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Assessment of the Epidemic Potential of the Marek's Disease Virus in the Russian Federation

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Abstract: Marek's disease virus is an oncogenic avian herpesvirus and the problem of oncogenicity of this virus for humans remains unexplored. This pathology appeared in broiler chickens of 30 days and older, that is from now on the contact with poultry meat carries the risk of infecting people. This article analyzes the risks of the emergence of the epidemic potential of the Marek's disease virus in the Russian Federation taking into account the characteristics of modern pig and poultry farming. It was found that COVID 19 can serve as an additional factor in reducing the resistance of the population to herpesvirus infections. The COVID 19 epidemic is accompanied by folic acid deficiency which also increases the risk of contamination of diseases associated with DNA viruses, including an extended risk of animal viruse infection. Since, according to our estimates, Marek's disease occurred in at least 25% of broiler poultry farms in the Russian Federation, a possible expand in mortality from neoplasms of the reproductive system for the Russian Federation as a whole can contribute to the dynamics of oncological diseases of reproductive organs and breast cancer. Since 2011 a contagious form of intestinal pathology, vesicular enteritis, has widely spread at poultry farms in the Russian Federation. During periods of extending incidence of vesicular enteritis, we recorded cases of inflammation of the facial nerves and subfebrile temperature in contact persons, bursts of oncological diseases in veterinary personnel (ovarian cancer, breast cancer), abnormal and synchronous increases in the incidence of infectious larengotracheitis and Marek's disease in chickens under the age of 40 days which requires additional monitoring studies.

Keywords: zoonosis; Marek's disease; infections; vesicular enteritis; herpesvirus infection; breast cancer; COVID 19

Introduction

A number of animal viruses, in addition to their economic role in food production, may have zoonotic potential. Despite the fact that RNA viruses have a great zoonotic potential and are more likely to adapt to the human body [1], intensive contact with farm animals by personnel of poultry farms and pig farms creates risks for the emergence of an epidemic potential and for the DNA of viruses [1,2].

According to WHO the main source of infections for humans in recent years are animals [3]. Zoonoses is a significant proportion of new and existing human diseases. Zoonoses make up a significant proportion of all newly identified and many existing infectious diseases. Some diseases, such as HIV infection, start out as a zoonosis but later the strains mutate and only affect humans. Other zoonoses can cause periodic disease outbreaks such as Ebola virus disease and salmonellosis [3]. Others, such as the new coronavirus that causes COVID-19, have the potential to lead to global pandemics [4].

Marek's disease virus is an oncogenic avian herpesvirus [5]. The problem of oncogenicity of this virus for humans remains unresolved. It is known that the virus can multiply in the human body [6–

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8] and cases of cancer in groups of people after contact with this virus have already been recorded (unpublished data).

The aim of our study is to analyze the risks of the emergence of epidemic potential in the Marek's disease virus in conjunction with the current epidemic and epizootic situation in the Russian Federation taking into account the characteristics of modern pig and poultry farming.

Materials and Methods

Monitoring the incidence of vesicular enteritis and Marek's disease was carried out using the methods of pathoanatomical, histopathological studies in the period 2010-2022. Visits to poultry farms and agricultural enterprises were carried out throughout the Russian Federation, poultry farms in the Republic of Belarus and the Republic of Kazakhstan were also visited.

Histological studies of samples of pathological material were carried out by conventional methods. Pieces of pathological material were fixed in 10% buffered formalin solution. The tissues were dehydrated in alcohols of various concentrations, impregnated with xylene and then with paraffin. Histological sections were stained with hematoxylin and eosin. During the observation period 155 epizootics were examined including the analysis of 62 epizootics of vesicular enteritis.

An assessment of the incidence of malignant and benign tumors, cases of inflammation of the facial nerves, paresis of the limbs, stomatitis of people working in poultry farms was carried out on condition of anonymity at five large poultry farms in dynamics for 2012-2022.

The analysis of the growth of the incidence of ovarian cancer and breast cancer was carried out on the basis of available literature sources. When choosing literary sources for analysis, we were guided by such criteria as:

- the results of the assessment of the incidence of breast cancer and ovarian cancer in the population referred to the territory of the Russian Federation;
- scientific literature describes data on the incidence of breast cancer and ovarian cancer in the population for the period including 2011-2014;
- The population of the studied area exceeded 1 million people.
- Infection of broiler chickens with the Marek's disease virus of birds unfavorable for this disease was assessed by the results of PCR testing by the generally accepted method [16].

Numerical data on the production indicators of poultry farms, growing periods, productivity were taken from the reporting data of poultry farms, and expert estimates were also used.

The data were processed by the methods of variation statistics using MS Excel.

Results

Marek's disease virus is an oncogenic avian herpesvirus [5]. The problem of oncogenicity of this virus for humans remains unresolved. It is known that the virus can multiply in the human body [6–8] and cases of cancer in groups of people after contact with this virus have already been recorded (unpublished data).

Marek's disease (MD) is an infectious, highly contagious, chronic disease of chickens, widespread throughout the world, characterized by the development of massive lymphoid neoplasms, decreased immunity, and death of the bird [5]. The scientific literature notes the ability of a person to shed VBM virus within 70 days. We have successfully cultivated VBM on human cell cultures. Other herpesviruses are also capable of immortalizing human lymphocytes causing blast transformation, and many members of this family: Epstein-Barr virus (EBV), human herpesvirus type 6 (HHV-6), type 8 (HHV-8), herpes saimiri monkey virus – prototype models for studying viral carcinogenesis [9].

The sharp increase in the incidence of this infectious disease in broiler chickens, recorded by us over the past decade, in our opinion, significantly increases the risk of human infection.

In the period 2011-2021, according to our data, the causative agent of Marek's disease began to infect younger birds instead of ~70 days of age - 30 days. At the same time another herpesvirus

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infection that affects the respiratory system, ILT (infectious laryngotracheitis), has rejuvenated. The waves of two herpesvirus infections in chickens in the Russian Federation coincide in time with the appearance of the third infection - RSS (runting stunting syndrome / vesicular enteritis.

According to our observations RSS is very often accompanied by the appearance of BM. Mass distribution of RSS has been recorded by us since 2011, probably with breeding birds (spread with live vaccines is not excluded). A new form of vesicular enteritis was recorded by us in the Russian Federation during the summer of 2013. The spread through poultry farms was probably carried out from people (those who actively contacted with sick birds often had a temperature of 37 ° C during the year, inflammation of the facial nerves was periodically observed).

In 2011-2012, a case of malignant neoplasms of the mammary gland occurred in all employees working with a live VBM virus, one of the poultry farms in the Krasnodar region. In 2011-2012 and 2014-2016 two waves of BM (tumors combined with ovarian lesions in birds) were accompanied by an increase in the incidence of benign and malignant ovarian neoplasms in veterinary personnel, which may have been associated with the overall dynamics of the increase in the incidence of ovarian cancer in the country (Figure 1). At one of the poultry farms in the West Siberian region 21 people fell ill (they were operated on) and 2 people died. So far, there is no way to prove the presence of BM infection in these people and we can only talk about an indirect connection.

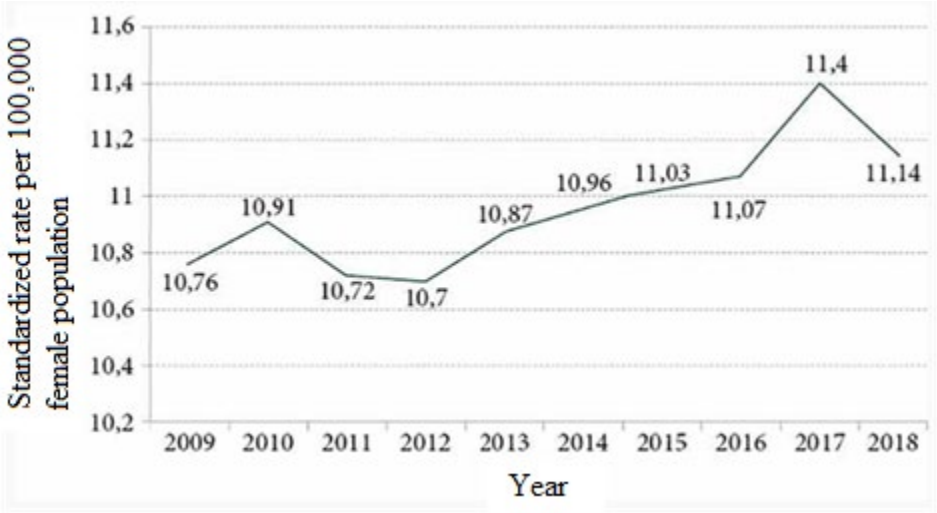

Figure 1. Dynamics of the incidence of ovarian cancer per 100 thousand female population [6].

An analysis of the incidence, mortality, and mortality from breast cancer in the female population of the Omsk region published in the scientific literature in a period from 2007 to 2014 [10] (Figure 2) also does not contradict the data on the incidence of Marek's disease and vesicular enteritis in chickens.

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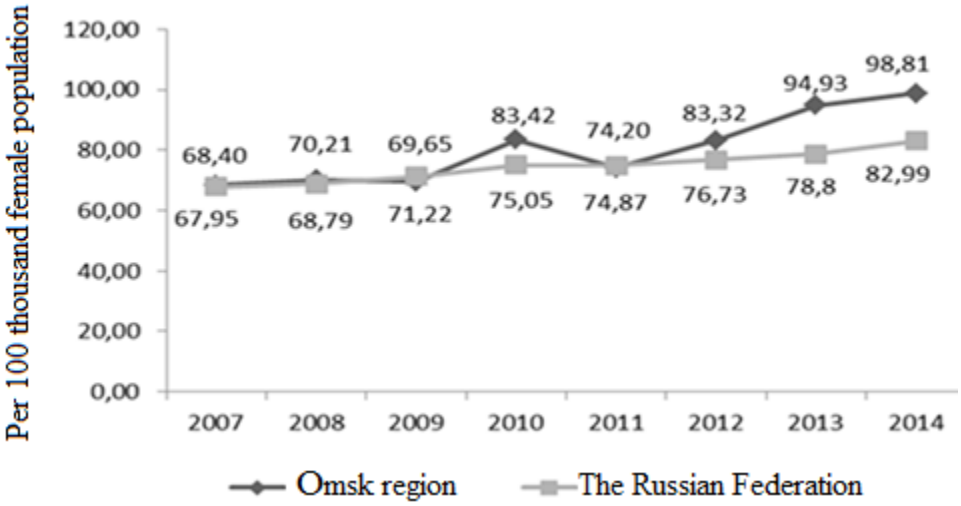

Figure 2. Dynamics of the incidence of breast cancer per 100 thousand female population [10].

To date, in our opinion, there are additional factors that increase the risk of infection of people with VBM:

1. BM appeared in broiler chickens of 30 days and older, i.e. henceforth contact with poultry meat carries the risk of infecting humans;

2. The COVID 19 epidemic is accompanied by folic acid deficiency [11], i.e. disruption of the folate cycle in humans which increases the risk of manifestation of diseases associated with DNA viruses, including an increased risk of infection with animal viruses [12,13];

3. COVID 19 reduces the resistance of the population to herpesvirus infections (see also point 2).

It is noteworthy that the dynamics of the incidence of ovarian cancer in the Russian Federation [14], in general coincides with the curve of the incidence of breast cancer [10] which indicates a possible commonality of the mechanisms provoking the development of these diseases (Figure 3).

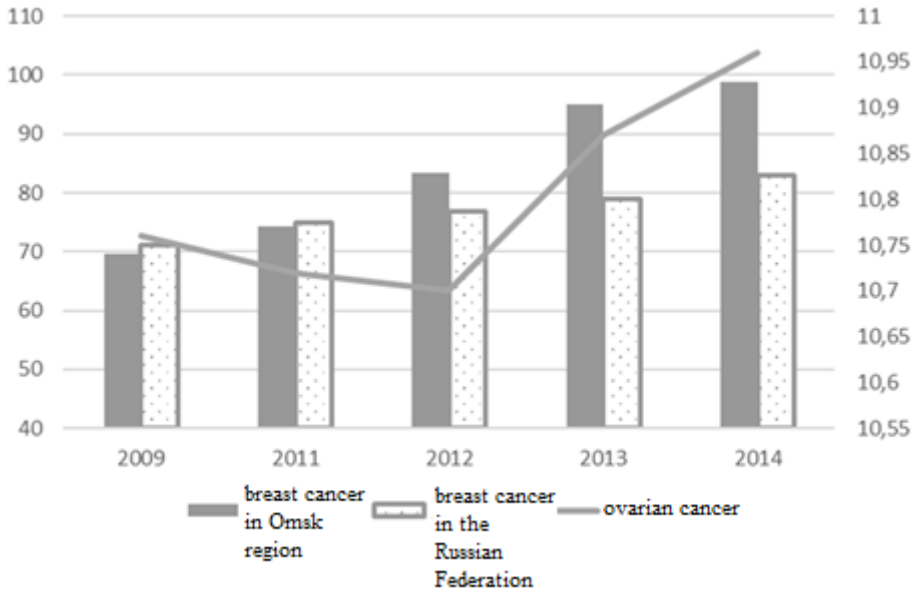

Figure 3. The number of diseases of breast cancer and ovarian cancer in% 2009-2014. Note: РМЖ is breast cancer, РЯ is ovarian cancer.

In view of the fact that the "rejuvenation" of herpesvirus infections in chickens was recorded by us in 2010-2012 and was accompanied, among other things, by inflammatory lesions of the

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reproductive system of chickens (ovaries) we consider it necessary to test the hypothesis about the effect of viral agents from chickens on the incidence of lesions of the mammary glands and ovaries in women.

The question is natural - what should be the minimum efficiency of the transfer of an infectious agent from chickens to humans followed by the manifestation of a neoplasm, so that this fact could be revealed in the course of an epidemiological analysis by medical infectious disease specialists? Thus, we can record an increase in the incidence of breast cancer in the Russian Federation by 14.9 people per 100,000 population from 2007 to 2014 [10]. The increase in the incidence of ovarian cancer was 0.38 per 100,000 people [14] in 2009-2018. That is, even the presence of an additional factor in the form of a viral agent from chickens could provoke the development of a malignant neoplasm from 150 to 3.8 people per 1 million of the population. Correlation coefficient between the incidence of breast cancer and ovarian cancer in the Russian Federation in 2009-2014 was positive and reached 0.61 according to Pearson and 0.486 according to Spearman (not significant). For the Omsk region the correlation coefficient was 0.73, which suggests the presence of a common factor affecting both analyzed parameters.

Infection of broilers with the causative agent of vesicular enteritis, according to our estimates is ~ 30%, similar or greater infection with VBM (up to 60-80% by slaughter according to the results of PCR testing). As a result, during the year the population of the region should come into contact with 4.3 million carcasses of broiler chickens infected with the Marek's disease virus and 1.5 million carcasses infected with the causative agent of vesicular enteritis (excluding cross-contamination of carcasses during processing). With an average annual consumption of poultry meat of 60-80 kg per capita one can expect contact with 24 - 28 broiler carcasses per year of a regular consumer of poultry products, on average. This intensity of public contact with infected poultry should guarantee a high risk of exposure to all viruses for persons involved in the cooking poultry dishes (mainly women, food workers and poultry enterprises). Since BM according to our estimates was found in at least 25% of broiler poultry farms in the Russian Federation a possible increase in mortality from neoplasms of the reproductive system for the Russian Federation as a whole can contribute to the dynamics of oncological diseases of the reproductive organs and breast cancer.

Conclusions

1. Since 2011 a contagious form of intestinal pathology, vesicular enteritis has distributed widely at poultry farms in the Russian Federation. The safety of this infection for the population remains unexplored.
2. During periods of increasing incidence of vesicular enteritis we recorded cases of inflammation of the facial nerves and subfebrile temperature in contact persons, bursts of oncological diseases in veterinary personnel (ovarian cancer, breast cancer), abnormal and synchronous increase in the incidence of ILT and BM in chickens under the age of 40 days, which requires additional monitoring studies to assess the safety of this nosology for the population.
3. The spread of COVID 19 suggests that the risk of human infection with herpesvirus infections from animals may also increase which requires monitoring of zoonotic herpesviruses in risk groups among the population of the Russian Federation.

References

1. Wozniakowski G., Samorek-Salamonowicz E. Animal herpesviruses and their zoonotic potential for cross-species infection //Annals of Agricultural and Environmental Medicine. – 2015. – Т. 22. – №. 2.
2. Blair A., Zahm S. H. Agricultural exposures and cancer //Environmental health perspectives. – 1995. – Т. 103. – №. suppl 8. – С. 205-208.
3. Wolfe N. D., Dunavan C. P., Diamond J. Origins of major human infectious diseases //Nature. – 2007. – Т. 447. – №. 7142. – С. 279-283.

 doi:10.20944/preprints202301.0413.v1

4. Zoonoses // World Health Organization URL: https://www.who.int/ru/news-room/factsheets/detail/zoonoses (accessed 20.09.2022).
5. Sharma J. M. et al. Public health implications of Marek's disease virus and herpesvirus of turkeys. Studies on human and subhuman primates //Journal of the National Cancer Institute. – 1973. – T. 51. – №. 4. – C. 1123-1128.
6. Beasley J. K. et al. Transmission of Marek's disease by poultry bouse dust and chicken dander //American Journal of Veterinary Research. – 1970. – T. 31. – C. 339-344.
7. Purchase H. G. et al. Public health concerns from human exposure to oncogenic avian herpesviruses //Journal of the American Veterinary Medical Association. – 1986. – T. 189. – №. 11. – C. 1430-1436.
8. Laurent S. et al. Detection of avian oncogenic Marek's disease herpesvirus DNA in human sera //Journal of general virology. – 2001. – T. 82. – №. 1. – C. 233-240.
9. Lvov N.D. Human herpesviruses - systemic, integrative, lymphoproliferative immunooncopathology // BC. - 2012. - T. 20. - No. 22. - S. 1133-1137.
10. Shirlina N. G., Stasenko V. L., Shcherbakov D. V. The burden of breast cancer in the female population of the Omsk region // Modern problems of science and education. – 2016. – no. 5. - S. 63-63.
11. Hayashi M. et al. Enhancement of mRNA synthesis from Marek's disease virus genome in the lymphoblastoid cell line, MDCC-MSB1, by 5-azacytidine //Journal of Veterinary Medical Science. – 1994. – T. 56. – №. 2. – C. 287-291.
12. Pejaković S. et al. Role of DNA methylation and CpG Sites in the viral telomerase RNA promoter during gallid herpesvirus 2 pathogenesis //Journal of Virology. – 2020. – T. 94. – №. 23. – C. e01488-20.
13. IuG I. et al. Issues on evolution of CpG islands in genome of Marek's disease virus //Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii. – 2010. – №. 1. – C. 84-86.
14. Leonov M. G. et al. Onco-epidemiological features, analysis of diagnosis and detection of ovarian cancer in Russia // Effective pharmacotherapy. - 2020. - T. 16. - No. 11. - S. 18-21.
15. Donchenko A.S., Yushkov Yu.G., Afonyushkin V.N. Search for candidate genes of the Marek's disease virus that can increase its pathogenicity during promoter demethylation. Bulletin of Russian Agricultural Science. - 2009. - No. 1. - P. 73–75.
16. Afonyushkin V.N., Gorodov V.S., Kilp A.S., Sigareva N.A. The role of methylation of herpesvirus promoters in the realization of pathogenic potential on the example of Marek's disease / Bulletin of NSAU (Novosibirsk State Agrarian University). 2022. No. 3 (64). pp. 83-92.
17. Yushkov Yu.G., Afonyushkin V.N., Gorodov V.S., Filipenko M.L., Boyarskikh U.A., Dudareva E.V. Issues of the evolution of CPG islets in the Marek's disease virus genome Journal of microbiology, epidemiology and immunobiology. 2010. No. 1. S. 84-86.