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Basic reproduction number for certain infectious porcine diseases: estimation of required level of vaccination or depopulation of susceptible animals

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SUMMARY
Basic reproduction number (R_0) is one of the fundamental quantitative characteristics in epidemiology of infectious human and animal diseases. This parameter reflects the biological properties of the infectious agent, the social and economic aspects of animal husbandry, natural factors associated with the habitat of the animal population invaded by the virus (microorganism), as well as the effectiveness of methods selected for infection control, in particular, the implementation of preventive measures; it also allows foreseeing the number and probability of occurrence of new secondary outbreaks in the area at risk of the disease spread. The paper presents data on the estimation of basic reproduction number (R_0) for a range of infectious porcine diseases. A systematic analysis has been undertaken with respect to the publications available on the estimation of R_0 for various virus isolates of African swine fever, classical swine fever, foot-and-mouth disease, porcine reproductive and respiratory syndrome, Aujeszky's disease, hepatitis E, encephalomyocarditis, porcine circovirus type 2, as well as pleuropneumonia associated with *Actinobacillus pleuropneumoniae*, and diseases caused by pathogenic isolates of *Mycoplasma hyopneumoniae.* Based on the obtained R_0 values, recommendations for the veterinary services are made on preventive vaccination of pigs against the above mentioned diseases in the areas at risk of infection spread. The necessary conditions for wild boar depopulation aimed to prevent new African swine fever outbreaks are identified, namely, the elimination of at least 75% of the wild boar population living in the risk zone within the period of time equal to one infectious period.

Key words: infectious porcine diseases, basic reproduction number (R_0), vaccination, depopulation, wild boars.

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Базовая скорость репродукции для некоторых инфекционных заболеваний свиней: оценка необходимого уровня вакцинации или депопуляции восприимчивого поголовья животных

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РЕЗЮМЕ

Одной из основных количественных характеристик в эпидемиологии/эпизоотологии инфекционных заболеваний человека и животных является базовая скорость репродукции (R_0). Данный показатель отражает как биологические свойства самого инфекционного агента, социально-экономические способы ведения животноводства, природные факторы обитания той популяции животных, в которую внедряется вирус (микроб), так и эффективность выбора методов борьбы с инфекцией, включая проведение профилактических мероприятий, а также позволяет предвидеть количество и вероятность возможного появления новых вторичных очагов инфекции в зоне риска распространения заболевания. В работе представлены данные по оценке базовой скорости репродукции (R_0) для ряда инфекционных болезней свиней. Проведен систематический анализ имеющихся публикаций по оценке этого показателя для различных изолятов вирусов африканской чумы свиней, классической чумы свиней, ящура, репродуктивно-респираторного синдрома свиней, болезни Ауески, гепатита Е, энцефаломиокардита, цирковируса типа 2, а также актинобациллезной плевропневмонии и заболеваний, вызываемых патогенными изолятами *Mycoplasma hyopneumoniae*. На основе полученных количественных значений показателя R_0 даны рекомендации ветеринарным службам по проведению профилактической вакцинации свиней от перечисленных заболеваний в зонах риска распространения инфекции. Определены необходимые условия по депопуляции дикого кабана для предотвращения возникновения новых очагов африканской чумы свиней: уничтожение за время, равное одному инфекционному периоду, не менее 75% обитающей в угрожаемой зоне популяции животных.

Ключевые слова: инфекционные болезни свиней, базовая скорость репродукции (R_0), вакцинация, депопуляция, дикие кабаны.

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INTRODUCTION

Basic reproduction number (R_0) is one of the fundamental quantitative characteristics in epidemiology of infectious human and animal diseases. In population biology, the concept of basic reproduction number is a central one for the "parasite – host" system and is expressed as the average number of offspring that one parasite is able to produce; the number of offspring will depend on the biological characteristics of the parasite [1].

For infectious animal diseases, R_0 is the average number of secondary cases one primary case would "generate/reproduce" in a completely susceptible population during the period of time equal to one infectious period [1, 2].

That is, when one infected individual is introduced into some closed population and has contacts with other animals in it, before the diagnosis is made with subsequent isolation (usually during the infectious period), a certain number of susceptible animals become infected.

Basic reproduction number directly reflects the biological properties of the infectious agent, the social and economic aspects of animal husbandry, natural factors associated with the habitat of the animal population invaded by the virus (microorganism), as well as the effectiveness of methods selected for infection control, in particular, the implementation of preventive measures. A biological agent can invade and persist in the animal population when $R_0 > 1$. In equilibrium, each case in a homogeneously mixing population of susceptible animals produces only one secondary case that later either recovers or dies, i.e. here $R_0 = 1$. When $R_0 < 1$, the epidemic process will die out.

In epizootiology (veterinary epidemiology), the interaction between a population of parasites (biological agents) and their hosts (animals) with a direct infection transmission mechanism is expressed as a simple phenomenological model of the "state and transition" type or the so called "SIR model" (see figure). This model divides the population into several classes (states): S – susceptible animals, I – infectious animals, and R – immune (recovered) or removed animals. That is, when a biological agent is introduced into a population of susceptible animals and they become infected, they transition to the state of infection with subsequent development of post-infection immunity (recovery) or removal from the population (death, emergency slaughter of animals) – the R state.

Based on the "state and transition" model theory developed by A. G. McKendrick and W. O. Kermak in 1927–1933, Head of the Mathematical Division of the World Health Organization N. Bailey suggested a mathematical model of the epidemic process that represents a system of

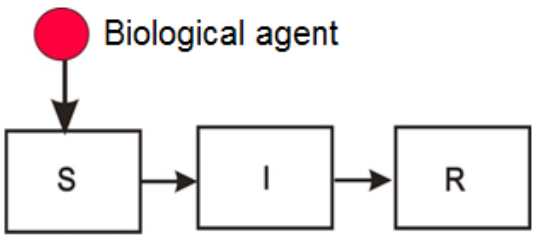

Fig. A simple phenomenological model (SIR model) of the epidemic process

Рис. Простая феноменологическая модель эпизоотического процесса типа SIR

differential equations [1]. The theory of the mathematical model of epidemics starts with considering a homogeneously mixing herd consisting of an animal population of size *N*. Let *S* be the number of susceptible animals, *I* – the number of diseased animals (the sources of infection) and *R* – the number of removed animals in this herd at time *t*, i. e. $S + I + R = N$. It was assumed that the average number of new cases (ΔI) among susceptible animals (*S*) in a certain time interval (Δt) will be proportional to both the number of the sources of infection and the number of susceptibles. If the frequency of contacts between animals within the herd is constant and equals β, then the average number of new cases of the disease during this interval of observation Δt will be $\beta SI\Delta t$, i.e. $\Delta S = -\beta SI\Delta t$.

The transition equation $S - I - R$ can be expressed as a system of differential equations:

$$\frac{\partial S}{\partial t} = -\beta SI$$
$$\frac{\partial I}{\partial t} = \beta SI - \gamma I$$
$$\frac{\partial R}{\partial t} = \gamma I$$

subject to initial condition $(S, I, R) = (S_0, I_0, 0)$ at time $t = 0$.

In this system of equations, the parameter γ (infected animal removal rate) is introduced, i.e. the number of diseased animals removed from the herd during time interval Δt will be $\gamma I\Delta t$.

A classical equation for calculation of R_0 from the above mentioned system of equations will be represented as follows:

$$R_0 = \beta/\gamma.$$

When $R_0 > 1$, infection continues to spread.

MATERIALS AND METHODS

The data of foreign and domestic researchers in the veterinary field are used in the paper. The researchers estimated R_0 by means of experiments in susceptible animals infected with various biological agents using a SIR model of dynamics of observed animal state transitions. To estimate the level of susceptible animal vaccination required to ensure the prevention of highly dangerous animal disease spread (*P*), the following commonly accepted formula was used [3]:

$$P = 1 - 1/R_0.$$

The same formula was used to calculate the required level of wild boar depopulation in the area at risk of African swine fever (ASF) spread.

RESULTS AND DISCUSSION

In the context of an increase in the number of ASF cases in both domestic pigs and wild boars in some European and Asian countries, veterinary specialists carry out extensive research to study the spatiotemporal dynamics of ASF spread [4, 5]. To estimate the dynamics of potential spread of the disease among animals on a farm (a closed population) if even a single animal is infected, as well as between farms, it is necessary to foresee the number and probability of potential new secondary outbreaks of infection in the area at risk of ASF spread. This is a condition for strict control to be implemented with respect to animal and animal product movement/trade at a certain distance from the primary outbreak. One of the possible epidemiological parameters can be the estimated R_0 value showing that, if an ASF outbreak occurs, then new outbreaks can occur in the area of potential risk of infection spread during the period of time equal to one infectious period. Probabilistic quantification of a potential animal disease epidemic, i.e. how many secondary cases can be produced in a herd, if even a single animal becomes diseased (within-herd R_0) or how many secondary outbreaks can occur in the area at risk of infection spread (between-herd R_0) depending on a variety of social, natural and economic factors, is of particular interest for epidemiology. In view of this, the scientific publications available on this topic have been analyzed; the results reported in the publications are presented in Table 1.

The results obtained show that, if even a single ASF case is detected on a farm (within a herd), the number of subsequently affected susceptible animals can vary between 2 and 15 (for serotype II), and the infectious period can last up to 14 days, and this appears to be attributable to the specificity and structure of production [6–9]. In the papers published by Russian researchers [10], basic reproduction number was estimated to range from 4 to 11 within domestic pig populations, and from 2 to 3 – for between-farm spread (for serotype II). In terms of the development of an epidemic, this suggests that, if one animal on a farm is ASFV-infected, it should be expected that subsequently, at the end of one infectious period, at least 11 other animals will become diseased (in some cases – up to 47 animals, as it was determined for serotype I on the island of Malta) [11, 12]. In case of ASFV serotype II spread from the primary outbreak area (a farm) to other farms in the area at risk, from 2 to 17 new outbreaks should be expected to occur during the infectious period [7, 10]. For ASFV serotype IX, the value of R_0 can be about 3 [13].

Due to the lack of effective vaccines for emergency vaccination of animals, one of the ways to control the spread of infection may only be the rapid slaughter (within the incubation period) of all animals in the area at risk of infection spread; besides, quarantine must be strictly observed, and relevant restrictions must be complied with [14]. The necessary condition for preventing the further spread of infection from the primary outbreak area in the area at risk (with regard to the territory of the Russian Federation) is the depopulation of at least $P = 1 - 1/2 = 0.5$ (or 50%) of susceptible animal population in the immediate risk zone [10].

One of the measures taken to eradicate ASF in wild boars is their depopulation (shooting) in the area at risk of infection spread around the primary outbreak of the disease (an animal that has died from ASF or a positive diagnosis established when carrying out diagnostic shooting in the territories inhabited by wild boars). Taking into account the obtained R_0 values for wild boar populations with the maximum R_0 value of up to 4 (3.77) [15, 16], the necessary and sufficient condition for depopulation (the upper confidence limit) to prevent the further spread of the disease will be determined as follows: $P = 1 - 1/4 = 0.75$ (or 75%). This means that, in case a wild boar that has died from ASF is found in some area, at least 75% of the population must be eliminated in the relevant range immediately (within the infectious period of 6 to 15 days). The range of one family usually encompasses a 2 to 5 km radius; but, depending on the natural conditions and landscape, some animals can travel up to 12 to 25 km within several days [17]. For example, if there is a population consisting of 30 boars (about 3–4 families) in the area at risk, then, after even one infected animal has been detected, at least 23 boars must be rapidly (within one

Table 1
The estimated values of within-herd and between-herd basic reproduction number for ASF based on the results of literature data analysis

Таблица 1
Оценочные величины внутристадной и межстадной базовой скорости репродукции для АЧС по результатам проведенного анализа литературных источников

Publication	Genotype	Isolate	Duration of infectious period (days)	Between-herd R_0	Within-herd R_0
S. A. Belyanin et al. (2011)	II		6.8 (5.0–8.6)	–	–
H. C. De Carvalho Ferreira et al. (2013)	I	Malta-78 Netherlands-86	6.8 ± 1.8 4.6 ± 1.4	–	18.0 (6.9–46.9)
J. Pietschmann et al. (2015)	II	Armenia-08	2–9	–	6.1 (0.6–14.5) 5.0 (1.4–10.7)
C. Guinat et al. (2015)	II	Georgia 2007/1	3–14	–	2.8 (1.3–4.8) within a pen 1.4 (0.6–2.4) between pens
V. M. Gulenkin et al. (2011)	II	Russia	5–15	2–3	4–11
M. B. Barongo et al. (2015)	IX	Uganda	–	3.24 (3.21–3.27) 1.63 (1.6–1.72) 1.9 (1.87–1.94)	–
F. I. Korennoy et al. (2017)	I	Ukraine, 1977	7 (within a farm) 19 (between farms)	1.65 (1.42–1.88)	7.46 (5.68–9.21)
C. Guinat et al. (2018)	II	Russia	4.5–8.3	4.4–17.3	–
I. Iglesias et al. (2016)	II	Russia	– (wild boar)	1.58 (1.13–3.77)	–
A. Marcon et al. (2020)	II	Czech Republic Belgium	6 (wild boar)	1.95 1.65	–

incubation period, i.e. 15 days according to the OIE recommendations) eliminated, and appropriate diagnostic tests must be carried out. Only in this case the required and sufficient conditions will be fulfilled to prevent the further spread of ASF in the wild boar population.

Table 2 presents the R_0 values for a number of porcine diseases. These values were obtained by foreign researchers when performing experiments on infection of susceptible animals with a field virus or by means of mathematical modelling using the transmission rate (β) values determined while analyzing the development of natural epidemics [18–21].

The data presented in Table 2 show that for such an infectious disease as classical swine fever the maximum value of R_0 can be about 81.3 (for weaner pigs) [23, 24]. This means that it is necessary to ensure that preventive vaccination conducted in a herd induces protective immunity in 99% of animals [(1 – 1/81.3) × 100%]; therefore, the vaccines used should have high immunogenicity.

To prevent the spread of infection in the area at risk (between the farms), the emergency vaccination (or depopulation) of at least 67% of animals in this area should be carried out [(1 – 1/2.9) × 100%] with $R_0 = 2.9$ [20, 25].

The results obtained by P. L. Eble et al. with respect to FMD show that immunization with a single vaccine dose performed within the study failed to protect pigs in the closed animal population (herd) against the disease transmission. Only as a result of vaccination with a four-fold vaccine dose, the disease might not continue to spread, but might reach equilibrium (with the death or recovery of one animal, $R_0 = 1$) due to the possible development of not fully stable immunity in some animals within the vaccinated animal population [19]. These results indicate that vaccines with high protective activity (immunogenicity) should be created for immunization of pigs, and appropriate vaccination schedules should be developed taking into account the possibility of implementing a DIVA strategy.

The vaccine against Aujeszky's disease used within the study published by M. C. M. De Jong and T. G. Kimman which ensures that at least 90% of animals in the population are protected is able to prevent the further spread of infection within the farm (herd) with $R_0 = 10$ [18].

In order to prevent the transmission of porcine reproductive and respiratory syndrome in a herd, it is necessary to induce protective immunity in at least 91%

Table 2
The estimated values of within-herd and between-herd basic reproduction number for certain porcine diseases based on the results of literature data analysis

Таблица 2
Внутристадная и межстадная оценочные величины базовой скорости репродукции для некоторых болезней свиней, полученные по результатам проведенного анализа данных литературы

Publication	Disease (genome/strain)	Duration of infectious period (days)	Between-herd R_0	Within-herd R_0
A. Stegeman et al. (1999)	classical swine fever	18	2.9	–
E. Weesendorp et al. (2009)	classical swine fever Paderborn strain Brescia strain	–	–	36 17
D. Klinkenberg et al. (2002)	classical swine fever	–	3.39 (between pens)	15.5 (within a pen)
H. Laevens et al. (1999)	classical swine fever	32	–	13.7 81.3 (for weaner pigs)
M. Andraud et al. (2008)	porcine circovirus type 2	35	1.47	5.9 (1.8–10.1)
M. Kluivers et al. (2006)	encephalomyocarditis	–	–	1.4 (within a pen)
H. Maurice et al. (2016)	encephalomyocarditis	–	–	4.2
H. Maurice et al. (2002)	encephalomyocarditis	–	–	1.24 (0.39–4.35)
V. Spyrou et al. (2004)	encephalomyocarditis	–	–	9.87 (a combined estimate for several viruses)
M. C. M. De Jong, T. G. Kimman (1994)	Aujeszky's disease	–	–	10 (non-vaccinated) 0.53 (vaccinated)
P. L. Eble et al. (2008)	foot-and-mouth disease	2.3–6.5	–	40 (non-vaccinated) 11 (single-dose vaccinated) 1 (four-fold-dose vaccinated)
A. G. J. Velthuis et al. (2003)	*Actinobacillus pleuropneumoniae*	from 2 days to several weeks (in case of chronic disease)	10	–
T. Meyns et al. (2004)	*Mycoplasma hyopneumoniae* (virulent isolates)	positive after inoculation 14–32	–	1.47 (0.68–5.38)
E. Pileri (2015)	porcine reproductive and respiratory syndrome, genotype 1	12–14	non-vaccinated 2.78 (2.13–3.43) vaccinated 0.53 (0.19–0.76)	3.53 (2.89–4.18) farm 1 7.11 (3.55–10.68) farm 2
C. Charpin et al. (2012) [22]	porcine reproductive and respiratory syndrome, genotype 1	7–63	–	2.6 (1.8–3.3)
M. Bouwknegt et al. (2008)	hepatitis E	49 (block 1) 13 (block 2)	–	8.8 (4–19) (contact exposure)

of vaccinated animals [(1 – 1/10.68) × 100%] with the maximum R_0 value of 10.68 [18, 26]. The studies conducted show that, if appropriate preventive vaccination has been carried out in the area at risk prior to the outbreak, the disease will not continue to spread between the farms, because the maximum R_0 value is 0.76 [26]. If there are any susceptible animals on the farms, it is necessary to induce protective immunity in at least 71% of animals in the area at risk of infection spread with the maximum R_0 value of 3.43 [(1 – 1/3.43) × 100%].

As for porcine circovirus type 2, in order to prevent the further spread of infection (with the maximum R_0 value of 10.1), it is necessary that immunization should induce protective immunity in 90% of animals [27]. A similar result was found for encephalomyocarditis (with $R_0 = 9.87$) [28–31].

In case of hepatitis E, vaccination-induced protective immunity (for the maximum R_0 value of 19, as determined in the course of experiments on contact infection of pigs) should be about 95% [32].

It was determined that for the virulent isolate of *Mycoplasma hyopneumoniae* [33] the vaccination carried out on a farm should protect at least 81% of animals [(1 – 1/5.38) × 100%] with the upper confidence limit for R_0 being $R_0 = 5.38$. With the said level of pig population protection, the disease should not occur on the farm if infection is introduced into the population.

The data obtained for *Actinobacillus pleuropneumoniae* [21] indicate that, even if there is only one infection outbreak area (a farm), the animals in the area at risk of further spread of the disease should be vaccinated using vaccines with high immunogenicity. Livestock vaccination should cover at least 90% of the total number of farms [(1 – 1/10) × 100%].

CONCLUSION

The above mentioned basic reproduction number (R_0) values for some infectious porcine diseases are indicative of a certain variability in the value of R_0. Apparently, the R_0 values may be dependent on the conditions in which laboratory experiments are carried out, the age group of the animal population selected for experiments, the methods of infection, the virulence of the virus used for infection, etc. Nevertheless, the estimation of R_0 makes a certain scientific contribution to basic applied epidemiology of a number of infectious porcine diseases and is necessary when planning such anti-epidemic activities as preventive immunization or depopulation of susceptible animals aimed to prevent disease outbreaks and the further spread of infection. In particular, with regard to wild boar depopulation in the area at risk of ASF spread, the necessary condition for stopping the further spread of infection is the elimination of at least 75% of the wild boar population living in the risk zone within the period of time equal to one infectious period.

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