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ASSESSMENT OF BASELINE CYTOGENETIC PARAMETERS IN BLOOD ERYTHROCYTES AND BUCCAL EPITHELIAL CELLS OF HEALTHY CATTLE AND SMALL RUMINANTS IN THE ALMATY REGION

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Baseline cytogenetic parameters in healthy livestock are essential for evaluating stress and mutagenic effects under environmental conditions. This study aimed to establish reference values of genome instability in cattle and sheep of different sex and age groups in the Almaty region. Cytogenetic analysis was conducted on "Kazakh fat-tailed coarse-wooled" sheep and "Alatau" cattle using two minimally invasive assays: the micronucleus (MN) test in peripheral blood erythrocytes and the cytome assay in buccal (nasal) epithelial cells. The research quantified genome instability and described the spectrum of cytogenetic abnormalities. Baseline values of MN were determined in both species. In cattle, MN frequency in erythrocytes and reticulocytes ranged from 0–0.5% and 0.1–0.8%, while in nasal epithelial cells the average MN level was 0.015% and other abnormalities reached 0.025%. In sheep, MN frequency varied from 0.1% to 1.2% (mean 0.31%). The mean MN level in buccal epithelium was 0.028%, whereas karyological abnormalities reached 0.04%. Comparative evaluation showed higher genome instability in females than males and in young animals versus adults, demonstrating the influence of physiological factors. The study provides reference values for cytogenetic biomarkers and identifies typical abnormalities in epithelial cells of farm animals. These results can support biomonitoring programs and improve assessment of livestock genetic health under environmental and anthropogenic stressors.

Key words: *buccal epithelium, cattle, erythrocytes, karyologic disorders, micronucleus test, nasal epithelium, sheep.*

АЛМАТЫ ӨҢІРІНДЕГІ САУ ІРІ ҚАРА ЖӘНЕ ҰСАҚ МҮЙІЗДІ МАЛДЫҢ ҚАН ЭРИТРОЦИТТЕРІ МЕН БУККАЛЬДЫ ЭПИТЕЛИЙ ЖАСУШАЛАРЫНДАҒЫ НЕГІЗГІ ЦИТОГЕНЕТИКАЛЫҚ КӨРСЕТКІШТЕРДІ БАҒАЛАУ

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Сау ауыл шаруашылығы жануарларындағы бастапқы цитогенетикалық көрсеткіштер қоршаған орта факторларының стресс туғызатын және мутагендік әсерлерін бағалауда аса маңызды болып табылады. Осы зерттеудің мақсаты – Алматы өңіріндегі әртүрлі жыныс және жас топтарына жататын ірі қара және ұсақ малдардағы геномдық тұрақсыздықтың анықтамалық (референт-

тік) мәндерін белгілеу. Зерттеу қазақтың құйрықты қылшықжүнді қойларына және алатау тұқымды ірі қара малдарына жүргізілді. Цитогенетикалық талдау перифериялық қан эритроциттеріндегі микроядролық тест және буккал (мұрын) эпителий жасушаларындағы цитома-талдау әдістері арқылы жүргізіліп, геномдық тұрақсыздық деңгейін сандық бағалауға және цитогенетикалық аномалиялар спектрін сипаттауға мүмкіндік берді.Ірі қара малдарда эритроциттердегі микроядролардың жиілігі 0–0,5% аралығында, ал ретикулоциттерде 0,1–0,8% деңгейінде болды. Мұрын эпителийінде орташа микроядролар деңгейі 0,015%, ал басқа кариологиялық бұзылыстар 0,025%-ға жетті. Қойларда микроядролар жиілігі 0,1–1,2% (орташа 0,31%), буккал эпителийінде 0,028% деңгейінде анықталды, ал кариологиялық бұзылыстар 0,04%-ға дейін жетті. Салыстырмалы талдау нәтижесінде аналық малдар мен жас жануарларда геномдық тұрақсыздықтың жоғары екені анықталды, бұл физиологиялық факторлардың ықпалын көрсетеді. Алынған деректер мал шаруашылығындағы генетикалық денсаулықты бағалау және қоршаған орта мен антропогендік стрессорлардың әсерін бақылау үшін пайдаланылуы мүмкін.

Түйінді сөздер: *ауыз қуысы эпителийі, ірі қара мал, эритроциттер, кариологиялық бұзылыстар, микроядролық тест, мұрын эпителийі, қой.*

ОЦЕНКА БАЗОВЫХ ЦИТОГЕНЕТИЧЕСКИХ ПОКАЗАТЕЛЕЙ В ЭРИТРОЦИТАХ КРОВИ И КЛЕТКАХ БУККАЛЬНОГО ЭПИТЕЛИЯ ЗДОРОВОГО КРУПНОГО И МЕЛКОГО РОГАТОГО СКОТА АЛМАТИНСКОГО РЕГИОНА

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Базовые цитогенетические показатели у здоровых сельскохозяйственных животных важны для оценки стрессовых и мутагенных воздействий внешней среды. Целью настоящего исследования было установление референсных значений геномной нестабильности у крупного и мелкого рогатого скота различных пола и возраста в Алматинском регионе. Анализ проводили на овцах породы «Казахская курдючная грубошёрстная» и КРС породы «Алатау» с использованием микроядерного теста в эритроцитах периферической крови и цитоме-анализа клеток буккального (носового) эпителия, что позволило количественно оценить уровень геномной нестабильности и выявить спектр цитогенетических нарушений. У крупного рогатого скота частота микроядер в эритроцитах и ретикулоцитах составляла 0-0,5% и 0,1-0,8% соответственно, а в эпителии носовой полости средний уровень микроядер достигал 0,015%, при этом кариологические аномалии – 0,025%. У овец частота микроядер варьировала в пределах 0,1-1,2% (в среднем 0,31%), в буккальном эпителии – 0,028%, с аномалиями до 0,04%. Показано, что у самок геномная нестабильность выше, чем у самцов, а у молодых животных выше, чем у взрослых, что отражает влияние физиологических факторов. Полученные референсные значения могут использоваться для биомониторинга генетического статуса сельскохозяйственных животных и оценки воздействия природных и антропогенных стрессоров.

Ключевые слова: *буккальный эпителий, крупный рогатый скот, эритроциты, кариологические нарушения, микроядерный тест, носовой эпителий, овцы.*

Introduction

For the successful development of domestic animal husbandry, as well as for the rational treatment and prevention of diseases in farm animals, comprehensive and detailed studies of their health are essential. Modern and timely vaccination is one of the fundamental mechanisms ensuring the well-being of industrial livestock farming, along with a properly selected diet and appropriate animal housing conditions. A substantial body of data has been accumulated regarding the use of various vaccines and vaccination schedules [1, с. 127, 2, с. 43]. Vaccination is mandatory for all animals; however, each administered vaccine induces significant changes in the organism at both the cellular and systemic levels [3, с. 97, 4, с. 361].

Damage to the genetic apparatus of cells has been demonstrated in relation to various DNA- and RNA-containing viruses. These phenomena have been confirmed for several viruses that cause human diseases, including hepatitis [5, с. 17], rubella [6, с. 47], retroviruses [7], AIDS [8, с. 301], SARS-CoV-2 [9, с. 50], and

others [10, c. 224], including certain vaccine preparations [11, c. 63]. In other words, viruses are capable not only of inducing immunosuppressive conditions following illness and/or vaccination, but also of acting as biogenic mutagens, triggering genetic disruptions and chromosomal rearrangements [10, c. 224]. However, data on genome instability associated with viral diseases and vaccine preparations in animals are extremely limited in the scientific literature [4, c. 361, 10, c. 224, 12, c. 98].

At the initial stage of research on virus-induced mutagenesis in farm animals, it is essential to investigate the reference (baseline) values of genome instability in cattle and small ruminants. One of the key indicators of health, genome stability, and the organism's adaptive potential is cytogenetic homeostasis. It can be characterized using the micronucleus test, which involves the quantitative assessment of cells containing micronuclei and other cytological abnormalities [13, c. 25].

Micronuclei are extranuclear segments of chromatin that arise due to genetic and structural abnormalities, as well as dysfunction of the mitotic spindle apparatus. They are rarely formed during mitosis in normal cells; however, if the cells exhibit genomic instability or the organism has been exposed to genotoxic agents, the frequency of micronuclei formation increases. For this reason, micronuclei are widely used in epidemiology and cytogenetics as biomarkers to assess the genetic profile or genome instability resulting from external exposure or the mutagenic potential of agents capable of causing chromosomal aberrations in somatic cells [14, c. 17].

The most convenient approaches for in vivo micronucleus analysis include the examination of micronuclei in peripheral blood erythrocytes [15, c. 71] and the cytome assay of buccal epithelial cells [16, c. 159]. These methods are informative and minimally invasive, making them suitable for evaluating and monitoring genetic damage in animals. Moreover, their low cost and ease of sample preparation make the micronucleus test an ideal choice for genetic, environmental, and epidemiological research.

The aim of the present study was to assess the reference (baseline) values of genome instability in cattle and small ruminants (sheep) of various sex and age groups in the Almaty region, as well as to characterize the spectrum of abnormalities detected in peripheral blood erythrocytes and buccal epithelial cells.

Purpose. To establish baseline (reference) cytogenetic indicators of genome instability in healthy cattle and sheep of different sex and age groups in the Almaty region by assessing micronuclei and karyological abnormalities in peripheral blood erythrocytes and epithelial cells (nasal in cattle, buccal in sheep).

Tasks. To determine baseline (reference) values of micronuclei and karyological abnormalities in cattle and sheep using peripheral blood erythrocytes and epithelial cells (nasal in cattle, buccal in sheep); to compare baseline cytogenetic indicators across age groups in both species and sex groups in sheep; and to assess erythropoietic activity in cattle via reticulocyte frequency and examine its association with micronucleus frequency.

Materials and Methods

Ethical approval: This study was approved during a meeting of the Local Ethical Commission at the Institute of Genetics and Physiology of the Science Committee of the Ministry of Higher Education and Science of the Republic of Kazakhstan, №2 on May 23, 2024.

Subjects: To assess the cytogenetic status of farm animals (sheep and cattle), a micronucleus analysis was performed in peripheral blood erythrocytes and a cytome assay was conducted in buccal epithelial cells of sheep and nasal epithelial cells of cattle. Biological samples were collected from 37 sheep of the "Kazakh fat-tailed coarse-wooled" breed and 16 cattle of the "Alatau" breed, representing various sex and age groups. Cytogenetic preparations were made from the collected samples of blood and buccal/nasal epithelium.

Preparation of peripheral blood erythrocyte smears: Peripheral blood samples were collected using a vacuum blood collection system into tubes containing K_2EDTA as an anticoagulant. Smears were prepared using standard laboratory procedures [16, c. 159]. The air-dried blood smears were fixed in 96% ethanol for 30 minutes, then air-dried again and stained with a 4% Romanowsky–Giemsa solution for 20 minutes. The frequency of micronuclei and cytological abnormalities was evaluated in normochromic erythrocytes under a Zeiss AxioLab A.1 microscope using oil immersion at 16×100 magnification. During cytogenetic analysis, all structural abnormalities in erythrocytes deviating from normal morphology were recorded. Up to 20,000 erythrocytes per individual animal were examined. Photodocumentation was carried out for the most characteristic abnormalities observed in the peripheral blood erythrocytes.

Preparation of buccal/nasal epithelial cell smears: Buccal epithelial samples (from the oral cavity of sheep) and nasal epithelial samples (from cattle) were collected using a cytobrush. After collection, the brush was placed in a 15 mL tube containing 5 mL of physiological saline. Following vigorous shaking, the brush was removed, and the cells were pelleted by centrifugation at 1000 rpm for 5 minutes. The supernatant was discarded, the pellet was resuspended, and 5 mL of fresh saline was added. This washing procedure was repeated three times. After the third wash, 0.5–1 mL of the supernatant was left, in which the cell pellet was resuspended. The cell suspension was then applied onto microscope slides and air-dried. Staining was performed without fixation using a 10% Romanowsky–Giemsa solution for 10 minutes [17, c. 98]. This staining method yields clean and evenly colored preparations. The frequency of micronuclei and karyological abnormalities was assessed using a Zeiss AxioLab A.1 light microscope at 16×40 magnification. At least 1,000 cells were analyzed for each animal.

Assessment of erythropoiesis level: To evaluate the level of erythropoiesis, reticulocyte analysis was performed. Supravital staining of reticulocytes was carried out using brilliant cresyl blue (BCB). In an Eppendorf-type tube, 50 µL of BCB solution was mixed with 50 µL of blood, incubated for 1–1.5 hours at room temperature (18–25°C), and smears were prepared using standard methods [16, c. 159]. The stained preparations were ready for analysis the following day. In this staining method, erythrocytes appear greenish-gray, and the granular-filamentous substance (reticulum) is stained blue. The number of reticulocytes was counted per 1000 erythrocytes and expressed as a percentage. The analysis was performed using a Zeiss AxioLab A.1 light microscope at 16×100 magnification.

Statistical analysis: For statistical calculations, the arithmetic mean and its standard error (M±SE) were calculated as percentages per 100 cells. The significance of differences between means was evaluated using Student's t-test. The threshold for statistical significance was set at $p \leq 0.05$. Statistical analysis was performed using Microsoft Excel (Microsoft Corporation, Redmond, Washington, DC, USA).

Results and Discussion

Study of baseline cytogenetic parameters in peripheral blood erythrocytes of cattle.

A comparative analysis of the frequency of micronuclei and reticulocytes in cattle groups of different sex and age is presented in Figure 1. Cytogenetic analysis of cattle erythrocytes revealed an average micronucleus frequency of 0.37 ± 0.04%. Young animals exhibited a higher level of micronuclei compared to adults, likely associated with increased erythropoietic activity in younger animals. No significant sex-related differences in the frequency of micronuclei were observed among young cattle. It was not possible to obtain biological samples from mature breeding bulls; therefore, it was not feasible to assess sex-based differences in micronucleus frequency among adult cattle. An elevated level of micronuclei was observed in pregnant cows, which may also be attributed to intensified erythropoiesis during pregnancy.

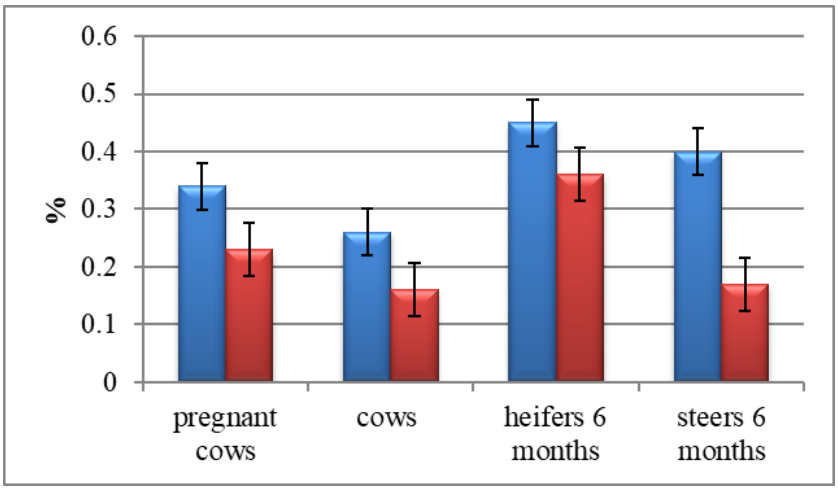

*Figure 1 – F*requency of micronuclei in erythrocytes and reticulocytes in peripheral blood of cattle of different age and sex.
Row 1 – Frequency of micronuclei in erythrocytes; Row 2 – Frequency of reticulocytes

The examined animals showed an average reticulocyte frequency of 0.2%. Elevated erythropoietic activity above this level was observed in pregnant cows and heifers. In 6-month-old heifers, the erythropoiesis level was significantly higher than in young bulls, indicating a sex-related difference.

A comparative analysis of micronucleus frequency and reticulocyte levels revealed a significant positive correlation (+0.72) between these parameters in the studied animals. This indicates that the higher the erythropoietic activity (i.e., the rate of erythroid cell division), the more frequently cytogenetic abnormalities in the form of micronuclei occur.

Table 1 presents the reference values for micronuclei and reticulocyte content in the blood of Alatau cattle from the Almaty region.

Table 1 – Reference values of micronuclei frequency in erythrocytes and reticulocytes in peripheral blood of cattle of different ages and sexes

Variant	Number of cells viewed	Reference values of MN, %	Reference values of reticulocytes, %
Pregnant cows	60000	0,2-0,8	0,1-0,5
Cows	50000	0,1-0,6	0,1-0,5
Heifers 6 months	60000	0,2-0,8	0,1-0,4
Steers 6 months	70000	0,2-0,6	0-0,3
Average	230000	0,1-0,8	0-0,5

Among the cytological abnormalities, erythrocytes of atypical size were observed, primarily macrocytes and microcytes. In some young animals, poikilocytosis was detected–an alteration in the normal shape, thickness, and volume of cells. The most commonly observed forms were acanthocytes, echinocytes, spherocytes, and dacrocytes (Figure 2). Such abnormalities may be associated with underlying health issues, including anemia, helminthic infestations, and diseases of internal organs and systems.

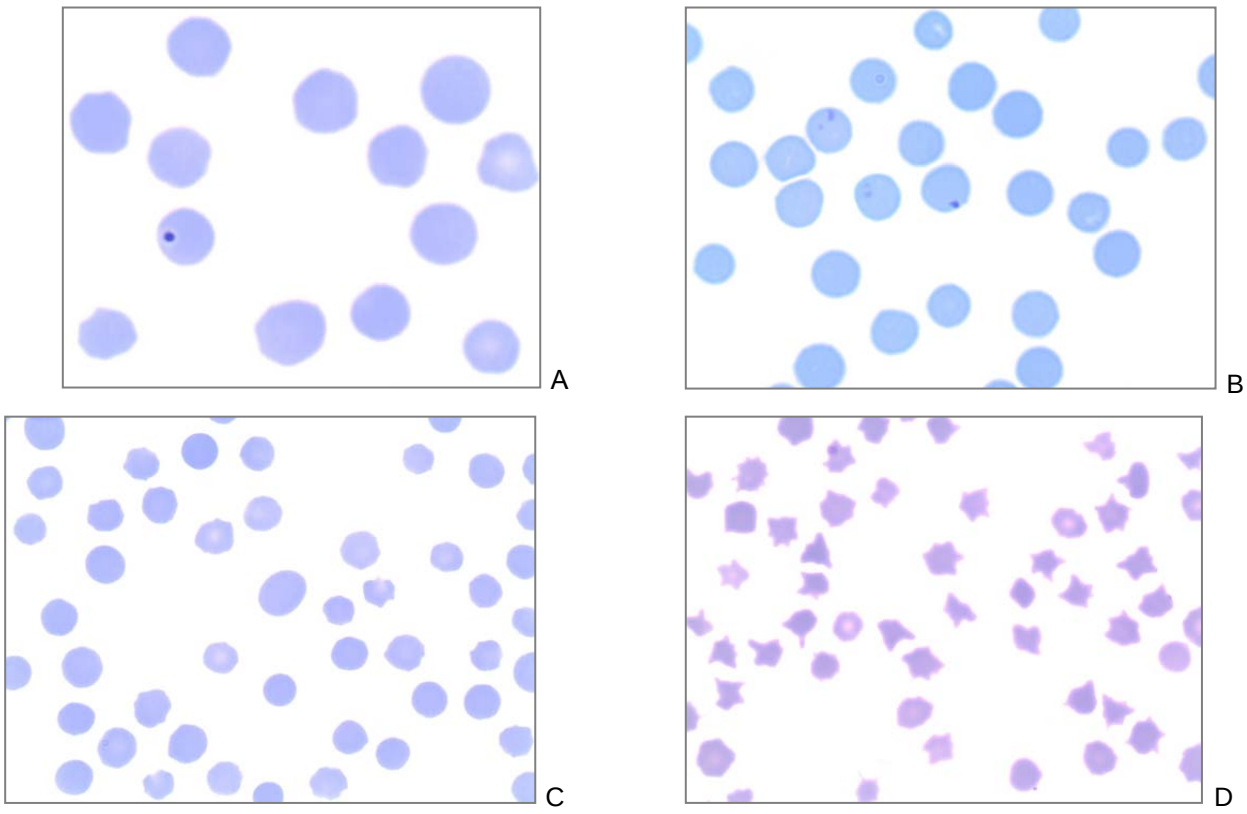

Figure 2 – Preparations of cattle peripheral blood erythrocytes; A – micronucleus; B – reticulocytes; C – macrocyte, D – poikilocytosis in calf erythrocytes. Magnification 10 x 100

Cytome analysis in nasal buccal epithelial cells of cattle.

The cytome analysis of nasal epithelial cells in cattle revealed an average micronucleus frequency of 0.015% (Figure 3). No significant differences were observed between age or sex groups. The average frequency of karyological abnormalities detected by the cytome assay was 0.025%. Similarly, no statistically significant sex- or age-related differences were found. However, as with the analysis of micronuclei in peripheral blood erythrocytes, a trend toward increased abnormalities was noted in pregnant cows and 6-month-old heifers (Figure 3).

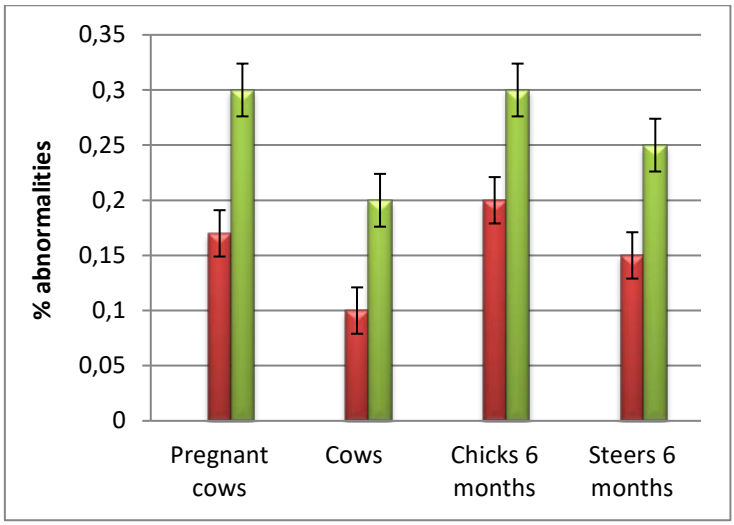

Figure 3 – Frequency of micronuclei and karyologic abnormalities in cattle nasal epithelium. Row 1 – frequency of micronuclei; Row 2 – frequency of karyologic abnormalities

The reference values for the frequency of micronuclei and karyological abnormalities in the nasal epithelium of cattle are presented in Table 2. The spectrum of detected abnormalities in the nasal epithelium corresponds to that observed in buccal epithelium and includes micronuclei, nuclear buds, nuclear invaginations, binucleated cells, and chromatin condensation (Figure 4). The most frequently observed abnormalities were circular nuclear indentations and early stages of cellular degradation, characterized by chromatin condensation.

Table 2 – Reference values of micronuclei (MN) frequency and karyologic abnormalities in cattle nasal epithelium

Variant	Number of cells viewed	Reference values of MN, %	Reference values, karyologic disorders, %
Pregnant cows	6000	0,1-0,5	0,2-0,8
Cows	5000	0,1-0,5	0,1-0,6
Heifers 6 months	6000	0,1-0,4	0,2-0,8
Steers 6 months	7000	0-0,3	0,2-0,6
Average	23000	0-0,5	0,1-0,8

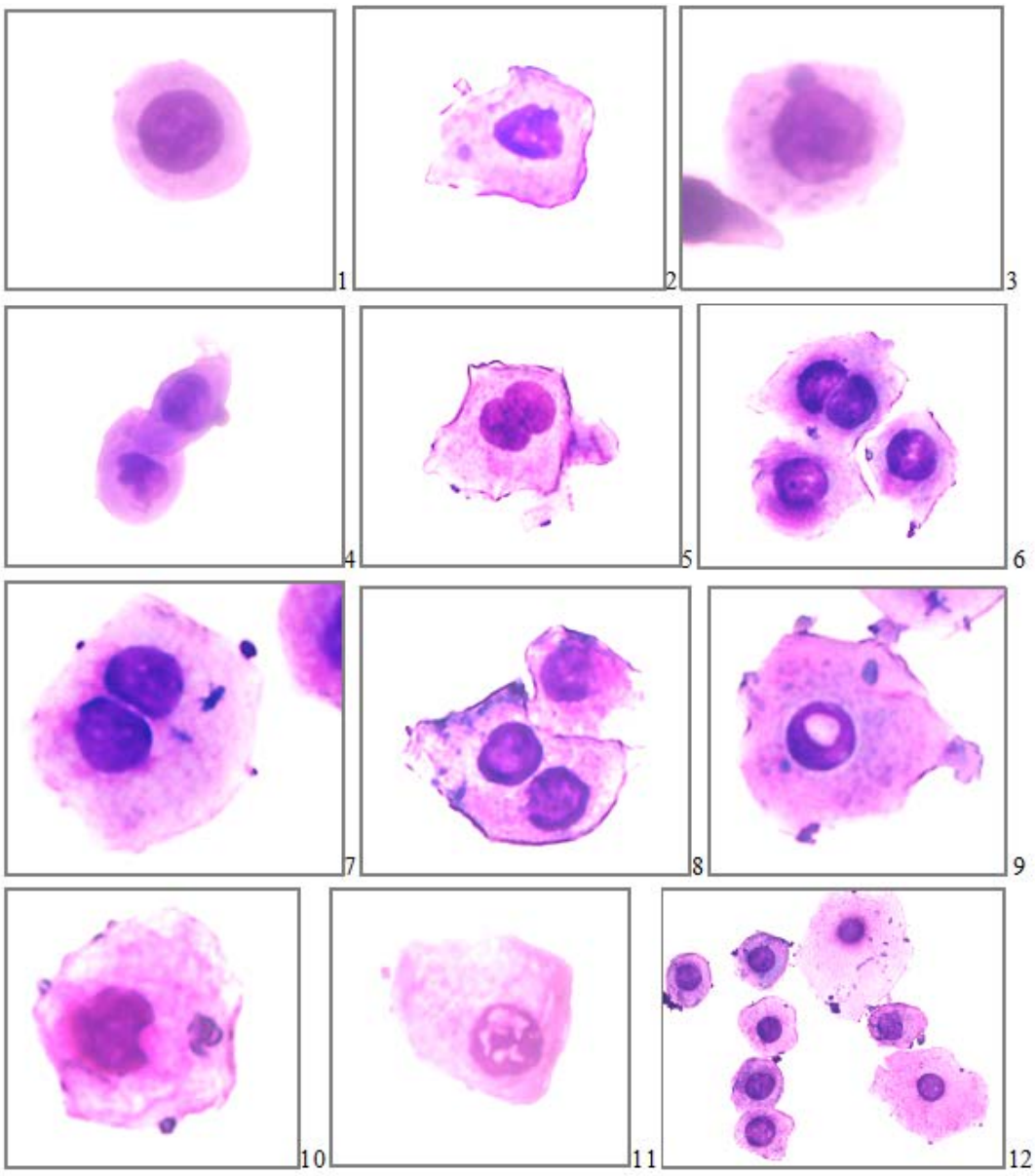

Figure 4 – Cytogenetic and karyologic disorders in cattle nasal epithelium
1 – normal cell, 2 – cell with micronucleus, 3 – nuclear bud, 4 – invagination of the nucleus,
5, 6 – circular notch, 7 – adjacent nuclei, 8 – bi-nuclear cell, 9 – nuclear vacuole, 10 – perinuclear vacuole,
11 – chromatin condensation, 12 – buccal epithelium cells in the nasal cavity

Study of baseline cytogenetic parameters in sheep.

A similar analysis of cytogenetic parameters in erythrocytes and buccal epithelial cells was conducted in sheep. Sheep erythrocytes are among the smallest among mammals, measuring 4.2–4.4 µm in diameter, compared to 5.1–5.2 µm in cattle (Figure 5).

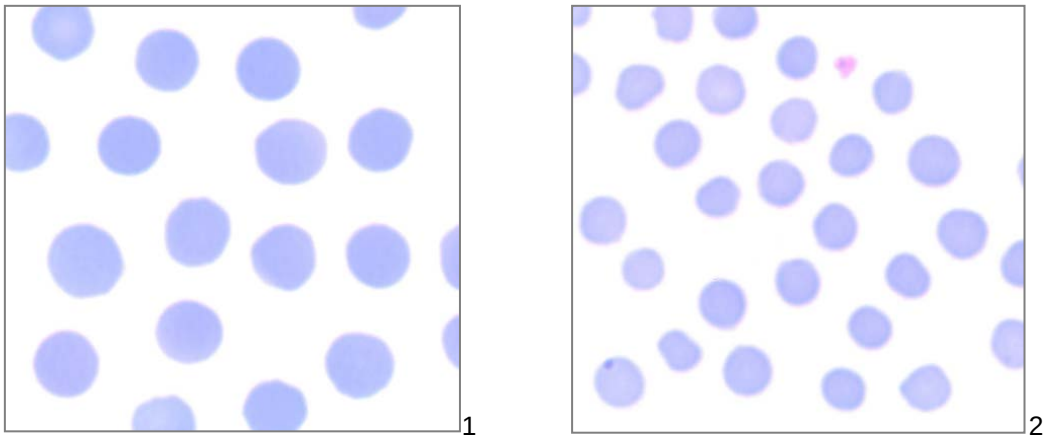

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Figure 5 – Demonstration of different red blood cell sizes in cattle (1) and sheep (2)

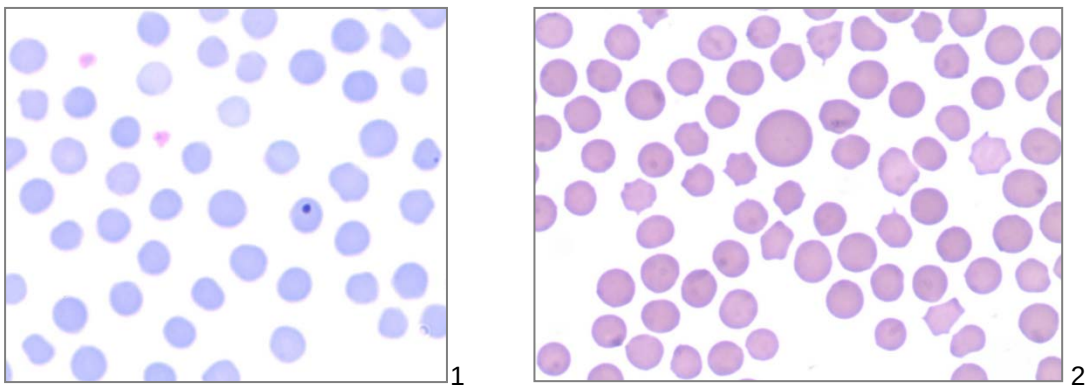
The results of the cytogenetic analysis of sheep erythrocytes are presented in Table 3.

Table 3 – Micronucleus analysis of erythrocytes in sheep of different age and sex

Variant	Number of cells viewed	Frequency of micronuclei in erythrocytes, %	Reference values, micronuclei frequency in erythrocytes, %
6 months10♀	60000	0,55±0,03*	0,5-1,2
18 months10♀	10000	0,20±0,04	0,1-0,3
Pregnant sheep 7 ♀	70000	0,27±0,02	0,1-0,5
Average ♀	230000	0,34±0,01	0,1-0,2
6 months 7 ♂	70000	0,40±0,02*	0,1-0,8
18 months 3♂	60000	0,13±0,01	0,1-0,2
Average ♂	130000	0,26±0,01	0,1-0,8
Average	360000	0,31±0,01	0,1-1,2
p≤0,05			

The frequency of micronuclei in peripheral blood erythrocytes of sheep varied by age. Young animals exhibited a higher level of micronuclei compared to adults. Among 6-month-old animals, sex-based differences were also observed: females showed higher micronucleus frequencies than males of the same age group. The highest levels of micronuclei were recorded in 6-month-old ewe lambs.

Among cytological abnormalities, erythrocytes of atypical size were detected, primarily macrocytes, while microcytes were not observed. In some cases, poikilocytosis was noted in young animals, including echinocytes, acanthocytes, and dacrocytes (Figure 6).



1 2

Figure 6 – Peripheral blood erythrocyte smears of sheep; micronucleus (1) and poikilocytosis (2) in sheep erythrocytes, magnification 10 × 100

The analysis of sheep blood smears stained using supravital staining to detect reticulocytes and assess the level of erythropoiesis did not reveal the presence of reticulocytes in their peripheral blood. However, this is not considered a pathological finding; rather, it reflects a species-specific feature of sheep erythropoiesis, in which fully matured normochromic erythrocytes are released into the bloodstream in healthy animals. Under conditions of increased erythropoiesis due to anemia or blood loss, reticulocytes can be detected at a level of up to 0.05% in sheep.

Cytome analysis in buccal epithelial cells of sheep

For the cytome analysis in sheep, buccal epithelial cells (from the inner cheek lining) were collected. The average frequency of micronuclei in the buccal epithelium of sheep was 0.028%. Age- and sex-based analysis of micronucleus frequency revealed the same trend as observed in peripheral blood erythrocytes: females showed higher genome instability than males, and young animals had higher rates than adults (Figure 7).

The average frequency of karyological abnormalities in the cytome analysis of sheep was 0.04%. The highest frequency was recorded in 6-month-old animals. No statistically significant differences were found between sexes.

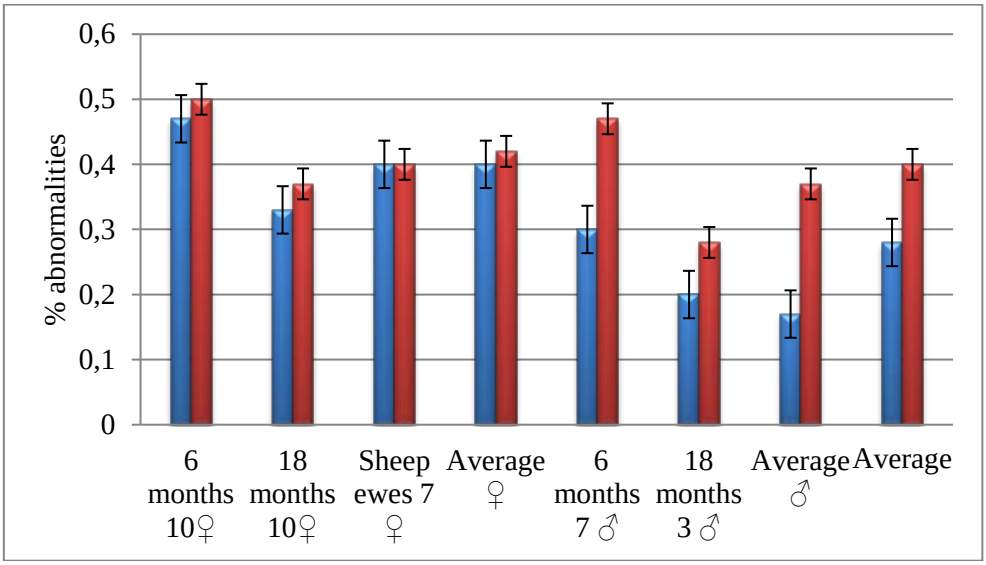


Figure 7 – Frequency of micronuclei and karyological abnormalities in the buccal epithelium of sheep. Row 1 – frequency of micronuclei; Row 2 – frequency of karyological abnormalities

Some individual animals showed abnormally elevated levels of micronuclei, nuclear protrusions, and apoptotic cells. These animals were identified within the "Ewe" group and were excluded from the analysis, as they likely exhibited underlying health issues. The reference values for the frequency of micronuclei and karyological abnormalities in the buccal epithelium of sheep are presented in Table 4.

Figure 4 shows microphotographs of buccal epithelial cells, which differ morphologically and in the range of karyological abnormalities from nasal epithelial cells. These cells are generally larger, irregular in shape, have a lower nucleus-to-cytoplasm ratio, and exhibit a broader spectrum of karyological abnormalities. The detected abnormalities included nuclear buds, protrusions, binucleated cells, cytoplasmic and nuclear vacuolization, chromatin condensation, apoptosis, and degenerative changes.

Table 4 – Reference values for micronucleus frequency and karyological abnormalities in the buccal epithelium of sheep of different age and sex

Variant	Number of cells viewed	Reference values of MN, %	Reference values, karyologic disorders, %
6 months10♀	6000	0,1-0, 4	0,1-0,8
18 months10♀	1000	0,1-0,5	0,2-0,4
Pregnant sheep 7 ♀	7000	0, 1-0,4	0,2-0,6
Average ♀	23000	0, 1-0,5	0,1-0,8
6 months 7 ♂	7000	0, 1-0,7	0,2-1,3
18 months 3♂	6000	0, 1-0,7	0,1-0,8
Average ♂	13000	0, 1-0,7	0,1-1,3
Average	36000	0, 1-0,7	0,1-1,3

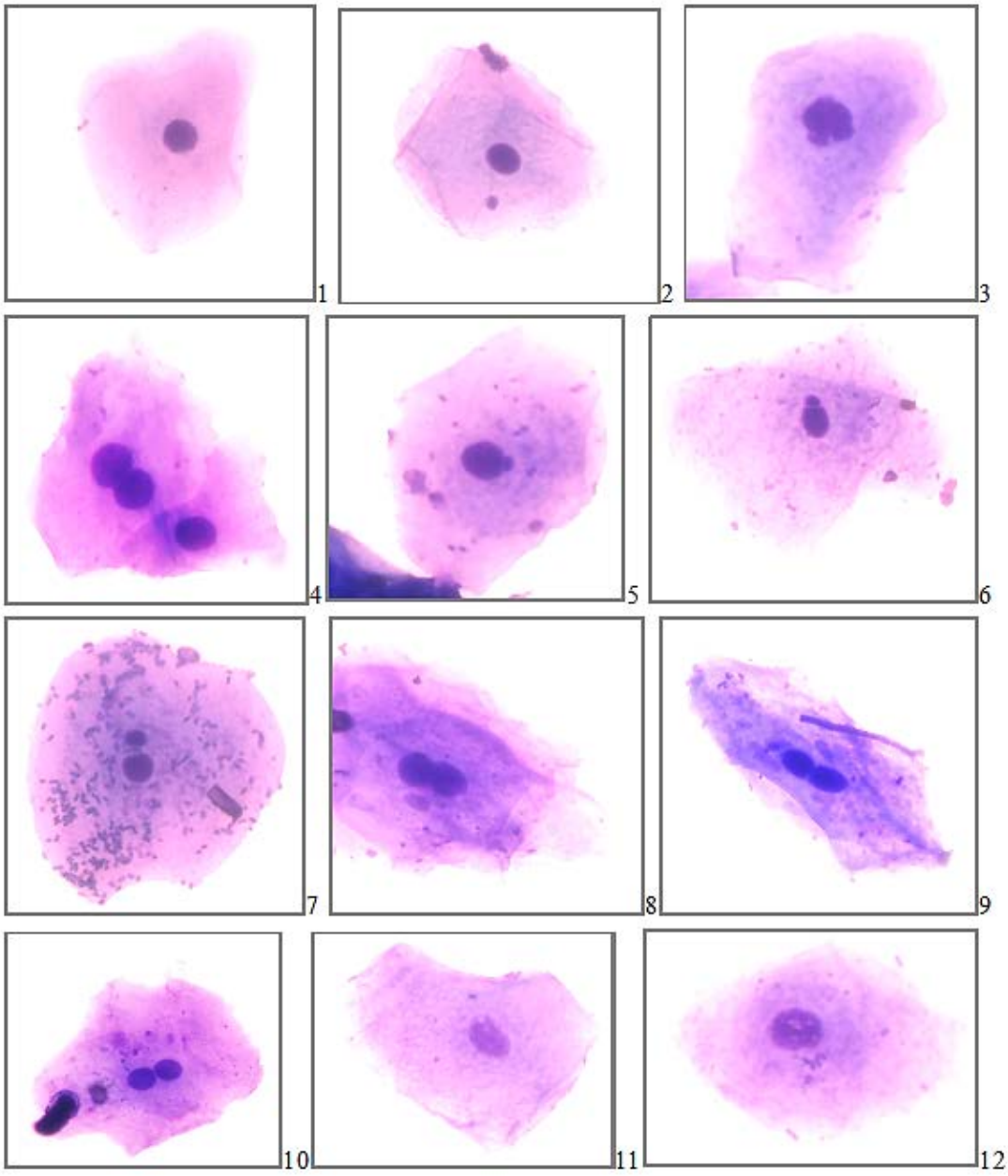


Figure 8 – Cytogenetic and karyologic disorders in buccal epithelium of sheep oral cavity
1 – normal cell, 2 – micronucleus, 3 – invagination of nucleus, 4 – circular notch, 5 – protrusion of “bubble” type, 6 – protrusion of “tongue” type, 7 – protrusion of “broken egg” type, 8 – lobed nucleus, 9 – adjacent nuclei, 10 – binuclear cell, 11 – perinuclear vacuole, 12 – chromatin condensation

In recent years, morphometric [18, c. 1130] and genetic criteria [19, c. 143] have been increasingly used to assess genome instability, health status, and the organism’s sensitivity to biotic and abiotic factors of various origins. The primary method for evaluating mutagenic effects is the analysis of unstable chromosomal aberrations, which result in the formation of micronuclei.

Changes in micronucleus frequency in the studied animal groups allow for the assessment not only of the degree of mutagenic exposure but also of individual, genetically determined sensitivity to mutagens, infectious agents, and pharmaceuticals. This, in turn, enables the identification of at-risk health groups. It is well known that the degree of mutagenic impact is assessed based on the baseline (control) values of cytogenetic indicators, particularly micronucleus frequency. According to various authors, this indicator varies over a fairly wide range: for sheep, from 0.33% to 0.87%; and for cattle, from 0.46% to 1.8% [20,c. 34]. Moreover, differences in micronucleus frequency among animals may be influenced by various factors.

In recent years, morphometric [18, c. 1130] and genetic criteria [19, c. 143] have been increasingly applied to assess genome instability, health status, and the organism’s sensitivity to various biotic and abiotic factors. The main method for evaluating mutagenic effects remains the analysis of unstable chromosomal aberrations, the consequence of which is the formation of micronuclei.

Changes in micronucleus frequency among studied animal groups make it possible to assess not only the degree of mutagenic exposure but also the individual, genetically determined sensitivity to mutagens, infectious agents, and pharmaceutical substances, thereby allowing for the identification of risk groups in terms of health status. It is widely recognized that the degree of mutagenic exposure is evaluated based on baseline (control) values of cytogenetic indicators such as micronucleus frequency. According to various authors, this parameter varies within a fairly broad range: from 0.33% to 0.87% in sheep, and from 0.46% to 1.8% in cattle [20,c. 34]. It has also been reported that the differences in micronucleus frequency among animals may depend on various factors.

For example, statistically significant differences in the frequency of erythrocytes with micronuclei have been reported between Birlik-type (0.52%) and Suyunduk-type (0.33%) Edilbaev sheep. The authors attribute this to the higher adaptive potential of Suyunduk sheep to adverse environmental conditions compared to Birlik sheep [20,c. 34]. Other studies have reported variations in micronucleus frequency depending on age and sex within the Romanov sheep breed: 0.48% in ewes, 0.56% in rams, and 0.87% in lambs [20,c. 34]. Our results support these findings, showing a higher frequency of micronuclei in young animals (0.5%) compared to adults (0.17%). According to the literature, the most pronounced age-related differences are observed in lambs during the hematological crisis, especially on the first day of life, when many physiological and hematological adjustments occur during and immediately after birth [21, c. 106352]. These indicators can be explained by several factors: First, the relative immaturity of the cellular component of the immune system in young animals, which is responsible for eliminating erythrocytes with micronuclei; Second, the selective breeding of only the healthiest and most valuable animals; And third, the naturally higher level of erythropoiesis in young stock. In support of the latter, we demonstrated a statistically significant positive correlation (+0.72) between reticulocyte frequency and the level of micronuclei in the animals examined.

The study by Elkina et al. [22, c. 136] showed a significantly higher frequency of micronucleated erythrocytes in domestic livestock species compared to musk oxen. There is also evidence of greater genome instability in animals with high milk productivity and elevated red blood cell parameters compared to less productive individuals [19, c. 143]. These results are consistent with the findings of Santovito (2024) [23, c. 93], which demonstrated not only breed-related differences in cytogenetic abnormalities among dogs but also a significantly higher frequency of such abnormalities in purebred dogs compared to crossbreeds.

Studies demonstrating varying levels of genome instability in farm animals living under different environmental conditions are not surprising and serve several important functions. They provide insight into the animals' genomes and their adaptive potential, as micronucleus frequency has been shown to correlate with the oxidative stress index [24, c. 503170]. In addition, such animals can be used as bioindicators to assess the ecological status of the region under study [25,c. 138058].

An additional parameter associated with both physiological condition and cytogenetic indicators is the level of erythropoiesis, which reflects the regenerative activity of the bone marrow. This can be evaluated by the content of reticulocytes in the blood [16, c. 159, 26]. Reticulocytes are young erythrocytes found in small amounts in peripheral blood. Unlike mature erythrocytes, they contain residual RNA and mitochondria, aggregated into a granular reticular structure (reticulum), which is revealed through supravital staining of blood smears. As erythrocytes mature, this reticular network disappears. Accelerated erythropoiesis is characterized by an increased proportion of reticulocytes, while suppressed erythropoiesis results in a decrease. Depending on the degree of maturity, five types of reticulocytes are distinguished: 1 – with a nucleus and granularity in the form of a dense ring around it; 2 – with a granular-reticular structure resembling a tangle; 3 – with dense network-like granularity; 4 – with thread-like granular-reticular material; 5 – with isolated granules located in different areas of the cytoplasm. Under normal conditions, nearly 80% of reticulocytes belong to types 4 and 5 [27, c. 27].

The presence of type 1–3 reticulocytes in blood smears indicates enhanced regeneration of erythroid cells. High reticulocytosis is typically observed in cases of blood loss and hemolytic anemias.

As an alternative to cytogenetic analysis of lymphocytes and peripheral blood erythrocytes, the cytome assay (analysis of micronuclei and karyological anomalies) in epithelial cells offers an even less invasive method for assessing genetic status. Compared to lymphocytes, epithelial cells have a limited capacity for DNA repair; therefore, buccal and nasal epithelial cells may more accurately reflect genome instability events [28, c. 241]. Being in direct contact with inhaled and ingested genotoxic agents, epithelial tissues are the first to exhibit their mutagenic effects, and the frequency of micronuclei and karyological abnormalities can reveal pathological changes long before clinical symptoms appear [28, c. 241, 29, c. 76].

In theory, any epithelial tissue (e.g., cervical, vaginal, esophageal, urethral, urinary tract, conjunctival, nasal, buccal, bronchial epithelium, etc.) can be used for micronucleus assessment. However, buccal and nasal mucosal cells are more accessible and preferred for cytome analysis, as they represent the first line of contact with many hazardous substances and infectious agents. It is important to consider the characteristics of each epithelial tissue, as they differ in both micronucleus frequency and the spectrum of cytological abnormalities. In our study, nasal epithelium was used for cattle due to technical constraints.

The analysis of buccal epithelium is widely used in human studies. In animals, especially farm animals, this method is only beginning to be applied for assessing genome instability and the general health status of the organism. Therefore, establishing reference values and the spectrum of detectable abnormalities is an important step toward promoting its broader use. Moreover, the micronucleus assay results in peripheral blood

erythrocytes and buccal/nasal epithelial cells in small and large ruminants show strong correlations–+0.75 and +0.88, respectively. This correlation has also been demonstrated in the literature, such as in a study on mice under stress, where sharp changes in erythrocyte electrophoretic mobility were accompanied by an increase in epithelial cells showing various pathological alterations [30, c. 108]. However, one should take into account the different response times to induced exposure. While the timing of response is not critical for evaluating baseline indicators or chronic effects, it becomes a significant factor when assessing acute exposure. In erythrocyte micronucleus analysis, the time between exposure and the first observable increase in micronucleated erythrocytes in the bone marrow is typically between 8 and 12 hours. Considering erythrocyte maturation, the initial appearance of micronuclei in peripheral blood can be expected after 24–36 hours, followed by a decline [31, c. 7]. The stratified squamous non-keratinized nasal and buccal epithelium is renewed by the division of basal layer cells, where micronuclei are initially formed. As basal cells mature, they gradually migrate to the surface layer, which is used for cytological analysis. The time required for basal cells to reach the surface is individual and depends on the nature of the exposure. Various researchers estimate that buccal epithelial cells reach the surface layer within 3–14 days and may exhibit nuclear damage during this time. Therefore, the optimal observation period is 5–10 days after exposure, with a return to baseline levels within 2–3 weeks [29, c. 76]. Thus, in response to acute exposure, it takes approximately one week for aberrant buccal epithelial cells to mature and appear in the surface layer for detection.

Another important consideration in cytome analysis in animals is the following. In studies involving human buccal epithelial cells, significant attention is paid to recording destructive nuclear abnormalities (karyopyknosis, karyorrhexis, and karyolysis), which are then used to calculate the repair index, reflecting the dynamics of carcinogenesis. However, before collecting epithelial samples, human subjects are typically instructed to rinse their mouths several times to eliminate naturally aging and dying cells. In animals, this is practically impossible, even when using flushing tools. Therefore, the analysis of destructive abnormalities in buccal and nasal epithelial cells in animals is not reliable, and these types of abnormalities should be excluded from evaluation. Another observed feature in cattle is the presence of occasional buccal epithelial cells in samples collected from the nasal cavity. This is likely due to the animals licking their noses, leading to the transfer of buccal epithelial cells into the nasal passages. As a result, such cells should be differentiated during the analysis of nasal epithelium in cattle – a task that typically poses no difficulty – and excluded from the evaluation.

Conclusion

The cytogenetic analysis of preparations from sheep and cattle established baseline values for micronuclei and karyological abnormalities. It was found that the reference cytogenetic indicators in healthy animals vary by sex (in sheep) and age (in both sheep and cattle). In adult animals, these values were lower than in young animals, likely due to increased erythropoietic activity in the latter. In sheep, males exhibited lower cytogenetic indices compared to females. A few individual animals showed elevated levels of cytogenetic abnormalities, which may be associated with subclinical health issues and/or feeding or housing conditions, although no clinical symptoms were observed at the time.

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