Ecole
Nationale
Vétérinaire
Toulouse

Postweaning *E. coli* diarrhea
Colitoxicosis
Edema disease

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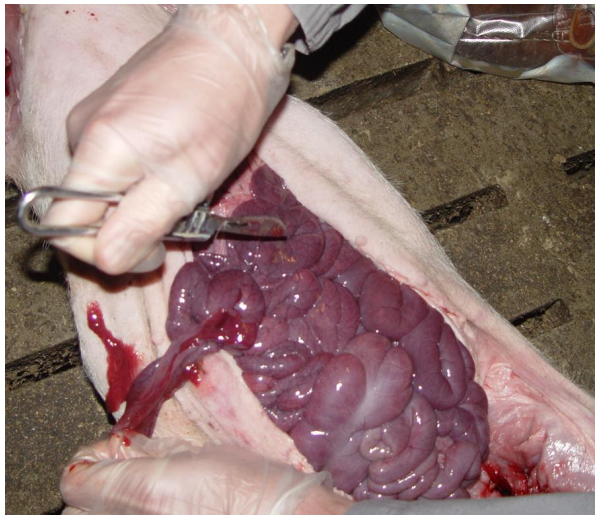
Mantova, 18th of February 2010

« Why and How »

Whatever the problem,
we have always 2 questions to answer
.

- « How » to rectify the problem as soon as possible ?
- « Why » the problem occurs ?



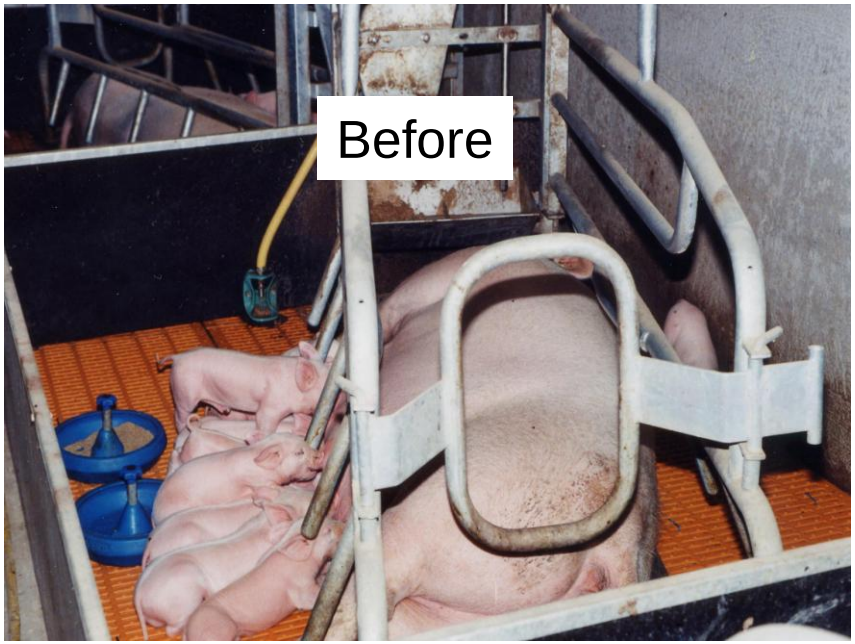
PWD

- « Common », non fatal,
- Classical prophylaxis
  - France:
    - In feed: « colistine 1er âge »
    - water: colistine
  - North America / DK / Spain: Zn0
- Effect on growth
- *E. coli*

  F4 (K88) (classic)

  F18 (edema disease + enterotoxins)
- PWD = pathology of transition

Disease of transition

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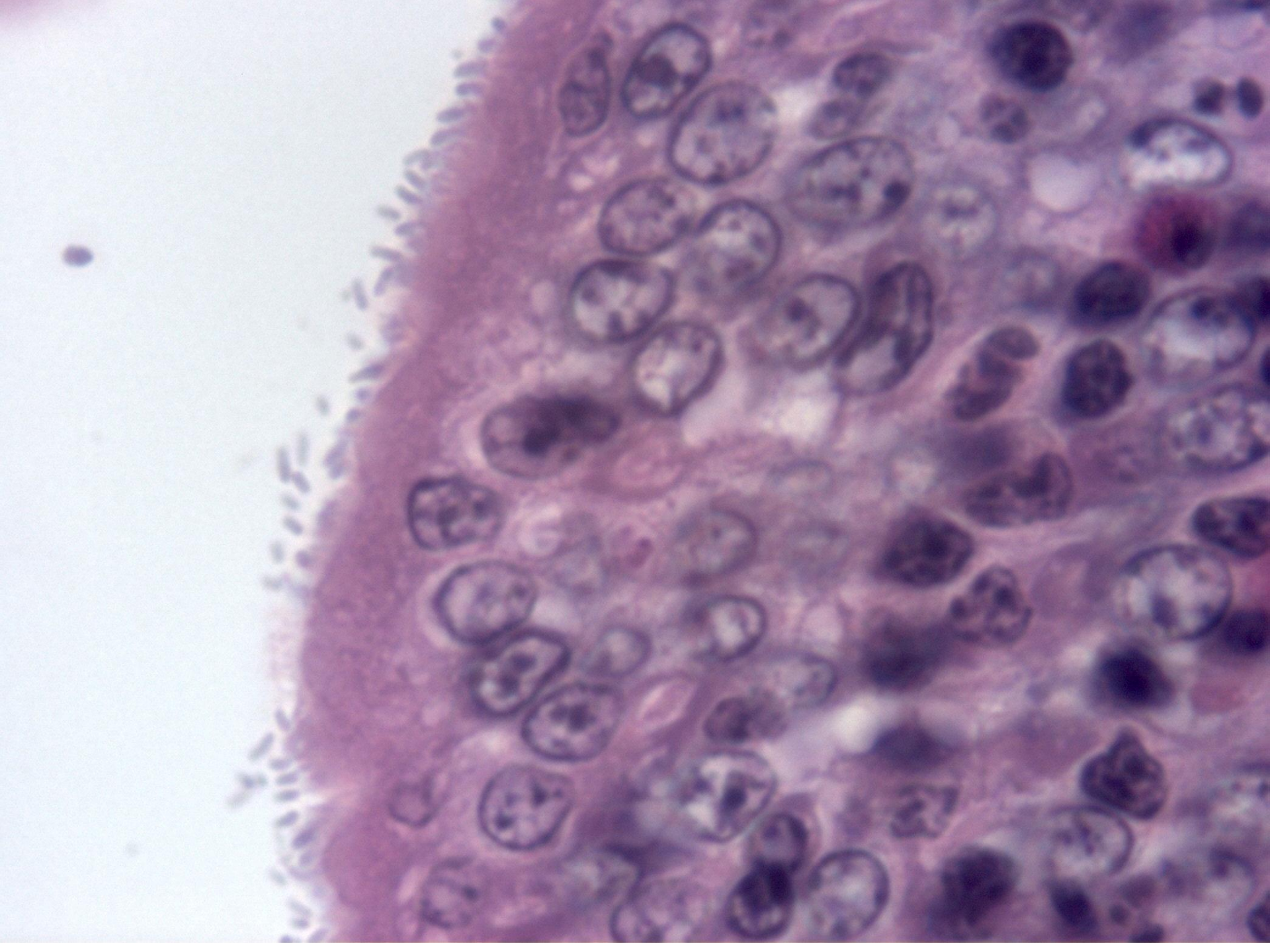
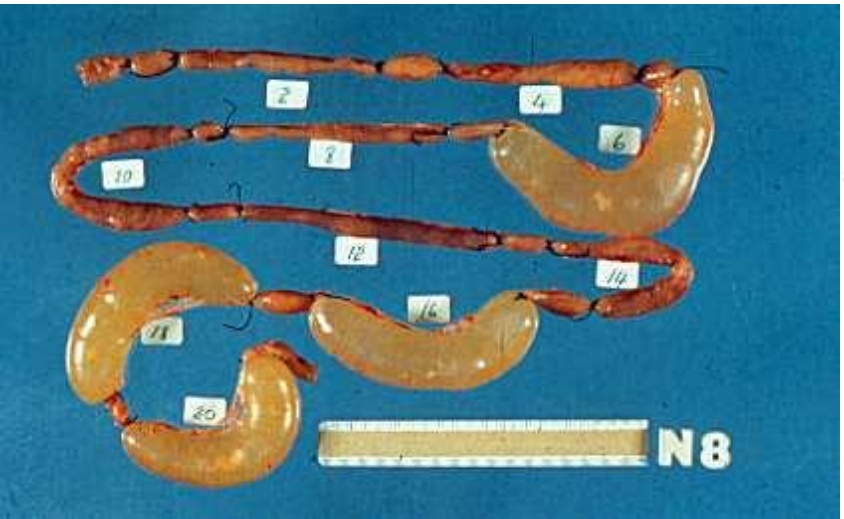
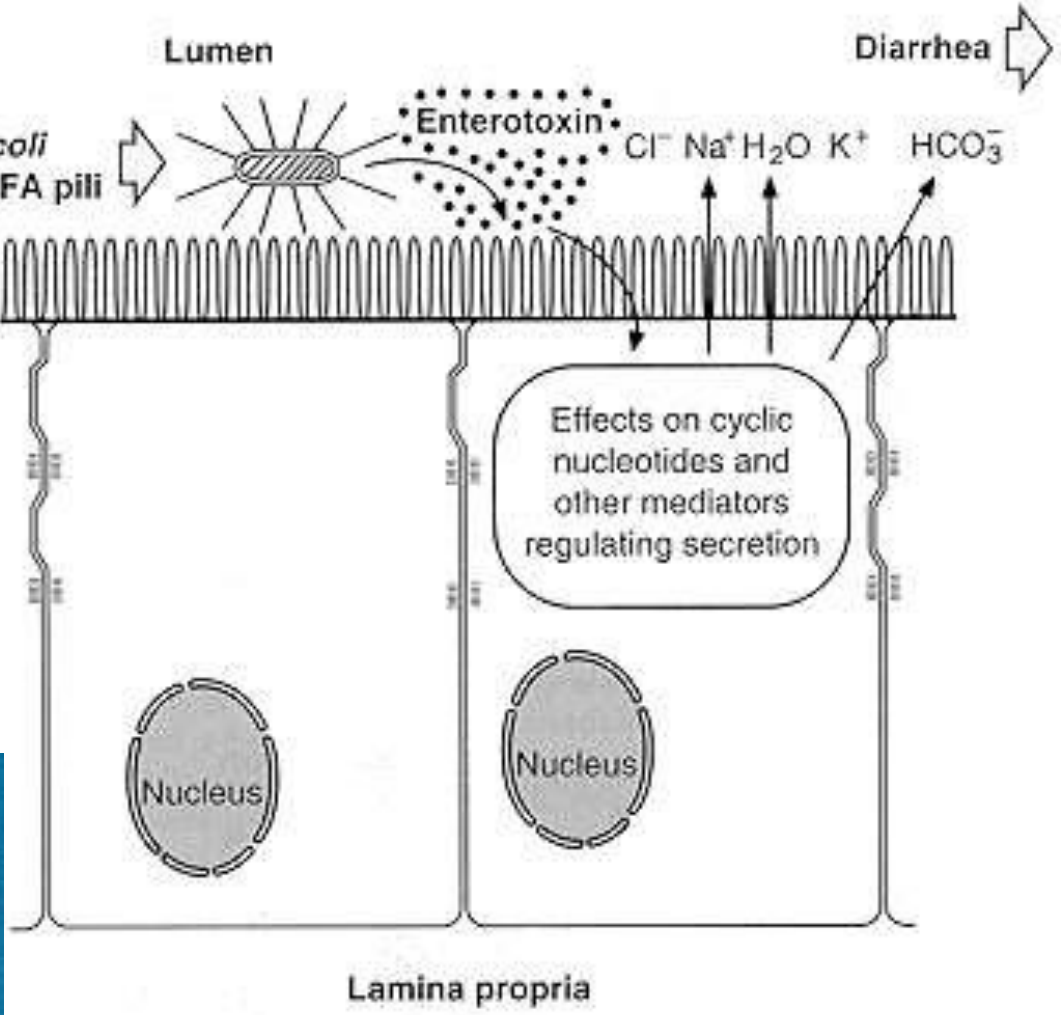


E. coli: Fimbriae (adhesins)

F4 = K88 ab, **<u>ac</u>**, ad

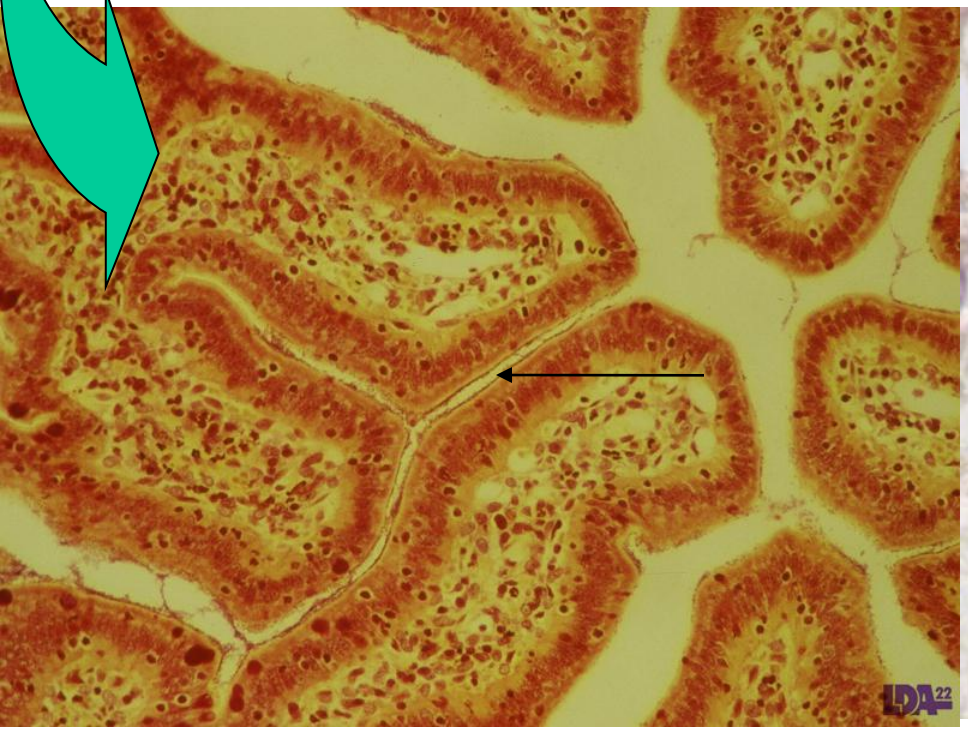
F18 = F107 (**<u>ab</u>**, ac)



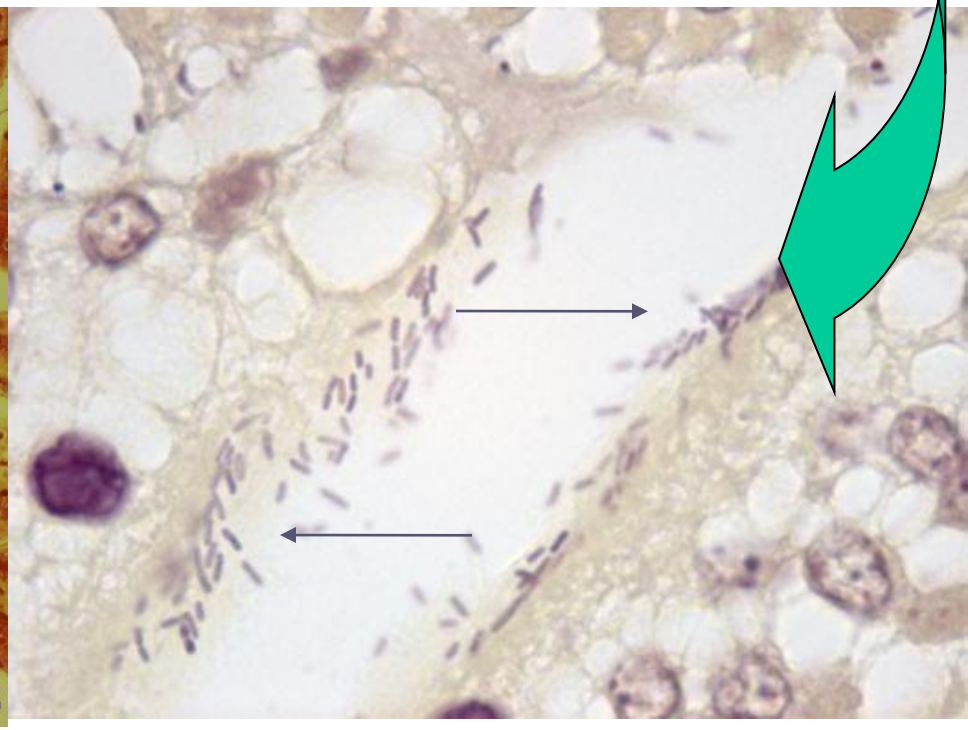


- Villis are normal
- Gram negative bacteria on the mucosa

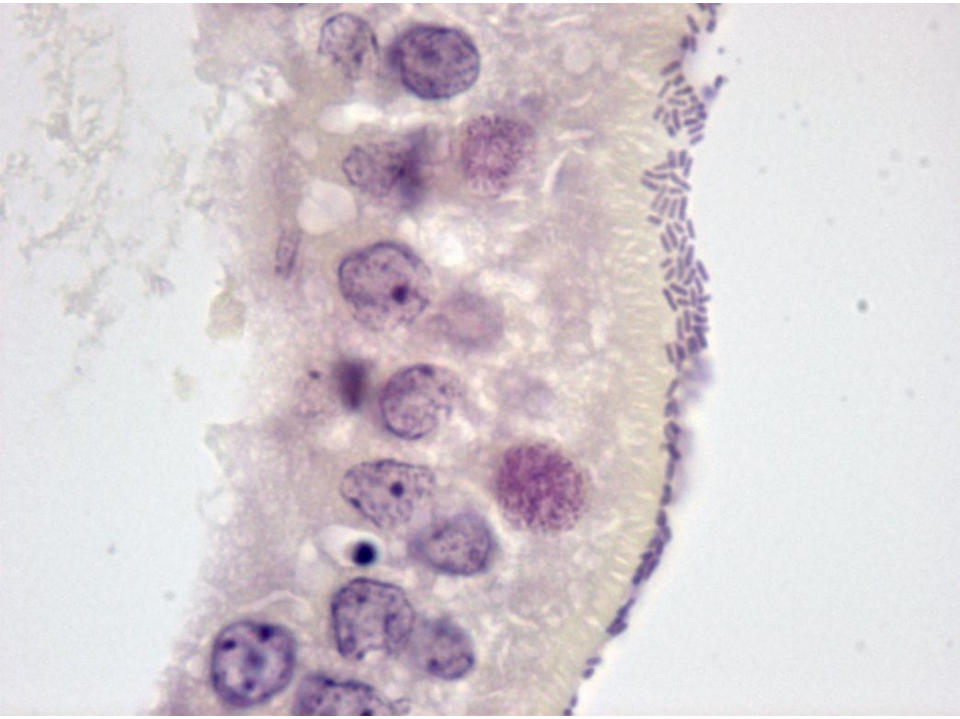
HES coloration



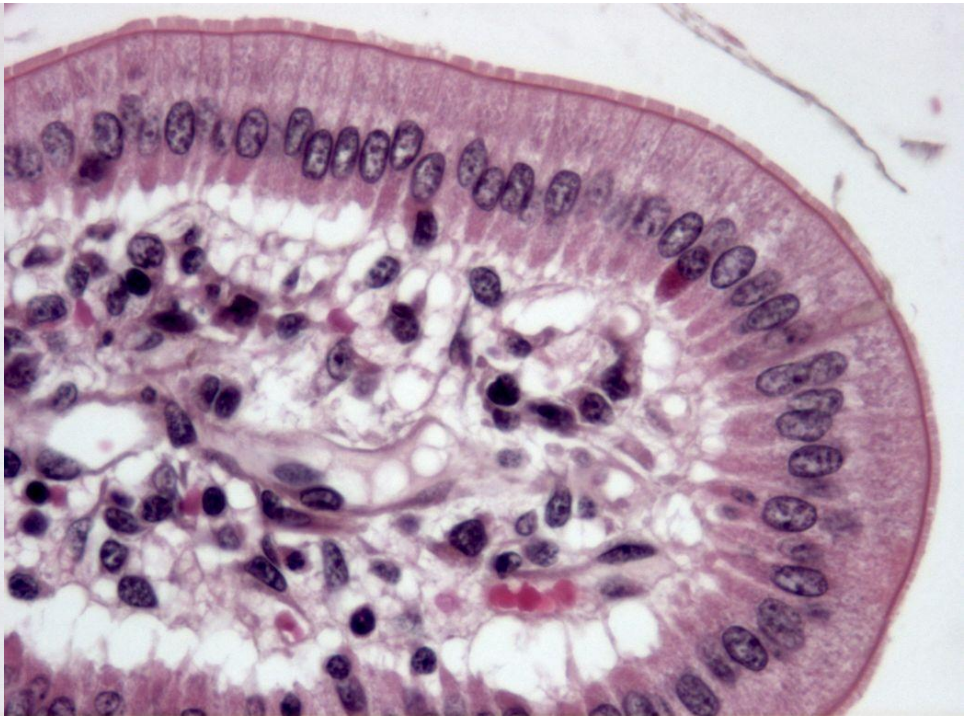
Gram coloration(x 1000)



PWD (*E. coli*) (Gram)

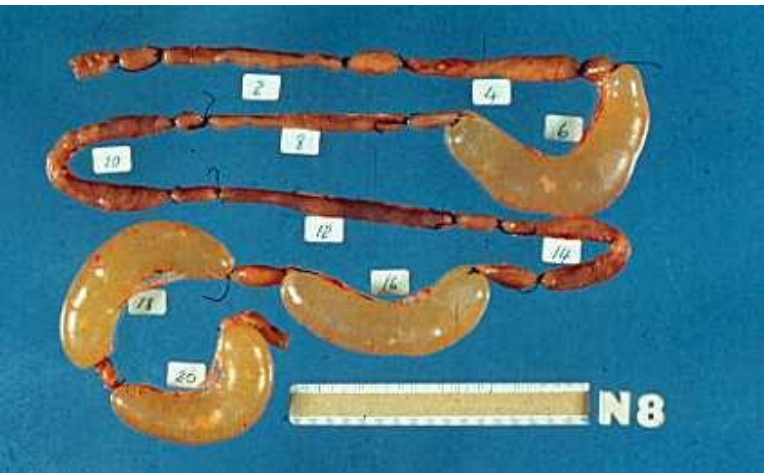


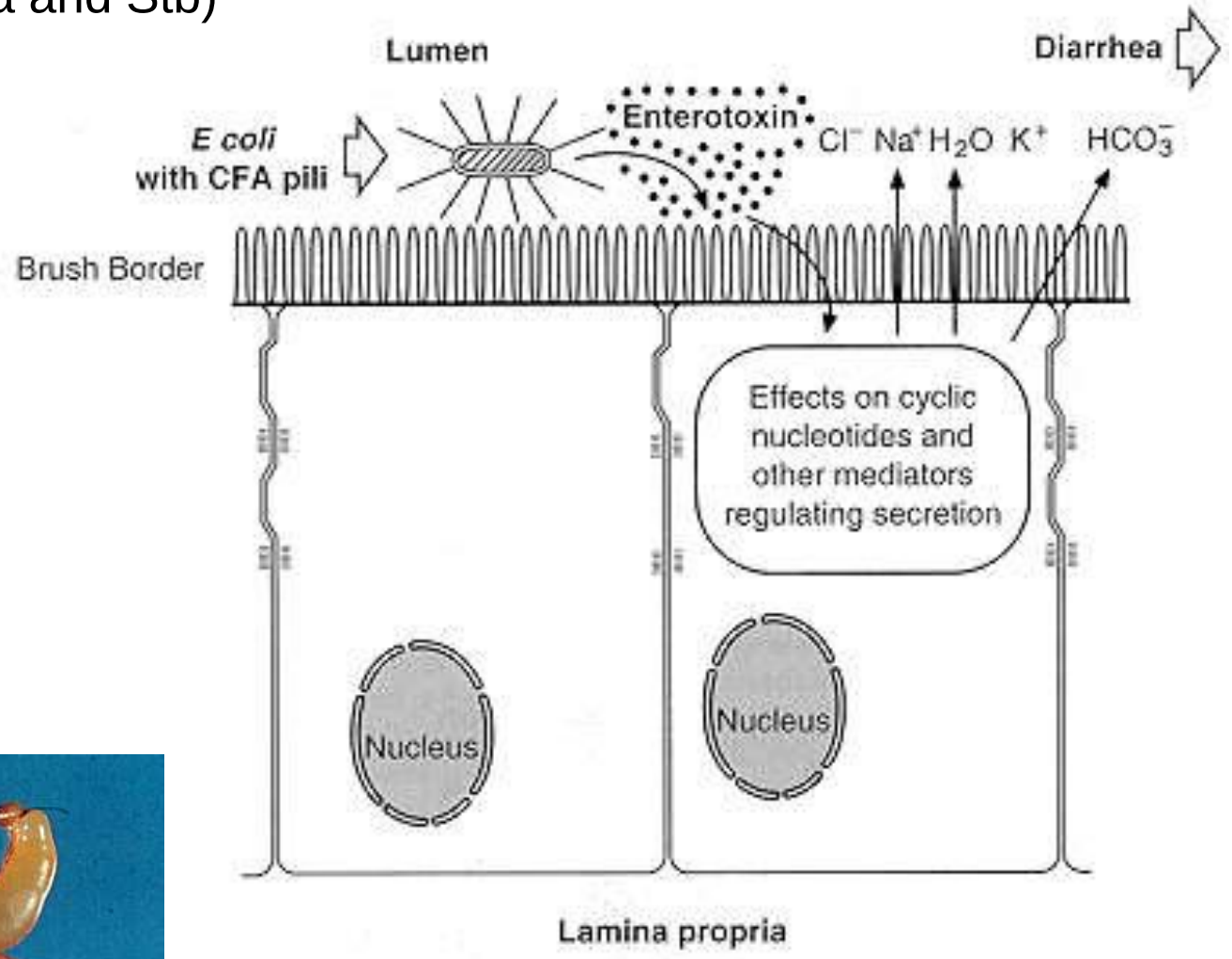
Normal brush border (HES)

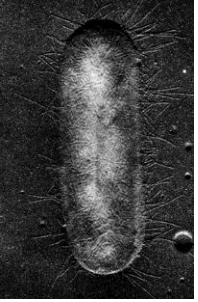


E. coli: Enterotoxins

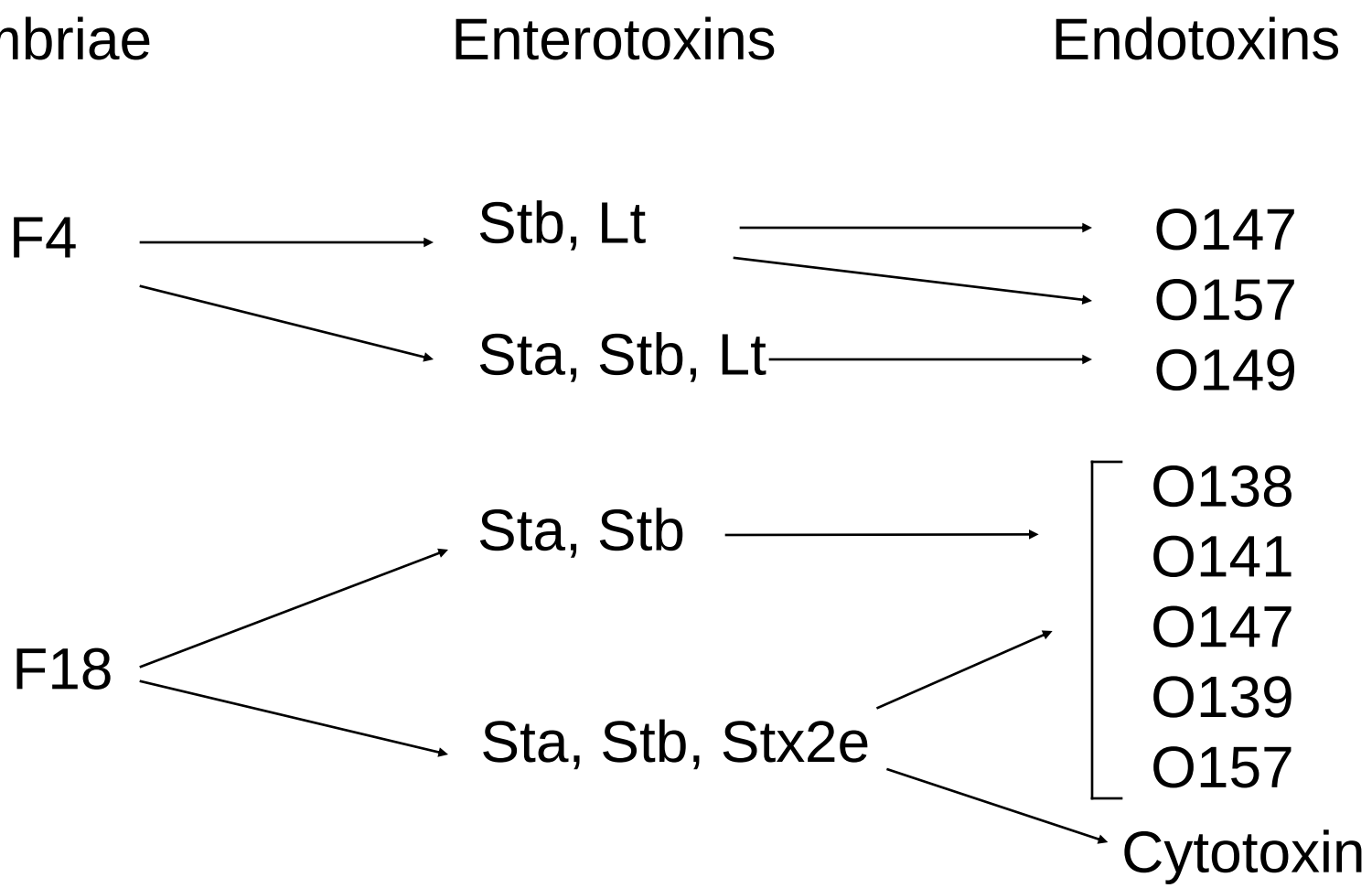
Heat Stable (ST: Sta and Stb)
Heat Labile (LT)
Shiga Toxin (Stx2e)





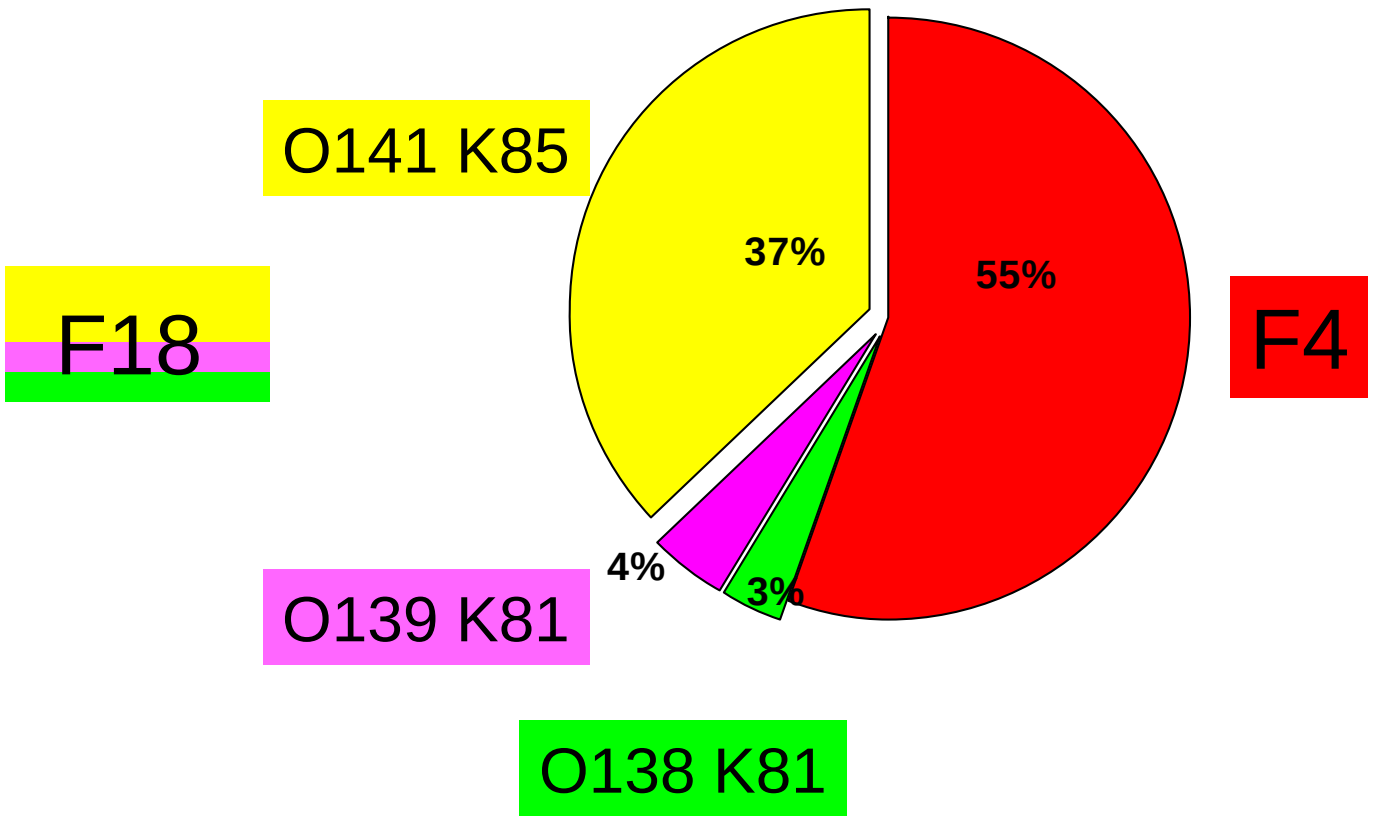


Postweaning *E. coli* diarrhea



The French situation (Labofarm, 2009)

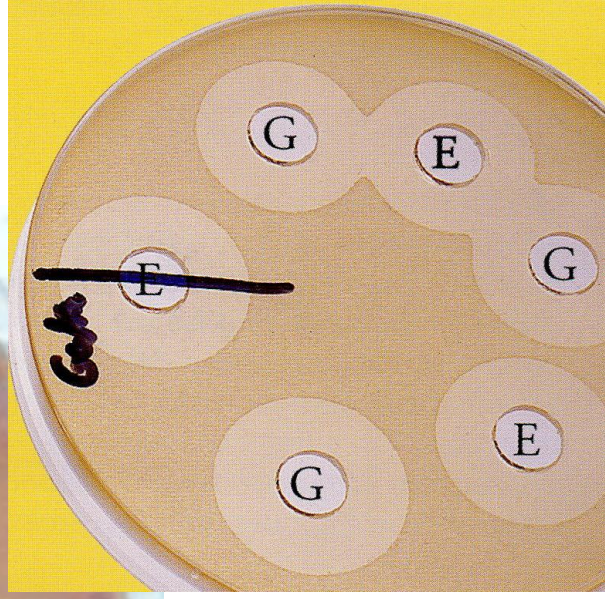
E. coli (PWD) 2002-2008



Le Guennec, 2009

Table 3: Patterns of susceptibility to disease

Adhesin	Age of susceptibility	Lineage-specific
987P	0-2 weeks	no
K99	0-2 weeks	no
K88	0-8 weeks (likely)	yes (autosomal dominant)
F18	3-8 weeks (likely)	yes (autosomal dominant)

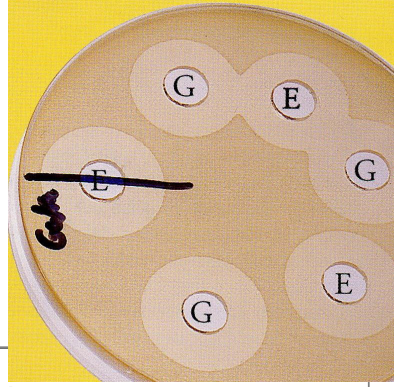


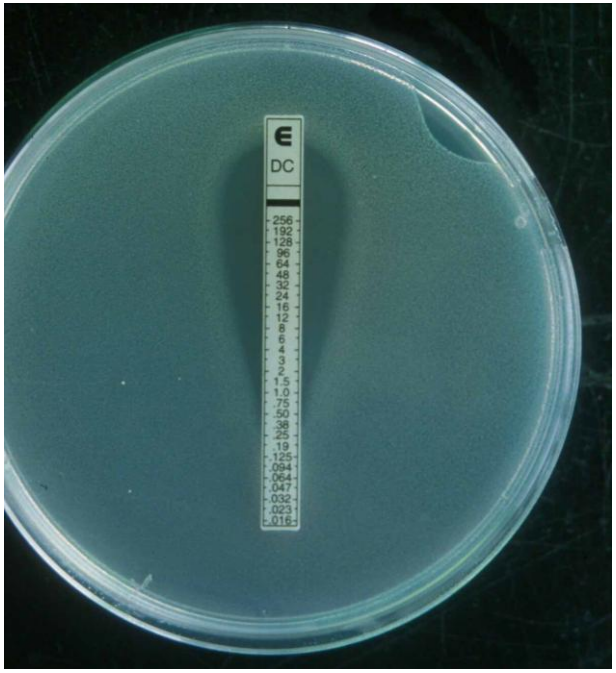
Hemolytic F4 *E. coli*

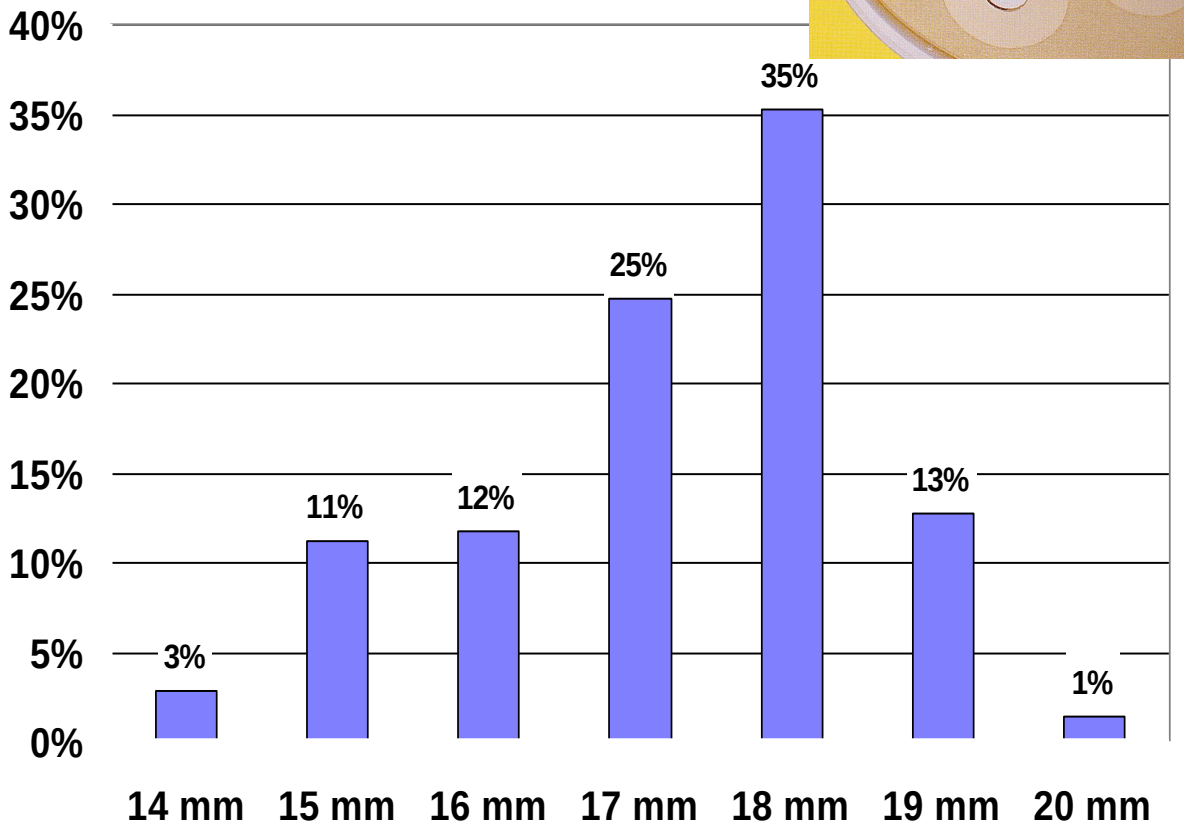
AntibioR

Antibiotic	**% Resistant**	**N=1300**
Gentamicine	5	
Néomycine	10	
Apramycine	2	
Amoxicilline	51	
Céfalexine	3	
Ceftiofur	1	
TMP sulfa	59	
Flumequine	15	
Marbofloxacine	8	
Enrofloxacine	8	
Florfenicol	2	

- E test if diameter below 18mm

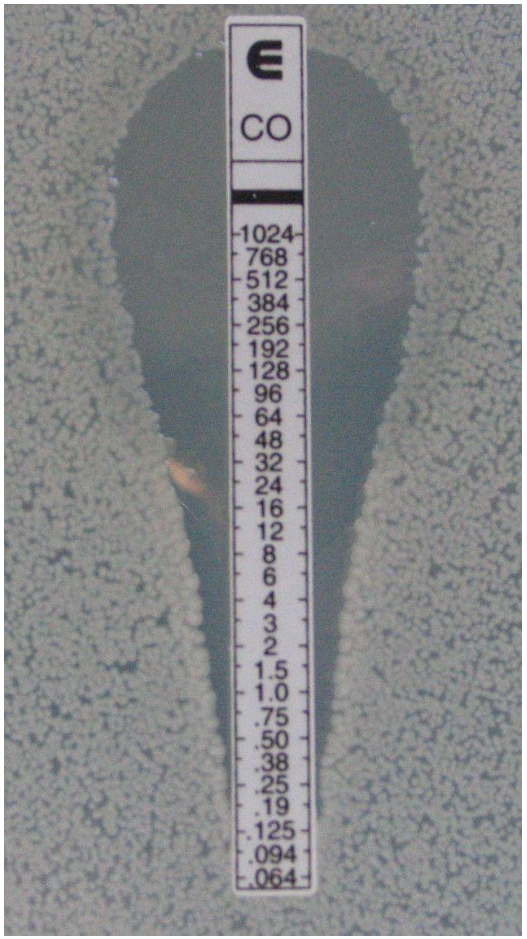




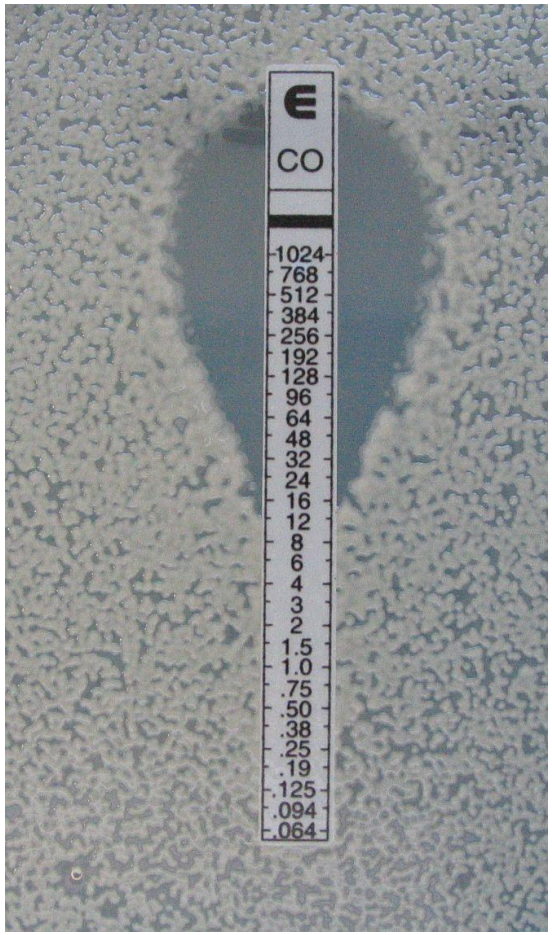


Colistine : some strains are R

S 0,19 µg/ml



R 16 µg/ml



MIC : relation diameter and E-Test

Diameter	Number of strains	MIC by E Test		% strains with MIC ≥ 2 µg/ml
		>2 µg/ml	<2 µg/ml	
<15 mm	1	**1**	0	100 %
15 mm	7	**7**	0	100 %
16 mm	11	**9**	**2**	82 %
17 mm	15	**2**	**13**	15 %
18 mm	22	0	**22**	0 %
≥ 19 mm	14	0	**14**	0 %

PWD: pathophysiology (herd)

Agressions Résistance

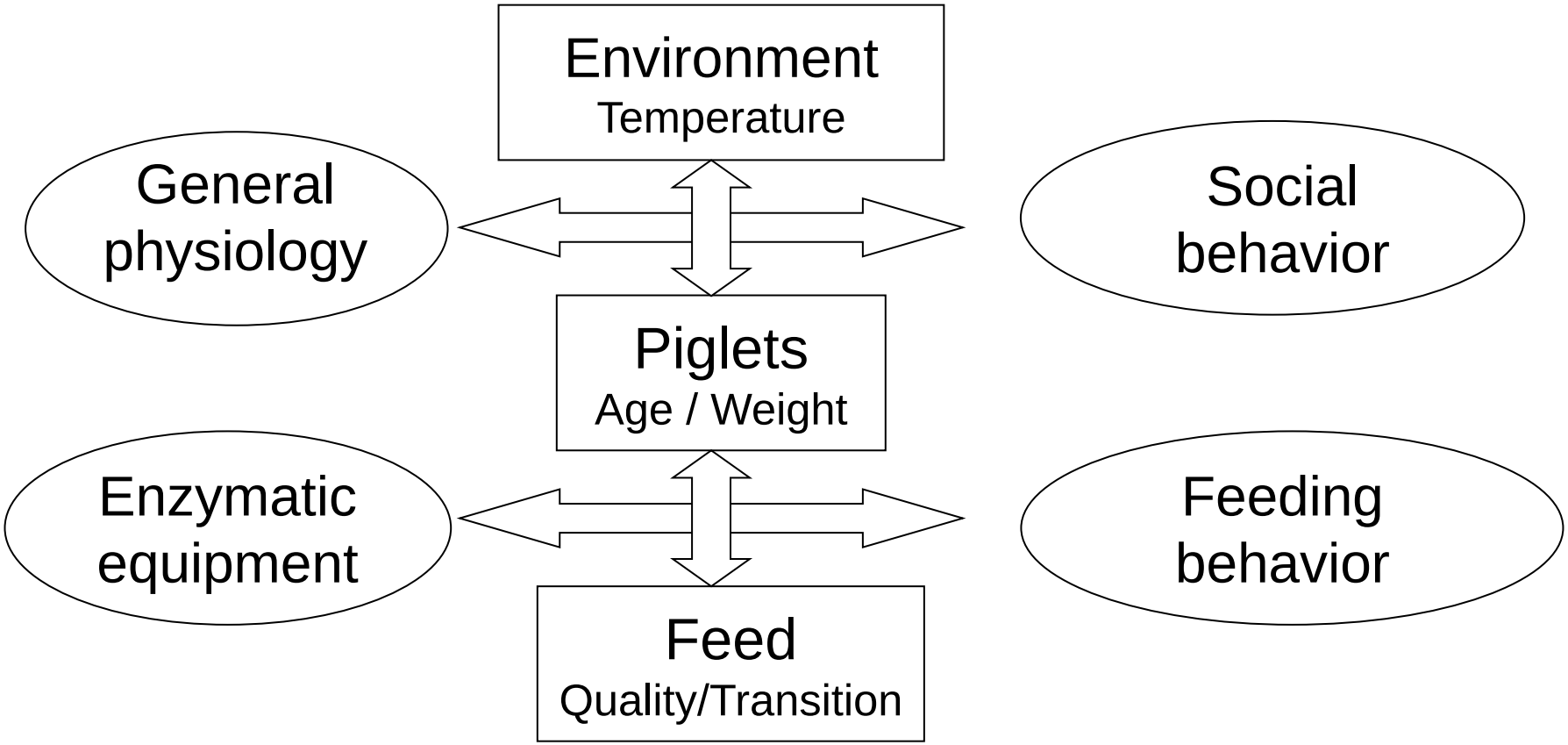
Résistance

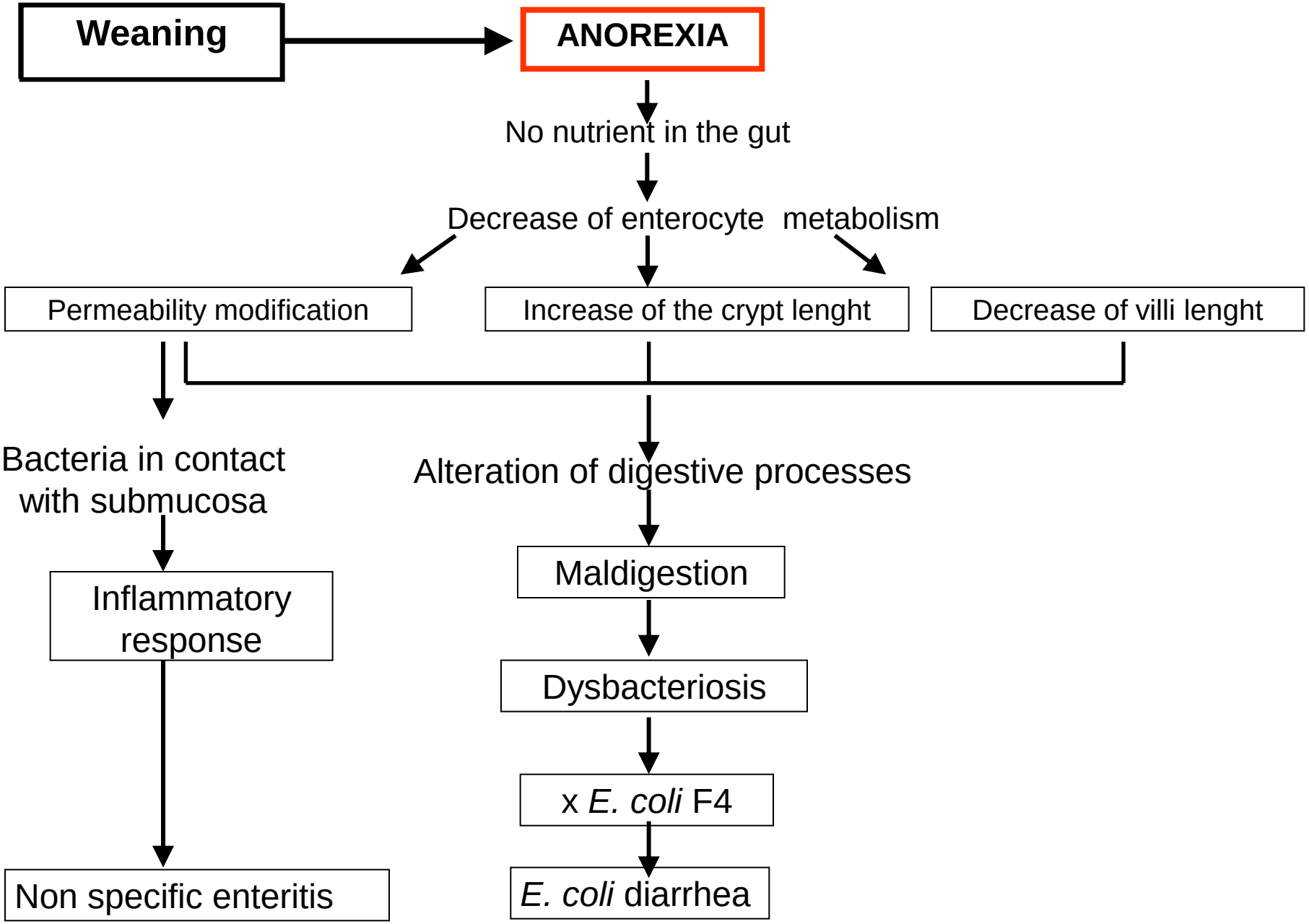
Agressions

Résistance

Agressions

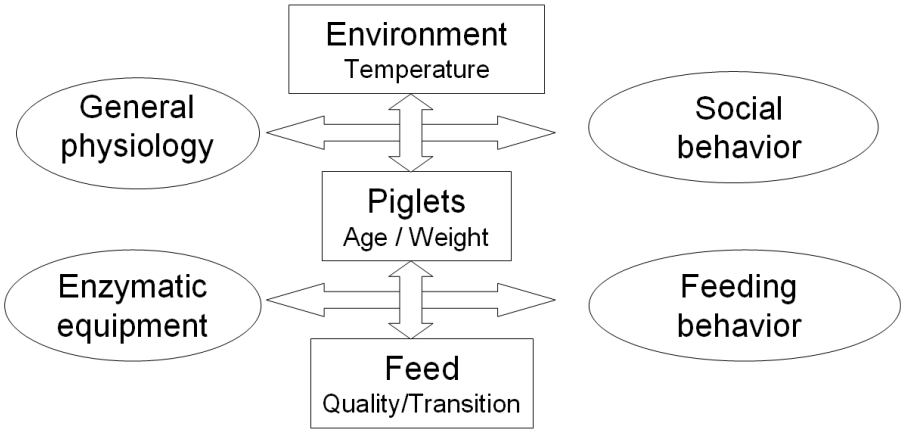
PWD: pathophysiology (herd)



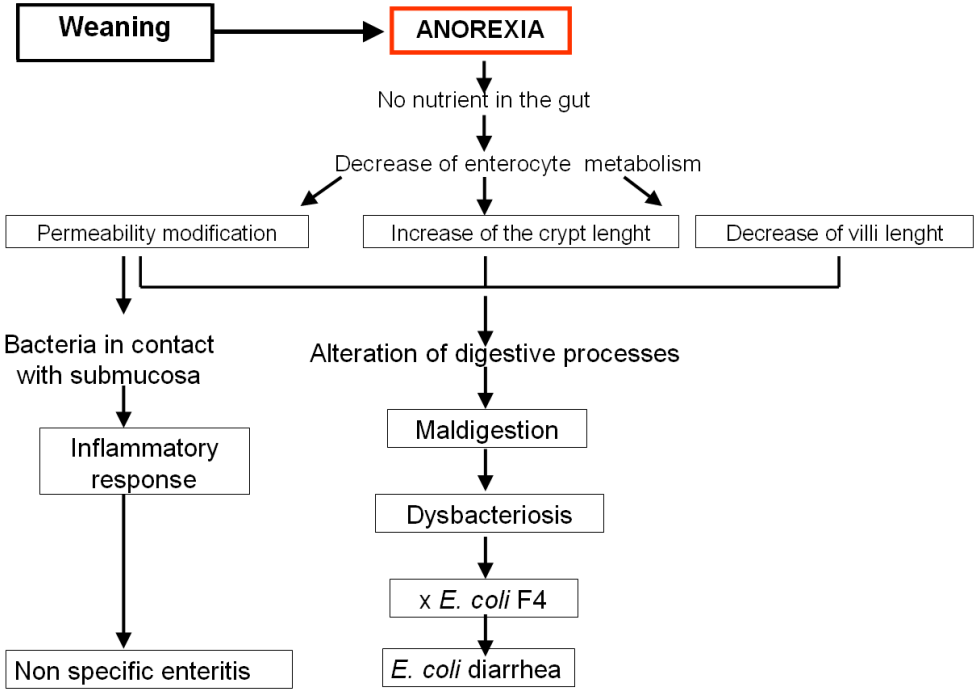


Adapted from David Guillou, 2008

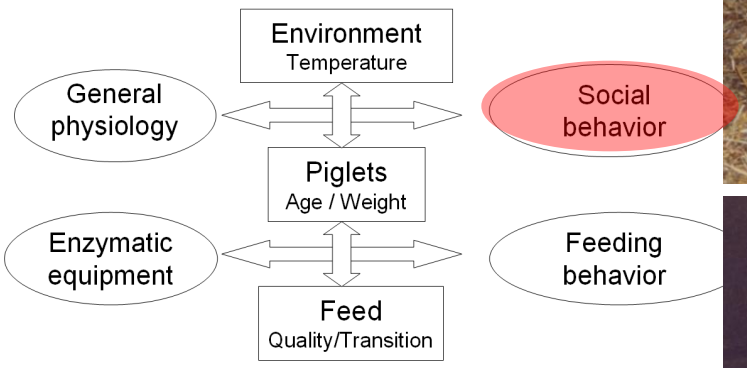
Herd level



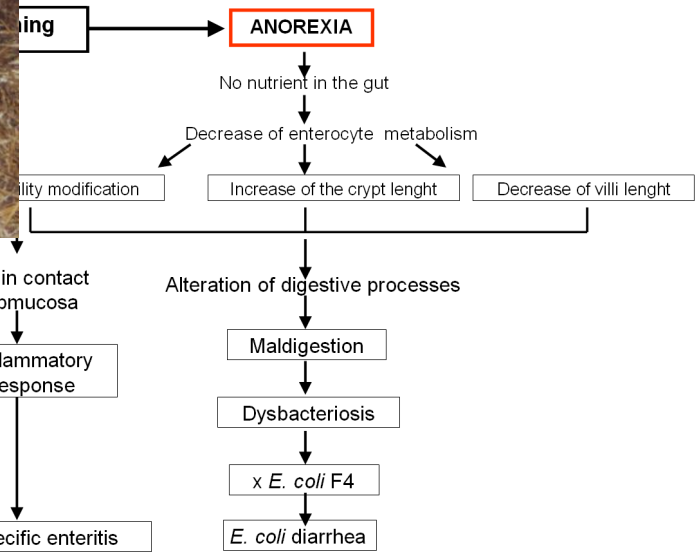
Piglet level



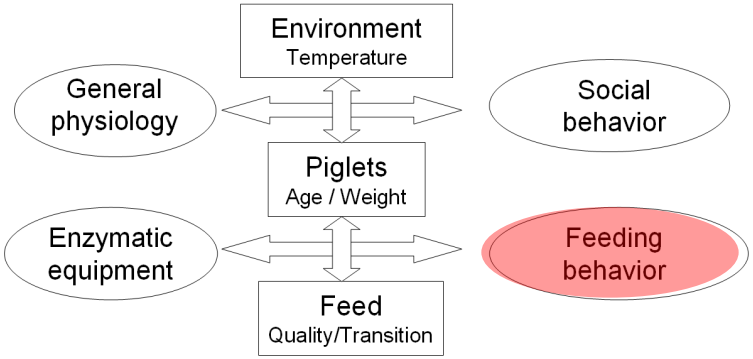
Herd level



Piglet level



Individually measured feed intake characteristics and growth performance of group-housed weanling pigs: Effects of sex, initial body weight, and body weight distribution within groups[1,2]



. C. van der Peet-Schwering*, J. W. Schrama†,
, H. Everts§, L. A. den Hartog, and A. C. Beynen§

ion on individual feed intake characteristics
of group-housed weanling pigs[1,2]

E. M. A. M. Bruininx*[3], G. P. Binnendijk*, C. M. C. van der Peet-Schwering*,
J. W. Schrama†, L. A. den Hartog‡, H. Everts§, and A. C. Beynen§

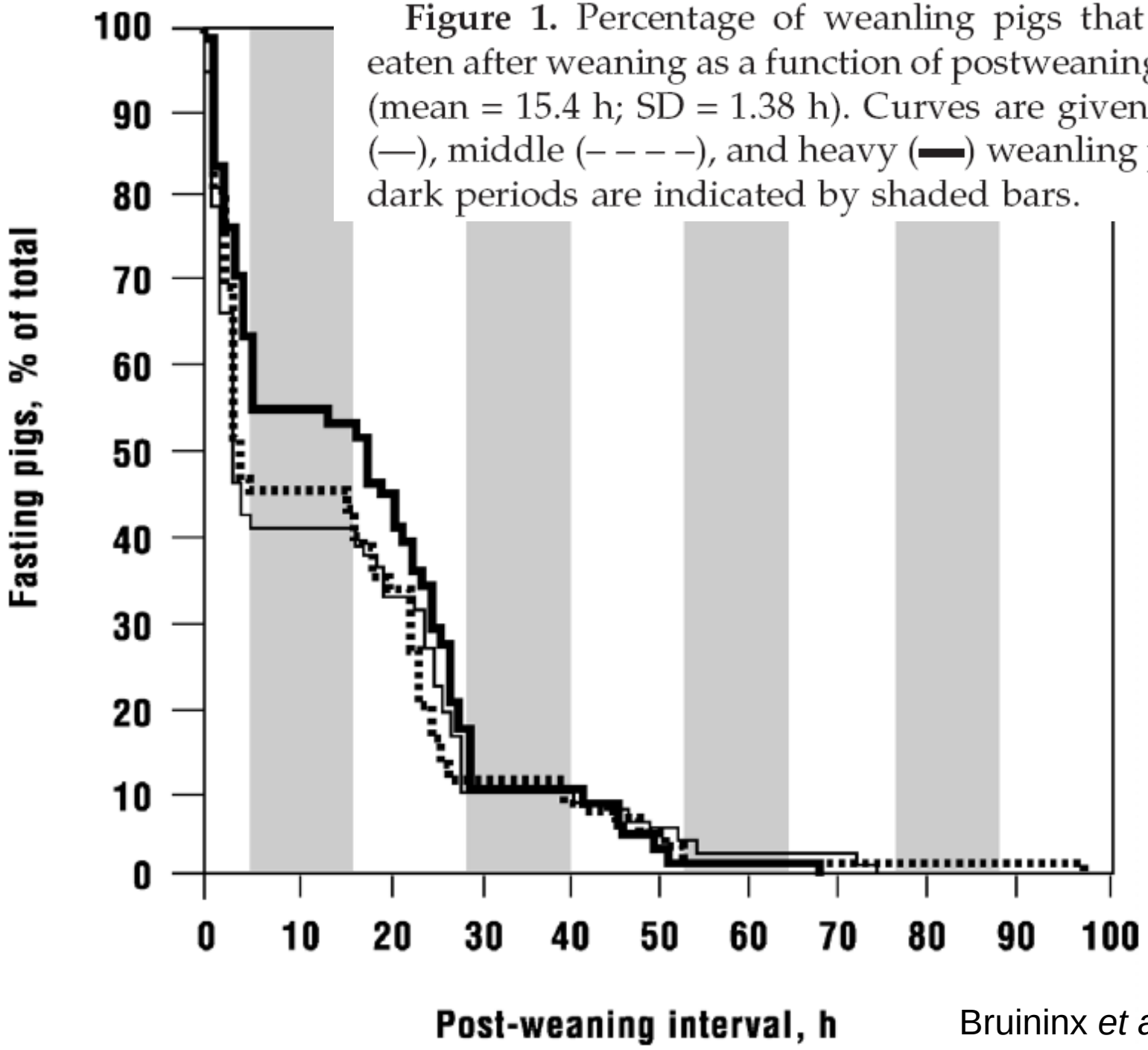
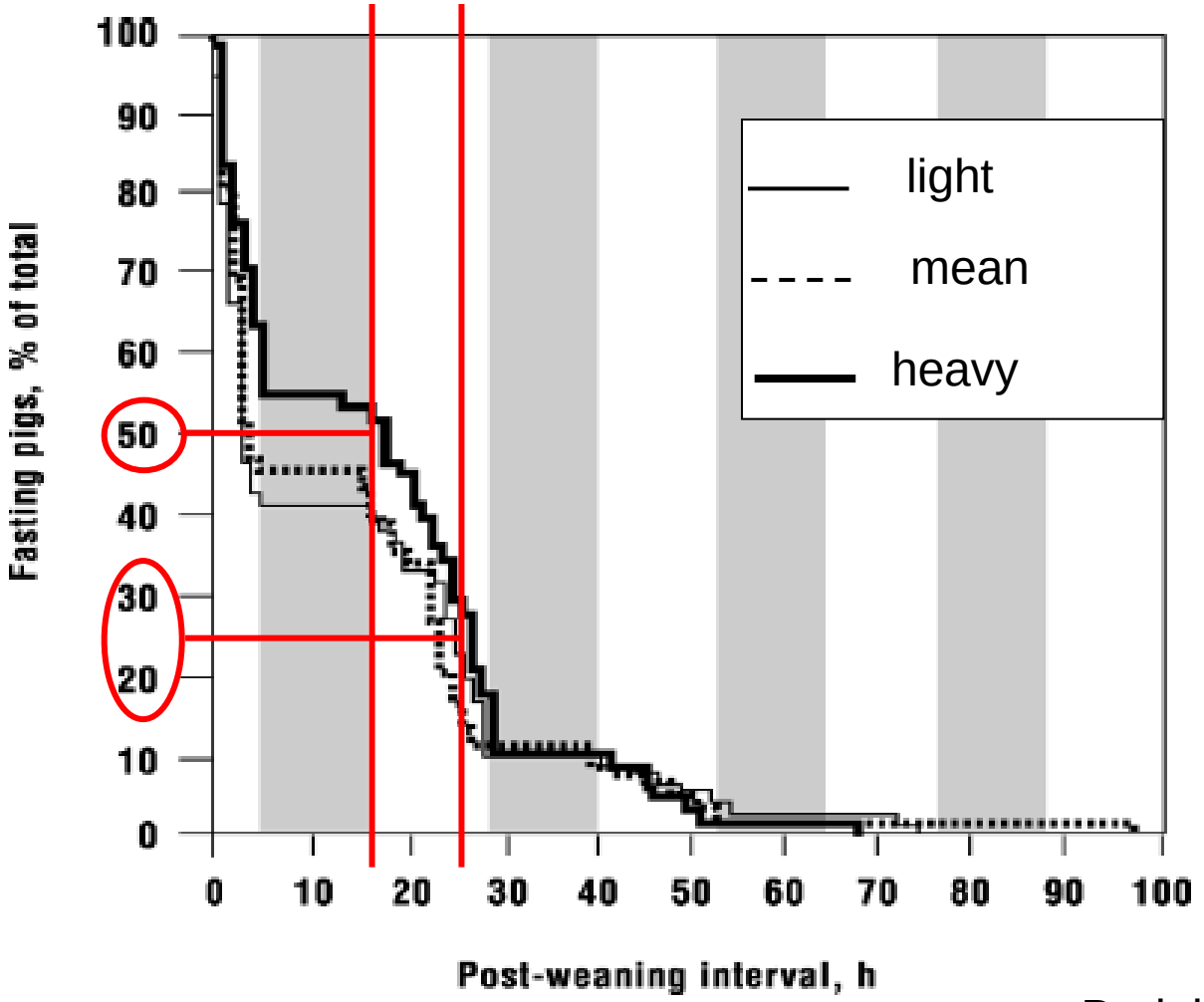


Figure 1. Percentage of weanling pigs that had not eaten after weaning as a function of postweaning interval (mean = 15.4 h; SD = 1.38 h). Curves are given for light (—), middle (– – – –), and heavy (▬) weanling pigs. The dark periods are indicated by shaded bars.

Bruininx *et al.*, 2001

Post-weaning anorexia

although duration is limited



Bruininx *et al.*, 2001

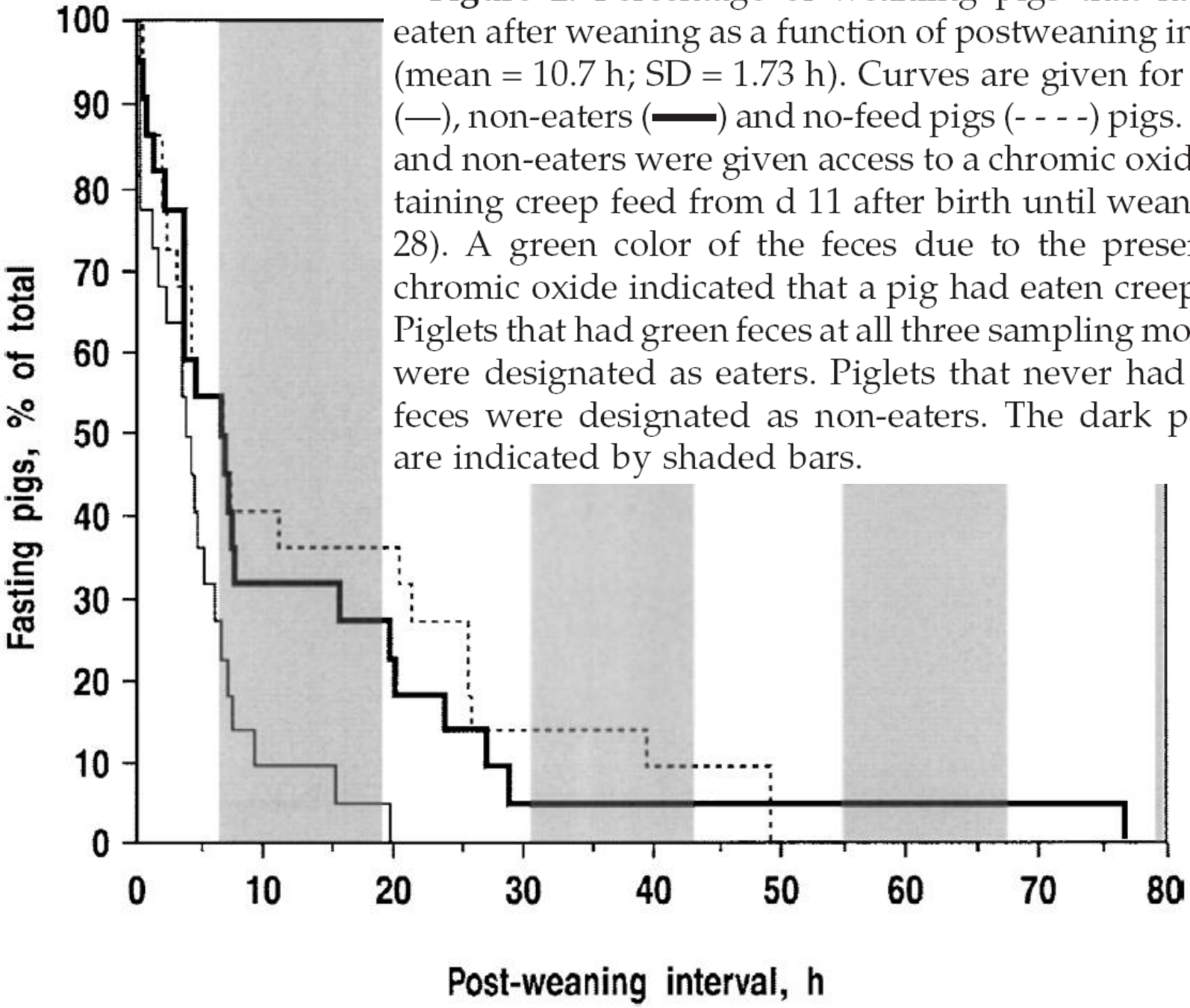


Figure 2. Percentage of weanling pigs that had not eaten after weaning as a function of postweaning interval (mean = 10.7 h; SD = 1.73 h). Curves are given for eaters (—), non-eaters (▬) and no-feed pigs (- - - -) pigs. Eaters and non-eaters were given access to a chromic oxide containing creep feed from d 11 after birth until weaning (d 28). A green color of the feces due to the presence of chromic oxide indicated that a pig had eaten creep feed. Piglets that had green feces at all three sampling moments were designated as eaters. Piglets that never had green feces were designated as non-eaters. The dark periods are indicated by shaded bars.

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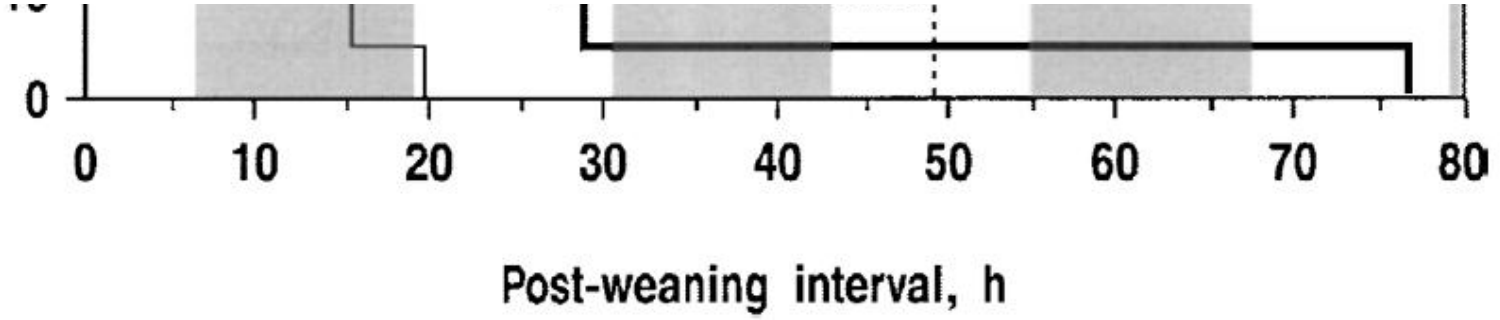

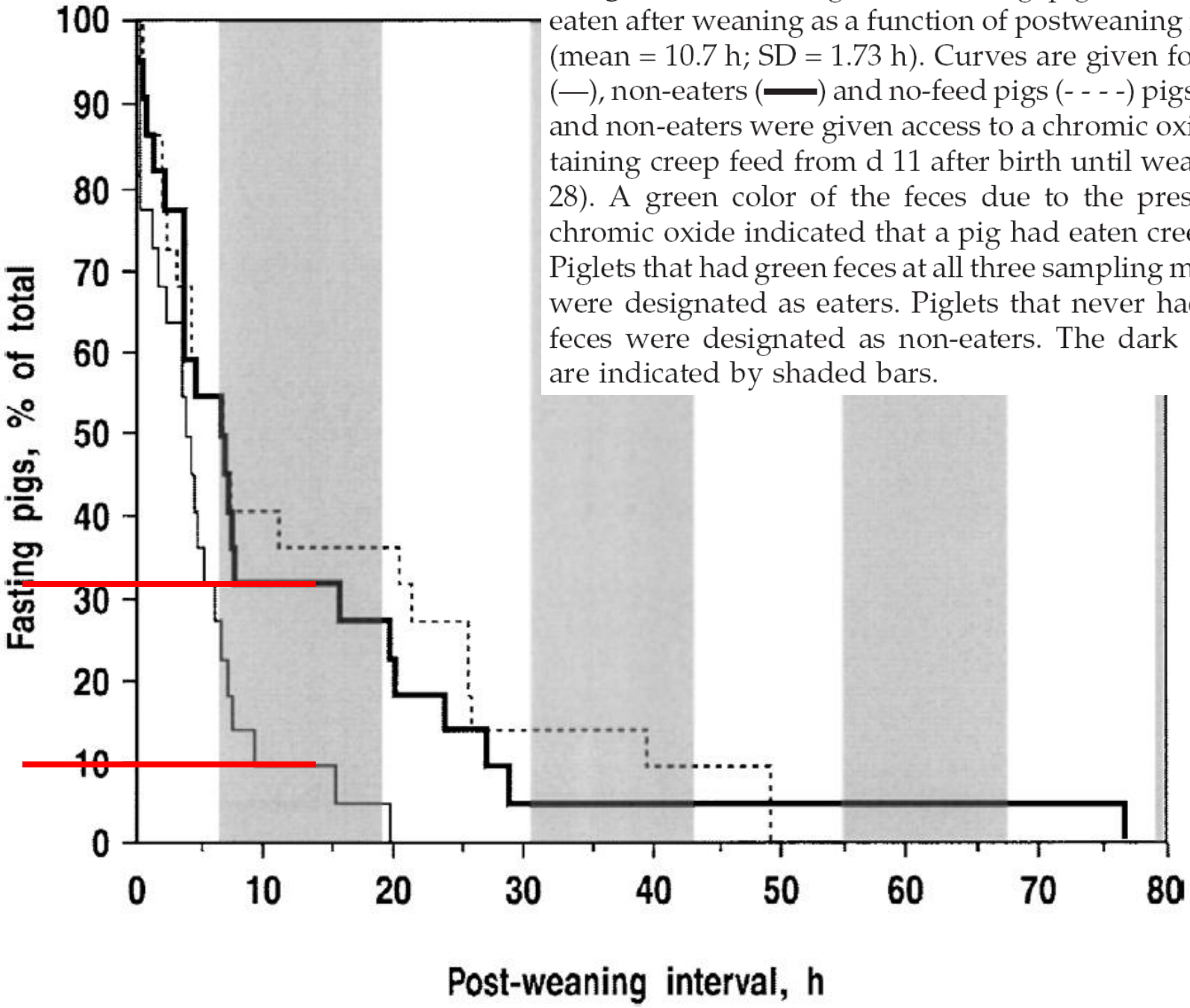

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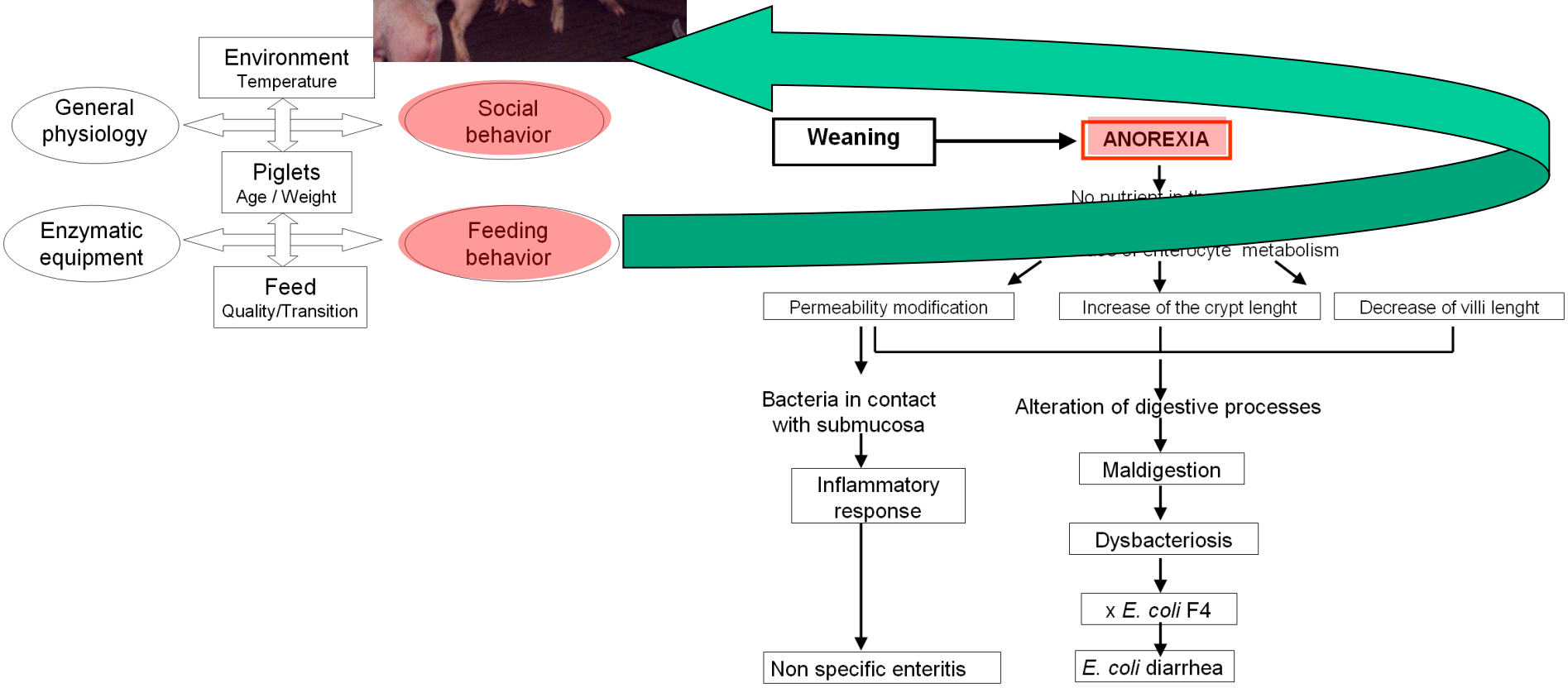
Housing: t°


Environment
Temperature
General physiology
Social behavior
Piglets
Age / Weight
Enzymatic equipment
Feeding behavior
Feed
Quality/Transition
Weaning
ANOREXIA
metabolism
Permeability modification
Increase of the crypt lenght
Decrease of villi lenght
Bacteria in contact with submucosa
Alteration of digestive processes
Inflammatory response
Maldigestion
Dysbacteriosis
x E. coli F4
Non specific enteritis
E. coli diarrhea

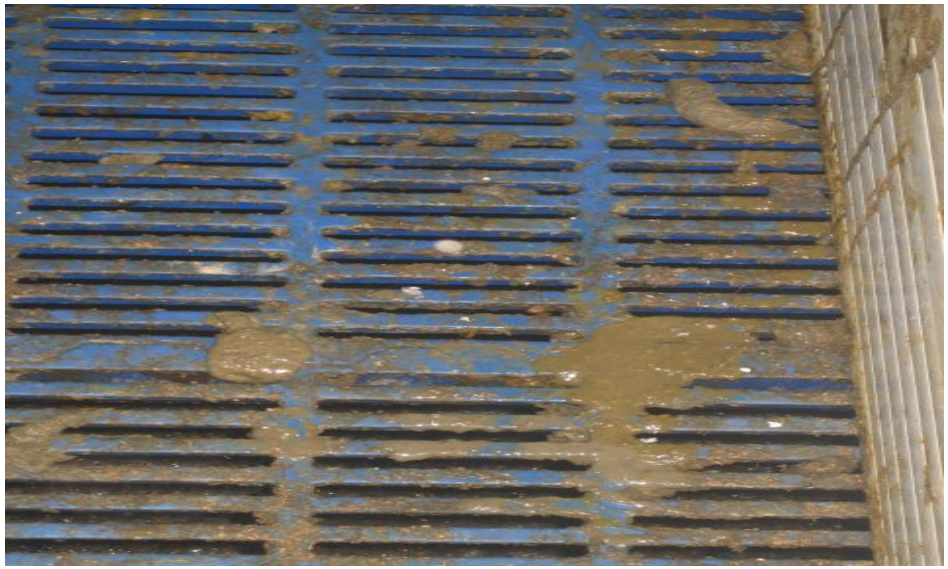
Postweaning *E. coli* diarrhea

Physio Global	***Physio digestive***	***Behavior & feed***	***Feed changes composition***	***Feed changes immuno***
⇩	⇩	⇩	⇩	⇩
Syndrome of adaptation	Less absorption	Feed consumption	Enzymatic adaptation	End of lactogenic protection
⇩	⇩	⇩	⇩	⇩
Decrease stress (t C, housing)	Feed quality and feed transition	Feed quality and feed transition	1-pre-weaning 2-digestive capacity	1-Antibiotic 2-Vaccination 3-Ecologic manipulation
Yes, but	Yes, but	Yes, but	Yes, but	Yes, but

Italy / Denmark / France

Postweaning *E. coli* diarrhea

Human componant: How >>> Why



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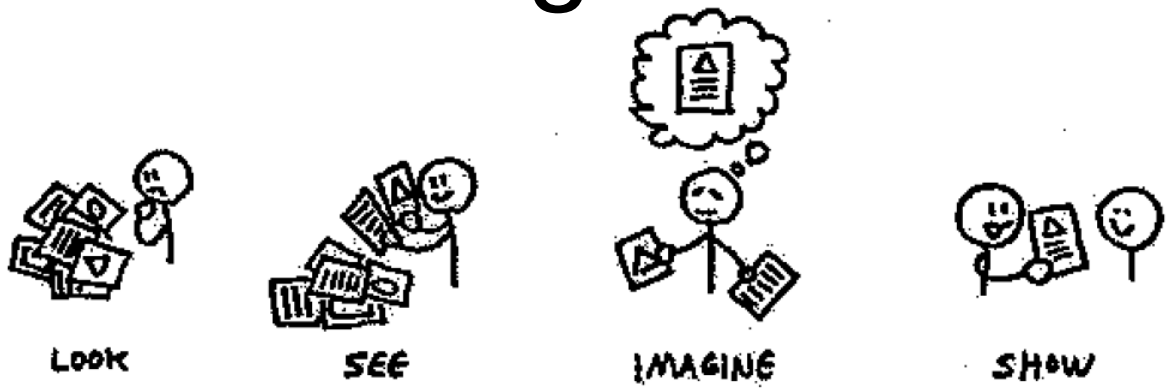
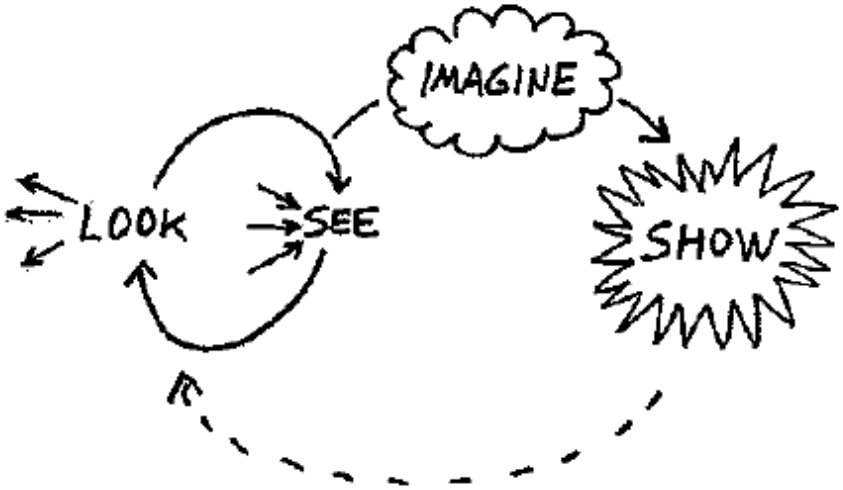
Postweaning *E. coli* diarrhea diagnosis

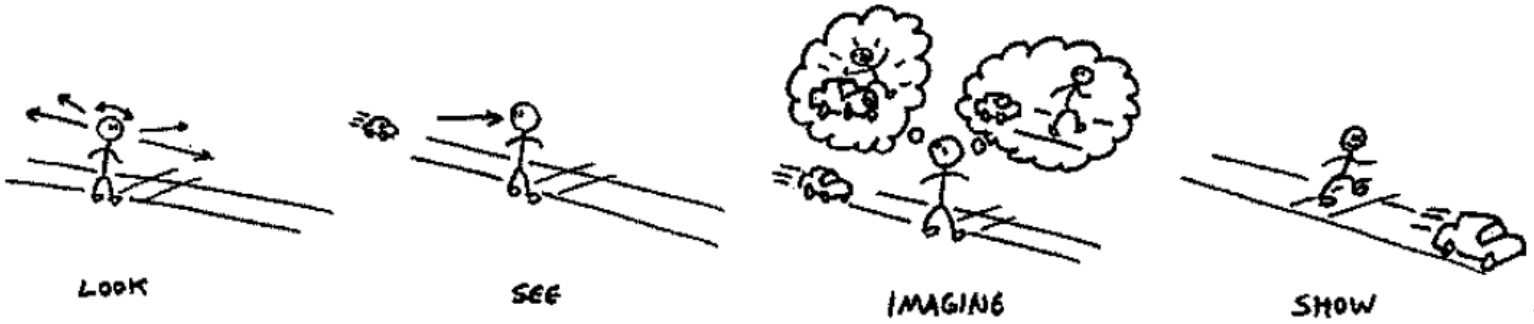


The four-step visual thinking process when creating a report.



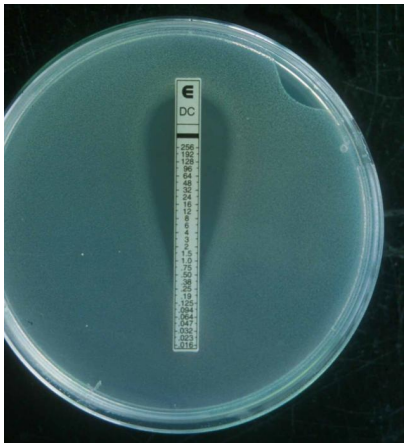
The visual thinking process, as it really happens.

Postweaning *E. coli* diarrhea diagnosis



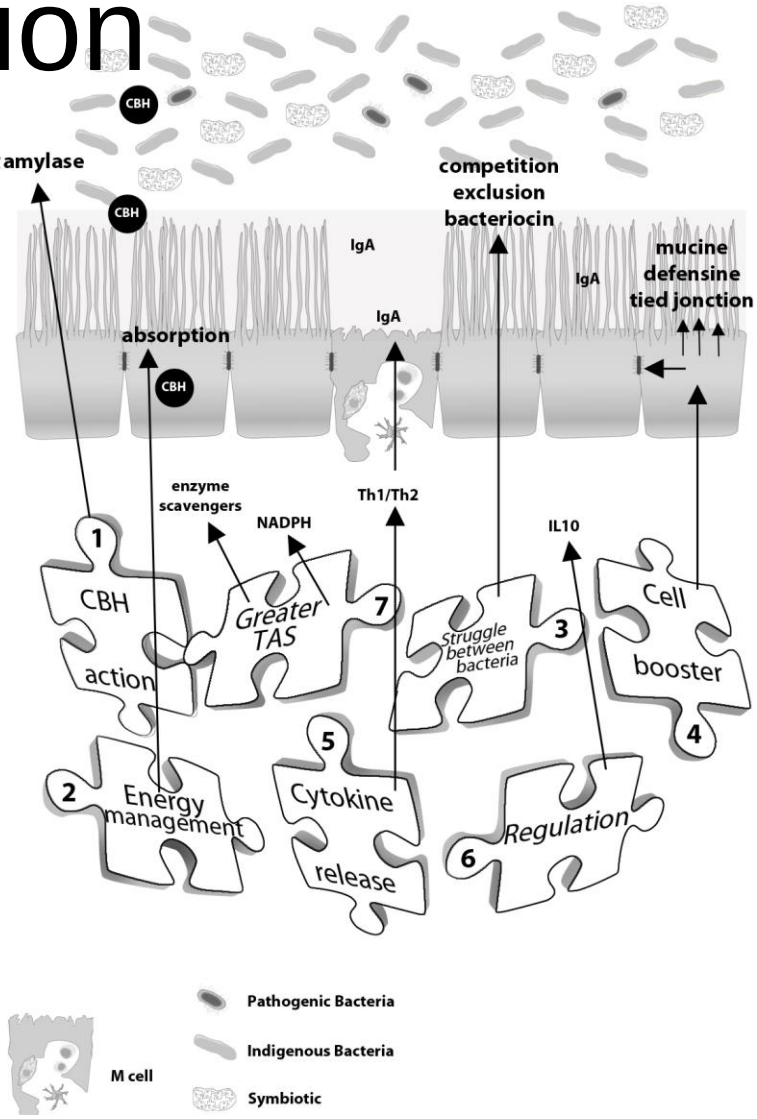
The four-step visual thinking process when crossing a street.

- Clinical and epidemiological: major even if …
  The six W (and mainly « When »)
- Pathology (gross and histo): why ?
- Bacteriology: why except
- Differential: uncommon diseases are …



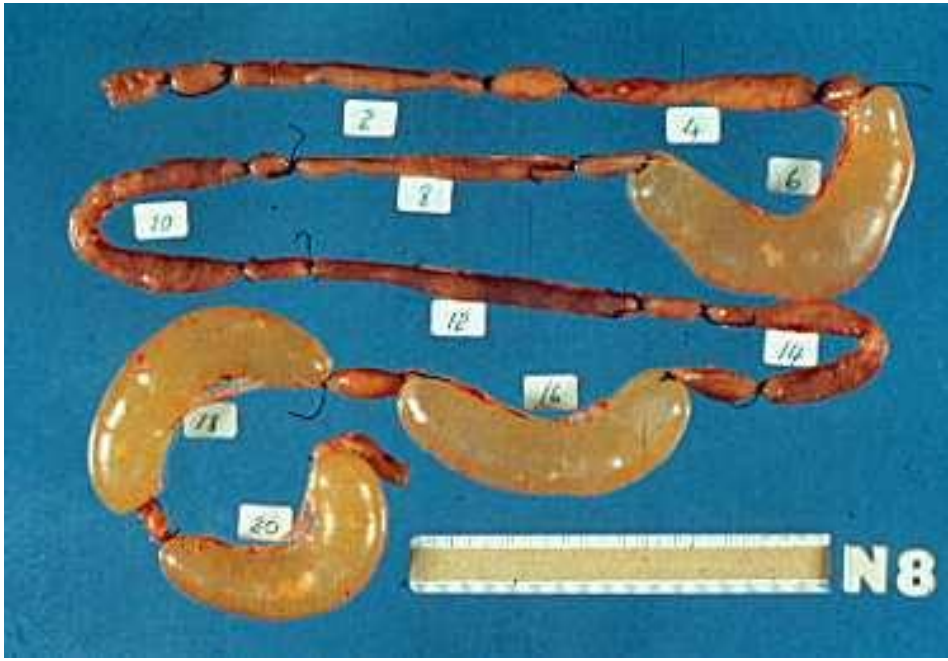
Postweaning *E. coli* diarrhea prevention

- Antibiotic or Ab-like
  - Antibiotics: Yes but …
  - ZnO (2500ppm): Yes but .
- Symbiotics
  - Prebiotic: Yes but …
  - Probiotic: Yes but …



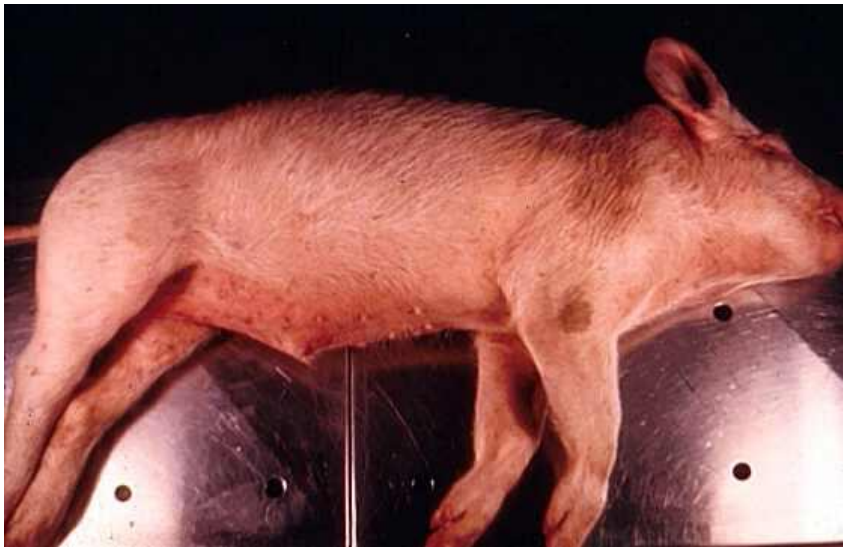
Postweaning *E. coli* diarrhea prevention

J. Fairbrother, GREMIP, Canada:
Live *E. coli* strain:
F4+/Sta-STb-LT-

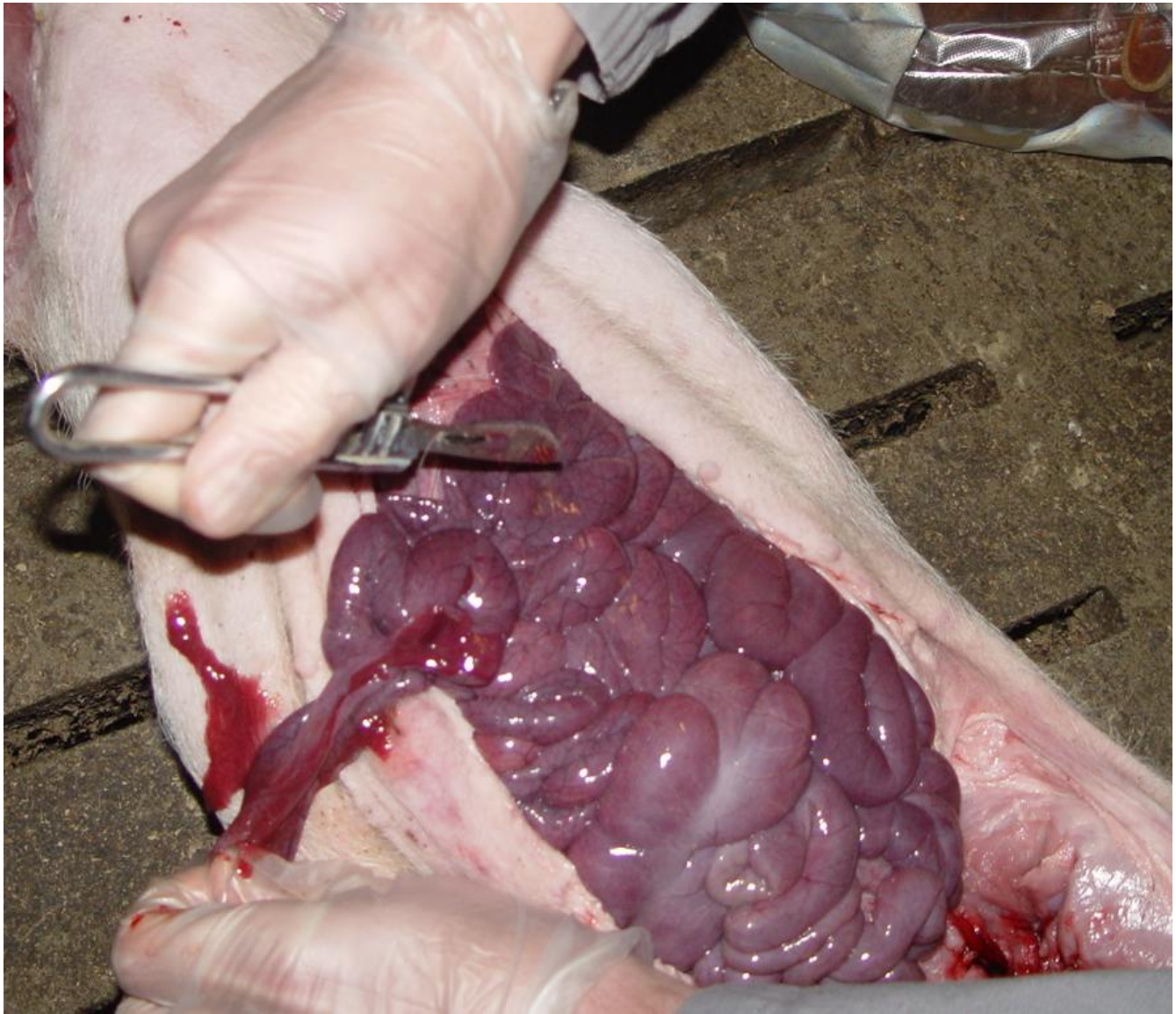


Post-weaning acute death

- Classical case
  - Enzootic acute deaths
  - Heavy pigs
  - No previous symptoms
- Differential diagnosis
  - Colitoxicosis
  - Edema disease
  - Mulberrey Heart Disease
  - *Streptococcus suis*
  - *Haemophilus parasuis*



Colitoxicosis
Hemorragic gastro-enteritis

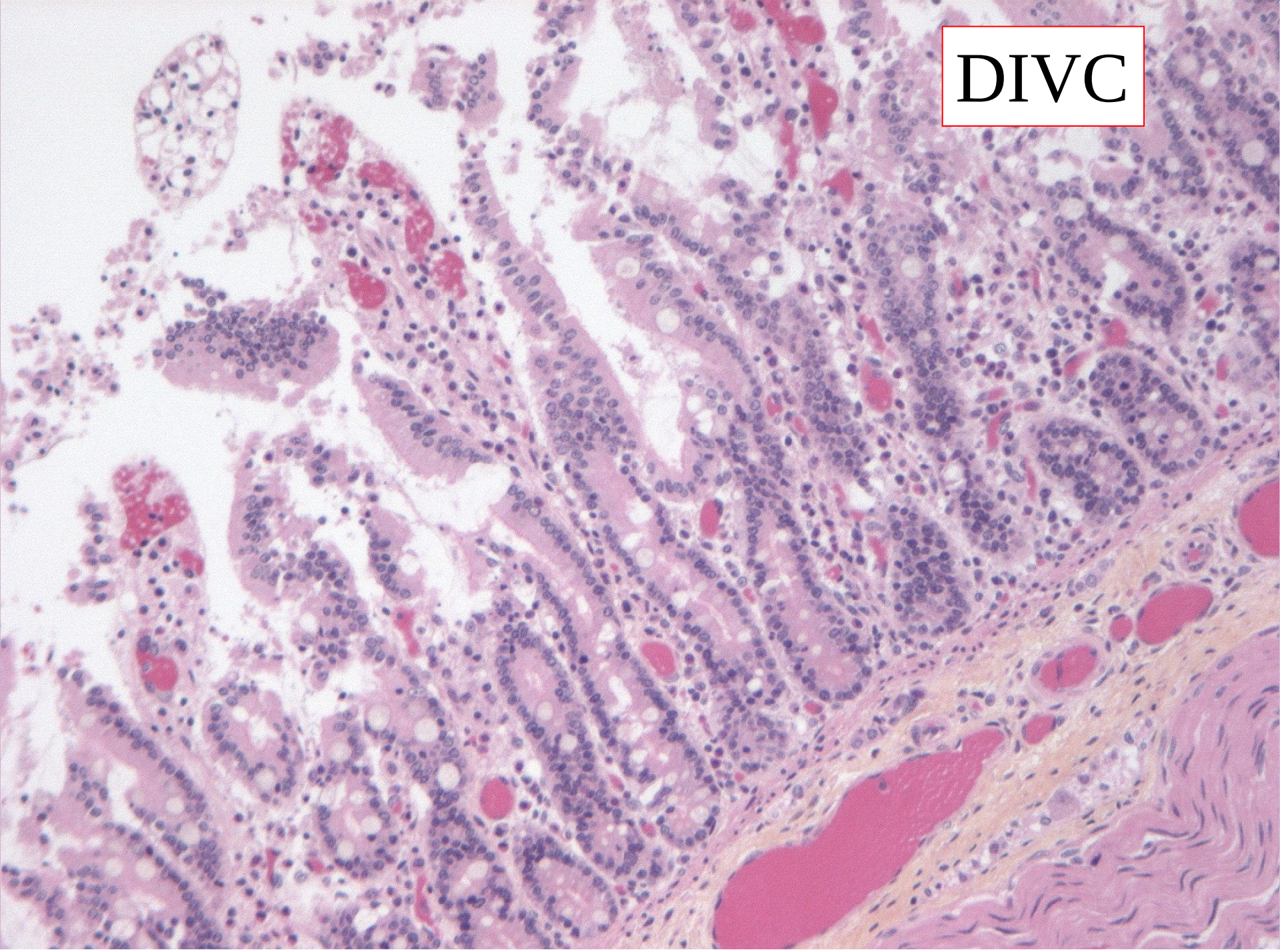


Colitoxicosis
Hemorragic gastro-enteritis

- Infectious but not contagious
- Major disease (acute death of heavy piglets)
- Digestive *E. coli* (F4) accident
  - **massive** colonisation all small intestin (**<u>24-36h</u>**)
  - **massive** LPS production and LPS release

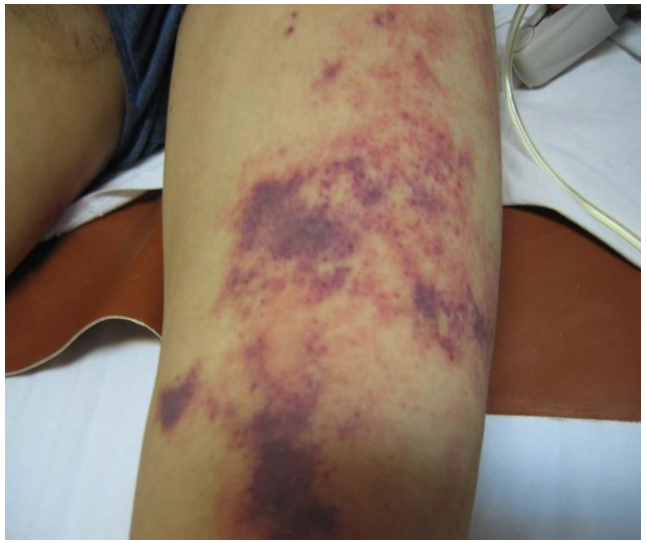
    Disseminated intravascular coagulation

    Toxic Chock


DIVC

- Toxic shock-like syndrome (TSLS)

S. suis, Human and China

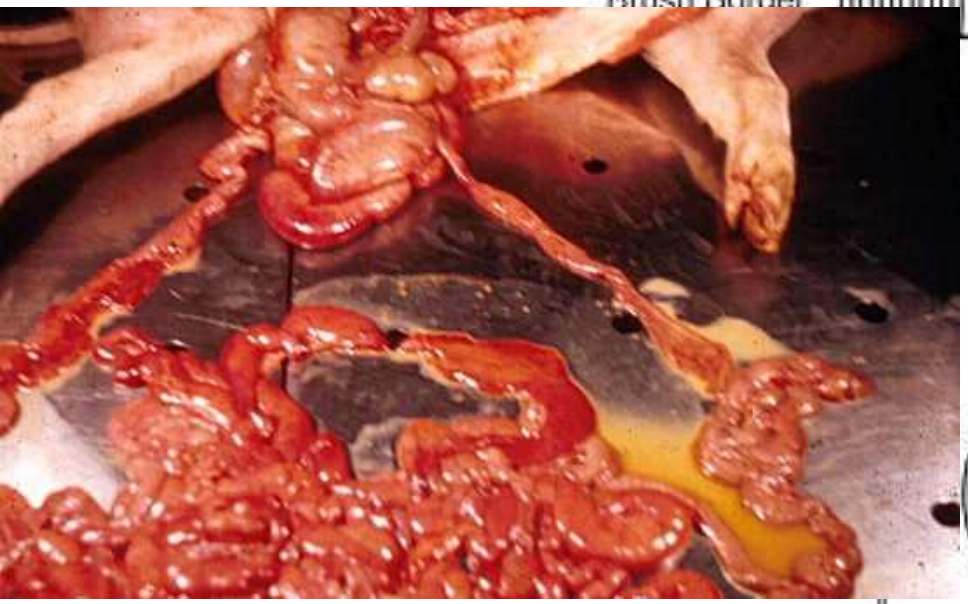



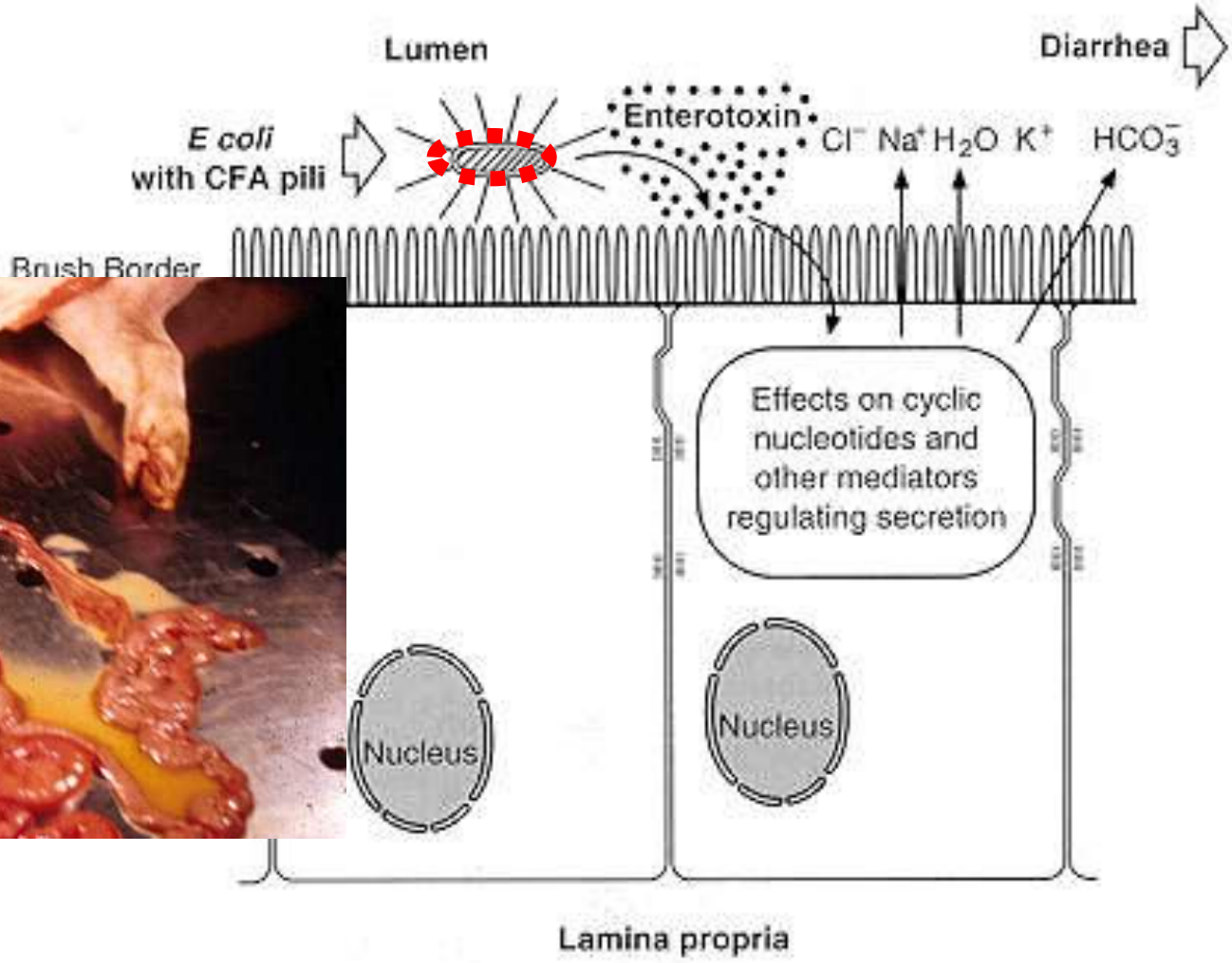

Gottschalk, 2008

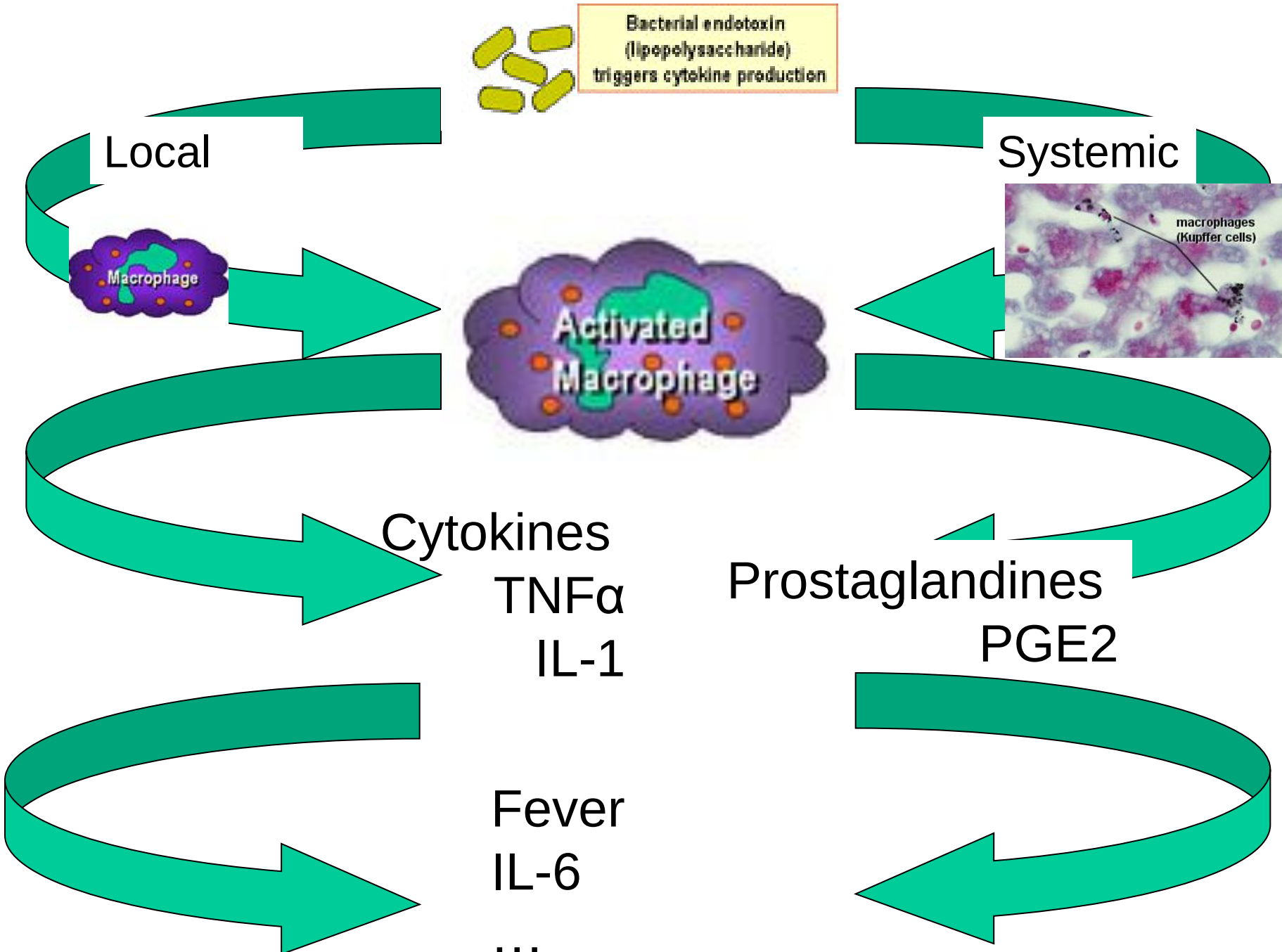
E. coli: Endotoxins (LPS)

Disseminated intravascular coagulation

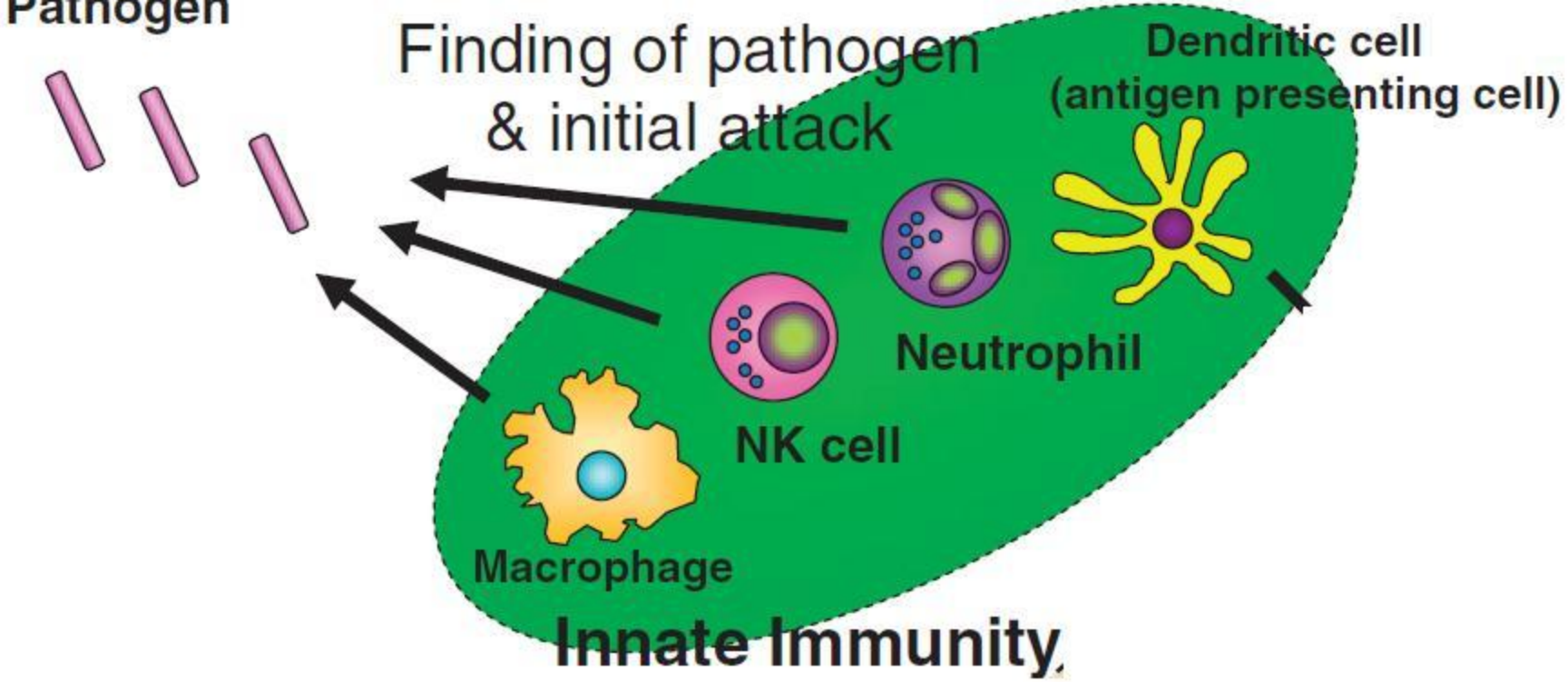
Toxic Chock

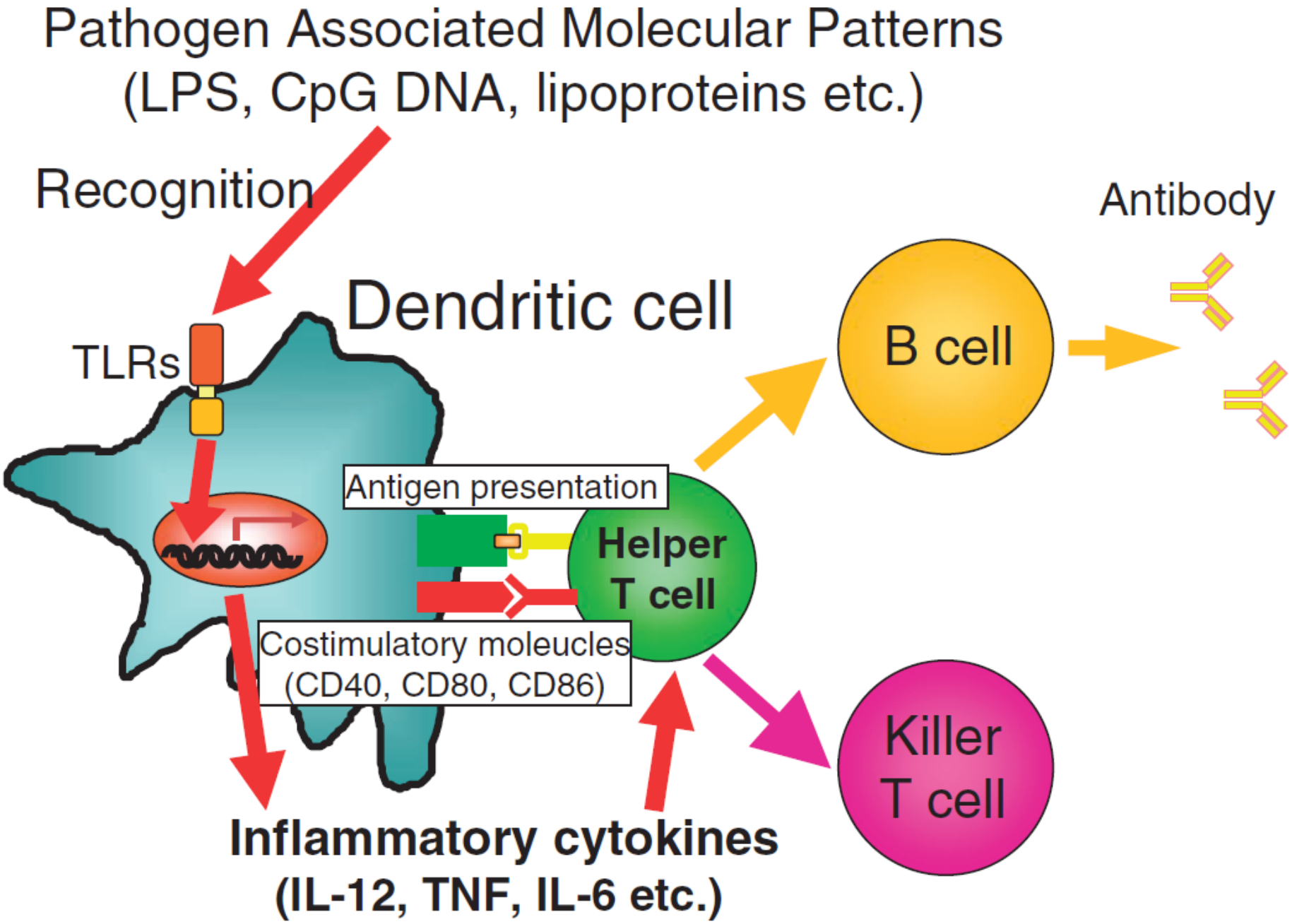


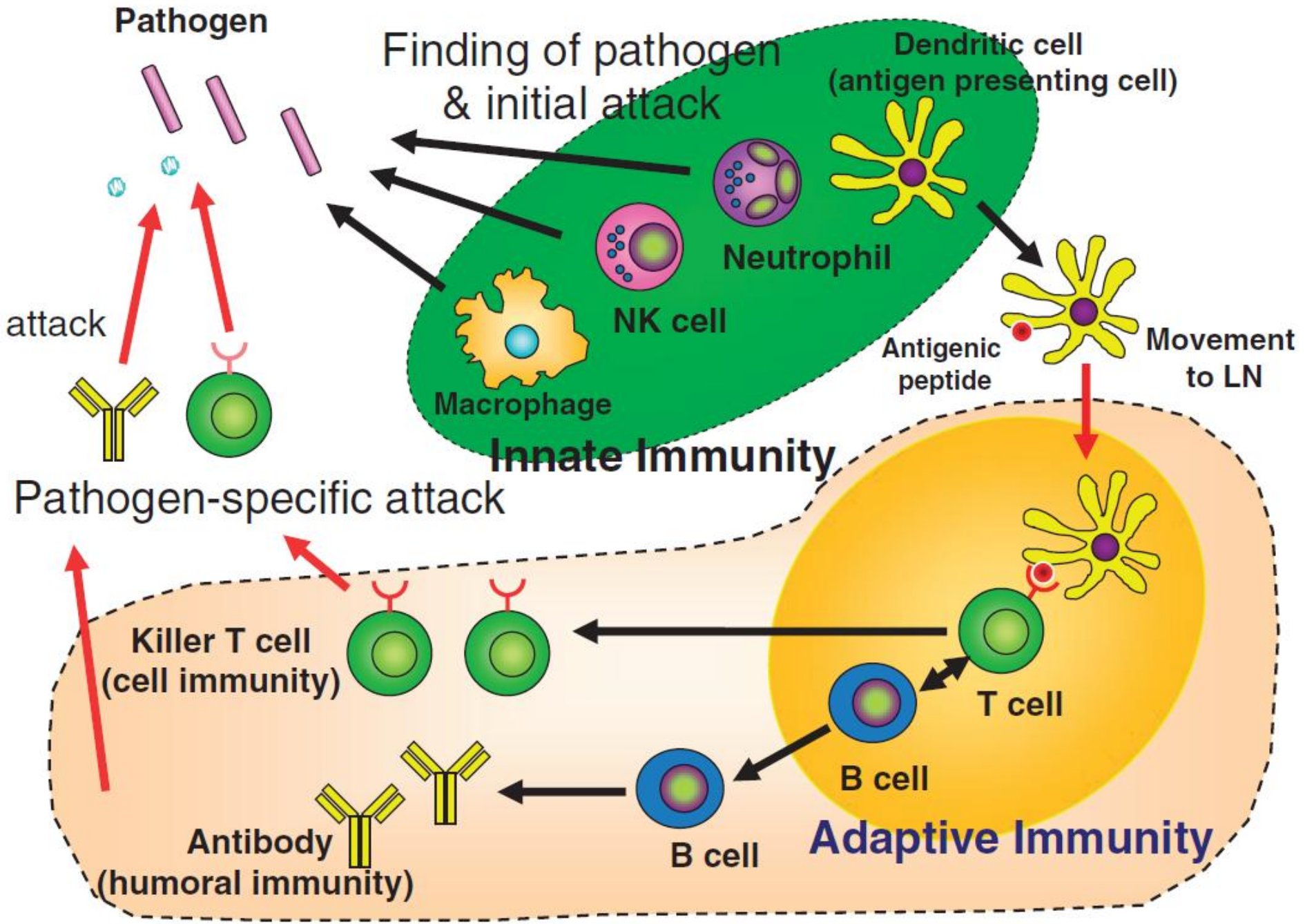


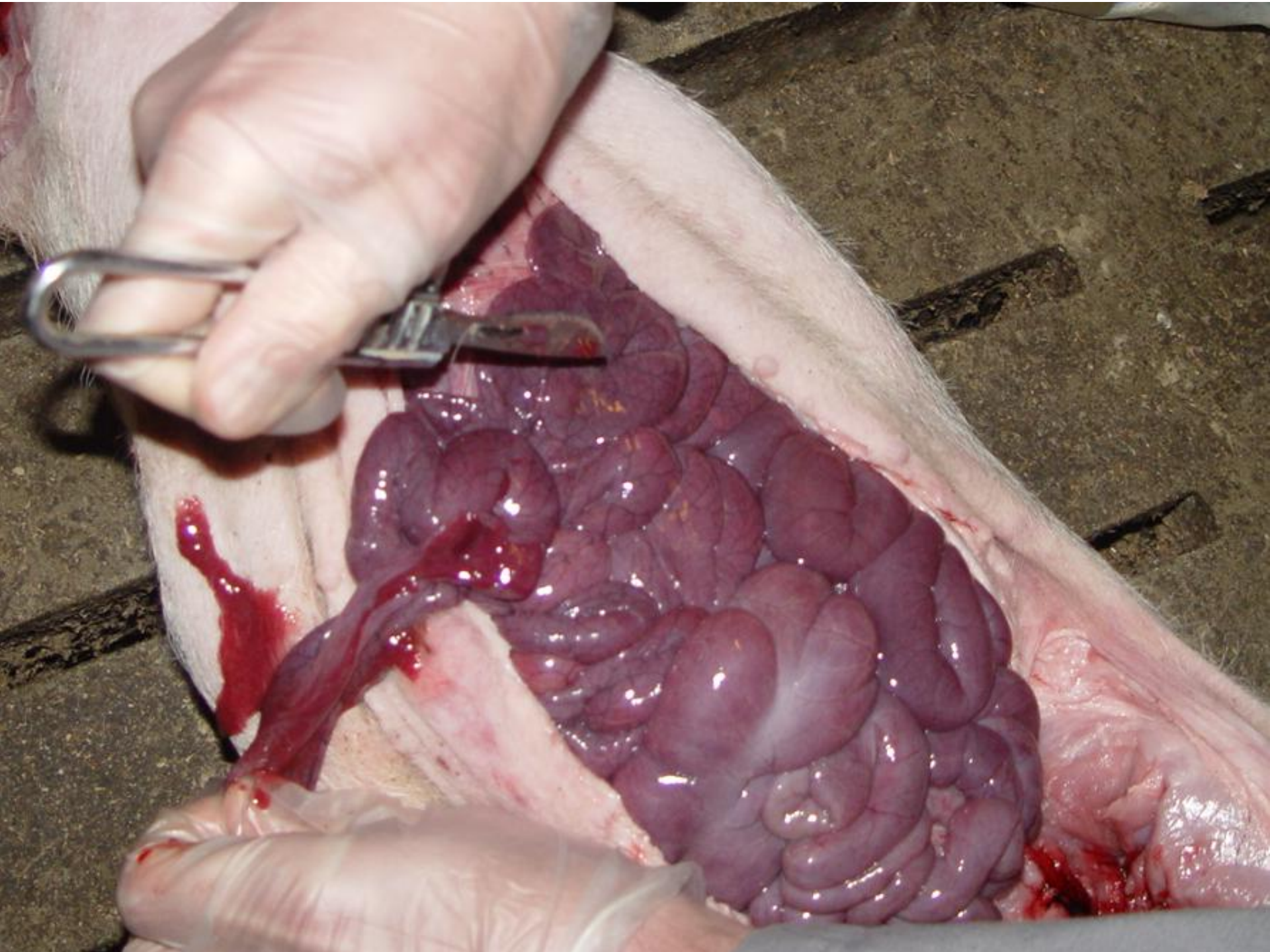

Bacterial endotoxin
(lipopolysaccharide)
triggers cytokine production
Local
Systemic
Macrophage
Activated
Macrophage
macrophages
(Kupffer cells)
Cytokines
TNFα
IL-1
Prostaglandines
PGE2
Fever
IL-6
…

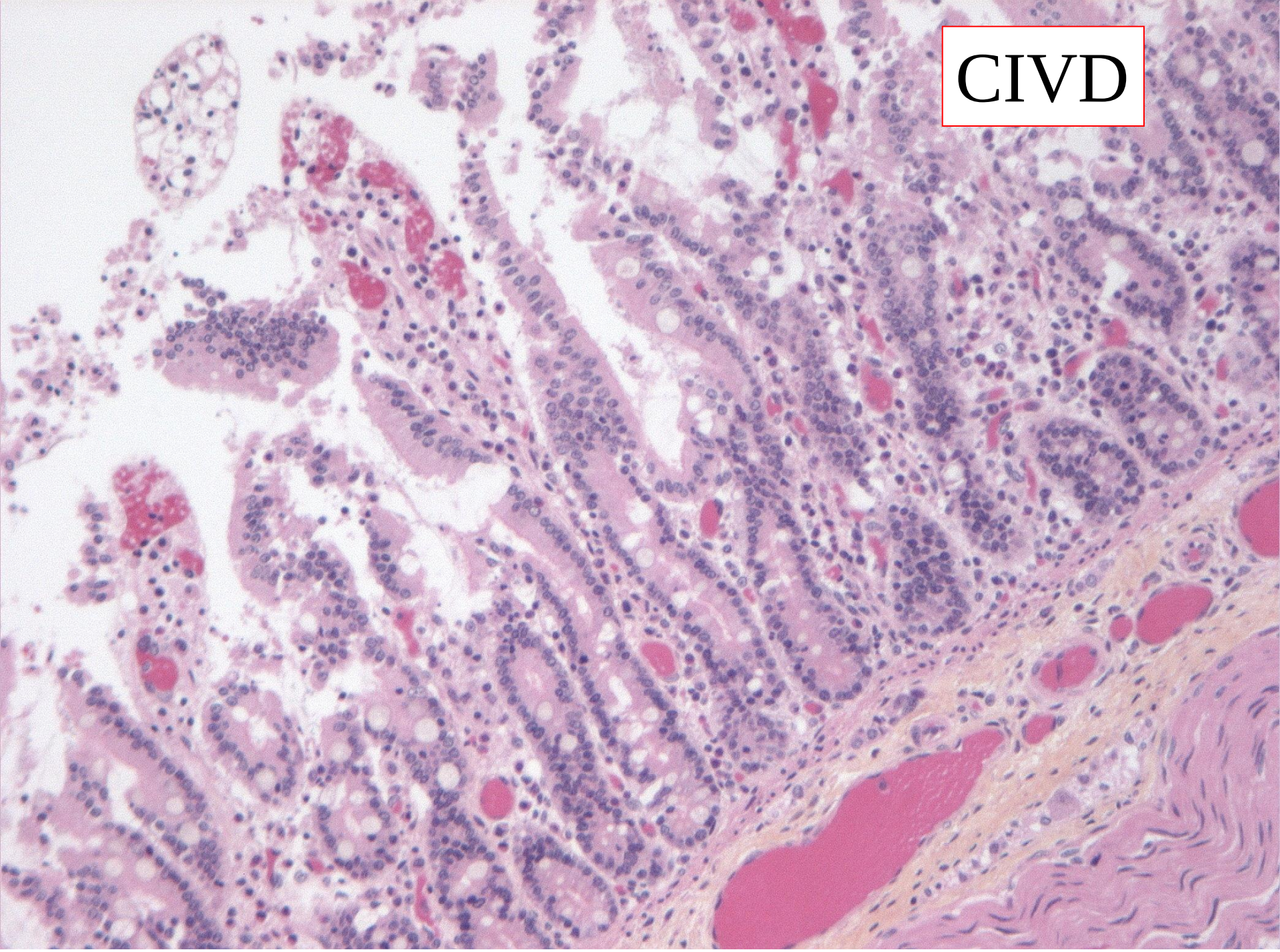
Reiner, 2009


Pathogen
Finding of pathogen
& initial attack
Dendritic cell
(antigen presenting cell)
Neutrophil
NK cell
Macrophage
Innate Immunity


Pathogen Associated Molecular Patterns
(LPS, CpG DNA, lipoproteins etc.)
Recognition
Antibody
Dendritic cell
TLRs
B cell
Antigen presentation
Helper
T cell
Costimulatory moleucles
(CD40, CD80, CD86)
Killer
T cell
Inflammatory cytokines
(IL-12, TNF, IL-6 etc.)


Pathogen
Finding of pathogen
& initial attack
Dendritic cell
(antigen presenting cell)
Neutrophil
NK cell
Macrophage
attack
Antigenic
peptide
Movement
to LN
Innate Immunity
Pathogen-specific attack
Killer T cell
(cell immunity)
T cell
B cell
Antibody
(humoral immunity)
B cell
Adaptive Immunity




CIVD

In all types of nursery

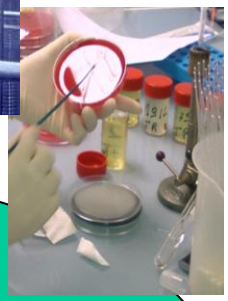
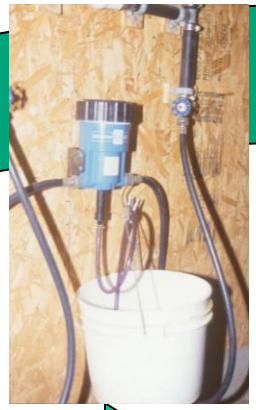
In all types of herds

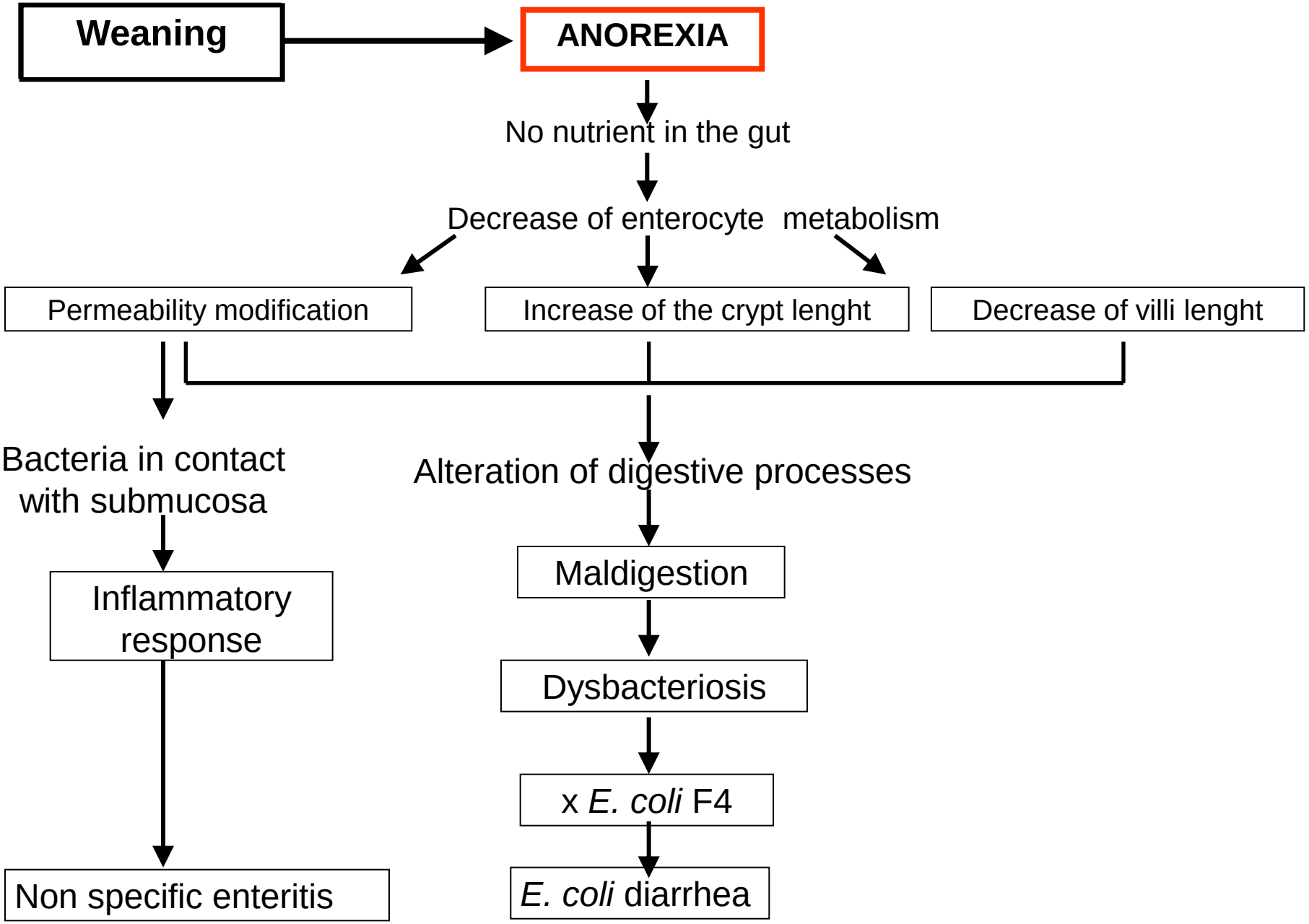
Two waves

1-PW

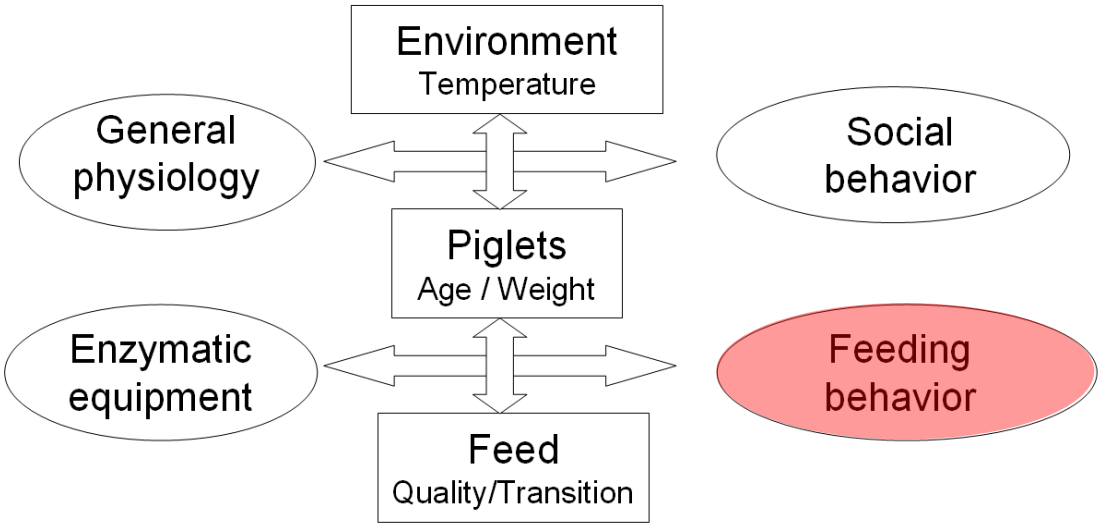
2-Post-transition

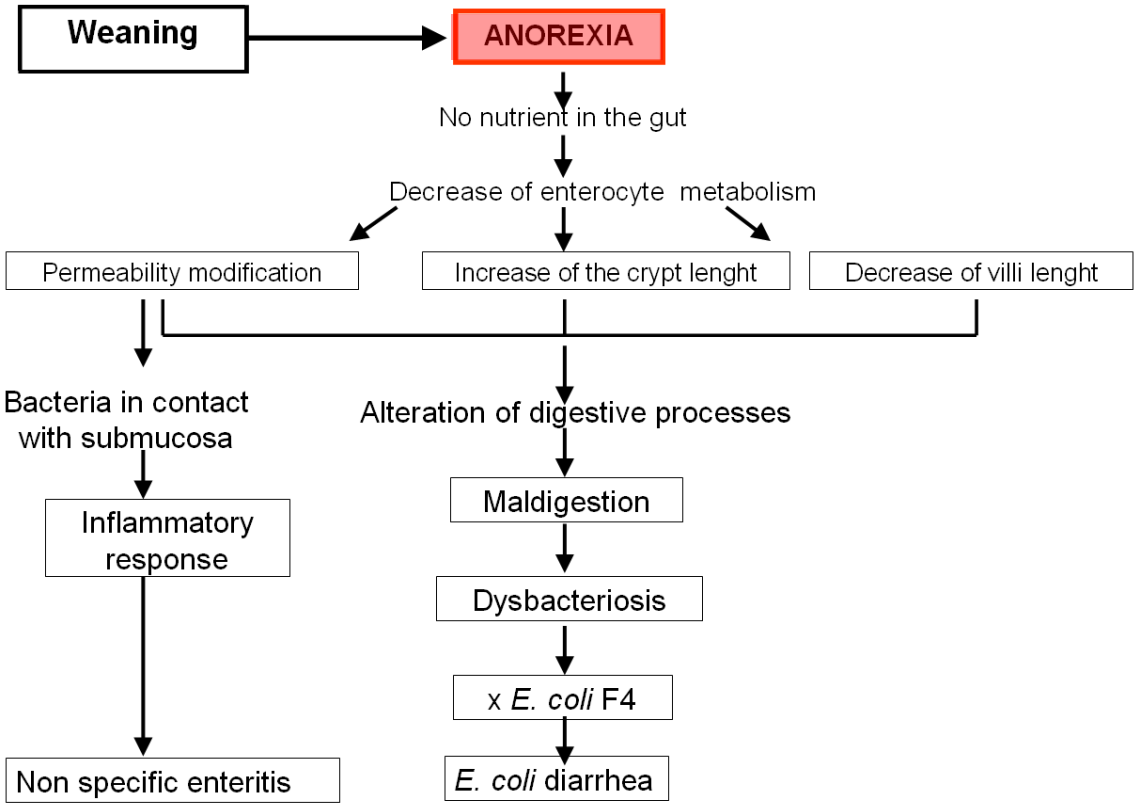
Antibiotics
Feeds (acidification, …)
TransitionS
Hygiene

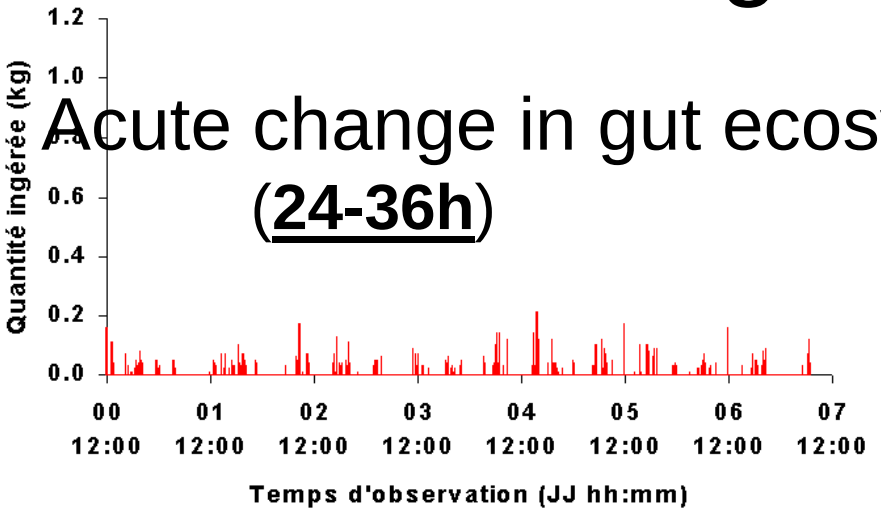
Adapted from David Guillou, 2008

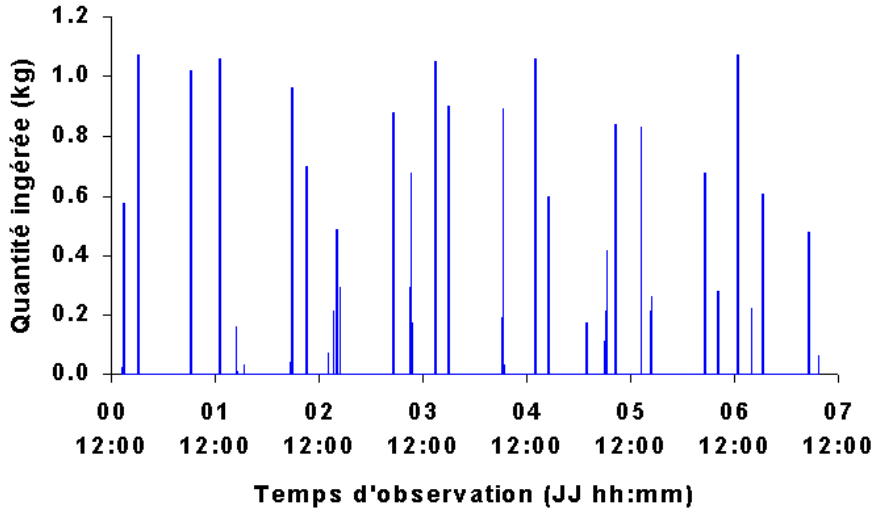

Environment
Temperature
General physiology
Social behavior
Piglets
Age / Weight
Enzymatic equipment
Feeding behavior
Feed
Quality/Transition


Weaning
ANOREXIA
No nutrient in the gut
Decrease of enterocyte metabolism
Permeability modification
Increase of the crypt lenght
Decrease of villi lenght
Bacteria in contact with submucosa
Alteration of digestive processes
Inflammatory response
Maldigestion
Dysbacteriosis
x E. coli F4
Non specific enteritis
E. coli diarrhea

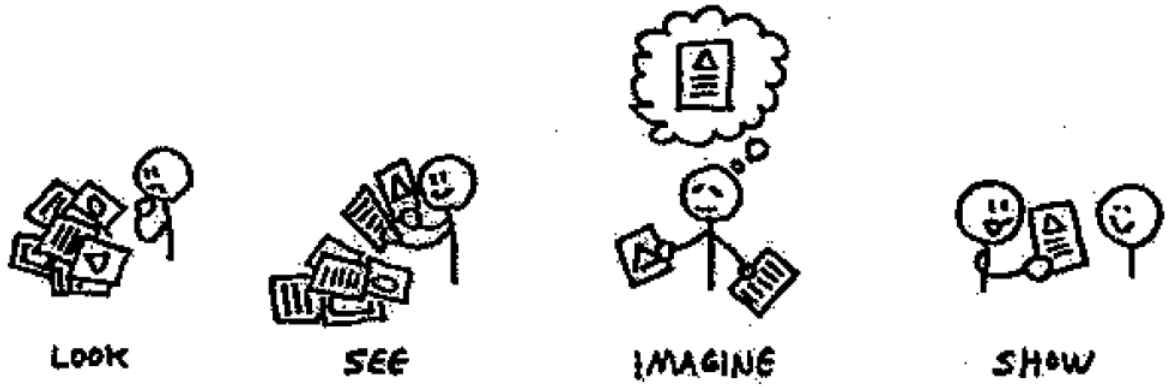
Colitoxicosis
Hemorragic gastro-enteritis

Acute change in gut ecosystem of one specific piglet (**<u>24-36h</u>**)

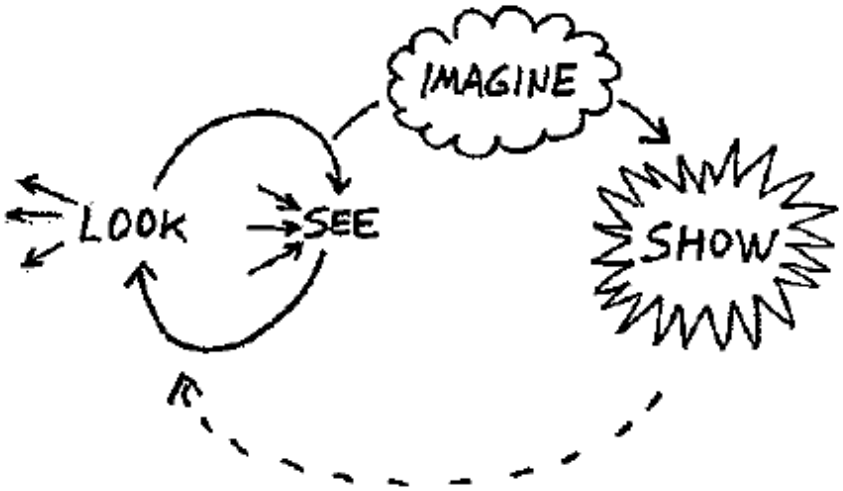




Colitoxicosis diagnosis

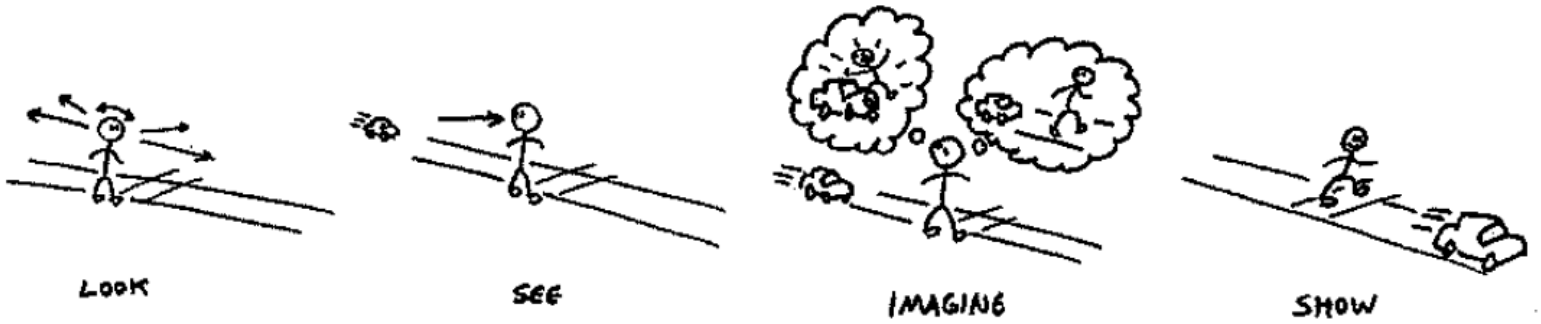


The four-step visual thinking process when creating a report.



The visual thinking process, as it really happens.

Colitoxicosis diagnosis

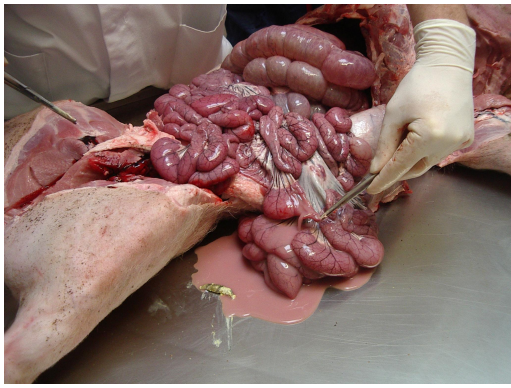


The four-step visual thinking process when crossing a street.

- Clinical and epidemiological:

What happens 24-36 hours before ?

- Pathology (gross)
- Bacteriology
- Differential:
  - Edema disease
  - Mulberrey Heart Disease
  - *Streptococcus suis or Haemophilus parasuis*



Colitoxicosis: pathophysio-diagnosis

- One question:
  What happens

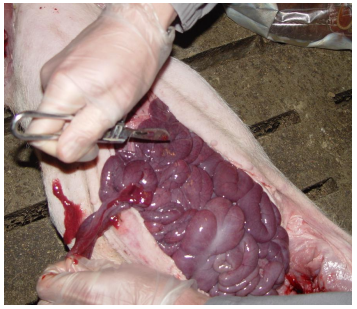
24-36 hours before ?

Gut accident
Infectious disease
Non contagious

1 3 5 7 9 11

Edema disease

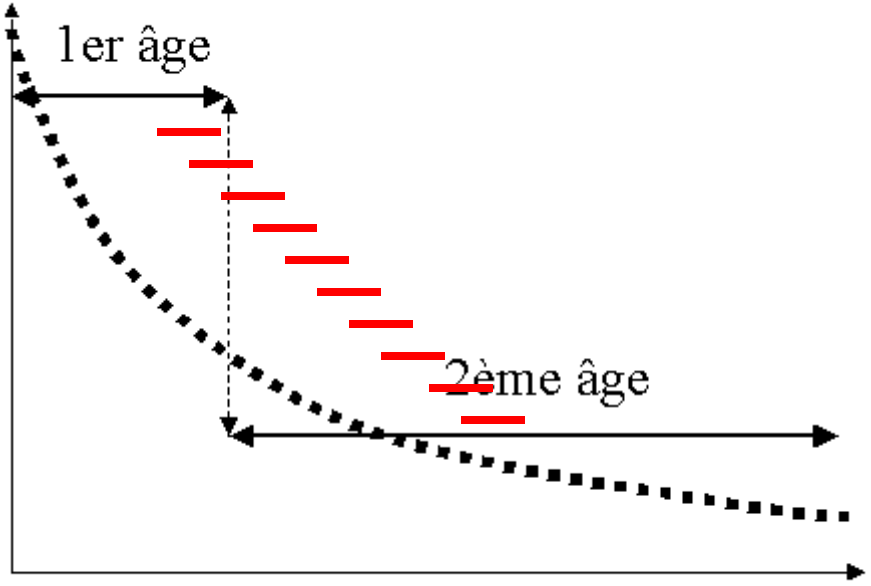
Colitoxicosis



1 3 5 7 9 11

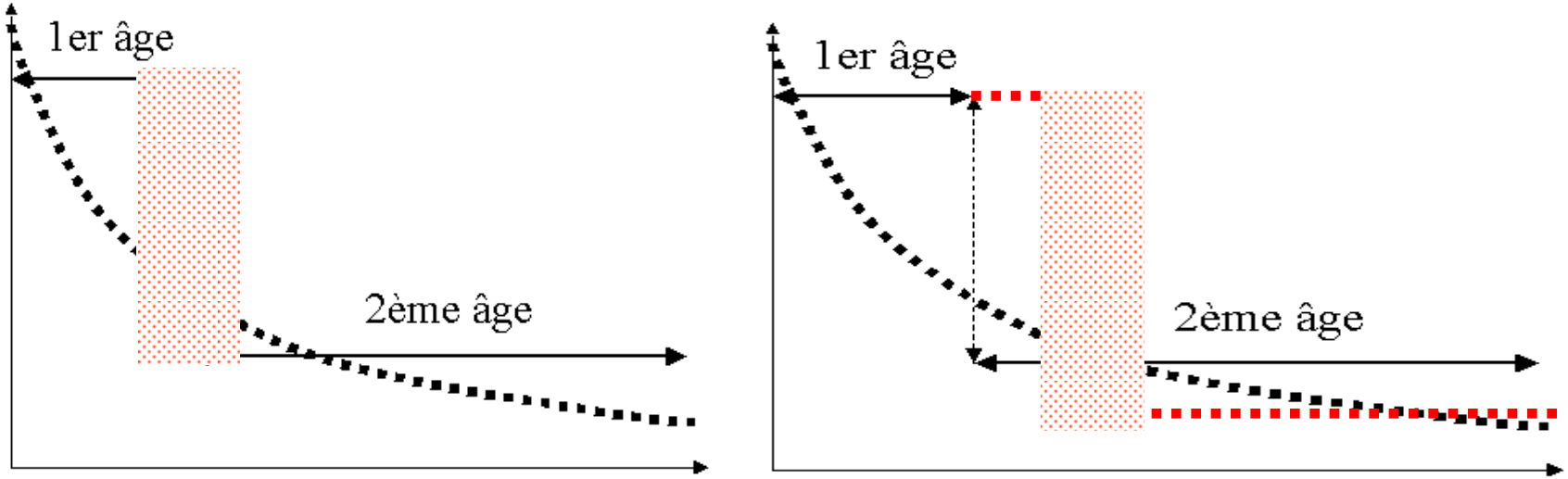
Colitoxicosis
Hemorragic gastro-enteritis

Acute change in gut ecosystem of one specific piglet (**<u>24-36h</u>**)



Colitoxicosis: pathophysio-diagnosis

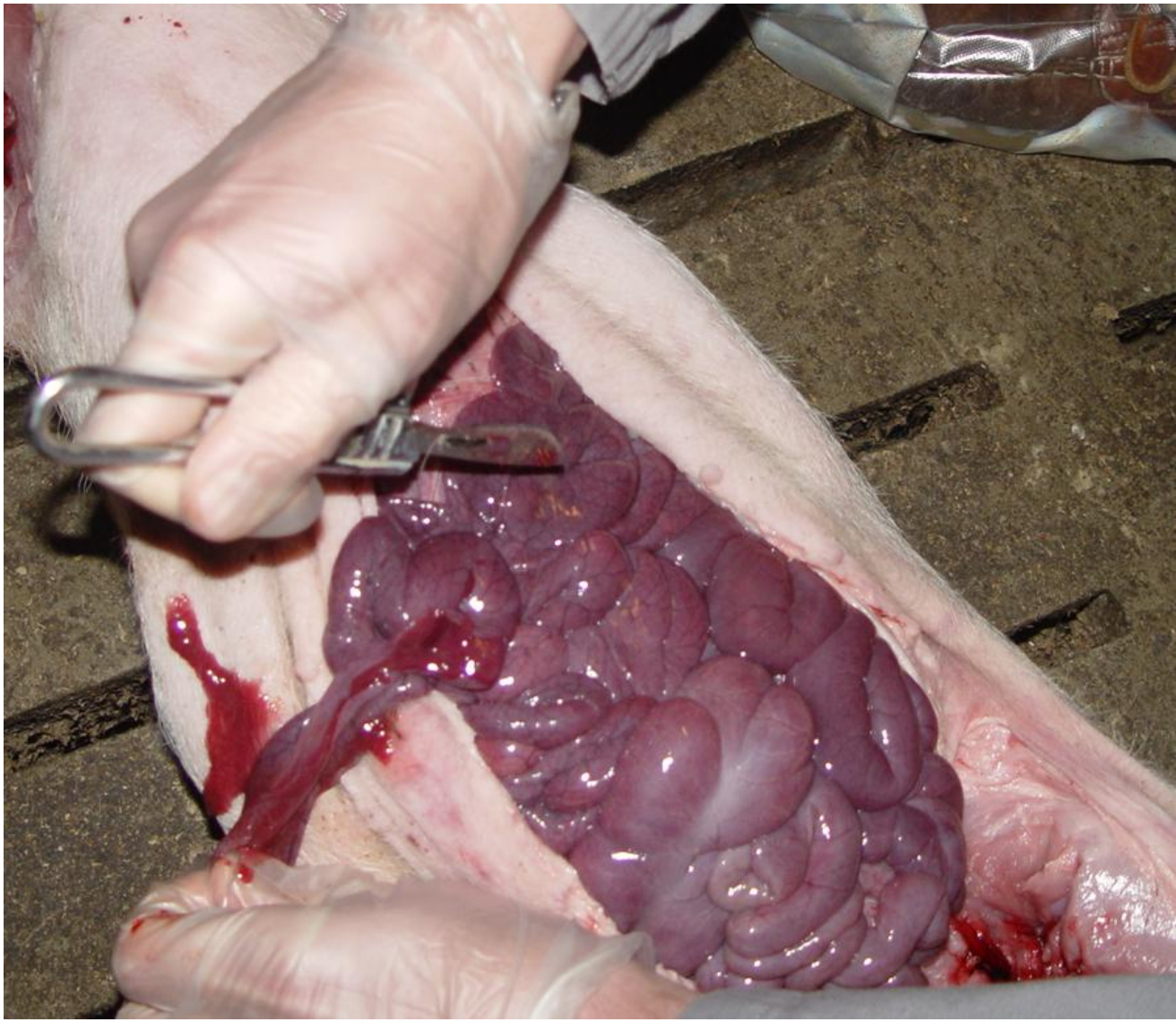
From « How » to « Why »



Pathology of transition:

- Counter-intuitive problem
- For well done … Too well done
- Piglet's feeding behavior

Colitoxicosis: treatment



Edema disease

- Infectious but NON contagious disease
- Prevalence increase
- Beautiful heavy piglets
- In all types of herds
- Weaners AND early growers
- Digestive accident with special *E. coli* (fimbriae F18)

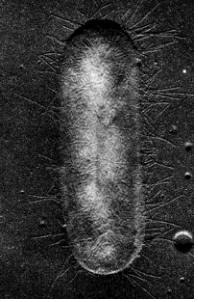
  -VTEC = VeroToxinogenic *E. coli*

  -STEC = ShigaToxigenic *E. coli*

  -EDEC = Edema Disease *E. coli*

  -EHEC = EnteroHemorrhagic *E. coli*

  ✓Slow acting colonisation all small gut



Edema disease

E. coli

Fimbriae	Enterotoxins	Endotoxins
F4	Stb, Lt	O147, O157
F4	Sta, Stb, Lt	O149
F18	Sta, Stb	O138, O141, O147, O149, O157
F18	Sta, Stb, Stx2e	Cytotoxin

Edema disease

Table 3: Patterns of susceptibility to disease

Adhesin	Age of susceptibility	Lineage-specific
987P	0-2 weeks	no
K99	0-2 weeks	no
K88	0-8 weeks (likely)	yes (autosomal dominant)
F18	3-8 weeks (likely)	yes (autosomal dominant)

Table 2: Serogroups of commonly isolated enterotoxigenic *E.coli* stains and their typical characteristics

Serogroup	Adhesin(s)	Toxin(s)	Hemolysins
Weaned pigs only			
O138	F18ab;ac	STa,STb±Stx2e	+
O139	F18ab	STa,STb±Stx2e	+
O141	F18ac	STa,STb±Stx2e	+
O157	F18ac	STa,STb±Stx2e	+

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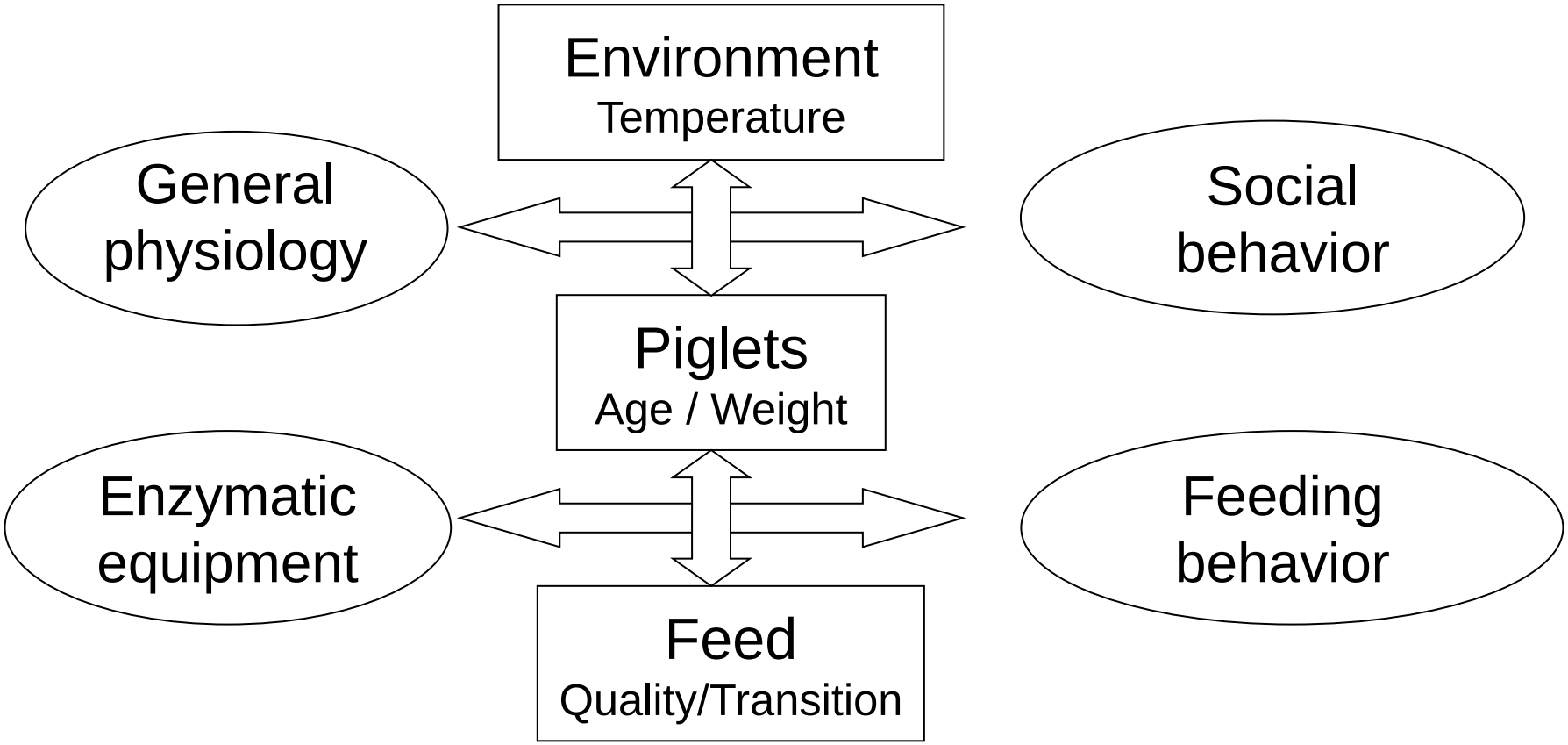
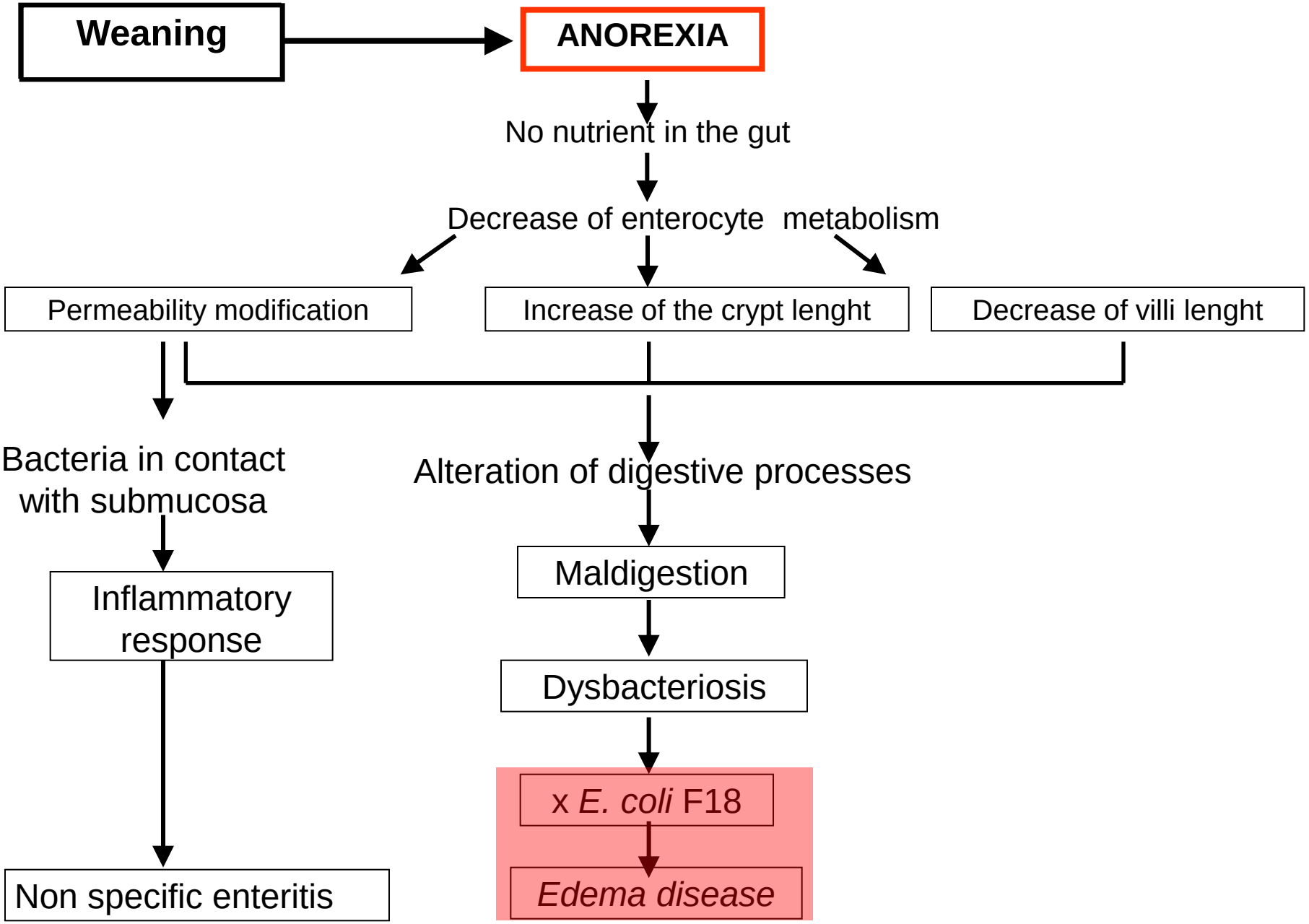
Virulence and fitness gene patterns of Shiga toxin-encoding *Escherichia coli* isolated from pigs with edema disease or diarrhea in Germany

Virulenz- und Fitnessgenprofile bei shigatoxinogenen Escherichia coli *von Schweinen mit Ödemkrankheit oder Diarrhoe in Deutschland*

Stefanie Barth, Abdybek Tscholshiew, Christian Menge, Reinhard Weiß, Georg Baljer, Rolf Bauerfeind

Edema disease

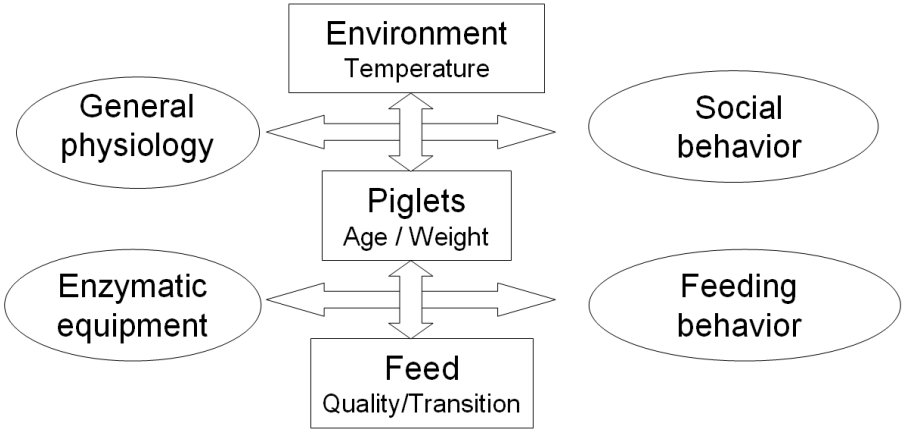




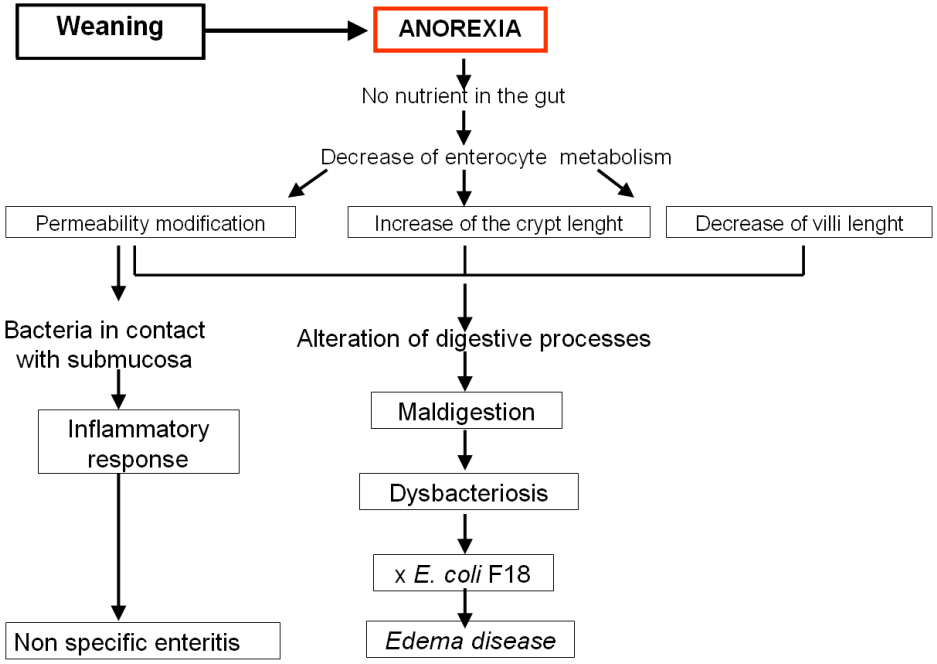
Adapted from David Guillou, 2008

Edema disease

Herd level



Piglet level



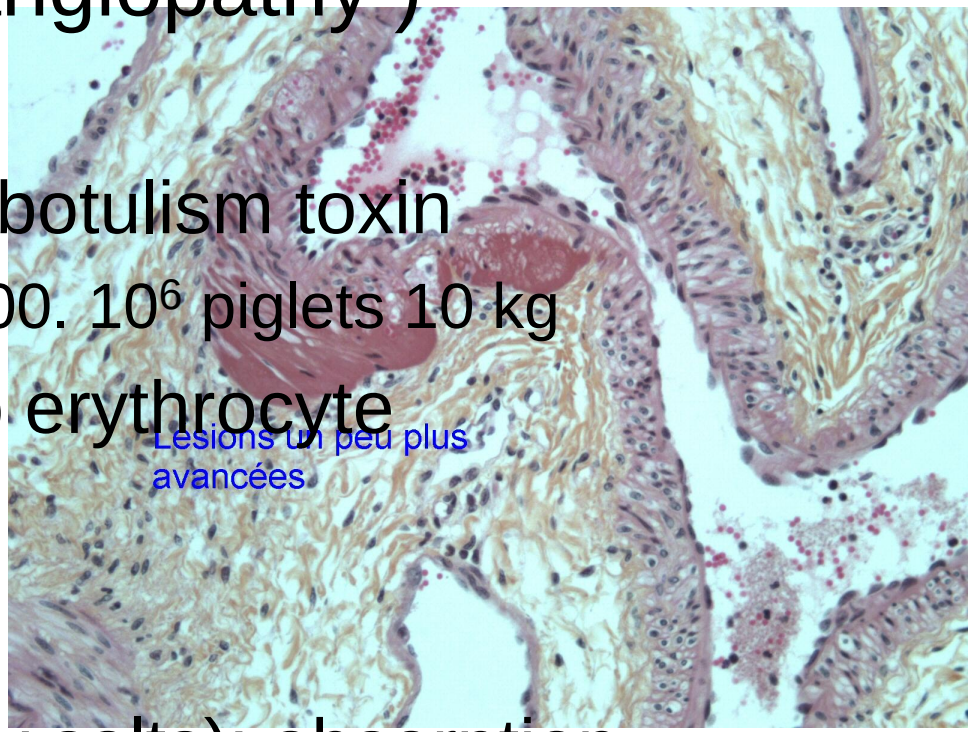
Edema disease

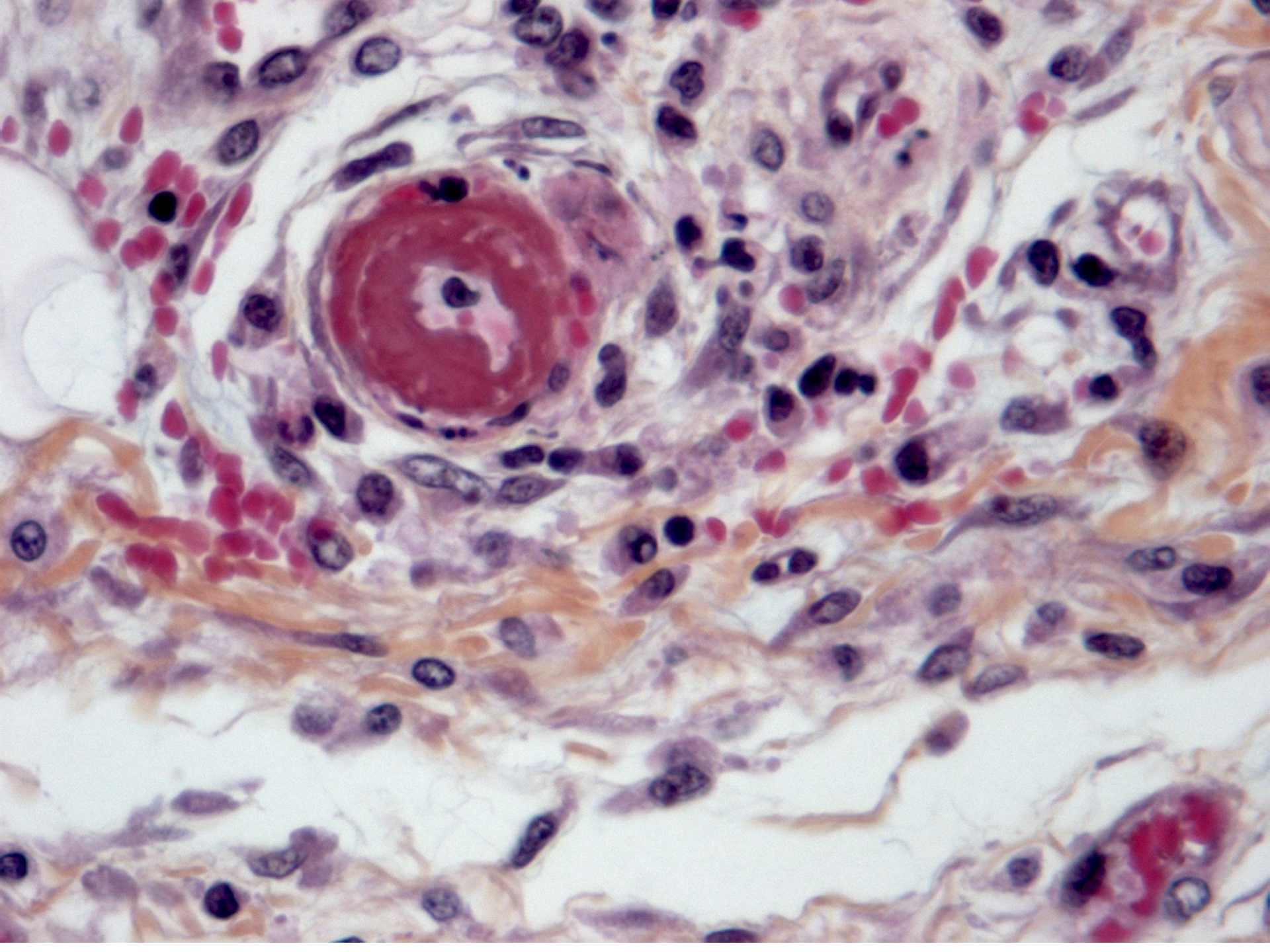
Physio Global	***Physio digestive***	***Behavior & feed***	***Feed changes composition***	***Feed changes immuno***
⇩	⇩	⇩	⇩	⇩
Syndrome of adaptation	Less absorption	Feed consumption	Enzymatic adaptation	End of lactogenic protection
⇩	⇩	⇩	⇩	⇩
Decrease stress (t C, housing)	Feed quality and feed transition	Feed quality and feed transition	1-pre-weaning 2-digestive capacity	1-Antibiotic 2-Vaccination 3-Ecologic manipulation
Yes, but	Yes, but	Yes, but	Yes, but	Yes, but

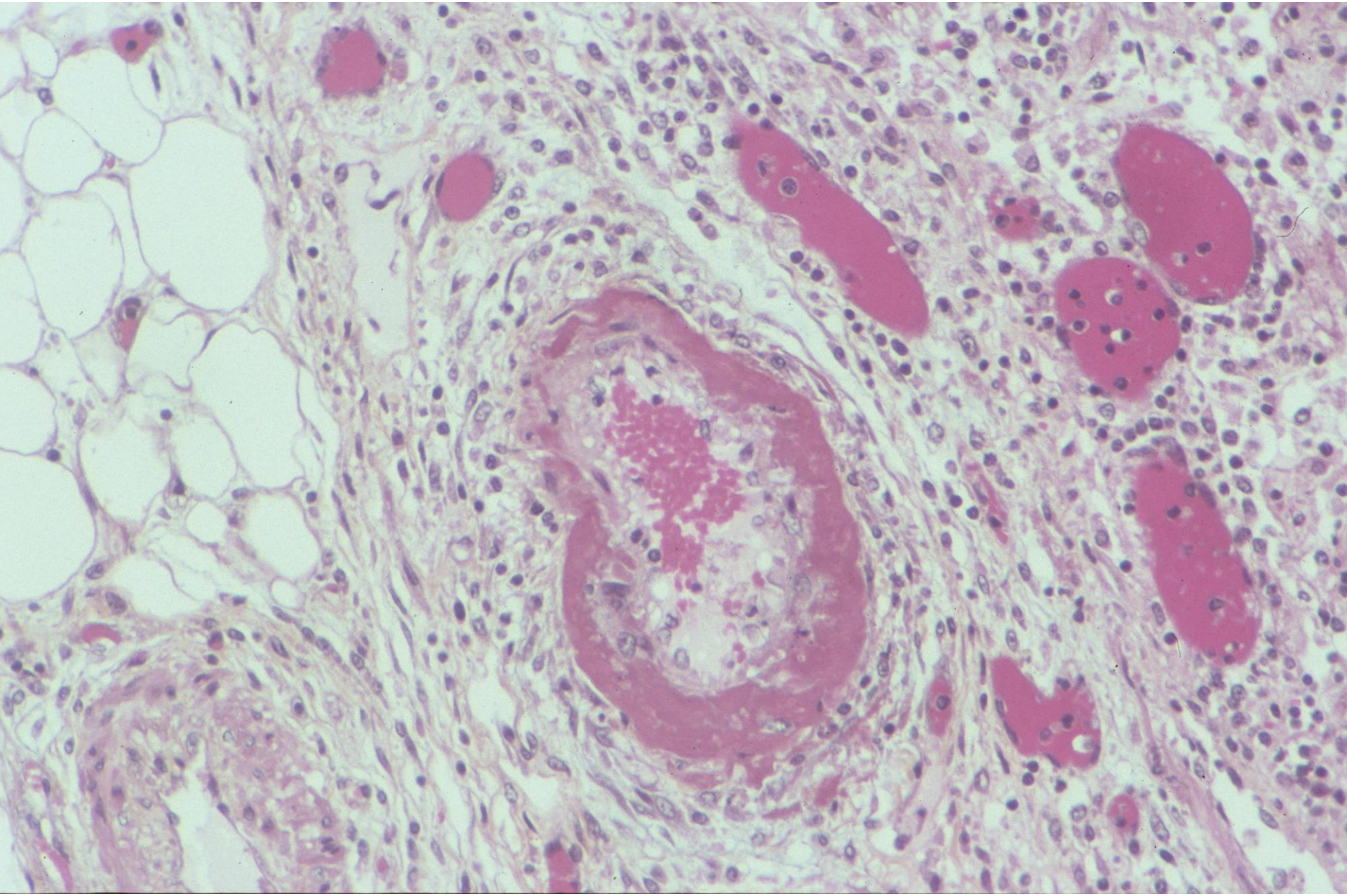
Denmark / France

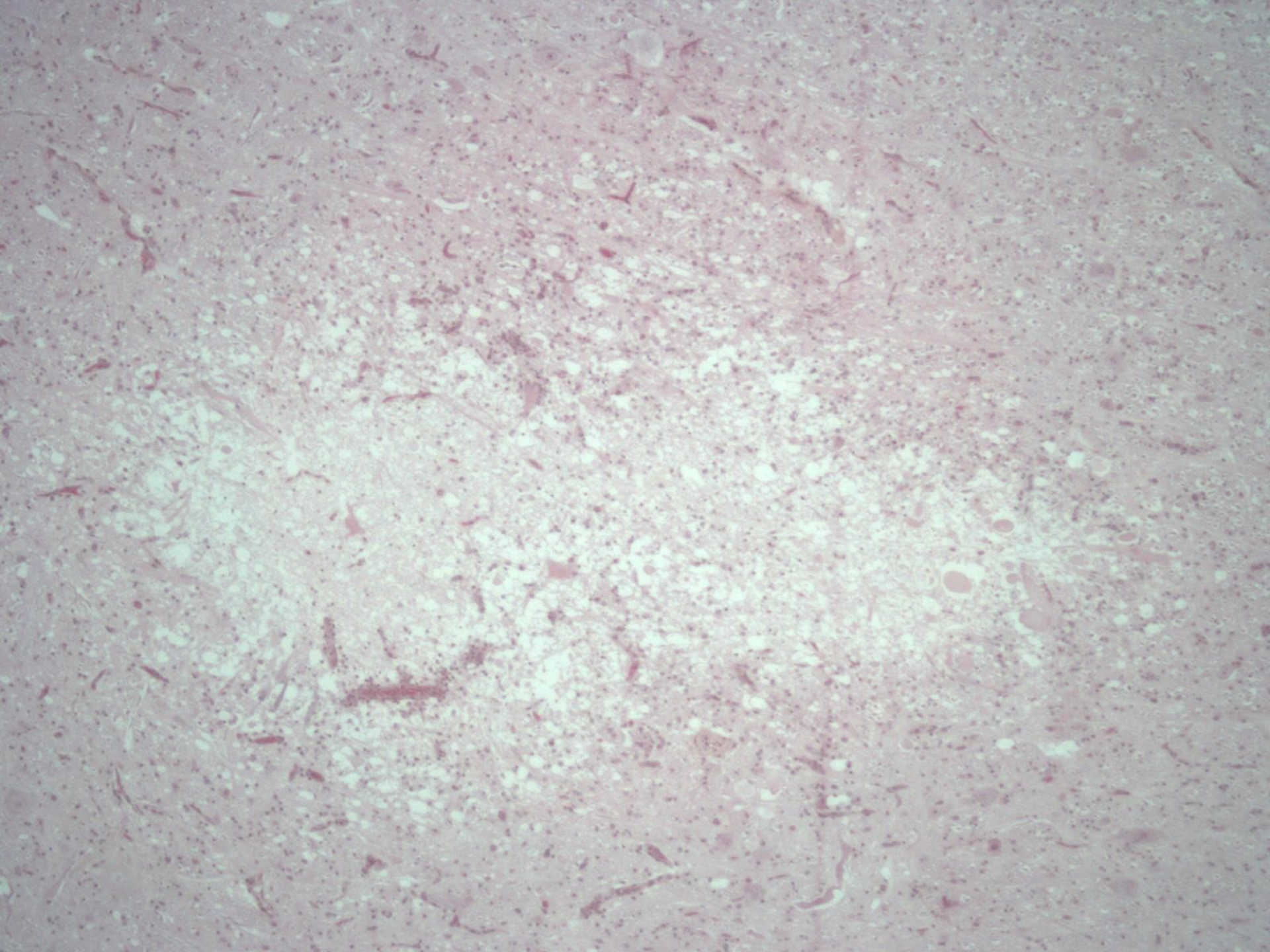
STx2e
toxinogenic disease

- IV: ED (degenerative angiopathy)
  - 0,000003mg/kg
  - 3x more toxigenic than botulism toxin
    - 1 gramme of toxin = † 100. 10^6 piglets 10 kg
  - Adhesion of the toxin to erythrocyte
- Oral:
  - Usually: no absorption
  - Gut manipulation (biliary salts): absorption
    - dysbacteriosis
      - Increase of biliary salts
      - expression of FUT-1



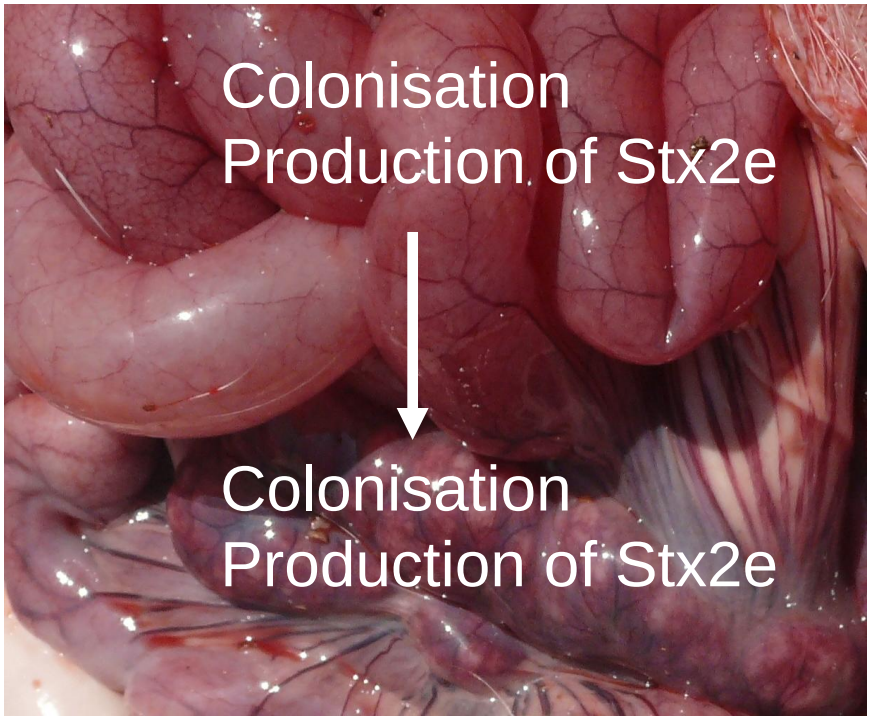






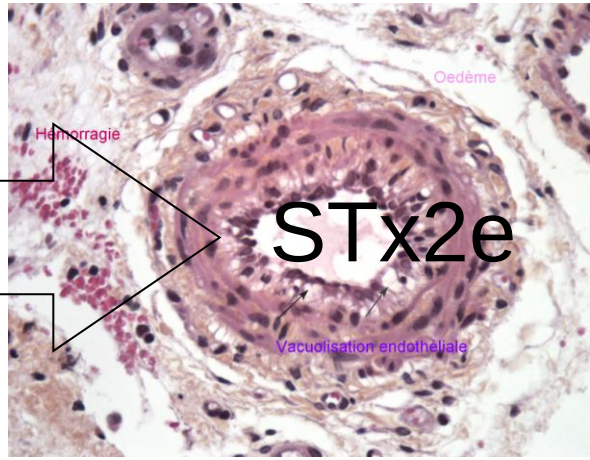
Edema disease

Gut incident



Fatal gut accident

Dysbacteriosis



Iatrogenic lysis
(i.e. antibiotics)

Massive release of Stx2e
- After bacterial lysis
- Non secreted (different from enterotoxins)

Isolation from lymphnodes

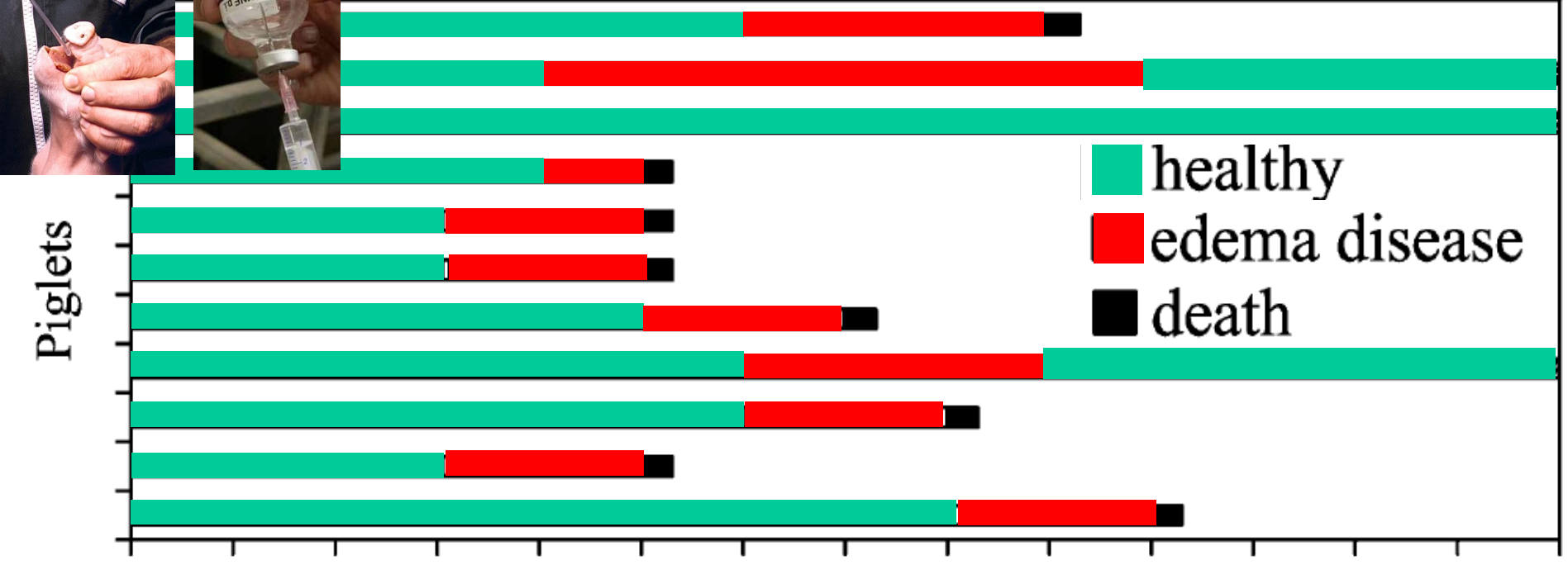
- Why it is of major importance ?
- Usually (textbooks): *E. coli* limited to gut lumen

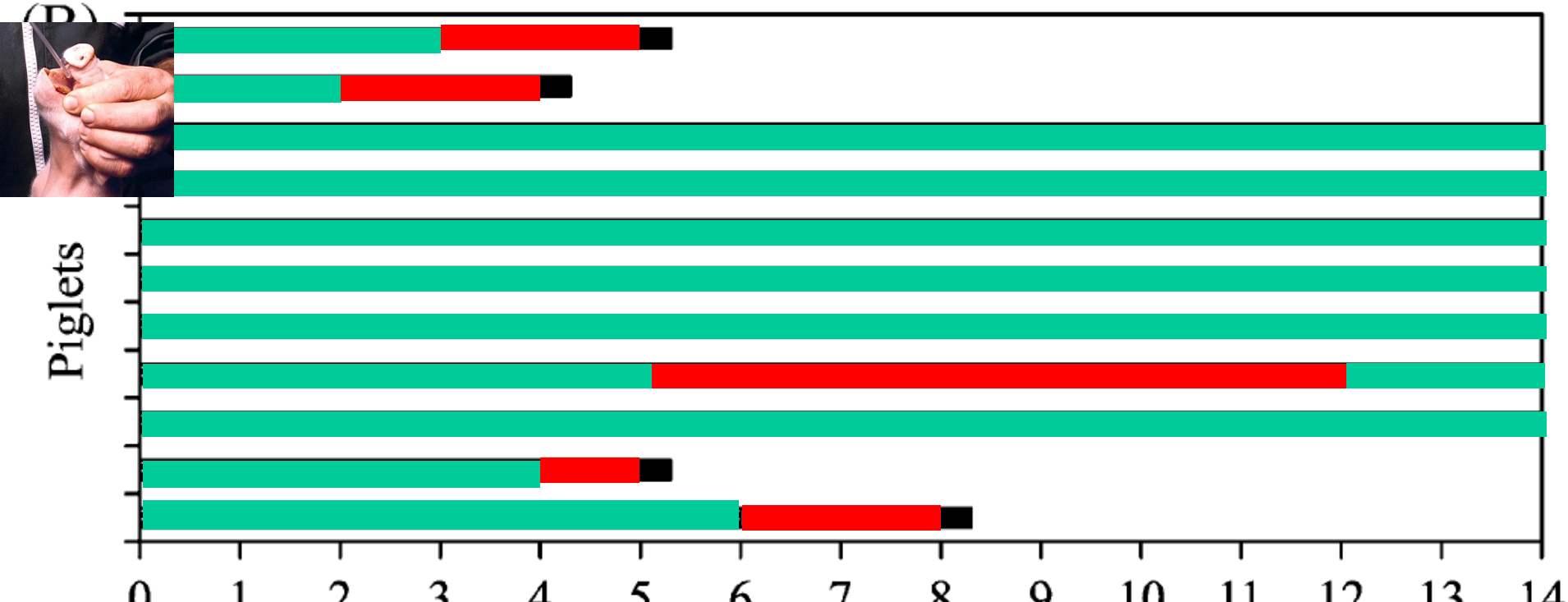
The effect of intramuscular administration of colistin on the development and course of experimentally induced oedema disease in weaned piglets

Lucie Konstantinova, Jaroslav Hamrik, Pavel Kulich, Vladimir Kummer, Jarmila Maskova, Pavel Alexa *

Veterinary Research Institute, Hudcova 70, 621 00 Brno, Czech Republic

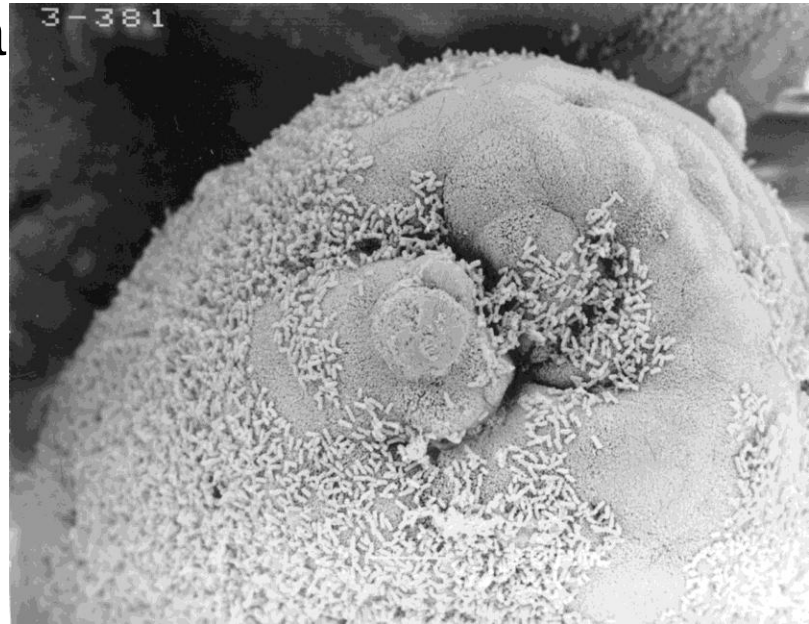
Veterinary Microbiology 128 (2008) 160–166


healthy
edema disease
death
Piglets


Piglets
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14

Konstantinova's results

- No colonisation (in fact: 1/22)
- Same intestinal multiplication in the two groupes (treated or not treated with colistine)
- Mesenteric lymphnodes colonized
- On a clinical point of view:
  - Lot A (treated) much more clinica



Konstantinova's hypothesis

- STEC lysis by colistine
  - Polypeptide: membrane lysis (like quinolones)
- Massive libération of Stx2e
  - STx2e non secreted (different from enterotoxins)
- Paradoxal situation

HUS
Hemolytic and uremic syndrome

In Japan, summer 1996…Hemorragic colitis and fatal HUS
Implication of *E. coli* entero-hémorragic (EHEC) with verotoxins

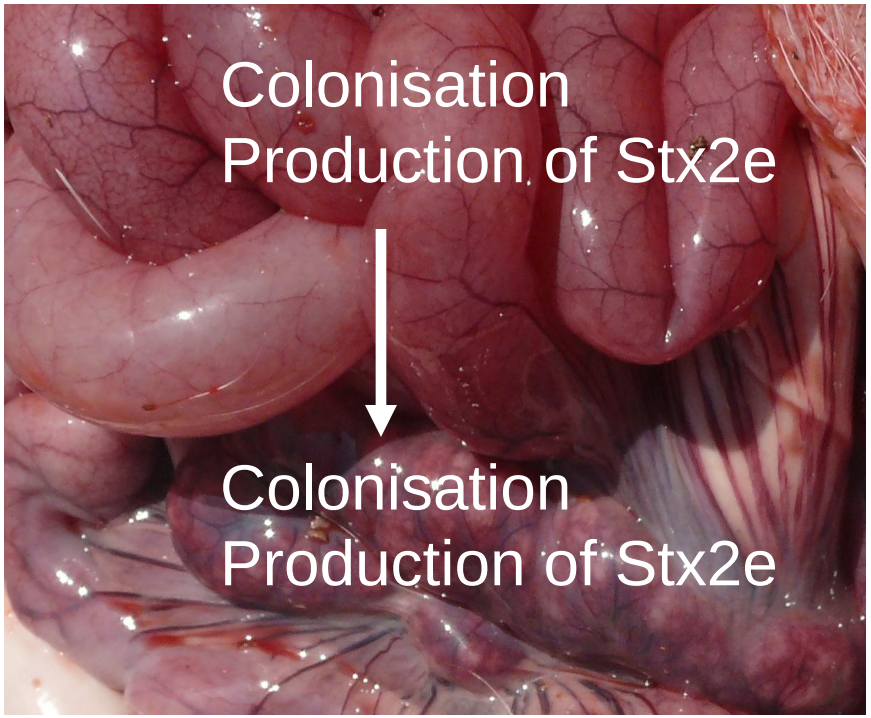
Wong et coll. 2000

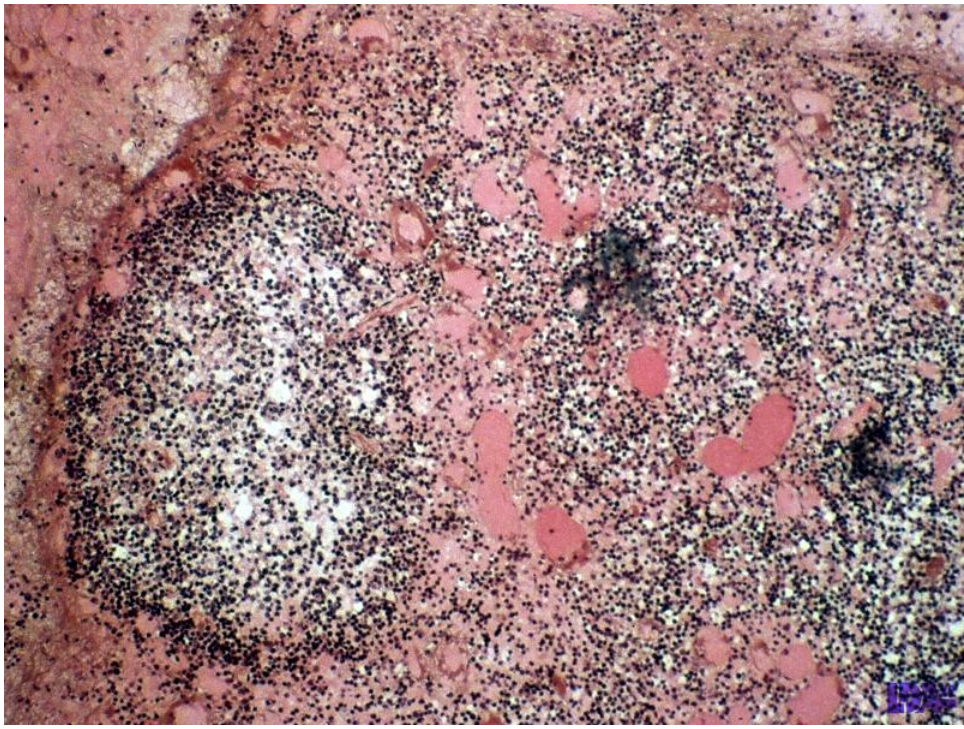
Increase of odds for HUS (50% versus 8%) between treated on non treated patients

« *We conclude that SOS-mediated induction of Shiga toxins and toxin-encoding bacteriophages may contribute to the emerging epidemiologic pattern of STEC (Shiga toxin-producing* E. coli*) disease* ».

Delayed digestive accident

6-8 days before clinical symptoms





Edema disease: pathophysio-diagnosis

- One question:
  What happens

6-8 days before ?

Edema disease

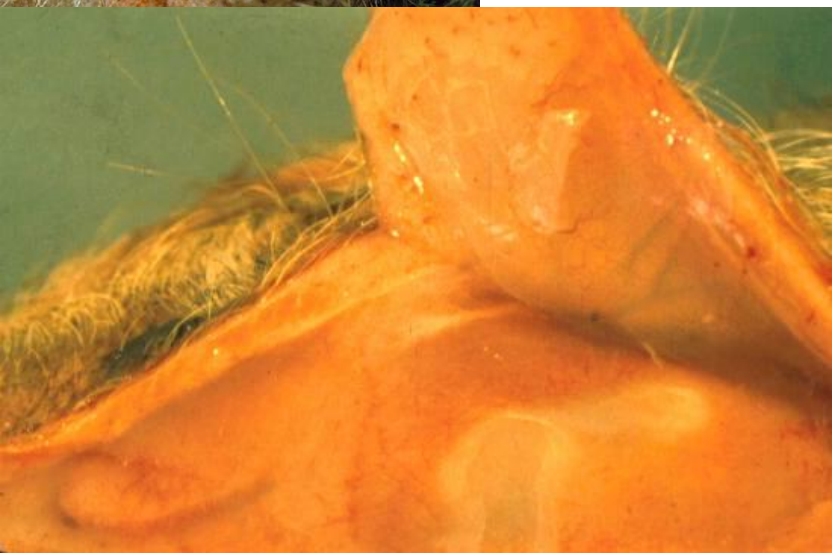
- Acute death
- Heavy and beautiful piglets
- Nervous symptoms

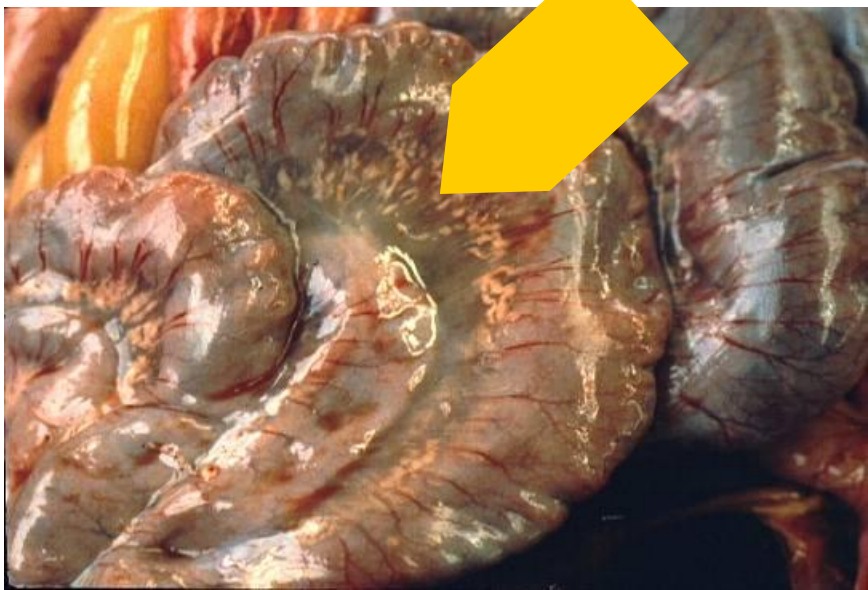
(confusion with *S. suis*)

- No fever (different from *S. suis*)

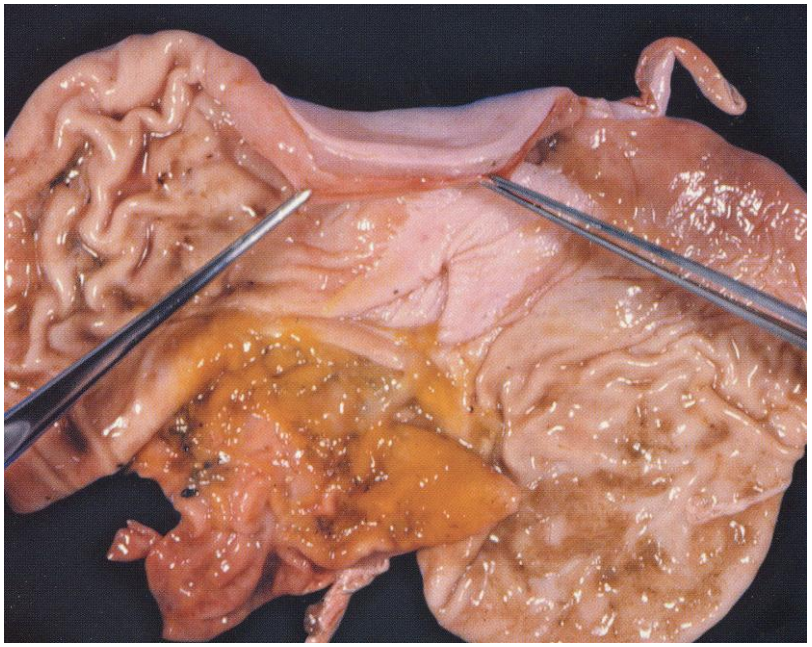

PLAY
0095

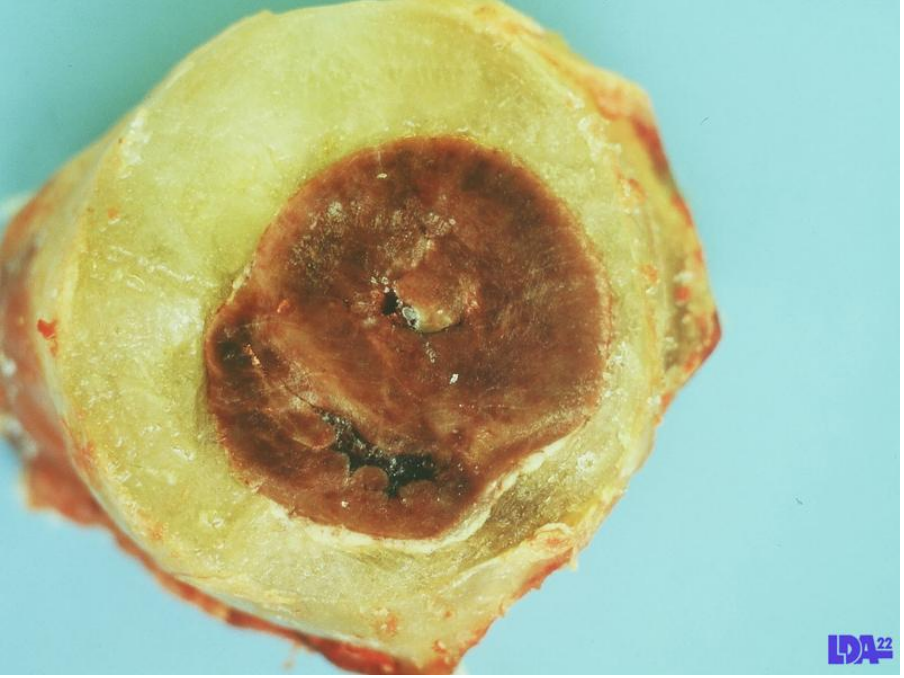
Edema disease

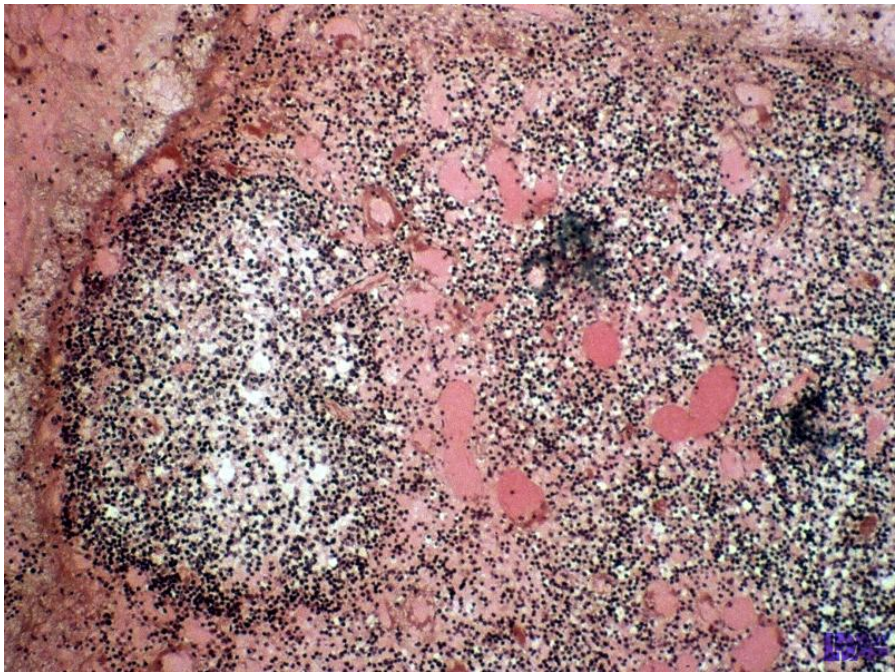




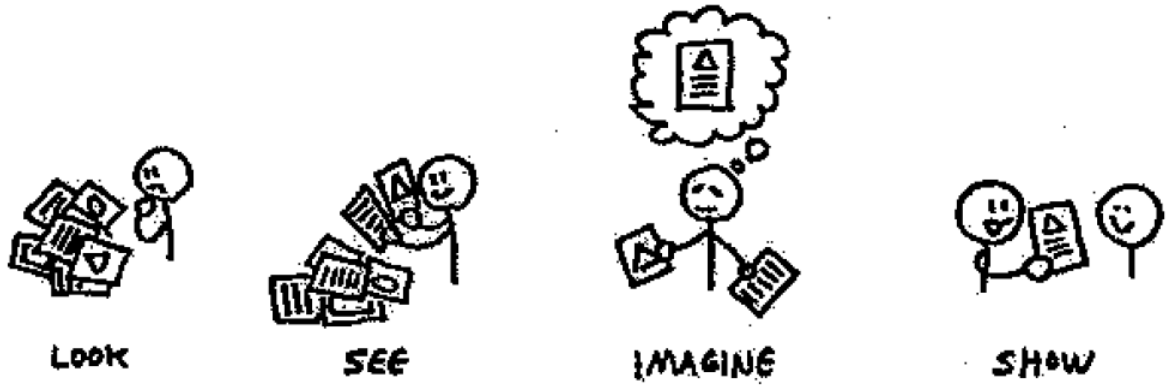
Edema disease



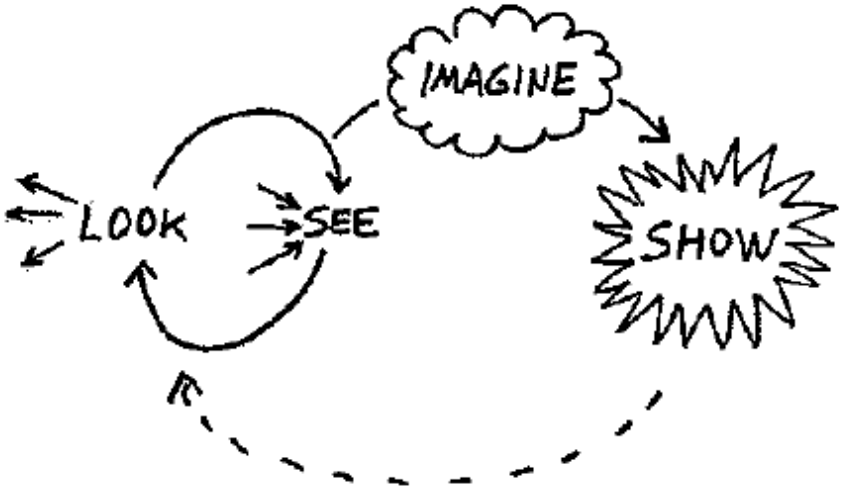




Edema disease diagnosis

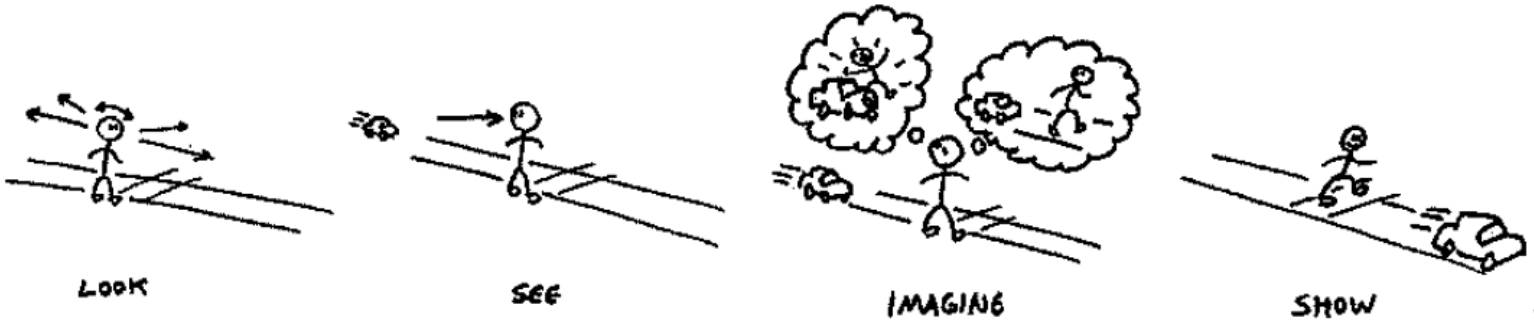


The four-step visual thinking process when creating a report.



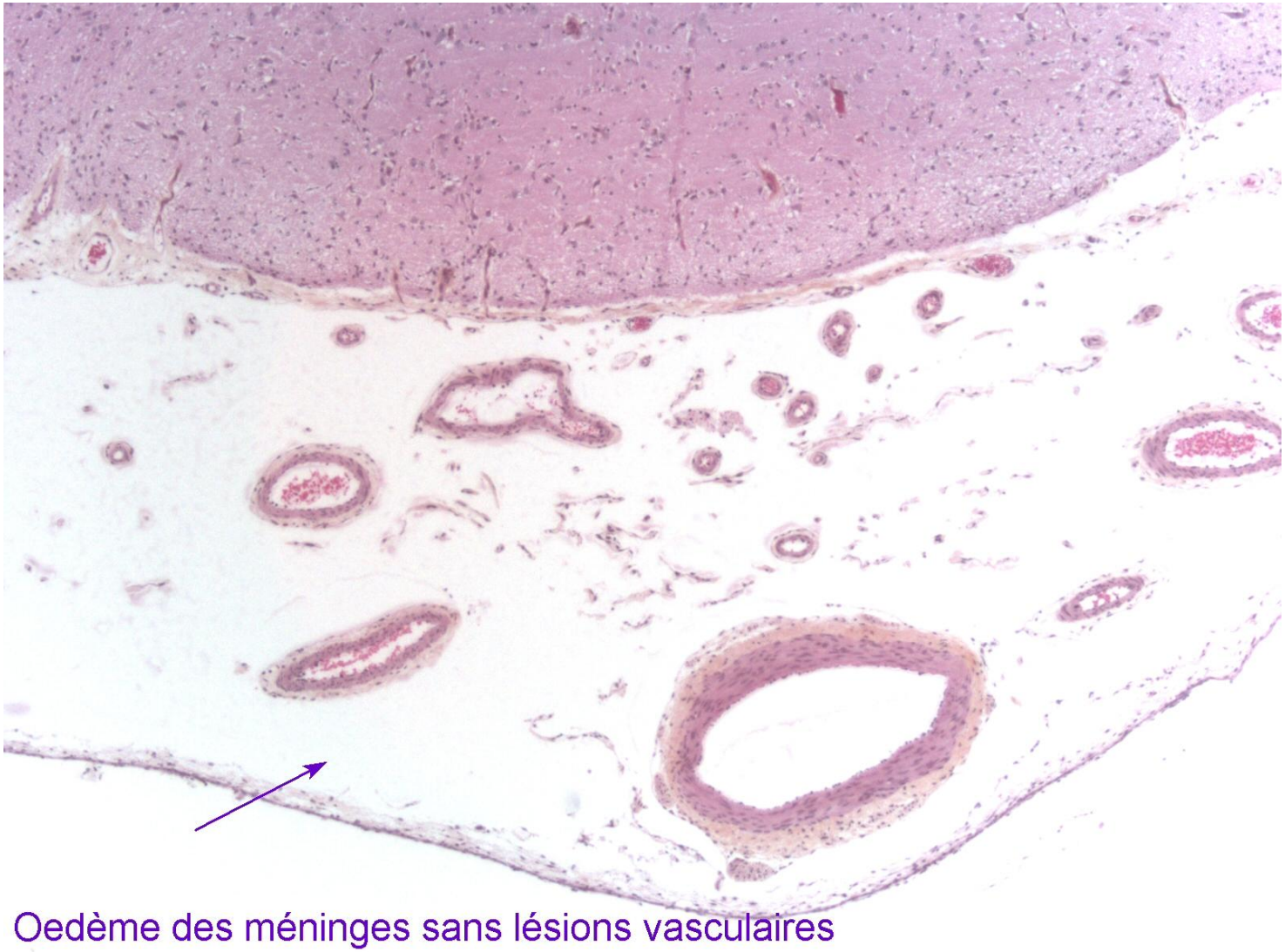
The visual thinking process, as it really happens.

Edema disease diagnosis



The four-step visual thinking process when crossing a street.

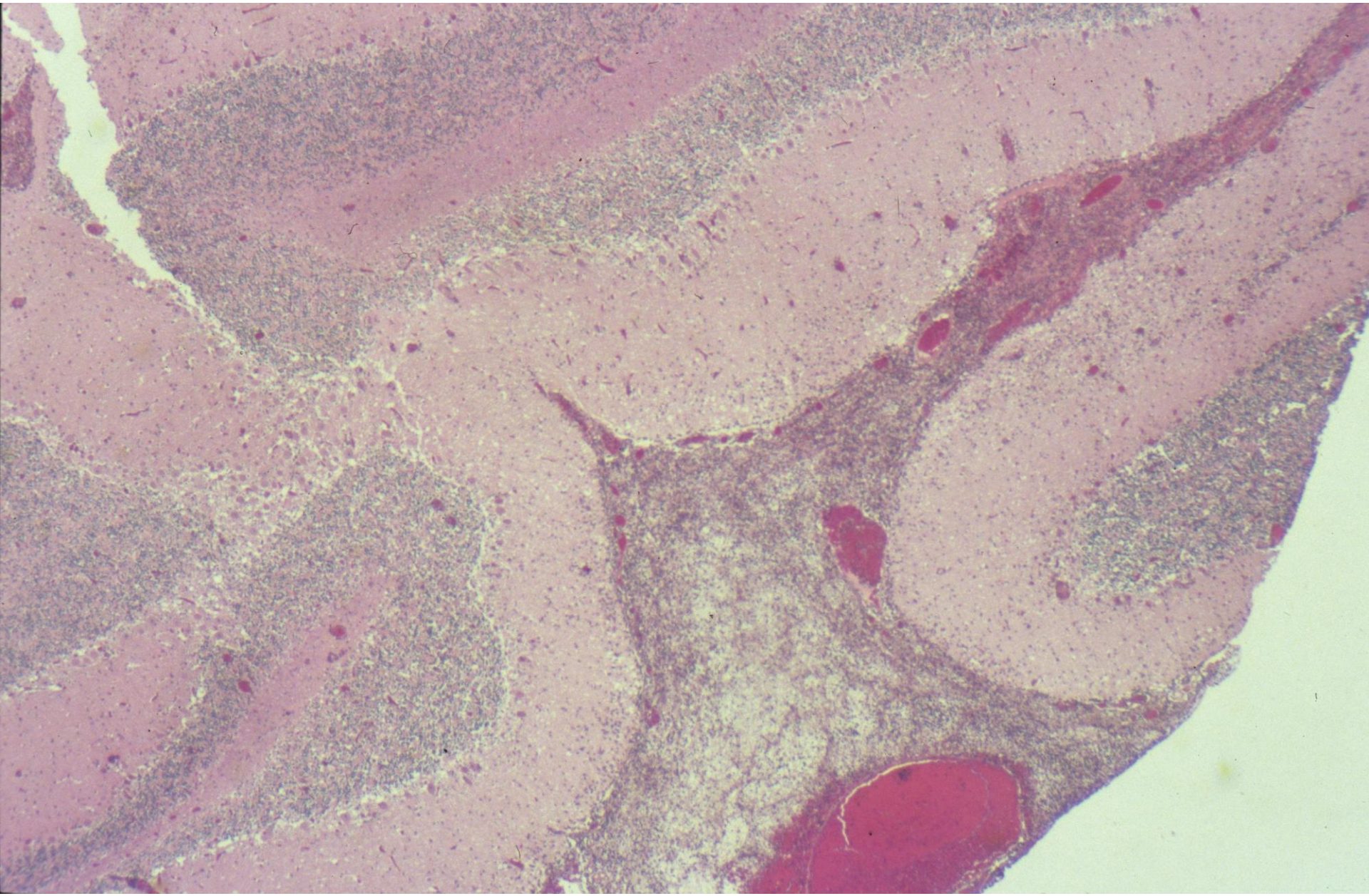
- Clinical and epidemiological:
  - Absence of fever
- Pathology (gross and histo)
- Bacteriology
- Differential:
  - Colitoxicosis
  - Septicemia (*S. suis / H. parasuis*)

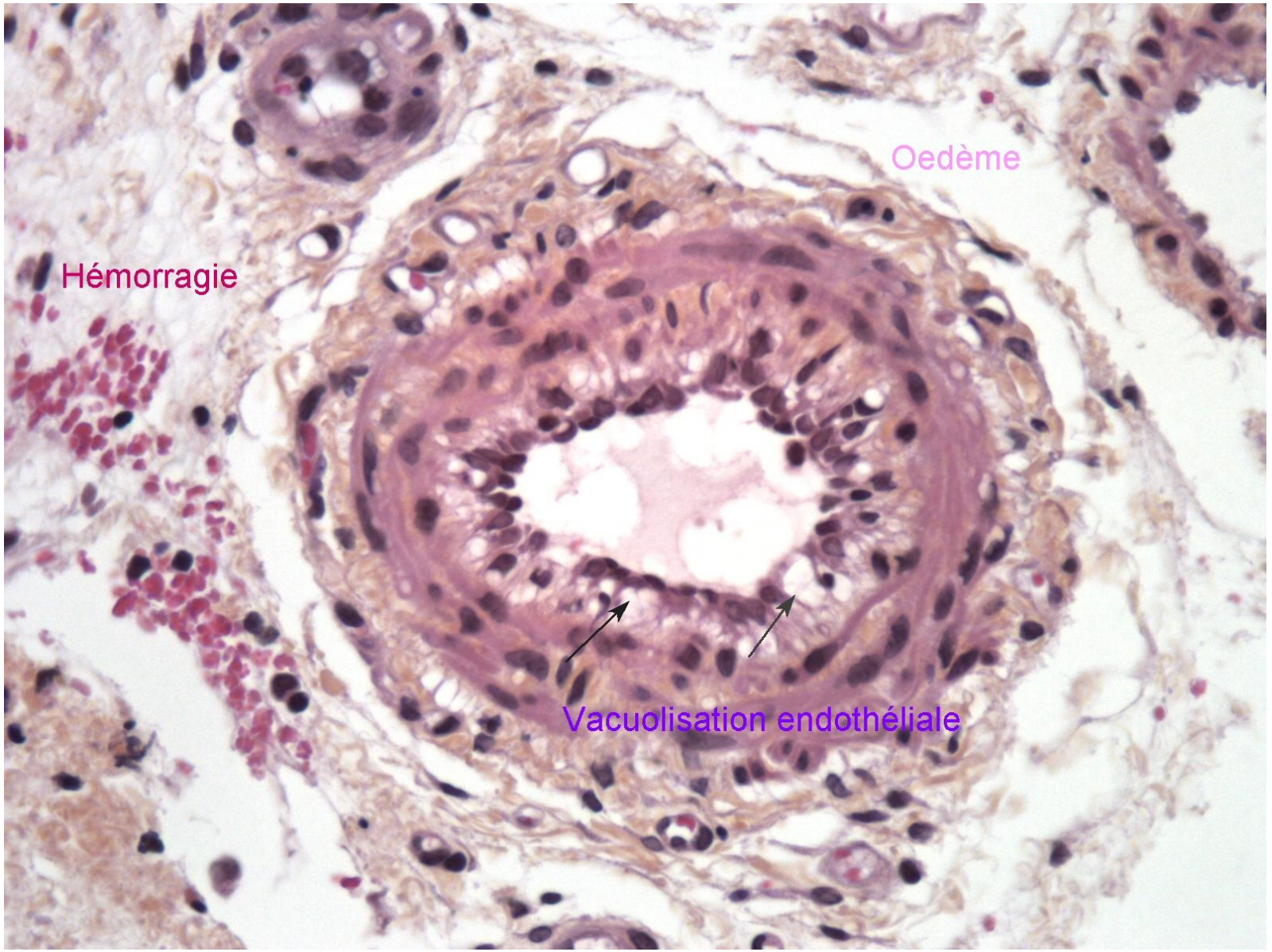


Oedème des méninges sans lésions vasculaires

Méninge, tronc cérébral.

Amenna, 2008

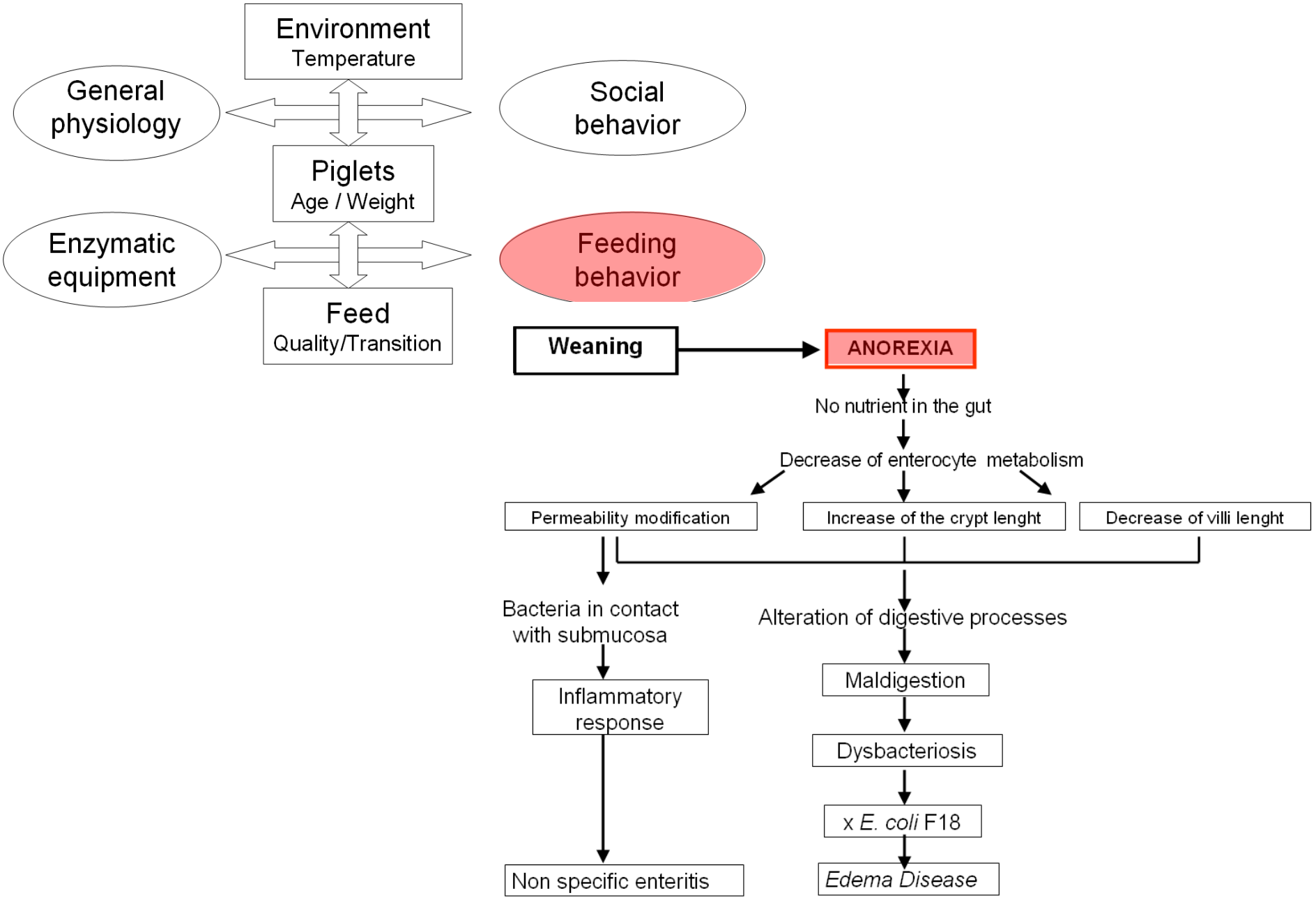




Angiopathy (mesenteric lymphnodes)

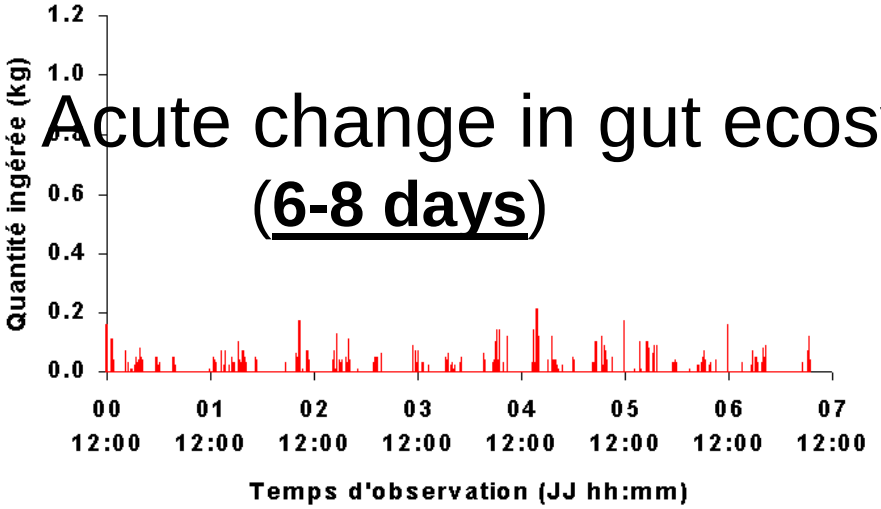
Amenna, 2008

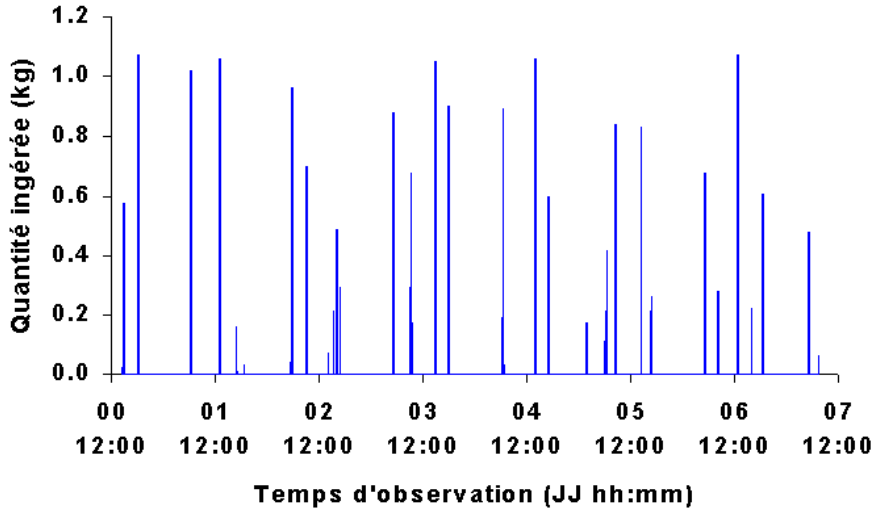

Lésions un peu plus
avancées


Environment
Temperature
General physiology
Social behavior
Piglets
Age / Weight
Enzymatic equipment
Feeding behavior
Feed
Quality/Transition
Weaning
ANOREXIA
No nutrient in the gut
Decrease of enterocyte metabolism
Permeability modification
Increase of the crypt lenght
Decrease of villi lenght
Bacteria in contact with submucosa
Alteration of digestive processes
Inflammatory response
Maldigestion
Dysbacteriosis
x E. coli F18
Non specific enteritis
Edema Disease

Edema disease

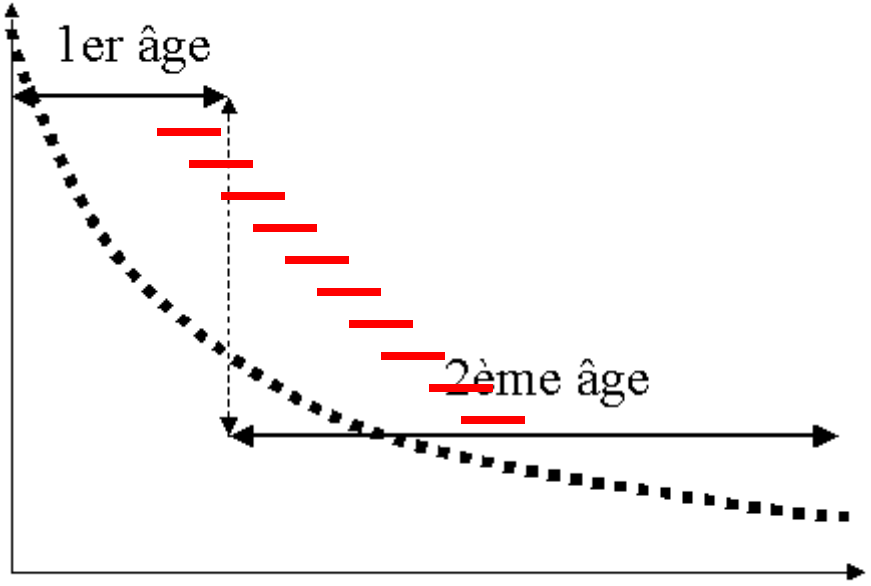
Acute change in gut ecosystem of one specific piglet (**6-8 days**)





Edema disease

Acute change in gut ecosystem of one specific piglet
(**6-8 days before**)

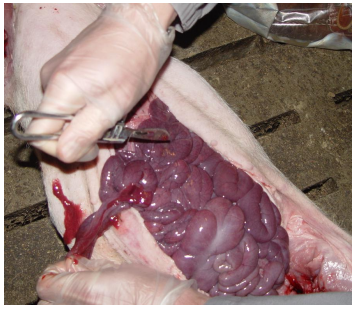


Gut accident
Infectious disease
Non contagious

1 3 5 7 9 11

Edema disease

Colitoxicosis



1 3 5 7 9 11

Last (but not the least) question: from where came the F18+Stx2e+ *E. coli* ?

- ✓Sows
- ✓Nursery


Robert, 2008

Last (but not the least) question: from where came the F18+Stx2e+ *E. coli* ?

- ✓Sows
- ✓Nursery

Waterborne E. coli

This Japanese paper (J. of Jap. Vet. Med. Assoc. 51 659-661) describes a condition over five months on a Japanese pig farm when some 270 piglets showed oedema of the eyelids and nervous systems some 10 days post weaning. Death invariably ensued.

Post mortem examinations revealed brain and intestinal lesions and E. coli 0139 was isolated from brains, lymph nodes and intestinal contents.

E. coli 0139 was detected from the water holding tank and in drinking water at various places on the farm. The problem disappeared after the water was chlorinated and the farm disinfected.

Edema disease

Enterotoxemia due to *Escherichia coli* in Weaning Piglets Water-Transmitted

Morio HADA*, Naomi HASHIMOTO, Toyoko FUKUTOMI and Kouken OKUDA

* *Okayama Livestock Hygiene Service Center, Mitsu-cho, Okayama 709-2123, Japan*

SUMMARY

From July to December in 1996 at hoggery in Okayama Prefecture, about 270 piglets showed edema of eyelids and nervous symptom about 10 days after weaning and acutely died. Three killed or dead pigs were necropsied, revealing histopathologically fibrinoid and hyaline degeneration of vascular walls in the brain stem and the submucosa of the small intestine. Verotoxigenic *Escherichia coli* (VTEC) O139 was isolated from the brain, lymph nodes and intestinal contents. VTEC O139 of the same serotype as isolats from the dead cases was also detected from storage tank and drinking water in the hoggery, and no more outbreaks occurred after chlorinating water and complete sweeping-out and disinfecting of the farmhouses.

——Key words : *E. coli* O139, enterotoximia, water-borne infection.

J. Jpn. Vet. Med. Assoc., 51, 659~661 (1998)

Edema disease prevention

J. Fairbrother, GREMIP, Canada:
Live *E. coli* strain:
F18+/Shigatoxin negative

Conclusions

- Why > How
  - When
- PWD
  - Principle of precaution
- Colitoxicosis
  - 24-36 hours
- Edema disease
  - 6-8 days
  - Counter-intuitive effects of antibiotics


i'm lovin' it
BURGER KING
KFC
STARBUCKS COFFEE