Antimicrobial Use in Livestock Production and Antimicrobial Resistance in the Asia-Pacific Region

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Antimicrobial resistance (AMR) is a growing global threat across drug classes and around the world. Although much of the evolving antimicrobial resistance can be attributed to (mis-)use of antimicrobials in humans, research by international scientific bodies supports the conclusion that the overuse of drugs in food animal production is a threat for continued availability of effective treatment of human diseases. Around 80% of total global antimicrobial use occurs in livestock, most of this use being for prophylactic purposes and growth promotion.

Resource-poor countries are particularly vulnerable to AMR as infectious diseases, including those caused by bacteria, are responsible for a large share of their disease burden and they therefore rely on effective antimicrobial medicines for treatment. Unfortunately, little quantitative information is available about antimicrobial use in the rapidly growing livestock sectors of Asia-Pacific countries but it has been estimated that the region constitutes nearly half of the global animal antimicrobial market, total sales in the region amounting to about US$ 1.8 billion in 2011.

At the 36th Session of the Animal Production and Health Commission for Asia and the Pacific (APHCA) delegates from 15 countries in the Asia-Pacific region presented and reviewed the extent of antimicrobial use (AMU) in livestock production and AMR in micro-organisms isolated from livestock and livestock products. (Details are available at: http://www.aphca.org/index.php?option=com_content&view=article&id=322&Itemid=257).

Antimicrobial Resistance in Asia-Pacific

Only limited data on the use of antimicrobials in farm animals in Asia can be found in the published literature and few countries in the region have sound information on the amount of antimicrobials used in livestock production. However, indirect evidence of widespread (mis-)use of antimicrobials in livestock production in the region is provided by the high prevalence of AMR to selected compounds found in enteric microorganisms isolated from food-producing animals and retail meat across a sample of Asian countries. Some findings from resistance studies conducted on *E. coli, C. jejuni* and *Salmonella spp*. isolates from poultry and poultry meat in the region are summarized in the following tables.

AMR in *E. coli* isolates from poultry

Country	No of isolates	Percentage of resistant isolates				
		AMP	CIP	CHL	GENT	TET
Cambodia	180	64	24	28	6	62
Indonesia	402	68	nd	11	14	81
Myanmar	13	60-70	46	60-70	8	60-70
Sri Lanka	?	88	35	18	15	73
Vietnam (M[1])	206	80	50	61	23	96
Vietnam (S[2])	202	71	20	66	16	92

AMP = Ampicillin; CIP = Ciprofloxacin, CHL = Chloramphenicol; GENT = Gentamicin; TET = Tetracycline
[1] Medium size farms, [2] Small farms

AMR in *C. jejuni* isolates from poultry

Country	No of isolates	Percentage of resistant isolates				
		AMP	CIP	ERY	GENT	TET
Cambodia	28	nd	61	18	nd	43
Cambodia	69	nd	20	3	0	nd
Philippines	12	83	92	31	92	92
Sri Lanka	?	20	83	9	5	43
Thailand	32	31	81	9	nd	41

AMP = Ampicillin; CIP = Ciprofloxacin, ERY = Erythromycin; GENT = Gentamicin; TET = Tetracycline

AMR in *Salmonella spp.* isolates from poultry

Country	No of isolates	Percentage of resistant isolates				
		AMP	CIP	CHL	GENT	TET
Bangladesh	12	75	0	0	0	50
Cambodia	152	17	3	6	1	21
Malaysia (live)	38	nd	nd	3	nd	14
Malaysia (meat)	11	55	9	46	40	55
Sri Lanka	?	7	nd	0	0	7
Thailand	211	49	1	28	12	59
Vietnam (M)	50	20	0	22	2	32
Vietnam (S)	36	17	3	19	3	33

AMP = Ampicillin; CIP = Ciprofloxacin, CHL = Chloramphenicol; GENT = Gentamicin; TET = Tetracycline
[1] Medium size farms, [2] Small farms

Although the above results do not stem from systematic and standardized assessments of the prevalence and extent of AMR, they clearly demonstrate that resistance to a range of compounds has become fairly common in bacteria isolated from poultry and poultry products. Across studies, more than half of the *E. coli* isolates tested showed resistance to Ampicillin and Tetracycline, followed by resistance to Chloramphenicol, Ciprofloxacin and Gentamicin. A high proportion of *C. jejuni* isolates was resistant to Ciprofloxacin and Tetracycline with generally lower prevalence of resistance to Erythromycin. Overall, the prevalence of AMR in *Salmonella spp*. isolates appears to be lower than in *E. coli* and *C. jejuni*, but a significant share of *Salmonella spp*. isolates was resistant to Ampicillin and Tetracycline. Most of the above isolates were resistant to more than one class of antimicrobials.

Consequences

Many previously 'easily' curable infectious diseases, both in humans and animals, are becoming increasingly difficult and costly to treat as single and multi-drug resistance grows. Proliferation of AMR will put many lives at risk. In addition to the cost of human suffering, the added health care cost occasioned by antimicrobial resistant infections (ARI) is staggering. One study in the USA estimated infection with antibiotic resistant microbes to be associated with an 11-day increase of hospitalization, increasing medical costs per patient by around US$20,000 with total societal costs amounting to approximately US$35 billion (year 2000). In addition, infection with AMR microbes resulted in a 2.2 fold increase in the risk of death as a consequence of infection.

Little quantitative information on the cost of AMR in Asia has been generated, but given Asia's high burden of gastrointestinal infections, a significant share of which is likely to be caused by pathogens associated with livestock, the cost cannot be trivial even without considering the additional losses ineffective drugs cause to the livestock industries. Society is at risk of losing one of the most important tools for human and animal disease management, at a time when animal and human population densities continue to increase overall and in a highly clustered fashion, which results in increased risk of transmission of microbes between species and of resistance genes between microbes.

Society can no longer rely mainly on the expectation that a continuous stream of new antimicrobials will come onto the market, as pharmaceutical companies find it increasingly difficult justify the investment into research and development in this area in an extremely competitive global market.

AMR is a complex problem and the contributing factors to its emergence and spread are diverse and multifaceted. Numerous stakeholders from across multiple sectors have a role to play in AMR containment but, unfortunately, coordinated containment activities have been lacking, especially at the regional level.

Ways Forward

APHCA delegates recognised that AMR is a global problem but that local action in each member country was needed to underpin regional and global risk reduction measures. A synthesis of feasible local actions is given below:

1. Undertake a *situational analysis* (to improve understanding of what is occurring with AMU and AMR) to understand the roles and motivations of all stakeholders in antimicrobial value chains in their respective countries;
2. Establish a *National Task Force on Antimicrobials* that is multidisciplinary and cross-sectoral to provide a forum to lead policy development and support action on AMU and AMR;

3. Improve *awareness* at different levels (including farmers and farmer organizations; veterinarians, para-veterinarians, veterinary faculty staff members; policy-makers; consumers and civil society);
4. Develop, review and improve *practical legislation and regulatory frameworks*, including compliance capacity, for AMU and AMR:
   - Develop national policy;
   - Develop guidelines and regulations to encourage responsible and prudent use of antimicrobials (e.g. on prescription for both animal and human AMU).
5. Build *capacity* (of both human resources and laboratory infrastructure) for monitoring AMU and surveillance of AMR:
   - Review current national capacity;
   - Explore options for capacity-building to fill gaps identified.
6. Undertake *monitoring and surveillance* of AMU and AMR:
   - Collect data on AMU (e.g. types and of volume of antimicrobials used, purpose of use);
   - Design and undertake targeted surveillance for AMR;
   - Explore options for developing a national programme for monitoring AMU and surveillance of AMR.
7. Promote *alternatives to AMU*, particularly improved infection control, good husbandry practices, and farm biosecurity;
8. Develop and implement communications and public *awareness* on AMU and AMR.

It is not feasible to undertake all of these quickly but it is important to undertake a situational analysis to understand the roles and motivations of all stakeholders in antimicrobial value chains in their respective countries. AMU is not just a technical issue and that addressing it and the risks from AMR require due consideration of social, economic, environmental, ethical and policy factors.