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

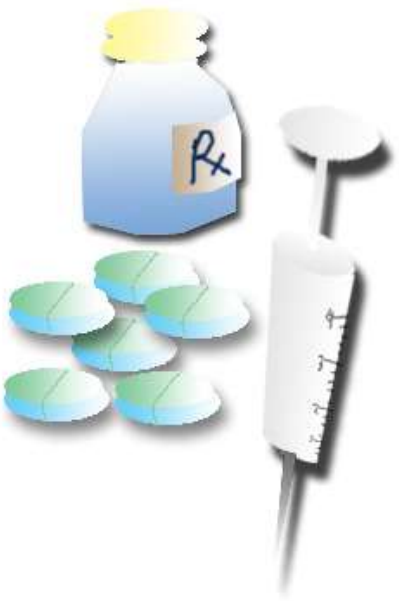
II. Adverse Effects of Antibiotic Drug Residues
   - A. Toxicological Effects
   - B. Immunological Effects
   - C. Microbiological Effects

III. Why do we have Antibiotic residues?

IV. What can we do?

Antibiotics

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)

Increasing world population

Advantages

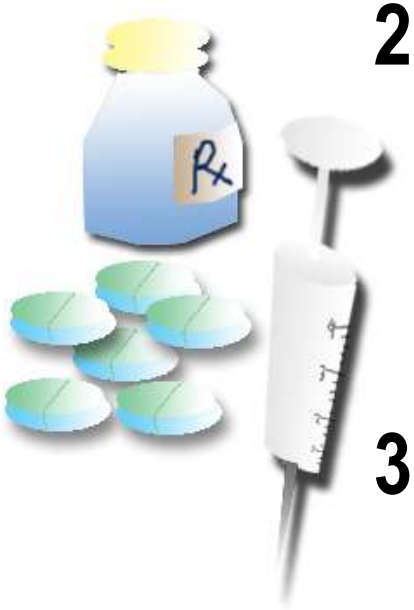
disadvantages

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

Concern:

Feb. 25, 1989, Philippine Daily Inquirer:

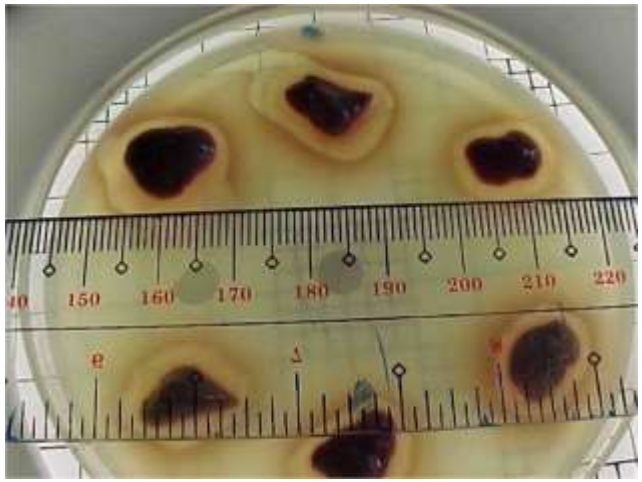
DOH Secretary Alfredo Bengzon remarked that *"veterinarians are abusing antibiotics by making these medicine a regular part of poultry & livestock feeds."*

– 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

Adverse Effects of Antibiotic Residues

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

Adverse Effects of Antibiotic Drugs

Toxicological Effects:

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

e.g., Tetracylines

– Discolored teeth, allergic reactions, peripheral blood changes

Adverse Effects of Antibiotic Drugs

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

Adverse Effects of Veterinary Drugs

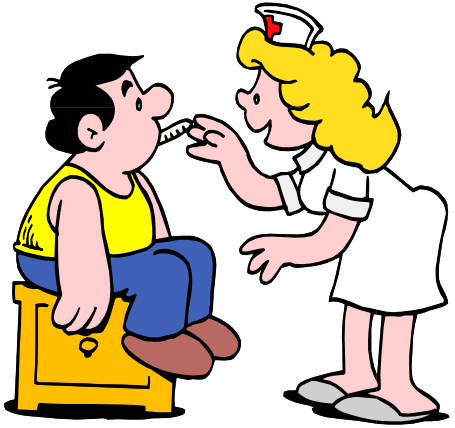
Immunological Effects:

e.g.,

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

- 1984: people w/ anaphylactic reaction after eating steak
- 1972: 2 people w/ 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

Microbiological Effects:



Typical Hospital Ward Scenario

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

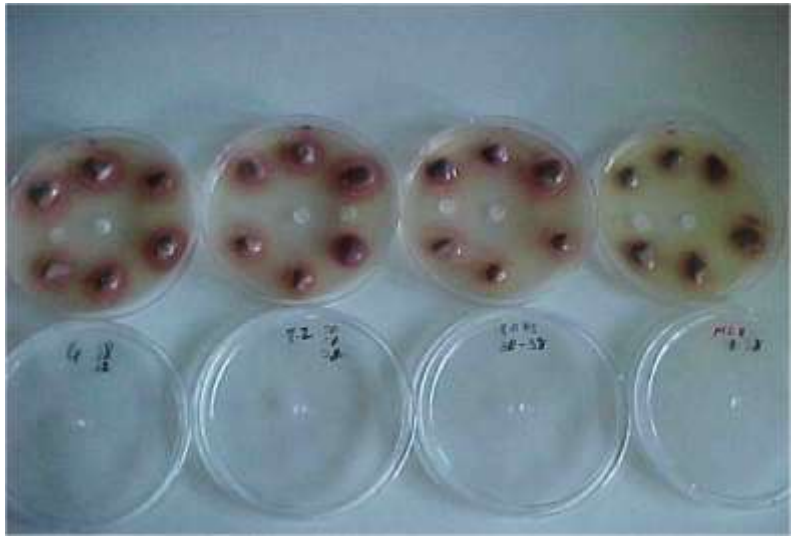
Antibiotic Resistance

Microbiological Effects:

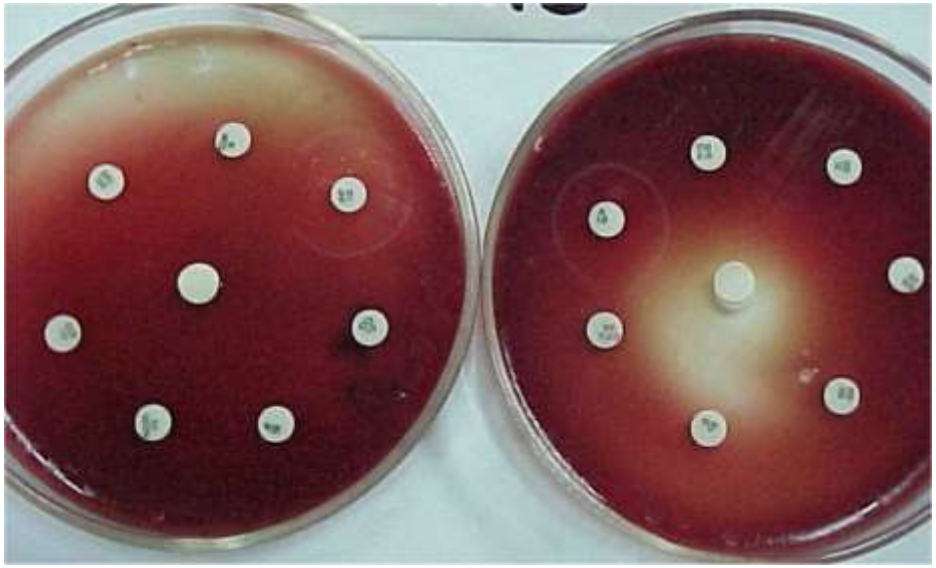
- Eliminate susceptible bacteria leaving resistant ones,
- alteration in gut microflora
- Interfere with food processing, e.g., fermented sausages, cheese production

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

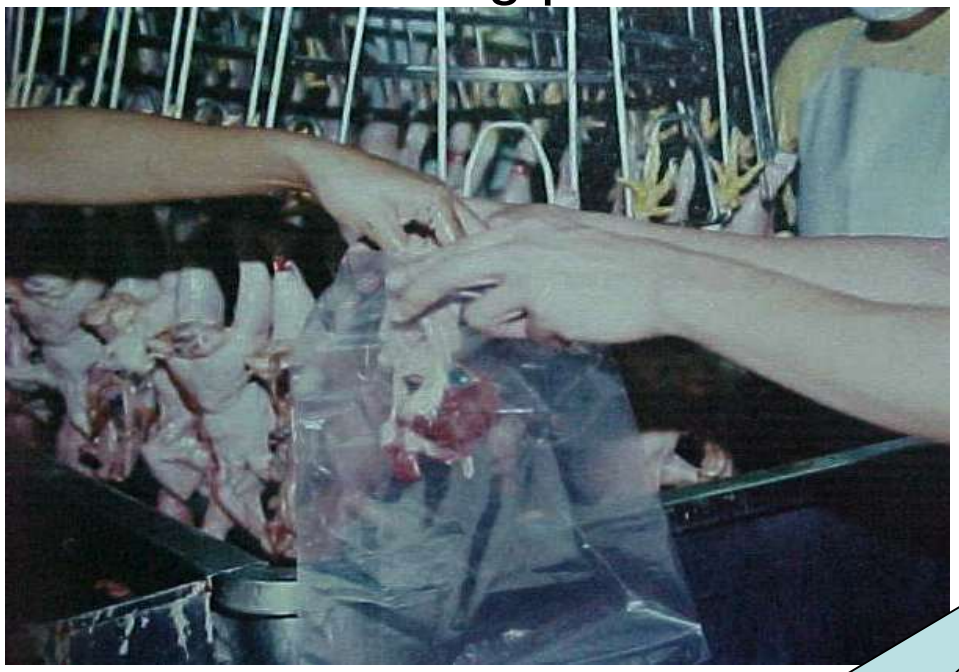


Multi-resistant *C. jejuni* isolates

Chickens: liver & ceca

Commercial producers'

dressing plant



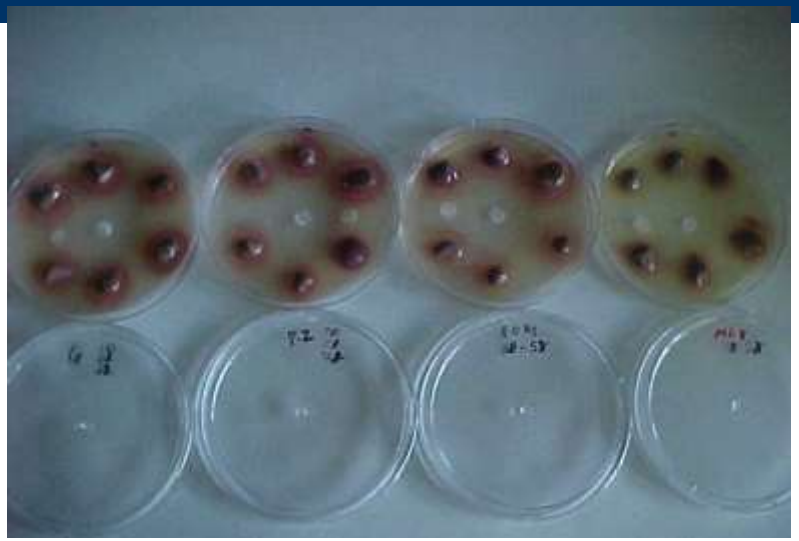
Backyard raisers'

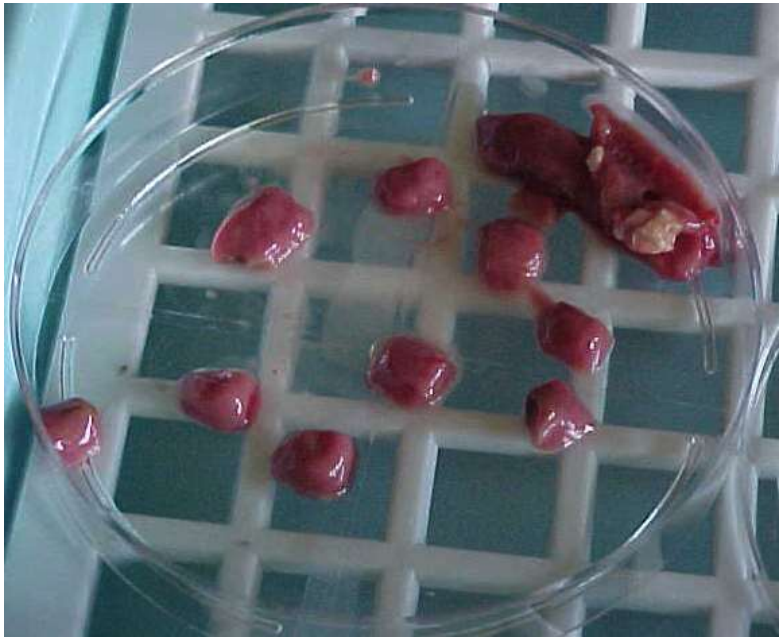
dressing plant

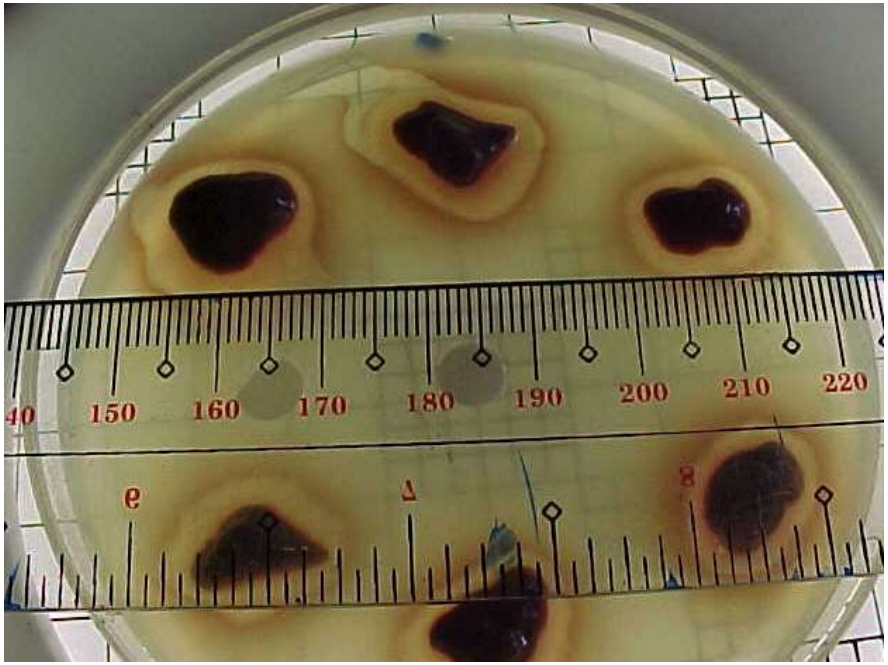
ceca

liver

Liver samples for Detection for antibiotic residues





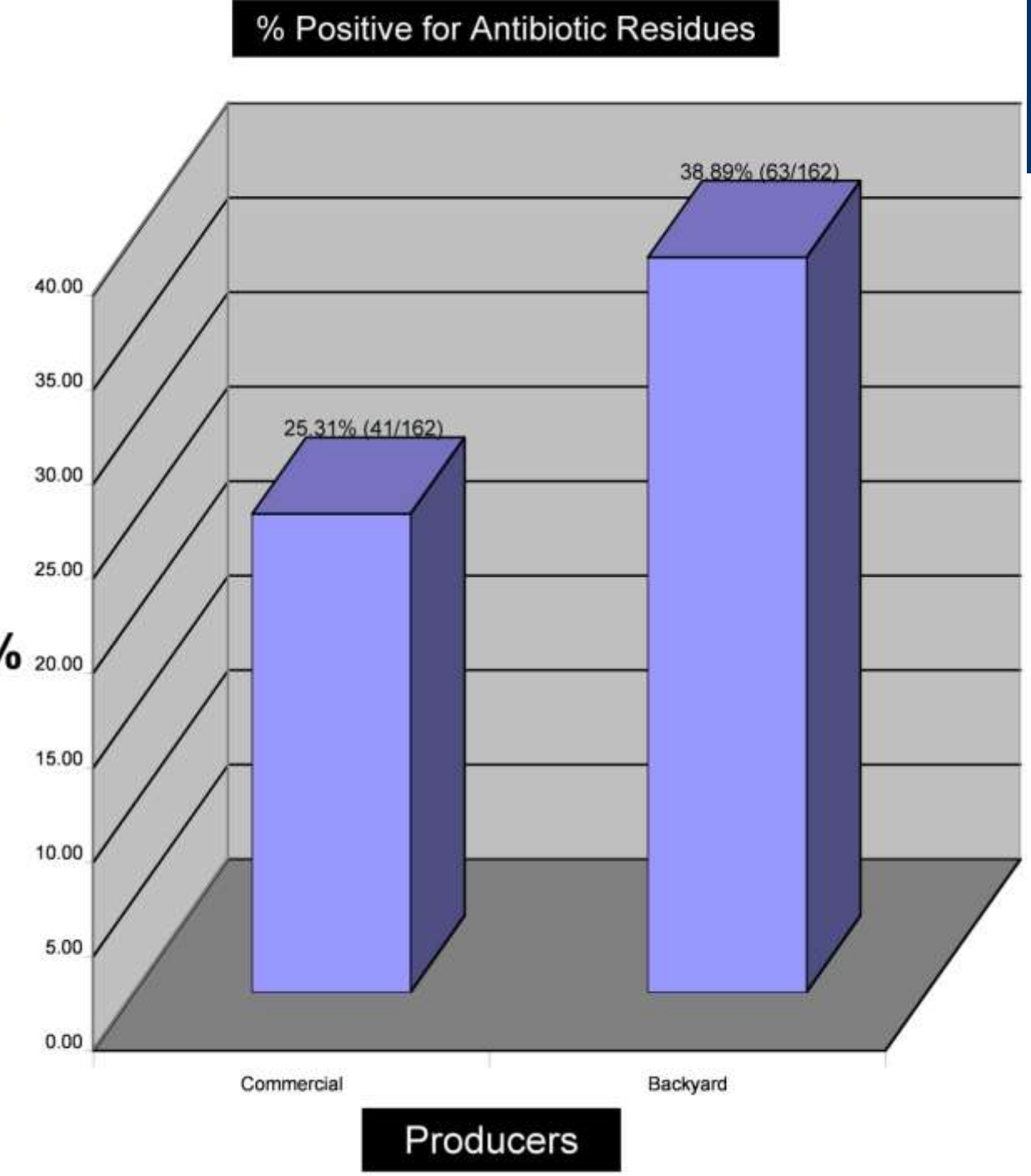


CECA: Isolation of *Campylobacter* sp.

Antibiotic Sensitivity Testing

ENRICHMENT & DIRECT methods, Confirmed as *C. jejuni* by PCR

Antibiotic Sensitivity Testing



Chickens tested positive for Antibiotic Residues

- **64.2%** (104/162) positives
- backyard raisers (39%) **>** commercial producers (25%)

  (p<.05)

  (P-value: **0.0001608**)

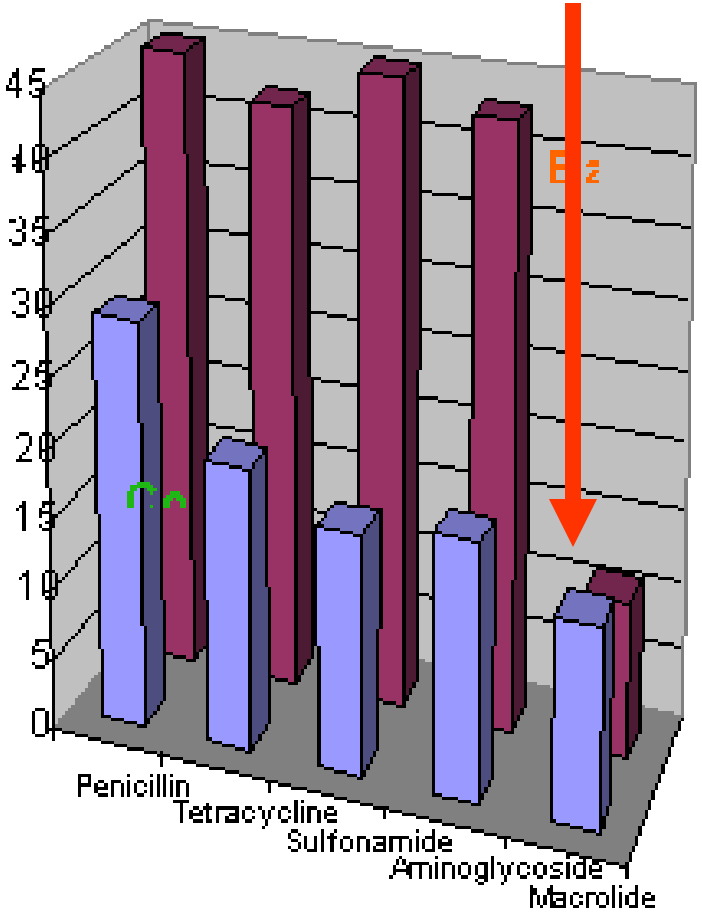
➢ Common use of antibiotics in poultry production

Residue vs Type of Antibiotic

Residue

least frequent type detected

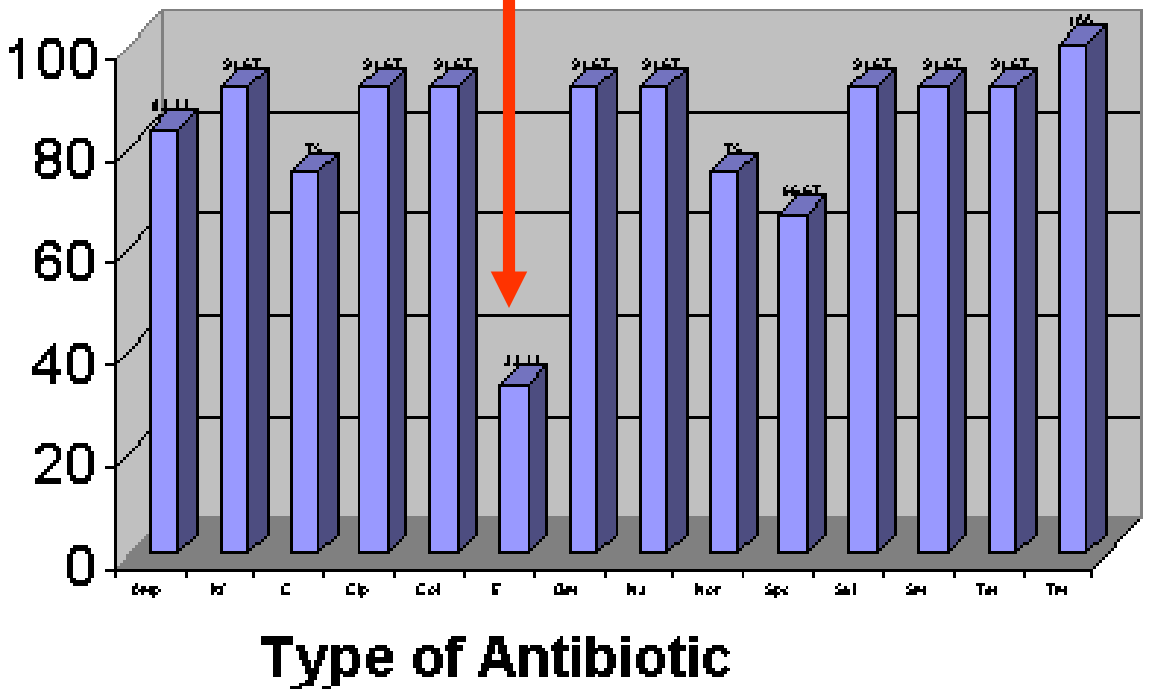
MACROLIDES



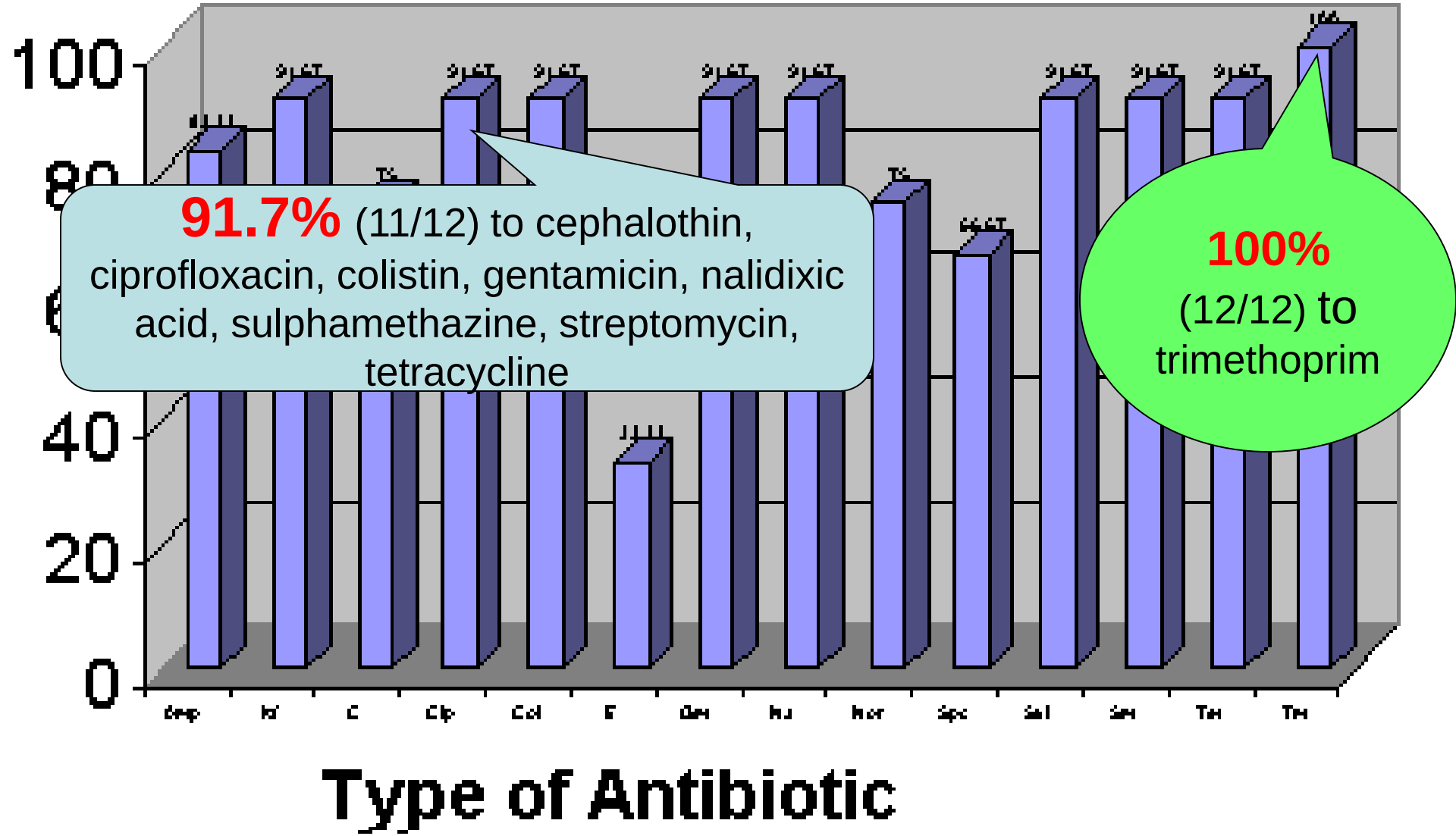
Resistance

Low resistance to Erythromycin

(a macrolide)



Antimicrobial profile of *C. jejuni* isolates: multi-resistance



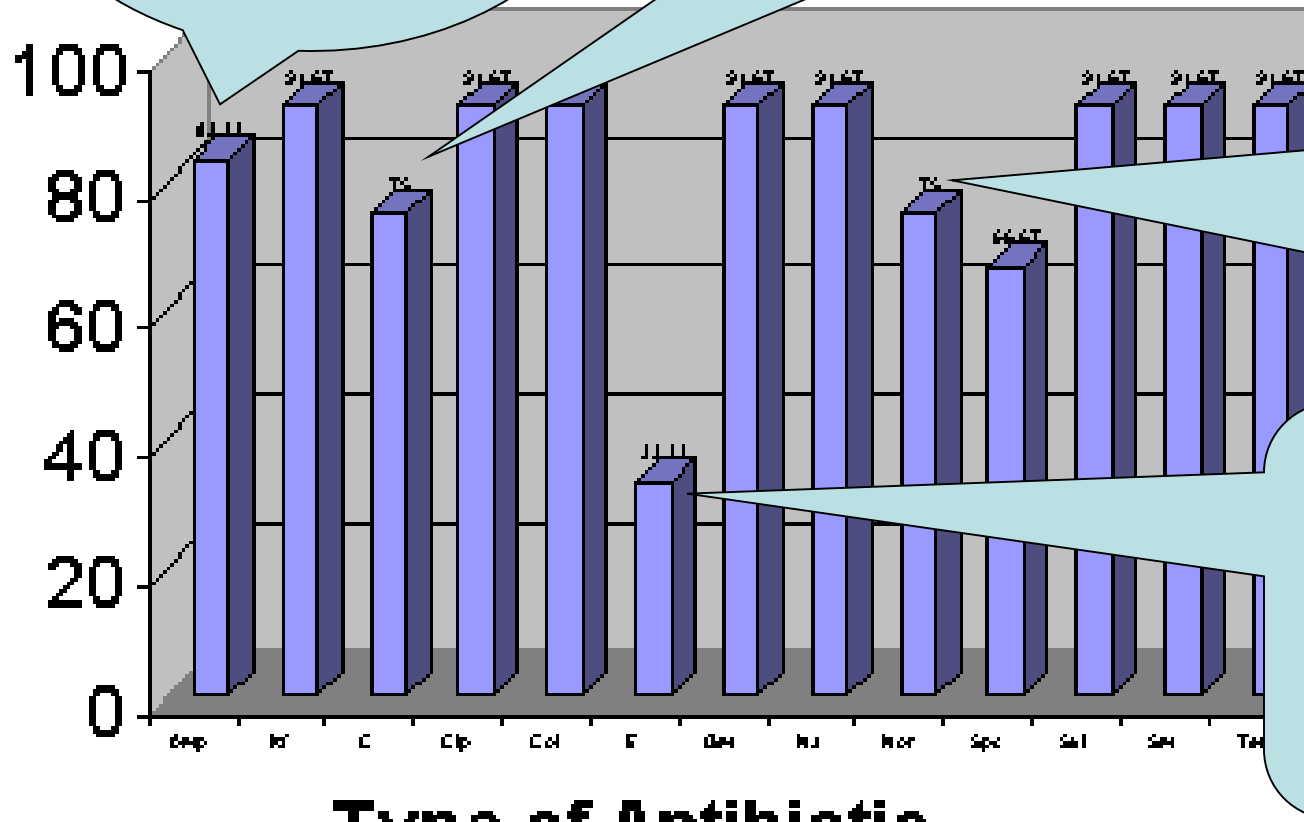
Antimicrobial resistance profile:

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



Penicillin residue & cephalothin

*** Significant** ($p < 0.05$)

P-values

ANTIBIOTIC TESTED	% RESIST-ANCE of *Campylo-bacter jejuni* ISOLATES	X^2 VALUES FOR TYPE OF ANTIBIOTIC RESIDUE DETECTED				
		Penicillin	**Tetra-cyclines**	Sulfas	**Aminogly cosides**	Macrolides
Ampicillin	83.3	.166	.58			.640
Cephalothin	91.7	**.020 ***	.1			.753
Chloramphenicol	75.0	.371	.157			.546
Ciprofloxacin	91.7	.640	.460		.460	.753
Colistin sulphate	91.7	.640	.460	.460	.460	.753
Erythromycin	33.3	**.028***	**.001***	.083	**.030 ***	.140
Gentamicin		.640	.460	.460	.4	.753
Nalidix		.640	.460	.140		.753
Norf		.371	1.00	1.00		546
Spe		.273	.083	.386		
Sup		.640	.460	.4		
Strep		.640	.140	.		
Tetracyc		.640	.460	.1		
Trimethoprim**	100					

Tetracycline residue & erythromycin

Penicillin residue & erythromycin

aminoglycoside residue & erythromycin

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

What is the significance of the statistically observed

CO- or **CROSS-RESISTANCE**?

Philippine Generics Law of 1988

= based on **Swann Report of 1969**

- 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

e.g., MDR-TB

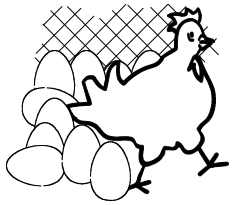
- **Antibiotic Residues**
- **Reservoir of resistant bacteria for human pop'n**

resistant strains → *restrict treatment options* → *more expensive treatment* → *treatment failure*

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 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?

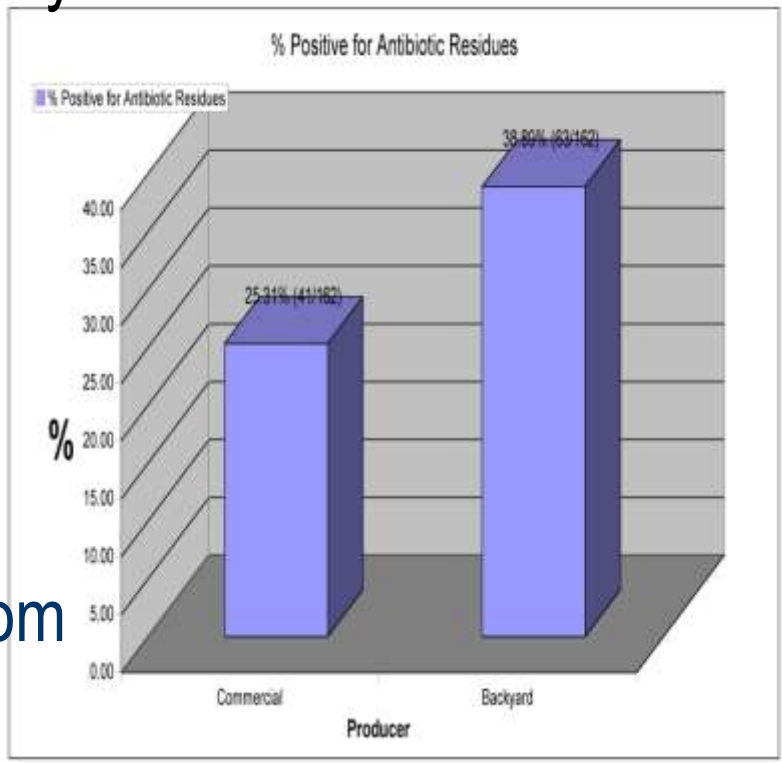
Why do we have residues?

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

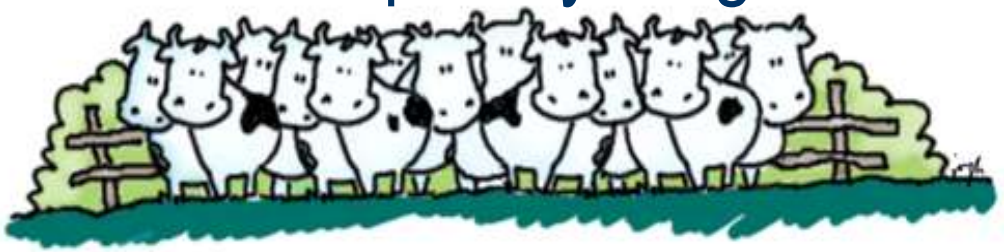
6. Common practice of long-term preventive use of subtherapeutic concentrations of drugs.

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

What can we do?

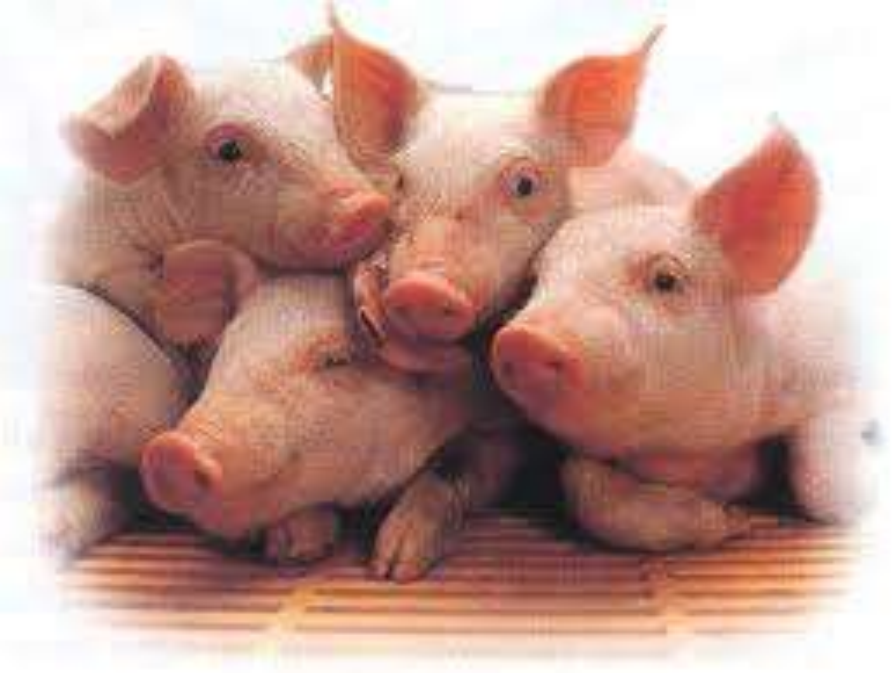
3. **Heightened surveillance** (through regular mandatory testing) by regulatory agencies for presence of residues.

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?