

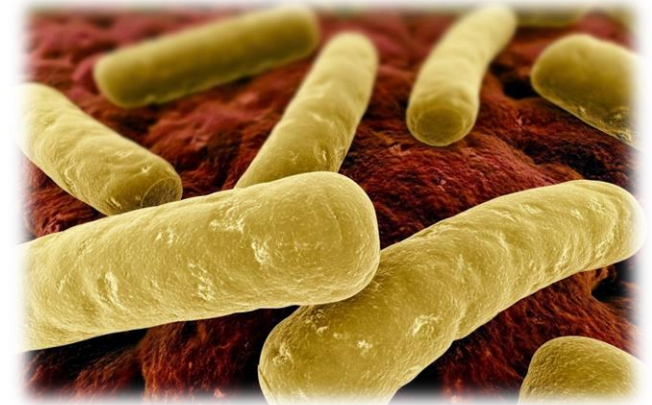
Clostridia

Historical Overview

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In 1930,

Bennetts isolated *Bacillus welchii* (later renamed *Clostridium welchii* and then *C. perfringens*) from intestinal lesions in a Black Orpington pullet, and attributed the bird's death to this organism.



Cont. ...

In the 1940's,

Mann described "six-day disease," in which he observed *C. perfringens* invading the intestinal walls of chicks.

Later,

McGaughey reproduced this condition in day-old chicks by feeding them cultures of *C. perfringens*.

Cont. ...

In 1961,

- › Parish described an intestinal disorder in a flock of 6-7 week-old cockerels;
 - › He named the disease NE
 - › He isolated *C. perfringens* from the intestinal tract of affected birds.
 - › Extracts from intestinal contents of diseased birds were lethal to chickens and mice.
 - › However, toxicity was neutralized by type B and type C antitoxin, and these isolates are now believed to have been type C.

Cont. ...

- › Parish also successfully reproduced the disease by per os administration of *C. perfringens*, with opium to slow peristalsis.
- › Since Parish's description of NE in England, the disease has been reported worldwide.

NE First Diagnosis

Western Australia in 1961,

- › NE was first diagnosed.
- › Within three years, it had been reported by 10 producers.



Cont. ...

Canada 1968 : 1971

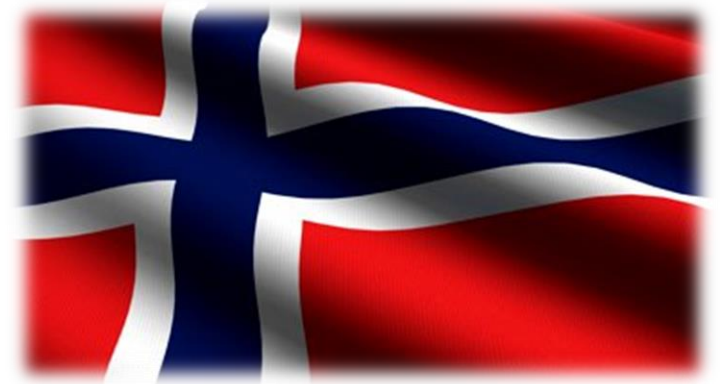
- › More than 1000 cases of NE were reported by veterinary diagnostic laboratories.



Cont. ...

Norway 1969 : 1989

- › Kaldhusdal and Skjerve revealed that the incidence of NE varied from 0% to 34% in chicken populations.



Thinking About Treatment and Prevention

- › As the number of outbreaks of the disease increased around the world, researchers began to investigate methods for treatment and prevention.
- › One method for prevention was addition of antibiotic growth promoters (AGPs) to poultry feed.



Antibiotics for Preventing NE

In 1948,

- › It was found that inclusion of dried fungal mycelia in poultry feed had increased growth rates and decreased mortality.
- › The growth promoting component was later found to be an antibiotic.

Cont. ...

1951,

- › The U.S. Food and Drug Administration (FDA) had approved use of antibiotics in animal feeds.
- › Such use has grown dramatically worldwide.
- › It is estimated that 50% of all antibiotics used in the Europe are given to animals.

Antibiotics Effect

- › AGPs are hypothesized to contribute to animal health by:
 1. Suppressing microbial growth which may induce subclinical disease.
 2. Reducing microbial destruction of essential nutrients.
 3. Increasing synthesis of vitamins or growth factors.



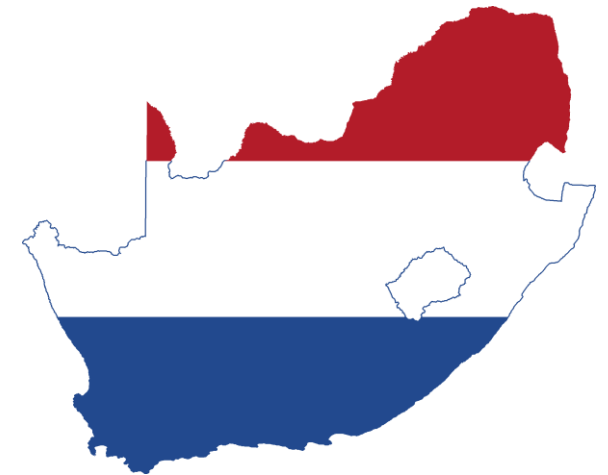
Cont. ...

- › Research has now shown that AGPs mainly work by inhibiting or killing intestinal microbial flora, particularly Gram-positive bacteria, thus making nutrients more available to the animal by eliminating competition.

Cont. ...

Netherlands in 1990,

- › An estimated 80,000 kg of antibiotics were used in humans, as compared to 300,000 kg in animals.
- › The broiler industry accounted for 26% of those veterinary antibiotics, translating to **430 mg per kg of meat per year.**



Cont. ...

Early 1970s, Netherlands

- › It was common practice for Danish poultry producers to include AGPs in poultry feed.

In the US,

- › 32 antimicrobial compounds are approved for use in broiler feeds without veterinary prescription.

Antibiotics Side Effect

These dramatic increases in use of AGPs have resulted in rising concerns about the overall effect of these products on human health.



Cont. ...

The largest concerns were:

1. The development of antimicrobial resistance by bacterial pathogens of animals.
2. The possible effects on consumers of drug residues in foods.
3. Animal pathogens will transfer antimicrobial resistance to human pathogens, and that humans will acquire these resistant pathogens by consumption of animal derived food products or exposure to the animals.

Cross Resistance

- › Some AGPs are able to instill cross-resistance to antimicrobials of classes used in human therapy.

- › Cross-resistance is instilled between:
 1. Avoparcin and vancomycin
 2. Virginiamycin and quinopristin/dalfopristin
 3. Tylosin/spiramycin and erythromycin
 4. Avilamycin and evernimicins

VRE

- › Among the most important cross-resistant bacteria are vancomycin-resistant enterococci (VRE), which have become a major concern as a nosocomial infection in Europe and US.
- › Use of avoparcin as an AGP may have created a reservoir of VRE in animal products, leading to emergence and spread of VRE in humans in Europe.
- › Pulsed-field profiles of human VRE isolates were identical or closely related to those of poultry isolates.
- › VRE were found in poultry only where avoparcin had been used to prevent NE.

Pristinamycin

- › Enterococci resistant to pristinamycin, a new antimicrobial for treatment of VRE infections, have been isolated from humans and domestic animals.
- › Pristinamycin belongs to the same antimicrobial class as virginiamycin, another major AGP, also inferring the role of AGPs in generating antimicrobial resistant human pathogens.

Lincomycin

- › **Clindamycin** is not approved for use in animal feeds in Japan, and high level resistance of poultry enterococci to this antimicrobial may be due to cross-resistance to **lincomycin**, which has long been used by Japanese poultry producers.

Antibiotic Ban

BANNED!!

- › In consequence to these concerns, many countries in Europe have banned the use of AGPs.
- › Beginning in the 1970s, countries of what is now the European Union began eliminating the use of AGPs.

Positives of AGP Ban

1. The prevalence of VRE in animals has decreased dramatically, although these findings have not been uniform.
2. The rate of VRE isolation rate from poultry in The Netherlands decreased by nearly 50%.

Cont. ...

3. Prevalence of isolates of *E. faecium* resistant to avoparcin, avilamycin, vancomycin, virginiamycin, and erythromycin in Denmark decreased significantly.
4. The Netherlands, Germany, and Italy reported decreased prevalence of VRE from poultry and humans since the avoparcin ban.

Negatives of AGP Ban

1. Increased number of outbreaks of NE and other clostridial diseases, especially in western Europe.
2. In France, incidence of NE rose from 4% in 1995 to 12.4% in 1999.

Cont. ...

3. In Norway, Sweden, Denmark, and elsewhere, an immediate increase in the number of NE cases was followed by a decline to pre-ban levels with the introduction of the coccidiostats narasin and salinomycin.

Finally

- › Most countries outside Europe still control NE with combinations of AGPs and ionophores, but in Europe, particularly the Nordic countries, NE is controlled by use of ionophores, good hygienic practices, and modified diets.

SOLVEDA®

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scientific Office:

12 Abbas El Akad St., 9th district, El Obour City, Egypt

Tel. and fax: +2 02 43126096

Cellular: +2 0120 51 00 700

E-mail: info@solveda.net

Factory

192 small industrial area, El Obour City B/C, Egypt

Tel.: (+2) 02 4487 40 50

(+2) 02 4487 44 80

Website: www.solveda.net