cooked foods, and ready-to-eat foods.
- Avoid consumption of raw (unpasteurized) milk or foods made from raw milk.
- Wash hands, knives, and cutting boards after handling uncooked foods.

Additional recommendations for persons at high risk (those immunocompromised by illness or medications, pregnant women, and the elderly):

- Avoid soft cheeses (e.g., Mexican-style, feta, Brie, Camembert, and blue-veined cheese). (There is no need to avoid hard cheeses, cream cheese, cottage cheese, or yogurt.)
- Leftover foods or ready-to-eat foods (e.g., hot dogs) should be reheated until steaming hot before eating.
- Although the risk for listeriosis associated with foods from delicatessen counters is relatively low, pregnant women and immunosuppressed persons may choose to avoid these foods or to thoroughly reheat cold cuts before eating.

People at risk (YOPI)

Young

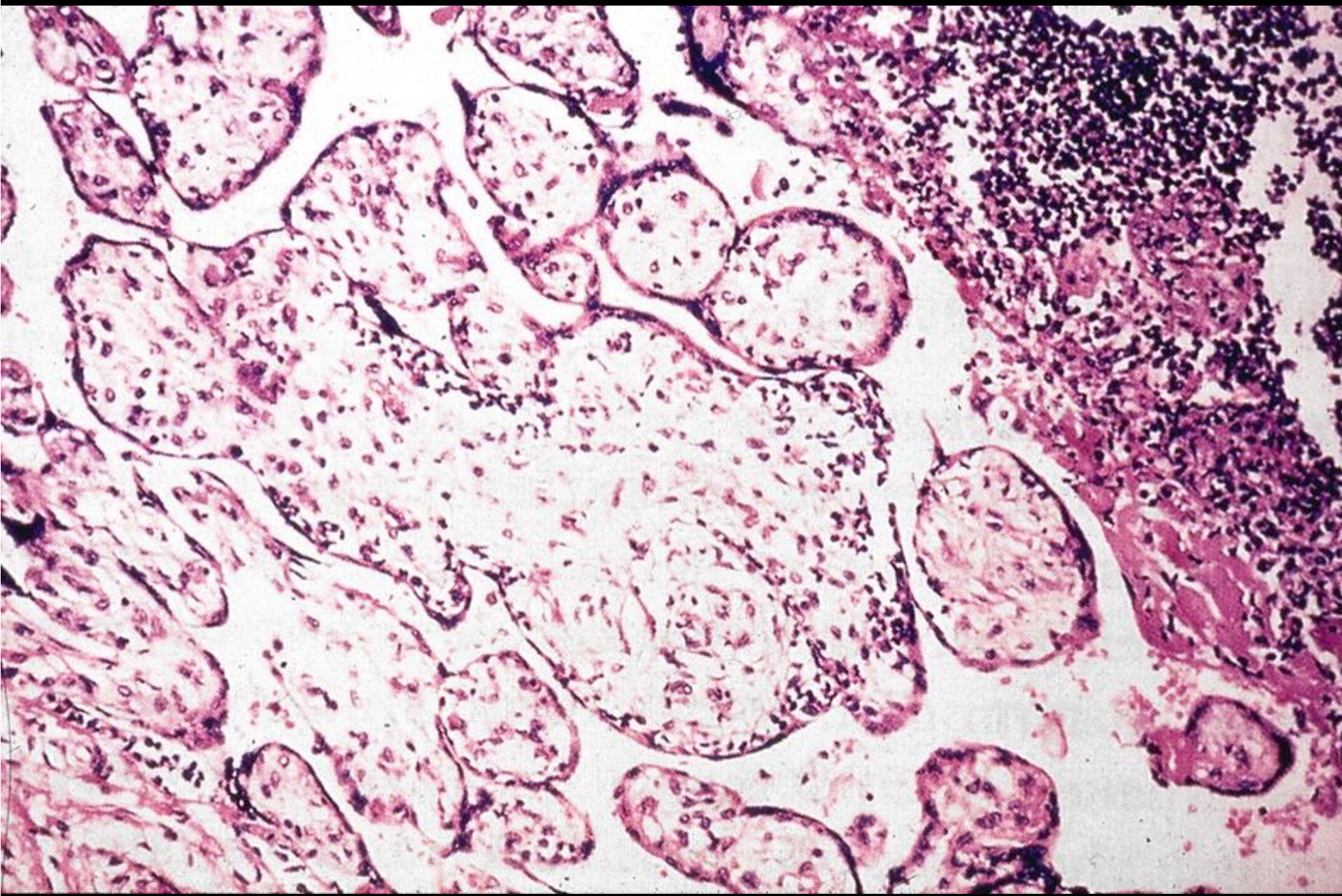
Old

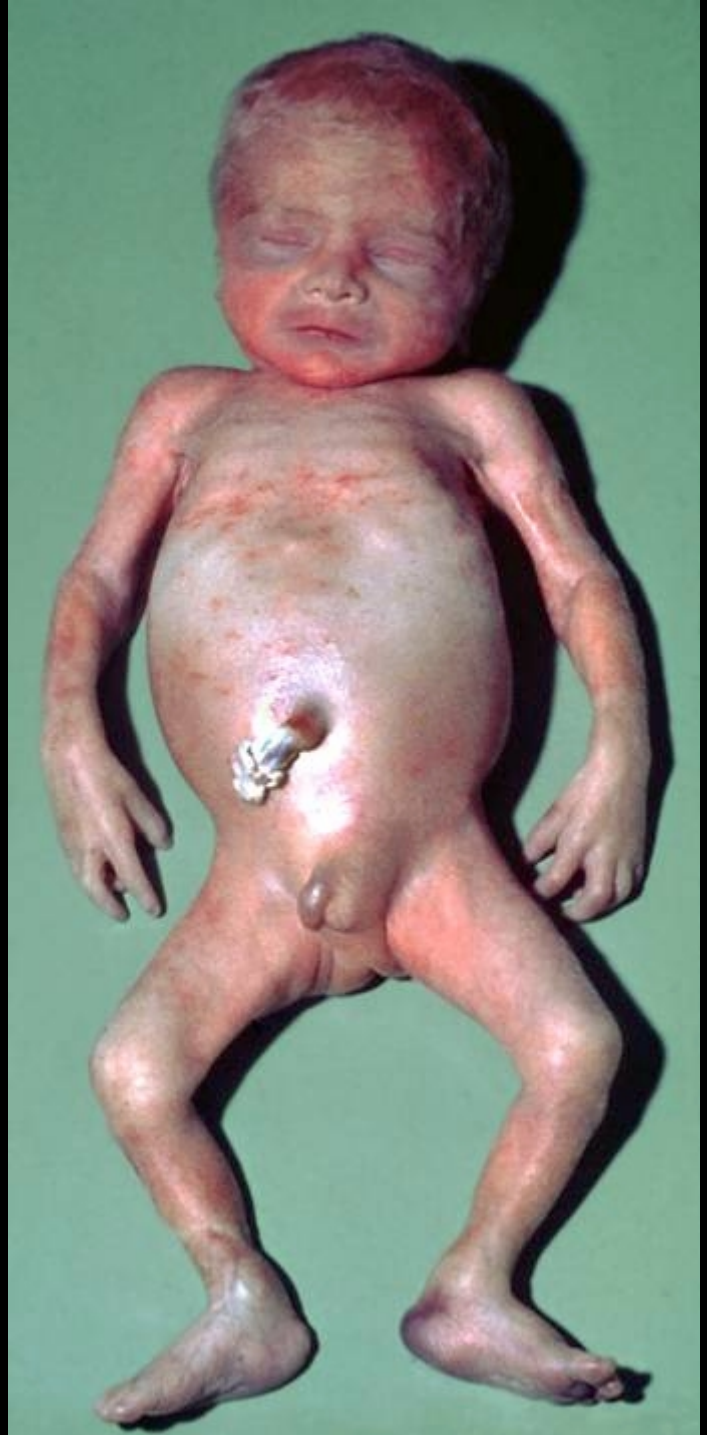
Pregnant

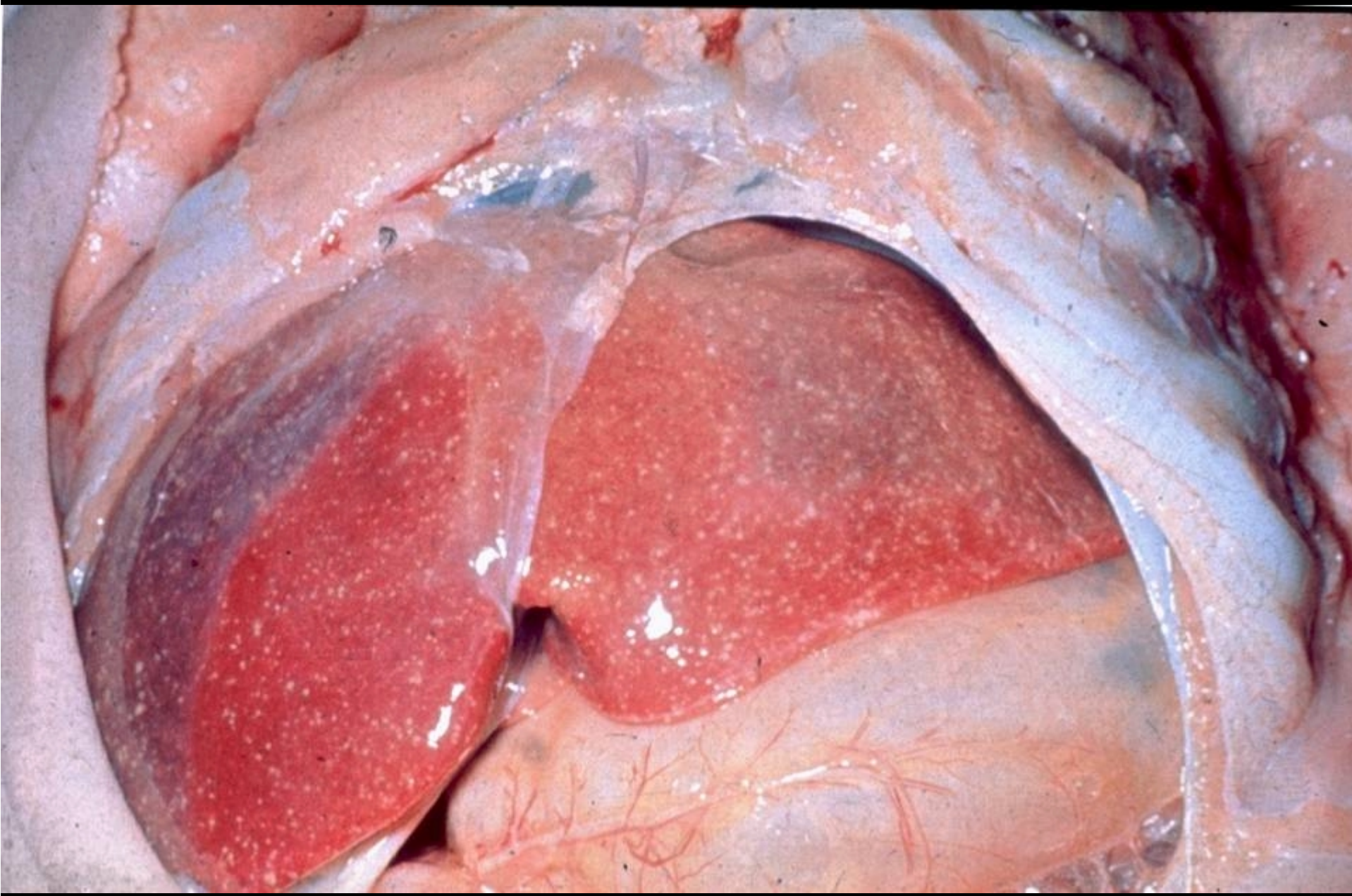
Immuno-compro-mised

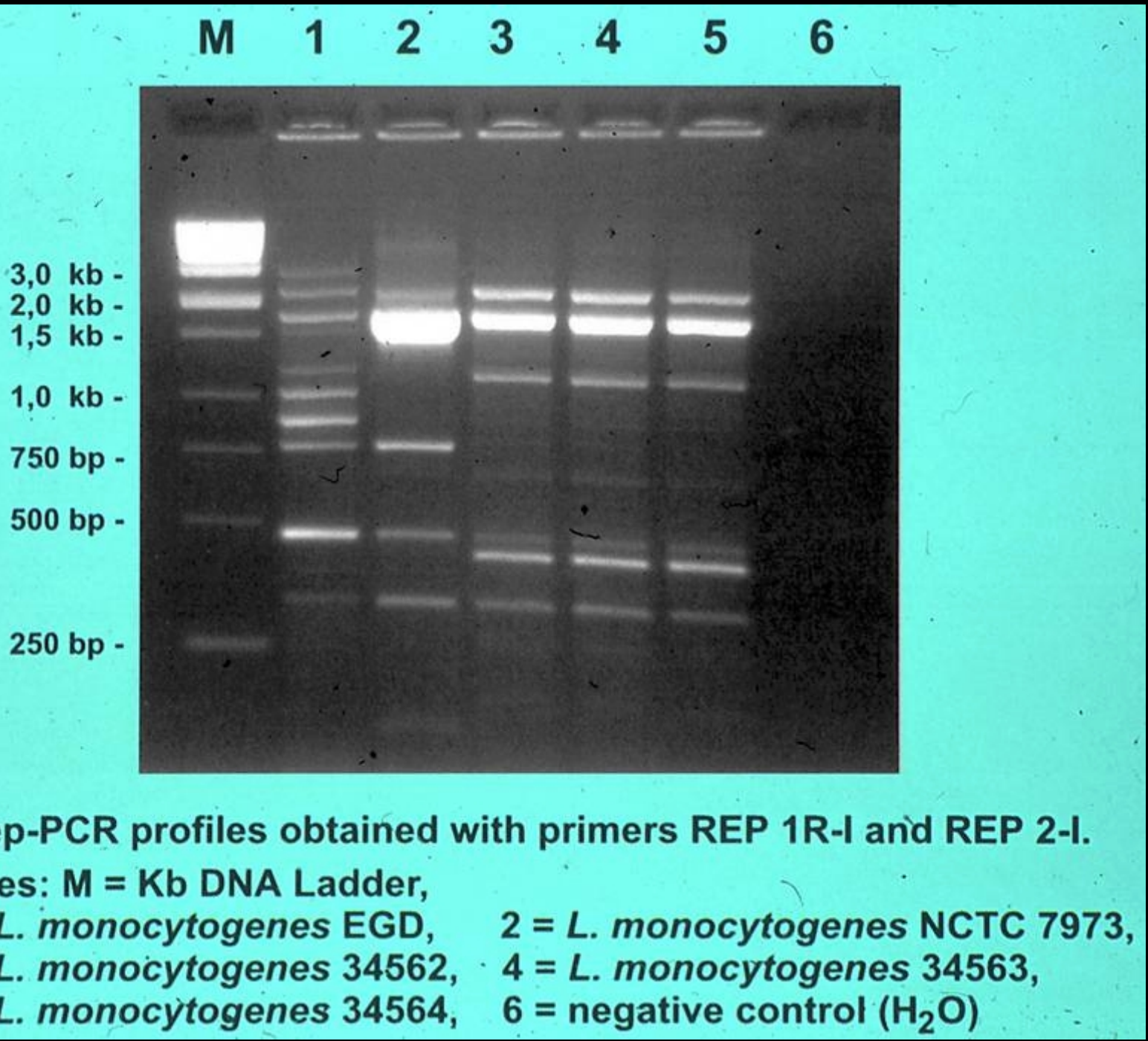
Incidence of listeriosis in certain populations at risk (per 100,000 individuals a year)

Normal population	0.7
Aged persons (> 70 years)	2
Alcoholics	5
Diabetic people	5
Iron overload	5
Pregnant women	12
Cancer patients	15
Steroid therapy	20
Lupus erythematodes	50
Kidney transplant recipient	100
Chronic lymphatic leukemia (CLL)	200
AIDS	600
Leukemia (AML+ALL)	1,000



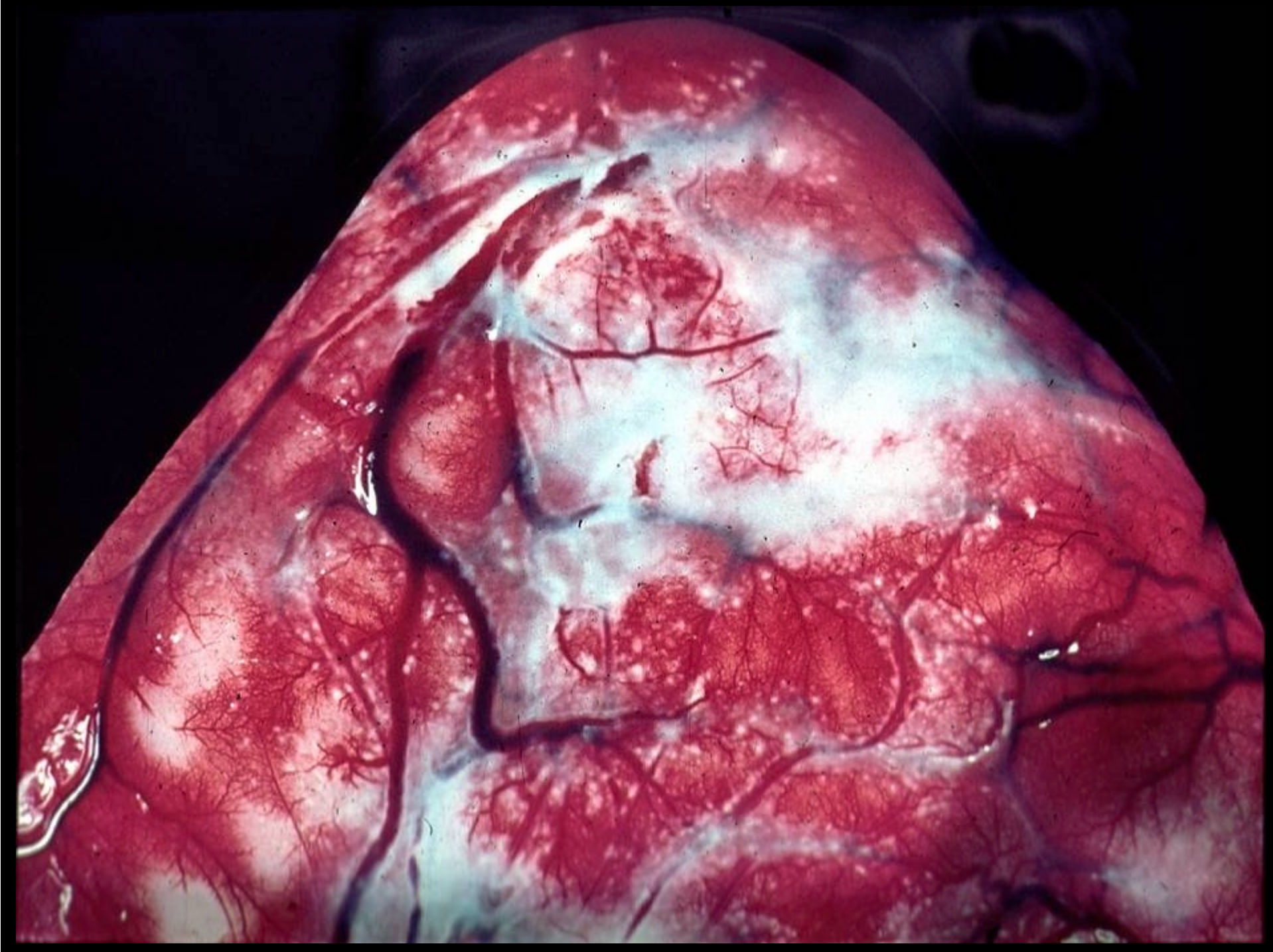


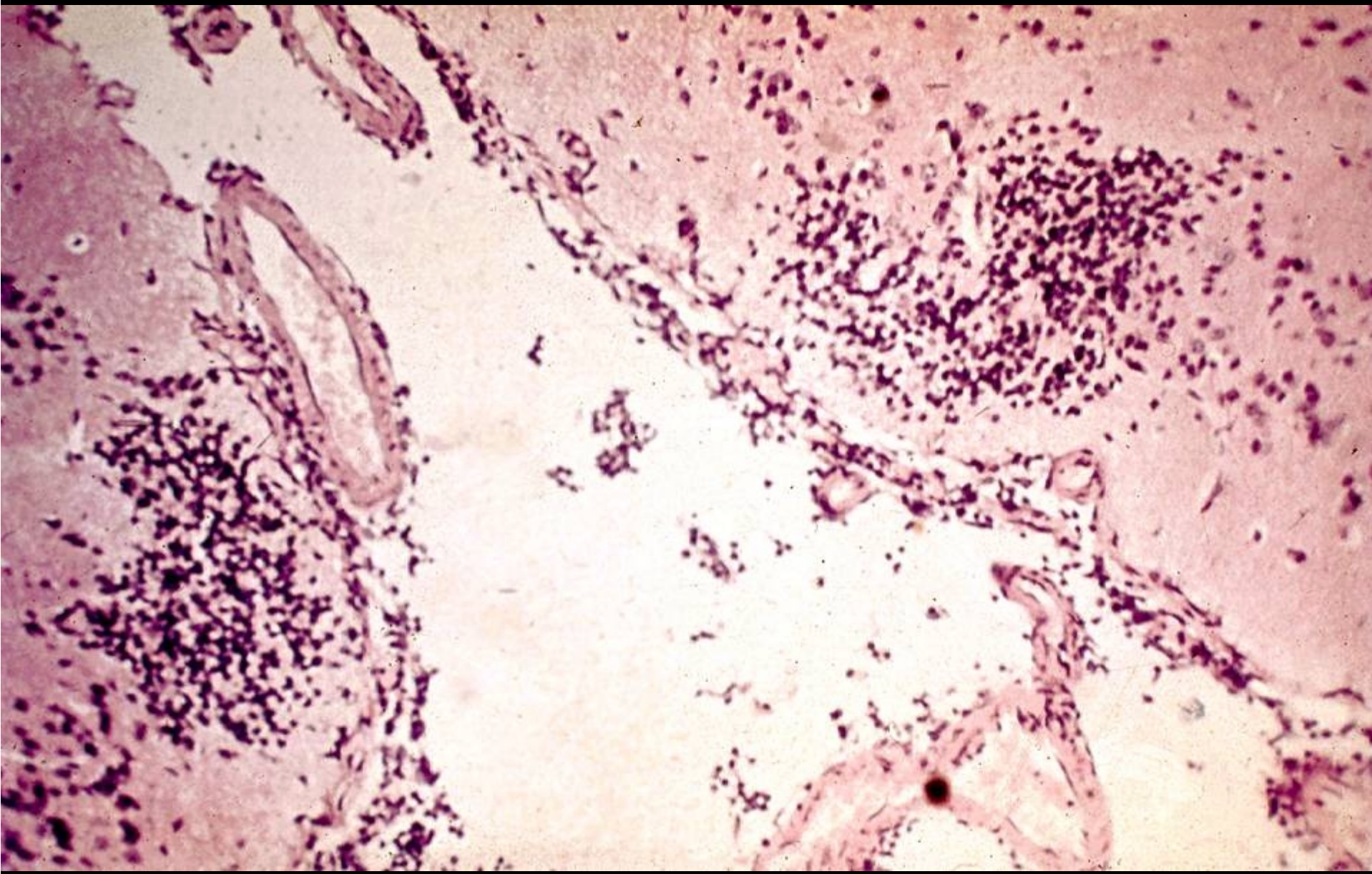


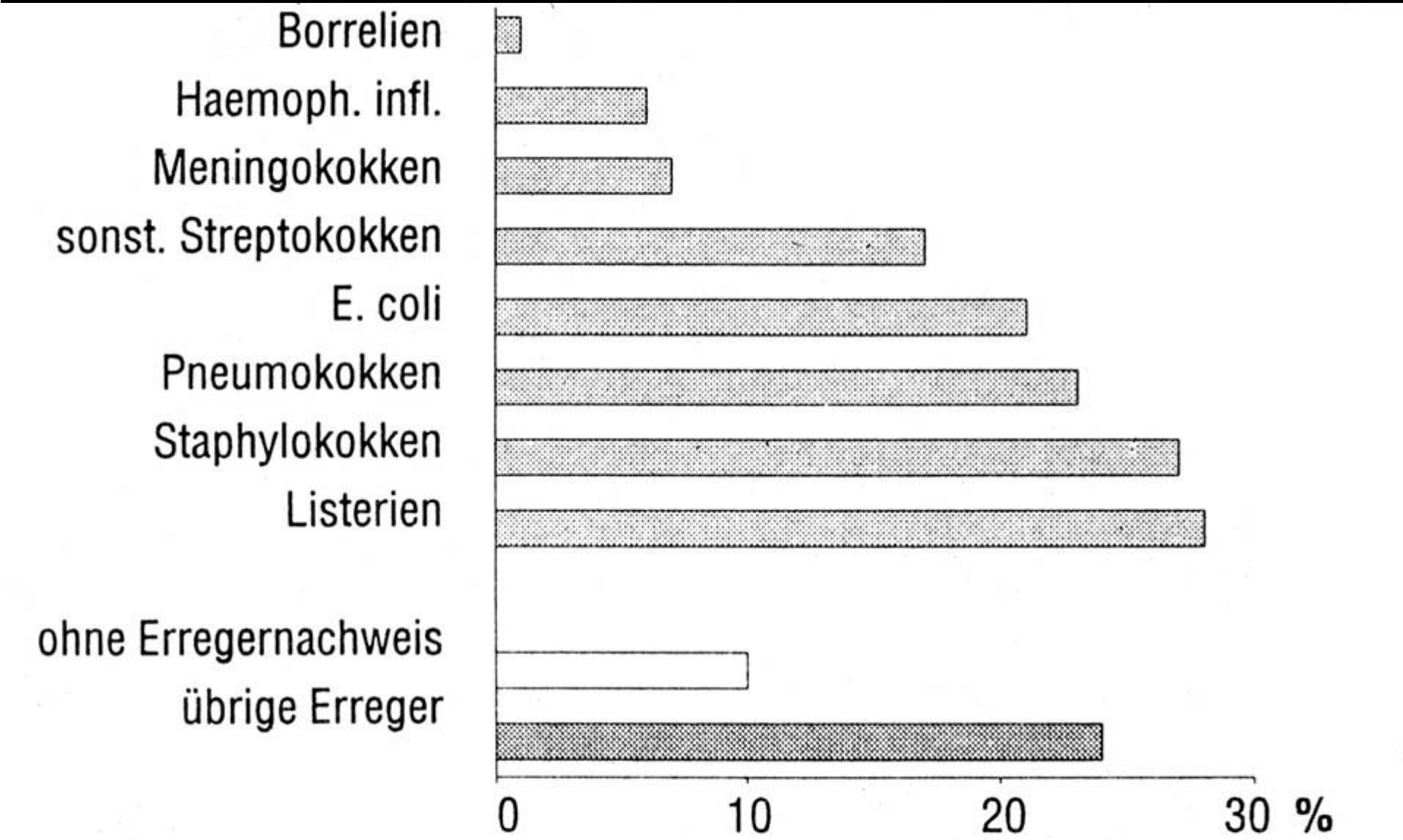


rep-PCR profiles obtained with primers REP 1R-I and REP 2-I.

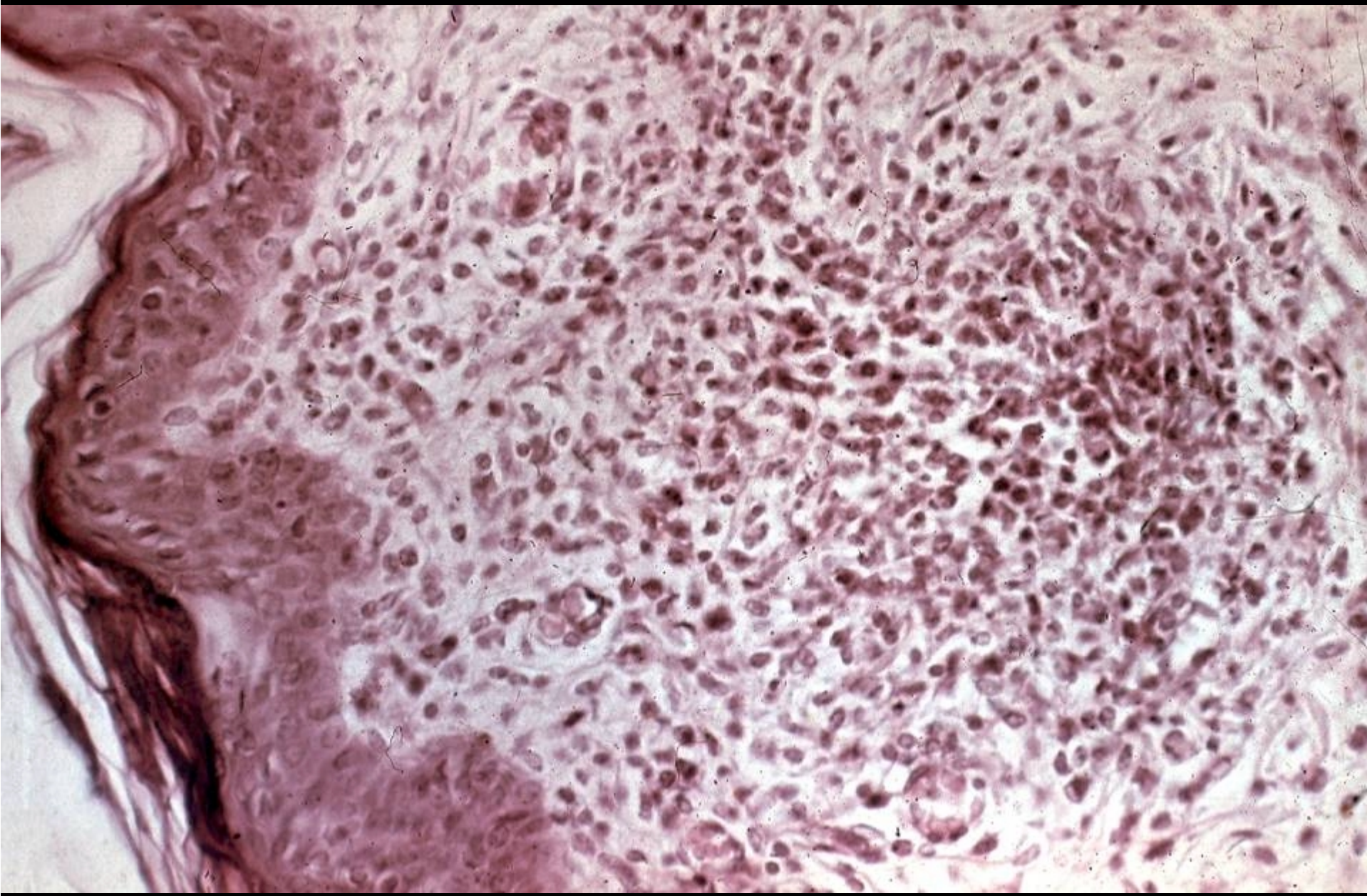
Lanes: M = Kb DNA Ladder,
1 = *L. monocytogenes* EGD, 2 = *L. monocytogenes* NCTC 7973,
3 = *L. monocytogenes* 34562, 4 = *L. monocytogenes* 34563,
5 = *L. monocytogenes* 34564, 6 = negative control (H_2O)

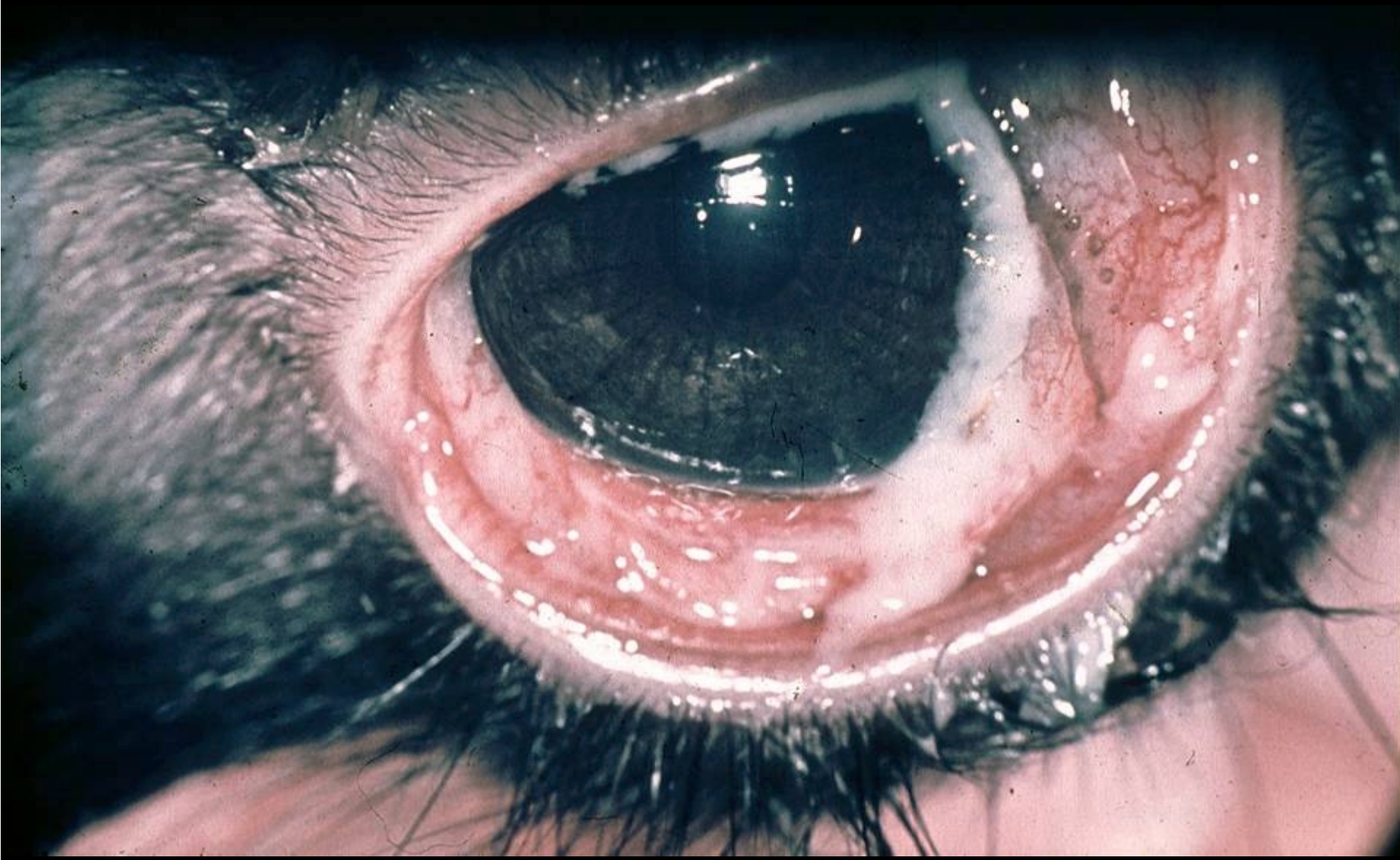






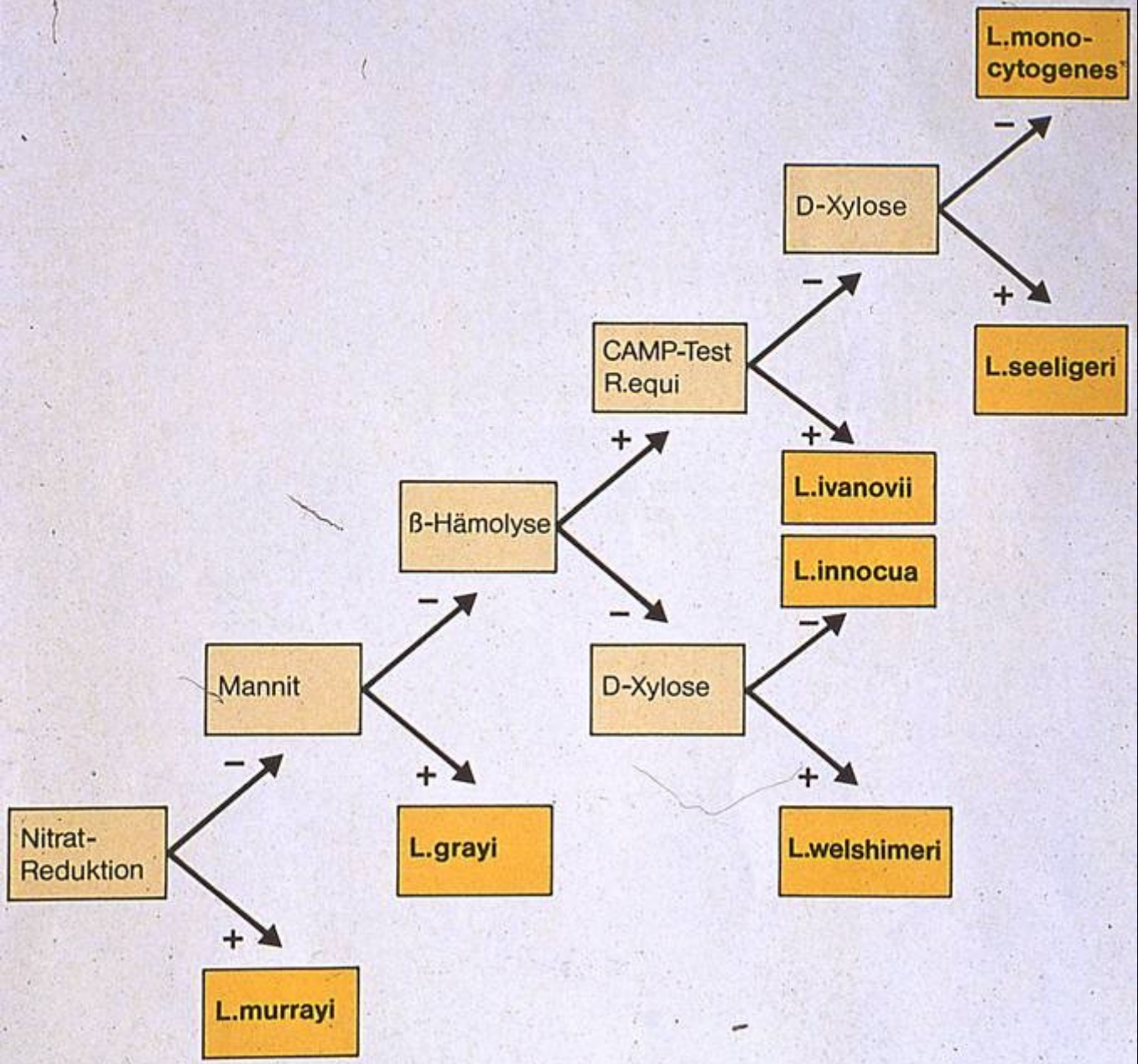
Gemeldete bakterielle Meningitis in den neuen Bundesländern und Berlin 1992–1997: Letalität (auf der Basis 343 gemeldeter Sterbefälle)

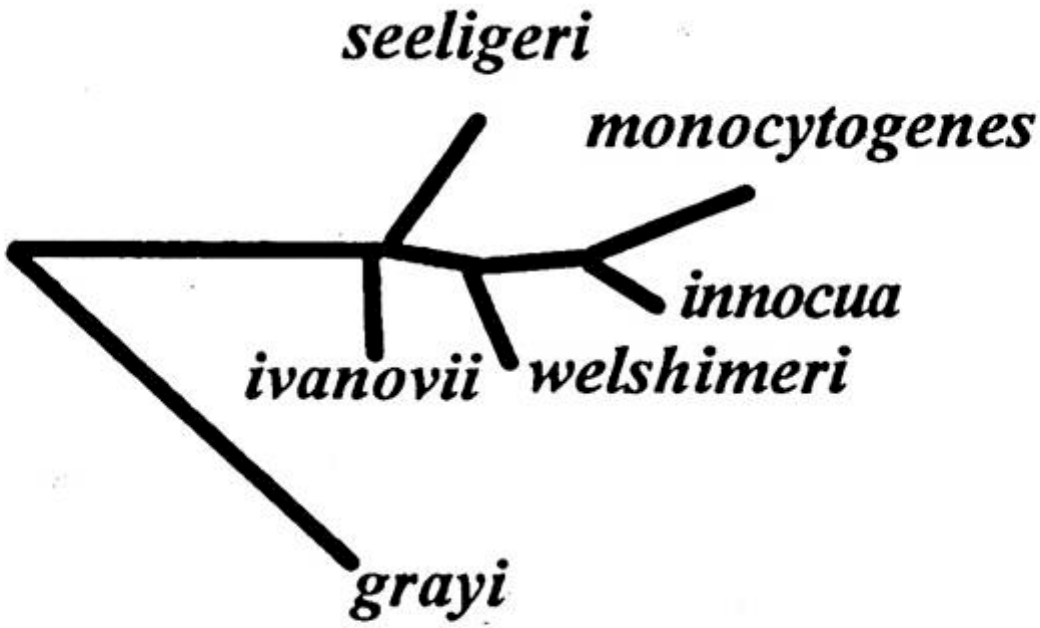





Joseph Lister 1827-1912
antiseptic surgery
30c
TRANSKEI
John Meyer
C44 1982

Differenzierung von Arten der Gattung Listeria





Taxonomic relatedness of the *Listeria* species based on 16S ribosomal RNA sequence data (adapted from Collins *et al.*, 1991).

Occurence of **Listeria** species.

	L monocytogenes	L ivanovii	L innocua	L seeligeri	L welshimeri
Human listeriosis cases	+ + +	+		(+)	
Animal listeriosis cases	+ + +	+ +			
Human healthy carriers	+ + +	+ +	+ + +	(+)	(+)
Animal healthy carriers	+ + +	+ +	+ + +	+ +	+
Food	+ + +	+ +	+ + +	+ + +	+ +
Environment	+ + +	+ + +	+ + +	+ + +	+ +

(+): 1 strain
\+ : 2 - 10 strains
\+ + : 11 - 50 strains
\+ + + : more than 50 strains

Serovare von Listeria monocytogenes

(nach SEELIGER, 1977, unveröffentlicht)

	Bezeichnung	O - Antigene	H - Antigene
	1/2a	I II (III)	AB
	1/2b	I II (III)	ABC
	1/2c	I II (III)	B D
	3a	II (III) IV	AB
	3b	II (III) IV	ABC
	3c	II (III) IV	B D
	4a	(III) (V) VII IX	ABC
	4ab	(III) V VI VII IX	ABC
	4b	(III) V VI	ABC
	4c	(III) V VII	ABC
	4d	(III) (V) VI VIII	ABC
	4e	(III) V VI (VIII)(IX)	ABC
	5	(III) (V) VI VIII X	ABC
	7 ?	(III) XII XIII	ABC
Listeria spec.*	6a (4f)	(III) V VI VII IX XV	ABC
	6b (4g)	(III) V VI VII IX X XI	ABC

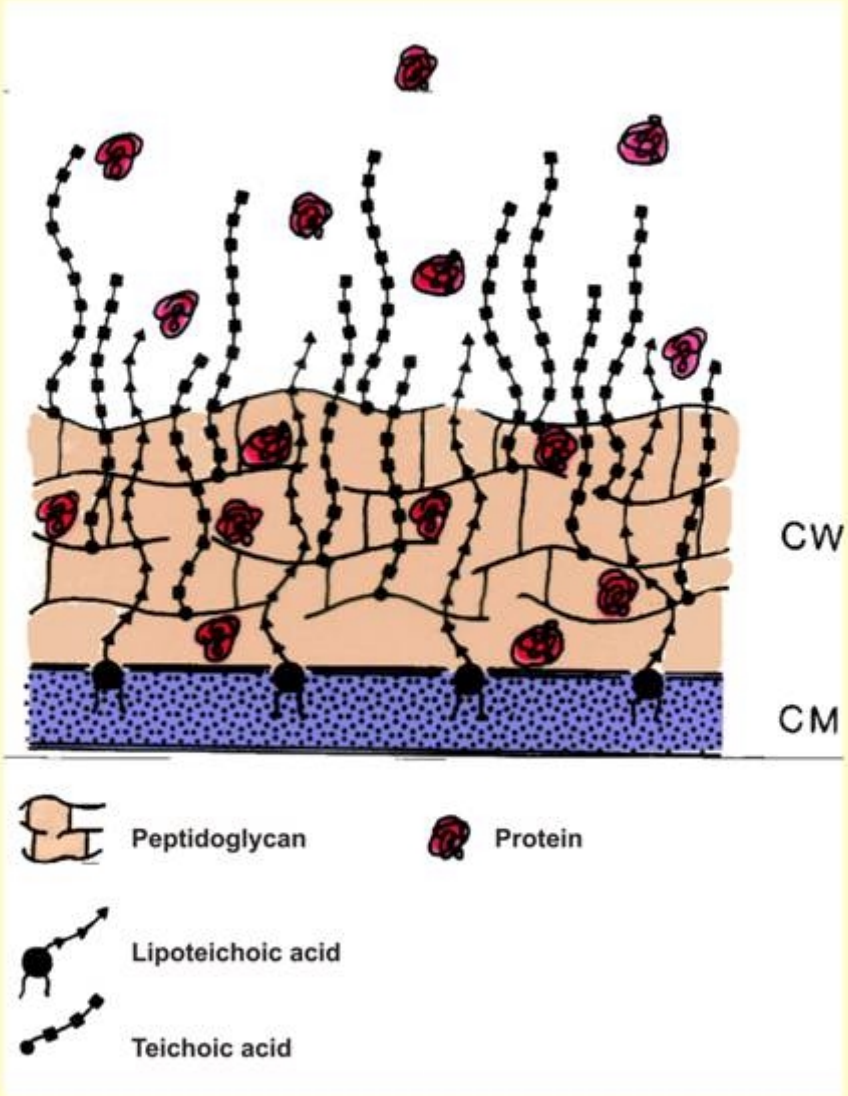
* nicht haemolysierende Stämme ; weitere Antigenkombinationen sind bekannt, aber nicht aufgeführt.

Serovar distribution in **Listeria** species.

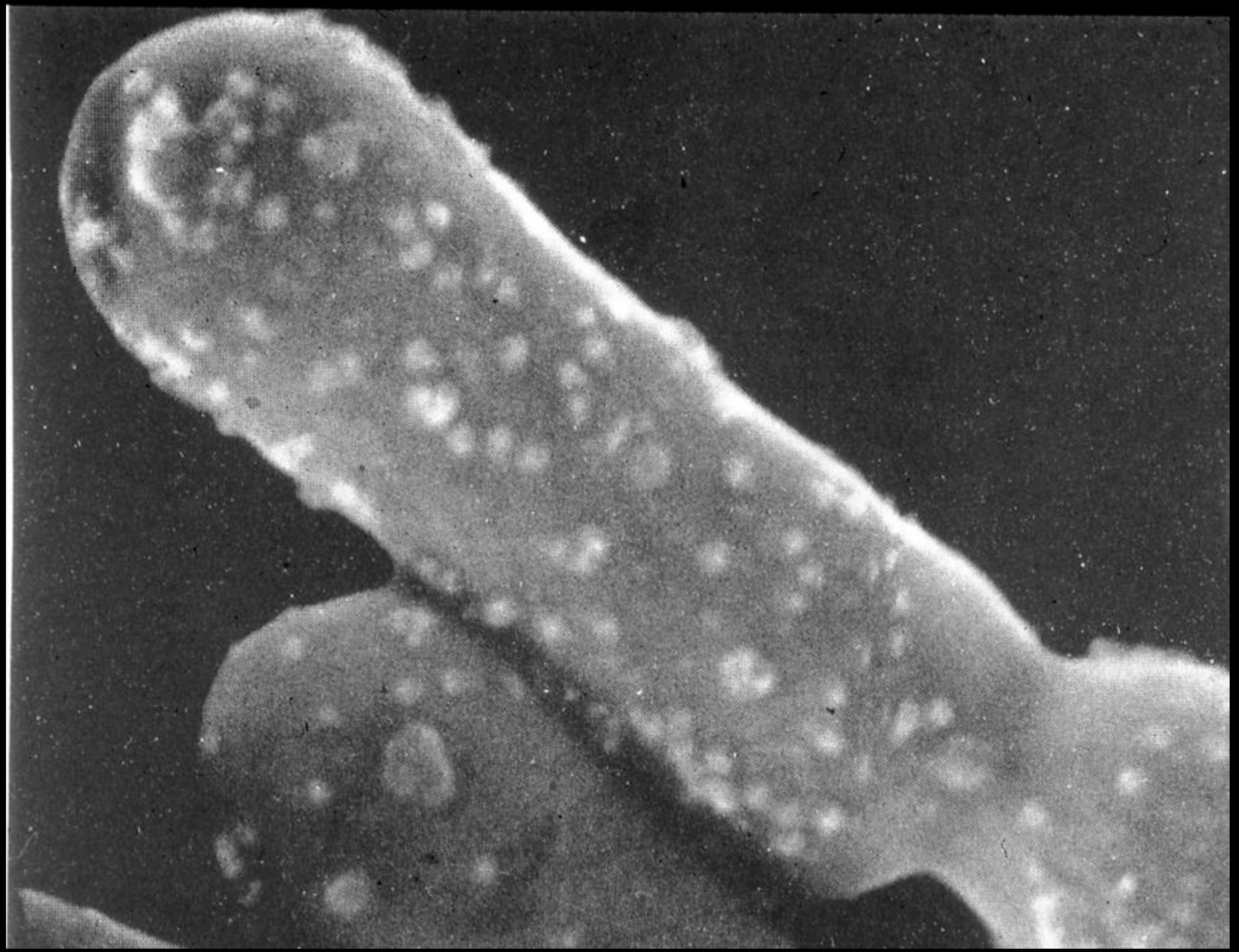
Serovars	L monocytogenes	L seelfgeri	L welshimeri	L innocua	L ivanovii
1/2a,b,c	+++	+++	+		
3a,b,c	++	++			
4a,ab,b,c,d,e	+++	+	+	+	
6a,b,U.S.		++	++	+++	
5					+++

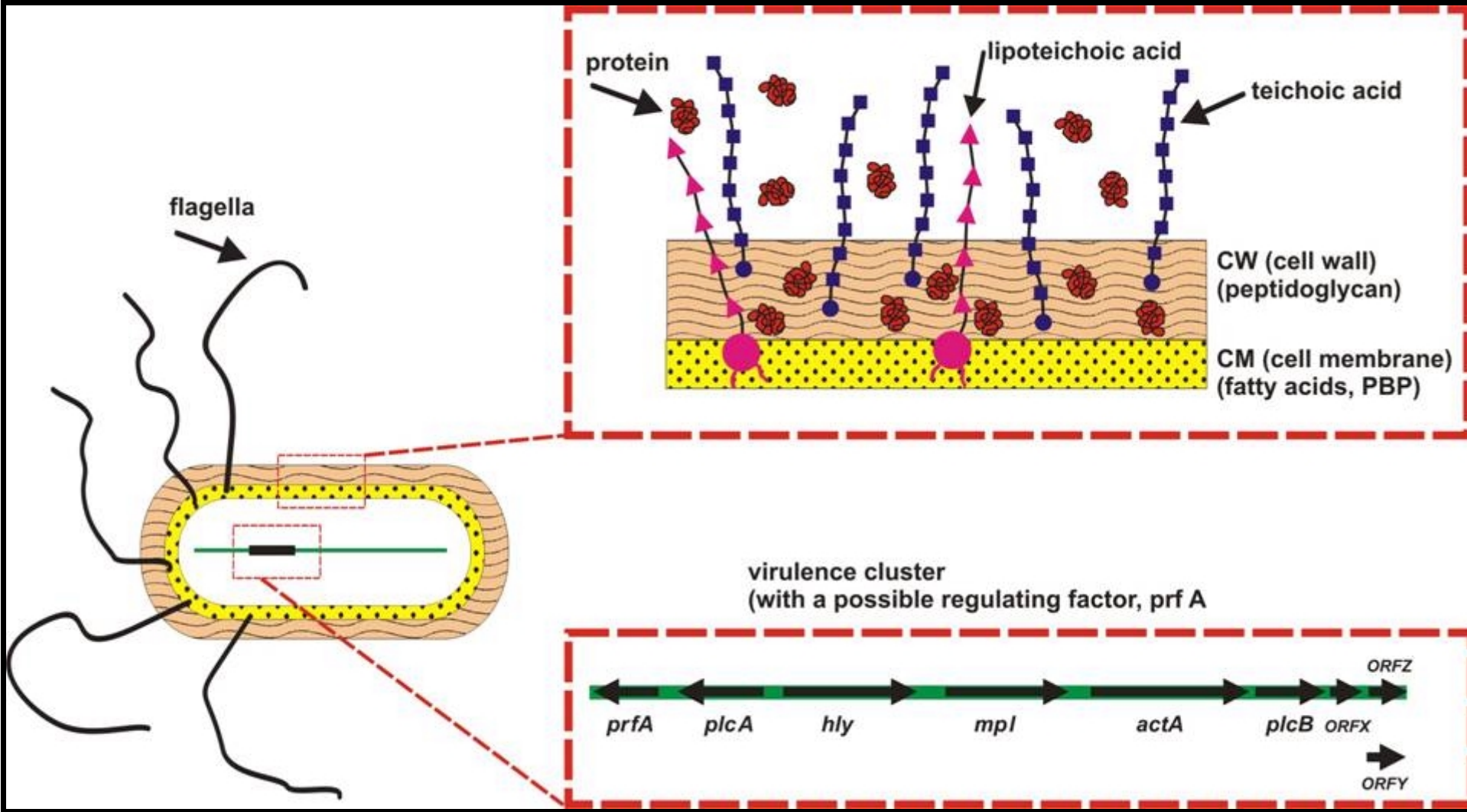
\+ : 1 to 10 strains
++ : 11 to 50 strains
+++ : more than 50 strains
U.S. : undesignated serovars

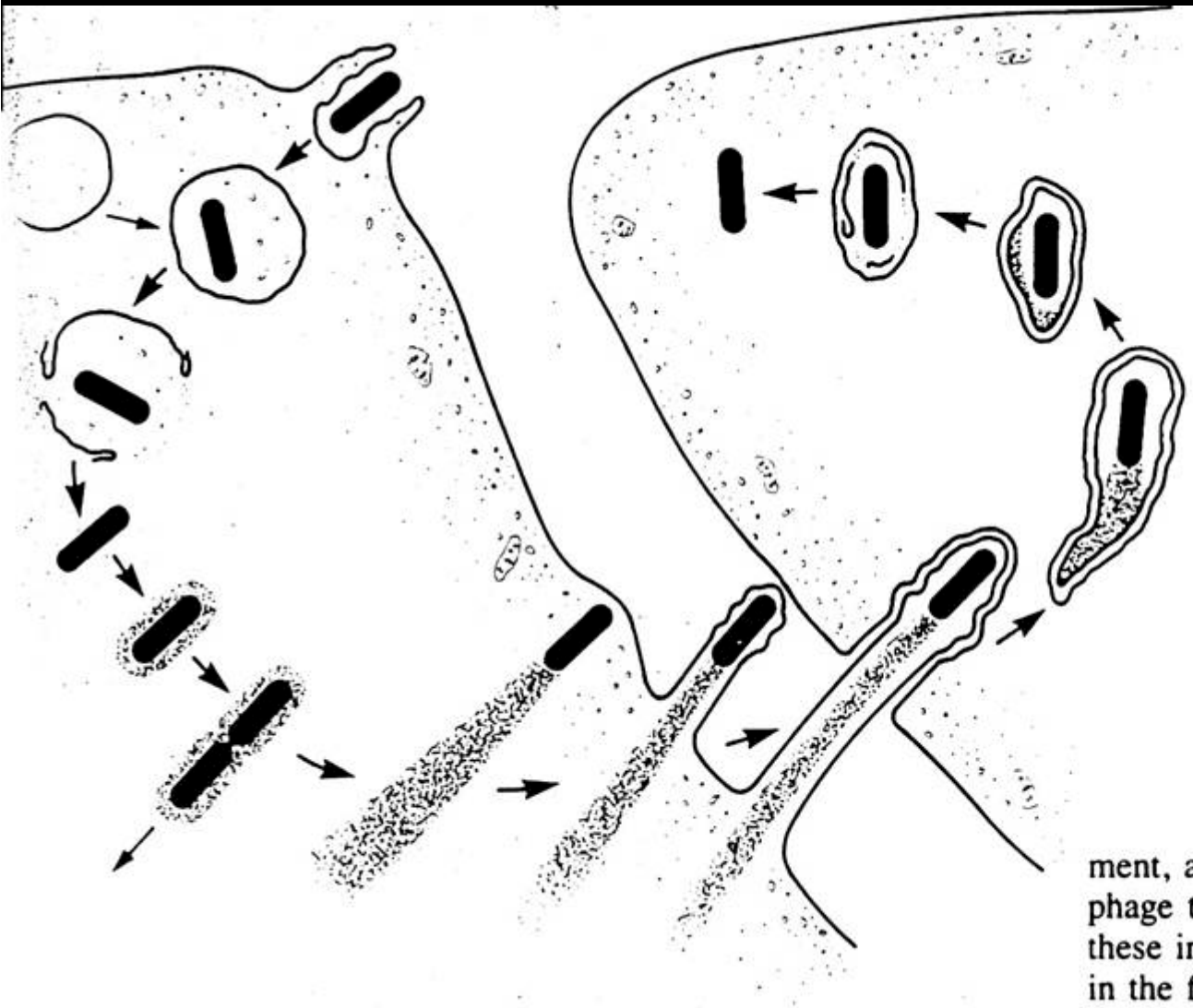
General organisation of the cell wall of strains of *Listeria* showing the possible arrangements of polymers



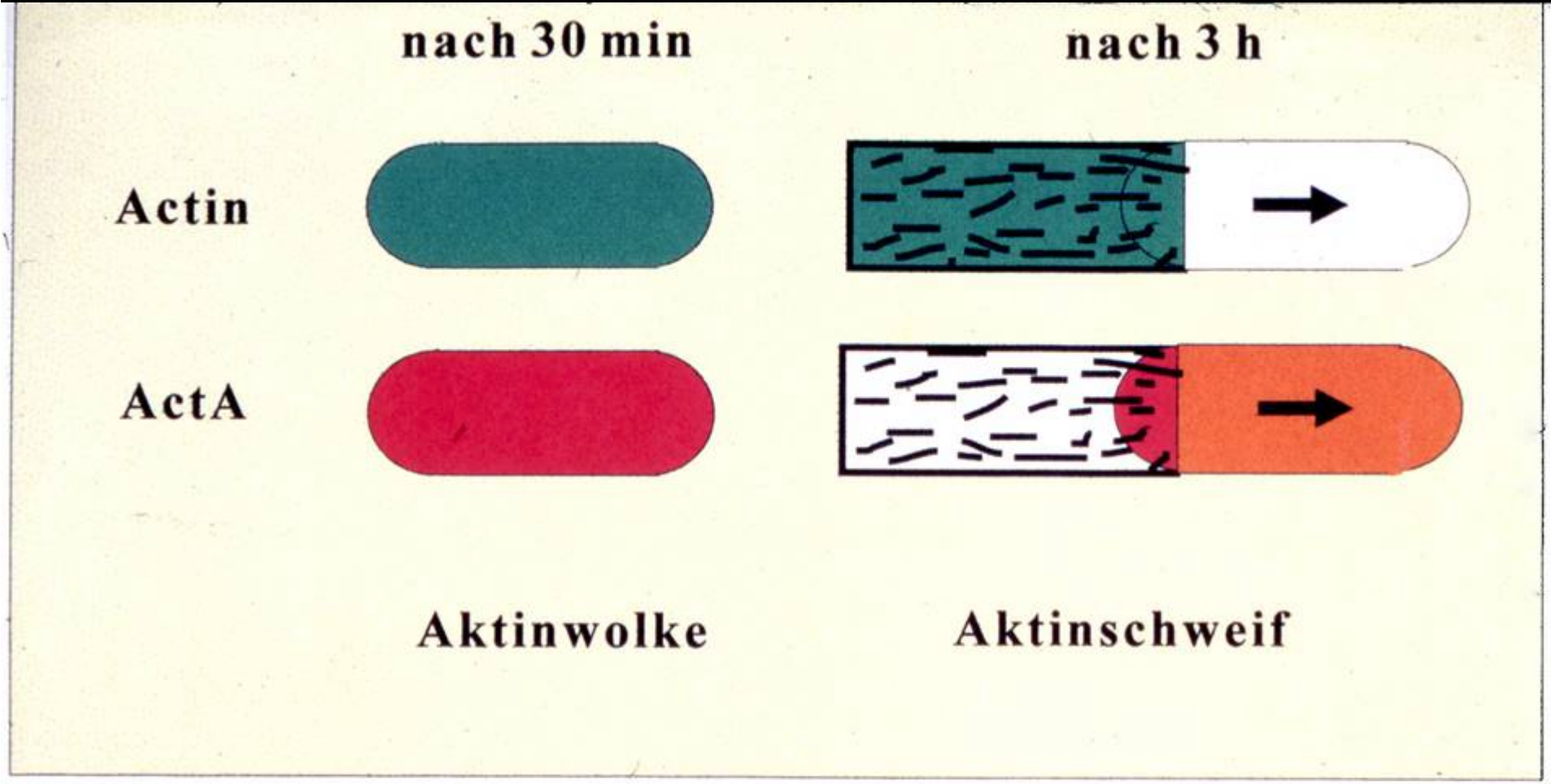
nach Fiedler 1988



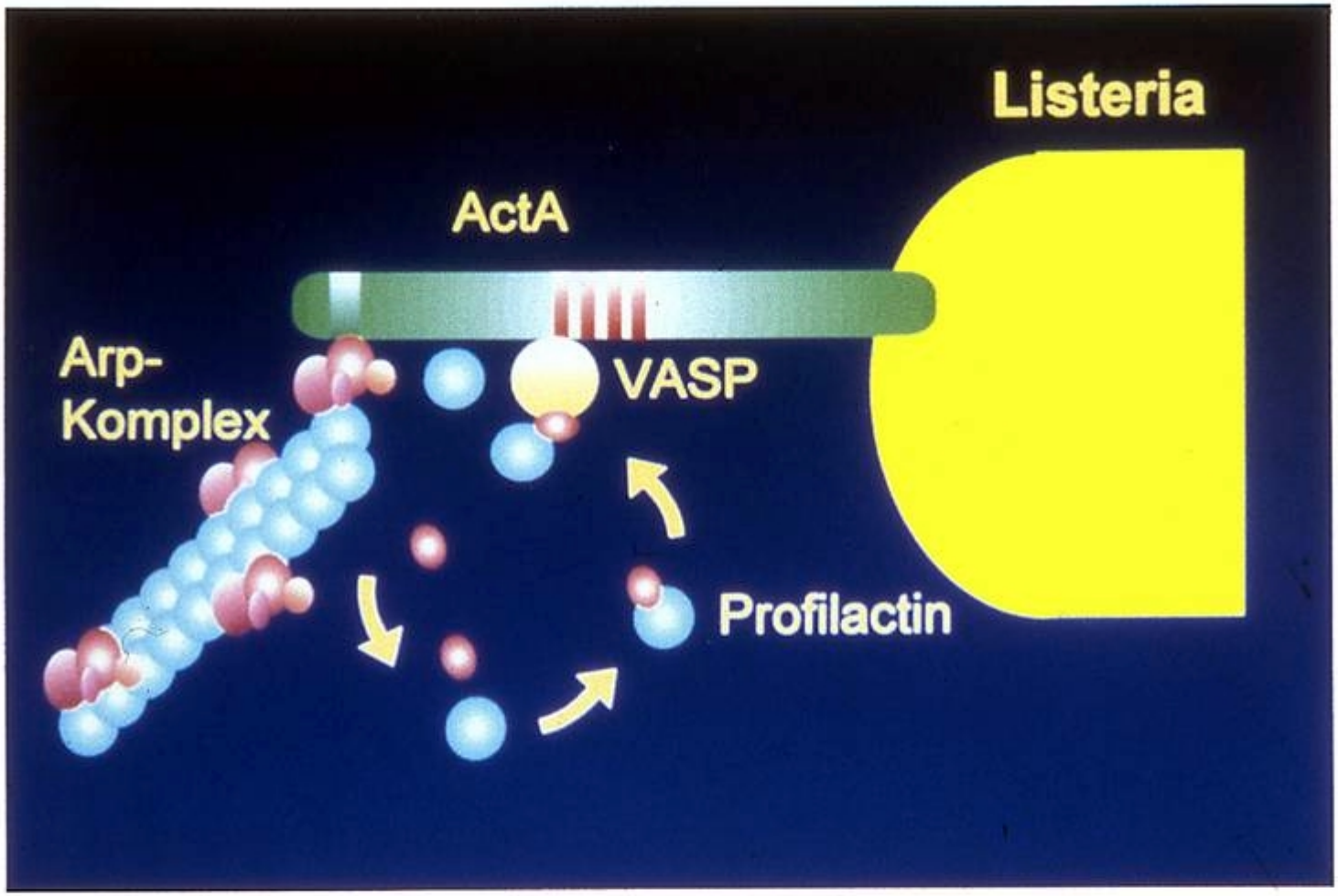

protein
lipoteichoic acid
teichoic acid
CW (cell wall)
(peptidoglycan)
CM (cell membrane)
(fatty acids, PBP)
flagella
virulence cluster
(with a possible regulating factor, prf A
ORFZ
prfA
plcA
hly
mpl
actA
plcB
ORFX
ORFY



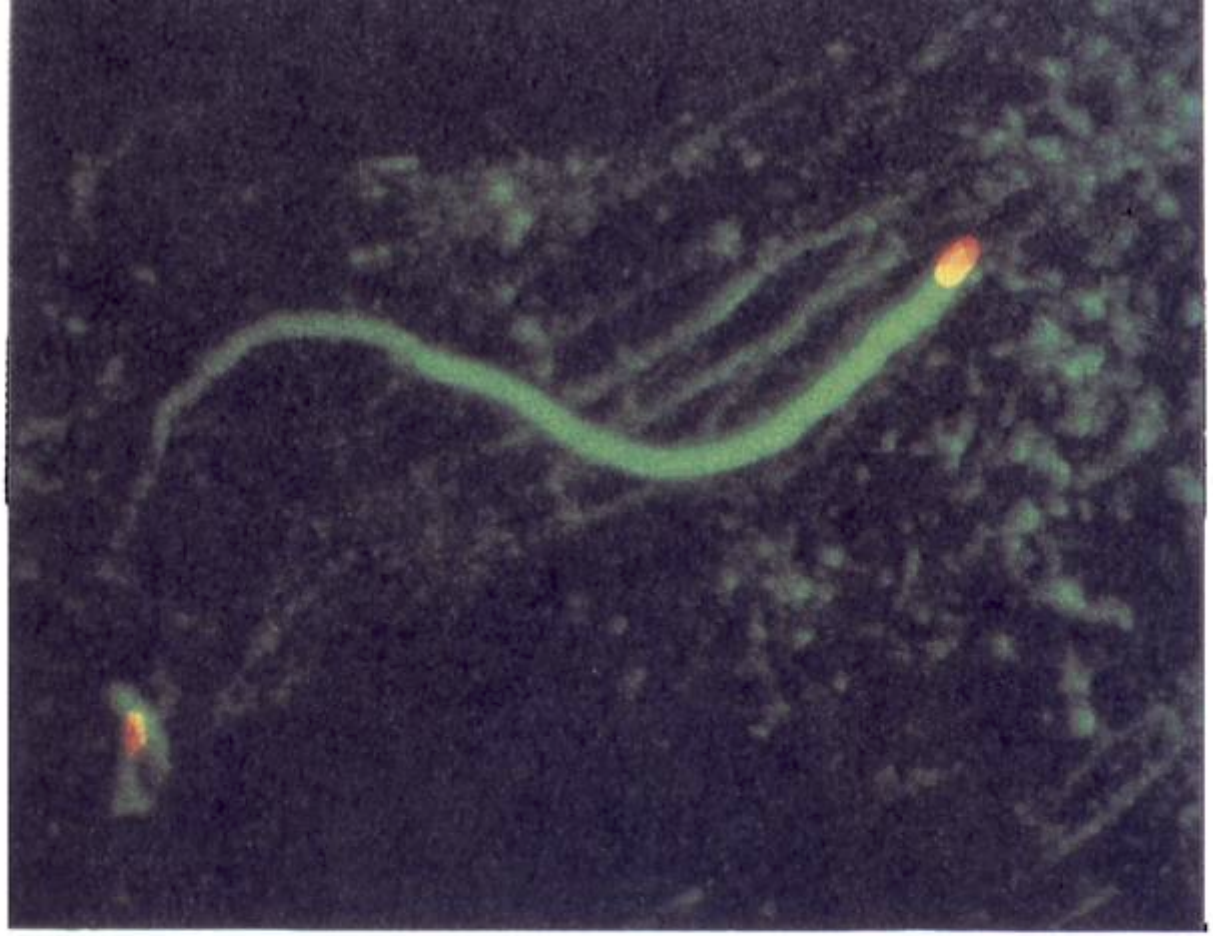
Stages in the entry, growth, movement, and spread of *Listeria* from one macrophage to another. Photographs illustrating all these intermediate stages have been presented in the figures.



Modell einer "Polarisierung" des aktiven ActA im Zytoplasma der Wirtszelle. Das aktive ActA ist hier rot dargestellt, in einer frühen Phase ("Aktinwolke") findet es sich auf der ganzen bakteriellen Oberfläche. Später wird es größtenteils durch Phosphorylierungen inaktiviert (hier orange wiedergegeben), so daß die aktive Form nur noch an dem bakteriellen Pol anzutreffen ist, an dem sich auch der Aktinschweif formiert.

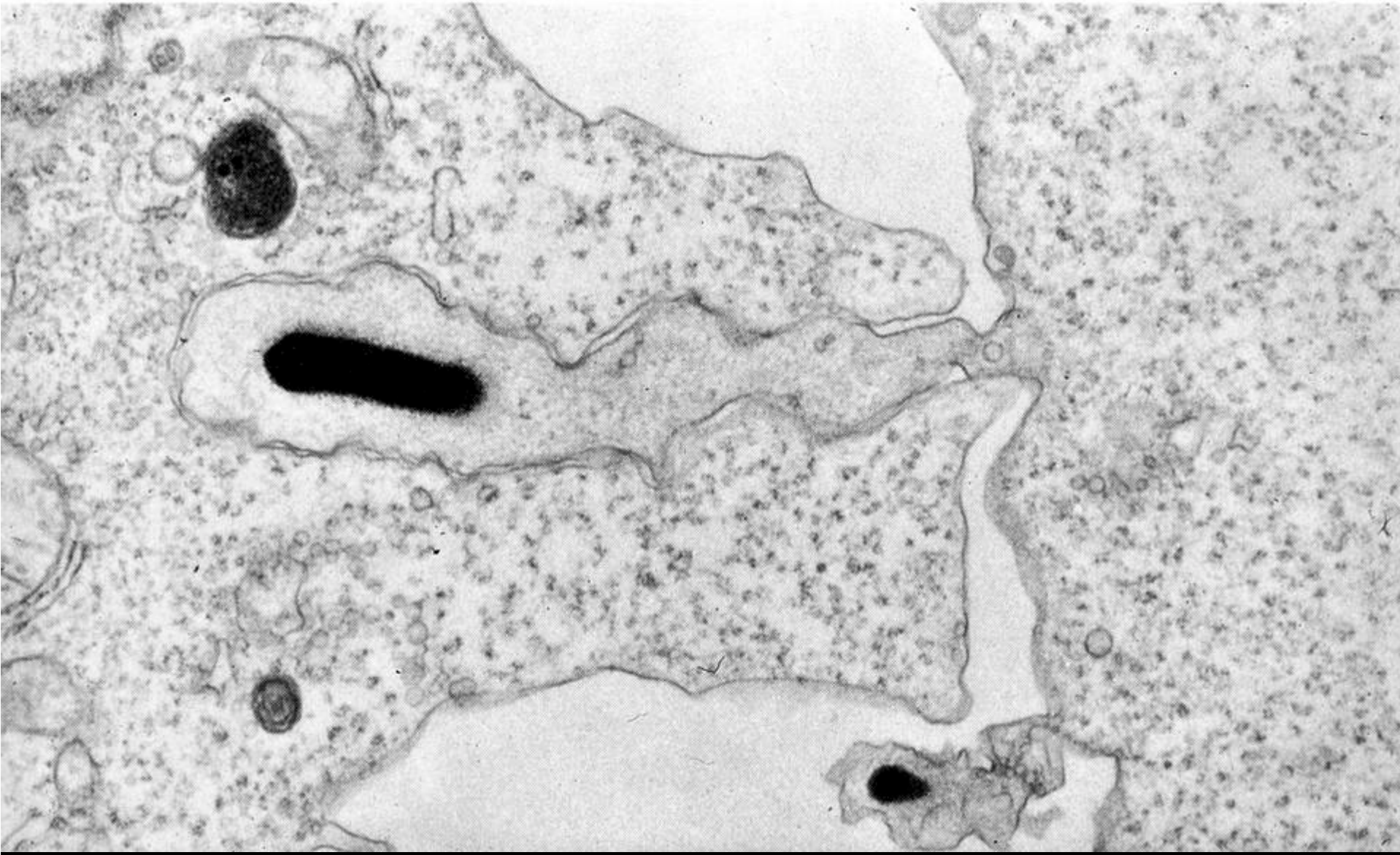


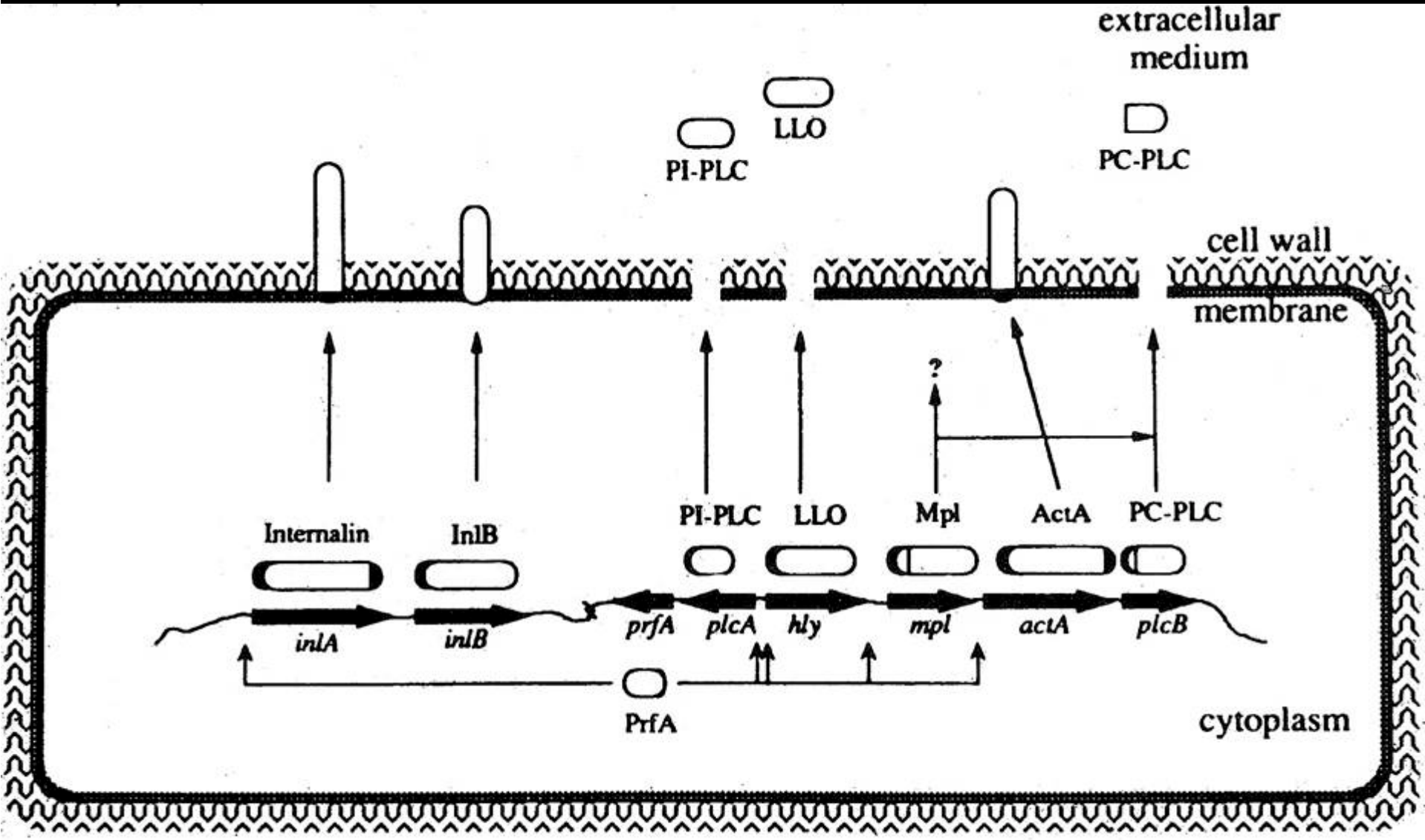
Schematische Darstellung der Funktion des ActA-Proteins. Die vier Prolin-reichen VASP-Bindungsstellen und das N-terminal gelegene Motiv sind durch entsprechende Färbungen im ActA-Molekül angedeutet.



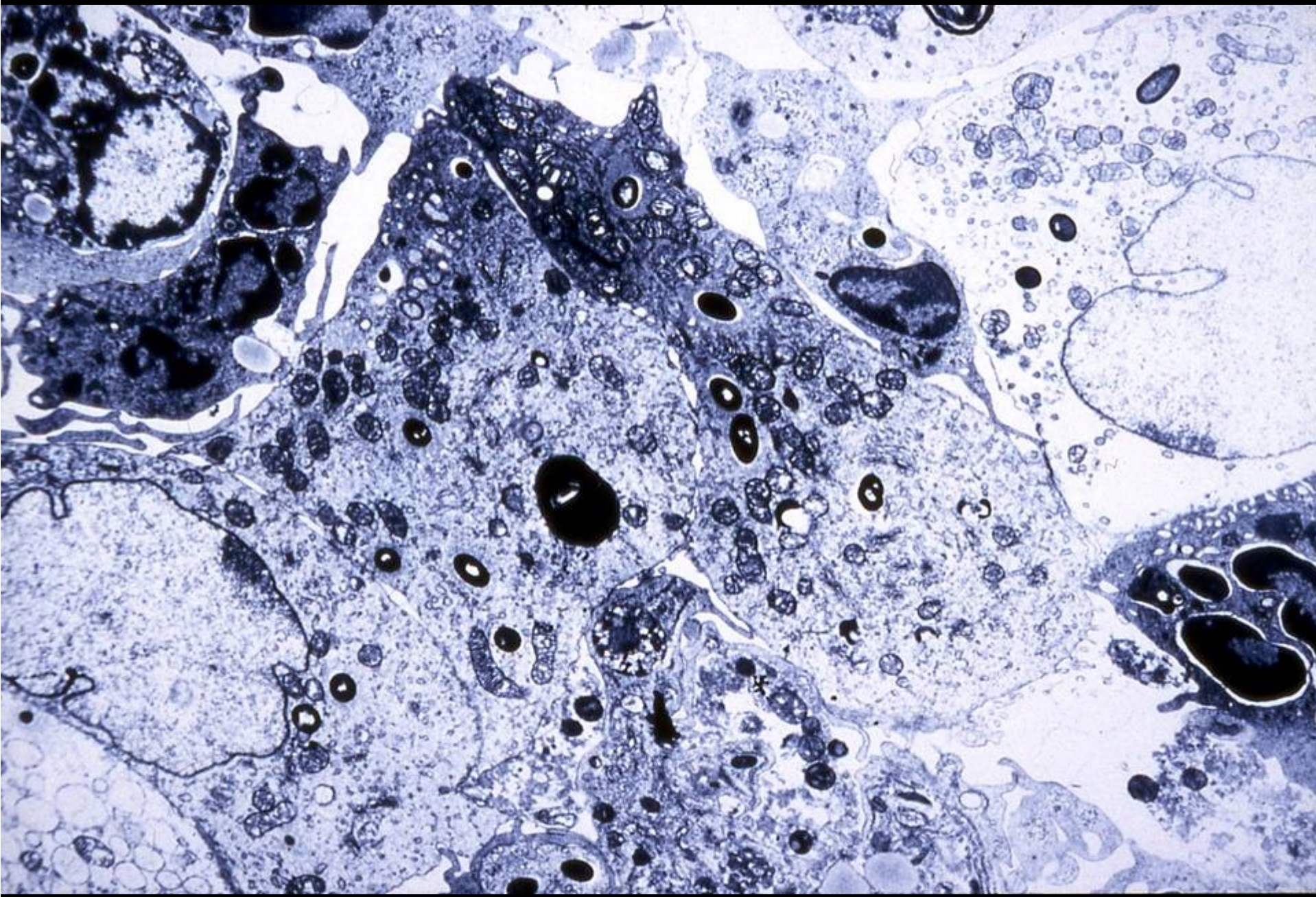
Directional actin assembly by *L. monocytogenes*, with filamentous actin assembled at one bacterial extremity. Shown is a double immunofluorescence confocal laser scanning micrograph of a Vero cell infected for 5 h and treated with anti-*L. monocytogenes* antiserum (bacterium; red) and fluorescein isothiocyanate-phalloidin (F-actin; green). (Reprinted with permission from *Molecular Microbiology*, vol. 13, no. 3, 1994, front cover.)

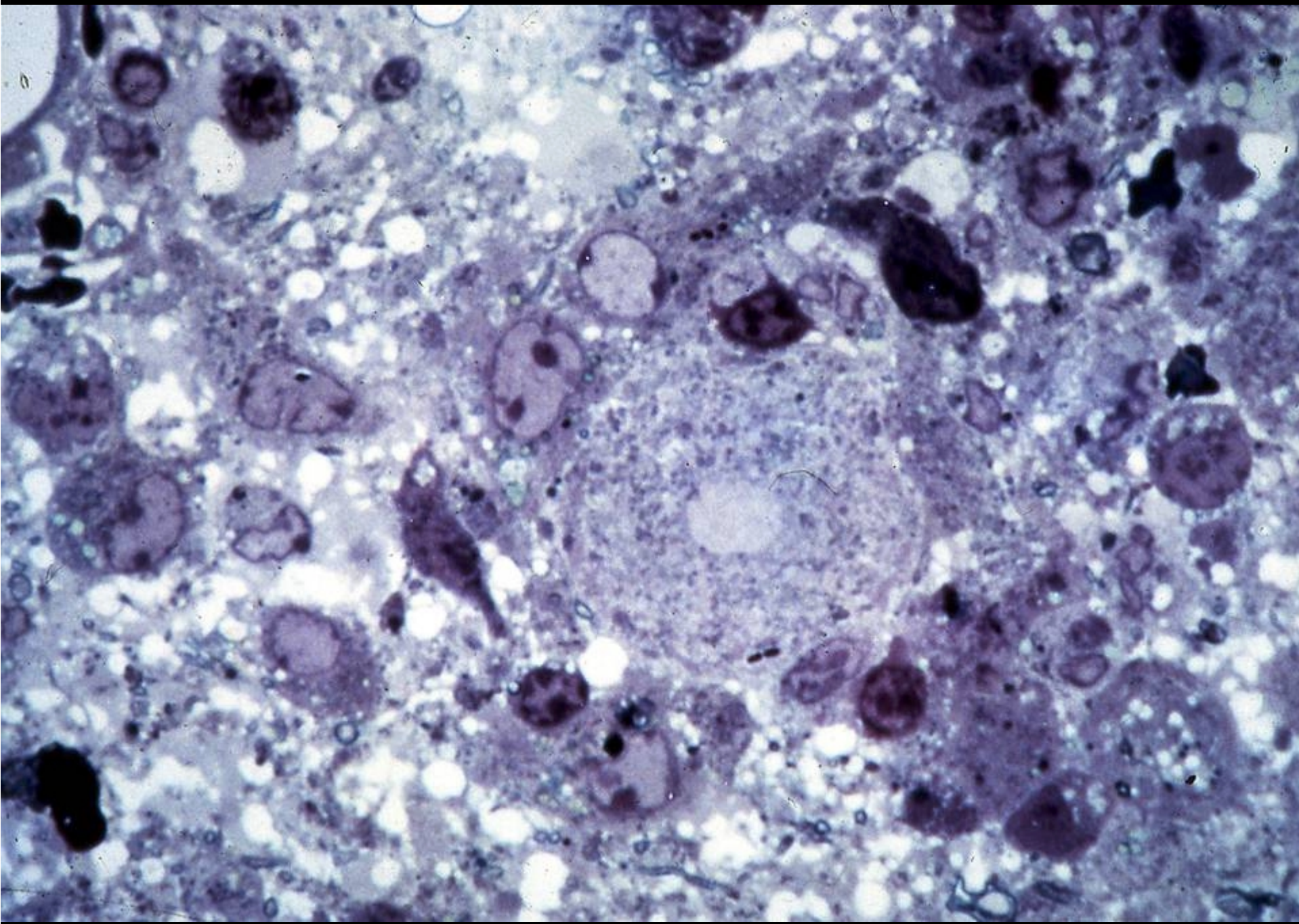
L. monocytogenes Cell-to-Cell Spread

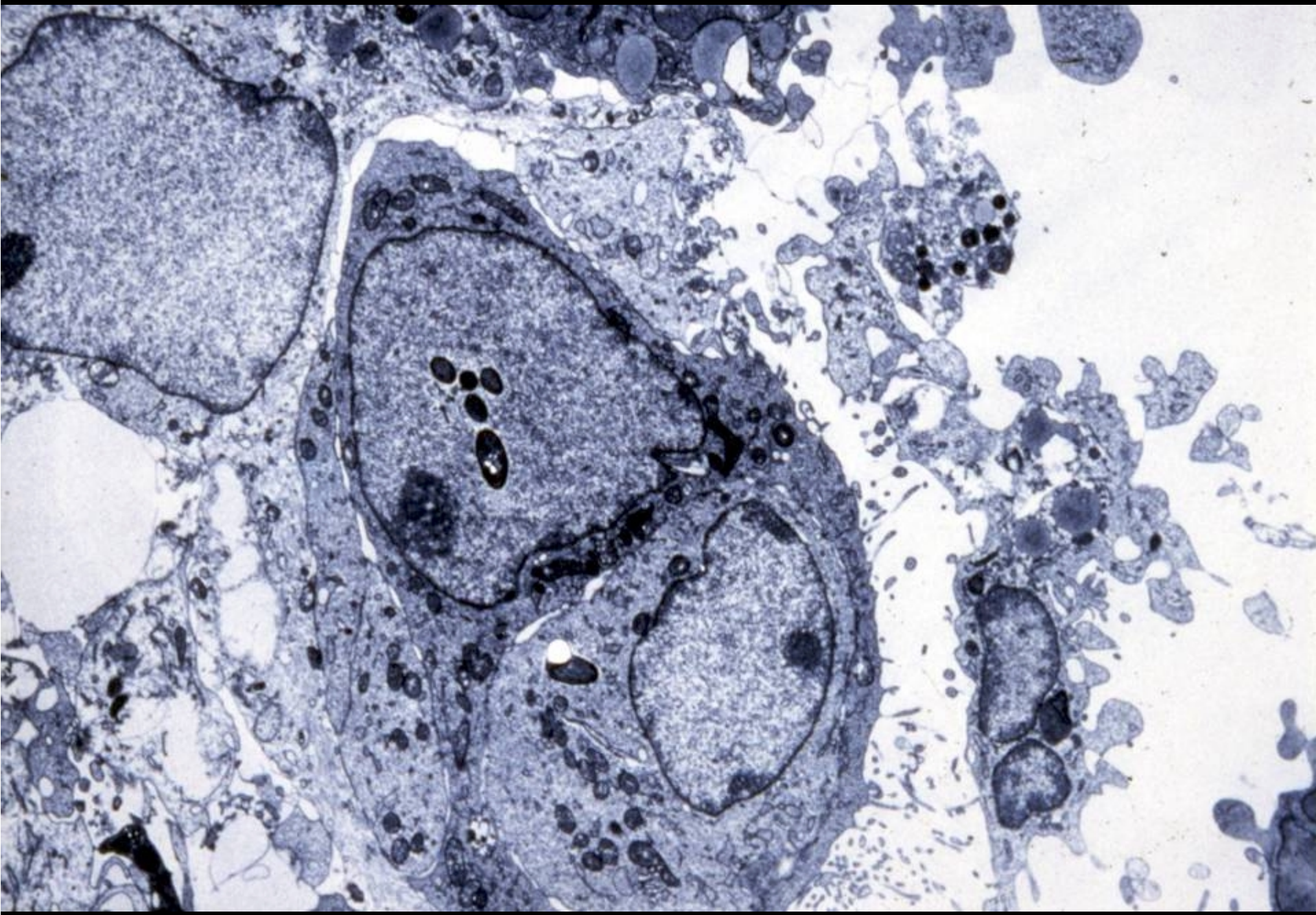


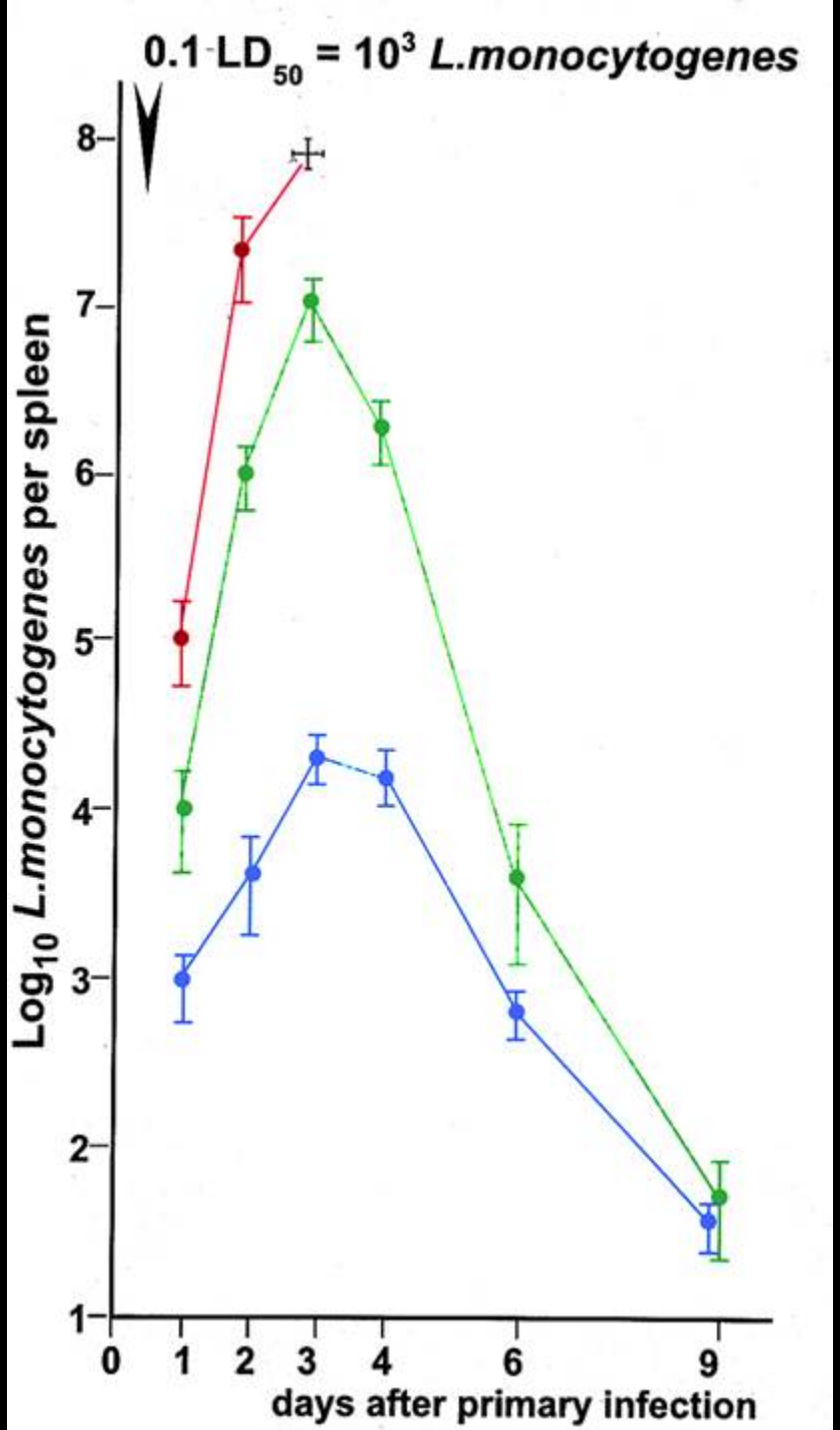


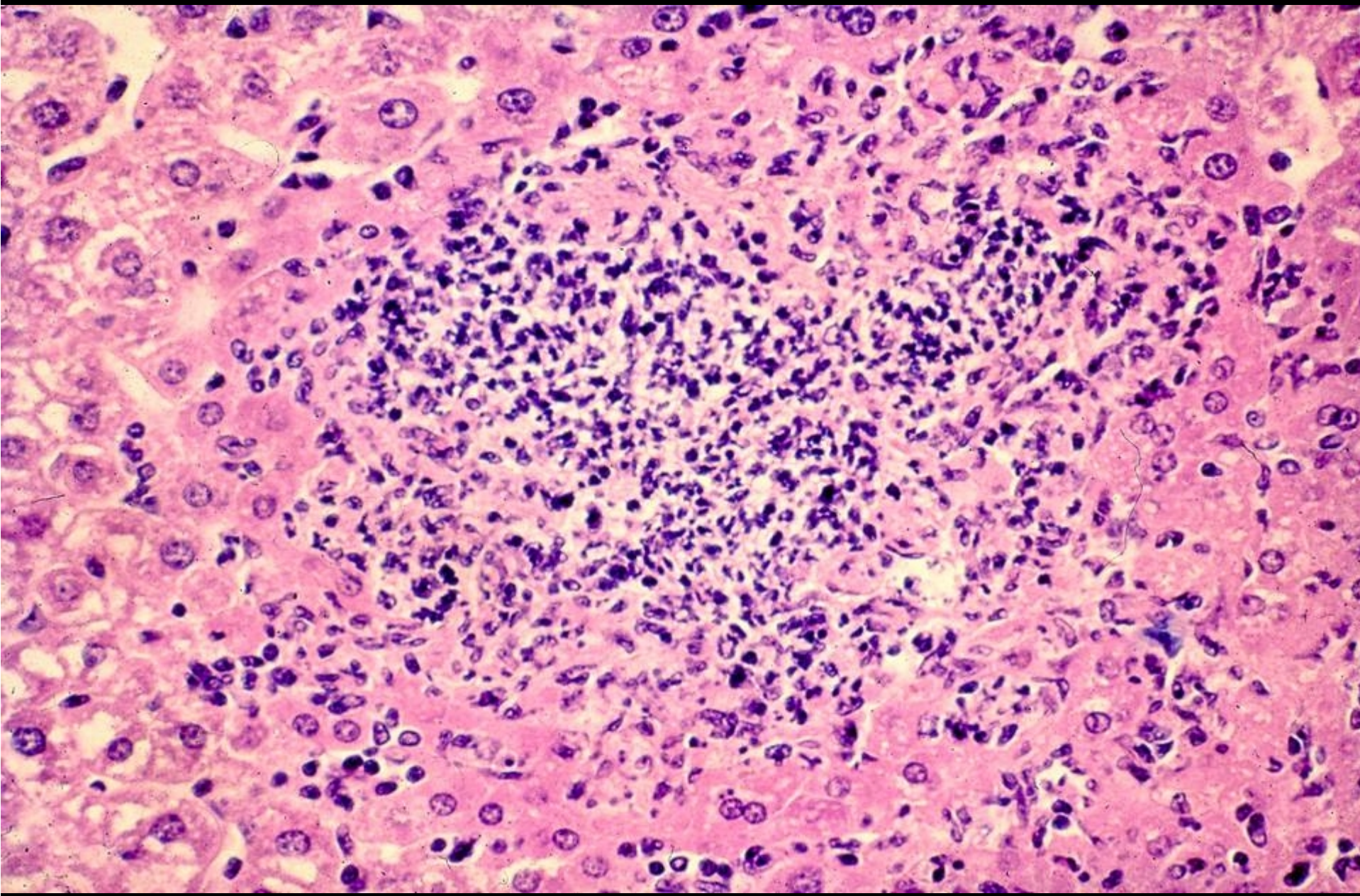
Schematic representation of the genes and gene products of *L. monocytogenes.*

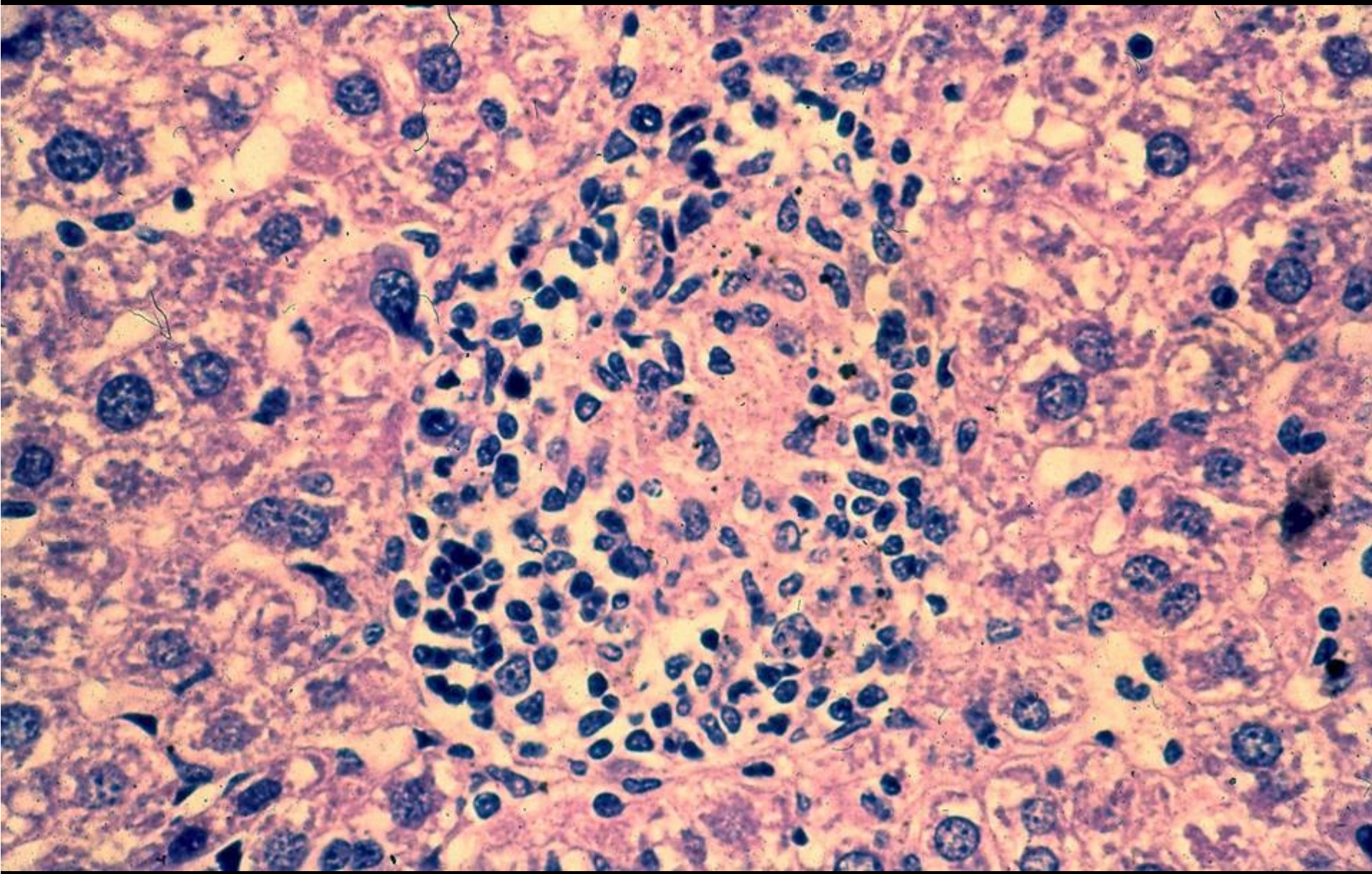


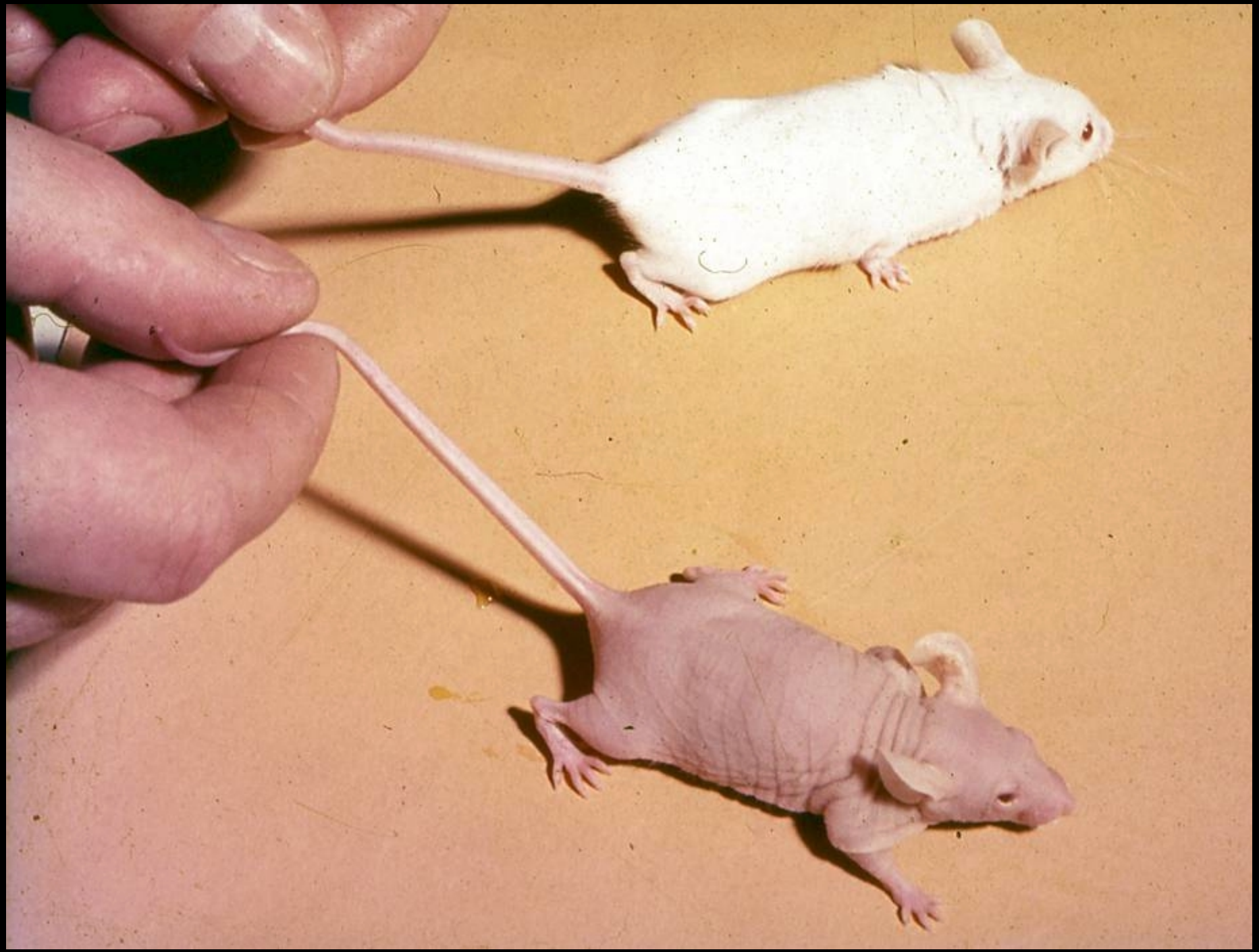


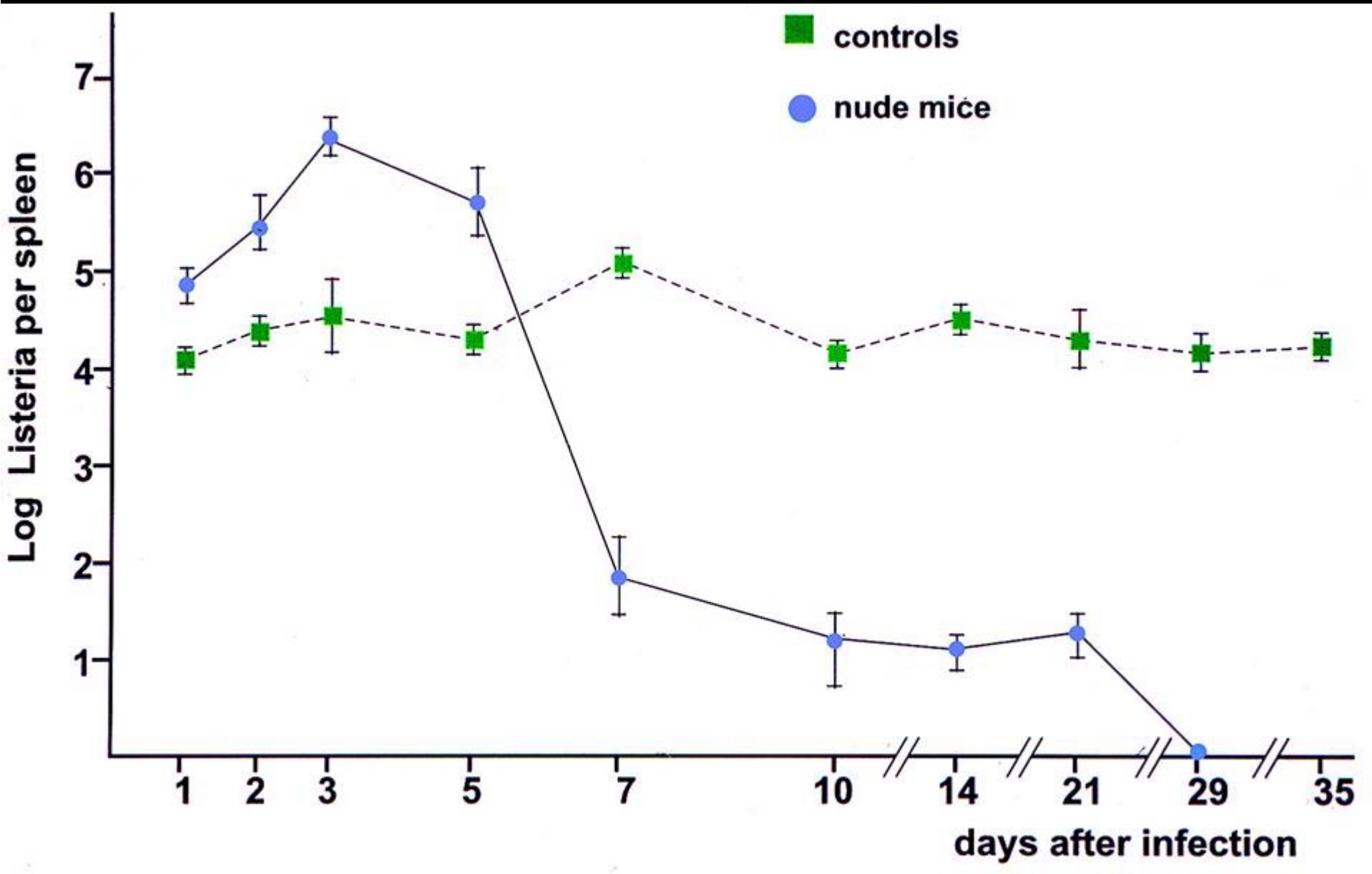


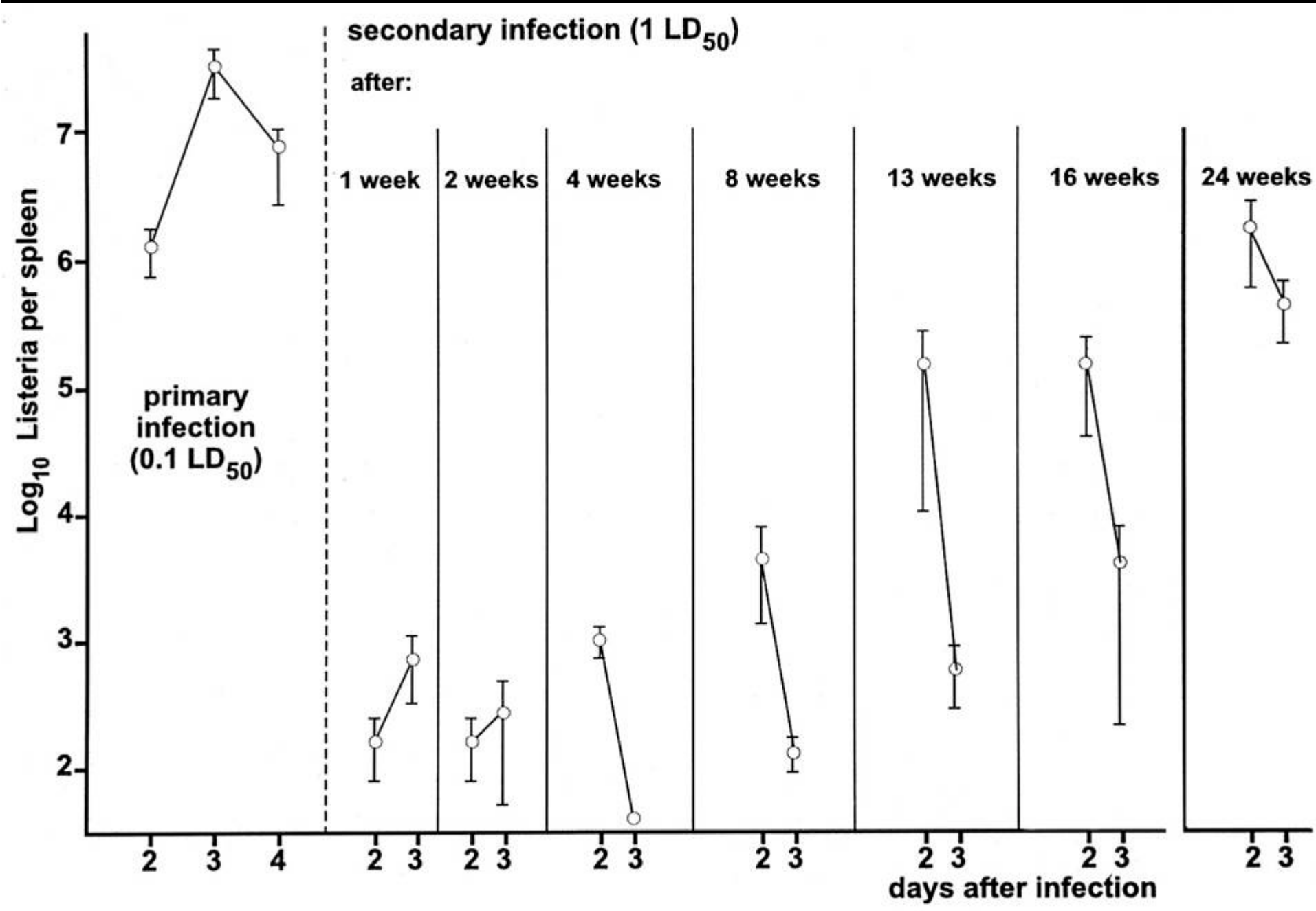

0.1 LD50 = 10^3 L.monocytogenes
Log10 L.monocytogenes per spleen
8
7
6
5
4
3
2
1
0
1
2
3
4
6
9
days after primary infection

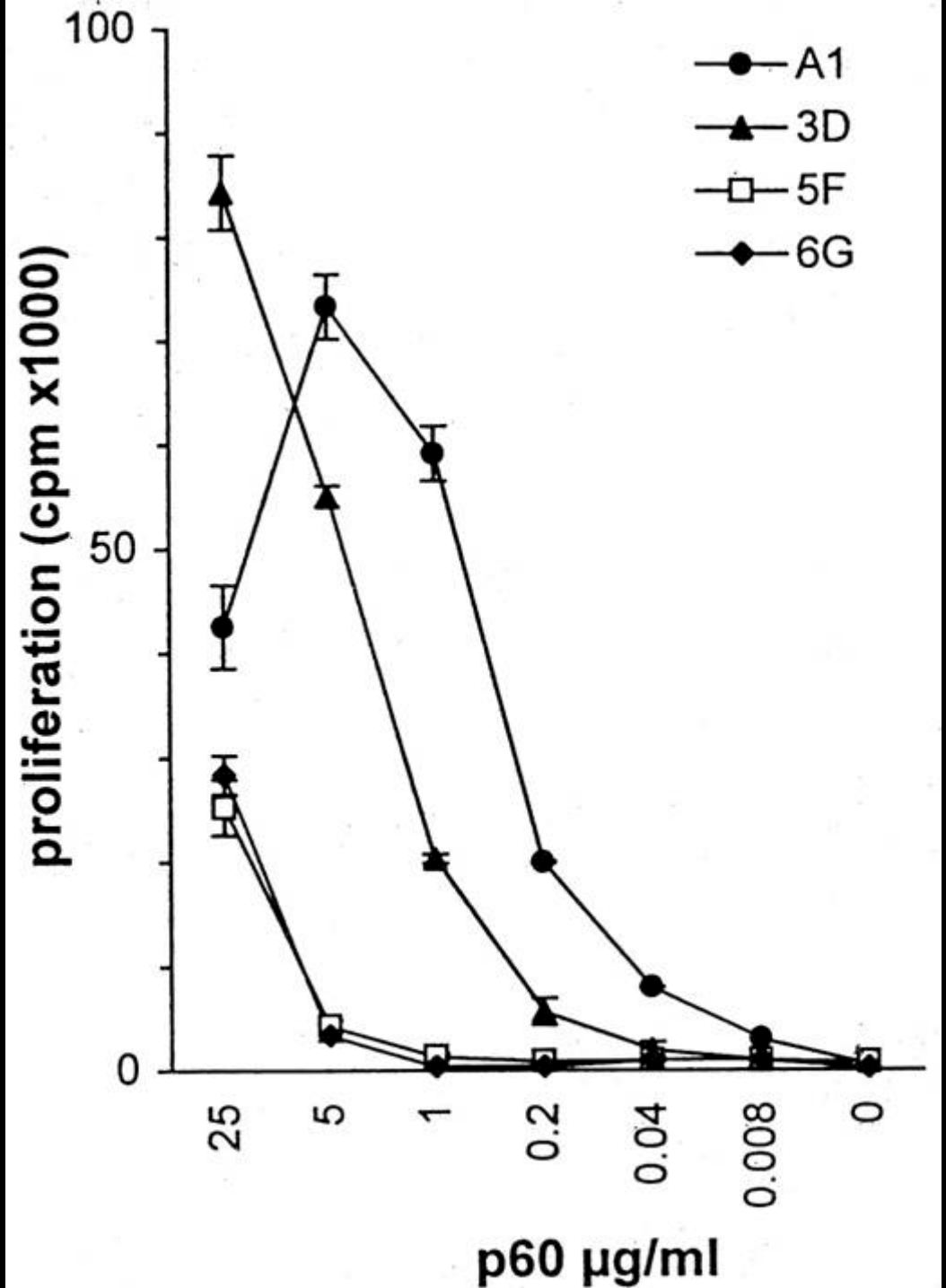




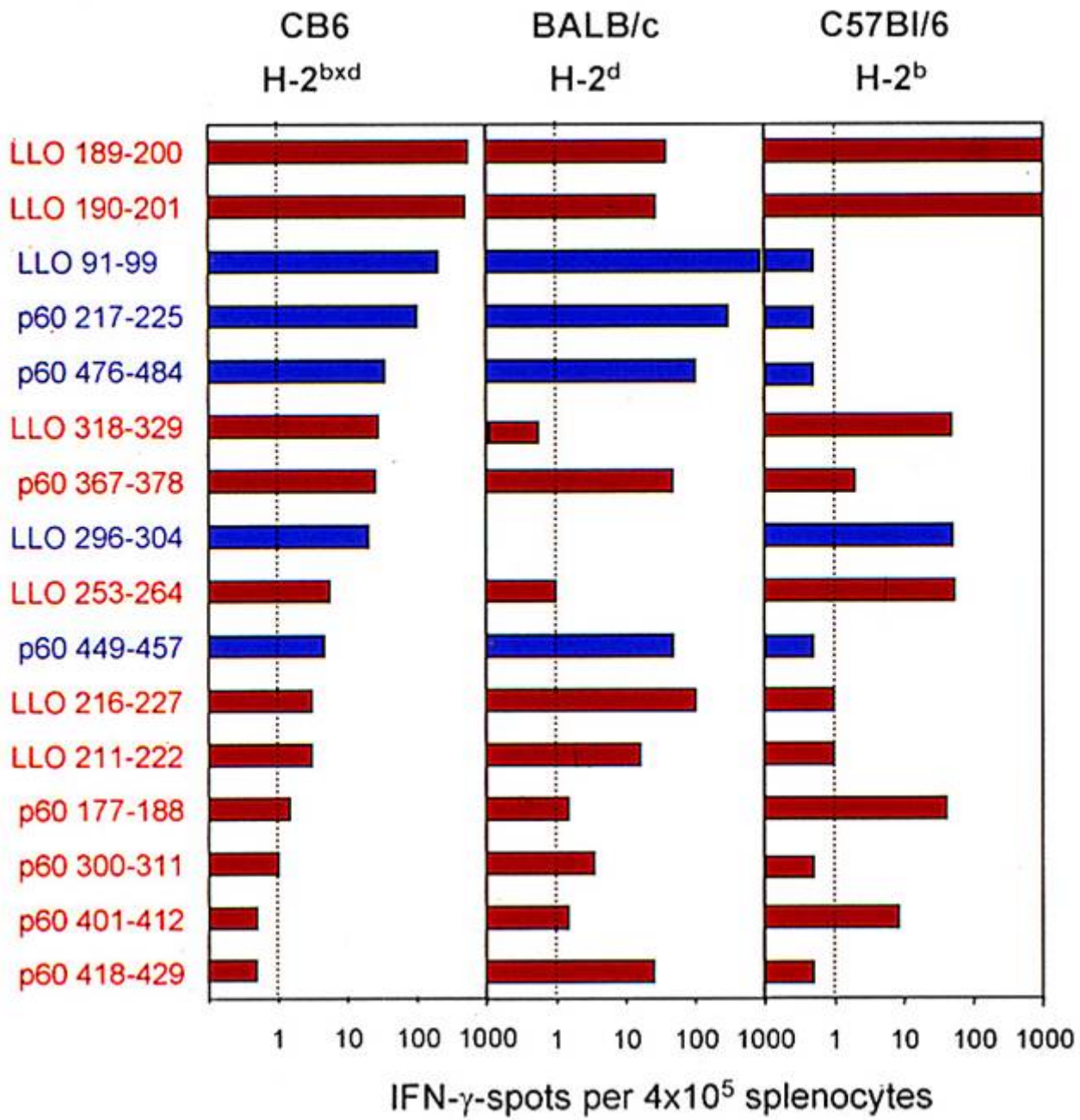



controls
nude mice
Log Listeria per spleen
7
6
5
4
3
2
1
1
2
3
5
7
10
14
21
29
35
days after infection


secondary infection (1 LD50)
after:
1 week
2 weeks
4 weeks
8 weeks
13 weeks
16 weeks
24 weeks
primary infection (0.1 LD50)
Log10 Listeria per spleen
7
6
5
4
3
2
2 3 4
2 3
2 3
2 3
2 3
2 3
2 3
2 3
days after infection


100
50
0
proliferation (cpm x1000)
A1
3D
5F
6G
25
5
1
0.2
0.04
0.008
0
p60 µg/ml

Hierarchy of T cell epitopes in CB6 mice



Antimicrobial activities of natural compunds against *Listeria monocytogenes*

Allyl isothiocyanate from diverse plants (Lin et al., J.Food Protect. 63, 2000, 727)

Herb extracts (Prototeca one and two) (Cutter, J.Food Protect. 63, 2000, 601)

Eucalyptus and other oils (Harkenthalet al., Pharamazie 54, 1999, 460)

Sulfur cpmpounds from cabbage (Kyung and Fleming, J. Food Protect. 60, 1997, 67

Furocoumarins from parsley (Manderfield et al., J. Food Protect. 60, 1997, 72

Essential oils from plants (Aureli et al., j. Food Protect. 55, 1992, 344

Med Microbiol Lett 1996; 5: 1 - 7

Alan P. Johnson*[1], James McLauchlin[2], Saroj Shah[2] and Marina Warner[1]

In vitro activity of 10 antimicrobial agents against strains of *Listeria* from 515 cases of human listeriosis in the UK.

Antimicrobial agent	MIC range (mg/l)	MIC_{50} (mg/l)	MIC_{90} (mg/l)
Ampicillin	0.25-2	0.5	0.5
Penicillin	0.12-1	0.5	1
Chloramphenicol	≤2-8	8	8
Ciprofloxacin	≤0.5-8	2	4
Erythromycin	≤0.25	≤0.25	≤0.25
Gentamicin	≤2-16	≤2	4
Rifampicin	≤0.25	≤0.25	≤0.25
Tetracycline	≤0.5-256	2	4
Trimethoprim	≤0.5-1	≤0.5	≤0.5
Vancomycin	1-4	2	2

In vitro susceptibilities of 82 *Listeria monocytogenes* strains to 22 antimicrobial agents.

Antimicrobial agents	Range (μg/ml)	MIC (μg/ml)	
		50%	90%
Ampicillin	0.12-1	0.5	1
Gentamicin	≤ 0.25-0.5	≤ 0.25	≤ 0.25
Rifampin	≤ 0.008-0.06	≤ 0.008	0.03
Chloramphenicol	4-16	8	8
Tetracycline	0.12-32	0.5	1
Co-trimoxazole	≤ 0.03-0.06	≤ 0.03	0.06
Imipenem	0.03-0.12	0.06	0.06
Meropenem	0.06-0.12	0.12	0.12
Erythromycin	0.06-0.25	0.06	0.12
Azitromycin	0.5-1	1	1
Ciprofloxaein	0.5-2	1	1
Ofloxacin	2- 4	4	4
Levofloxacin	0.5-2	1	1
Sparfloxacin	0.5-2	2	2
Grepafloxacin	0.25-1	0.5	1
Trovafloxacin	0.12-0.5	0.25	0.5
Moxifloxacin	0.12-1	0.25	0.5
Gemifloxacin	0.06-0.25	0.12	0.25
Clinafloxacin	0.06-0.25	0.12	0.12
Vancomycin	1- 2	1	1
Teicoplanin	0.12-0.5	0.25	0.5
Linezolid	1-1.5	1.5	1.5

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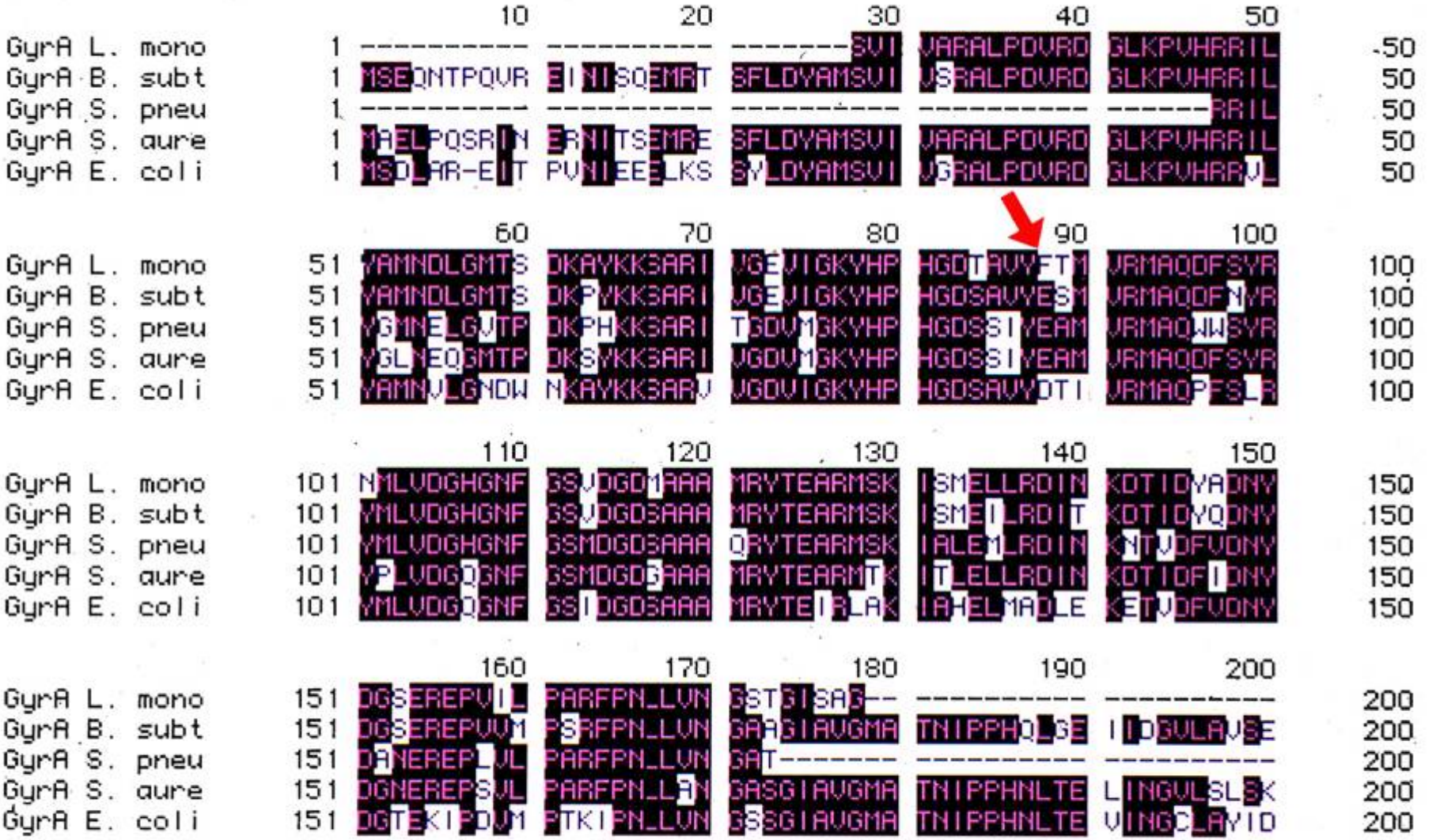
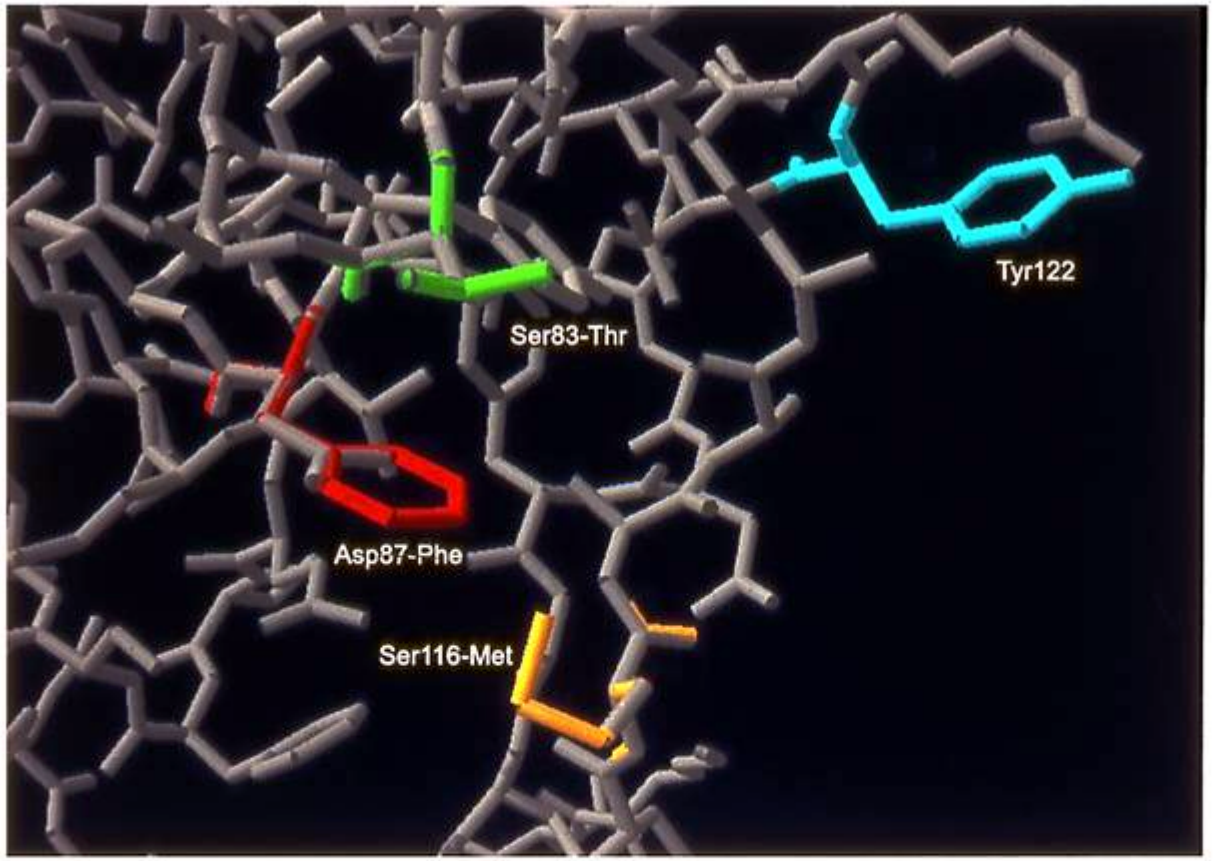
In vitro susceptibility of Listeria monocytogenes to various antibiotics

agent	range of MIC values (mg/l)	interpretation of inhibitory action		
		susceptibel	intermediate	resistant
penicillin	0.06-2	●		
ampicillin/ amoxycillin	0 06-0 5	●		
azlodllin	0.5-2	●		
cephalotin	0 25-16		●	
cefotaxime	4->128			●
cefepime	4->64			●
imipenem	0.03-0.12	●		
gentamicin	0 06-4	●		
sisomicin	0.01-0.12	●		
netilmicin	0 06-32	●		
amikacin	<0.06-32	●		
kanamycin	0 5-2		●	
streptomycin	0.5-4		●	
nalidixic acid	>128			●
D-ofloxacin	>64			●
levofloxacin	1-4		●	
ciprofloxacin	0.5-2		●	
CI 934	0 25-1	●		
Bay Y 3118	0.06-0.25	●		
vancomycin	0 12-0 5	●		
teicoplanin	0.12-0.5	●		
daptomycin	0.25-4		●	
cotrimoxazole	0.06-0.5	●		
chloramphenicol	2-8		●	
rifampicin	0.04-0.25	●		
fosfomycin	4-2048			●
clindamycin	0.25-4		●	
tetracycline	0 12 0 5	●		

DNA gyrase

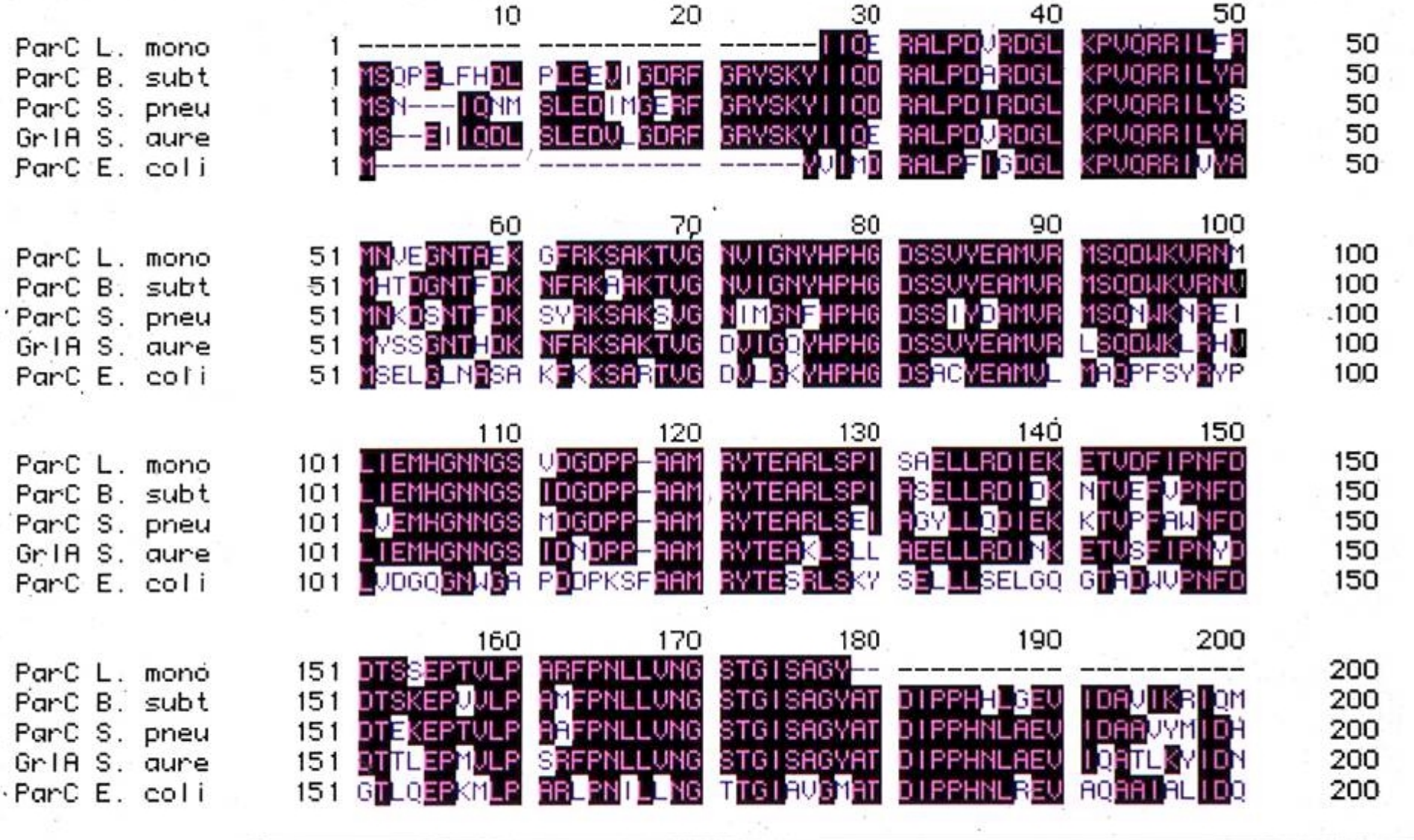


Alignment of the quinolone resistance-determining regions (QRDRs) located in the N-termini of GyrA (subunit A of DNA gyrase)



Structural alignment between GyrA of *E. coli* and of *L. monocytogenes* displaying the important amino acid variations. A section of the QRDRs near the active site Tyr122 (blue) is shown. Differences in the sidechains at the mutational hot spots Ser83 and Asp87 (*E. coli*) are coloured green and red, respectively. In this view, the additional methyl group of threonine is pointing to the right, as does the aromatic ring of phenylalanine. The altered sidechain at position 116 is marked in yellow.

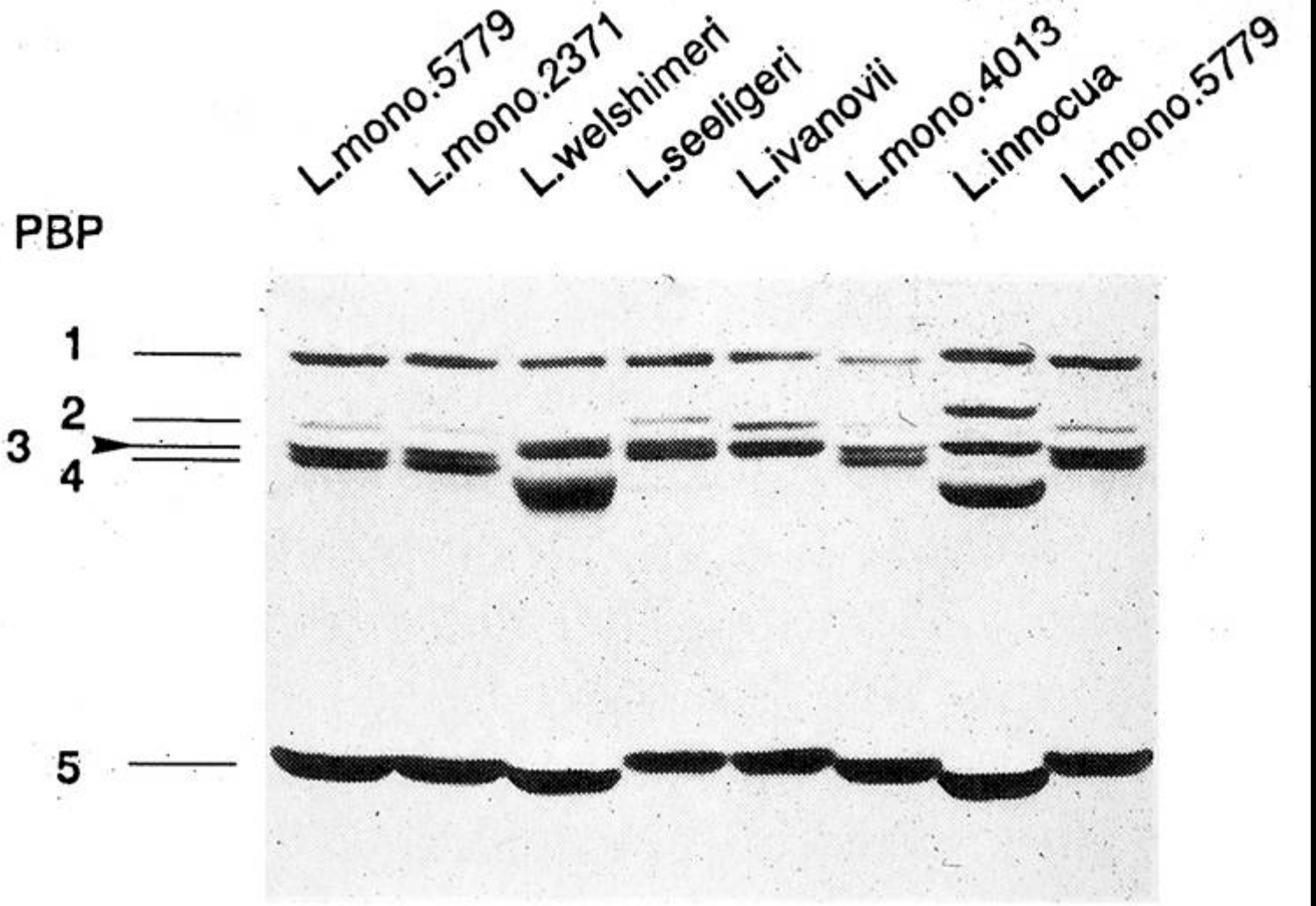
DNA topoisomerase IV



Alignment of the quinolone resistan-edetermining regions (QRDRs) located in the N-termini of ParC (subunit A of DNA topoisomerase IV)

Susceptibility of *L. monocytogenes* to cephalosporins and few other ß-lactams (MIC values: mg/l)

	SLCC 5835 (EGD)	SLCC 7140	SLCC 4949
Ampicillin	0.5	2	0.5
Cephalothin	4	4	0.25
Cefoxitin	32	64	2
Cefuroxime	128	128	0.5
Cefotaxime	64	128	0.25
Cefepime	64	128	8
Cefpirome	32	64	1
Mecillinam	64	128	8
Aztreonam	>2048	>2048	4



Penicillin-binding protein (PBP) profiles of five *Listeria* species. Membranes were incubated with [^{3}H]-propionyl ampicillin and prepared for SDS-PAGE as described in the text. The PBPs of *L. monocytogenes* are schematically indicated on the left, with the arrow marking the position of PBP

Numbers of

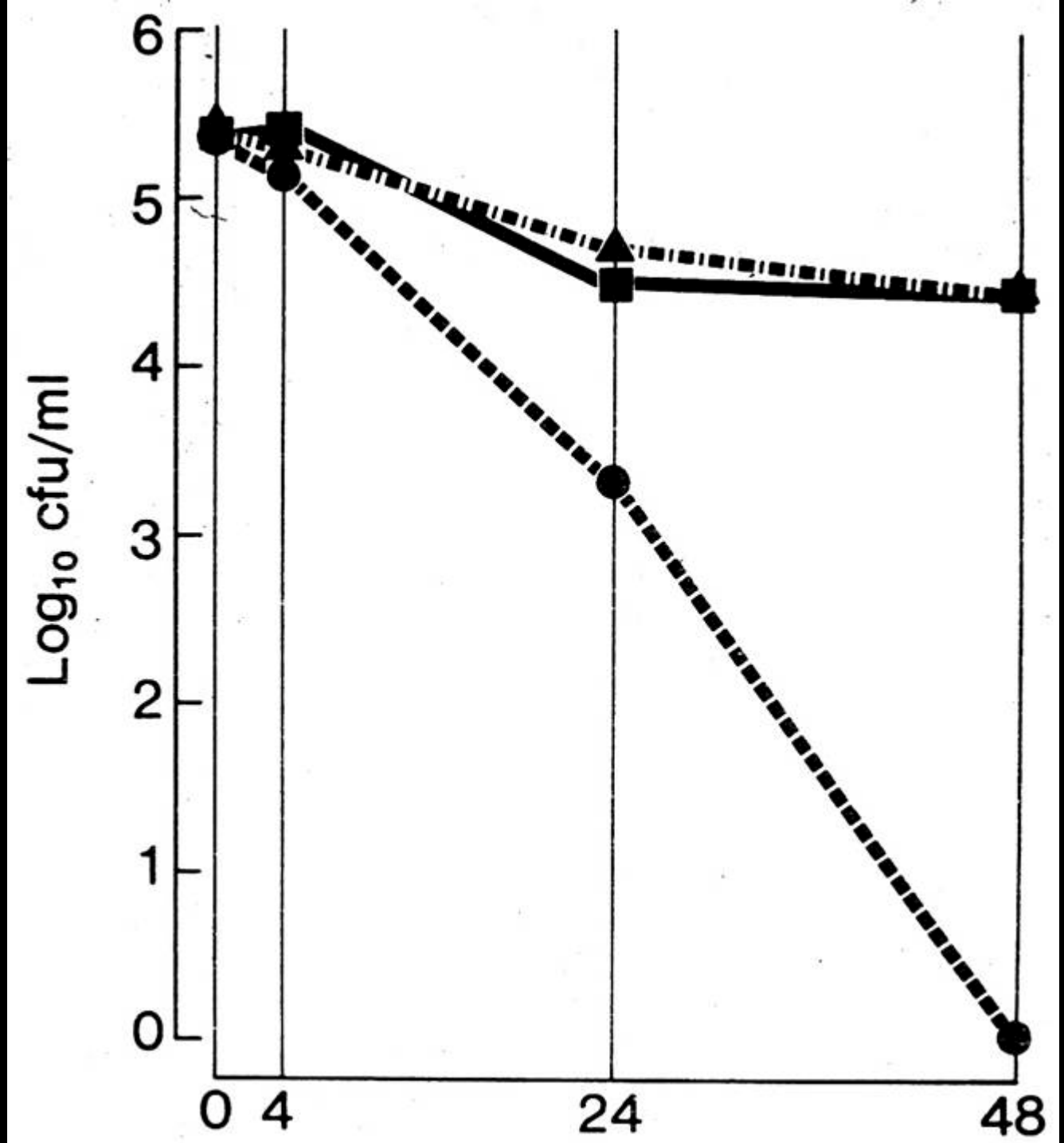
Penicillin Binding Proteins

from *Listeria monocytogenes* per cell

PBP 1	:	120
PBP 2	:	80
PBP 3	:	145
PBP 4	:	130
PBP 5	:	600

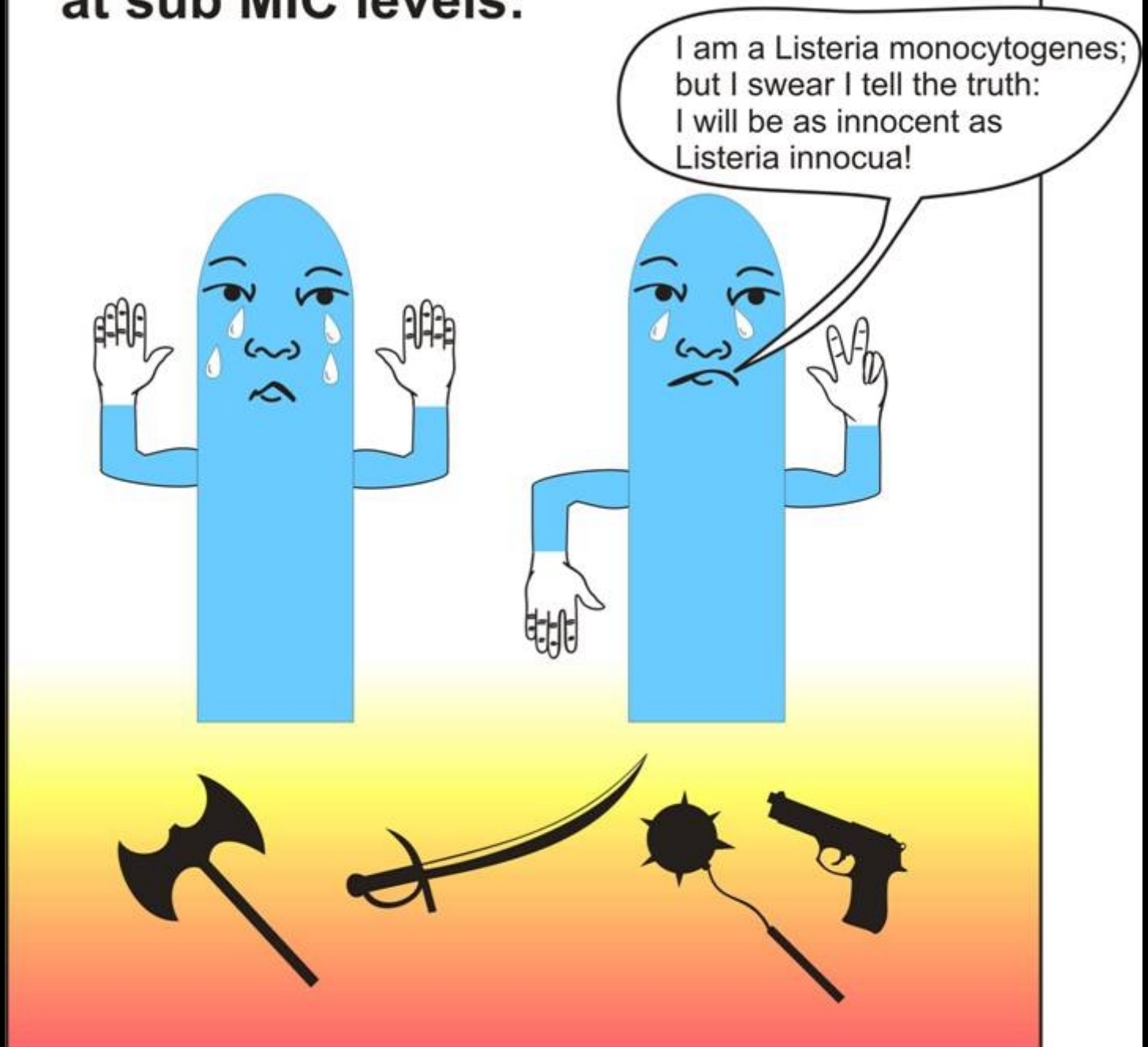
PBP 3 of Listeria ssp.

- identical in all Listeria ssp.
- involved in the last stages of peptidoglycan synthesis
- essential (blockage of this enzyme has deleterious consequences for the bacterial cell)
- does not bind cefotaxime
- does not bind aztreonam


6
5
4
3
2
1
0
Log10 cfu/ml
0
4
24
48

agent	range of MIC values (mg/l)	interpretation of inhibitory action			interpretation of bactericidal action		
		susceptibel	intermediate	resistant	yes	tolerant or weak	no
penicillin	0.06-2	●				●	
ampicillin/ amoxycillin	0.06-0.5	●				●	
azlocillin	0.5-2	●				●	
cephalotin	0.25-16		●				●
cefotaxime	4->128			●			●
cefepime	4->64			●			●
imipenem	0.03-0.12	●				●	
gentamicin	0.06-4	●			●		
sisomicin	0.01-0.12	●			●		
netilmicin	0.06-32	●			●		
amikacin	<0.06-32	●			●		
kanamycin	0.5-2		●			●	
streptomycin	0.5-4		●			●	
nalidixic acid	>128			●			●
D-ofloxacin	>64			●			●
levofloxacin	1-4		●				●
ciprofloxacin	0.5-2		●				●
CI 934	0.25-1	●				●	
Bay Y 3118	0.06-0.25	●				●	
vancomycin	0.12-0.5	●			●		
teicoplanin	0.12-0.5	●			●		
daptomycin	0.25-4		●				●
cotrimoxazole	0.06-0.5	●			●		
chloramphenicol	2-8		●				●
rifampicin	0.04-0.25	●					●
fosfomycin	4-2048			●			●
clindamycin	0.25-4		●				●
tetracycline	0.12-0.5	●					●

at sub MIC levels:



Prerequisites for the intracellular activity of an antibiotic

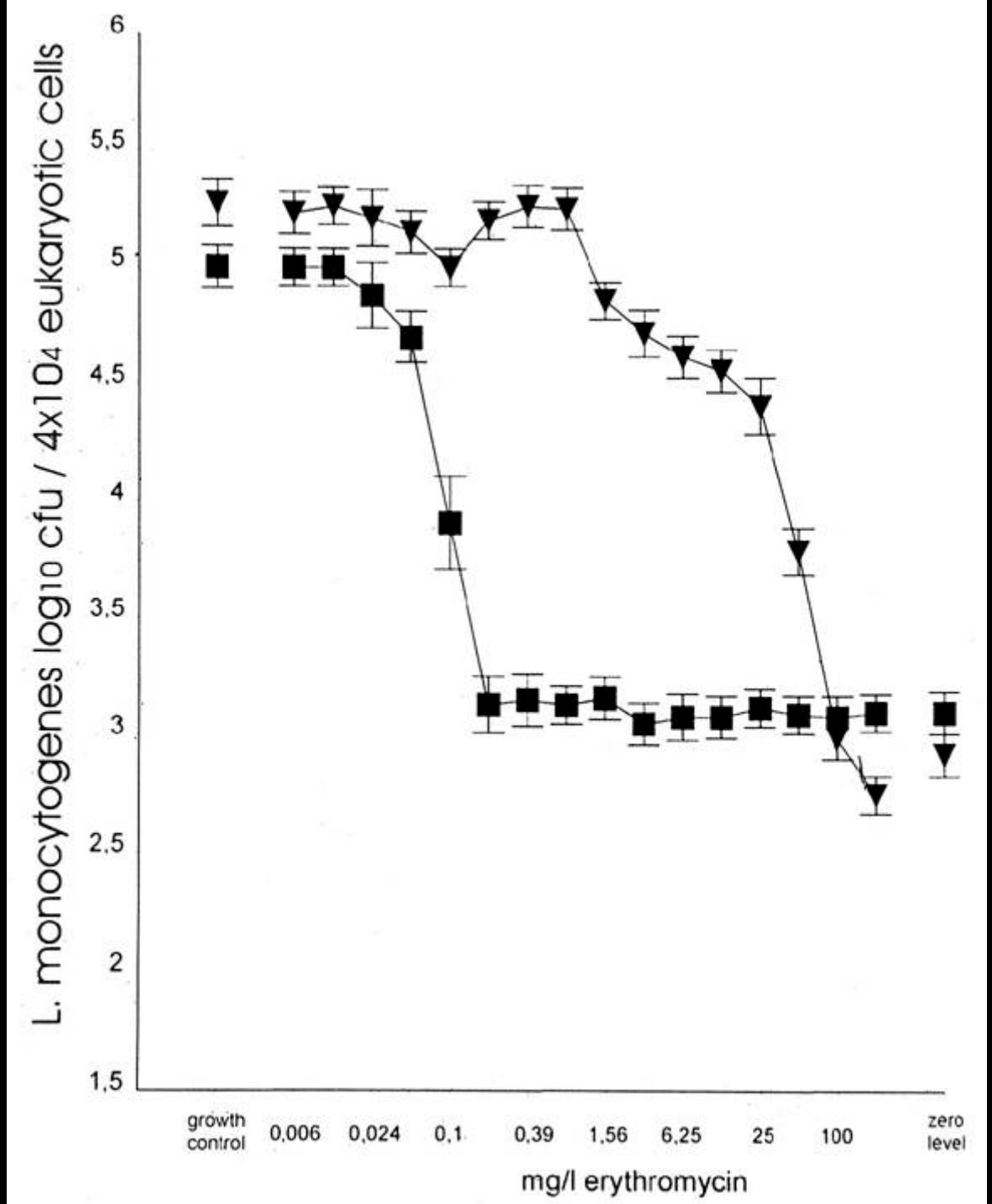
- Penetration into the cell by diffusion or active transport
- Intracellular persistence and eventually accumulation (import higher than export)
- Distribution within the cell to the proper compartment where the pathogen resides

a) cytosol
b) lysosome
c) phagocytic vacuole
d) nucleus

- Stability and activity in the particular environmental condition

Locations of spontaneous expression of the MDR-gen

Duodeum	++
Jejunum	++
Ileum	+++*
Uterus epithelium of pregnant rats	+++
Uterus epithelium of non-pregnant rats	+
Placenta (trophoblasts)	+++
Testis (seminiferous epithelium)	+++
Kidney (cortex)	++
Kidney (medulla)	—
Capillary endothelium in brain	+++


L. monocytogenes log10 cfu / 4x10⁴ eukaryotic cells
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
growth control
0,006
0,024
0,1
0,39
1,56
6,25
25
100
zero level
mg/l erythromycin

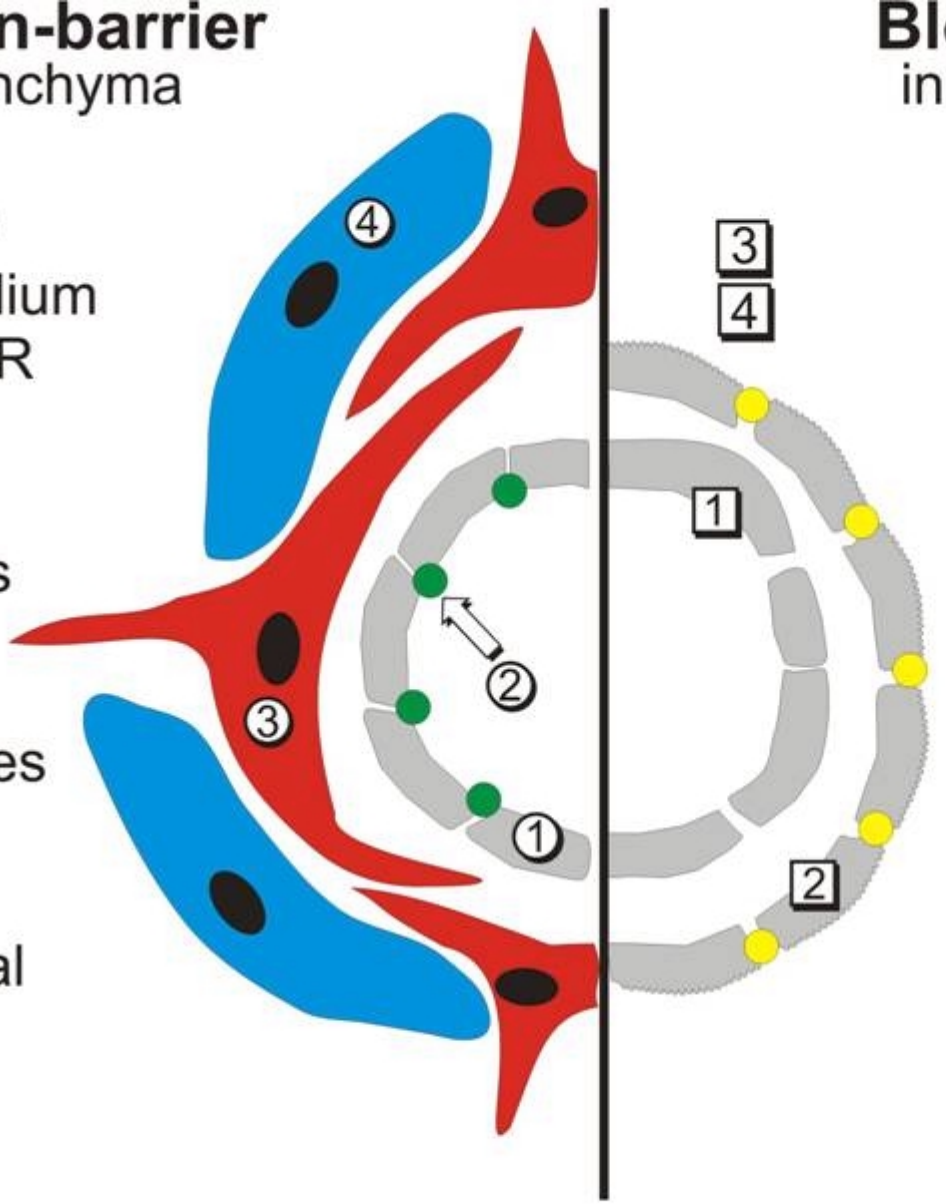
Blood-brain-barrier
in the parenchyma

① capillary endothelium with MDR

② tight junctions

③ astrocytes

④ microglial cells



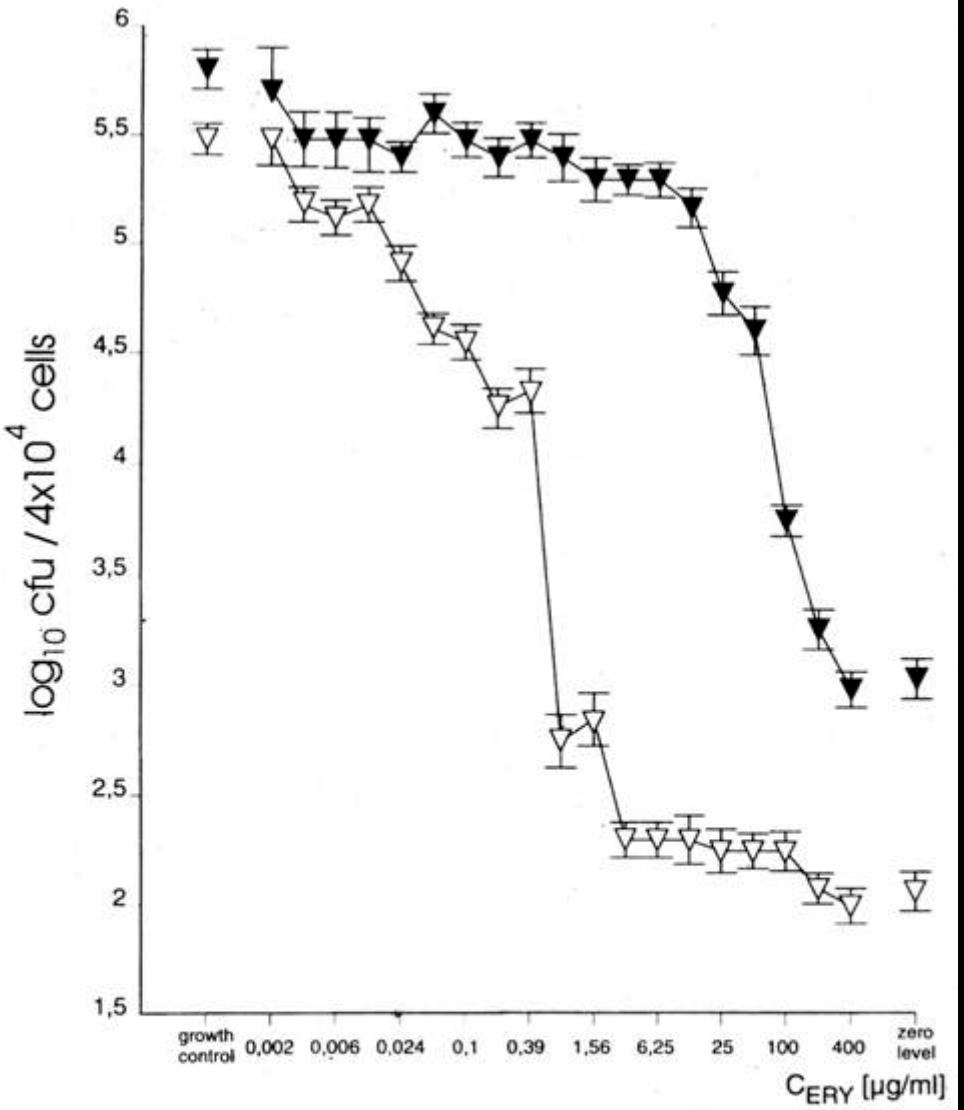
Blood-CSF-barrier
in the choroid plexus

1 capillary endothelium:
- no tight junctions
- partially fenestrated
- with MDR?

2 epithial cells from the choroid plexus (with tight junctions)

3 no astrocytes

4 no microglia



Reversal of the susceptibility of *L. monocytogenes* by verapamil. KBV-1 cells were incubated without verapamil (▼) and with verapamil (▽). In this experiment, vinblastine was included in the supernatant for the whole incubation time of 24 hours. However, similar results were obtained without vinblastine or with gentamicin, or with a shorter incubation time of 5 hours.

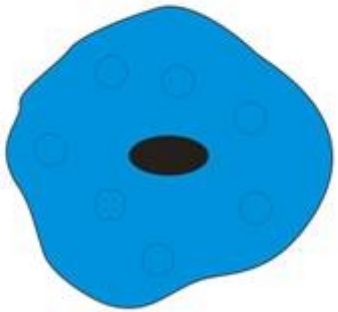
	KBV-1	G185
Erythromycin	+	+
Clarithromycin	+	+
Azithromycin	+	+
Fusidic acid	+	—
Clindamycin	+	—
RP 59500	+	—
Rifampicin	(+)	—
Ciprofloxacin	(+)	—
Ofloxacin	(+)	—
Cotrimoxazole	(+)	—
Doxycycline	(+)	—
Chloramphenicol	—	—
Fosfomycin	—	—
Vancomycin	—	—

Intrazelluläre Verteilung von Antibiotika

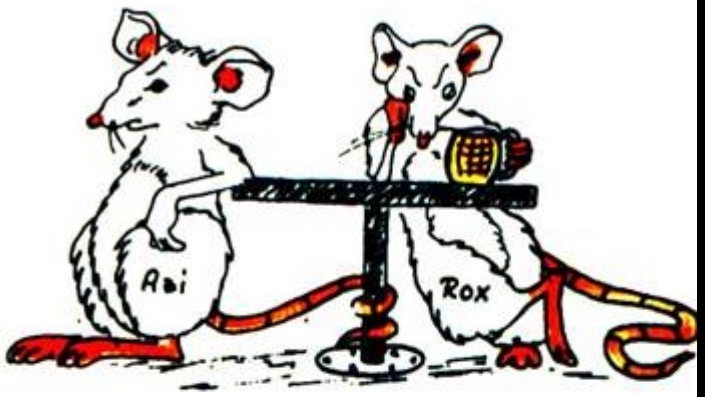
Teicoplanin

Aminoglykoside

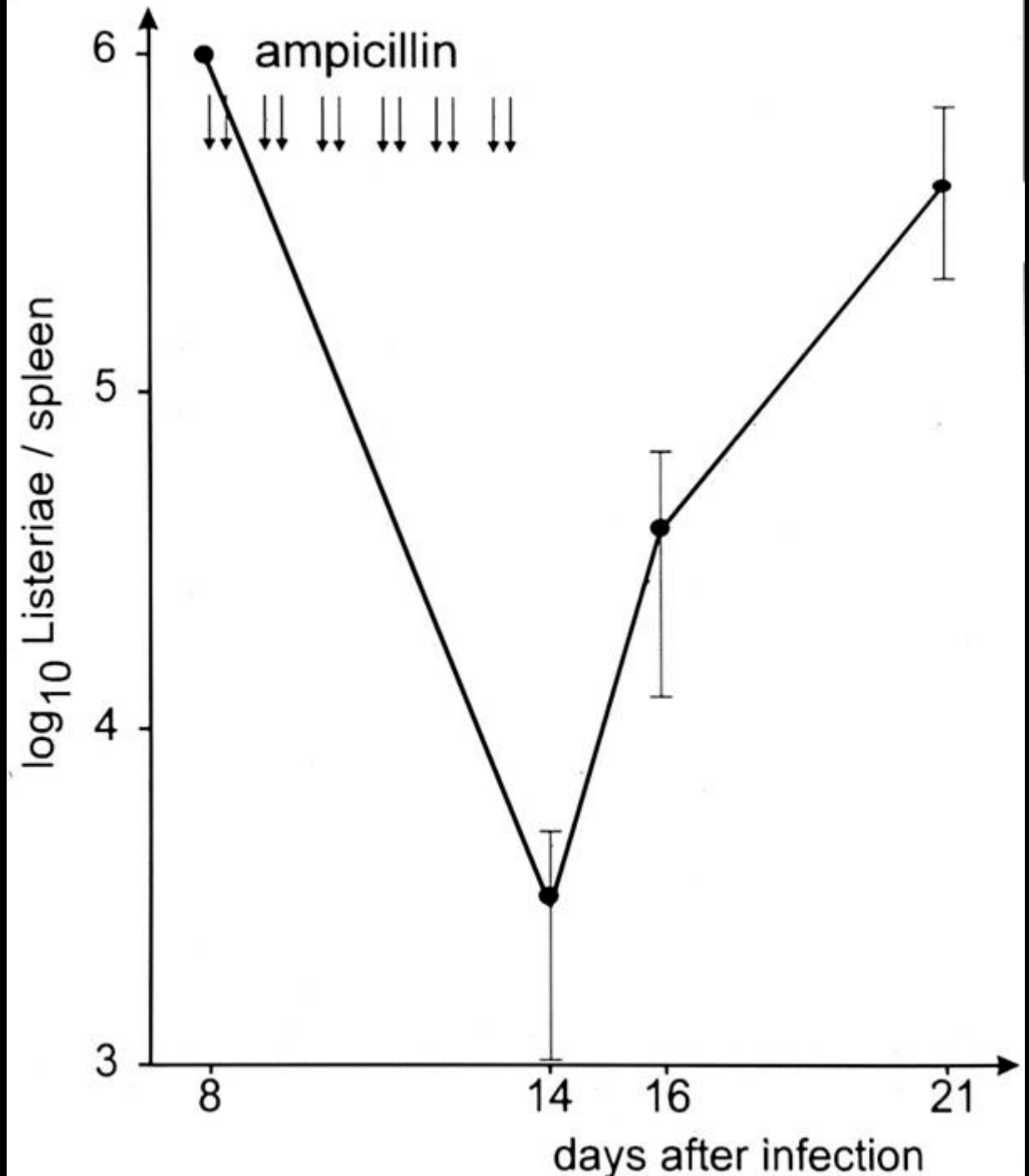
Makrolide



Azithromycin;
Chinolone



Beuw


ampicillin
6
5
4
3
log10 Listeriae / spleen
8
14
16
21
days after infection