“How Many AMR Deaths Will It Take Before We Act?”

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Antibiotics have been used in animal husbandry for decades with two main purposes:

- **Medical treatment of infections**
- **Improvement of animal growth** → optimizing the absorption of nutrient through reduction of bacterial growth in the intestinal tract

**Antibiotic Growth Promoter (AGP)**

AGP use was further encouraged after 1953 following the publication of *Nutritional Effects of Antibiotics* by Thomas Jukes and William Williams.
Global Trends in Antimicrobial Use in Food Animals

• Global use of antimicrobials in food animal production is projected to increase by 67 percent from 63,000 tons in 2010 to 106,000 tons by 2030.

• Estimated global average annual consumption of antimicrobials to produce 1 kg of meat:

Deaths Attributable to AMR Every Year

At least 700,000 deaths worldwide are caused by drug-resistant bacteria each year, slashing about US$100 trillion from the combined gross domestic product and an additional $210 trillion from secondary effects.

In 2014, Dr. Harry Parathon, chairman of the Antimicrobial Resistance Control Committee (ARCC) Ministry of Health, reported that at least 130,000 people died per year due to antimicrobial resistance. There are no new figures being published ever since.

Source: The Review on Antimicrobial Resistance chaired by Jim O’neill (May, 2016); UN IACG on AMR final report (April, 2019); Program Pengendalian Resistensi Antimikroba, presentation by Dr Harry Parathon
How does antibiotic resistance occur?

1. High number of bacteria. A few of them are resistant to antibiotics.
2. Antibiotics kill bacteria causing the illness, as well as good bacteria protecting the body from infection.
3. The resistant bacteria now have preferred conditions to grow and take over.
4. Bacteria can even transfer their drug-resistance to other bacteria, causing more problems.
Drivers of AMR

- Misuse and overuse of antimicrobials; poor access to quality, affordable medicines, vaccines and diagnostics; lack of awareness and knowledge; population movement
- Lack of access to clean water, sanitation and hygiene; poor infection and disease prevention and control in health care facilities and farms
- Discharge of waste from health care facilities, pharmaceutical manufacturing and farms
- Misuse and overuse of antimicrobials; poor infection and disease prevention and control in food & feed
- Poor infection and disease prevention and control; transmission of resistant pathogens in food production, storage, distribution and preparation

Source: UN IACG on AMR final report (April, 2019)
Antimicrobials are given to food producing animals.

Drug resistant bacteria develop in animals.

Drug resistant bacteria can spread to the environment.

...and to food.

Drug resistant bacteria can be transferred to people by eating food.

...and can be more severe and difficult to treat than those from drug susceptible bacteria.

Antimicrobial Resistance (AMR) along the food chain

Source: WHO (2017)
The Occurrence on MCR-1 Gene Bacteria in Indonesia

PREVALENCE OF mcr-1 COLISTIN RESISTANCE GENE IN Escherichia coli ALONG BROILER MEAT SUPPLY CHAIN IN INDONESIA

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Running title: Prevalence of mcr-1 gene in Escherichia coli along broiler meat supply chain

“The MCR-1 gene was found in 89.66% colistin resistant E.Coli isolates.”
– Dr Maria Fatima Palupi

ABSTRACT

Colistin is the last drug choice for dealing with carbapenem-resistant Enterobacteriaceae; therefore, this drug is very crucial for human health. The discovery of a plasmid-mediated colistin resistance gene, mobilized colistin resistance-1 (mcr-1), signals a significant global health threat. Colistin sulfate is an antimicrobial agent which has been approved for use in broilers in Indonesia. The purposes of this study were to measure the prevalence of colistin resistant E. coli and to detect the mcr-1 colistin resistance gene in E. coli, and E. coli O157:H7 in the entire supply chain of broilers in Bogor Regency, West Java Province, Indonesia. Samples were taken from flocks that use colistin sulfate (cloacal swabs, drinking water, and litter), small-scale poultry slaughterhouses (fresh meats and plucker swabs), traditional markets (fresh meats), and small restaurants (cooked meats). Isolation of E. coli was done on each sample and 493 isolates were obtained. All E. coli isolates were then tested for their susceptibility to colistin sulfate by the agar dilution method. Detection of mcr-1 gene from colistin resistant isolates (minimum inhibitory concentration > 2 µg/mL) was conducted using polymerase chain reaction. The prevalence of colistin resistant E. coli from all isolates was 11.76% (CI 95%; CL 9.21–14.91%), and the prevalence of mcr-1 gene was 10.55% (CI 95%; CL 8.13–13.57%). There was a very good agreement between colistin resistance phenotype and mcr-1 gene (κ = 0.939). The mcr-1 gene was found in 89.66% colistin resistant E. coli isolates. Two colistin resistance and mcr-1 carrying gene isolates were identified as E. coli O157:H7 serotype. This study was the first research on mcr-1 gene in Indonesia which covers the entire supply chain of broiler meat from farms to consumers. These results showed the necessity to emphasize a reduced use of colistin sulfate in broiler management and to improve biosecurity measure, not only in farms but also in the entire supply chain of broiler meat.

Keywords: broiler, colistin, Escherichia coli, mcr-1, supply chain
“Prevalence of MCR-1 Colistin Resistance Gene in *E. Coli* along Broiler Meat Supply Chain in Indonesia”

The sample for this study was taken from 4 pathways:

1. Flocks that use colistin sulfate (cloacal swabs, drinking water, and litters);
2. Small-scale poultry slaughterhouses (fresh meat and plucker swabs);
3. Traditional markets (fresh meats);
4. Small restaurants near the traditional market (cooked meats).

All of the *E. Coli* isolates were tested for their susceptibility to colistin sulfate by the agar dilution method. Based on the study, the MCR-1 gene was found in 89.66% colistin resistant *E. Coli*.

These results showed the necessity to emphasize a reduced use of colistin sulfate in broiler management and to improve biosecurity measure, not only in farms but also in the entire supply chain of broiler meat.

Indonesia’s National Action Plan on AMR (2017-2019)

There are five strategic objectives covered on the NAP:

1. Improve awareness and understanding of antimicrobial resistance through effective communication, education and training.
2. Strengthen the knowledge and evidence base through surveillance and research.
3. Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures.
4. Optimize the use of antimicrobial medicines in human and animal health.
5. Develop the economic case for sustainable investment in new medicines, diagnostic tools, vaccines and other interventions.

Yet urgent matters, such as investing in the development of new molecules, international coordination and maximum antibiotic consumption targets in animal husbandry, have not been addressed.

The NAP lacks of enforcement, including law enforcement.
Key Challenges in Implementing NAP

**Awareness & political will**
Many countries need a stronger narrative that can engage both policymakers and the general public, by linking AMR to national interests, such as food, health, environment and economic development.

**Data & technical capacity**
Countries need data on antimicrobial resistance, use and access but science in these areas is expensive and complex, and many countries lack the technical capacity and know-how to analyse such data and develop data-informed actions.

**Finance**
Public and private sector finance is required to build the systems and support infrastructure to prevent infection in the first instance, and then enable sustainable access to, and use of antimicrobials.

**Coordination**
A lack of human, technical and financial resources, combined with complex logistics and ways of working, hampers coordination, across both sectors and stakeholder groups.

**Monitoring**
Few countries have their own monitoring systems, and even fewer have incorporated these into wider health and agriculture systems.

Source: UN IACG National Action Plans (June, 2018)
China Study: Cost of an AMR Outbreak
Based on the 2003 severe acute respiratory syndrome (SARS) outbreak model

China’s antibiotic profile
- Produce: 90% of the world’s antibiotic crude drugs
- Export: 70% of the world’s total antibiotic
- Consumption: 160,000 tons/year (50% percent of the total global consumption)
- Consumption in livestock: 50% of antibiotic consumption

Direct cost of an AMR outbreak:
467 billion Yuan = $67 billion
In the first 2 weeks of AMR outbreak (for animal husbandry sector alone)

Economic Analysis of AMR Shock to Demand for Food Animal Product:
- Domestic production of food producing animals would shut down and foreign exports to the domestic market would come to a full stop.
- Demand for domestic meat and poultry products would drop drastically while the demand for antibiotics-free foreign products that come from high-standard countries may increase substantially.
- Consequences for the domestic production as unemployment would rise and security of food supply would be under threat in addition to the massive deaths of humans and animals.

### China Study: Cost of an AMR Outbreak

Based on the 2003 severe acute respiratory syndrome (SARS) outbreak model

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**Causes of Antibiotic Misuses in China**

<table>
<thead>
<tr>
<th>Causes</th>
<th>descriptions</th>
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<tbody>
<tr>
<td><strong>1 Maximizing output</strong></td>
<td>Producers administer low doses of antibiotics to healthy food animals to promote faster growth and offset the effects of overcrowding and poor sanitation. Roughly over 60 percent of antibiotics used by food producing animals was directed to promoting faster growth of the animals.</td>
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<td><strong>2 lack of skills &amp; food safety consciousness</strong></td>
<td>Small-scale farmers placed high expectations on the power of drugs to secure animals’ health. Many continued to use the same drugs for a long time and when the effectiveness of the drugs declined they tried to use them more intensively or combine with other antimicrobials. Also many farmers relied on their past experience or commercial ads in their choice of veterinary medicine. Human medicine is often used food animals.</td>
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<td><strong>3 Inadequate institutional support</strong></td>
<td>Administration of antibiotics is shared by two government agencies. Lack of accountability is inevitable. Conflict of goals is another problem. The Ministry of Agriculture is responsible for both the development of agriculture and administration of the country’s antibiotics use in animals. Confusion in responsibilities among producers, local and central governments also exists.</td>
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<td><strong>4 Absence of role by vets</strong></td>
<td>High demand by animal pets induced vets into urban cities. The role of vets is often taken over sales people from antibiotics companies.</td>
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AMR consequences for Indonesia?

• Various global studies found **high antibiotic residues in commercial poultry meat and milk tanks**. There is no guarantee this is not happening in Indonesia.
• Indonesia is among the **top 4 countries with the highest risk of a potential multi-drug resistant bacterial outbreak**—along with China, India, and Pakistan.
• **An export downturn of shrimp** (one of the major export commodities):
  o Total value of fisheries export, including shrimp: **$ 4.2 billion** (2017).
  o The EU has banned the importation of products of animal origin produced using antibiotics. This step will possibly be followed by Japan and the US, top 2 destinations for Indonesian shrimp exports.
  o Competition with zero-antibiotic shrimp of Ecuador in the US market.
• **Tourism** will come to a virtually **complete stand still**.
• **Bilateral trade** will be seriously affected.
• **Foreign direct investment** will include so much **risks** that investors will choose for other option.
Recommendations

• The discovery of the MCR-1 gene in Palupi’s study should sound alarm bells. Therefore, we **urgently need alternative feed additives to antibiotic growth promoters.** → Rapid authorization of alternatives to AGP.

• Solve the issue within the inter-ministerial governance of AMR in Indonesia:
  • Complex challenges that involve intersection between various stakeholders’ interest, including profit motives.
  • Complexities between different government agencies in term of regulations and focuses (Ministry of Health, Ministry of Agriculture, Ministry of Marine Affairs and Fisheries)

• A national emergency approach is required with the involvement of all relevant ministries, **scientists** and key stakeholders, such as **food producers** and **consumer groups**, as stipulated in the National Action Plan. Indonesia must come up with **effective tangible actions** that are **realistic** and **implementable**.

**With President Joko “Jokowi” Widodo preparing for his second term in office, there is no better moment to take the AMR threat more seriously.**
Thank you!