

Additive-Polygenic Inheritance of Reproductive System Diseases in Holstein Cows in Subpopulations

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Abstract— The revealed gynecological pathologies in Holstein cows can occur under the influence of different allelic systems and have a polygenic character. As a result of the research, a link between the reproductive traits and adaptability was established, which were characterized by low heritability and were subject to inbreeding depression. Selection rates increased from generation to generation by an average of 13.8 %, but did not always lead to changes in disease rates. The correlation coefficient between the milk yield of cows for 305 days of first lactation and the service period was -0.227 ± 0.013 (F test 5.2), the coefficient of linear regression of the service period for milk yield for 305 days of first lactation -0.45 ± 0.033 . A positive correlation ($r = +0.52 \pm 0.012$) was found between the milk yield of full-aged cows for 305 days of lactation and the number of cows eliminated due to infertility ($r = +0.52 \pm 0.012$). Genetic and environmental factors together exceeded the threshold of adaptability, so the body's ability to resist became weakened. Correlation coefficient of daughter-mother on duration of diseases $+0.33 \pm 0.022$, on age of animals at the beginning of disease $+0.36 \pm 0.021$. The recurrence rates of gynecological pathologies in cows from the first to the second lactation are $+0.807$, from the second to the third $+0.892$, from the first to the third $+0.454$. From the data obtained, it follows that heritability depends on factors, each of which has a relatively small impact on variability and is determined by many genes. Signs with a threshold deviation are not associated with the efficiency of breeding productivity. Gynecological pathologies in offspring arise under the influence of different allelic systems.

Keywords—reproductive diseases in cattle, heritability, resistance, susceptibility, frequency of exposure.

I. INTRODUCTION

The reproductive function of cattle refers to complex biological processes that ensure the reproduction and adaptation of animal populations. Studies on the possibility of assessing the genome of cows and its relationship with adaptation on the basis of a one-step method [1]. Adaptive selection of Holstein breed on Sakhalin took place during 28-30 generations. In the ever-changing conditions of feeding and maintenance, there has been an accumulation of genetic variability of traits responsible for fitness. The etiology of diseases of the reproductive system in animals with a genetic predisposition has not been studied enough. Especially great value it acquires at the adaptations of animals in extreme climatic conditions of breeding. A statistically significant relationship between productive longevity and culling ages was established [2]. To improve longevity, an economic

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model of adjusted productive life of a herd of dairy cows is proposed [3]. To improve longevity, an economic model of adjusted productive life of a herd of dairy cows is proposed [3]. The solution to this problem can be approached by considering the genetic nature of these diseases. Physiological mechanisms of manifestation of these signs are different, so the genes responsible for their manifestation also differ to some extent. Most often, these diseases occur when the interaction of the predisposing genotype with environmental factors reaches a certain threshold state [5].

Morbidity of animals in the population is characterized by the frequency of their manifestation. Infecting agents are pathogenic. Although the very manifestation of the trait is subject to the law "all or nothing", the degree of its manifestation can vary widely (due to the influence of other genetic factors and environmental factors, or both). The incidence of the disease can spread in a small population partly due to the founder effect [6].

As the population grows, allele frequencies will generally continue to reflect the original small group. Because the founder of a small population, gene drift can play an important role in determining the genetic memory of subsequent generations, and allele frequencies can change. Since the founder population comes from a small number of animals, that these animals with a particular disease share a common genetic profile rather than having several different disease mutations or susceptibility alleles. This homogeneity is important because genetic heterogeneity can make the identification of any particular disease allele very difficult.

This group of diseases is characterized by multifactorial (due to many loci) control of stability and susceptibility under significant influence of environmental conditions (additive-polygenic inheritance [7]. When certain values of predisposition - the so-called threshold of susceptibility-are exceeded, the mechanism of multifactorial disease development is triggered [8].

The occurrence of most reproductive traits in animals is quite complex, so a direct assessment of all the factors of influence is almost impossible, since many different genes are involved in the susceptibility and each of them contributes. In this regard, the result of genetic analysis obtained by the method of variation statistics becomes preferable. It allows to use methods of phenotypic correction and penetrant control in related groups (frequency of gene manifestation, determined by the number of individuals within the related group).

Genetic analysis is possible on the condition that susceptibility is determined by multifactorial.

II. METHODS

The objective is to study the degree of genetic predisposition to gynecological diseases of cows of Sakhalin population of Holstein breed at adaptive selection.

The frequency of occurrence of pathologies of the reproductive system in cows of the Sakhalin population of the Holstein breed for five overlapping generations was investigated. The genetic conditionality and the nature of resistance to gynecological pathologies were assessed by clinical genealogical and genetic-statistical methods. The data obtained in the experiment were processed using the application program Statistica 8.0 ("StatSoft Inc.", USA.) The tables show the average values \bar{x} and the error S_x . The differences were considered statistically significant at $p < 0.05$. For the analysis genealogical schemes of lines and related groups with indication of all cases of diseases were made. The incidence rate was calculated within related groups, by which they were compared with each other and with the population frequency. The influence of kinship relations and the degree of inbreeding on the frequency of reproductive pathologies in animals was studied. In genetic analysis, the Chi-square assent criterion was used to compare observed frequencies with those expected in discrete classes. Traits were divided into two phenotypic classes, with a single threshold separating them. Gradations of classes were considered as norm and susceptibility. The frequencies for genetic analysis are replaced with average susceptibility so that the distribution is normal. The normalized values are taken from the truncated normal distribution table [9].

The group averages are expressed in fractions of the standard deviation with respect to the threshold [10]. The correlation between kinship groups and the population was determined from the threshold deviations:

$$t = \frac{X_r - X_p}{i} \tag{1}$$

where X_r – average deviation from threshold in related group;

X_p – average deviation from threshold of population;

i – average deviation of susceptible animal from average.

Due to the environmental factors of similarity between parents and their descendants, the heritability of susceptibility was defined as the ratio of the genetic variant to the General phenotypic.

The following formula is used to calculate the inbreeding coefficient (F_x):

$$F_x = \Sigma (1/2)^n (1 + Fa), \tag{2}$$

where n is the number of individuals in any lineage, including the parents of X , the common ancestor of Fa , and all individuals of a given lineage connecting the parents to their common ancestor. Susceptibility and resistance frequencies were determined:

$$P = \frac{P_1}{n}, \tag{3}$$

where P – frequency (proportion of ill animals);

$$q = \frac{P_0}{n} \tag{4}$$

where q – frequency (proportion of healthy animals);

$$\delta = \sqrt{pq} \text{ – standard deviation;} \tag{5}$$

$$S_x = \frac{p\sqrt{1-p}}{n} = \frac{\sqrt{p-q}}{n} \text{ the error of the arithmetic average} \tag{6}$$

Power of influence index (r_w) in the analysis of variance:

$$r_w = \frac{\delta_x^2 - \delta_z^2}{\delta_x^2 + (n_0 - 1)\delta_z^2} \tag{7}$$

where δ_x^2 – between – groups variance δ_z^2 bintra – groups variance

A test (F^* - criterion) ($F = \frac{S_y^2}{S_x^2}$) was considered as a ratio of sample variances. When this value is greater than the critical value at a given level of significance, the null hypothesis was rejected.

The following pathologies were studied in cows persistent ovarian corpus luteum, ovarian hypofunction, ovarian cysts, ovarian sclerosis, uterine subinvolution and endometritis. Diagnosis of pregnancy was carried out on the 19th-23rd, 28-32, 38-45 days after artificial insemination by transrectal echographic examination with Easi-Scan-3 "BCF Technologi" ultrasound scanner, with a linear sensor 4.5-8.5 MHz. According to clinical signs and scanner SIUI CTS 7700, as well as rectal studies revealed the causes and extent of reproductive dysfunction. When ovarian cysts were detected in cows, they were differentiated into follicular and corpus luteum cysts.

To identify the genetic predisposition to gynecological diseases of cows of the Sakhalin population, data on 2417 heads of sick animals and dropped out of the herd due to infertility were analyzed. The studies were carried out according to the guidelines for diagnosis, veterinary control of the reproductive function of cows. The diagnosis took into account the factors that cause these pathologies: high milk productivity during the period of milking, inflammatory processes of the uterus, errors in feeding, in particular, feeding with poor-quality feed, inactivity, change in the behavior of sick animals.

III. RESULTS

The frequency of groups of gynecological diseases in cows in a number of generations was: $p = 0.1916 \pm 0.0045$. Coefficient of phenotypic variability: $Cv = 22.8\%$ of genetic variability $Cv_g = 8.6\%$. Comparison of observation frequencies in discrete classes of diseases with their expected values according to the Chi-squared compliance criterion corresponded to the normal distribution and had a single-mode configuration (F -criterion 5.5). Selection rates increased from generation to generation (1.1-6.2 % first generation; 1.5-9.2 % fifth generation). On average, the selection pressure increased from 3.4 % in the first generation to 4.8% in the fifth one. The frequency of diseases in this case were in the range $0.0022 \pm 0.00751 - 0.1916 \pm 0.0045^{***}$ in the first generation, 0.0430 ± 0.00531 -Insert tag (Alt+2) $0.1415 \pm 0.0075^{***}$ in the fifth. However, this did not always lead to significant changes in disease rates. This is due to the fact that the genes of many loci together affect the traits responsible for susceptibility in accordance with the newly formed combinations. As a result, frequencies with small deviations in several overlapping generations of selection are formed (Table 1).

TABLE I. INTENSITY OF SELECTION AND FREQUENCY DISTRIBUTION OF GYNECOLOGICAL DISEASES IN SAKHALIN COWS IN OVERLAPPING GENERATIONS, P

Disease	Population (n =2417) $p \pm S_x$	I generation		II generation		III generation		IV generation		V generation	
		$p \pm S_x$	Selection ratio %	$p \pm S_x$	Selection ratio %	$p \pm S_x$	Selection ratio %	$p \pm S_x$	Selection ratio %	$p \pm S_x$	Selection ratio %
Persistent corpus luteum of ovaries	0.1489±0.00251	***0.1916±0.00452	5.2	***0.1750±0.00401	4.8	**0.1252±0.00507	5.9	***0.1167±0.0047	6.2	***0.1415±0.00754	6.3
Hypofunction of ovaries	0.0289±0.01407	0.0176±0.01401	1.2	-	0.7	0.0322±0.01386	1.3	0.0296±0.01354	1.5	0.0861±0.01365	1.5
Ovarian sclerosis	0.0103±0.03594	0.0044±0.03982	1.1	0.0055±0.03983	2.2	0.0132±0.03977	2.4	0.0191±0.03964	2.5		2.6
Ovarian cyst	0.0268±0.01514	0.0022±0.01533	5.4	**0.0335±0.01533	5.9	0.0132±0.01528	5.5	0.0087±0.01531	6.6	*0.0430±0.00531	7.2
Endometritis	0.0550±0.00730	0.0022±0.00751	6.2	0.0726±0.00724	8.2	0.0398±0.00739	7.5	0.0487±0.01545	9.1	0.0523±0.00734	9.2
Subinvolution of uterus	0.0910±0.00433	***0.1101±0.00425	1.4	***0.1024±0.00432	2.0	0.0986±0.00403	2.1	***0.0662±0.00435	2.2	0.0769±0.00447	2.3
Average	0.3595	0.0712±0.00214	3.4	0.0778±0.00174	3.9	0.0537±0.00185	4.1	0.0482±0.00169	4.7	0.0667±0.00297	4.8

^a. S_x – arithmetical mean error,

^b. p – frequency of diseases in generations,

^c. n – number of diseased animals,

^d. * – reliably at $p \leq 0.01$,

^e. ** – reliably at $p \leq 0.001$;

^f. *** – reliably at $p \leq 0.0001$.

Studies have suggested the presence of a complex of causes of exposure to these diseases. In most cases, the influence of various biological and stochastic factors was observed. Complications brought errors in feeding and infection. Signs of fertility can be classified as threshold and quantitative. This gradation indicates a hidden variation, which is negatively correlated with the phenotypic value of the main breeding feature-milk yield of cows for 305 days of lactation. Thus, over many generations, there is an accumulation of both phenotypic and genetic variability that characterizes susceptibility as such. The correlation coefficient between the milk yield of cows for 305 days of first lactation and the service period was -0.227 ± 0.013 (F test 5.2) The coefficient of linear regression of signs of reproduction to the sign of productivity, respectively ($b_{yx} = 0.45 \pm 0.033$ service-period of milk yield for 305 days of the first lactation). A positive correlation ($r = +0.52 \pm 0.012$) was found between the milk yield of full-aged cows for 305 days of lactation and the number of cows eliminated in terms of fertility. It follows that genetic and environmental factors together exceeded the

threshold of adaptability, so the body's ability to resist became weakened. Correlation coefficient of the daughter-mother on duration of diseases ($r = +0.33 \pm 0.022$), on age of animals at the beginning of disease ($r = +0.36 \pm 0.021$). The coefficients of recurrence of gynecological pathologies in cows from the first to the second lactation $+0.807$, from the second to the third $+0.892$, from the first to the third $+0.454$, respectively This tendency has been manifested in several generations and from a breeding point of view it probably corresponds to this situation.

Since the value of the selection coefficient varied significantly from one generation to another, it is necessary to assess the impact of inbreeding. The vulnerability was discovered a graded continuum of increasing susceptibility to disease with increasing coefficient of inbreeding. Consequently, an increase in the frequency of major pathologies associated with an increase in the degree of inbreeding indicates a multifactorial effect of susceptibility (Fig.1).

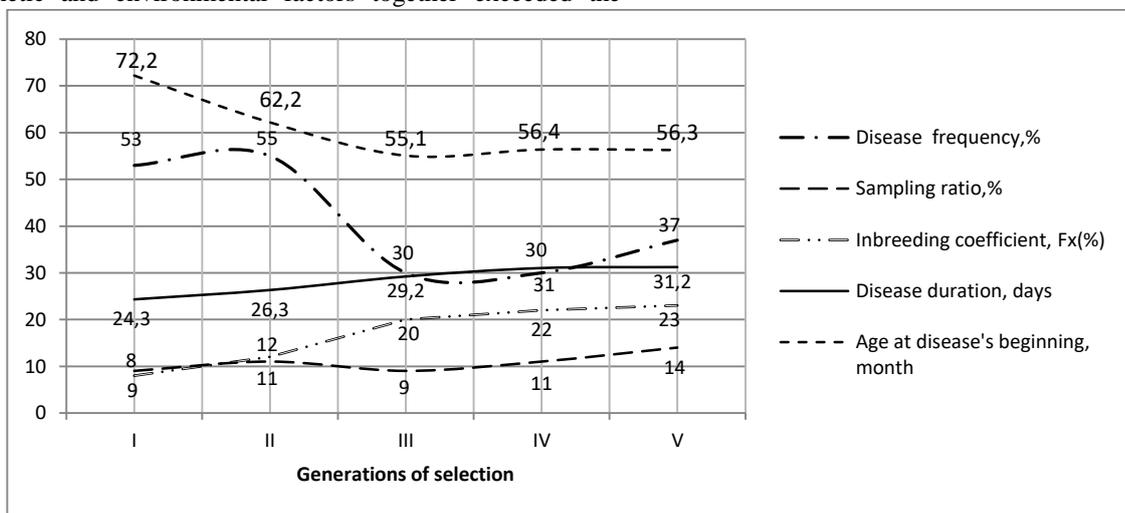


Fig. 1. The influence of inbreeding on susceptibility to diseases of the reproductive traits in cows of the Sakhalin population in discrete generations

The observed phenotypic differences, both in the mean values and in the selection effect, can also be attributed to the non-genetic effect. However, the response to selection may be cumulative in nature due to the long length of time.

TABLE II. HERITABILITY OF MULTIFACTORIAL SIGNS OF SUSCEPTIBILITY-SIGNS OF SENSIBILITY OF HAVE COWS SAKHALIN COWS WITH SINGLE-MODE FREQUENCY DISTRIBUTION

Disease	Cattle amount <i>n</i>	<i>p</i> , %	Phenotypic variance δ^2_T	Genetic variant 2_s	Heritability coefficient
Persistent corpus luteum of ovaries	360	41.2	49.21	11.31	0.23

Hypofunction of ovaries	70	8.01	27.14	8.41	0.31
Ovarian sclerosis	25	2.86	16.66	2.33	0.14
Ovarian cyst	65	7.44	26.24	0.52	0.02
Endometritis	133	15.2	35.90	3.94	0.11
Subinvolution of uterus	220	25.2	46.22	10.16	0.22

From the data obtained, it follows that gynecological diseases differed in the degree of genetic determination. The values of heritability coefficients depended on many factors, each of which has a relatively small impact on variability and is determined by many genes. Genetic analysis presumably indicated that related groups with the additive effect of many loci differed in the set of polyallel systems (Fig.2).

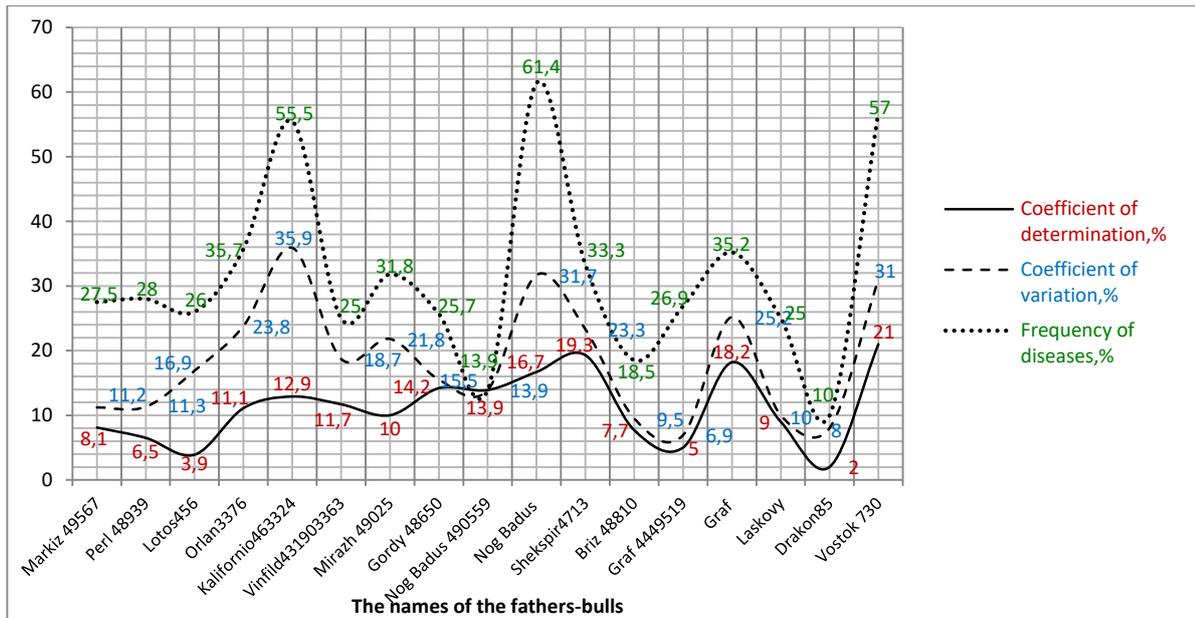


Fig. 2. Additive-polygenic effect of susceptibility to gynecological diseases of cows-daughters of bulls of Sakhalin population

This figure shows additive-polygenic inheritance of gynecological pathologies in offspring. The incidence of disease in the daughters of bulls varied significantly and depended on the total action of alleles causing the pathological condition. Pathological phenotype was manifested when the total effect of genetic and environmental factors reached or exceeded the threshold value of the coefficient of

determination. This trend is observed when calculating the relationship of traits in related groups and populations by threshold deviations. The offspring obtained from animals of the evaluated lines and related groups with different degrees of susceptibility and resistance to diseases differed significantly in the distribution of the observed frequency values (Table 3).

TABLE III. CORRELATION OF SUSCEPTIBILITY TO GYNECOLOGICAL DISEASES IN DAUGHTERS OF BREEDING BULLS AND POPULATION

Line	Fathers	Amount of daughters, n	<i>p</i> , %	<i>x</i>	<i>i</i>	<i>t</i>
Vis Bek Ideal 1013415	Markiz 49567	40	27.5	0.61	1.22	0.29
	Perl 48939	25	28.0	0.58	1.20	0.27
	Lotos456	46	26.0	0.64	1.25	0.30
	Orlan3376	42	35.7	0.35	1.03	0.09
	Kalifornio463324	18	55.5	0.00	0.78	-0.3
	Vinfild431903363	22	31.8	0.46	1.11	0.18
Reflection Sovering 198998	Mirazh 49025	35	25.7	0.64	1.24	0.31
	Gordy 48650	86	13.9	1.08	1.59	0.52
	Nog Badus 490559	57	61.4	0.00	0.79	-0.3
	Shekspir4713	18	33.3	0.44	1.09	0.17
	Briz 48810	27	18.5	0.92	1.46	0.45
	Graf 4449519	71	35.2	0.38	1.05	0.12
Montvik Chiftein 95679	Laskovy	26	26.9	0.61	1.22	0.29
	Drakon85	64	25.0	0.67	1.27	0.32
Population	Vostok 730	10	10.0	1.20	1.75	0.54
		2121	41.1	0.253	0.966	

The index of power of influence (r_w) for fathers was 19.8 %, including 11.22% for lines, respectively. It should be noted that the frequency of susceptibility to diseases significantly depended on the feeding conditions of animals, and concern only the phenotypic values of signs.

IV. CONCLUSION

1. The causes of genetic pathologies of the reproductive system in subpopulations may be related to the result of adaptive selection.

2. Reproductive traits, closely related to adaptability, are characterized by low heritability and are particularly susceptible to inbred depression.

3. Signs with threshold deviations are not associated with the efficiency of breeding productivity. Gynecological pathologies in offspring arise under the influence of different allelic systems.

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