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Antimicrobial resistance in animal health

2021 review

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Introduction

European **Antibiotic Awareness** Day is taking place on 18 November 2021. For this occasion, ANSES is publishing the results of several monitoring programmes that it carries out to prevent the emergence and spread of **antibiotic-resistant bacteria** in farm and domestic animals in France.

Antimicrobial resistance is the result of **antibiotic use** leading to the selection of resistant bacteria. The emergence and spread of resistant bacterial strains call into question the **efficacy of antibiotics** in both humans and animals. Indeed, these resistant bacteria can be transferred from animals to humans and vice versa, by direct contact or through the food chain or the environment. Controlling antimicrobial resistance is therefore a major challenge, requiring **an overall "One Health" approach.**

In this review, the Agency presents the results of its monitoring programmes on **animal exposure to antibiotics,** via the sales survey of veterinary medicinal products, as well as **levels of resistance** in pathogenic bacteria isolated from animals and the food chain. Thanks to around 10 years of effort to reduce the use of antibiotics in veterinary medicine, the overall level of antimicrobial resistance in animals continues to **decrease**.
However, there is no room for complacency, as shown by the **trend reversal** observed over the past few years in certain animal species, both for sales of antibiotics and for the antimicrobial resistance of certain bacterial strains.

1

Sales survey of veterinary medicinal products: animals still less exposed to antibiotics

The French Agency for Veterinary Medicinal Products (ANMV), which is part of ANSES, has been monitoring **sales of veterinary antibiotics** and animal exposure to these products since 1999. It does this based on sales of veterinary medicinal products reported by marketing authorisation holders.
The quantity of antibiotics sold has been **steadily decreasing**, with 415 tonnes of antibiotics sold in France in 2020 versus 422 tonnes in 2019. This corresponds to less than one third of the quantity of antibiotics sold in 1999 (1311 tonnes).

However, the tonnage of antibiotics sold does not reflect the **actual exposure of animals** to antibiotics: this depends on the dosage of the medicinal product, the duration of administration, and depopulation trends for the different animal species considered. The Agency took into account the recommendations for use for the medicinal products studied and the estimated weights of the animal populations, to determine the level of exposure of animals to antibiotics.

A decrease that has been stagnating over the past few years

Compared to 2011, which marked the start of the EcoAntibio plan aiming to reduce the use of antibiotics, the **overall exposure of animals has decreased by 45.4%.**

Exposure to antibiotics has declined for all species since 2011:
- **22.5%** for cattle,
- **55.5%** for pigs,
- **64.4%** for poultry,
- **39.9%** for rabbits,
- **11.8%** for cats and dogs.

However, over the past few years, this decrease seems to have levelled off, and animal exposure to antibiotics has been **stable or even increasingly slightly** depending on the species. For example, while it continued to decrease between 2019 and 2020 for poultry and pigs (respectively by -9.7% and -3.2%), it increased for rabbits (+2.5%), cattle (+2.9%) and cats and dogs (+5.1%).

Animal exposure to antibiotics has fallen by **45.4%** since 2011.

The use of critical antibiotics continues to decline

Special attention has been paid to critical antibiotics, i.e. antibiotics of importance in human medicine. Their use in animals has **decreased sharply** since 2013: by 87.3% for fluoroquinolones and by 94.3% for third- and fourth-generation cephalosporins. This trend is continuing, since between 2019 and 2020, the exposure of all species to fluoroquinolones and newer-generation cephalosporins **declined by 9.3% and 3.9% respectively.** Although the frequency of treatment with critically important antibiotics has fallen to a very low level since 2017, it will be necessary to remain vigilant and monitor trends in the coming years.

Colistin is another closely monitored antibiotic for which transferable resistance mechanisms in bacteria have been reported. The rate of exposure to this antibiotic has decreased by 66% versus the reference level in 2014-2015. Exposure to colistin has declined in all sectors, although exposure by the **oral route increased** in cattle last year.

What are critical antibiotics?

Certain antibiotics are considered critically important because they are the only ones or are among the few that can treat serious diseases in humans. Their use is therefore regulated in veterinary medicine and should only be considered as a last resort.

A survey of veterinary practices

This year, the report on the sales of veterinary medicinal products presents the results of a survey of veterinarians who were asked about their antibiotic **prescription practices.** This survey, which 467 veterinarians completed, was prepared by ANSES-ANMV in collaboration with the Monitoring Committee for Veterinary Medicinal Products.

Most practitioners stated that they had **reduced** prescriptions of antibiotics for rabbits, pigs and poultry between 2019 and 2020. These remained **stable** for other domestic animals.

According to the veterinarians who participated, one of the factors encouraging them to prescribe fewer antibiotics has been the use of **vaccines and alternative treatments** such as phytotherapy and aromatherapy.

The development of **"antibiotic-free" specifications** in the poultry, pig and rabbit sectors, and the transition to organic farming systems for cattle and goats, will also lead to a decrease in the use of antibiotics. Indeed, in organic farming, the use of synthetic antibiotics is prohibited.

Other reasons were more isolated: for example, some veterinarians affirmed they had administered more antibiotics to cattle due to **weather conditions** that had promoted respiratory diseases and mastitis (inflammation of the udder). The use of certain antibiotics decreased in 2020 due to s**upply shortages.**

To find out more, read the report on the sales survey of veterinary medicinal products containing antimicrobials in France – 2020 (Fr).

Increased antibiotic use in pets: an effect of COVID?

Between 2019 and 2020, turnover generated from sales of medicinal products for dogs and cats **increased by 8.6%.** This increase may have been due to COVID-19 and the resulting lockdowns. Several assumptions have been put forward: since owners spent more time with their animals, they were able to pay **more attention to signs of disease.**

Moreover, as certain treatments and surgical procedures had to be **delayed**, some diseases may have been treated at more advanced stages than usual and required more antibiotics. However, it is too early to demonstrate a clear causal link.

2

RESAPATH monitoring: antimicrobial resistance still on the decline, but vigilance required for cats, dogs and horses

Since 1982, the French surveillance network for antimicrobial resistance in pathogenic bacteria of animal origin (RESAPATH) has encompassed 71 veterinary analytical laboratories involved in monitoring this resistance on a voluntary basis. The laboratories send ANSES the results of antibiotic resistance tests performed at the request of veterinarians for healthcare purposes.

In 2020, **51,736 antibiograms** were collected. The most represented species were dogs (27.3%), cattle (19.7%), poultry (19.7%) and cats (10.8%). Monitoring focused primarily on the *Escherichia coli* bacterium, considered indicative of trends in antimicrobial resistance since it is a known reservoir of resistance genes, which it can transmit to other bacteria.

Resistance to critically important antibiotics remains low

Fluoroquinolones and third- and fourth-generation cephalosporins are critical antibiotics. The proportion of strains resistant to these antibiotics has remained **very low** for several years (below 8%).

However, this year was marked by a **slight increase in resistance to third- and fourth-generation cephalosporins** in horses and dogs.

Colistin

Resistance to colistin, another antibiotic of interest, **remains low** in all animal species.

Resistance to other antibiotics: cats, dogs and horses should be closely monitored

The rate of antimicrobial resistance has **decreased** to varying degrees depending on the sector and antibiotic since the start of the monitoring programme. This decrease is continuing for poultry, pigs and cattle. However, a trend **reversal** has been observed in the past two years for **dogs, cats and horses**. This increase has been particularly pronounced for amoxicillin and amoxicillin-clavulanic acid: for example, the rate of amoxicillin-resistant strains in cats, which was 30% in 2018, rose to over 40% in 2020. This phenomenon therefore needs to be monitored.

Multidrug-resistant bacteria

Bacteria are said to be **multidrug resistant** when they are non-susceptible to more than three tested antibiotics. The development of multidrug resistance can lead to **therapeutic dead-ends**, when there are no longer any medications effective against a bacterial strain.

Since 2011, there has been a **decrease** in the proportion of multidrug-resistant *Escherichia coli* strains in most animal species.

The proportion of multidrug-resistant strains is highest in cattle (15% in 2020) and lowest in poultry (2 to 3%).

Only the trend in horses is a cause for concern: between 2011 and 2020, multidrug-resistant strains tended to **increase**, although their percentage did not exceed 9% in 2020. Along the same lines, the number of strains susceptible to all tested antibiotics is tending to decrease in horses, whereas it is increasing in other species.

Staphylococci: different levels of resistance depending on the bacterial species

The resistance of *Staphylococcus aureus* to methicillin, which is a major indicator of antimicrobial resistance in humans, remains limited in strains isolated from animals.
However, resistance to this antibiotic in *S. pseudintermedius* is common, accounting for 15-20% of strains in 2020 depending on the species and disease. This is another Staphylococcus species that is pathogenic for domestic carnivores but does not affect humans.

To find out more, read the RESAPATH annual report for 2020 (Fr).

3

Monitoring of antimicrobial resistance in food-producing animals: a harmonised system at European level

In France, the **European surveillance scheme** for antimicrobial resistance is coordinated by the Directorate General for Food (DGAL). It is an active surveillance system based on the sampling of bacteria of interest from **healthy food-producing animals.** Depending on the bacterium and farming sector, samples are collected on the farm (surface sampling), at the slaughterhouse (in intestinal contents) or at distribution (in meat).

As the **National Reference Laboratory** (NRL) for antimicrobial resistance, ANSES implements these annual surveillance plans. The results for France are published in the DGAL's report on surveillance and control plans. At European level, they are included in a report by the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC).

Monitoring bacteria of importance to human health

Three groups of bacteria are monitored: **Salmonella** and **Campylobacter**, which are the leading causes respectively of foodborne illness outbreaks and bacterial gastroenteritis in humans in Europe,

and *Escherichia coli*, known to be a reservoir of antimicrobial resistance genes. These genes can be transmitted to bacteria in humans via the food chain. The NRL has published a report reviewing changes in antimicrobial resistance observed since this harmonised European scheme was introduced in 2014.

Salmonella: varying trends depending on the antibiotic and species

While there is little or no resistance to antibiotics of critical importance to human health, the rate of resistance to certain other antibiotics (penicillin, tetracycline and sulfonamides) can be high in Salmonella at the slaughterhouse. For example, over half of all strains isolated from pigs, calves and turkeys are resistant to tetracycline.

Levels of resistance to sulfonamides are high in calves (34.9% of isolated strains) and very high in pigs (58.8% of strains). Lastly, 44.1% of strains isolated from pigs are resistant to ampicillin, which is a penicillin.

Campylobacter: its resistance to certain antibiotics remains high

From 2014 to 2020, the resistance of Campylobacter jejuni strains remained stable for all tested antibiotics, except for tetracycline, to which resistance decreased significantly, by 9% in chickens and 15% in turkeys. Rates of resistance in Campylobacter remain high to very high for fluoroquinolones (67.8% of the chicken strains isolated in 2020) and tetracyclines (63.7% of chicken strains in 2020), but the susceptibility of Campylobacter to macrolides, the antibiotic class most commonly used to treat campylobacteriosis in humans, has been preserved.

Escherichia coli: a situation that has improved overall

Since 2014, more and more Escherichia coli strains have been susceptible to all tested antibiotics, regardless of the animal species of origin. This rate has increased by 54% in turkeys, 48% in chickens and 40% in calves. However, resistance to ampicillin has increased in all strains isolated from pigs.

Lastly, there are fewer Escherichia coli that produce extended-spectrum β-lactamase (ESBL) or cephalosporinase – enzymes enabling bacteria to resist certain critically important antibiotics in humans – in the intestinal contents of all of the animal species studied and in chicken meat.

For more information, read the report on the monitoring of antimicrobial resistance in zoonotic and commensal bacteria isolated from food-producing animals and food thereof (Fr).

4

Research to improve monitoring and understanding of antimicrobial resistance

Efforts to control antimicrobial resistance are also supported by research work.

Improving the monitoring of antimicrobial resistance in animals

Over the past few months, ANSES has published several studies aiming to improve monitoring systems for antimicrobial resistance. An initial publication demonstrated the **complementary nature** of the monitoring programmes implemented by RESAPATH and the NRL for antimicrobial resistance. Carried out in different contexts, in diseased animals for the former and in food-producing animals for the latter, they sometimes highlight different trends.

ANSES is calling for the creation of a **European antimicrobial resistance surveillance network in veterinary medicine (EARS-Vet).** Just like the national monitoring conducted by RESAPATH, it would monitor the resistance levels of bacteria collected from diseased animals. Its creation would help better define the appropriate use of veterinary antibiotics in Europe. Lastly, ANSES is also exploring the possibility of monitoring the resistance of bacteria, such as mycoplasmas, that are **not currently covered** by the monitoring systems.

To find out more about this research, read our news update from 30 September 2021.

What role do dogs play in the spread of antimicrobial resistance?

Man's best friend, dogs may be able to transmit antibiotic-resistant bacteria to humans. The project on Dynamics of the spread, persistence and evolution of AMR between humans, animals and their environment (**DYASPEO**), coordinated by ANSES, was selected this past spring n the call for projects of the Priority Research Programme on antimicrobial resistance, set up by the French Government. It aims to clarify the role of pets in the spread of antimicrobial resistance.

To find out more about this project, read our news update from 11 March 2021.

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ANSES, French Agency for Food, Environmental and Occupational Health & Safety

The French Agency for Food, Environmental and Occupational Health & Safety (ANSES) provides public decision-makers with the scientific benchmarks needed to protect humans and the environment against health risks. It studies, assesses and monitors all the chemical, microbiological and physical risks to which humans, animals and plants are exposed, thereby helping the public authorities take the necessary measures, including in the event of a health crisis. A national agency working in the public interest, ANSES comes under the responsibility of the French Ministries of Health, the Environment, Agriculture, Labour and Consumer Affairs.

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