Prudent Use of Antimicrobials in Veterinary Medicine

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Discovery of Penicillin and Emergence of Penicillin Resistant Bacteria

1928  Discovery of the penicillin by Fleming
1940  Purification of the penicillin by Florey & Chain
1940  Emergence of penicillin resistant bacteria
1941  Confirmation of clinical effects
1945  Start of the industrial production
       Awarded a Novel Prize
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Awarded a Novel Prize

Alexander Fleming
Howard W Florey
Ernst B Chain

*Penicillum notatum*

*Staphylococcus aureus*
The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant.

In Alexander Fleming’s speech accepting the 1945 Nobel Prize in Physiology or Medicine.
Antimicrobial Resistance Threats in USA

**NATIONAL SUMMARY DATA**

Estimated minimum number of illnesses and deaths caused by antibiotic resistance*:

- At least 🌞2,049,442 illnesses,
- 🐦23,000 deaths

* bacteria and fungus included in this report

Estimated minimum number of illnesses and death due to *Clostridium difficile* (C. difficile), a unique bacterial infection that, although not significantly resistant to the drugs used to treat it, is directly related to antibiotic use and resistance:

- At least 🌞250,000 illnesses,
- 🐦14,000 deaths

**WHERE DO INFECTIONS HAPPEN?**

Antibiotic-resistant infections can happen anywhere. Data show that most happen in the general community; however, most deaths related to antibiotic resistance happen in healthcare settings, such as hospitals and nursing homes.
History of Antimicrobials use in animal

1928  Discovery of penicillin

1946  Growth promotion effect of sulfa drugs and streptomycin as food additive in chicken

1949  Practical use in USA

1953  Practical use in UK

Contribution of stable supply of safe livestock products VS Antimicrobial Resistance

- antibiotics
- synthetic antimicrobials
Relationship between quantity of antimicrobials use and prevalence of resistant *E. coli* in Japan

Effect of antimicrobials use

- **Selection** of antimicrobial resistant bacteria
  - Pathogenic bacteria acquire antimicrobial resistance
  - A big risk
  - Plasmid, transposon
  - Dissemination of antimicrobial resistant bacteria
  - Pathogenic bacteria acquire antimicrobial resistance
  - Use of antimicrobials


Emergence of resistant *Campylobacter* in fecal samples of pigs by the administration of fluoroquinolone

(A) Fluoroquinolone-resistant *Campylobacter* (logCFU/g) over time (Days)

- **Not-treated**
- **Enrofloxacin 5.0mg/kg/day-i.m.**
- **Norfloxacin 5.0mg/kg/day-p.o.**

(B) Fluoroquinolone-resistant *Campylobacter* (logCFU/g) over time (Days)

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The pigs were treated with fluoroquinolones on days 1-5 (asterisks).

Transmission of Antimicrobial Resistant Bacteria between Animal and Human

- **Human**
  - Antimicrobial drug
  - Selection pressure
- **Animal**
  - Antimicrobial drug
  - Antimicrobial growth promoter
  - Selection pressure
- **Environment**
  - Agrichemical
  - Selection pressure
- **Food**
WHO Global Action Plan on Antimicrobial resistance

At the Sixty-eight World Health Assembly in May 2015, the World Health Assembly endorsed a global action plan to tackle antimicrobial resistance.

To achieve this goal, the global action plan sets out five strategic objectives:

1. to improve awareness and understanding of antimicrobial resistance;
2. to strengthen knowledge through surveillance and research;
3. to reduce the incidence of infection;
4. to optimize the use of antimicrobial agents
5. to increase investment in new medicines, diagnostic tools, vaccines and other interventions.

One Health approach
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One Health approach
Prudent use of antimicrobials is an integral part of good veterinary practices. It is an attitude to maximise therapeutic efficacy and minimise selection of resistant micro-organisms.

Federation of Veterinarians of Europe
Emergence factor of Antimicrobial Resistant Bacteria

- **Overuse** of antimicrobials
- **Misuse** of antimicrobials

Prudent Use of Antimicrobials

By veterinarian, herder, farmer, fisherman *etc.*
Guidelines for the responsible and prudent use of antimicrobial agents in veterinary medicine

In OIE International Standards on Antimicrobial Resistance 2003

Guideline provide guidance for the responsible and prudent use of antimicrobials in veterinary medicine with the aim of protecting both animal and human health.

● Responsibilities of the regulatory authorities

the veterinary pharmaceutical industry

pharmacists

veterinarians

livestock producers

What can you do as veterinarians?

We need to collectively ensure the responsible and prudent use of antibiotics in animals to preserve their effectiveness.

1. Only prescribe and dispense antibiotics for animal under your care and only if necessary.
2. Conduct antimicrobial sensitivity testing before prescribing or administering an antibiotic.
3. Educate animal owners on the risks associated with misuse of antibiotics.
4. Promote sound animal husbandry hygiene methods, vaccination strategies, and periodically review farm records to ensure compliance with your prescriptions.
5. Keep your knowledge on antibiotics use recommendations up to date.

World Antibiotic Awareness Week 2015
Prudent Use Guidelines in the world

- USDA/FDA (2012); Guidance for Industry # 209 The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals
- European Union (2015); Guidelines for the Prudent Use of Antimicrobials in Veterinary Medicine 2015/C 299/04
- Federation of Veterinary of Europe; Antibiotics Resistance & Prudent Use of Antibiotics in Veterinary Medicine
- American Veterinary Medical Association; Judicious use of Antimicrobials
- American Veterinary Medical Association (2008); Judicious Use of Antimicrobials for Treatment of Aquatic Animals
- American Association of Feline Practitioners (2009); Basic Guidelines of Judicious Therapeutic Use of Antimicrobials
- American Association Bovine Practitioners; Prudent Antimicrobial Use Guidelines for Cattle
- Canadian Food Inspection Agency; Prudent Use of Veterinary Drugs in Livestock Feeds
- Canadian Veterinary Medicine Association; Guidelines on the Prudent Use of Antimicrobial Drugs in Animals
- Alliance for the Prudent Use of Antibiotics: Antibiotics Use in Food Animals
- Bayer; Guidelines for the Use of Quinolones in Veterinary Medicine
“Prudent Use Guidelines” were established in 2013 and distributed to promote prudent use of antimicrobials.

Leaflets explaining prudent use guideline for veterinarians and livestock farmers.

Prudent Use Guidance for Livestock Farmers

- To prevent selection, emergence and spread of AMR bacteria, prudent use is important.

- **STOP AMR**
  - Keep efficacy of antimicrobials in animal and human

- **ACTION**
  1. Keep animals health
  2. Use on the prescription
  3. 

Yamamoto, MAFF
Main Points of Prudent Use Guidelines

i) **Prevention of infection**

It is essential to prevent infection by appropriate management of feeding, sanitation and vaccines.

- The standards of Rearing Hygiene Management
- The guidelines on good hygienic practice

ii) **Definite diagnosis**

Identify the cause of infection and determine treatment measures based on veterinarian’s definite diagnosis
Main Points of Prudent Use Guidelines

iii) **Effective use of antimicrobials**

- Choose effective antimicrobial drugs with microbial sensitivity test
- Fluoroquinolones, 3rd generation cephalosporins, etc. should be used as the second choice drug, only if the first choice drug is not effective

iv) **Information sharing**

Share information about AMR bacteria among the relevant parties
JVAR : Japanese Veterinary Antimicrobial Resistance Monitoring System

- Sales of Antimicrobial
- Resistance in animal pathogens
- Resistance in Zoonotic and Indicator bacteria
- Pharmaceutical companies
- Healthy animals
- Diseased animals

Japanese Veterinary Antimicrobial Resistance Monitoring System (JVARM)
JVARM has started collaboration with JANIS (Japan Nosocomial Infectious Surveillance: AMR surveillance in the human health sector) in order to establish the integrated surveillance system recommended by WHO based on One Health Approach.

Analyze and evaluate data, provide two types of information, Open Report and Feedback Report.

JANIS (Since 2000)

JANIS DATA FORMAT

MIC data

http://www.nih-janis.jp
Integrate the JVARM data into the JANIS system

JANIS server program can calculate

- SIR judgement from MIC
- resistant rate
- multi-antimicrobial resistant rate

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Copy of JANIS Server

Annual report in same format

JVARM data

MIC data (E. coli :2003-2013)
Antimicrobial use in Japan

(MAFF and MHLW in 2002)
Sale of Antimicrobials in Companion animals

<table>
<thead>
<tr>
<th>Antimicrobials</th>
<th>Kg</th>
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<tbody>
<tr>
<td>Aminoglycoside</td>
<td>2200</td>
</tr>
<tr>
<td>Cephalosporin</td>
<td>300</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>100</td>
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<tr>
<td>Penicilene</td>
<td>900</td>
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<tr>
<td>Peptide</td>
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<tr>
<td>Lincosaminid</td>
<td>10</td>
</tr>
<tr>
<td>Sulfonamide</td>
<td>30</td>
</tr>
<tr>
<td>Fluoroquinolone</td>
<td>100</td>
</tr>
<tr>
<td>other</td>
<td>0</td>
</tr>
</tbody>
</table>

Total 7,071 kg

JVARM, 2012
Sale of Antimicrobials in animals as active compound in Japan
Change of resistance(%) in *Escherichia coli* isolates from animals
Change of resistance(%) in *Escherichia coli* isolates from animals

- **Cattle**
  - Ampicillin
  - Cefazolin
  - Cefotaxime
  - Kanamycin
  - Gentamicin
  - Dilidrostreptomycin
  - Streptomycin
  - Oxytetracycline
  - Tetracycline
  - Chloramphenicol
  - Colistin
  - Enrofloxacin
  - Nalidixic acid
  - Ciprofloxacin
  - Trimethoprim
  - Trimethoprim-sulfamethoxazole

- **Pig**
- **Broiler**
- **Layer**
Change of resistance(%) in *Escherichia coli* isolates from animals

![Graphs showing the change of resistance for different antibiotics across different animal species.](Image)
Cephalosporin resistance rate in *E. coli* isolates from healthy broilers

9.7%: Withdrawal of the off-label use of ceftiofoul at hatcheries

Conclusion

1. Antibiotic resistance has emerged as a very significant health care problem due to the overuse and misuse of antimicrobials in human and veterinary medicine and in agriculture.
2. The spread and enlightenment of the prudent use guideline for the clinical veterinarian and farmer is insufficient.
3. The antimicrobial in the field of aquaculture is not to appoint prescription legend drug.
4. Antimicrobial for human is empirically used in a companion animals, and the emergence of drug resistant bacteria and antimicrobial consumption is unclear.
5. Because monitoring in the environment is not carried out, an effect of antimicrobial agrochemicals to the environmental microorganism is unclear.
Antimicrobial Resistance: No action today, no cure tomorrow!

WHO, 2011
Thank you for your attention!