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# Neonatal Colibacilosis & Clostridiosis

*Brief overview & Practical approach*

Oriol Boix Mas

Corporate Product Manager

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# Neonatal Clostridiosis

*Brief overview & Practical approach*

Oriol Boix Mas

Corporate Product Manager

What percentage of sows have recurrent neonatal diarrhoea in Europe despite current vaccination against *E.coli* & *C.perfringens* type C?

Why?

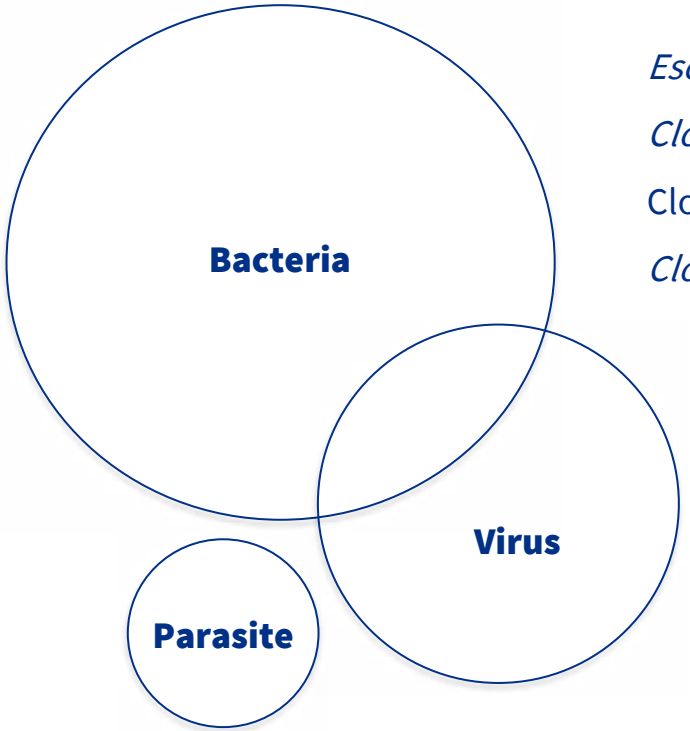
## CURRENT SITUATION

1. New farms
    - High replacement which implies a high ratio of gilts/batch
    - Antibiotic reduction

2. Hyperprolific sows
    - Competition for colostrum
    - More piglets = density
    - Management and personnel technology
        - Split nursing
        - Adoptions

3. Animal welfare
    - Gestation in groups
    - Dirty sows
    - Lack control feeding curve

# *Who is our enemy?*




*Escherichia coli*

*Clostridium perfringens* type C

Clostridium perfringens type A

*Clostridioides difficile*

Rotavirus

Coronavirus (PED / TGE)

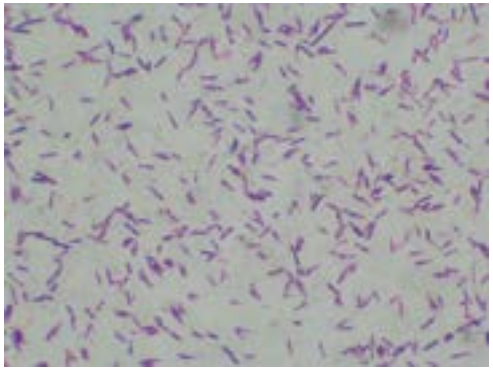
Seneca virus

Coccidiosis

# *Clostridioides difficile*

***Clostridium perfringens* type A**

- Gram positive anaerobe bacteria
- Difficult to culture
- Toxins involved on the pathogenesis
  - Toxin A and Toxin B



**Source:** Dr. Rodrigo Otavio

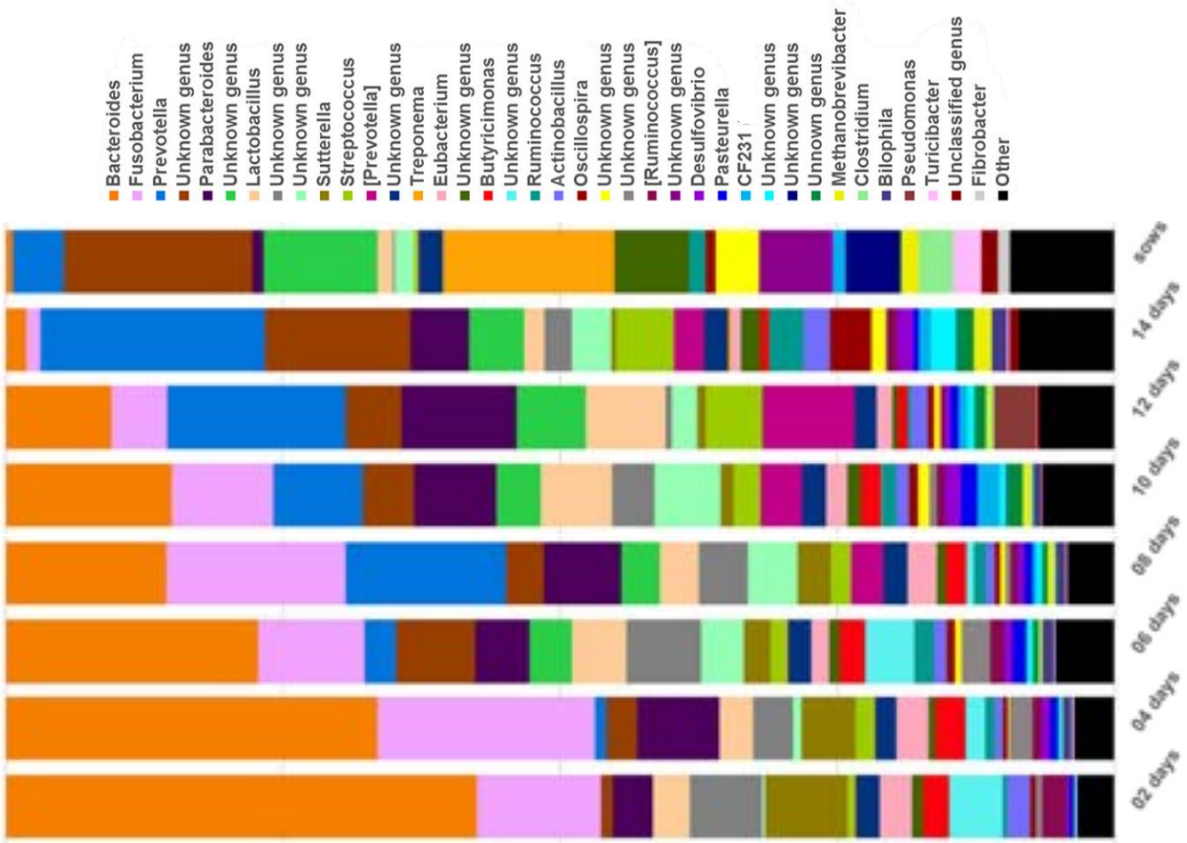
- Spore forming, rod-shaped
- Extremely resistant in the environment
- Can be found in environment, soil & water, air or domestic animals

**Diarrhea in piglets 1-7 days of age**

- Development of microbiota
- Source of infection: sow

Why do piglets have diarrhoea and sows don’t?

# Pathogenesis and epidemiology

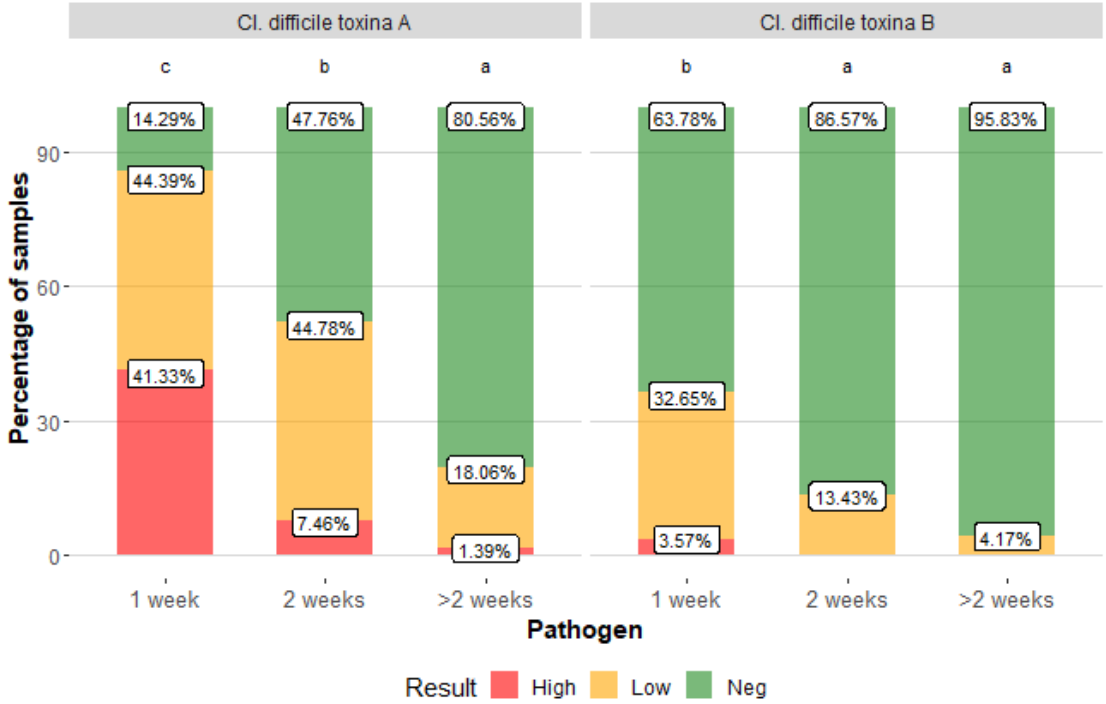




Microbiology Spectrum

RESEARCH ARTICLE

Neonatal Piglets Are Protected from *Clostridioides difficile* Infection by Age-Dependent Increase in Intestinal Microbial Diversity


Cl. difficile toxina A
Cl. difficile toxina B
c
b
a
b
a
a
14.29%
44.39%
41.33%
47.76%
44.78%
7.46%
80.56%
18.06%
1.39%
63.78%
32.65%
3.57%
86.57%
13.43%
95.83%
4.17%
Percentage of samples
90
60
30
0
1 week
2 weeks
>2 weeks
1 week
2 weeks
>2 weeks
Pathogen
Result
High
Low
Neg

# Pathogenesis and epidemiology

**Diarrhea in piglets 1-7 days of age**

- Development of microbiota
- Source of infection: sow

- **Possible triggers**
  - Dose, antibiotic use and time of infection.
  - Poor passive transfer of immunity through colostrum
  - Piglet environment with high infection pressure

Pathogenesis and toxins

# Effect of age, dose and antibiotic therapy on the development of *Clostridium difficile* infection in neonatal piglets

Paulo H.E. Arruda [a], Darin M. Madson [a,*], Alejandro Ramirez [a], Eric Rowe [b], Joshua T. Lizer [c], J. Glenn Songer [a,c]

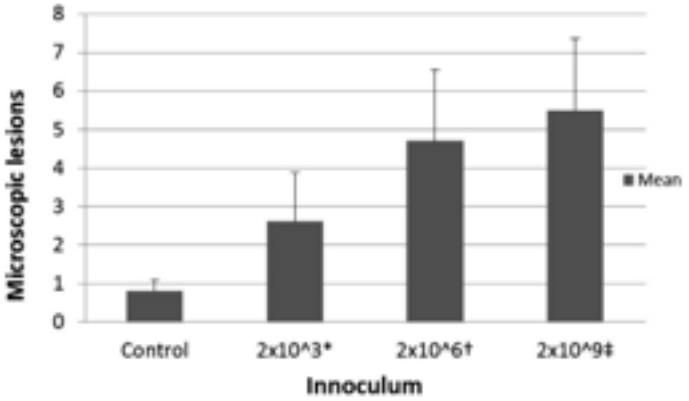
[a] Department of Veterinary Diagnostic and Production Animal Medicine, College of Veterinary Medicine, Iowa State University, Ames, IA 50011, USA
[b] Biomedical Science Department, College of Veterinary Medicine, Iowa State University, Ames, IA 50011, USA
[c] Veterinary Microbiology and Preventive Medicine Department, College of Veterinary Medicine, Iowa State University, Ames, IA 50011, USA

Clinical signs

Low concentration (40%)
High concentration (80%)

Macroscopic lesions

Low < High concentration



# Pathogenesis and epidemiology

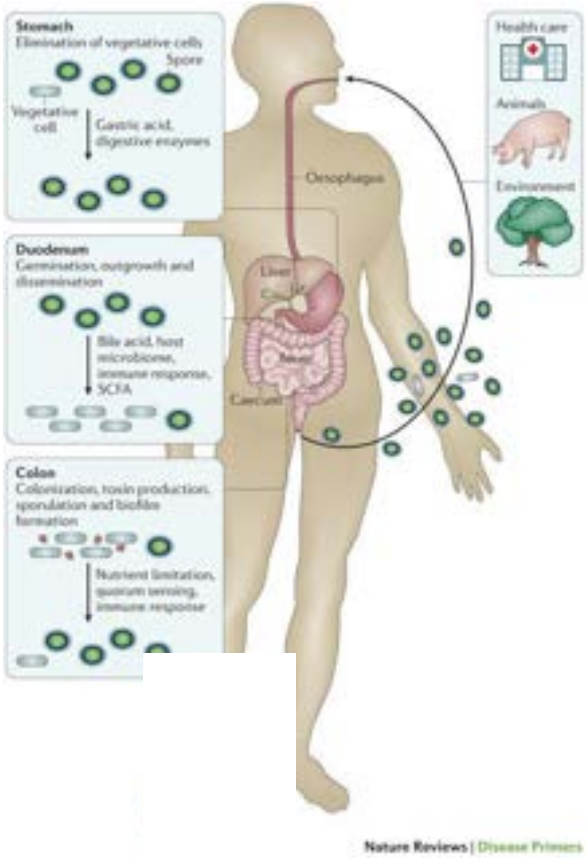
Fecal-oral transmission

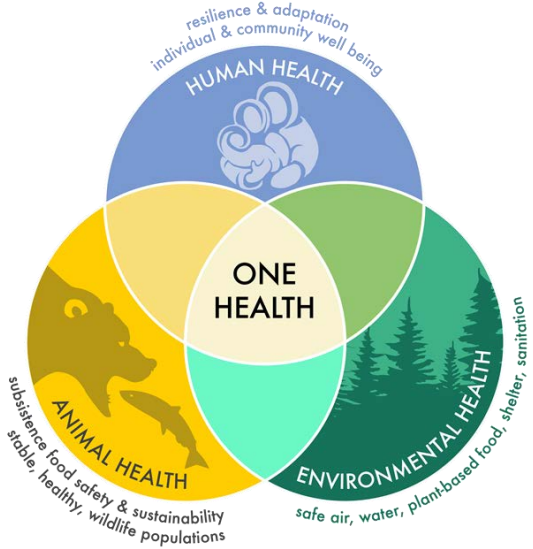
Animals

Air

Humans

# Pathogenesis and epidemiology




Smits, W.. et al. Nat Rev Dis Primers 2, 16020 (2016).

# Study finds superbug C. difficile can jump between pigs and humans, providing evidence of zoonotic spread

by European Society of Clinical Microbiology and Infectious Diseases

"Our finding indicates that **C. difficile is a reservoir** of antimicrobial resistance genes that can be **exchanged** between animals and humans"

https://phys.org/news/2022-04-superbug-difficile-pigs-humans-evidence.html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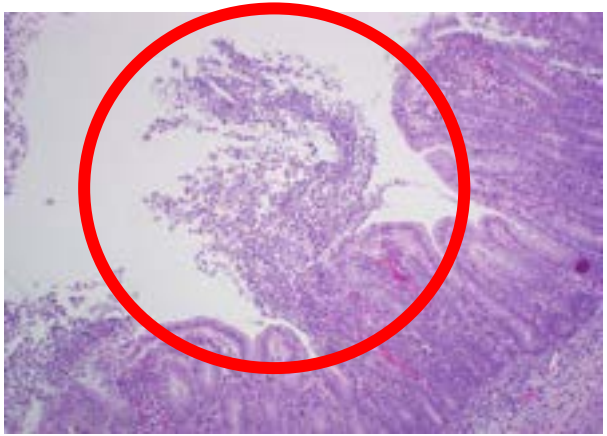
- **Gross Lesions**
  - Mesocolonic edema
  - Not pathognomonic

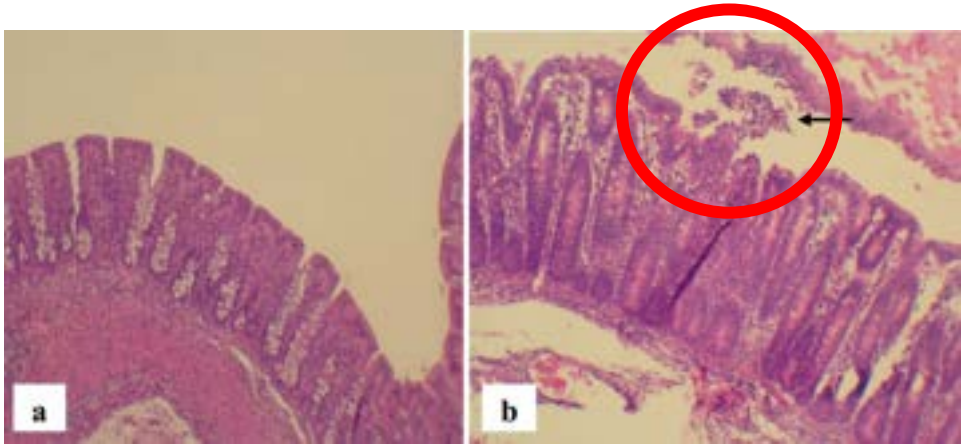
- **Histopathologic Lesions**
  - Ulcerative fibrinopurulent colitis
  - Focal erosions and ulcerations with variable amounts of fibrin and neutrophils

(volcano-like lesion)

# Pathogenesis and epidemiology



Source: Dr. Paulo Arruda




Source: Dr. Rodrigo Otávio

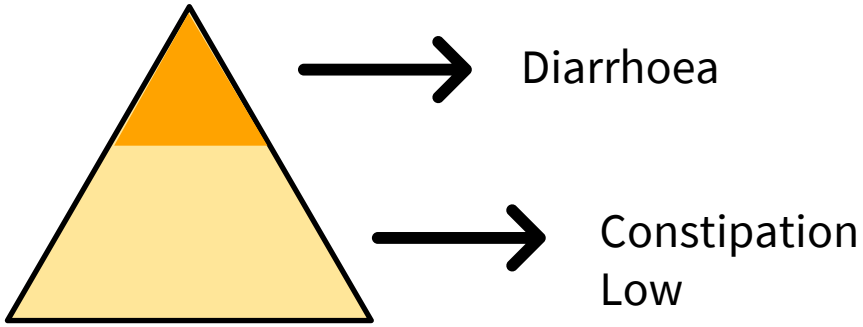
# Clinical signs

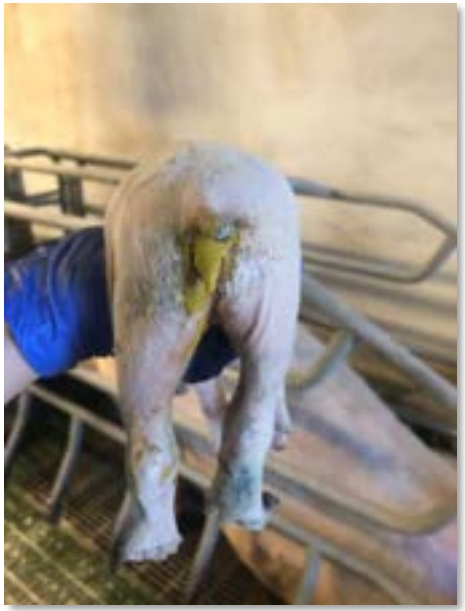
Pasty to watery yellow diarrhea soon after birth

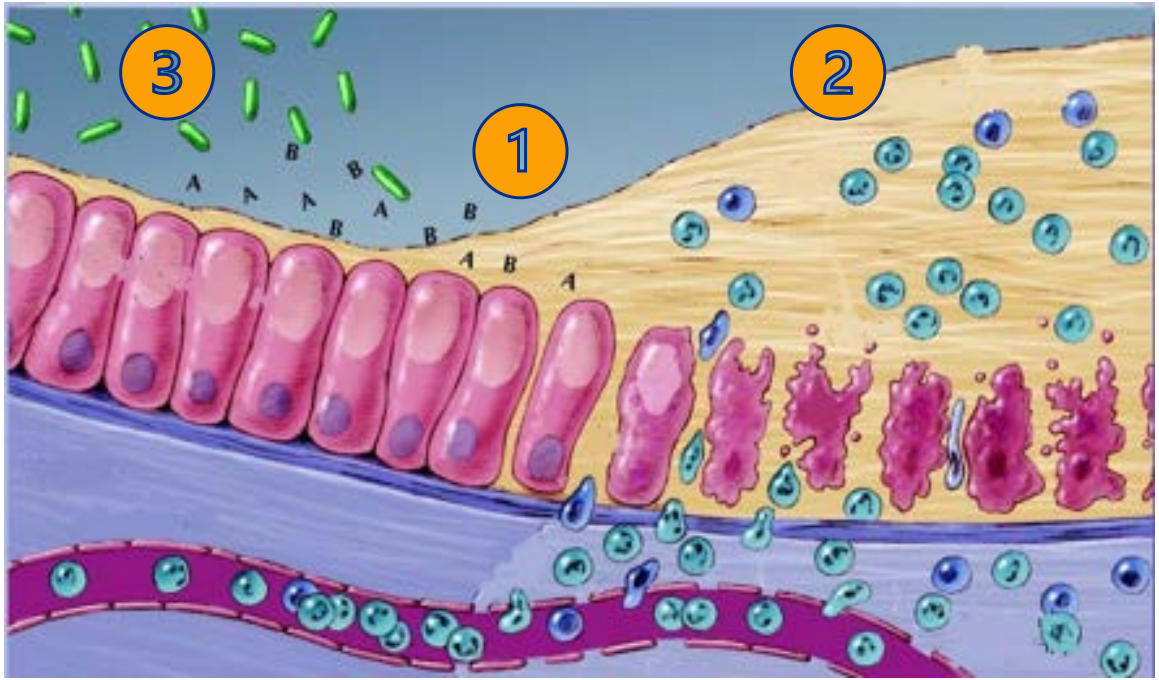
May cause sudden death but mortality usually low

Co-infection can increase mortality

Subclinical Infection: Lower weaning weights






## Diagnosis

1. Toxin detection

   ↑ SP ↓SE

2. Lesion detection

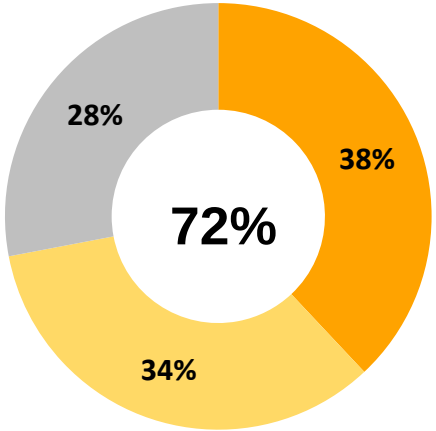
   ↑ SP ↑ SE

3. Bacteria detection

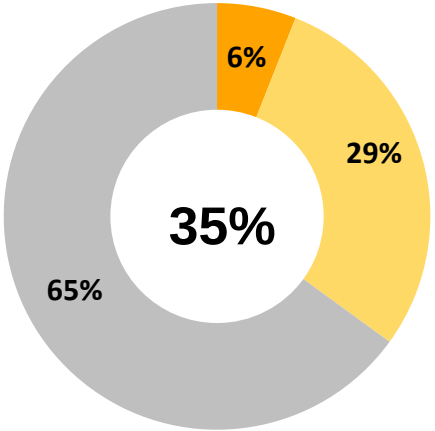
   ≈ SP ↑ SE

## PREVALENCE

*C.difficile – A toxin*




*C.difficile – B toxin*



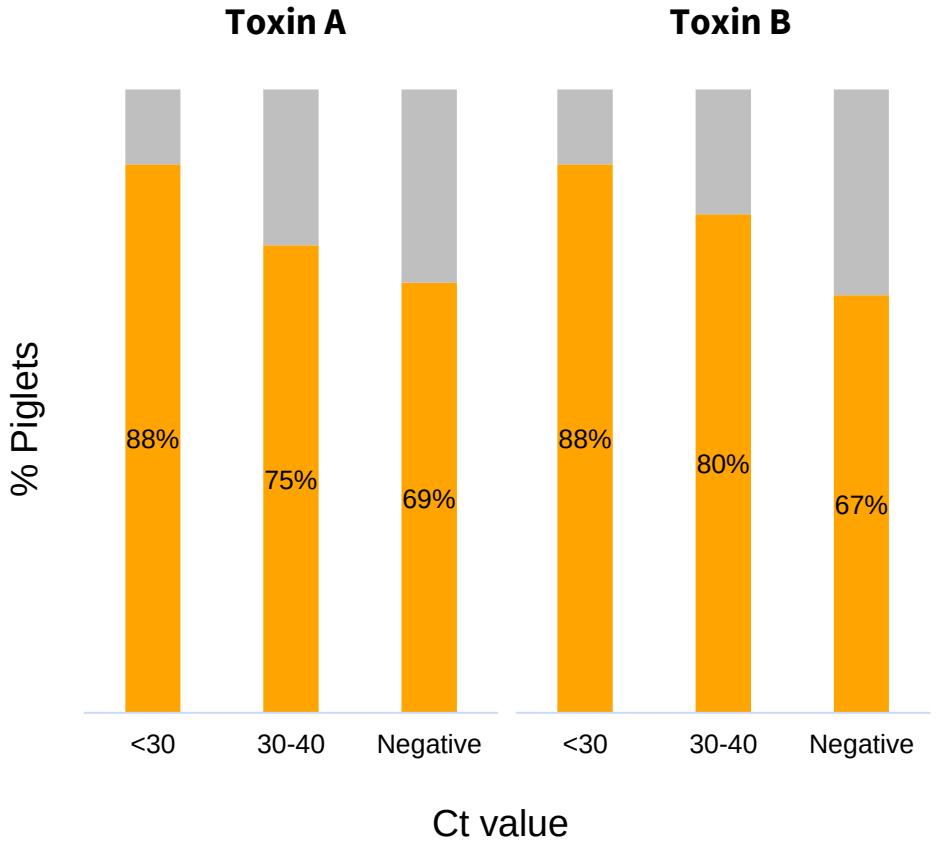

HIGH / MEDIUM / NEGATIVE

¿WHICH IS THE ROLE OF THE BACTERIA LOAD?

↑ *C.difficile*

↓ Valor Ct

↑ Diarrhoea



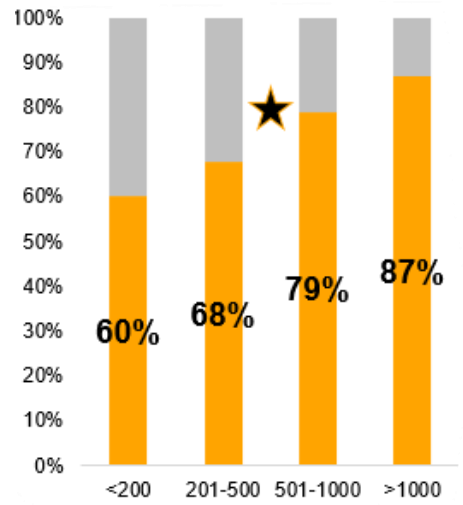

**DIARRHOEA**
**HEALTHY**

# 4. ASSOCIATED RISK FACTORS

POSITIVE PCR NEGATIVE PCR

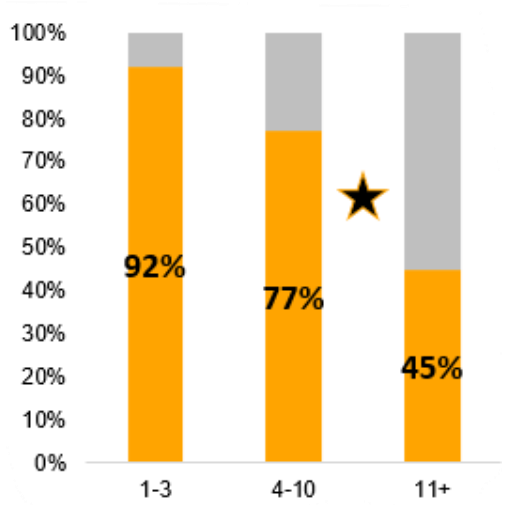
## FARM SIZE

> 500 sows



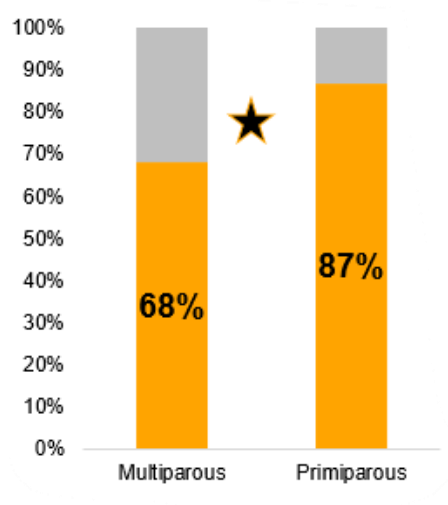

## AGE

< 10 days




## PARITY

Gilts > Multiparous



Farm size

Ct

Age

+

Parity

How is the diagnosis approached?

# Practical Case – Spain 2021

1

**Anamnesis**

Diarrhea 5 days old

Penicillin (12% litters)

Poor body condition

Yellowish diarrhea

2

**Lesions**

3

**PCR**

**High quantity**
**+++**
**Medium quantity**
**++**
**Low quantity**
**+**

HIPRA DIAGNOS

| | *C. difficile A toxin* PCR-REAL TIME | *C. difficile B toxin* PCR-REAL TIME |
|---|---|---|
| 10 Dias A5148 | NEG | NEG |
| 3 Dias N7056 | POS +++ (Ct 26) | POS ++ (Ct 34,8) |
| 4 Dias 7803 | POS +++ (Ct 28,6) | POS + (Ct 37,6) |
| 3 Dias 9498 | POS +++ (Ct 25,1) | POS ++ (Ct 33,4) |

# Practical Case – Spain 2021

1 **Anamnesis**

Diarrhea 5 days old

Penicillin (12% litters)

Poor body condition

Yellowish diarrhea

2 **Lesions**

3 **PCR**

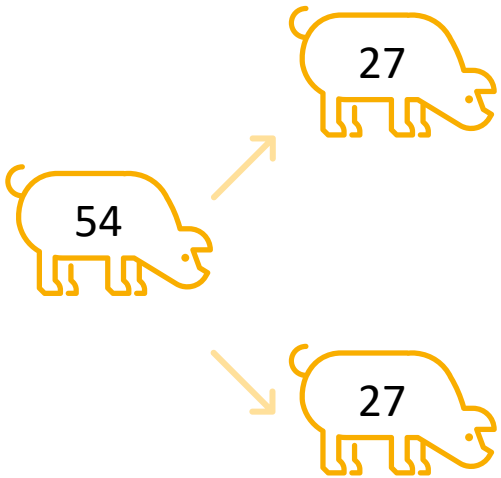
**High quantity**
**+++**

4 **HP**

# Practical Case – Spain 2021

| | Piglet 1 | Piglet 2 |
|---|---|---|
| **Small intestine** | ✓ | ✓ |
| **Colon** | Edema mesocolon | Edema mesocolon |
| **Limphonodes** | ✓ | ✓ |

# Practical Case – Spain 2021




SUISENG Coli/C + SUISENG Diff/A

SUISENG Coli/C

Vaccination Plan:

6 & 3 weeks BF

# Practical Case – Spain 2021

## 1 CLINICAL SIGNS

### PIGLETS WITH ND

34%*

### LITTERS WITH ND

24%*

* Diferencias estadísticamente significativas ($p<0.05$)

# Practical Case – Spain 2021

## 2 WEANING WEIGHT

| | | Result | |
|---|---|---|---|
| **ADG (g/d)** | | 186 g/d<br>156,8 g/d | ↑ 29 g/d* |
| **Kg at weaning** | SUISEN Cell C + SUISEN Delta<br>vs<br>SUISEN Cell C | 6,1 Kg<br>5,3 Kg | ↑ 800 g* |
| **% piglets < 5kg** | | 21%<br>44% | ↓ 50 %* |

* Diferencias estadísticamente significativas ($p<0.05$)

# Practical Case – Spain 2021

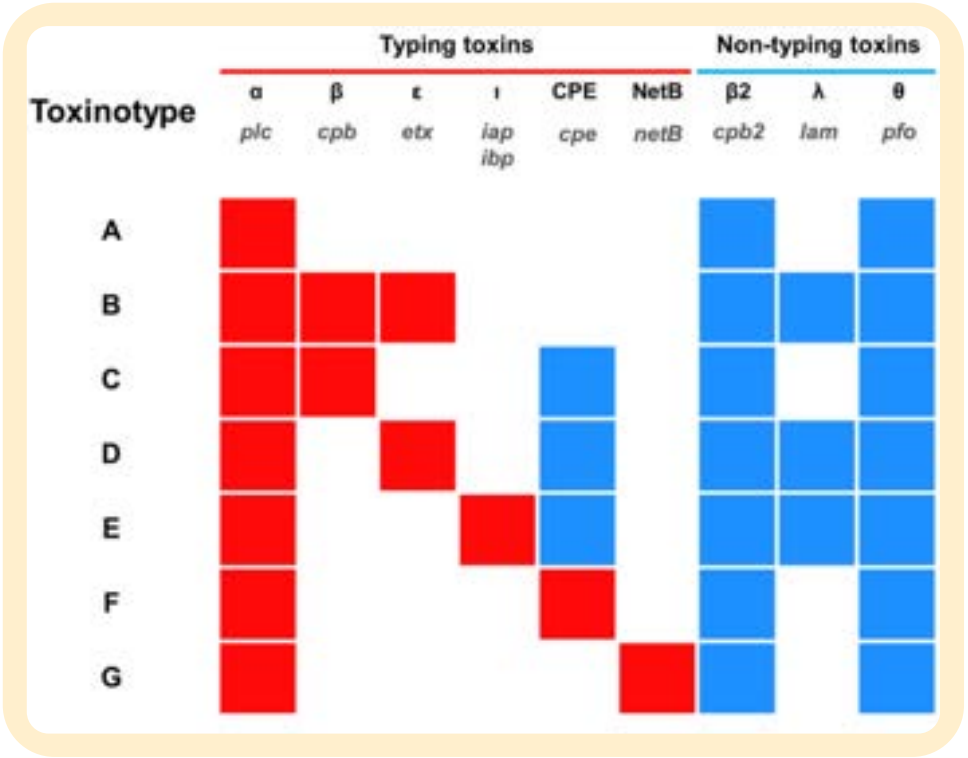
3 ANTIMICROBIAL INJECTIONS

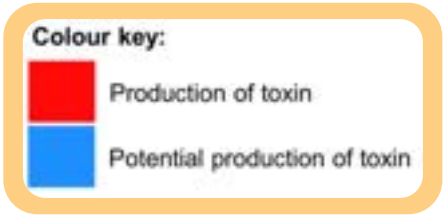
| % Piglets treated with antibiotics | |
|---|---|
| Control | 43,3 % |
| SUISEN® Diff/A | 22,5 % |

**50%**

*Clostridioides difficile*

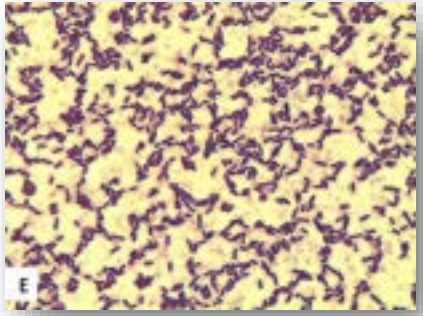
# *Clostridium perfringens type A*




*Raymond et al 2018*

- Anaerobic bacilli, Gram positive
- Spore formers.
- Commensal in more than 90% of piglets



**Source:** Dr. Rodrigo Otavio

- Short generation time: multiply to $10^8$ to $10^9$ cells/g in a few hours

- Alpha-toxin

## Pathogenesis and epidemiology

- Endemic → piglet microbiota flora
  - Found within healthy and sick pigs and environment

- Faecal-oral transmission
  - Sow to piglet
  - Piglet to piglet
  - Environment to piglet

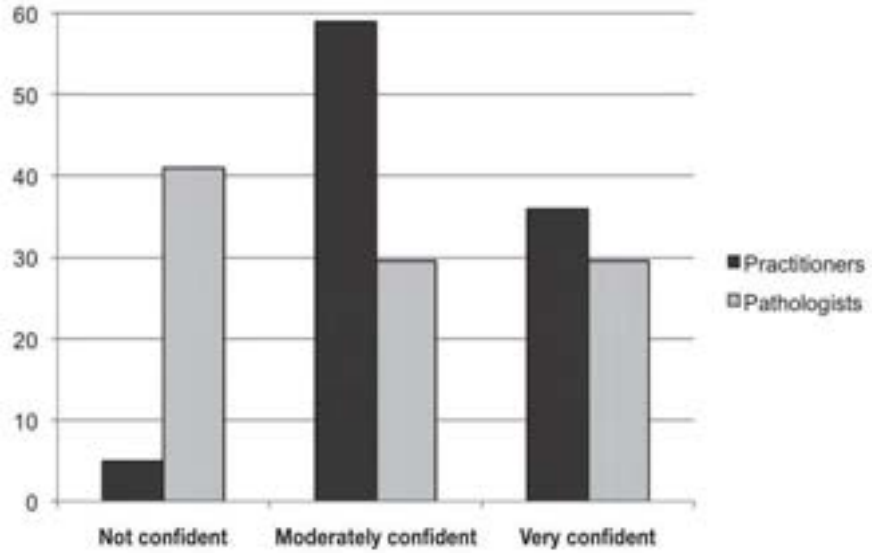
- Disease cannot be experimentally reproduced

Pathogenesis and epidemiology

**How do swine practitioners and veterinary pathologists arrive at a diagnosis of *Clostridium perfringens* type A enteritis in neonatal piglets?**

Gloria Chan, Abdolvahab Farzan, John F. Prescott, Robert Friendship

2013




Vets:

90% moderate/ Very confident

Pathologists:

70% moderate or low confident

# Clinical signs

- Affect piglets in the first week-of-life
- Non-specific diarrhea: Watery to pasty yellow diarrhea
- Morbidity: 5-50%
- Mortality: 0-10%
- Co-infections, management, environment, genetics

# Clinical signs

Research Square

**Co-infection of porcine epidemic diarrhea virus and Clostridium perfringens type A enhances disease severity in weaned pigs**

Contents lists available at SciVerse ScienceDirect

The Veterinary Journal

journal homepage: www.elsevier.com/locate/tvjl

A novel watery diarrhoea caused by the co-infection of neonatal piglets with *Clostridium perfringens* type A and *Escherichia coli* (K88, 987P)

Xiaocen Wang [a,1], Wenzhi Ren [b,1], Ying Nie [a], Liqing Cheng [a], Wei Tan [a], Chong Wang [a], Libin Wei [a], Rui Zhang [a], Guangmou Yan [a,*]

Article

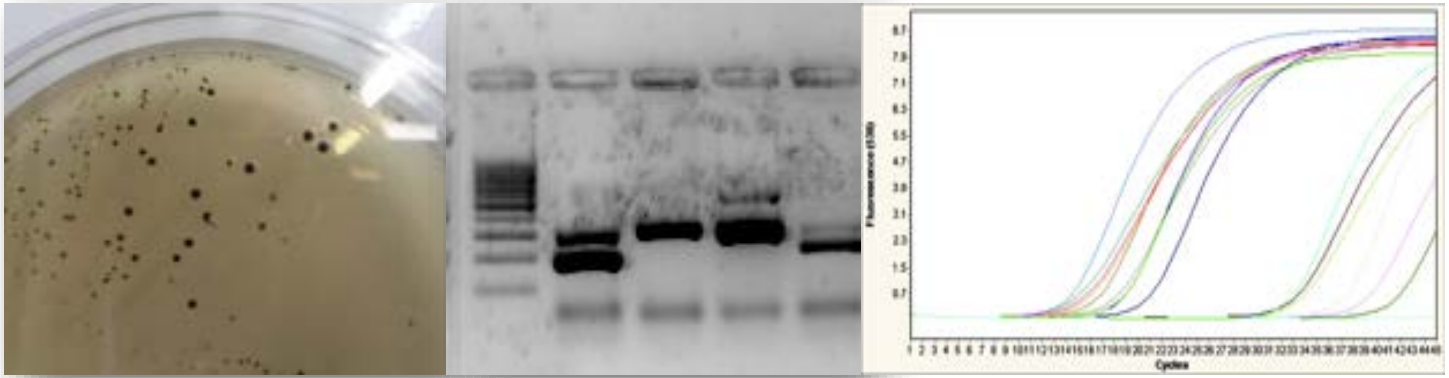
**Microbiological Findings and Associated Histopathological Lesions in Neonatal Diarrhoea Cases between 2020 and 2022 in a French Veterinary Pig Practice**

Gwenaël Boulbria [1,2,*], Charlotte Teixeira Costa [3], Nadia Amenna-Bernard [3], Sophie Laboé [3], Valérie Normand [1,2], Théo Nicolazo [1], Florian Chocteau [4], Céline Chevance [1,2], Justine Jeusselin [1,2], Mathieu Brissonnier [2] and Arnaud Lebret [1,2]

| Simultaneous Detection of Pathogens | Piglets (n = 106) | |
|---|---|---|
| | Number | % |
| Rotavirus type A (RVA) + *Clostridium perfringens* (*C. perfringens*) type A | 19 | 17.9 |
| *C. perfringens* type A + *Enterococcus hirae* (*E. hirae*) | 9 | 8.5 |
| RVA + *C. perfringens* type A + *E. hirae* | 7 | 6.6 |
| Rotavirus type C (RVC) + *C. perfringens* type A | 5 | 4.7 |
| RVA + *E. hirae* | 4 | 3.8 |
| *C. perfringens* type A + *Escherichia coli* (*E. coli*) | 3 | 2.8 |
| RVA + RVC | 2 | 1.9 |
| RVC + *C. perfringens* type A + *E. hirae* | 2 | 1.9 |
| *C. perfringens* type A + *E. hirae* + *E. coli* | 1 | 0.9 |
| RVA + RVC + *C. perfringens* type A | 1 | 0.9 |
| RVC + *E. hirae* | 1 | 0.9 |

## Diagnosis

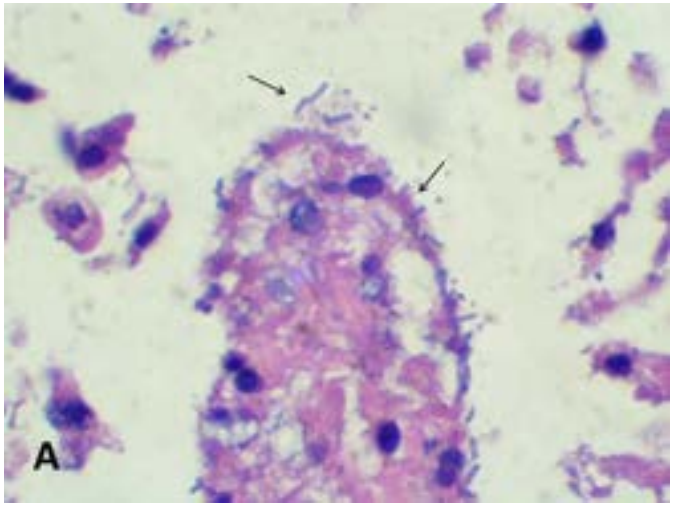
- Absence of other entero pathogens
- Detection of C. perfringens type A: isolation, qPCR



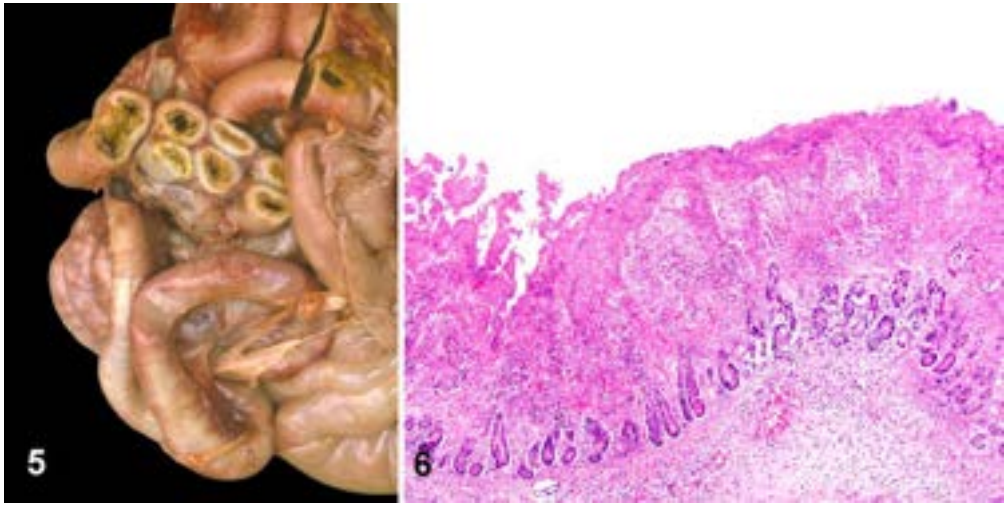
Source: Dr. Rodrigo Otavio

## Diagnosis

- Histopathologic
  - Abundant large, gram-positive bacilli in upper small intestine
  - Mild micro-ulcerations of villus tips



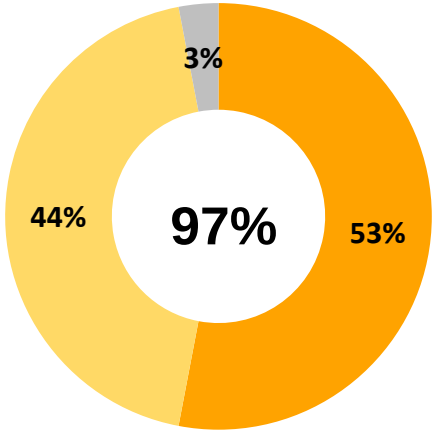

Source: Dr. Rodrigo Otavio




Source: Francisco Uzal

## PREVALENCE

*C.difficile – A toxin*



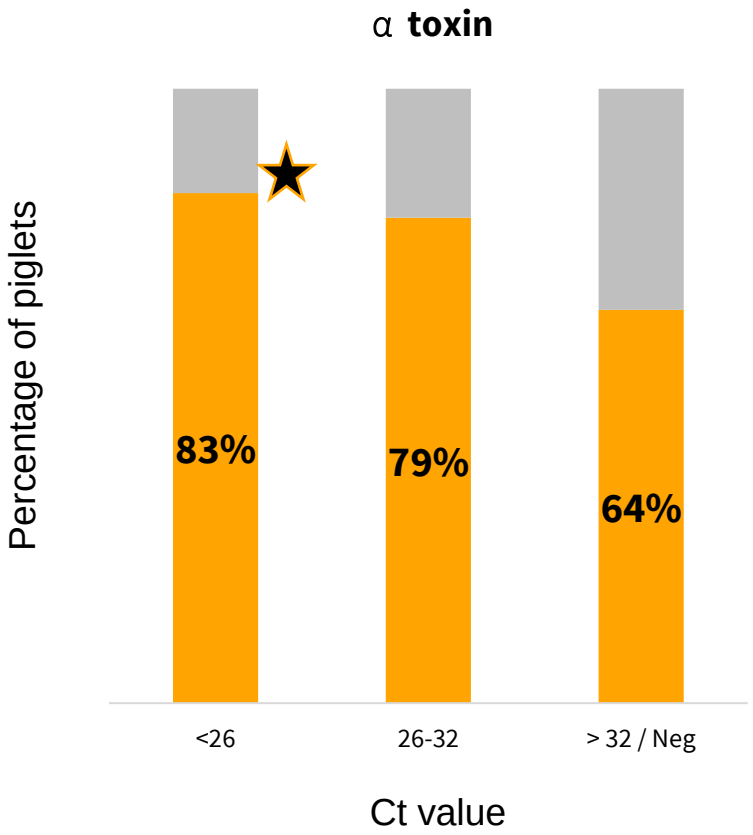

HIGH / MEDIUM / NEGATIVE

# WHAT IS THE ROLE OF THE BACTERIAL LOAD?

↑ *C.perfringens* type A

↓ ↓ ↓ Ct value

↑ diarrhea




**DIARRHEA**
**HEALTHY**