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Hedgehogs and antibiotic resistance: A review

[1, 2, 3] **Andreia Garcês**
[1] INNO, Veterinary Laboratory, R. Cândido de Sousa 15, Braga, Portugal
[2] Cooperativa de Ensino Superior Politécnico e Universitário, CRL -CESPU, R. Central Dada Gandra, Gandra, Portugal
[3] CITAB, University of Trás-os-Montes and Alto Douro, Quinta de Prados, Vila Real, Portugal

Corresponding Author: **Andreia Garcês**

Abstract
Antimicrobial resistance has become a concern for public health in the last decades due to overuse and misuse of antibiotics. Hedgehogs live in close contact with humans, their pets, and livestock. Their numbers have been rising in gardens, farms, and green areas in the cities. This close contact with humans and pets poses a potential risk for zoonotic transmission. These animals are host to a wide variety of viruses, bacteria, fungi and parasites some of which are considered zoonotic. Antibiotic resistance (AMR) in hedgehog knowledge is still very scarce, but the few studies performed show that they are hosts of AMR and play an important role in their dispersion in the environment. Also, because they live in close contact with humans, and same species are pets, they are more vulnerable to acquiring these pathogens. In the present study, we aim to compile the latest studies that describe the presence of antibiotic-resistant in hedgehogs.

Keywords: Hedgehogs, One Health, Bacteria, Zoonoses, Antibiotic-Resistant

1. Introduction

Antimicrobial resistance (AMR) has always existed, but the overuse and misuse of antibiotics in the last decades have generated an increase in antibiotic resistance strains [1]. The Centres for Disease Control and Prevention (CDC) and The World Health Organization (WHO) have already declared that AMR is one of the biggest public health problems of our time [2]. AMR is a global concern that is no longer entirely confined to human health contexts, but also to animal and environmental health [3]. Wildlife can acquire antibiotic-resistant bacteria from humans, domestic animals, or environmental sources (e.g., water bodies). They can be the host of these resistant strains but also disseminate them in the environment and contaminate other animals or even humans [3, 4]. This dissemination of resistance through wild animals is an issue for the management of resistance. However, antimicrobial resistance surveillance programs rarely focus on wildlife, and therefore little is known about the mechanisms of dissemination and acquisition of AMR in wild animals [3, 5].

Hedgehogs are small nocturnal mammals that belong to the Order Eulipotyphla [6, 7]. They are easily identified by their spines over the dorsal and lateral body [8]. This species is native to Europe, Asia and Africa, and is one of the most common and widely distributed mammal species [7, 9]. They are extremely adaptable and may be found in rural and urban areas [8] Hedgehogs are omnivores, with a diet composed of insects, worms, snails, frogs, snakes, bird eggs, fungi, fruits, vegetables and cat food when available [2, 9]. Some species hibernate during the winter in some regions [7]. According to the IUCN UCN Red List of Threatened Species hedgehog species are classified as Least Concerned [10, 11]. Although not considered threatened, some populations have been declining in the last decades due to diverse factors associated with human presence, which include habitat fragmentation, road traffic collision, predation by pets, garden machines and food shortage [12].

Hedgehogs live in close contact with humans, their pets, and livestock. Their numbers have been rising in gardens, farms and green areas in the cities [12]. Some species, the European hedgehog (*Erinaceus europaeus*), and the African hedgehog (*Atelerix spp*. and *Hemiechinus spp*.) are popular as pets [9]. Close contact with humans and pets poses a potential risk for zoonotic transmission [2]. These animals are host to a wide variety of viruses, bacteria, fungi and parasites some of which are considered zoonotic or have the potential of affecting other animals. Some of these agents that they are carriers are ticks, fleas, mites, ringworm, *Toxoplasma gondii*, influenza virus, yellow fever, *Salmonella enteritidis*, *Anaplasma phagocytophilum*, leptospirosis, or foot and mouth disease [8]. This close contact also so makes them prone to obtain AMR from Humans and domestic animals and disseminate these resistant strains.

Surprisingly, very few studies regarding AMR in hedgehogs have been performed. Consequently, this review aims to summarise information about AMR in hedgehogs and show that this specie may be a possible sentinel for the study of AMR.

2. Material and methods

For this review, we conducted a literature search through the main web search engines, such as Google Scholar, ResearchGate, Web of Knowledge, and PubMed, as well as in other grey bibliographies available online. The search terms included combinations of hedgehogs, Erinaceus, antibiotic resistance, zoonoses, bacteria, resistance strains, and one health. As inclusion criteria, only works that describe information regarding antibiotic resistance in hedgehogs were included.

3. Methods of transmission and dispersion of Antibiotic resistance

The acquisition and dispersion of AMR can happen by many routes, although not fully understood, direct contact with humans and otter animals, contaminated soils and water are some of the sources of acquisition. Fig 1 is a schematic representation of the dispersion and acquisition of AMR by hedgehogs.

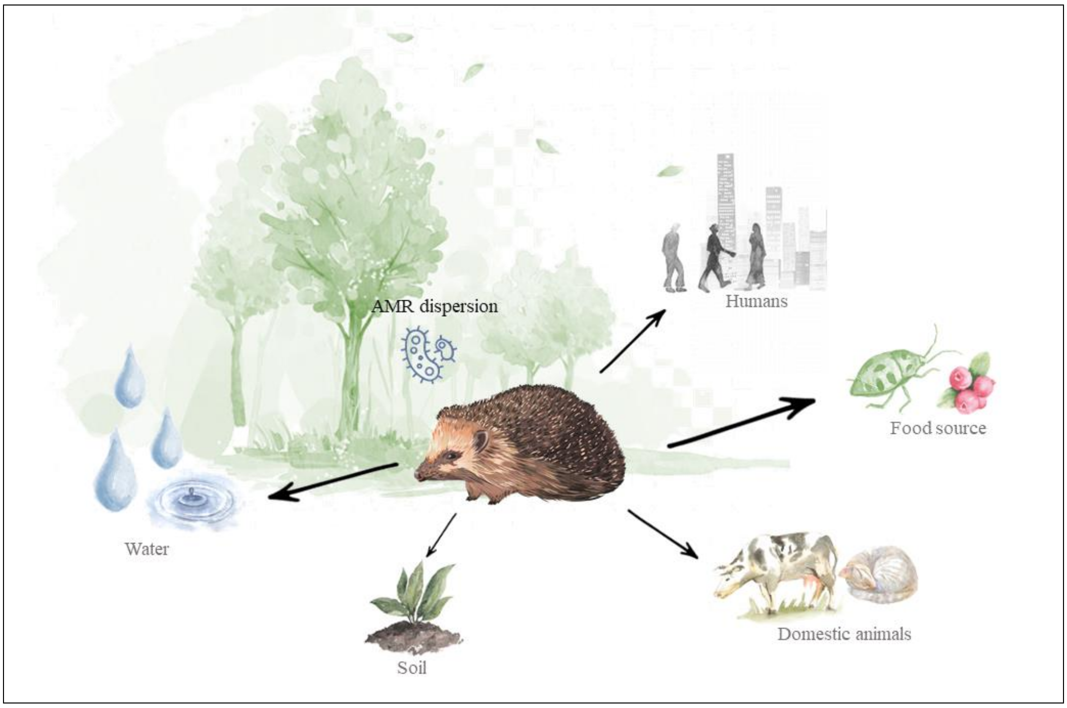

Fig 1: Schematic representation of the possible routes of spread of antibiotic resistance bacteria by hedgehogs

3.1 Direct contact with humans or other animals

Humans and domestic animals can be in contact with hedgehog species that live or feed near habitations and gardens. Wild hedgehogs are attracted to gardens in residential areas and rural villages, where garden owners supply food (cat food and food disposal) and water for them [7]. There is also the potential sharing of food and water bowls with the pets that live in that gardens [2]. Hedgehogs easy become familiar with human presence, which makes them one of the few wild mammals people are prone to come into physical contact with. Humans can directly touch the wild animals when they are trapped, wounded, or taken up to a veterinarian [5]. Another source of contamination is the ingestion of faeces. Hedgehogs' faeces can be touched by humans or their animals or be ingested by contaminated food and water [5, 13].

3.2 Water bodies

Many studies have described the presence of AMR bacteria in treated in rivers, ponds, lakes and even seawater. Additionally, there is strong evidence of resistance genes exchange between environmental bacteria and human pathogens in aquatic systems [5, 14]. These AMR found in water can originate either from human or from domestic animal populations by sewage discharge, livestock effluents, aquaculture or leaching from open dumps with hospital residues [5, 15]. AMR can be transmitted to hedgehogs because they inhabit, feed, and drink the water in these aquatic environments contaminated. Also, they can defecate near the bodies of water and contaminate the waters with pathogenic bacteria [5].

3.3 Soil

AMR exists naturally in soil communities due to the production of antibiotics by some soil bacteria and fungi, faeces and urine deposition of manure use or the effluent flows. The higher diversity of AMR bacteria occurs in areas where humans are present [5]. Wind also plays a role in AMR dispersion, because it spread small particles of soil contaminated. Animal species, including those feeding in exposed fields, could be infected by AMRB and spread them further [5].

3.4 Food sources

Another source of contamination can be the food source. Insects play a role in the propagation of antibiotic-resistant bacteria between humans-animals-environment since they live near contaminated water bodies and dumpsters and can acquire this AMR bacteria [16]. Fruit and vegetables also can be contaminated with a particle of faeces, or soil that transport AMR [5].

4. Antibiotic resistance in Hedgehogs

Two great groups of bacteria were studied in hedgehogs: *Enterobacteriaceae* and *Staphylococcus* spp. A total of 20 papers are consulted for this review.

4.1 Enterobacteriaceae

One of the most studied bacteria in hedgehogs are enterobacteria and other Gram-Negative from the gastrointestinal flora [8]. Their gastrointestinal flora is very similar to that of other animals and humans, and therefore they can be asymptomatic carriers of various pathogenic agents [9].

Table 1 is summarized the studies performed on different species of hedgehogs on *Enterobacteracea* and the AMR observed. Table 2 are represented the strains and resistances of *Salmonella* spp. in hedgehogs. This bacteria is of particular importance as a zoonotic agent to humans [9].

Table 1: Summary of the studies performed in different species of hedgehogs on *Enterobacteriaceae,* according to the number of animals, countries, year, type of sample, specie of bacteria isolated and antibiotic resistances

Specie	Number animals	Country	Year	Type of Sample	Bacteria Isolated	Antibiotic resistance	Ref.
Erinaceus concolor	8	Iran	2011	Faeces	*Escherichia coli, Proteus spp, Pseudomonas spp, Shigella spp, Yersinia spp, Salmonella spp, Klebsiella spp*	Ampicillin and tetracycline (53.3%), polymyxin E (44.8%), amoxicillin-clavulanate (34.5%)	[8]
Atelerix albiventris	4	Indonesia	2020	Rectal Swab	*Eschericia coli. Proteus mirabilis*	Erythromycin (100%) and Penicillin G (100%). One *P. mirabilis* isolates resistant to the antibiotics Erythromycin, Fosfomycin, Chloramphenicol, Penicillin G, Streptomycin, and Tetracycline	[17]
Erinaceus europaeus	90	Netherlands	2010-2012	Faeces	*Escherichia coli*	71% presented E. coli, 86% AmpC producing E. coli and 41% ESBL-producing *E.coli*	[18]
	37	Italy	2017-2018	Intestine, liver, spleen, kidney and lung fresh and formol	Various	Detected 4.2 *tet* genes per animal - 52% tet(M) gene, 41%tet(K) and tet(X), 32% tete (X) gene and 31% tet(M) gene	[19]
	114	Spain	2020	Faecal	*Klebsiella spp., Escherichia coli, Citrobacter freundii, Serratia spp., Proteus mirabilis, Enterobacter cloacae, Shigella spp.*	Genetic variants detected: blaCTX-M-15 (19.3%), blaSHV-28 (10.5%), blaCMY-1 (9.7%), blaCMY-2 (8.8%), and blaOXA-48 (1.7%). 52% of the isolates showed an MDR phenotype and 30.8% had an extended (XDR) profile	[12]
Erinaceus europaeus and *Atelerix algirus*	49	Spain	2016-2017	Rectal swabs	*Klebsiella spp., Escherichia coli, Citrobacter freundii,*	13,5% multirresistente samples. Drug resistance genes detected were: CMY-2, CTX-M-3, SHV-2, CMY-1, SHV-1, CTX-M-15, TEM-1, SHV-12, SHV-28, SHV-11, OXA-48.	[20]

Table 2: Summary of the studies performed in different species of hedgehogs on *Salmonella* spp, according to the number of animals, countries, year, the serotype of salmonella strain and respective antibiotic resistances. All samples originated from faecal and rectal swabs.

Specie	Number animal	Country	Year	Serotype	Antibiotic resistance	Ref.
Ateleri albiventris	200	Chile	2017-2018	*S. entérica* serotypes Muenchen, Infantis and IV43:z4,z23	Multiresistance to diverse antibiotics	[9]
	25	Burkina Faso	2010	*S. Ank, S. Banana, S. Drac, S. Monschaui, S. Muenster, S. Senftenberg, S. Stanley, S. group G 13,22:z:-*	Streptomycin, ampicillin, sulphonamides; nalidixic acid	[21]
Hemiechinus auritus	30	Istambul	2019	*Salmonella Typhimurium 4,5,12: i: 1,2*	Ciprofloxacin	[22]
Erinaceus europaeus	26	Spain	2013-2014	*S. Kottbus* 6,8:e,h:1,5	Ampicillin, trimethoprim/ sulfamethoxazole, sulfonamide, streptomycin, tetracycline, nalidixic acid	[23]
	170	UK	2012–2015	*S. Enteritidis* phage type (PT)11, PT66 biotype, *S. Enteritidis* multi-locus sequence-type (ST)183	Ampicillin, chloramphenicol, gentamicin, sulphonamide, trimethoprim, spectinomycin, tetracycline	[24]

Staphylococcus spp

Several studies have been performed regarding different species of Staphylococcus isolated from hedgehogs.

In a study performed in 1965 samples of skin, paws, anus, and nasal samples from 59 hedgehogs (*E. europaeus*) were collected from urban parks and gardens in diverse regions of New Zealand, which showed that 85 % of the animals carried strains of *S. aureus.* Of the 124 coagulase-positive strains isolated, 86.3 % were resistant to penicillin G. All strains examined were sensitive to streptomycin, chloramphenicol, tetracycline, erythromycin and celbenin. Of the forty strains examined for B-lysin production, 83% were positive. Of 118 strains, seventeen were phage group I, three phage group II, and twenty-five phage group III [25]. Another study performed in Spain (Aragón), between 2012 and 2015 from nasal and rectal samples isolated *S. aureus, S. equorum, S. sciuri, S. simulans* and *S. vitulinus*. The isolated agents presented resistance to penicillin, cefoxitin, fusidic acid, erythromycin, clindamycin, lincomycin, streptomycin and tetracycline [26].

Methicillin-resistant Staphylococcus aureus (MRSA) is one of the greatest problems of public health nowadays [26, 27]. MRSA are a carrier of mecA/mecC genes, which are one of the mechanisms that enable them to be resistant to antibiotics such as methicillin and other penicillin-like antibiotics [28, 29]. Hedgehogs are a natural reservoir of mecC-MRSA [7]. Several studies have described the presence of the genes mecC and mecA in hedgehogs in several countries as shown in table 3.

Some studies, such as Smith *et al*. 1965 [25] and Ramussen *et al*. 2019 [30], showed that the occurrence of mecC-MRSA seemed to be higher in males than in females, although was not statistically significant. This phenomenon can be associated with their mating behaviour with multiple females and the fights with other males during the mating season. Also, males have larger territories than females, thus they have more contact with other individuals (34).

Table 3: Specie, location of isolation, year, type sample of MRSA, genes and clonal lineages

Specie	Country	Year	Type sample	Genes	Clonal lineages and spa type	Ref.
Erinaceus europaeus	Budapest	2020	nasal and skin	mecA, mecC	ST130, spa type (t19701) and belonged to SCCmec type XI. It carried an exfoliative toxin (etE)	[31]
	Sweden	2003 and 2011	Blood and skin	mecC	CC130 and ST130 associated beta-lactamase gene blaZ (spa-types: t843, t5771)	[32]
		2017	nostrils, oral cavity and the perineal area	mecC	CC130, spa-types were identified (t843, t978, t3391, t9111, t10751, t10893, t11015, t15312)	[28]
	German	2013	Blood and skin	mecC	CC130-MRSA-XI, CC599-MRSA-XI	[33]
	Austria	2010 - 2012	Nasal and perineal swabs	mecC	ST130, with spa types t843, t10513 or t3256, or to ST2620, with spa type t4335	[34]
	Denmark	2017	Nose, tonsil	mecC	CC130 (spa-types: t528, t843, t1048, t3256, t3570, t6220, t17133) and CC1943 (spa-types: t978, t2345, t3391, t8835, t16868), spa-type t843 (CC130).	[30]
	Spain	2012 -2015	Nasal and rectal swabs	mecA	Genetic lineage CC1, typed as ST1-t386-SCCmecIVa-agrIII and harboured the blaZ, erm(C), ant(6)-Ia and aph(3´)-IIIa resistance genes.	[35]

Smith and Marples, 1960 [25], observed that 45% of wild hedgehogs (*E. europaeus*) presented a chronic mycotic infection produced by a dermatophyte specie known as *Trichophyton erinaceid*. The development of these dermatophytes in animal skin seems to offer an ideal environment for the colonization and rapid multiplication of *S. aureus*. These fungi produced an antibiotic substance biologically similar to penicillin G, with an anti-staphylococcal activity in vivo and in vitro, which could have provided a selective pressure to the development of resistance in this bacteria's strain that resided in the ringworm infection [25, 31]. The study reported a 86% prevalence of MRSA in these animals [25].

In 2021, a similar screening was performed in the wild Swedish hedgehog population (*E. europeus*). Twenty-three animals that had *T. erinacei* that carried the genes pcbAB, pcbC and penDE, which encodes penicillin biosynthesis enzymes. Of these animals, 14 carried mecC-MRSA [36]. This study also showed that there was a higher incidence of *T. erinacei* during winter months when hedgehogs hibernate, so it should be expected a higher prevalence during hotter seasons. The identification of these penicillin-producing *T. erinacei* in hedgehogs is important since this dermatophyte might influence the skin bacterial flora of the hedgehogs. This selective pressure could facilitate the emergence of resistant variants of bacteria such as mecC-MRSA. The selection of mecC-MRSA on hedgehogs also could be influenced by the presence of the blaZLGA251 gene which produces beta-lactamase and it is near the mecCon the SCCmec XI [36]. These studies showed that European hedgehogs seem to be the main reservoirs of mecC-MRSA, which explain that mecC-MRSA mainly has been found in Europe and *E. europaeus* [36].

5. Conclusions

This review concludes that hedgehogs are hosts of antibiotic resistances and pathogenic bacteria. Their close contact with humans made them more susceptible to acquiring these resistant bacteria and spreading them. This represents a health problem not only for humans and ecosystems but also for the species itself. Hedgehogs have unquestionably important as a biological indicator of environmental health. They could use as a sentinel of antibiotic resistance in the environment. Nevertheless, there are still considerable knowledge gaps, as these animals are often forgotten and neglected in wildlife epidemiological surveillance and disease control. More studies under the One Health system are necessary for the future to better understand the role of hedgehogs in the spread and acquisition of antimicrobial.

6. Conflict of interests

The authors have not declared any conflict of interests.

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