

Monitoring of the Occurrence and Dissemination of Antimicrobial Resistance in *Salmonella* Strains by the Geographic Information Program QGIS

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Abstract— In recent decades, the antimicrobial resistance has become a global problem for veterinary and medicine. Control of the spread of resistant strains of microorganisms among food-producing animals requires a comprehensive approach, including monitoring of resistance, detection of mechanisms of antimicrobial resistance of microorganisms isolated from food-producing animals. The susceptibility of 207 *Salmonella* strains isolated from sick and dead food-producing animals, animal products and feed in the Leningrad region from 2004 to 2016 to antimicrobials of to nine pharmacological groups was studied by the disc-diffusion method. The program QGIS 2.18 was used by the authors to visualize the detection and spread of resistant strains of *Salmonella* in the Leningrad region. It was established that during the considered period there was an increase in the number of areas in which resistant strains were isolated, as well as the number of groups of antimicrobials to which *Salmonella* strains were resistant. Since 2009, the isolation and spread of multi drug resistant (MDR), and since 2015 - extremely resistant strains of *Salmonella* in the Leningrad region has been noted. The usage of the geographic information program allows not only to visualize the presence of resistant strains and the spread of strains over large areas, but also to mark on the map the biological properties of strains, serological variant, sources of isolation, profile of resistance and other data. Thus, QGIS is a valuable tool for monitoring resistance. The obtained data can serve as a basis for the development of a system of measures to reduce resistance both at the individual farm and at the regional level.

Keywords—monitoring, resistance, *Salmonella*, geographic information systems.

I. INTRODUCTION

This in recent decades, the antimicrobial resistance has become a global problem for veterinary and medicine. The widespread use of antimicrobials in agriculture for the prevention and treatment of infectious diseases of animals, often unjustified and irrational (low doses, long intervals between administration, short courses of treatment), leads to a long content in the body of animals antimicrobials in sub-therapeutic concentrations, which contributes to the selection of resistant forms of microorganisms [1, 2]. The increase in the number of antimicrobial resistant strains isolated from animals and from food is noted everywhere, including our country [3]. Clinically healthy animals may be carriers of strains resistant to ten or more antimicrobials. The spread of antimicrobial resistant strains result in decrease of the effectiveness of treatment of bacterial infections in animals,

an increase in morbidity, mortality and long-term bacterial carriage [2].

The resistance of microorganisms of the same species to antimicrobials, even those belonging to the same pharmacological class, can vary greatly within the region, depending on many factors.

In this regard, control of the spread of resistant strains among food-producing animals requires a comprehensive approach, including sensitivity monitoring, the study of mechanisms of resistance to antimicrobials of microorganisms isolated from productive animals, food and feeds. The obtained data can serve as a basis for the development of a system of measures to reduce resistance both at the individual farm and at the regional level.

Many countries around the world have established antimicrobial resistance monitoring systems, including integrated surveillance of isolation of microorganisms from food-producing animals, from food, and from humans. Various geographic information systems are used to visualize the distribution of resistant strains within the region.

II. METHODS

The sensitivity to antimicrobials of 207 *Salmonella* strains isolated in the Leningrad region from 2004 to 2016 from sick and died food-producing animals, animal products and feed was determined. Susceptibility was tested by disco-diffusion method to the antimicrobials (pharmacological groups): amphenicols (chloramphenicol), quinolones (nalidixic acid, ciprofloxacin, pefloxacin), penicillins (ampicillin, amoxicillin/clavulanic acid), cephalosporins (ceftazidim, cefepim, cefotaxime), carbapenems (meropenem), sulfonamides and trimethoprim/sulfamethoxazol, tetracyclines (tetracycline), aminoglycosides (streptomycin, gentamicin, tobramycin, amikacin), nitrofurans (nitrofurantoin). The study and interpretation of the results were carried out in accordance with regulatory documents [4, 5]. The production of extended spectrum beta-lactamases (ESBL) was confirmed by the double disc method. ESBL class was determined in polymerase chain reaction with specific primers [6, 7, 8]. In the format of the Microsoft Office Excel 2007, a database the results of the susceptibility *Salmonella* strains was formed. *Salmonella* strains were divided by serological variant, by the area of isolation, by types of sources of isolation (poultry, cattle, pigs, poultry products, dairy and meat cattle breeding, pig breeding, feed), as well as by sensitivity to antimicrobials: (susceptible,

resistant to 1 – 2 groups of antimicrobials, MDR, including extremely resistant) [9].

By use the QGIS version 2.18 and open data on the administrative-territorial division of the Russian Federation in the ESRI shape format from the OpenStreetMap project (OSM), data on the isolation of *Salmonella* strains with different resistance to antimicrobials were applied to the map of the Leningrad region, divided into districts, separately for each year of the analyzed period. In the legend of the map, different colors were designated for strain categories: susceptible, resistant to 1-2 groups of antimicrobials, MDR, extremely resistant. The territory of the district was painted in accordance with the category of isolated strains. Areas of the region in which *Salmonella* this year were not isolated were

designated by separate color. The project included in text format data for each region on the susceptibility of the isolated *Salmonella* strains, indicating the serological variant and the source of isolation.

III. RESULTS

Since *Salmonella* strains, differing in sensitivity to antimicrobials, were isolated over a long period (2004-2016) in significant areas of the Leningrad region, to identify the temporal and spatial trends in the occurrence and distribution of resistant strains, we conducted a cartographic analysis of the data.

Figures 1 - 3 illustrate how the isolation geography of antimicrobial resistant strains spread has changed.



Fig. 1. Isolation of *Salmonella* strains in the Leningrad region in 2004 and their susceptibility to antimicrobials



Fig. 2. Isolation of *Salmonella* strains in the Leningrad region in 2009 and their susceptibility to antimicrobials

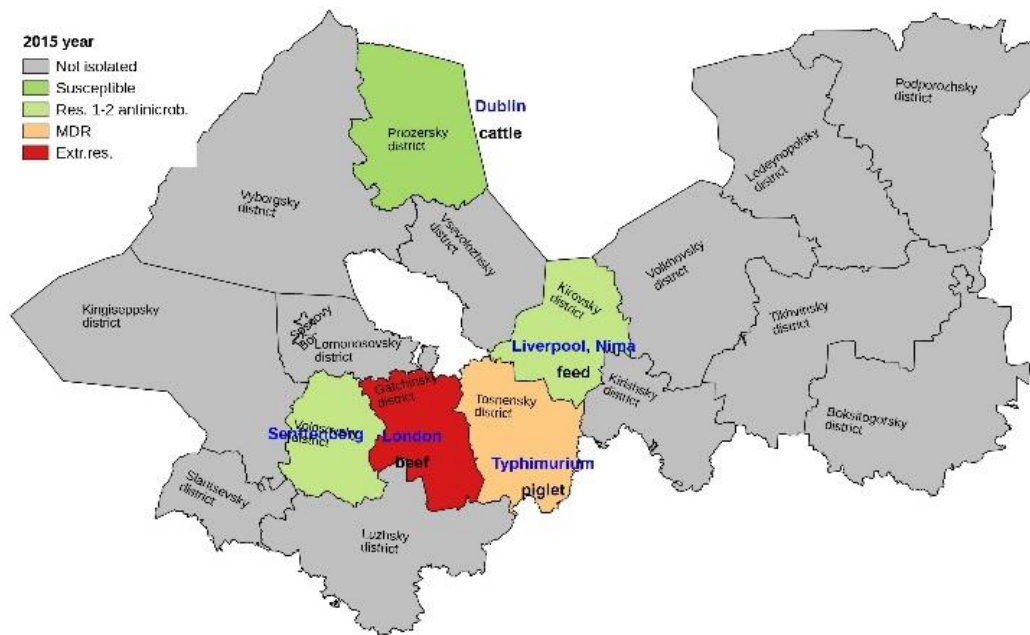


Fig. 3. Isolation of *Salmonella* strains in the Leningrad region in 2015 and their susceptibility to antimicrobials

In the 2004 - 2006 isolation of resistant to one and two groups of antimicrobials or MDR strains was noted only in one of the districts of the Leningrad region:

In 2004 – in Lomonosovskiy district – strains of *S. Enteritidis* isolated from poultry, were resistant to tetracyclines and nitrofurans; in 2005 – strains of *S. Dublin* isolated from died calves in Vsevolzhskiy district were resistant to tetracyclines and penicillins, with one strain producing ESBL class CMY-2; in 2006 in Vsevolzhskiy district strain of *S. Dublin* isolated from cattle, was resistant to tetracycline. In 2007, *Salmonella* strains resistant to one group of antimicrobials were found already on the territory of two districts-Volosovskiy district (strain *S. Java*, isolated from the corpse of a calf resistant to quinolones) and Gatchinskiy district (*S. Derby* strain, also isolated from the corpse of a calf resistant to tetracyclines). In 2008, no resistant *Salmonella* was isolated. Since 2009, the geography of isolation of antimicrobial resistant strains has expanded: in 2009, 2010 and 2013, their isolation was noted in three districts.

In 2009, *Salmonella* resistant to 1-2 groups of antimicrobials were isolated in Gatchinskiy district (*S. Infantis* isolated from milk whey, resistant to tetracycline and quinolones) and Tosnenskiy district (*S. Choleraesuis* isolated from pigs, resistant to quinolones). In the same year in Leningrad region have started to detect MDR strains. *S. Haifa* strain resistant to penicillins, cephalosporins and quinolones producing ESBL of STX-M class was isolated from chicken in Volosovskiy district. *S. Typhimurium* strain isolated from died pig was resistant to amphenicols, penicillins, aminoglycosides, tetracyclines and sulfonamides in Tosnenskiy district.

In 2010, *Salmonella* strains resistant to one and two groups of antimicrobials were isolated in Volosovskiy district (*S. Dublin*, isolated from the internal organs of a died calf, resistant to tetracyclines) and Tosnenskiy district (isolated from pigs *S. Choleraesuis* strains, resistant to quinolones and *S. Typhimurium* strain, resistant to sulfonamides and penicillins). MDR strains in the same year were isolated in Lomonosovskiy district (*S. Infantis* isolated from chickens, resistant to tetracyclines, quinolones and nitrofurans) and

Tosnenskiy district (*S. Typhimurium* strains isolated from the corpses of piglets and pigs had several phenotypes of resistance: most strains were resistant to amphenicols, penicillins, aminoglycosides, tetracyclines and sulfonamides, but there was one strain resistant only to penicillins, aminoglycosides, tetracyclines and sulfonamides, there were variants of sensitivity to different antimicrobials within the same pharmacological group).

In 2011, all resistant strains of *Salmonella* were isolated in Tosnenskiy district from died pigs. Strains of *S. Derby* were resistant to penicillins and tetracyclines, several strains of *S. Typhimurium* had the same resistance profile. The MDR strains of *S. Typhimurium* isolated in 2011 had a predominant resistance profile "amphenicols, penicillins, aminoglycosides, tetracyclines, sulfonamides", but there were also strains of the same serological variant resistant to three groups of antimicrobials: penicillins, tetracyclines, sulfonamides or amphenicols, penicillins, tetracyclines.

In 2012, tetracycline-resistant strains of *S. Derby* were isolated from pork and chicken meat in Sosnovy Bor town. In the same year, the isolation of MDR strains of *S. Typhimurium* with the already known resistance profile "amphenicols, penicillins, aminoglycosides, tetracyclines, sulfonamides" from died piglets and pigs in Tosnenskiy district it was noted. In the same area, a strain of *S. Dublin* resistant to amphenicols, aminoglycosides, tetracyclines, sulfonamides was isolated from the died calf.

In 2013, the MDR strains of *Salmonella* were detected in the Volkhovskiy, Lomonosovskiy and Tosnenskiy districts (*S. Agona* isolated from pigs in the Volkhovskiy district, were resistant to amphenicols, penicillins and aminoglycosides, the strains of *S. Typhimurium*, isolated on the territory of Lomonosovskiy district, were resistant to amphenicols, penicillins, aminoglycosides, and sulfonamides; a strain of *S. Dublin* isolated from internal organs of died cows in the Tosnenskiy district was also resistant to amphenicols, penicillins, aminoglycosides and sulfonamides and has produced ESBL AmpC class).

In 2014, resistant strains were isolated in four districts. Strains of *S. Infantis* isolated from poultry products in the

Volkhovsky and Kirovsky districts had the same resistance profile "quinolones, sulfonamides, tetracyclines, aminoglycosides, nitrofurans". In Gatchinsky district, *S. Senftenberg* strain resistant to amphenicols, sulfonamides, tetracyclines and nitrofurans was isolated from meat and bone meal, and *S. Rissen* strain resistant to sulfonamides, tetracyclines and aminoglycosides was isolated from yeast in Volkhovsky district. Thus, animal feed components can serve as a source of resistant strains and resistance genes. In Tosnensky district, extremely resistant strains of *S. Typhimurium* resistant to amphenicols, penicillins, aminoglycosides, tetracyclines, sulfonamides, nitrofurans were isolated from died pigs.

In 2015, the detection of extremely resistant strains has already been recorded in the Gatchinsky district (*S. London* strain isolated from beef, resistant to quinolones, amphenicols, penicillins sulfonamides, tetracyclines, nitrofurans). MDR strains of *S. Typhimurium* resistant to amphenicols, penicillins, aminoglycosides, sulfonamides, tetracyclines were isolated from died pigs in Tosnensky district. Strains of *S. Infantis* resistant to quinolones, sulfonamides, tetracyclines, nitrofurans and *S. Typhimurium* resistant to sulfonamides, tetracyclines and aminoglycosides were isolated from poultry products in Gatchinsky and Tosnensky districts. Strains of *S. London* and *S. Typhimurium* resistant to amphenicols, sulfonamides, tetracyclines and penicillins were isolated from beef in Gatchinsky district. *Salmonella* strains resistant to one or two groups of antimicrobials were isolated in Volosovsky district (*S. Senftenberg*, isolated from chicken flour, resistant to quinolones), Gatchinsky district (*S. Ruzizi* strain, isolated from poultry products, *S. Newlands* strain, isolated from beef were resistant to nitrofurans, *S. Mbandaka* strain, isolated from feed, resistant to sulfonamides and aminoglycosides.), Kirovsky district (strains of *S. Nima* and *S. Liverpool* isolated from fish meal were resistant to nitrofurans) and Tosnensky district (*S. Enteritidis*, resistant to nitrofurans).

In 2016, resistant *Salmonella* strains were isolated in five districts of the Leningrad region. A nitrofurant-resistant strain of *S. Enteritidis* was isolated in the Priozersky district, where previously resistant strains were not detected. In Gatchinsky district, tetracycline-resistant strains of *S. Give*, *S. Kapemba* and *S. Newlands* were isolated from beef; strains of *S. Agona* and *S. Newlands* resistant to the same antimicrobial were found in feed. Strains resistant to two groups of antimicrobials were isolated in the Gatchinsky district (resistant to tetracyclines and sulfonamides strains *S. Brandenburg* and *S. Typhimurium* isolated from beef and having the same resistance profile strains *S. Senftenberg* and *S. Isangi* detected in feed, also strain *S. Montevideo* isolated from feed, resistant to quinolones and sulfonamides). MDR strains were isolated in Volosovsky, Gatchinsky, Lomonosovsky and Tosnensky districts. *S. Infantis* strain with resistance profile "quinolones, sulfonamides, tetracyclines, aminoglycosides" was isolated from minced chicken in Gatchinsky district, *S. Reading* strain was isolated from turkey, resistant to quinolones, sulfonamides and tetracycline, and strain *S. Typhimurium*, isolated from quail, resistant to sulfonamides, tetracyclines and aminoglycosides. In 2016, the detection of MDR strains from feed was noted: *S. Montevideo*, isolated in Tosnensky district from meat and bone meal, was resistant to quinolones, aminoglycosides and nitrofurans and *S. London*, isolated in Volosovsky district from the same source, had a widespread resistance profile " amphenicols, penicillins, aminoglycosides, tetracyclines, sulfonamides»

When analyzing the information received, attention is drawn to the distribution in the Leningrad region of *Salmonella* strains having a resistance profile "amphenicols, penicillins, aminoglycosides, tetracyclines, sulfonamides" and its variants, consisting in the absence of one or two of the five pharmacological groups of antimicrobials. These strains belonged not only to serological variant *S. Typhimurium*, but also *S. Agona* (2013), *S. Dublin* (2012, 2013), *S. London* (2015, 2016), and were isolated, as a rule, from died piglets or pig products in the Volkhovsky, Gatchinsky, Lomonosovsky and Tosnensky districts. Other common resistance profiles had *S. Infantis* strains isolated from poultry or poultry products. The profile "quinolones, tetracyclines, nitrofurans" was detected in strains of this serovar in 2010 and 2012 on the territory of Lomonosovsky district and the Sosnovy Bor town. Strains with the stability profile "quinolones, sulfonamides, tetracyclines, aminoglycosides, nitrofurans" were isolated in 2014-2016 on the territory of Gatchinsky, Lomonosovsky, Kirovsky and Tosnensky districts.

It is noteworthy that in the last years of survey, 2015 and 2016, resistant *Salmonella* strains began to be detected in animal feed components.

IV. CONCLUSION

Thus, visualization of the isolation and spread of resistant strains, especially over several years, allows us to make a holistic view of the occurrence of resistant strains of microorganisms and to trace the trends of their dissemination. QGIS allows you to map in different layers information such as serological variant, resistance profile, economic relations, feed source, feed intake, applied antimicrobials, and other data. With the help of the QGIS program, it is possible to analyze strains by isolation sources, serological variants, take into account the temporal dynamics of the spatial spread of resistant strains in significant areas, and forecast the spread of resistant strains in the region. This approach makes it possible to monitor the spread of resistant strains much more effectively and to develop measures to reduce the resistance of zoonotic agents, especially causing disease in both animals and humans [10].

In the European Union, ArcGIS 9.3 is used for monitoring resistance within ECDC. [11]. In a number of countries, geographical information systems are used as an auxiliary tool in the resistance monitoring system: DANMAP (Denmark), NARMS (USA), ONERBA (France), NETHMAP/MARAN (Netherlands), SWEDRES/SVARM (Sweden) [12, 13, 14, 15]. These systems focus mainly on strains isolated from humans. In Russia, the AMRmap resistance monitoring system has been created, which allows analyzing and visualizing data on the susceptibility to antimicrobials of microorganisms isolated from humans. The AMRmap database includes regularly updated data accumulated as part of prospective multicenter epidemiological antibiotic resistance studies conducted by the Research Institute of Antimicrobial Chemotherapy (IAC) and the Interregional Association for Clinical Microbiology and antimicrobial chemotherapy (IACMAC). In 2017, the database contained information on the susceptibility to antimicrobials of more than 40,000 clinical isolates of microorganisms isolated in 52 cities of the Russian Federation in 1997-2016, which were tested in the Central laboratory of IAC [16]. In our country, in veterinary medicine, GIS is used to monitor the spread of infectious diseases of food-producing animals in order to develop effective anti-epizootic measures [17, 18, 19]. For

monitoring the spread of resistant strains of *Salmonella* in the Russian Federation GIS is used for the first time.

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