Antibiotic Residues in Meat and Meat Products, Implications on Human Health

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Question

If you were offered a plate of this delicious lechon, will you accept and serve it to your family?

What if you were told that the animal source was treated with a drug before slaughter, would you serve it to your family?
Antibiotic Residues in Meat and Meat Products, Implications on Human Health

I. Introduction
   A. Antibiotic Drugs
   B. Withdrawal Period
   C. Antibiotic Drug Residues

II. Adverse Effects of Antibiotic Drug Residues
   A. Toxicological Effects
   B. Immunological Effects
   C. Microbiological Effects

III. Why do we have Antibiotic residues?

IV. What can we do?
Antibiotics – substances used to treat and prevent bacterial infection.

Have greatly enhanced
- human life expectancy,
- reduced mortality,
- improved the quality of life
- almost won the war against many infectious diseases.
3-fold Benefits in Use of Antibiotics in Animal Production

- **Producer** – production efficiency

- **Consumer** – more affordable, high quality protein

- **Animals** – improved health (increase feed efficiencies, growth promotion)
Current Animal Management

Intensive husbandry

• Large concentration of animals in confinement
• Close animal-to-animal contact
• Less space available
• Increase risk of disease transmission
• Mass medication via feed or water
• Widespread use of antibiotics to control disease & promote growth
In Animal production...

1. **Therapy** of immediate “serious” disease

2. **Prevention** of disease to which the animals are likely to be at risk in the future
   - *E.g.*, antibacterials, antifungals, antiparasitic prepn

3. **Performance improvement** or growth promotion
   - *E.g.*, subtherapeutic doses of antimicrobials

4. “**Anti-stress**” medication
   - *E.g.*, antibiotics, vitamins, minerals, amino acids, tranquilizers
Antimicrobials given as Feed Additives in Poultry

- Bacitracin
- Chlortetracycline
- Erythromycin
- Tylosin
- Neomycin
- Lincomycin
- Oxytetracycline
- Penicillin
- Streptomycin
- Virginiamycin
- Fluoroquinolones
- Sulfonamides

Concentration in Feed:
1 - 200 g per ton
Feb. 25, 1989, Philippine Daily Inquirer:

DOH Secretary Alfredo Bengzon remarked that “veterinarians are abusing antibiotics by making these medicine a regular part of poultry & livestock feeds.”

– Rash pronouncement had big impact/damage to veterinary profession
Drug Residues

**Antibiotic Drug Residues** – small amounts that remain in animal products and make their way into the food chain.

**Withdrawal Periods** – time between the disappearance of drug’s effects and the point at which the drug concentrations in tissues and body fluids reached a certain “safe” level

**Varies:**
- Drug used; pharmakokinetics
- Route of administration
- Animal species
Antibiotic Drug Residues: HAZARD to Food Safety
Toxicological Effects:

Dose Related:

– Acute: high doses = produce immediate toxicity

  e.g., Streptomycin in pregnant women
  • Damaged cranial nerve and cause congenital deafness

  e.g., Sulfonamides, Neomycin
  – Damaged to kidney
  – Damage to hearing
Toxicological Effects:

**Chronic:** small doses repeatedly ingested = can build up to toxic level

e.g., Tetracylines
- Discolored teeth, allergic reactions, peripheral blood changes
**Immunological Effects:**

- Allergenic residues (haptens) bind with protein forming antigens

- Symptoms: skin rashes, anaphylactic reaction

*E.g.,*

- Sulfonamides: skin rashes; asthma attacks
- Chloramphenicol: aplastic anemia
Immunological Effects:

- Penicillin: 3-10% of population hypersensitive; 10 IU (0.6g) can cause allergic reaction

- 1984: People with anaphylactic reaction after eating steak

- 1972: 2 people with anaphylactic reaction after eating pork with 0.02-0.04 ppm penicillin

- 3/15 developed hypersensitive reaction after drinking milk with 2.5 ug penicillin
**Antibiotic Resistance**

**Microbiological Effects:**

- **1930’s**
  - Bacterial infections
    - pneumonia
    - meningitis
    - bacteremia
    - typhoid fever
    - endocarditis
    - mastoiditis
    - syphilis
    - tuberculosis
    - rheumatic fever

  

- **Use of antibiotics**

- **1980s**
  - Non-infectious conditions
    - cancer
    - heart disease
    - diabetes
    - hypertension

- **2000s**
Microbiological Effects:

- Eliminate susceptible bacteria leaving resistant ones,

- Alteration in gut microflora

- Interfere with food processing, e.g., fermented sausages, cheese production
Microbiological Effects:

- Development of multi-resistant microorganisms
- Observed association between use of antibiotics in production with development of antibiotic resistance in local *Campylobacter jejuni*. 

Detection of antibiotic residues

Multi-resistant *C. jejuni* isolates
Chickens: liver & ceca

Commercial producers’ dressing plant

Backyard raisers’ dressing plant

ceca

liver
Liver samples for Detection for antibiotic residues
CECA: Isolation of *Campylobacter* sp.

Antibiotic Sensitivity Testing

ENRICHMENT & DIRECT methods, Confirmed as *C. jejuni* by PCR
% Positive for Antibiotic Residues

- **64.2%** (104/162) positives
- backyard raisers (39%) > commercial producers (25%) (p<.05) (P-value: **0.0001608**)

- Common use of antibiotics in poultry production
Residue vs Type of Antibiotic

- **Residue**
  - least frequent type detected
  - MACROLIDES

- **Resistance**
  - Low resistance to Erythromycin
    - (a macrolide)
Antimicrobial profile of *C. jejuni* isolates: multi-resistance

**91.7%** (11/12) to cephalothin, ciprofloxacin, colistin, gentamicin, nalidixic acid, sulphamethazine, streptomycin, tetracycline

**100%** (12/12) to trimethoprim
Antimicrobial resistance profile:

83% (10/12) to ampicillin related to penicillin as most common residue detected.

75% (9/12) resistant to chloramphenicol when it is supposed to be banned in food animals?

75% (9/12) resistant to norfloxacin related to use of fluoroquinolones in poultry.

33% (4/12) resistant to erythromycin related to macrolides as least detected antibiotic residue.
**Significant** (p <0.05) P-values

**X^2 VALUES FOR TYPE OF ANTIBIOTIC RESIDUE DETECTED**

<table>
<thead>
<tr>
<th>ANTIBIOTIC TESTED</th>
<th>Penicillin</th>
<th>Tetracyclines</th>
<th>Sulfas</th>
<th>Aminoglycosides</th>
<th>Macrolides</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin</td>
<td>83.3</td>
<td>.166</td>
<td>.584</td>
<td>.640</td>
<td></td>
</tr>
<tr>
<td><strong>Cephalothin</strong></td>
<td>91.7</td>
<td><strong>.020</strong> *</td>
<td>.140</td>
<td>.753</td>
<td></td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>75.0</td>
<td>.371</td>
<td>.157</td>
<td>.546</td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>91.7</td>
<td>.640</td>
<td>.460</td>
<td>.753</td>
<td></td>
</tr>
<tr>
<td>Colistin sulphate</td>
<td>91.7</td>
<td>.640</td>
<td>.460</td>
<td>.753</td>
<td></td>
</tr>
<tr>
<td><strong>Erythromycin</strong></td>
<td>33.3</td>
<td><strong>.028</strong> *</td>
<td><strong>.001</strong> *</td>
<td>.083</td>
<td><strong>.030</strong> *</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>.273</td>
<td>.83</td>
<td>1.00</td>
<td>.753</td>
<td></td>
</tr>
<tr>
<td>Nalidixic</td>
<td>.640</td>
<td>.460</td>
<td>.140</td>
<td>.753</td>
<td></td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>.371</td>
<td>1.00</td>
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<tr>
<td>Spectinomycin</td>
<td>.273</td>
<td>.083</td>
<td>.386</td>
<td>.940</td>
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<tr>
<td>Suphamethazine</td>
<td>.640</td>
<td>.460</td>
<td>.460</td>
<td>.753</td>
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<tr>
<td>Streptomycin</td>
<td>.640</td>
<td>.140</td>
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<td>.753</td>
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</tr>
<tr>
<td>Tetracycline</td>
<td>.640</td>
<td>.460</td>
<td>.460</td>
<td>.753</td>
<td></td>
</tr>
<tr>
<td>Trimethoprim**</td>
<td>.640</td>
<td>.460</td>
<td>.460</td>
<td>.753</td>
<td></td>
</tr>
</tbody>
</table>

* **CO- or CROSS-RESISTANCE** bet. **DIFFERENT** classes of antimicrobials

- Penicillin residue & cephalothin
- Tetracycline residue & erythromycin
- Aminoglycoside residue & erythromycin
What is the significance of the statistically observed CO- or CROSS-RESISTANCE?


- Antibiotics for humans should NOT be used on food animals,
  - e.g., Chloramphenicol banned in food animals

- Structurally SIMILAR drugs subject to resistance within SAME class of related antibiotics.

SIGNIFICANCE:
Observed CO- or CROSS-resistance shows that resistance to one antibiotic can confer resistance to other structurally DIFFERENT classes of antibiotics
Antibiotic supplementation in Animal production

Use of Antimicrobial agents in pro’d

Dev’t of antimicrobial resistance

Animal products: meat, milk, eggs

- Antibiotic Residues
- Reservoir of resistant bacteria for human pop’n

resistant strains restrict treatment options more expensive treatment treatment failure

e.g., MDR-TB
Antimicrobial Multi-resistance means...

- People can’t be effectively treated
- People are ill longer & have a higher risk of dying
- Prolonged epidemics
- Greater risk of infection
- 60% increase in mortality due to infectious agents, > 1/2 are resistant
- Increased cost of Tx = U$ 100 M - 10 B hospital cost of managing illnesses by resistant organisms
- Loss of confidence on health industry, pharmaceuticals
True story

- **APRAMYCIN** used only in animals due to unusual structure

  Enterobacteria of animal-origin became resistant to apramycin

- WHY? due to synthesis of PLASMID-mediated 3-N aminoglycoside acetyltransferase type IV which confers resistance to gentamicin (Chalus-Dancia et al., 1986)

- Plasmid spread among animal strains

- Plasmid later found in clinical isolates resistant to gentamicin from hospitalized human patients (Chalus-Dancia et al., 1991)

**SIG:** Spread of resistance involve transfer of antibiotic resistance genes from MO of animals to man
Why do we have Residues?
Why do we have residues?

1. When animal raisers give medication without availing themselves of veterinary services
2. Improper dosing
3. Non-observance of withdrawal period

= implied by detection of more animals from backyard raisers to be positive for antimicrobial residues vs commercial raisers
Why do we have residues?

4. Emergency slaughter of treated animals, sale from one farmer to another, then to the slaughterhouse without strict requirement of certification of treatment

5. Intensification of aquaculture, livestock production increasing susceptibility and risk of disease outbreaks

Problems

7. Lack of satisfactory data concerning the efficacy & safety of drugs

8. Lack of funding/interest to gather needed data. Evaluation is a long & tedious process.

9. Little interest in developing and applying for licensing of livestock & poultry drugs
Conclusion

What can we do?
What can we do?

1. Promote awareness of producers on importance of reading and observing label instructions on withdrawal requirement of drugs.

2. Promote appreciation of producers/raisers on adverse effects of improper use of antibiotics.
3. Heightened surveillance (through regular mandatory testing) by regulatory agencies for presence of residues.

Consumers cannot protect themselves. Residues often tolerate very high cooking temperature.

Thus, cooking is not an effective control measure to remove residues in animal products.
Healthy animals = healthy food = healthy consumers
Maraming salamat....
Questions?