ANTIMICROBIAL USAGE AND RESISTANCE DEVELOPMENT IN FOOD ANIMALS IN KENYA: AN EMERGING GLOBAL PROBLEM

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Global Antibiotic Resistance Partnership

CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
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BACKGROUND

Antibiotics -

-Natural or synthetic drugs which inhibit or kill bacteria or fungus.

-Have been used for over 65 years in medical and veterinary practice

Modes of action of antibiotics

1. Inhibition of nucleic acid synthesis

i)Fluoroquinolones (e.g. enrofloxacin norfloxacin etc)

Modes of action of antibiotics

ii)Rifampin)

2. Inhibition of metabolic pathways

(e.g Sulfonamide/Trimethoprim)

Modes of action of antibiotics contd…

3. Disruption of cell membrane
   (e.g. Polymixins & daptomycin
4. Inhibition of protein synthesis
   (e.g OTC. aminoglycosides (e.g. streptomycin), chloramphenicol)
5. Inhibition of cell wall synthesis -beta lactams (penicillins, cephalosporins, glycopeptides

What are the main uses of antimicrobials?

1. Specific therapy against known bacteria
2. Prophylaxis – e.g. Post operative care, intensive farming systems
3. Growth promotion in animal production

What is antimicrobial resistance?

-This is the ability of bacteria to survive exposure to one or more antimicrobials to which they would normally be susceptible.

-The gains in the use of antimicrobials is under threat due to frequent emerging resistance of cheap and effective ‘first choice or first line’ drugs.

Sequalae of increased AMR

- Delays in clinical recovery by patients (prolonged illness).
- Increased cost in therapy
- Greater risks of death or loss of production

How do bacteria become resistant to antibiotics?

i) Natural – e.g *E.coli* is resistant to penicillin

ii) Acquired resistance – due to *de novo* mutation or acquisition of resistance genes from other bacteria

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What are the mechanisms of acquired resistance?

-Bacteria produces enzymes that destroy antimicrobials

- Bacteria expresses efflux system that prevent antibiotic from reaching its intracellular target

- Bacteria modifies the drug's target site

- Drug undergoes an alternative metabolic pathway by bacteria

How do bacteria acquire new genetic material?

- Conjugation (mating)
- Transformation
- Transduction
- Acquisition of mobile genetic elements like transposons, integrons or gene cassettes

Where are the resistant genes located?

- Bacterial chromosomal DNA
- Plasmids (extra chromosomal DNA)

Why has resistance become an emerging issue?

1. Medical use accounts for more resistance in humans-70%
2. Veterinary use thought to account for <20 % of resistance
3. Agricultural use <3%?

Global concern for AMR

Initiatives

1997 WHO raised concern on this matter

1999 WHO Containment of AMR in medical use

2000 WHO Global Principles in Food Animals

1998 USDA/ FDA/ CDC Narms progamme

Global concern for AMR

DANMAP

SWEDRES

Norwegian Programme

Milestone in the development of antimicrobial resistance

Antim. Agent	Discovery	Clin. use	Res. Dev.
Penicillin	1940	1943	1943
Streptomycin	1944	1947	1947,1956
Tetracycline	1948	1952	1956
Erythromycin	1952	1955	1956
Vancomycin	1956	1972	1987
Nalidixic acid	1960	1962	1966
Gentamicin	1963	1967	1970
Fluoroquinolones	1978	1982	1986

Adapted from Schwarz and Chaslus-Dancla (2001)

Milestone in resistance development cont...

-AMR by itself is not new

- However the rate of increase is alarming compared to the world's ability to contain it

- There is dramatic upsurge in the spread of drug-resistance microbes

- AMR has thus become a "**public health issue worldwide"**

- Bacteria that are resistant to antimicrobials pose a threat to both human and animal health

- Essential life-saving antibiotics (e.g. fluoroquindones, 3rd generation cephalosporins become less effective against bacteria resulting in fewer alternatives

Milestone in resistance development cont...

-The misuse and overuse of antibiotics has reduced many cheap and common types ineffective against some bacteria

- Failures in clinical efficacy by antibiotics may lead to

  i) Prolonged illness – death and loss of production

  ii) Switching to second or third line drugs which are always much more expensive and sometimes much toxic

- Current trend of AMR development may suggest that some bacterial infections will have no effective therapy within the next ten years.

Why is AMR important in livestock production?

-Resistance in man is due to misuse and overuse by personnel and patient

- New emerging resistance in man is from food chain (meat, eggs, or exposure to faecal material)

Examples of food borne pathogenic bacteria:

Salmonella spp

Campylobacter

Commensal bacteria

Enterococcus spp

E. coli

What factors are likely to contribute to over usage of antimicrobials agents in food animals?

1. Lack of adequate knowledge on AMR by some cadre of livestock personnel
2. Empirical therapy based on clinical investigations rather than isolation, typing and of the pathogen
3. Availability of antibiotics over the counter in most developing countries
4. Insufficient regulatory and poor law enforcement
5. Industry may influence prescription patterns of some antibiotics

Issues related to AMR

- Several studies have demonstrated association between the use of antimicrobials in food animals and development of resistance e.g.. Fluoroquinolone resistant Salmonella and Campylobacter from animals and humans following use of fluoroquinolone in poultry
- FDA has recently banned use of fluoroquinolone in flock treatment in poultry
- In Kenya, Mapenay in his preliminary report has shown a correlation of antimicrobial use and resistance development
- VRE was shown to be due to the use of avoparcin as a growth promotant in food animals in Europe

Issues related to AMR cont...

-Vancomycin and all growth promotants have since been banned in Europe by 1997.

-After the ban prevalence of resistant *Enterococcus* in animals and poultry meat fell sharply

METHODOLOGY

1. Desk study from published literature
    - Ombui et al 1995 & 2000\
    - Mitema et al 2001
    - Kariuki et al 2002
    - Kikuvi et al 2006 and 2007
    - Ole- Mapenay 2007
    - Adelaide et 2008
2. Direct observation from retail chemist

Quantities (kg) of active substance of antimicrobial drugs per antimicrobial class administered in food producing animals in Kenya

	Year						
Antimicrobial class	1995	1996	1997	1998	1999	Total	Mean
Aminoglycosides	308.63	752.13	462.42	2421.52	843.88	4788.50	957.70
β-Lactams	352.90	572.86	480.65	1921.90	1195.45	4523.78	904.72
Tetracyclines	3664.41	15889.35	9215.98	7782.45	3324.75	39876.91	7975.38
Nitrofurans	5244.80	1155.00	55.00	660.00	385.00	7499.80	1499.96
Quinolones	25.08	7.70	6.28	177.57	252.14	468.78	93.76
Sulfonamides	6876.65	499.00	605.00	934.78	6604.40	15519.83	3103.96
Macrolides	0.00	165.00	0.00	7.79	0.00	172.79	34.56
Others (tiamulin)	24.75	69.30	23.76	0.00	0.00	11.81	23.56
Total	16497.22	19110.34	10849.09	13906.01	12605.62	72968.28	14593.66

Quantities of antimicrobial agents' consumption in kilograms 2000-2001

Antimicrobial agent	Year		Mean
	2000	2001	
Tetracycline	8481	9020	8751
Penicillin β-lactamase sensitive	504	521	513
Other Penicillins	18	18	18
Sulfa + Trimethoprim	148	86	117
Flouroquinolones	200	5204	2702
Aminoglycosides	318	127	222
Tiamulin	2	1	2
Others (Nitrofurans)	174	185	180
Total	**9845**	**15234**	**12540**

Table 3: Prevalence of resistance (%) to some antibiotics by *E. coli* in Kenya

[3]Adapted from Ole- Mapenay, 2007.

NA- Data not available.

Antimicrobial agent	Period		
	Prevalence (%) of resistance		
	1996-97	1998-99	2000-01
Tetracycline	60	13	14
Ampicillin	10	23	20
Cotrimoxazole	10	25	22
Streptomycin	NA	13	9
Chloramphenicol	8	NA	4
Nalidixic acid	1	0	NA
Ciprofloxacin	0	0	NA

Mean frequency of antimicrobial resistance among *Staphylococcus aureus* isolated from milk and meat in cattle samples in Kenya

	Percentage (%) resistance	
Antimicrobial agent	Milk isolates	Meat isolates
Ampicillin	22.7	61.9
Lincomycin	73.3	57.0
Co-trimoxazole	56.0	28.6
Penicillin	60.0	90.5
Minocycline	12.0	9.5
Erythromycin	13.3	19.0
Chloramphenicol	42.7	28.6
Methicillin	8.0	42.9

Adapted from Ombui *et al* 1995

Challenges

- Inadequate funding from government for in Public Health a challenge
- Equipment such as autoclaves, incubators and microscopes inadequate
- Collection of specimens not well supervised
- Several labs still require training support for their staff in order to undertake quality AST and surveillance.

Antimicrobial susceptibility tests for *Salmonella* isolates from food animals

Antimicrobial agent	MIC (µg ml-1)				% resistant
	Range	Mode	MIC_{50}	MIC_{90}	
Ampicillin	≤2 – 128	4	4	128	14.3
Chloramphenicol	4 – 128	8	8	8	7.1
Gentamicin	≤2 – 4	≤2	≤2	≤2	0.0
Kanamycin	≤2 - 16	8	8	16	0.0
Nalidixic acid	≤2 – 16	≤2	≤2	8	0.0
Streptomycin	4 – 64	16	16	64	14.3
Sulphamethoxazole/ trimethoprim (19:1)[a]	≤9.5/0.5 – 38/2	≤9.5/0.5	≤9.5/0.5	38/2	0.0
Tetracycline	≤2 - ≥256	4	4	16	7.1

Adapted from Kikuvi, 2006

What is the way forward and recommendation?

1. Prudent use of antimicrobial drugs in medical and veterinary medicine
2. Programmes to monitor the occurrence and development of antimicrobial resistance are highly desirable
3. Effective infection control (e.g. vaccinations) and hygienic practices should be implemented
4. Use of Critically Important Antibiotics (CIA) (3rd, 4th generation fluoroquinolones and cephalosporins) should be used only after antimicrobial susceptibility tests (AST)

5. Development of species guideline use of antimicrobial agents should be formulated in veterinary practice.

THANK YOU FOR LISTENING