Current understanding and knowledge gaps regarding wildlife as reservoirs of antimicrobial resistance

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ABSTRACT

Antimicrobial resistance (AMR) is a serious health issue shared across all One Health domains. Wildlife species represent a key intersection of the animal and environmental domains. They are a relevant but understudied reservoir and route of spread for AMR throughout the environment. Most wildlife AMR research thus far has focused on avian species, terrestrial mammals, and a selection of aquatic and marine species. Pathogens often identified in terrestrial wildlife include enteric zoonotic organisms such as Eschericia coli and Salmonella spp, in addition to nonenterics such as Staphylococci. Resistances have been commonly identified to antimicrobials important in veterinary and human medicine, including β-lactams, tetracyclines, aminoglycosides, and macrolides. Our emerging understanding of the dynamics of AMR distribution across life on Earth provides further opportunities for us to assess the risk it poses to veterinary and human health. Future work will require prioritizing which wildlife most exacerbates and indicates AMR in domestic animals. However, decreasing prices and increasing ease for metagenomic sequencing allows for synergies with expanding wildlife viral disease surveillance. Improved understanding of how wildlife impacts veterinary and human healthcare may increase opportunities for related research funding and global equity in such research. The companion Currents in One Health article by Vezeau and Kahn, JAVMA, June 2024, addresses in further detail the routes of spread of AMR across different animal populations and actions that can be taken to mitigate AMR with special consideration for wildlife sources.

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Antimicrobial resistance (AMR) is recognized a global health crisis.1 Veterinary researchers and practitioners play a critical role in identifying and mitigating AMR in collaboration with other professional sectors using a One Health approach. Within veterinary science and public health, significant attention has been given to antimicrobial use (AMU) and AMR in livestock populations. Work on companion animals as potential reservoirs of AMR is somewhat more recent. Significant knowledge gaps exist regarding how AMR, in the form of antimicrobial resistant bacteria (ARB), plasmidal DNA, and individual antimicrobial resistance genes (ARGs), as well as antimicrobial residues, propagate in the natural environment, away from the most intense anthropogenic activity. In veterinary medicine, spread to this environmental domain is likely most typified by wildlife.

Antimicrobials are produced naturally by many microbes across much of Earth’s biome, and thus AMR can be found in many ecosystems even in the absence of human activity.2 The spread of AMR is also aided by horizontal transmission, wherein ARGs are carried on mobile genetic elements, such as plasmids or transposons, that can be transferred between microorganisms. This is particularly common in bacteria and can even be mediated by viruses.3,4 However, AMU in human and veterinary medicine, as well as agriculture and industry, appears to substantially increase selection pressures for, and thus the prevalence of, AMR. The exact impact that AMU in a given One Health domain has on AMR in others is heavily debated, though most agree that spread does or at least could possibly occur between humans, animals, and the environment.

Selected Known Wildlife Reservoirs of AMR

Despite the relative lack of attention within the veterinary and public health professions, there have been hundreds of studies discussing wildlife populations in which AMR can be found. There is inherent systemic complexity in cause attribution and risk analysis. Additionally, little research robustly...
comments on how observed resistance profiles may differ from the preantibiotic era due to anthropogenic influence. Thus, it has been difficult to create a holistic picture of AMR in wildlife and how this information can best be used. However, researchers have focused on a relatively small subset of wildlife and peridomestic animal clades. These have been selected for a variety of reasons, including ease of sampling, perceived representativeness of AMR risk for domestic animal and human populations, and most strongly evidencing the spread of AMR from these domains. With this emerging body of work, we are gaining a more holistic sense of where different kinds of AMR are reservoired and in what amounts. This is discussed further below. Wildlife animals are grouped taxonomically and ecologically where possible, with a focus on vertebrates for brevity.

Migratory Birds and Waterfowl

Researchers have highlighted migrating avians as a significant risk for AMR spread. They can cross natural and artificial barriers, over both water and land, that isolate populations of many other non-flighted animals. Their migratory patterns, up to tens of thousands of miles/kilometers annually, could connect regions across hemispheres with otherwise different ARG and ARB prevalence. Migratory birds have been found to carry a diverse range of ARGs, including those conferring resistance to tetracycline, aminoglycosides, β-lactam, sulfonamide, chloramphenicol, macrolide-lincosamide-streptogramin, and quinolones. They also carry *Escherichia coli* with resistance to β-lactams, aminoglycosides, fluoroquinolones, tetracyclines, and sulfonamides.

Migratory waterfowl, such as gulls and geese, can be of particular focus due to their interfacing with aquatic and marine environments that can collect AMR from a wide range of effluents. They have been found to carry a variety of ARB, including *E. coli*, *Proteus mirabilis*, and *Salmonella* Typhimurium. These bacteria are often multidrug resistant (MDR), with some resistance to last-resort antimicrobials. Avians such as passerines, waterbirds, and raptors have been found to carry many types of ARB, including *E. coli*, *Staphylococcus*, and *Salmonella* spp. These bacteria often exhibit resistance to a range of antimicrobials, including amoxicillin, ampicillin, and rifampicin. Ducks and geese have been found to carry ARB such as *E. coli*, *Salmonella*, and *Campylobacter*.

In Chilean waterfowl, commonly MDR *Salmonella* serotypes have been detected. Waterfowl in Ohio have been found to shed MDR *E. coli* and *C. jejuni*, with some strains showing resistance to penicillin G, lincomycin, vancomycin, erythromycin, and bacitracin.

Scavenging Birds and Vultures

Scavenging birds, such as vultures, may feed on decaying animal tissue and other refuse. Many other types of birds, such as migratory birds and those common in urban environments, may at least opportunistically scavenge. They can be found adjacent to many anthropogenic activities worldwide and represent a critical intersection of livestock and wildlife health as well as interwildlife health as can be seen (Figure 1). Scavenging birds, such as vultures, may feed on recently deceased livestock or from their proximal environment, thus enabling the transfer of microbial communities common among domestic animals. Such birds have been found to carry multiple kinds of ARB, including *E. coli*. Vultures, particularly Egyptian and Griffon vultures, have been found to carry resistant *Salmonella*, *E. coli*, and other...
Enteric bacteria, with resistance to antimicrobials such as ampicillin, tetracycline, and trimethoprim/sulfamethoxazole. The use of antimicrobials in livestock farming has been identified as a key source of this resistance, with vultures consuming medicated livestock carcasses. The role of vultures in the spread of pig pathogens and pig-derived AMR has also been highlighted.

**Peridomestic and Urban Birds**

Urban birds encompass a wide array of avian species that spend much of their life cycle within the built environment. Among nondomestic animals, this potentially poses the greatest risk to veterinary and human health. Their peridomestic nature affords a high number of contact points with high-density effluents and potential domestic recipients of AMR, as visualized (Figure 2). They, as well as companion avian species, have been found to carry a range of AMR in their feces, including resistance to antimicrobials commonly used in human and veterinary medicine. However, similar to human activity, the role of urban birds in spreading clinically relevant AMR is complex and not fully understood.

**Wild Boars**

Studies have identified the presence of *Salmonella* and *Campylobacter*, as well as AMR, in indicator bacteria such as *Enterococcus faecium* and *E coli* in urban wild boars. Wild boars can carry a variety of ARB, including *S enterica, Campylobacter coli*, and *E coli* O157:H7. Wild boars in urban areas have been found to have higher levels of AMR in certain bacteria, such as *E faecium* and *E faecalis*, compared to rural wild boars. Lactobacilli isolated from wild boars have shown resistance to tetracycline and the presence of AMR determinants. In Japan, wild boars have been found to carry *Campylobacter* and *Salmonella* spp, some of which are resistant to enrofloxacin. MDR *E coli* producing extended-spectrum β-lactamases have been found in wild boars in central Europe. *Staphylococcus aureus* isolates from wild boars in Germany have shown genetic diversity and susceptibility to most antimicrobials. Despite a low prevalence, wild boars in Germany have also been found to carry MDR ARB.

**Wild Ungulates and Other Ruminants**

Wild ruminant populations are distributed worldwide, both as native and invasive species. Deer are also particularly popular game animals. This is a particular focus of public health risk assessment due to the bidirectional transfer of SARS-CoV-2 between North American white-tailed deer and humans. Some work has found that the prevalence of resistant bacteria in deer is low but that they can nonetheless serve as reservoirs and potential vectors for the spread of ARB. Studies in Scotland, Japan, and Germany have identified resistant *E coli* in deer, with resistance to tetracycline, cephalosporines, and other clinically important antimicrobials. A range of AMR and ARB have been found in wild cervids, including red deer, roe deer, moose, and reindeer. These include resistant *E coli, E faecalis, E faecium*, and *C jejuni*. The emergence and spread of cephalosporinases in wildlife further underscores the need for surveillance and mitigation measures. Wild ungulates, including buffalo, zebra, and wildebeest,
have been found to carry a range of ARGs, including tet(W) and blaCMY-2. Recent studies have also found these ungulates to harbor MDR E. coli, with resistance to antimicrobials commonly used in veterinary medicine.7,15,16,42–44

Mesocarnivores

Midsized carnivores, or mesocarnivores, include foxes, coyotes, skunks, otters, and many more mammals. They inhabit a wide swathe of the Earth’s landmass and demonstrate a large range of ecologies and behaviors. This includes lifestyles bringing them close to centers of human populations and activity.

A significant portion of research on AMR in wild mesocarnivores focuses on canids such as foxes and coyotes. Previous work has identified a high prevalence of AMR in zoonotic enteric pathogens, such as E. coli, in foxes.45 MecA-positive staphylococci have also been found in foxes.46 AMR in E. coli and enterococci isolates from foxes have been positively associated with human population density.47,48 There has also been a high level of ARGs detected in Andean foxes, particularly tetracycline resistance conferred by tet(Q).49 Vancomycin-resistant enterococci have also been found in red foxes.50 Additional studies have identified multiple AMR genes, including β-lactamases and multidrug efflux pumps, in the intestinal content of coyotes.51

ARB found in raccoons include E. coli and Salmonella. In Spain, raccoons were found to carry MDR E. coli, including extended-spectrum β-lactamase–producing strains.52 Significant work has also been conducted with raccoons and other mesocarnivores in Canada. These raccoons were found to shed resistant E. coli, including those with resistance to later-generation cephalosporins.53,54 In Costa Rica, raccoons were found to carry multiple Salmonella serovars resistant to ciprofloxacin and nalidixic acid.55

While some work has found only limited AMR in sea otters of the North Pacific, others have found more extensive resistance in Eurasian and Neotropical otters, the latter of which lives throughout Latin America.56–58 This includes resistant Salmonella and enterococci.

Large Carnivores

Research on AMR in large wild carnivores has mostly been conducted in big cats and bears, both from wild and captive populations. In captive Bengal tigers, E. coli with resistance to ampicillin, sulfamethoxazole-trimethoprim, nalidixic acid, and tetracycline were isolated.59 Carbapenem-resistant E. coli and Pseudomonas aeruginosa have also been found in Indian captive leopards.60 It was reported that MDR was found in enterococci in wild leopards in Brazil.61 Similarly, a high prevalence of ARGs was identified in wild felines in Chile.62 Norwegian Polar bears were found to have low levels of ampicillin resistance in their gut flora, possibly related to their isolation from large human settlements and other economic activity.63

Hedgehogs and Shrews

Hedgehogs and shrews represent a set of smaller mammals in which AMR profiles have been characterized. Wild hedgehogs, particularly the European hedgehog, have been found to carry MRSA and tetracycline resistance profiles.54,65 Shrews can reservoir various kinds of ARB, including E. coli, S. aureus, and P. aeruginosa.66–68 Though the presence of AMR in shrews is generally low, it can be elevated in areas with high livestock density and in coastal areas.7,69 This is likely due to routes of spread visualized in Figure 1.

Rats and Mice

Wild rats and mice collectively have a global distribution. They live in the natural environment and have also lived as peridomestic and domesticated inhabitants of urban settings for millennia. Rats can harbor a variety of ARB, including E. coli, Salmonella Typhimurium, K. pneumoniae, and P. aeruginosa.70 The presence of MRSA in rats is also a concern.71 Mice can carry a range of other pathogenic bacteria and ARGs, including those associated with gastrointestinal diseases and human pathogens.72

Fish

Aquatic animals, such as fish, can play a significant role in demonstrating how ARGs, antimicrobial residues, and ARBs distribute across the hydrosphere. Freshwater and their ecosystems can harbor many ARB, including Aeromonas, Edwardsiella, Acinetobacter, and Enterobacter.73–76 High levels of resistance to ampicillin, chloramphenicol, kanamycin, and streptomycin have been found in bacteria contained within fish mucus.77 ARB have additionally been identified in ornamental fish, including Citrobacter freundii.75,76 ARBs matching those of nearby trout farms have also been detected in aquatic environments in Turkey, potentially leading to anthropogenic AMR spread to nearby wild fish populations.79

Studies have identified high frequencies of resistance to ampicillin, streptomycin, and tetracycline in fish from Concepción Bay, Chile.80 The presence of MDR bacteria has been reported in coastal areas near aquaculture operations.81 In the Andaman Islands, fish bacteria from freshwater and marine sources have shown resistance to streptomycin, penicillin, and ampicillin.82

Cetaceans

Cetaceans, such as whales and dolphins, have a worldwide spread in marine environments as well as in some freshwater river ecosystems. AMR research in cetaceans has been especially active in regions such as the Northeastern coast of the US.83 Research has revealed Atlantic bottlenose dolphins to carry ARB, including E. coli, Plesiomonas shigelloides, A. hydrophila, and P. fluorescens.84 These have demonstrated resistance to erythromycin, ampicillin, and
ccephalothin. Research has also noted the presence of resistant *E. coli* and MRSA in bottlenose dolphins.\textsuperscript{45,86} Research in AMR within such marine ecosystems has also been active in the Northwestern coastal region of the US and the Southwest of Canada.

Seals and Walruses

AMR has been found in seals and walruses. In harbor seals and harbor porpoises, ARB were prevalent, with porpoises showing higher resistance.\textsuperscript{87} Rehabilitation of northern elephant seals increased the prevalence of AMR in commensal *E. coli*.\textsuperscript{88} *Enterococcus* spp in wild fur seals exhibited resistance to several antimicrobials.\textsuperscript{89} Bacterial isolates from pinnipeds stranded in California had MDR resistance profiles.\textsuperscript{90}

Knowledge Gaps and Future Directions

Overall, the current understanding of AMR in wildlife is limited. Findings thus far largely suggest that the presence of AMR in wildlife is reflective of AMU elsewhere, particularly those relevant to human medicine, with some findings showing associations with veterinary AMU. However, it is likely that this is at least partially a result of previous research having focused on these domains.

Prioritization of Future Work

Though increasing research on AMR to include a significant portion of the animal kingdom is likely unrealistic at present, strategic expansions of work to target wildlife populations most relevant to veterinary and public health can be prioritized.

Wildlife AMR research priorities thus far have focused on discovery-based surveillance, characterizing the impacts and source attribution of human activities, the reciprocal impacts on human and veterinary health, and the utility of wildlife as AMR sentinels. This does not seem liable to change in the near future. This may lead to a focus on peridomestic animals, whose ecologies are heavily reliant on human activities for food and the built environment for shelter. The number of interaction points with domestic animals or humans for such wildlife is higher than many other kinds of nondomestic animals. Similar investigations in rural peridomestic species will likely generate findings most significant to livestock. Further attention may be given to animals felt to have the most similar microbiome or pathogen profile to humans or veterinary species of interest.

Though there are emerging general trends of where focus should be given, it is nonetheless difficult to accurately predict what animals and ecological niches will yield findings most relevant to human and veterinary health or those that most strongly present a risk of spread across One Health domains. However, characterizing where clinically relevant AMR does not appear in high concentrations still remains of value to further establish overall trends in AMR prevalence.

Surveillance and Metagenomics

There is an overall need for improved surveillance of AMR in wildlife. Furthermore, the influence of various ecological and biogeographic factors on the occurrence of clinically important ARB in wildlife needs to be better understood.\textsuperscript{9}

AMR flow in the form of effluents makes detection via surface water and topsoils an important area of investigation. A developing body of practices and methods to capture large sets of resistomes, including for wildlife, focuses on metagenomics in environmental water and soil samples. Existing and emerging high-throughput metagenomic technologies and platforms will likely play an increasing role in environmental AMR detection. AMR in wildlife and environmental domains can be aided by metagenomics. Expansions on current sampling efforts and metagenomic methodologies could help to detect AMR in wildlife and wildlife-adjacent environments and can help to identify novel ARGs.\textsuperscript{6,89} If implemented, monitoring systems taking consistent measurements on a long-term basis could be important to establish temporal trends and, potentially, causal associations.\textsuperscript{16} Whole-genome sequencing should also be a focus of future work, especially to help determine the origin and directionality of spread for various ARB. Additionally, analyzing existing point prevalence surveys to synthesize into broader geographic or taxonomic knowledge, as has been done in livestock, remains a gap.\textsuperscript{91}

Wildlife as AMR Sentinels

Wildlife can serve as sentinels of AMR, providing valuable insights into how resistance is both distributed and transmitted across the world. Wild small mammals can indicate variation in AMR distribution and potential transmission to mammalian hosts.\textsuperscript{69} Additionally, the prevalence of wildlife AMR can be low in areas distant from human activity.\textsuperscript{16} This suggests that AMR presence in at least some wildlife species or ecological niches is indicative of AMU elsewhere and of AMR in associated wildlife populations. Continued surveillance of wildlife is crucial to better understand their role in the global dissemination of AMR.\textsuperscript{92}

Funding and Equity

Adding an AMR or antimicrobial residue surveillance component to any variety of wildlife or environmental sampling projects may serve as a feasible value-add to any such programming. This may create more opportunities for wildlife research, sometimes considered to be underfunded, via the potential relevance to the health of humans and domestic animals.

At present, much of the research related to AMR in wildlife is conducted in the Global North. It is possible that the rich biodiversity of the tropical climates, more prevalent across the Global South, can serve as an impetus to distribute the funding of
research more equitably. This is further compounded by the transmissible nature of AMR, especially considering the potential for spread across vastly disparate regions via migratory animals. Though likely differing in magnitude of occurrence, the ability of long-range migratory animals to spread disease may be thought of as analogous to the postulated role of air travel in spreading AMR among humans.

**Synergism with Transboundary Disease Surveillance**

Transboundary disease threats from wildlife, including those posed by AMR, represent a significant opportunity to expand One Health collaborations and overall infrastructure. Many different public health and agricultural authorities globally have expanded efforts to probe wildlife populations for emerging viral diseases in the wake of COVID-19. Sample collection and lab space, as well as other infrastructural, personnel, and funding synergies, could be considered in governmental and other research efforts.

**Conclusions**

AMR is present diffusely across Earth’s biosphere, including wildlife as recipients and spreaders. Though AMR exists naturally, anthropogenic influences can induce heightened levels in wildlife and throughout the environment. Further work is needed to examine the exact degree to which veterinary, medical, and industrial uses of antimicrobials influence AMR elsewhere and what risks this may create for veterinary and human medicine. As our global society creates further initiatives to incentivize judicious use across One Health domains, projects and entire systems are needed to advance our knowledge of where clinically relevant AMR, ARGs, ARB, and antimicrobial residues can be found. Veterinary, scientific, and other relevant communities must continue to keep these complex dynamics in mind as they continue playing a critical role in characterizing and mitigating AMR.

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**References**


20. Fallacara DM, Monahan CM, Morishita TY, Wack RF. Fecal shedding and antimicrobial susceptibility of selected...


63. Schaefer AM, Goldstein JD, Reif JS, Fair PA, Bossart GD. Antibiotic-resistant organisms cultured from Atlantic


