REVIEW ARTICLE

Emerging drug resistant pathogens from food animals: Balancing food security and safety in developing countries

Clement Meseko[1], Melvin Sanicas*[2], Dirga Rambe[3], Doudou Diop[4]

*Corresponding author's email address: melvin.sanicas@gmail.com

[1]*Animal Influenza Division, Infectious and Transboundary Animal Diseases, National Veterinary Research Institute, Vom Nigeria*
[2]*Clinical Development, Takeda Pharmaceuticals International AG, Zurich, Switzerland*
[3]*Internal Medicine, Omni Hospital, Jakarta, Indonesia*
[4]*Program for Appropriate Technology in Health (PATH), Dakar, Senegal*

ABSTRACT

Drugs are used essentially to treat illnesses in humans and animals. When metabolized in food animals, they are harmless, but residues may remain in tissues, meat and milk that can present risks in the food chain. A long-term consequence of drug residues in food of animal origin is the development and emergence of antimicrobial resistance (AMR). Generally, increasing the use of antimicrobials in medical and veterinary practice exacerbates AMR. Spread of infection or resistant pathogen or resistance genes in the environment can be explained by the close link between humans, animals, and the environment. The public health and economic impact of AMR have been estimated to be around 100 trillion US dollars each year and food animals are a major reservoir of AMR microorganisms in many low and middle income countries (LMIC). However,due to the lack of data on food-borne pathogens and antimicrobial usage is a challenge in the control of AMR in LMICs where the food industry is heterogeneous, largely informal, and unregulated. Emergence and transmission of AMR in developing countries are linked to food of animal origins, but the awareness of this relationship is low. Overall, the challenge of food insufficiency also described as food insecurity and a lack of adequate food safety measures can worsen the incidence and persistence of AMR. This review summarizes the issues and challenges of emerging drug resistant pathogens from food animals in developing countries, and highlights the importance of a holistic perspective in addressing AMR in humans in the context of the One Health approach.

Keywords: *food animals, foodborne pathogens, antimicrobial resistance, developing countries, One Health*

Introduction

Drugs are used for the prevention and treatment of illnesses or improvement of health and welfare in humans and animals. Naturally, drugs are metabolized and broken down to harmless products that are excreted from the body following their administration. However, some residues or metabolites remain in tissues, meat, milk and other food products and may present unforeseen risks in the food chain when consumed. Among the consequences and long-term effects of antimicrobial metabolites in food of animal origin is the development and emergence of antimicrobial resistance (AMR) [1]. Intensified use of antimicrobials in medical and veterinary practice also exacerbate AMR. Plants are typically consumed by animals, which are then consumed by humans. The food chain is one of several ways emerging AMR can be "transferred" to humans. Though pesticide may also be found as residues in vegetables when directly consumed by humans, most of the risks associated with antimicrobial residues are related to animal source foods [1,2].

The human-animal-environmental interface is interlacing, and the close interaction between the three components suggests that infections or resistance coming from humans or animals, foods or farms are likely to spread within the nexus [3,4]. Livestock production contributes significantly to the livelihood of peasant farmers in Africa and Asia. This also predisposes them to zoonotic diseases (also called zoonoses) which account for around 1 in 4 of the infectious disease burden in developing countries. In communities where humans live close to livestock and wildlife, the risk for zoonoses increase proportionally with the prevalence of poverty [5,6]. In 2010, the World Health Organization (WHO) estimated the burden of foodborne diseases globally to be a major public health problem, causing 600 million cases, 58% of which were due to pathogenic bacteria [7]. Emerging AMR in these pathogens may be spread in food animals to human and the environment.

Foods of animal origin and foodborne pathogens in AMR

Foods of animal origin play an essential role in human's diet, health and nutrition [8]. Livestock and game are important sources of high quality protein required in cell synthesis and growth. Protein plays a crucial role in various cellular functions including cell signaling, cell adhesion, and the interaction of the cells of the immune system [9]. Several life-sustaining biochemical reactions, such as anabolism and catabolism, are catalyzed by proteins [10].

The importance of animal protein intake by a human cannot be over emphasized, being critical for development, growth, and health. While there are many sources of protein, food of animal origin provides better quality protein – higher amino acid content and easier digestibility [11]. Though animal protein is essential and valuable, it is often more expensive and less affordable in developing countries where livestock production is increasing in volume through modern approaches and enhancement including the use of antibiotics.

Animal protein enhances the quality of plant-based diets and provides various micronutrients not found in sufficient quantities from plant sources. In developing countries, essential animal proteins are often inadequate, especially in children, older adults, and pregnant or breastfeeding women with increased nutritional requirements. These essential proteins are found in milk and seafood containing branched chain amino acids (BCAAs; leucine, isoleucine, valine) and taurine, which act beneficially on glucose metabolism and

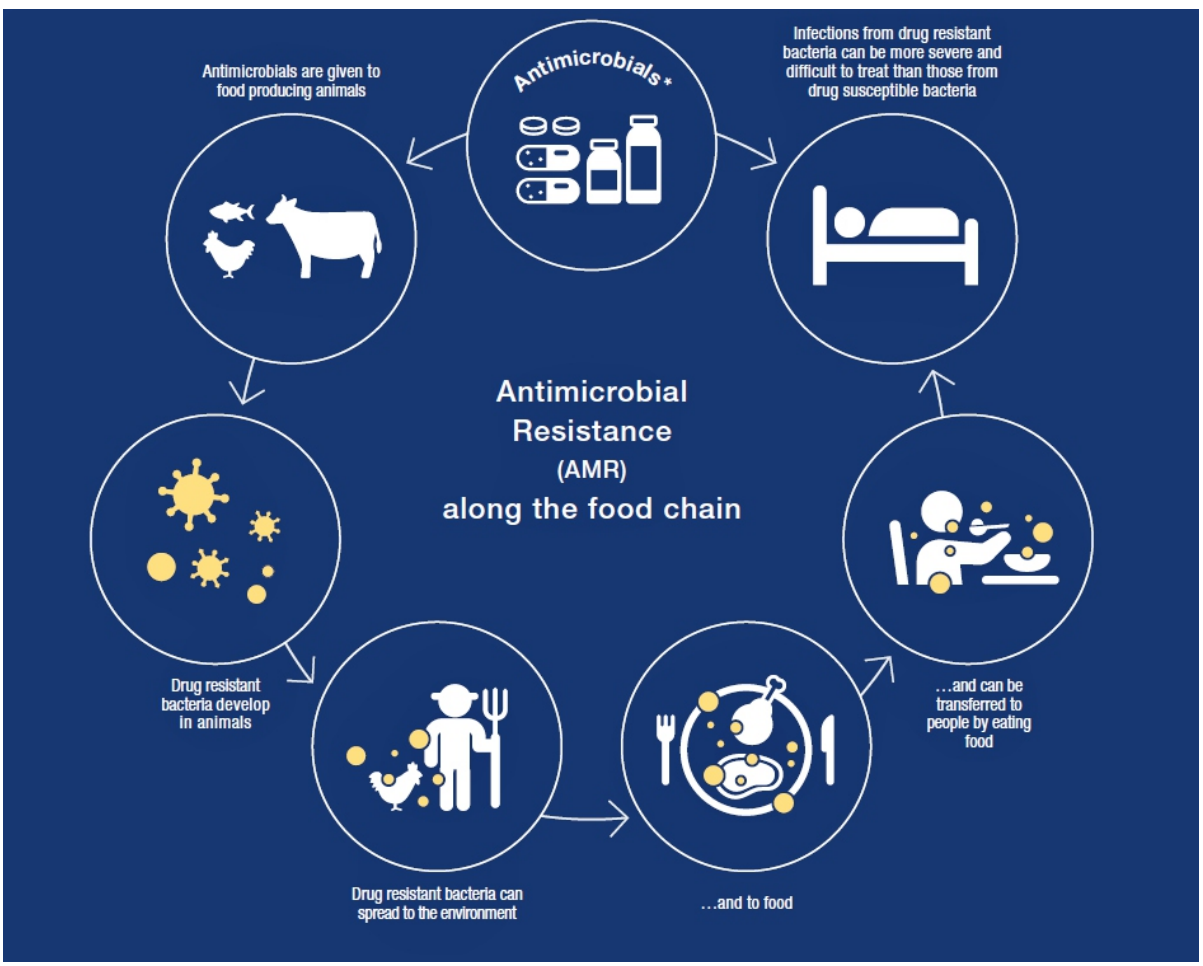

Figure 1. *Antimicrobial Resistance in the Food Chain infographic from WHO. This figure is covered by the Creative Commons Attribution 4.0 International License.*

blood pressure [12]. Compared to carbohydrate, proteins have higher food energy after fat among the three calorigenic nutrients. An average of 5.6 kcal g−1 concentrated calories, provided by protein diet, is essential in metabolism and delivery of high energy in unit mass compared to plant sources of food [13].

Food of animal origins is therefore essential, but high consumption of animal protein, processed meat, saturated fatty acids is a risk factor for potential carcinogens and infectious diseases [14,15]. Thus, while humans may depend on animals for food, the practice is not without some risks. Among these risks also are exposure to pathogens that may be inherent in animals. Zoonoses and livestock diseases are a major threat to global public health and welfare, hence it is important to control these diseases for agronomic health, food security, and for alleviating rural poverty especially in LMICs [16]. Many of these pathogens or microorganisms, bearing traits of AMR genes, may be transmitted from animal sources including food or the environment to humans [17]. Bacteria resistant to several antibiotics have been detected in meat and fresh produce and in humans in close contact with livestock in Ethiopia, Nigeria, and Kenya [17,18,19,20]. Apart from drug-resistant microorganism, drug residues in food of animal origin are also implicated in food safety. For instance, a high level of antimicrobial drug residues in animal meat has been shown in Kenya [21]. Similarly, injudicious use of antimicrobials was reported in small-scale poultry farms in Vietnam [22]. Researchers investigating livestock AMR globally found extensive AMR in India and China, while Kenya and Brazil are future hotspots. The investigators found that 73% of antimicrobials used in humans are also used in animals raised for food [23] and highlighted that food animals are a major contributor to the AMR problem in Africa, Asia and Latin America. In addition to animals, food from plants can also contain AMR pathogens through soil and water contaminated by AMR microorganisms from animals. Foodborne disease outbreaks by AMR pathogens have been reported from the use of animal wastes as organic fertilizer or from irrigation by contaminated surface water sources [24,25].

If no action is taken, diseases from AMR pathogens could cause 10 million deaths annually by 2050 and the economic consequence has been projected to be around 100 trillion US dollars. While bacteria acquire AMR by spontaneous mutations, some schools of thought implicate excessive use of antimicrobial compounds in food animals most often delivered in sub therapeutic doses in preventive medication and opinions are rife on banning utilization of essential antimicrobials on animals bred for food. This is because prolonged exposure to antibiotics increases mutation and replication of bacterial chromosomes responsible for resistance [26]. Horizontal gene transfer between human and animals occur and this is particularly applicable to zoonotic pathogens. While diseases caused by microbes may be prevented through biosecurity and chemotherapy, the more daunting and current public health challenge is the increase of AMR microbes in nature. Major progress towards the mitigation of this twenty-first century challenge has been the awareness of the mechanism involved in the emergence of AMR. Local, regional, and global campaigns by governmental, non-governmental organizations, and supranational organizations including WHO, Office International des Epizootics (OIE), and Food and Agriculture Organization (FAO) seek to bring AMR to the forefront of discussions. Several advocacy programs focus on strategy to control AMR and emphasize minimization of the use of antimicrobial in food animals [27]. Antimicrobial stewardship recognizes that food of animal origin plays a significant role in the emergence of AMR, and this may be through (i) spontaneous emergence of AMR in zoonotic pathogens that human may be exposed to in livestock and the environment and/or (ii) presence of drug residues in livestock-derived food such as meat, eggs, and milk [28]. The expansion of colonies of resistant microorganism eventually becomes dominant and resistance genes are horizontally transferred to susceptible animals and human in the population [21]. Furthermore, food insecurity and a lack of adequate food safety measures can increase the incidence and worsen the AMR problem.

Challenges of food safety and security in developing countries

Unsafe food containing pathogens, macroparasites or chemicals, cause serious diseases including diarrhea and cancers. It poses a significant threat to human health and welfare. People in developing countries are the most affected population. According to the WHO, 31 foodborne diseases (FBDs) in total caused more than 600 million cases, 420,000 deaths, and the loss of 33 million healthy life years (DALYs) in 2015. In addition, nearly one in ten people become sick each year from eating contaminated food [29]. The lack of proper hygiene or adequate sanitation coupled with a low awareness of good hygienic practices at various stages of the food chain contribute significantly to this crisis [30].

Many developing countries lack data on the prevalence, risk factors, or impact of foodborne illnesses locally [31] which results to formulation of control measures that do not address the real issues. Comprehensive epidemiological data is extremely important to establish proper food safety systems [32]. In many LMICs, the food trade is large, diversified, and mainly composed of an informal sector, making it challenging for the government to enforce food safety regulations [32]. Food safety implementation depends on individual and institutional capacity in the public and private sectors. In developing countries, technical capacity is often inadequate, mainly in food safety testing laboratories [33]. This situation is further complicated by lack of water and electricity supply, war, climate change, globalization of food trade, changes in animal husbandry practices, and the adoption of modern intensive agriculture [34,35].

Food insecurity leads to chronic undernutrition in over 820 million people globally. In 2019, 17.2% of the world's population lacked access to safe, nutritious, and adequate food. Ninety-nine percent of the world's undernourished are in developing countries [36]. According to the United Nations, there is food security "when all people, at all times, have physical, social and economic access to adequate, safe and nutritive food that meets their dietary requirements and food choices for an active and healthy life" [37]. Food safety and food security are closely linked. The Rome Declaration on World Food Security, organized by FAO, reported food safety as one of the main impediments to achieving food security in the world [38]. The economic status of households as well as global macroeconomic conditions affect food security [39]. Inadequate food security in developing countries is also determined by population growth, lack of access to food, poor infrastructure, low rates of agricultural production, patterns of international trade, infectious diseases, economic inequality, poor sanitation/ hygiene and water sources, climate change, natural disasters, and social conflict [39,40,41].

Emerging antimicrobial resistance related to animal sources

Over the past few decades, production of food from animal sources has spiked because of continuous growth of human population and the consequent increased demand for meat and poultry. This increased farming of livestock has resulted to the increased overall use of antimicrobials. Animals, like people, carry microbes in their gastrointestinal tract. Some of these microorganisms may be resistant to antimicrobials and can spread during the slaughtering process or through fecal carriage of resistant bacteria that can spread out in the environment [42]. The environment and wild animals can also be sources of resistance. Transmission of resistance to people can happen through several ways but the majority occurs through the food-borne route [42,43]. The primary cause of the emergence of AMR is the inappropriate use of antimicrobials including prophylactic medication, unessential or partial antimicrobial treatments in animal farming and livestock production. These practices resulted to not only the development of resistance in bacteria that cause animal diseases, but also in bacteria that are able to infect humans [43,44]. It is noteworthy that one out of five AMR infections in humans can be traced back to animal source foods and animals [44].

Bacterial species associated with agriculture food-producing animals are *Campylobacter jejuni*, *Salmonella enterica*, *Typhimurium* DT104, and *E. coli* O157:H7 [44,45]. *Salmonella* and *Vibrio* are potential pathogens associated with aquaculture and *Listeria monocytogenes*, *Aeromonas spp.*, and *Clostridium spp*. are threats to watch out for [44]. The use of fluoroquinolones, particularly ciprofloxacin, in

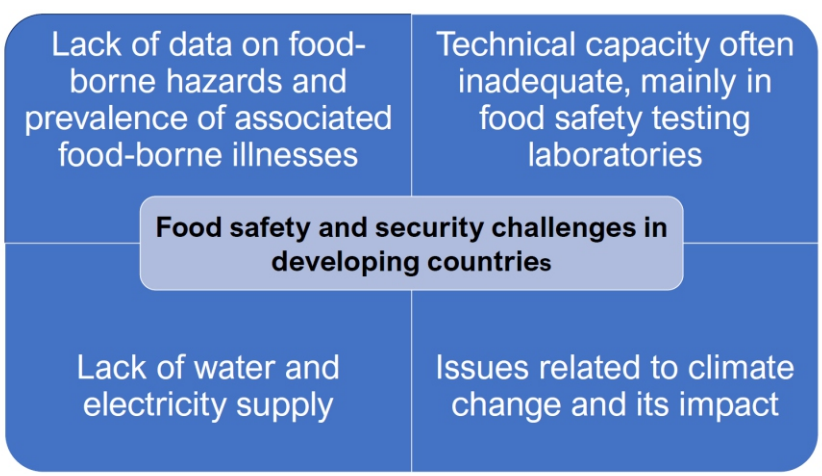

Figure 2. *Food safety and food security challenges in developing countries*

poultry production since 1995 led to the emergence of ciprofloxacin-resistant bacteria *Campylobacter*, which was subsequently detected in the breast meat of animals. The antibiotic avoparcin, used as an alpha-1-acid glycoprotein (AGP) in veterinary practice, promotes vancomycin resistance with the AGP antibiotic vinginicmycin which has a similar effect to streptogramin, a cyclic peptide antibiotic used in human medicine [44]. Cross-resistance occurring when a specific drug influences bacterial resistance and susceptibility to other antibiotics happen between antibiotics sharing the same mechanisms of action *e.g.* resistance between extended spectrum b-lactamases (ESBLs) caused cross-resistance within the class of penicillin and cephalosporins [44]. AMR to antimicrobial drugs could potentially reverse the benefits of the use of antimicrobials in controlling animal diseases, enhancing animal production, and protecting the health of humans [46]; animals' resistance to available antimicrobial agents makes treatments useless, lessens productivity and results to financial losses. To reduce the risk of AMR due to inappropriate use of antimicrobials in animals, there is a need to reinforce information resources in medical and veterinary professionals, patients, animal breeders and the public in LMICs to ensure better understanding and appreciation of the value of antimicrobials, especially antibiotics.

One health approaches to mitigating AMR

The rising threat of AMR must be addressed using a coordinated, holistic and multi-sectoral (One Health) approach because antimicrobials used in food-producing animals can be pharmacologically similar or the same to antimicrobials used in humans. Resistant pathogens from either of the three interlocking sectors: humans, animals or the environment can spread from one to the other, from one country to another, from one region to another as AMR pathogens are not limited by geography nor by human or animal borders. The WHO, FAO and OIE have coordinated efforts to ensure antimicrobial agents continue to be useful and effective by reducing the emergence and spread of AMR through responsible use of antimicrobials and better access to quality medicines. The WHO/FAO/OIE tripartite committee also produced a manual to assist countries as they draft new or refine existing national action plans aligned with objectives of the AMR Global Action Plan [47].

Factors unique to developing countries such as lax regulatory policies, socio-economic conditions and demographics make them an epicenter for AMR. In an evaluation of the national animal health systems performed by the OIE, more than 110 of about 130 countries, mostly from Africa and Asia, do not have pertinent policies to regulate import, manufacture, distribution, and use of antimicrobial agents [48]. In the South East Asia region (Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, Timor-Leste) the farming systems have been further developed over the years with support of the WHO and this led to a sharp increase in the consumption of fertilizers, pesticides, and antibiotics with a majority of the farmers lacking technical knowledge on AMR and how to reduce its impact [48]. The consequence of AMR in human health is already evident with the rise of multi-drug resistant tuberculosis (MDR-TB) that leads to the use of prohibitively expensive intravenous medicines. To reduce AMR in developing countries, political commitment, good governance, and multi-sectoral capacity building are crucial to implement global guidelines and establish appropriate policies and legislation for antimicrobial use and human and veterinary surveillance of AMR. The Philippine government was one of the first countries in the region to answer the call for action against the threat of AMR by creating an inter-agency committee with participation from the departments of health, agriculture, science and technology, interior and local government, trade and industry to formulate and implement the National Action Plan to Combat AMR in 2014 [49]. Human health and animal health authorities need to collaborate with stakeholders in the private and public sectors to align policies, strategies and activities nationally, regionally, and globally. Physicians should adhere to the "five rights" *i.e.* the right patient, the right drug, the right time, the right dose, and the right route and be regularly updated on the latest scientific information on AMR. Failure to do so increases the chances of antibiotic resistance. Chances are it can be worse, and drugs that are hitherto effective can become useless due to AMR. Moreover, physicians should maximize the use of vaccines, because vaccination as an effective way to prevent infections, prevent the need for antibiotics. Increasing coverage of existing vaccines and developing novel vaccines are important ways to tackle AMR and reduce preventable illness and deaths due to AMR pathogens. Veterinarians and animal health practitioners should prescribe antibiotics only when needed. As for humans, animals should be prescribed the right drug with the right dose at the right time using the right route relevant to the right species. Farm owners should comply with good animal husbandry practices and use antibiotics only when prescribed by a licensed veterinary practitioner. Wholesale distributors and retailers also share in the responsibility of fighting AMR, primarily by ensuring that antibiotics are only sold with prescriptions [50].

Conclusion

The role of food animals in AMR is not without controversy. It is important to recognize that AMR genes in animals and humans may evolve and move in ether directions. The underlying concern, however, is that inappropriate or excessive use of antimicrobial in food animals contributes to AMR emergence that could result to morbidity and mortality in humans [51]. In developing countries, several challenges exist: antibiotic self-prescription, poor sanitary conditions, lack of regulatory policies – all these conditions not particularly common in developed countries - foster the threat of AMR. Further to the local repercussions of these unique set of challenges and resistance trends, it is important to emphasize that local actions or inactions on AMR can lead to a global problem. Careful and rational use of antibiotics in the healthcare and agricultural sector is essential to slow the emergence of AMR and prolong the useful lifetime of currently-available antibiotics. In LMICs, public awareness and capacities for AMR stewardship need to be improved and strengthened. Effectively addressing AMR requires the animal, human, and environmental health sectors to join forces to reduce antimicrobial use in livestock production and maintain animal health, welfare and productivity, while safeguarding human life. The global strategy to fight AMR must take into consideration regional dynamics and national challenges.

References

1. National Research Council (US). (1999) Committee on Drug Use in Food Animals. The use of drugs in food animals: Benefits and risks. Washington (DC): National Academies Press (US); 3, Benefits and Risks to Human Health.
2. George A. (2019) Antimicrobial Resistance (AMR) in the food chain: Trade, One Health and Codex. Tropical Medicine and Infectious Disease. 4(1). pii: E54.
3. Okeke IN, Aboderin OA, Byarugaba DK, Ojo KK, Opintan JA. (2007) Growing problem of multidrug-resistant enteric pathogens in Africa.Emerging Infectious Disease. 13:1640–6.
4. Goel P, Ross-Degnan D, Berman P, Soumerai S. (1996) Retail pharmacies in developing countries: a behavior and intervention framework. Social Science & Medicine. 42:1155–61
5. Okeke IN, Laxminarayan R, Bhutta ZA, Duse AG, Jenkins P, O'Brien TF, *et al*. (2005) Antimicrobial resistance in developing countries. Part I: recent trends and current status. Lancet Infectious Diseases. 5:481–93.
6. Hart CA, Kariuki S. (1998) Antimicrobial resistance in developing countries. BMJ 317(7159):647-50.
7. Okeke IN, Lamikanra A, Edelman R. (1999) Socioeconomic and behavioral factors leading to acquired bacterial resistance to antibiotics in developing countries. Emerg Infect Dis. 5:18–27.
8. Howe PE. (1950) Foods of Animal Origin. JAMA 143(15):1337–1342.
9. Beisel R, William R. (1996) Nutrition and immune function: Overview. The Journal of Nutrition, 126(10):2611S–2615S.
10. Cooper GM. (2000) The cell: A molecular approach. 2nd edition. Sunderland (MA): Signer Associates. The Central Role of Enzymes as Biological Catalysts.
11. Elmadfa I, Meyer AL. (2017) Animal proteins as important contributors to a healthy human diet. Annual Review of Animal Biosciences 5(1):111-131.
12. Murphy SP, Allen LH. (2003) Nutritional importance of animal source foods. The Journal of Nutrition, 133(11):3932S–3935S,
13. Jiang B, Tsao R, Li Y, Miao M. (2014) Food safety: Food analysis technologies/techniques. Encyclopedia of Agriculture and Food System.
14. Hill M. (2002) Meat, cancer and dietary advice to the public. Eur. J. Clin. Nutr. 56(1):S36-41.
15. Biesalski HK. (2002) Meat and cancer: Meat as a component of a healthy diet. European Journal of Clinical Nutrition. 56: S2–S11.
16. Tomley FM, Shirley MW. (2009) Livestock infectious diseases and zoonoses 364 Phil. Trans. R. Soc. B.
17. Bengtsson-Palme J, Kristiansson E, Larsson D. (2018) Environmental factors influencing the development and spread of antibiotic resistance. FEMS microbiology reviews, 42(1), fux053.
18. Addis Z, Kebede N, Sisay Z, Alemayehu H, Wubetie A, Kassa T. (2011) Prevalence and antimicrobial resistance of *Salmonella* isolated from lactating cows and in contact humans in dairy farms of Addis Ababa: A cross sectional study. BMC Infectious Diseases. 11:222.
19. Fortini D, Fashae K, García-Fernández A, Villa L, Carattoli A. (2011) Plasmid-mediated quinolone resistance and β-lactamases in *Escherichia coli* from healthy animals from Nigeria. Journal of Antimicrobial Chemotherapy 66:1269–72.
20. Kikuvi GM, Ombui JN, Mitema ES. (2010) Serotypes and antimicrobial resistance profiles of *Salmonella* isolates from pigs at slaughter in Kenya. Journal of Infection in Developing Countries. 4:243–8.
21. Mitema ES, Kikuvi GM, Wegener HC, Stohr K. (2001) An assessment of antimicrobial consumption in

food producing animals in Kenya. Journal of Antimicrobial Chemotherapy. 24:385–90.
22. Choisy M, Van Cuong N, Bao T, Kiet BT, Ve Hien B, *et al*. (2019) BMC Veterinary Research 15:206.
23. Van Boeckel TP, Pires J, Silvester R, Zhao C, Song J, Criscuolo N, *et al.* (2019) Global trends in antimicrobial resistance in animals in low- and middle-income countries. Science 365(6459): eaaw1944.
24. van Hoek AH, Veenman C, van Overbeek WM, Lynch G, de Roda Husman AM, Blaak H. Prevalence and characterization of ESBL-and AmpC-producing *Enterobacteriaceae* on retail vegetables. Internat J Food Microbiol, 2015; 204:1–8.
25. Berendonk TU, Monaia CM, Merlin C, Fatta-Kassinos D, Cytryn E, *et al*. Tackling antibiotic resistance: The environmental framework. Nature Reviews 2015; 13:310–307.
26. Maclean RC, Millan AS. (2019) The evolution of antibiotic resistance. Science 365(6458):1082-1083.
27. Collignon P. (2013) Ban routine use of critically important antibiotics in food animals. BMJ 347:f4976.
28. Meseko C, Makanju O, Ehizibolo D, Muraina I. (2019) Veterinary pharmaceuticals and antimicrobial resistance in developing countries. In: Bekoe SO, Adesraku RK, eds. Veterinary pharmaceuticals.
29. World Health Organization (2015). WHO estimates of the global burden of foodborne diseases: Foodborne disease burden epidemiology reference group 2007-2015.
30. Report of Regional Conference For Asia And The Pacific. (2017). Food and Agriculture Organization of the United Nations.
31. Jaffee S, Henson S, Unnevehr L, Grace D, Cassou E. (2018). The safe food imperative: Accelerating progress in low and middle income countries. Washington, DC: World Bank.
32. Vipham JL, Chaves BD, Trinetta V. (2018). Mind the gaps: How can food safety gaps be addressed in developing nations? Animal Frontiers 8(4):16-25.
33. Oloo B, Daisy L, Oniang'o R. (2018) Food safety legislation in some developing countries. In: El-Samragy Y, ed. Food safety - Some global trends. IntechOpen.
34. Global Food Safety Partnership. (2019). Food safety in Africa: Past endeavors and future directions.
35. Othman N. (2007) Food safety in Southeast Asia: Challenges facing the region. Asian Journal of Agriculture and Development 4:83-92.
36. FAO, IFAD, UNICEF, WFP and WHO. (2019) State of food security and nutrition in the world 2019: Safeguarding against economic slowdowns and downturns.
37. FAO. (2002). The state of food insecurity in the world.
38. World Food Summit. (1996). Rome Declaration on World Food Safety.
39. Chawarika A. (2016). Food security and the developing world-emerging issues. MPRA Paper 71073, University Library of Munich, Germany.
40. Premanandh J. (2011). Factors affecting food security and contribution of modern technologies in food sustainability. Journal of the Science of Food and Agriculture 91:2707-2714.
41. Abdullah, Zhou D, Shah T, Ali S, Ahmad W, Din IU, Ilyas A. (2017) Factors affecting household food security in rural northern hinterland of Pakistan, Journal of the Saudi Society of Agricultural Sciences.
42. U.S. Department of Health & Human Services (2020) Antibiotic resistance, food, and food-producing animals
43. Meade E, Slattery MA, Garvey M. (2017) Antimicrobial resistance: An agent in zoonotic disease and increased morbidity. Journal of Clinical and Experimental Toxicology 1(1):30-37.
44. Economou V, Gousia P. (2015) Agriculture and food animals as a source of antimicrobial-resistant bacteria. Infection and Drug Resistance 8:49–61.
45. Haihong H, Cheng G, Iqbal Z, Ai X, Hussain H, Huang L, *et al.* (2014) Benefits and risks of antimicrobial use in food-producing animals. Frontiers in Microbiology.
46. FAO/OIE/WHO. (2016) Tripartite Collaboration on AMR.
47. Regidor SE, Somga SS. (2017) Philippines: Development of National Action Plans on AMR: Aquaculture Component, Project Accomplishments and Impacts. FAO.
48. Goutard FL, Bordier M, Calba C, *et al*. (2017) Antimicrobial policy interventions in food animal production in South East Asia. BMJ 358:j3544.
49. Lasco G, Sanicas M. (2019) To keep our antibiotics working, The Philippine Daily Inquirer.
50. Schwarz S, Cavaco LM, Shen J. (2018) antimicrobial resistance in bacteria from livestock and companion animals. Washington, DC: ASM Press. ISBN-0: 1555819796; ISBN-13: 978-1555819798; Pages: 712.
51. Price LB, Stegger M, Hasman H, Aziz M, Larsen J, Andersen PS, *et al*. (2012) *Staphylococcus aureus* CC398: Host adaptation and emergence of methiciliin resistance in livestock. mBio 3:e00305–11.