Integrated AMR surveillance for foodborne bacteria in Africa: Guidance from AGISAR

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Defining One health

• A collaborative, multisectoral, and trans-disciplinary approach working at the local, regional, national, and global levels.

• **Goal:** achieving optimal health outcomes recognizing the interconnection between humans (public health), animals (vets and others), plants (plant health), and their shared environment (ecologists and others)
Overview of One Health concept

One Health aims at providing holistic, multidisciplinary prevention and treatment of human and animal diseases.

Takes into consideration the interconnections among these ecosystems that influence the epidemiology of zoonotic diseases.

Unfortunately, multidisciplinary collaboration has crucial barriers to overcome - ‘single discipline’ established structures.
Why a "One Health " Approach?

- Antimicrobial Resistance TRULY Global
- Antibiotics are used in many settings
  - Clinical medicine, communities, animal husbandry / aquaculture, horticulture
- Same classes of antimicrobial agents are used in
- different sectors
- Any use will select for resistance
- Resistant bacteria and resistant genes do not recognize
- geographic or ecologic borders
EPIDEMIOLOGY OF ANTIMICROBIAL RESISTANCE
What comprises integrated surveillance of AMR in foodborne bacteria?

Integrated surveillance of antimicrobial resistance in foodborne bacteria is the collection, validation, analyses and reporting of relevant microbiological and epidemiological data on antimicrobial resistance in foodborne bacteria from humans, animals, and food, and on relevant antimicrobial use in human and animals.
WHO Advisory Group on Integrated Surveillance on Antimicrobial Resistance (AGISAR)

WHO AGISAR was established in December 2008 to support WHO's effort to minimize the public health impact of antimicrobial resistance associated with the use of antimicrobials in food animals. The Group comprises over 30 internationally renowned experts in a broad range of disciplines relevant to antimicrobial resistance.
The terms of reference for AGISAR

1. Develop harmonized schemes for monitoring antimicrobial resistance in zoonotic and enteric bacteria,
2. Support WHO capacity-building activities in Member States for antimicrobial resistance and antimicrobial usage monitoring.
Integrated surveillance a key element of AGISAR-AMR Containment strategy

- Documentation of the situation
- Identification of trends
- Input data for:
  - Establishing associations antimicrobial usage and antimicrobial resistance
  - Risk assessment
  - Evaluation of effectiveness of interventions
- Identify need for interventions
- Basis for focused and targeted research
- Basis for communication
How these objectives are achieved

• Development of guidance for integrated AMR surveillance
• National capacity building projects, including Pilot and National focused projects
• Review and maintaining the WHO List of Critically Important Antimicrobials for Human Medicine.
Small/pilot Projects and Country Projects

An integrated AMR surveillance system for bacteria commonly transmitted by food should provide data that can be used to:

• document the levels of AMR in different reservoirs;
• identify AMR trends over time and from place to place;
• describe the spread of resistant bacterial strains and genetic determinants of resistance;
• study the association between AMR and use of antimicrobial agents;
• generate hypotheses about sources and reservoirs of resistant bacteria;
• identify, and evaluate the effectiveness of interventions to contain the emergence and spread of resistant bacteria;
• develop targeted epidemiological and microbiological research for source attribution studies, identify risk factors and clinical outcomes of infections caused by resistant bacteria;
• inform risk analysis of foodborne antimicrobial resistance hazards;
• guide evidence-based policies and guidelines to control antimicrobial use in hospitals, communities, agriculture, aquaculture, and veterinary medicine (ONE-HEALTH)
• support awareness efforts aimed at mitigating current and emerging hazards.
Training Courses

Microbiology training
- Global/Region-specific pathogens (e.g. Salmonella, Campylobacter, E. coli, V. cholera).
- Quality assurance
- Biosafety
- Antimicrobial Susceptibility Testing

Epidemiology training
- Outbreak detection and response
- Evaluation of surveillance systems
- Study design
- Source attribution
- Burden of disease

Joint Epidemiology and Laboratory
- Joint case studies
- Integrated surveillance
- Risk assessment
- Country Plans of Action
- Advocacy and communication
- Information sharing networks

ZNPHI-CSE AMR Workshop 4-6 March 2019
Funding available

1. Small grants for focused projects (USD 15-30,000)
   • These projects should include characterization of foodborne pathogens in at least two of the following sectors; human, food and animal. Characterization should include antimicrobial susceptibility testing. The duration of the project is one year and the total amount requested from WHO should not exceed 15,000 USD.

2. Country pilot projects (USD 75,000)
   These projects implemented at country level should include:
   • Sampling and characterization of foodborne pathogens (Salmonella spp and Campylobacter as a minimum) in human, food and animal sectors.
   • Antimicrobial susceptibility testing should be performed in pathogens and indicator bacteria (E. coli, Enterococcus).
   • Monitoring of antimicrobial usage in animals and in humans.
   • An inclusion of an attribution component will be an asset.
Resources and calls for applications

- [WHO | WHO Advisory Group on Integrated Surveillance of ...](WHO link)
- [www.who.int/foodsafety/areas_work/antimicrobial-resistance/agisar/en/](WHO link)
Pilot projects spread out globally

- Costa Rica
- Colombia
- Peru
- Argentina
- Uruguay
- Senegal
- Gambia
- Burkina Faso
- Ghana
- Togo
- Cameroon
- Ghana
- Uganda
- Rwanda
- Tanzania
- Lebanon
- Uzbekistan
- India
- Viet Nam
- Bangladesh
- Ethiopia
- Cambodia
- Paraguay
- Venezuela
- Argentina
- Paraguay
- Not applicable
Pilot Project 2010-2016

![Bar chart showing the occurrences of different bacterial species over the years: Salmonella, Campylobacter, and E. coli. The chart includes data for human, food, animal, and environmental sources.](image)
Awards for – 2017/18

- Ecuador
- Argentina
- Suriname
- Chad
- Albania
- Iran
- Bhutan
- Palestine
- Japan
- Philippines
- Ethiopia
- Thailand
- Tanzania
- Zambia
- Zimbabwe
Some Sentinel integrated surveillance data
An integrated surveillance of antimicrobial resistance in *Salmonella* spp, *Campylobacter* spp *Escherichia coli* and *Enterococcus* spp from gut of healthy food animals and retail meat outlets as well as from human clinical specimens in selected regions in Kenya
MDR Invasive NTS in Africa: A Killer in Slums and Poor Rural Children.

Epidemiology and Genomics of Invasive Nontyphoidal *Salmonella* Infections in Kenya

Samuel Kariuki and Robert S. Gesare
Centre for Microbiology Research, Kenya Medical Research Institute, Nairobi

**Background.** In Kenya, invasive nontyphoidal *Salmonella* (NTS) disease causes severe bacteremic illness among adults with human immunodeficiency virus (HIV) and especially among children <5 years of age infected with HIV or malaria, or who are compromised by sickle cell disease or severe malnutrition. The incidence of NTS disease in children ranges from 166 to 568 cases per 1

DOI 10.1099/jmm.0.46375-0

Invasive multidrug-resistant non-typhoidal *Salmonella* infections in Africa: zoonotic or anthropoponic transmission?

Samuel Kariuki,1,2 Gunturu Revathi,3 Nyambura Kariuki,3 John Kiuru,1 Joyce Mwituria,1 Jane Muyodi,1 Jane W. Githinji,4 Dorothy Kagendo,1 Agnes Munyalo1 and C. Anthony Hart2

Published in final edited form as:

**Antimicrobial resistance and management of invasive *Salmonella* disease**

Samuel Kariuki1,2, Melita A. Gordon1,4, Nicholas Feasey4,6, and Christopher M Parry6,7
1Centre for Microbiology Research, Kenya Medical Research Institute, PO Box 43640-00100, Nairobi
S. Typhimurium Resistance Trends from 2013-2016 (N=147)
MAPPING HOTSPOTS

- Typhi
- Enteritidis
- Typhimurium
- Heidelberg
- Braenderup
- Other
• 15 patients treated at AGUH 1 year apart.
• 12 S. Typhimurium isolates from blood.
• Sensitive to – Chloramphenicol, Ciproxin and Cefoxitin.
• Resistant to Nalidixic acid, Cotrim, Ampicillin, Ceftriaxone and Aztreonam. MIC Ceftriaxone >256 ; MIC Ciprofloxacin=0.12.
• Resistance to β-lactams, including to ceftriaxone, was associated with carriage of a combination of blaCTX-M-15, blaOXA-1, and blaTEM-1 genes on 304 kb plasmid.
The Kenyan Cholera outbreak route
### Emergence of ESBL-producing *Vibrio cholerae* in 2012

<table>
<thead>
<tr>
<th>Isolate Number</th>
<th>ESBL enzymes present</th>
</tr>
</thead>
<tbody>
<tr>
<td>38/2012</td>
<td>CTX-M, TEM</td>
</tr>
<tr>
<td>39/2012</td>
<td>none- negative control</td>
</tr>
<tr>
<td>57/2012</td>
<td>CTX-M, TEM</td>
</tr>
<tr>
<td>52/2012</td>
<td>CTX-M</td>
</tr>
<tr>
<td>54/2012</td>
<td>CTX-M, TEM</td>
</tr>
<tr>
<td>58/2012</td>
<td>CTX-M, TEM</td>
</tr>
<tr>
<td>64/2012</td>
<td>CTX-M, TEM</td>
</tr>
<tr>
<td>68/2012</td>
<td>CTX-M, TEM</td>
</tr>
<tr>
<td>56/2012</td>
<td>CTX-M, TEM</td>
</tr>
<tr>
<td>43/2012</td>
<td>CTX-M</td>
</tr>
<tr>
<td>74/2012</td>
<td>CTX-M, TEM</td>
</tr>
<tr>
<td>73/2012</td>
<td>CTX-M, TEM</td>
</tr>
<tr>
<td>78/2012</td>
<td>CTX-M, TEM</td>
</tr>
<tr>
<td>75/2012</td>
<td>CTX-M, TEM</td>
</tr>
<tr>
<td>76/2012</td>
<td>CTX-M, TEM</td>
</tr>
<tr>
<td>44/2012</td>
<td>TEM</td>
</tr>
<tr>
<td>41/2012</td>
<td>CTX-M, TEM</td>
</tr>
<tr>
<td>45/2012</td>
<td>CTX-M, TEM</td>
</tr>
<tr>
<td>42/2012</td>
<td>CTX-M, TEM</td>
</tr>
</tbody>
</table>
WGS shows 3 main regions on the pVC_ESBL

1. SXT R319 carrying the floR-dhfrA1-strA-StrB-sul2 genes.
2. Class 1 integron carrying aadB-arr2-bla_{TEM1B}-cmlA-bla_{OXA-10}-arr2-aadA1 cassettes and with sul1 and a truncated qacEΔ1 gene at the 3’ conserved end.
3. Resistance genes inserted into the plasmid backbone encoding resistance to third generation cephalosporins (bla_{CTX-M-15}), aac(3)-IIc that confer resistance to Streptomycin, kanamycin and tobramycin and a putative gene for tunicamycin resistance.
Escherichia coli as a marker of contamination and AMR transmission along meat value chain
Susceptibility for *E. coli* from children treated at District Hospital 2010-2013, (n=325)

Highest prevalence of resistance was observed for commonly used antimicrobials including ampicillin, co-trimoxazole, streptomycin and amoxillin-clavulanic acid.
Antibiotic susceptibility patterns for E. coli isolated from poultry in small scale farms in Thika, n=350

Note small (4%) resistance to ceftazidime, co-amoxiclav (7%), ciprofloxacin (4%)
Resistance phenotypes *E. coli* from poultry in small scale farms in Thika town and Thika chicken slaughter house; N=300
Antibiotic susceptibility patterns for *E. coli* isolated from effluent in abattoirs and their proportions in percentage; N=55

**Antibiotic susceptibility patterns among the organisms isolated from effluent in abattoirs**

- **Ampicillin**
- **Co-Trimoxazole**
- **Kanamycin**
- **Augmentin**
- **Tetracycline**
- **Ciprofloxacin**
- **Nalidixic acid**
- **Chloramphenicol**
- **Gentamycin**
- **Ceftriaxone**
- **Streptomycin**

Proportion in %

- **Sensitive (s)**
- **Intermediate (I)**
- **Resistant (R)**

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<table>
<thead>
<tr>
<th>District</th>
<th>Village</th>
<th>No. of Households/questionnaires covered</th>
<th>Type and total No. of animals reared</th>
<th>Most common antibiotic/drug used for treatment/prophylaxis/growth promotion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thika west</td>
<td>Kiganjo</td>
<td>5</td>
<td>3100 chicken</td>
<td>Fluquin (Enrofloxacin); Biosol (Trimethoprim sulphamethoxazole); Hipralona Entos (Enrofloxacin); Fosbac; Molar plus multivitamins</td>
</tr>
<tr>
<td>Landless</td>
<td></td>
<td>6</td>
<td>6524 chicken</td>
<td>Hipralona Entos (Enrofloxacin); Agdoxythyl; Keplox 2.5%; Colive; Alamycin; Levacide; Neoxy-vitamin WSP; OTC plus (Oxytetracycline)</td>
</tr>
<tr>
<td>Muthaiga</td>
<td></td>
<td>4</td>
<td>3896 chicken</td>
<td>Neoty-VCA WSP; Aliseryl WS; Biosol (Trimethoprim sulphamethoxazole); Fosbac</td>
</tr>
<tr>
<td>Munyu</td>
<td></td>
<td>5</td>
<td>5060 chicken</td>
<td>Kepcox; Coacidistat; Bremalan; Levacide poultry; Bedgen-40 liquid; Medicated liquid paraffin; Alamycin</td>
</tr>
<tr>
<td>Athena</td>
<td></td>
<td>1</td>
<td>1000 chicken</td>
<td>Amoxyvet; Fosbac; Levacide</td>
</tr>
<tr>
<td>Gatundu North</td>
<td></td>
<td>13</td>
<td>7760 chicken</td>
<td>Aciracox; Levacide; Poltricin; Vita poultry (multivitamin); Oxytetracycline; Doxyvet- SOS, Neoxy vitamin; Oxyfurazole; Limoxin; Amitotal; Egg boost</td>
</tr>
<tr>
<td>Gatono</td>
<td></td>
<td>4</td>
<td>4780 chicken</td>
<td>Trimovet; Alamycin; Amidiostat</td>
</tr>
<tr>
<td>Kihingo</td>
<td></td>
<td>1</td>
<td>500 chicken</td>
<td>Multiflox (multivitamin)</td>
</tr>
<tr>
<td>Gaisugi</td>
<td></td>
<td>2</td>
<td>500 chicken</td>
<td>OTC plus (oxytetracycline); Alamycin</td>
</tr>
<tr>
<td>Nguna</td>
<td></td>
<td>1</td>
<td>13,000 chicken</td>
<td>Bedgen O liquid; Limoxin</td>
</tr>
<tr>
<td>Nyando</td>
<td>Ko bango</td>
<td>1</td>
<td>650 chicken</td>
<td>Oxytetracycline</td>
</tr>
<tr>
<td>Kisumu East</td>
<td>KARI</td>
<td>2</td>
<td>127 chicken</td>
<td>Biotrim- vet plus; Aliseryl WS</td>
</tr>
<tr>
<td>Kisauni</td>
<td></td>
<td>2</td>
<td>100,000 Chicken; 10,00 Cows</td>
<td>Fosbac; Aidamycin</td>
</tr>
<tr>
<td>Kwale</td>
<td></td>
<td>4</td>
<td>4300 Chicken; 11 cows</td>
<td>Biotrin; Esb3 30%; veriben</td>
</tr>
</tbody>
</table>
For antibiotic use at small holder settings, evidence abounds everywhere!
Veterinary Antimicrobials Imported into Kenya through the Single Window system (July 2016-January 2017)

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Quantity (Kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxytetracycline Hydrochloride</td>
<td>2,560,861</td>
</tr>
<tr>
<td>Tylocin</td>
<td>1,026,000</td>
</tr>
<tr>
<td>Penicillin + Streptomycin</td>
<td>830,004</td>
</tr>
<tr>
<td>Amprolium</td>
<td>443,877</td>
</tr>
<tr>
<td>Chlorotetracycline</td>
<td>234,879</td>
</tr>
<tr>
<td>Penicillin</td>
<td>64,654</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>21,652</td>
</tr>
<tr>
<td>Gentamycin</td>
<td>16,200</td>
</tr>
<tr>
<td>Sodium sulphadimidine</td>
<td>11,245</td>
</tr>
<tr>
<td>Sulfamethoxazole + Trimethoprim</td>
<td>3,322</td>
</tr>
<tr>
<td>Ampicillin + Cloxacillin</td>
<td>856</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>321</td>
</tr>
<tr>
<td>ZNPHI-CSE AMR Workshop 4-6 March 2019</td>
<td></td>
</tr>
</tbody>
</table>
AMU in Livestock production – crucial insights from KAP study
Commonly used antimicrobials

• The most commonly used antibiotics in livestock production are:
  – **Treatment**- Penicillin + Streptomycin combo for cattle and pigs and Biotrim for chicken
  – **Prophylaxis**- Penicillin G for cattle, Alamycin (Oxytetracycline) for chicken and Tetracycline for pigs
  – **Growth promotion**- Neoxy Vitamins (Oxytetracycline + Neomycin) for cattle, Alamycin (Oxytetracycline) for chicken and oxytetracycline for pigs. Others used for growth promotion include Penicillin G for cattle and Neoxy Vitamins (Oxytetracycline + Neomycin) for chicken

• Majority of farmers were aware of antimicrobial resistance, but fear of losses from disease led to more use.

• Biosecurity was widely practiced, if improved could reduce the need for antibiotic use
Individual vet. supplier, Agro-vet shop and regular pharmacy/chemist were the common sources of antibiotics to farmers with **Individual vet. supplier (75%)** being the most common supplier of antibiotics to farmers.
Major findings among food animals

• Meat products contaminated with \textit{E. coli}, \textit{Salmonella}, \textit{Campylobacter}; highest contamination rates in retail meats at lower end markets

• Contamination rates higher in chicken at retail markets compared to the commercial abattoir higher for \textit{E. coli}, \textit{Salmonella} and \textit{Campylobacter} in comparison to beef.

• Antimicrobial resistance highest among isolates from poultry, then pigs and cattle

• Poor hygiene at local settings major risk factor for contamination and AMR
Major findings among food animals

• Oxytetracycline most commonly used antibiotic, especially among poultry small scale farmers.
• In addition farmers often used fluoroquinolones (including norfloxacin and enrofloxacin), erythromycin, variety of sulphonamides and co-trimoxazole in both poultry and cattle rearing.
• Antimicrobials easily obtainable from shops barely 10-15 min walking distance.
• Most stockists could give information on usage but generally farmers gave different doses of antibiotics and multivitamins to their flocks.
• Less than 20% of farmers understood the dangers of misuse of antibiotics
The GARP-MoH-MoALF One-Health Team

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