Current Situation of Control Measures of Drug Residues in Main Foods of Animal Origin in Palestine

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- Introduction.
- Extent of Antibiotics in Food.
- Legislations.
- Antibiotic Residues in Sheep and Cattle Meat.
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واقع الرقابة الصحية البيطرية على المنتجات الحيوانية

- **الابقار والاغنام**:
  - 13 مسلخ بالضفة وغزة، 8 بالضفة منها 5 مذابح.....
  - الحيوانات التي بها علامات لاعطاء ادوية مع افات مرضية كلية اخرى يتم اتلافها.
  - عدم وجود جهة رقابية لاخذ عينات عشوائية لفحصها.
  - لا دراسات عن مدى انتشار الادوية البيطرية باللحوم.
- **لحوم الدواجن**:
  - مشكلة مسالخ الدواجن مثل مشكلة مسالخ الحيوانات الكبيرة: عددها قليل ولا تغطي السوق المحلي، والباقي يتم ذبحه في محلات ذبح عشوائية.
  - عدم وجود جهة رقابية لاخذ عينات عشوائية لفحصها.
  - رسالة ماجستير: 24% من العينات تحتوي مضادات حيوية.

- **الحليب ومنتجاته**:
  - المزارع المزودة لمصانع الالبان والاجبان يتم فحص الحليب عند الاستلام بالمصنع ورفض الايجابي.
  - الحليب من الابقار المعالجة بمضاد حيوي وعقاقير اخرى يتم بيعها على حده ويمكن انتاج جبنة منها.
  - عدم وجود جهة رقابة لاخذ عينات عشوائية لفحصها.

- **في الاتحاد الاوروبي**: رقابة كاملة على الادوية، تعهدات وضمانات بالالتزام بفترة الامان للادوية، عينات عشوائية: الموجبة منها يتم اتلافها مع اجراءات عقابية للمزارع.

- A Residue is defined as ‘a residue of substances having a pharmacological action, or their metabolites and other substances transmitted to food products, which are likely to be harmful to human health’.

- A large number of drugs used to control or prevent infections or to promote growth are considered essential in production systems.

- Almost all chemicals administered knowingly or unknowingly to animals result in some trace residue remaining in the carcass or food.

- There is a growing consumer resistance to the presence of unwanted residues in food.

- The principal consumer concerns are:
  - drug resistance,
  - toxicity,
  - potential allergy, and;
  - carcinogenic effect.

- Detection of unwanted residues presents a new challenge to food hygienists.

- Traditional inspection methods cannot guarantee the detection of residues since many of the drugs used are rapidly absorbed from the site of administration, and, in common with those that are given to animals parenterally or orally, do not produce lesions which can be routinely observed.

Therapeutic products that cause concern:

1- Antimicrobials: the major group of chemical residue in meat. These are a diffuse group containing several classes of compounds used to treat or prevent bacterial infection.

2- Pesticides: including anthelmintics, ectoparasiticides and antiprotozoals.

3- Hormones: which are used for therapeutic purposes in various fertility treatments or for growth promotion and are administered as injection or implant.

4- Environmental contaminants: herbicides, heavy metals, and fungicides.

5- Additives: these are employed to prevent the onset of spoilage, to promote binding properties and to enhance flavor and nutritive value in the preservation and processing of food.

- When farm animals are treated with antibiotics, drug residues settle in the animal's tissue.

- Residues end up not only in the meat, but also in other products of animal origin such as milk, eggs and honey.

- The presence of antibiotics residues and their associated harmful health effects on humans make the control of veterinary drug residues an important measure in ensuring consumer protection.

Traditional inspection procedures need to be complemented by an increasingly wide range of sophisticated laboratory analysis.

- Antimicrobials are generally used in farm animals for therapeutic and prophylactic purposes.

- They include a large number of different types of compounds, which can be administered either in feed, in drinking water or by injection.

- Some practices involve in the use of ‘‘cocktails’’ (mixtures of small amounts of several substances).

Pathological Effects produced by Antibiotic Residues in Food

- Transfer of antibiotic resistant bacteria to the human.
- Immunopathological effects
- Autoimmunity
- Carcinogenicity (Sulphamethazine, Oxytetracycline, Furazolidone)
- Mutagenicity
- Nephropathy (Gentamicin)
- Hepatotoxicity
- Reproductive disorders
- Bone marrow toxicity (Chloramphenicol)
- Allergy (Penicillin)

- Antimicrobial residues in food disrupt the intestinal microflora and increase the development of resistant bacteria in the general population.

- Drug resistance has gained its importance due to its ability of transmission to other enteric pathogens which have posed a serious public health problem.

- In addition soil microflora which receives antimicrobial residues via birds manure may affect the human health as a source of developing resistant microorganisms

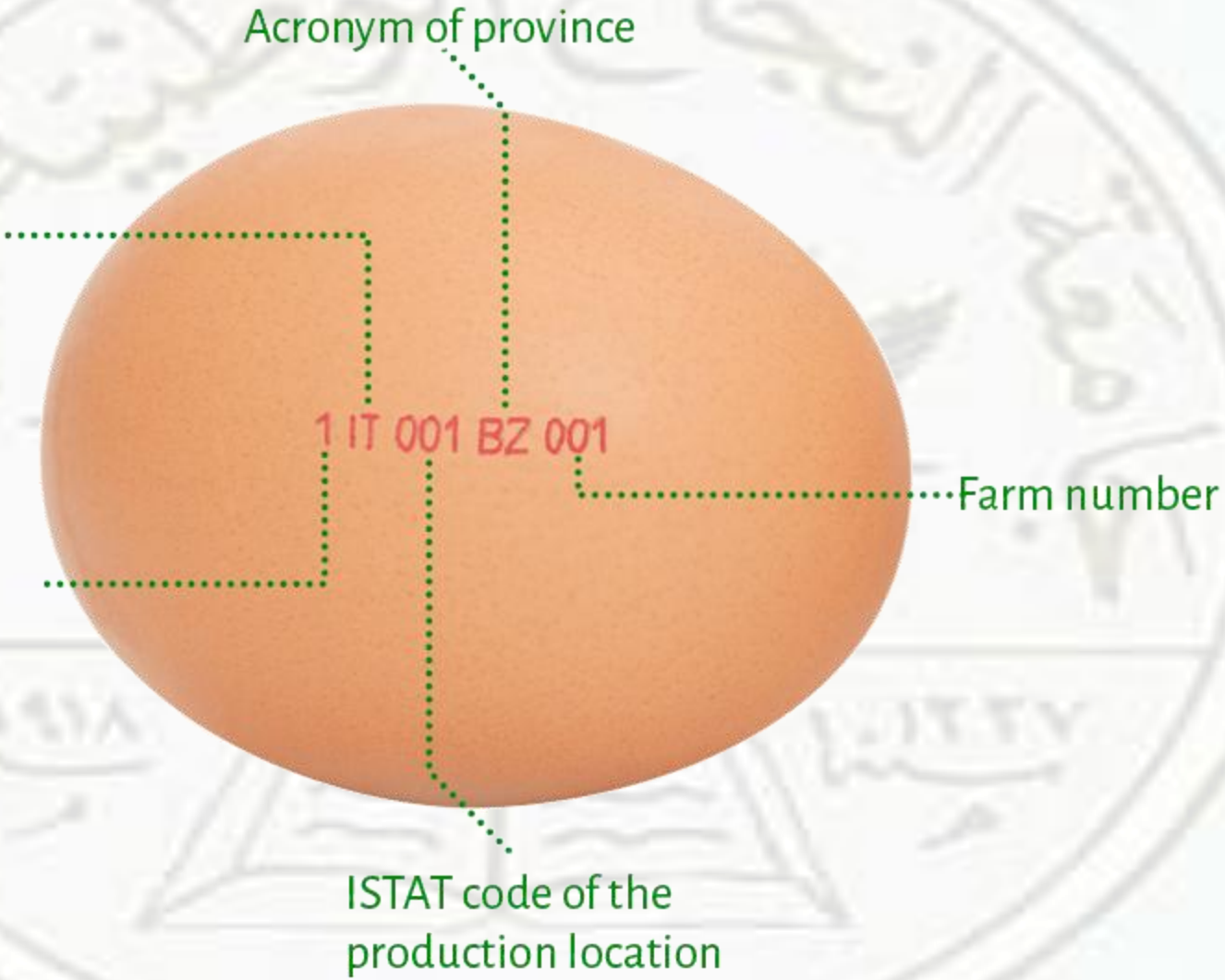
- Within the European Union, the use of antibiotics is regulated by the law.

- In many countries, maximum residue limits MRL have been determined and are checked on a random basis.

- When animals are treated with antibiotics, a waiting period is required before slaughter.

- As a result of these strict controls, the discovery of large quantities of antibiotics in meat has become rare.

Example code of the Egger farm



- Mostly, antibiotics are found in low quantities in poultry. Beef or other animal products such as milk, eggs and honey rarely contain residues.

- Antimicrobial residues are detected by chemical, biological and immunological methods.

- Detection methods can be classified by their degree of quantification into qualitative, semi-quantitative and quantitative methods.

Maximum residue limits (MRL) in EU

- It is the maximum concentration of residue accepted by EU in a food product obtained from an animal that has received a veterinary medicine or that has been exposed to a biocidal product for use in animal husbandry.

- The EU requires by law that foodstuffs, such as meat, milk or eggs, obtained from animals treated with veterinary medicines or exposed to biocidal products used in animal husbandry must not contain any residue that might represent a hazard to the health of the consumer.

- Some substances are considered to represent a hazard to the safety of the consumer at any level.

- These substances must not be used in veterinary medicines for use in food producing animals or in biocidal products for use in animal husbandry, and are included in table 2 (prohibited substances) of the annex to Commission Regulation (EU) No 37/2010.

- In the case of meat from bovine and porcine animals and meat from poultry, a trade document or certificate conforming to a model laid down by European Community legislation shall accompany the food and state that the animals are free of drug residues.

Pharmacologically active Substance	Marker residue	Animal Species	MRL	Target Tissues	Other Provisions (*according to Article 14(7) of Regulation (EC) No 470/2009*)	Therapeutic Classification
Amoxicillin	Amoxicillin	All food producing species	50 µg/kg 50 µg/kg 50 µg/kg 50 µg/kg 4 µg/kg	Muscle Fat Liver Kidney Milk	For fin fish the muscle MRL relates to 'muscle and skin in natural proportions'. MRLs for fat, liver and kidney do not apply to fin fish. For porcine and poultry species the fat MRL relates to 'skin and fat in natural proportions'. Not for use in animals from which eggs are produced for human consumption.	Anti-infectious agents/Antibiotics
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Table. - 1. Maximum Residues Limit (MRL) (ug/kg) for veterinary residues.

ANTIBIOTIC	MRL
Benzyl penicillin	4
Ampicillin	4
Amoxycillin	4
Oxacillin	30
Cloxacillin	30
Dicloxacillin	30
Tetracycline	100
Oxytetracycline	100
Chlortetracycline	100
Streptomycin	200
Dihydrostreptomycine	200
Gentamycine	200
Neomycin	100
Sulphonamides	100
Trimethoprime	50
Spiramycin	200
Tylosine	50
Erythromycine	40
Quinalones	75
Polymyxine	50
Ceftiofur	100
Cefquinome	20
Nitrofurans	0
Nitromidazoles	0
Other chemotherapeutics (Chloramphenicol, Novobiocine)	0

قانون أمراض الحيوانات
قانون رقم (39) لسنة 1954

المادة (8)
صلاحية الفحص والمعالجة

1- للطبيب البيطري أو مفتش المواشي أن يكلف صاحب أي حيوان لفحص حيوانه أو تلقيحه أو معالجته على أي وجه آخر أو وسمه أو تعليمه بصورة أخرى أو رشه أو غسله أو تعقيمه بأية صورة أخرى، أو وضعه تحت الحجر الصحي طيلة المدة التي يعينها إذا رأى في أي وقت من الأوقات من الضروري أو المستحسن إجراء ذلك منعاً لتفشي المرض.

2- يجوز لأي طبيب بيطري:

أ - أن يحظر على أي شخص ذبح أي حيوان تحت المعالجة وفاقاً لأحكام الفقرة (1) أو تحت معالجة أي شخص مجاز كطبيب بيطري أو تحت المعالجة البيطرية بأية صورة أو يكون تحت الحجر الصحي مدة من الزمن، و

ب- أن يحظر استعمال نتاج ذلك الحيوان بما في ذلك الحليب للمدة التي يستصوب تحديدها، و

ج- أن يسمح بذبح الحيوان أو استعمال نتاجه وفاقاً للشروط التي يعينها.

The main purpose of meat inspection is to detect and prevent public health hazards such asfood-borne pathogens chemical contaminants in meat Yet existing inspection practises often date back decades and might not always adequately protect public health. Traditionally, inspection techniques (visual, palpatory and by incision) for the presence of gross lesions or flaws such as bruises or broken bones have satisfied public health objectives. However these techniques are not always suitable for detecting food-borne diseases such as campylobacteriosis, salmonellosis and virulent strains of *E.coli*, or contamination by chemical substances such as steroids or veterinary drug residues.

Chemical hazards were also included and mainly fall into three areas: the residues of veterinary drugs (such as antibacterial substances or sedatives), unauthorised or prohibited anabolic substances (such as growth hormones or meat quality enhancers) and other chemical contaminants.

- In the West Bank and the Gaza Strip, there are 13 ruminant slaughterhouses, including eight in the West Bank and five in the Gaza Strip, in addition to nine poultry slaughterhouses in the West Bank and one in Gaza.

- From the 8 slaughterhouses in the West Bank, just 3 are effectively serving the areas they cover.

- In these working slaughterhouses no testing for antibiotic residues is performed. Suspected cases with generalized lesions are condemned.

Residue Testing Procedures: Cattle and Swine

There are basic principles you should keep in mind when you are deciding whether or not a carcass may contain residues. The in-plant screening tests provide guidance and should be used as primary tools in the first step of the residue program.

The following is a list of the pathologies and conditions that warrant retention and testing of carcasses. Symptoms are described to help PHVs determine when to retain and test carcasses.

- Peritonitis and surgery – carcasses with active peritoneal inflammation associated with fibrinous exudate or fetid ascitic fluid, no matter how limited the extent of the lesions or with ventral abdominal cellulitis secondary to percutaneous abomasal surgery. Findings of surgical devices (suture, toggles, fistula devices, etc.) are only significant if they are associated with active (i.e. the presence of fibrin as opposed to chronic peritonitis with fibrous adhesions) peritoneal inflammation.

- Injection sites – carcasses with lesions associated with injections. Injection sites are likely to be found in a variety of locations including the neck, shoulder, thorax, axilla, ventral abdomen (along the subcutaneous abdominal vein), flank, hindquarter, pelvic area (perirectal) and tail. Also, look for cellulitis that is away from pressure points (e.g., tubor isschii, hip joint, stifle joint). These are generally found in the semimembranosis and semitendinosis muscle.

- Pneumonia – carcasses with acute, subacute and chronic active pneumonias; with pleural cellulitis resulting from reticulo peritonitis complex; or with embolic pneumonia.

- Pleuritis – inflammation of the pleura lining in the thoracic cavity and lungs

- Pericarditis – carcasses with fibinous or fibrinosuppurative pericarditis.

- Endocarditis – carcasses with endocarditis and acute pulmonary, renal or other embolic lesions.

- Signs of treatment – leakage around jugular veins; subcutaneous, intramuscular, or intraperitoneal signs of treatment; signs indicative treatment by mouth such as discoloration from particles found in any part of the digestive tract.

- Septicemia, pyemia or generalized disease – carcasses that are being condemned for septicemia, pyemia, or other inflammatory/infectious conditions. On antemortem or postmortem inspection – depression, elevated or subnormal body temperature, hyperemic skin, congested mucous membranes, dehydration, poor body condition, in association with an injury or inflammatory condition such as abcesses, arthritis, pneumonia, mastitis, metritis, or diamond skin

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(d) where there are serious grounds for suspecting the presence of residues or contaminants, an analysis by sampling of residues not resulting from the hunting process, including environmental contaminants. When a more extensive inspection is made on the basis of such suspicions, the veterinarian must wait until that inspection has been concluded before assessing all the game killed during a specific hunt, or those parts suspected of showing the same abnormalities;

Lesions that may lead to the presence of antimicrobials in animals:

- Fluorescence in the bone marrow: tetracycline.
- Abscesses and necrosis at different body sites: suspension of injection sites.
- Microcysts at the ovaries, muco- or hydrometra: sex-hormones.
- Icterus, hepatopathy: copper.
- Atrophy of the thymus: corticosteroids.


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Antibiotic Residues in Broilers

- Chicken meat, rather than other commodities, such as milk or beef, is largely consumed in the Palestinian territories by consumers of all ages.

- It is clear that poultry production is becoming more and more prominent sector and it needs to be improved and developed.

- Intensive farming, which is a natural response to increasing demand, may put pressure on farmers and veterinarians to use more and more antimicrobials in terms of types and quantities.

Table (2.2): Poultry production in Palestinian territories **[9]**

Region	Broilers	Layers	Broilers mothers	Turkey
2009/2010				
Gaza strip	7,556,507	311,280	22,790	34,670
West Bank	23,554,904	1,233,736	376,633	486,460
Total	31,111,411	1,545,016	399,423	521,130
2010/2011				
Gaza strip	16,373,467	297,678	2,200	-
West Bank	20,174,056	1,328,779	534,988	318,420
Total	36,547,523	1,626,457	537,188	318,420
2012/2013				
Gaza strip	8.218.180	351.199	-	8.093
West Bank	23.297.203	1.425.579	994.620	538.320
Total	**31,515,383**	**1.776.778**	**994.620**	**546.413**

- Results confirmed the presence of antibiotic residues in poultry meat samples collected from different sites in West Bank and Gaza Strip.

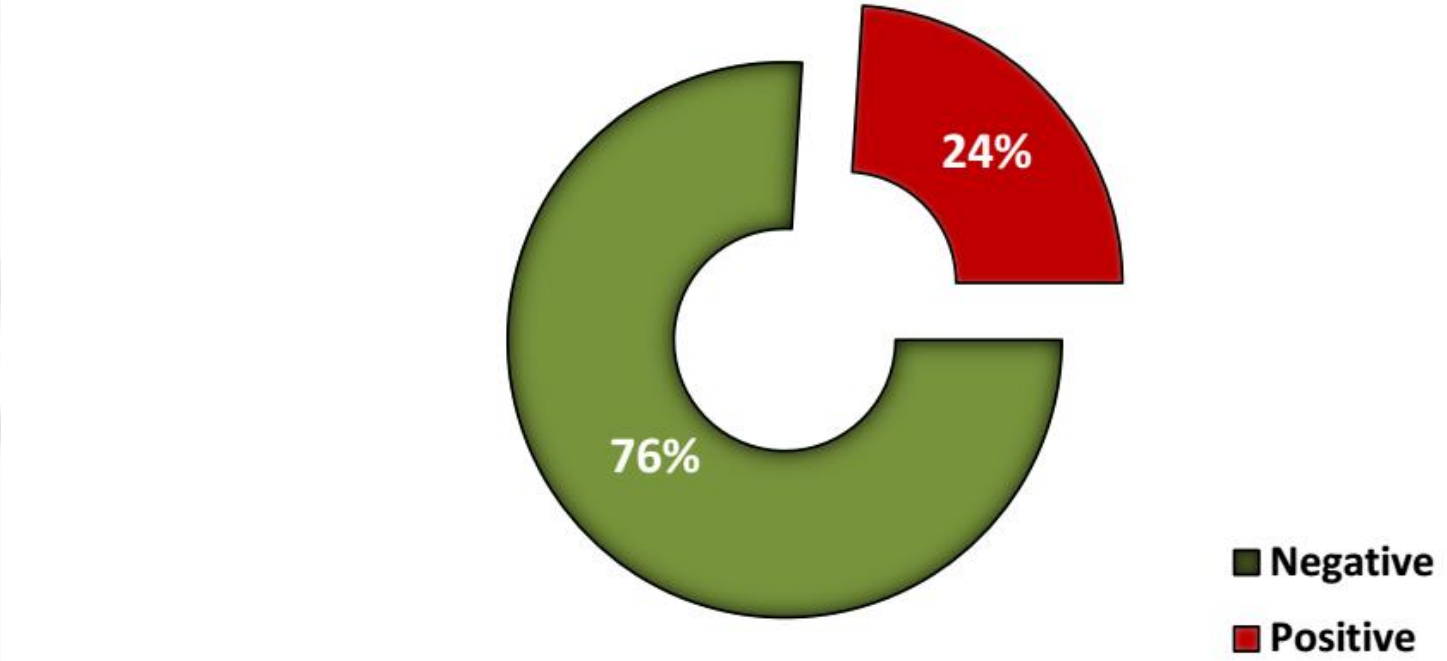

Figure (4.2): Overall positive samples of antibiotic residues.

Emergence of resistant bacteria in chicken

- In animals, antimicrobials resistant enteropathogens (e.g., *Salmonella*, *Campylobacter*, *Yersinia*, and some strains of *Escherichia coli*) are of special concern to human and animal health because these bacteria are most likely to be transferred through the food chain to humans, or resistance genes in commensal bacteria may be transferred to the zoonotic enteropathogens.

- In all cases, the hypothesis is that the food chain is the main mean of transmission.

- Direct physical contact, shared environments, and exposure through vectors and fomites are all routes for bacterial transmission between animal species.

- Poultry is considered a leading source for foodborne infections caused by *Campylobacter* and *Salmonella*.

- Food surveillance most commonly isolates *Salmonella* from fresh meat, commonly from poultry and less frequently from eggs, beef, fishery products, vegetables and milk

Testing milk for antibiotic Residues

- The approach to the control of antibiotic residues in milk is complex.
- The primary control is on farm and begins with the correct prescription and administration of the antibiotics and the careful adherence to withdrawal periods.
- In short, milk producers must ensure that milk from animals under treatment or in the withdrawal period does not enter the food chain.

- The primary controls are complemented by the testing of milk for antibiotics, undertaken by Dairy Plants at various points in the supply chain, including on farm.

- It is up to individual food business operators (including milk producers) to determine their own sampling and testing regime, taking account of other testing undertaken in the distribution chain, including any testing carried out on their behalf.

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2. Regulation (EC) No 853/2004, (Annex III, Section IX, Chapter I.III.2, 4 and 5) requires that:

i) food business operators must initiate procedures to ensure that raw milk is not placed on the market if it contains antibiotic residues in excess of regulated limits (Maximum Residue Limit – MRL);

ii) food business operators must inform the competent authority where this requirement is not met, and take corrective measures; and

iii) a representative number of random samples of raw milk be tested to monitor the effectiveness of the initiated procedures.

Thus, there is no requirement to test **all** raw milk collected from milk production holdings but food business operators should ensure that appropriate testing is in place to meet the requirement of (i) above. Such testing may be undertaken by food businesses at various points in the supply chain, including on farm.

Antibiotic Residue in Honey

- Because of potential health risks, the use of antibiotics in beekeeping is generally banned in many countries.
- No maximum residue limits are defined (zero tolerance).
- where a large part of the global honey supply is produced. Testing for residues is therefore relevant particularly in imported honey.

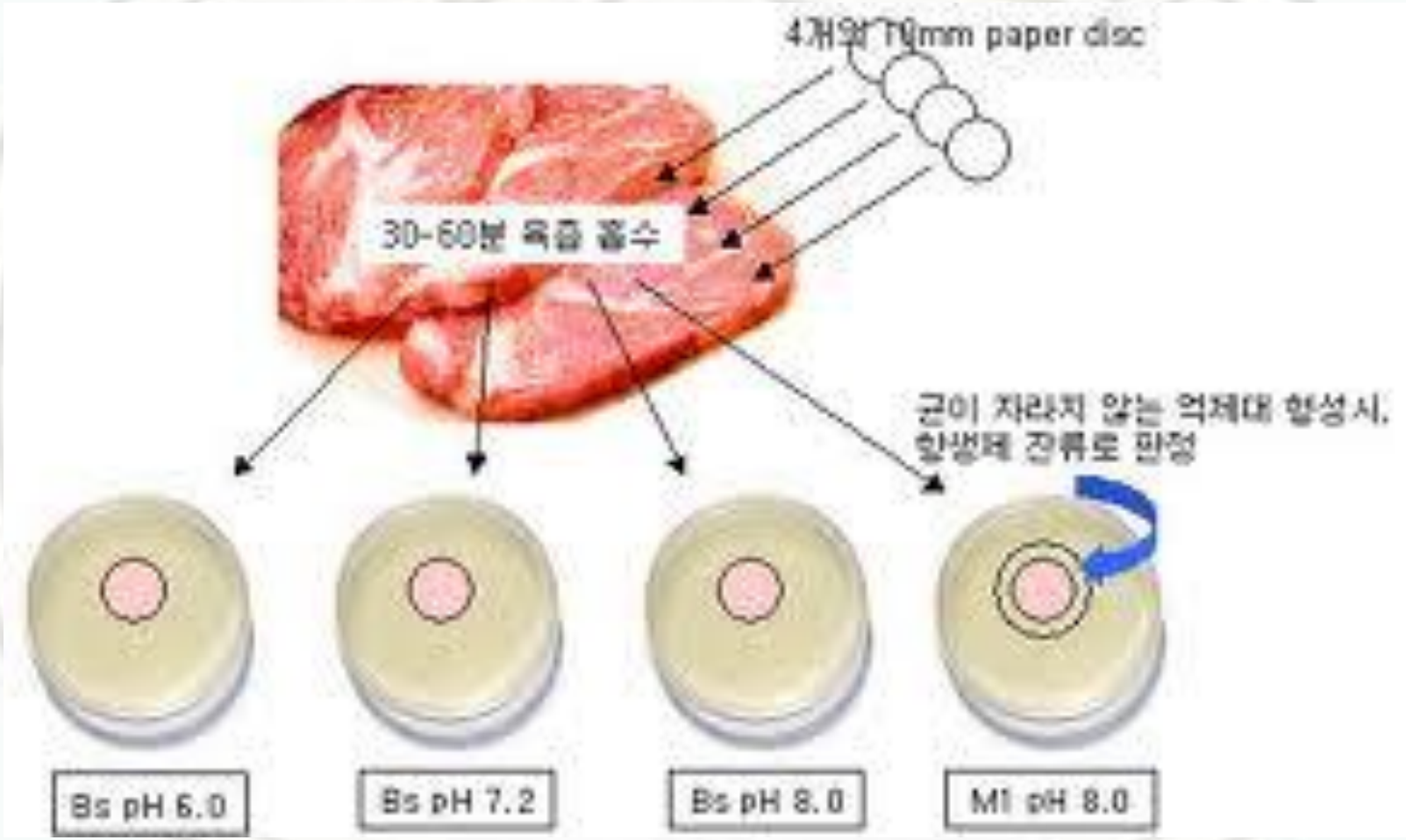
Tests for antimicrobial agents in foods of animal origin:

- **Testing samples from kidneys and muscles**
- **Four-plate test (FPT):**
  - It is one of the basic microbiological methods used for the detection of antibiotics in food.
  - This test has the advantage of requiring simple apparatus and limited training for analysts, and of having rapid turnaround and broad spectrum detection.
  - It is an agar diffusion test.
  - Food samples are applied to four plates of agar medium, three of which are inoculated with *Bacillus subtilis* spores at pH 6, 7.2, and 8, and with *Micrococcus luteus* at pH 8

– Trimethoprim is incorporated into the pH 7.2 medium to enhance the sensitivity of the test for sulphonamide residues.

– Diffusion of the active antibiotic is detected by the formation of clear zones of inhibition on one or more plates after overnight incubation.

– The reliability and sensitivity of the tests are monitored by applying 6 mm diameter filter-paper discs containing standard quantities of known antibiotics in each run.


4개의 10mm paper disc
30-60분 육즙 흡수
균이 자라지 않는 억제대 형성시,
항생제 감류로 판정
Bs pH 6.0
Bs pH 7.2
Bs pH 8.0
M1 pH 8.0

Conclusion

- Palestine has no specific regulations regarding the use of antimicrobials or the maximum allowable antimicrobial concentrations in food. Rules might be the same for other countries.

- Additionally, there are no systems to monitor the presence of antimicrobial residues in animal products in Palestine.

Recommendations

Guidelines for the Establishment of a Regulatory Programme for Control of Veterinary Drug Residues in Foods (CAC/GL 16-1993) (under revision).

Official or officially-recognised programmes for chemical hazards and contaminants should include measures to:

- control the registration and use of veterinary drugs and pesticides so that residues do not occur in meat at levels that make the product unsafe[25] for human consumption, and
- provide monitoring and surveillance systems that establish baseline data and guide a risk-based approach to control of such hazards in meat.

- A certificate conforming to a model laid down by the Ministry of Agriculture should accompany the animals/birds introduced for the slaughterhouse that clearly state that the animals are free of drug residues.

- Given the potential hazards presented by the presence of antimicrobial residues in food of animal origin on human health, and that there is an intensive, un-regulated and uncontrolled use of antimicrobials in the food industry in our area, it is of utmost importance to investigate this issue and to generate data that would serve as a baseline data for researchers as well as for decision makers.

- A monitoring policy should be implemented to ensure the conformity of meat sold with international/Palestinian standards.

- Thus, it is recommended that rules should be taken to ensure observing proper withdrawal periods before marketing and drug control in veterinary use.

- Rapid screening procedures for the analysis of antibiotic residues and instant grading and prohibition of food containing antibiotics more than MRL.

- Penalties.

- In the operational implementation, it was necessary to provide veterinary control number certificate to the animal food business, apply the good farming practice and HACCP, monitor program and surveillance for antibiotic residue, and develop the supervision for veterinary public health.

- The first step in residue prevention is to make individuals and organizations aware of the problem through education by veterinary personnel, organizations, and literatures and governmental agencies.

- Irrational use of antibiotics in field veterinary practices should be avoided.

- Development of simple and economic field test to identify drug residue in edible animal products.

- Nation wide monitoring and periodic surveillance of microbial residue in food.

Thank you for your attention