Argentina-United Kingdom

BILATERAL WORKSHOP ON ANTIMICROBIAL RESISTANCE IN THE ENVIRONMENT

PRODUCTIVE PROCESSES AND THEIR RELATION WITH THE ENVIRONMENT

Red de Seguridad Alimentaria CONICET
Biotechnology and Biological Sciences Research Council (BBSRC)
Natural Environment Research Council (NERC)
Department of Health and Social Care (DHSC) United Kingdom

Museo Argentino de Ciencias Naturales
BUENOS AIRES, September 10-13, 2018
Surface 2800 km$^2$
3700 km long
1400 km wide

- Buenos Aires
  - Ciudad Autónoma de Buenos Aires
  - Gran Buenos Aires
- Pampeana:
  - Resto de Buenos Aires, Córdoba, Entre Ríos, La Pampa, Santa Fé.
- Cuyo:
  - Mendoza, San Juan, San Luis
- Noreste Argentino - NEA
  - Corrientes, Chaco, Formosa, Misiones
- Noroeste Argentino - NOA
  - Catamarca, Jujuy, La Rioja, Salta, Santiago del Estero, Tucumán
- Patagonia:
  - Chubut, Neuquén, Río Negro, Santa Cruz, Tierra del Fuego

Fuente: INDEC
- Current cattle stock reaches 53533787 heads
- Production of 2.5 M meat tons (7600 M U$S)
- Milk production estimated in 500 M liters
- Broilers stock estimated in 43 M
- Sheep stock 15 M
- Pigs stock 5.2 M
ANTIMICROBIALS USE

Mainly USED in intensive exploitations

Feed lots, poultry farms and pig farms

Antimicrobials are used as growth promoters, prophylactics, metaphylactics and therapeutics

People are understanding the problem of using growth promoters

However, there is still a lot of work to do
Antimicrobial use in Feed lot

Metaphylactic at entry

Therapeutic when symptoms are detected

In general injectable

Sometimes oral in feed

Some used antimicrobials are Enrofloxacin, danofloxacin, Ceftiofur, Florfenicol, Oxytetracycline and Tilmicosin. Sometimes an antimicrobial is used in combination with an antiinflammatory agent like ketoprofen or diclofenac
Antimicrobial use in Broilers

In water or feed

Therapeutic when symptoms are detected generally in water

Oral in feed metaphylactic or growth promoter

Some used antimicrobials are Amoxi, Apra, Bacitra, ceftio, tetracyclines, colistin, enro, macrolides, florfenn, fosfo, aminoglycosides, linco, monensin, salino, sulfa/trimeto, virginiamicin. Sometimes used in combination with ketoprofen or diclofenac. Bromhexine used too.
Antimicrobial use in Pigs

Therapeutic when symptoms are detected

In general injectable

Sometimes oral in feed

Normally used antimicrobials are apramicin, enrofloxacin, danofloxacin, Ceftiofur, Florfenicol, Oxytetracycline, Macrolides, aminoglycosides, Furazolidone, sulfas/trimeto, bacitracin, virginiamycin, carbadox.
TREATMENT OF SLUDGES

Feedlot: Sludge is stored and composted. After 6 months and two years, is used for fertilization

Milk farms: Mud from corrals the same than in feed lot. Milking barn manure is kept suspended and then used for fertilization.

Pigs, manure is stored in pits. Then, anaerobic lagoons. Surface water could be reused. Muds used as fertilizers.

Poultry, the beds are changed every 4-5 production cycles. The removed material is composted and used as fertilizer.
Bacteria have an advantage of 3500 million years of experience on the planet above humans.

Bacteria responded successfully to every challenge nature has put in their pathway.

Are they who cross our path...?
Bacteria are everywhere.!!!

Number of bacteria in earth:

500,000,000,000,000,000,000,000,000

Five million trillion trillon

Every person in this room will add 37 million bacteria to the air every hour.
We are bacteria

1,5 kg of our body are bacteria

WHAT IS THE MICROBIOME? BACTERIOME?

100 trillion bacteria

Develop a critical role in health
Bacteria can reproduce very fast

That is a great advantage

In favorable conditions a bacterium can divide every 20 min

In 10 h, a bacterium can generate 1 billion bacteria

Bacteria can exchange genetic material

And that is another great advantage
Lastly viruses started to be considered in health

Further than pathogenic viruses,

The majority of viruses are antibacterial

Bacteriophages play a critical defensive role

Phages concentrate in mucus
Penicillin: Fleming, 1928
Sulfonamides: Germany, 1935
Penicillin was developed Florey
During second world war

ANTIMICROBIAL REVOLUTION STARTS

ANTIMICROBIAL RESISTANCE WAS DESCRIBED BY
FLEMING IN THE FIFTIES
ANTIBACTERIANOS

Penicillin, sulfamides, chlortetracyclin 1930
Estreptomycin, chloranfenicol
Erytromycin, Vancomycin, Rifamycins 1940
Meticilin, Gentamicin, Ampicillin, Cefalotin, Quinolones 1950
Carbenicillin, new Cefalosporins, Trimetoprim 1960
Cefotaxime, Clavulanic, imipenem-Cilastatin, Rifaximine 1970
Monobactams, new Quinolones, new macrolides 1980
Estreptogramins, Oxazolidinones, Pleuromutilins, Lipopéptides, Glicilciclones, Teixobactine 1990
Penicillin resistance
Gentamicin resistance
Ampicillin resistance
Teixobactine
How antimicrobials are used?

In human medicine antimicrobials are used therapeutically or prophylactically.

In Veterinary Medicine, antimicrobials can be used in four different ways: prophylactic, metaphylactic, therapeutic and as growth promoters.

GROWTH PROMOTERS USE IS UNDER SEVERE QUESTIONING IN THE WORLD NOWADAYS.
This was not causing concern until the sixties. The Swann Committee was formed for evaluating the use of ATBs as growth promoters. In 1986, Sweden banned growth promoters. Denmark and Finland supported and press in 1995. Denmark experimented from 1998 to 2000.

Sources: Human therapeutics: The Danish Medicines Agency. Antimicrobials for animals: Until 2000, data are based on reports from the pharmaceutical industry of total annual sales from the Federation of Danish pig producers and slaughterhouses (1994-1995) and Danish Medicines Agency and Danish Plant Directorate (1996-2000). Data from 2004-2015 are based on data extracted from VetStat.
One world, one health

Humanity has become aware of the link between human and animal diseases.

60% of human infectious diseases are animal origin. 75% emerging human diseases and 80% pathogens potentially biological weapons are animal origin too.

Regular human nutrition with milk, eggs and meat proteins is critical, and if it fails it represents a serious public health issue.
THERE ARE THREE HUMAN POPULATIONS AT RISK

Urban population
Hospital population
Rural population
- Control over the counter availability of antimicrobials
- Instruct the general population against automedication
- Consensus building with pharmaceutical companies on the number of tablets in a box
- Instruct the general population in returning unused pharmaceuticals to the drugstore
- Train physicians in the correct use of antimicrobials

Etc, etc, etc.......
- Good manufacture practices
- Effluent treatments according to law.
- Monitoring by Regulatory Agencies
- Rational use of antiseptics
- Prudent and rational use of antimicrobials
  - Diagnostic
  - Breakpoints
  - Pk/Pd
- Training in the use of clothes, sterile materials, hands washing
- Professional cleaning of surgeries
- Design of safe and efficient effluent treatment plants
- Avoid application of antimicrobials directly in the environment
- Use insecticides under good agricultural practices and integrated pest control
- Avoid use of resistance determinants in the production of transgenic materials
Industry uses antimicrobial resistance genes as "marquers" to measure efficacy of the production process.

Genes used in GMO production:
- gene blaTEM1 Penicillin resistance
- gen aph3’-2 (nptII) Kanamycin and neomycin resistance
- gen aph3’-38 Amikacin resistance
- gen aad3”9 Streptomycin and y Spectinomycin

There are transgenic seeds including AMRG approved in Argentina:
- Corn bt 176 (Novartis), gene bla (betalactamase).
- Corn Mon810 (Monsanto), gene nptII (neomycin fosfotransferase).
- Cotton Mon531 (Monsanto), gene nptII ygen aad, (aminoglicoside adenililtransferase).
- Correct antimicrobial use (prudent and rational)

- Safety of animals, operators, consumers, environment

- Good Agriculture Practices

- Good Clinical Practices
Increase knowledge in fish physiology and Pharmacology

- Necessity of immunotherapy
- Implementation of Good Practices
- Special consideration of feed
-Quality starts with agricultural primary production

-Hygiene along the chain

-Good Manufacture Practices
THE CONSUMER WHO Gold Rules

HAND WASHING

HYGIENE COOKING

CORRECT COOKING
CONTACT INGESTION

Seawage wastes

SEA RIVERS LAKES

HUMAN ANTIMICROBIALS

FOOD

CONTACT INGESTION

VETERINARY ANTIMICROBIALS
WHAT SHOULD WE HAVE IN MIND?

1. Any antimicrobial treatment selects resistance.

2. There are no frontiers between countries to stop resistance.

3. There are no frontiers between species.

4. In antimicrobial therapy, we have no other tool that good diagnosis, Breakpoints and Pk/Pd, knowledge is growing here.

5. One of the keys is the understanding of the flow of resistance determinants. **ENVIRONMENT**
THE BEST ANTIMICROBIAL TREATMENT

1. The one that is not done, because there is not infection

2. The best second it that based in diagnosis, rational use, treating humans and animals on the basis of Pk/Pd and treating animals with antimicrobials that are not first line in human medicine

WHAT DO WE DO WITH ANTIMICROBIALS THEN?

USE IT THE LEAST POSSIBLE, BUT ALL THE NECESSARY
MUCHAS GRACIAS