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IMPROVEMENT OF METHODS IN HORMONAL REGULATION OF REPRODUCTIVE FUNCTION IN COWS AND SHEEP

MONOGRAPH

MINISTRY OF HIGHER EDUCATION, SCIENCE AND
INNOVATION OF THE REPUBLIC OF UZBEKISTAN

SAMARKAND STATE UNIVERSITY OF VETERINARY MEDICINE,
ANIMAL HUSBANDRY AND BIOTECHNOLOGY

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UDC: 619: 636.2: 636.3: 577.1
BBK: 28.672.538.14

Nurmukhamedov B.M.
Improvement of methods in hormonal regulation of reproductive function in cows and sheep. Monograph. Samarkand State University of Veterinary Medicine, Animal Husbandry and Biotechnology Publishing Center, 2024 - 220 pages

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The monograph is recommended for printing by the Council of the Samarkand State University of Veterinary Medicine, Animal Husbandry and Biotechnology
№ 3 dated 14 November 2024 y.

The monograph describes the results of many years of research by the author and the literature data covers the issues of reproduction of cows and karakul sheep, outlines the methods of the hormonal function of the ovaries, regulation of the reproductive function of the ovaries and the elimination of infertility in animals.

Methods of using prostaglandins in veterinary practice are discussed. The proposed complex of developments to combat infertility will increase the livestock and profitability of cattle breeding and astrakhan breeding.

ISBN: 978-9910-8946-3-3

Designed for veterinarians, zooengineers, karakul breeders, scientists, bachelors, undergraduates and scientific applicants in the specialty of veterinary medicine and animal science.

INTRODUCTION

An important reserve for increasing the gross production of meat, milk and wool is the intensive conduct of animal husbandry on an industrial basis, as well as the elimination of infertility and barrenness, which are still significant in many farms of the country. Due to infertility, a large number of cows and sheep are discarded every year, and a lot of calves, lambs and milk are not received. That is why great attention is paid to the issue of preventing and eliminating infertility, increasing the reproductive capacity of animals.

The respected first President scientifically decided and adopted No. PP-308 dated March 23, 2006 "On measures to stimulate an increase in the livestock population in personal subsidiary, dekhkan and farms", dated April 21, 2008 No. PP 842 "On additional measures to enhance incentives increasing the number of livestock in personal subsidiary, dekhkan and farms and the decision to produce livestock products "and dated December 29, 2015 №PP-24/60, as well as the Law of the Republic of Uzbekistan on Veterinary Medicine to ensure inviolable implementation.

Under the influence of unfavorable factors, disorders arise in the reproductive system in the form of a decrease in generative, hormonal, secretory and motor functions. So, during obstetric and gynecological studies of 29245 cows, carried out by us in many farms of Voronezh, Tambov, Lipetsk and other regions, it was revealed from 15 to 30% of animals with periods of infertility from two months or more on the basis of ovarian hypofunction (20-35 %), persistence of the corpus luteum (5-7.5%), cystic changes in the gonads (8-15%), retention of the placenta, subinvolution of the uterus and endometritis (20-60%).

However, despite the great importance and urgency of the problem under consideration, the issues of the etiology and pathogenesis of postpartum and gynecological diseases, methods of their prediction, early diagnosis, prevention and treatment have not yet been sufficiently developed and covered in the literature. Therefore, currently used in veterinary practice, various methods of prevention and treatment of postpartum and gynecological diseases in cows and sheep, hormonal methods of regulation functional disorders of the ovaries in the conditions of industrial livestock farming require further improvement and development.

At the same time, the use of hormonal drugs in the practice of veterinary medicine and animal husbandry was often empirical and therefore did not always give the expected results. This phenomenon can be explained not only by insufficient knowledge of the effect of exogenous gonadotropin and other hormones on specific structures of the gonads, which are in different functional states and in violation of their generative ability, but also by the fact that the development of scientific and practical provisions on the regulation of sexual function was not based on deep knowledge about the structure and function of the ovaries. In particular, in the literature, the issues of cytogenesis of reproductive, follicular and connective tissue cells, follicles and corpus luteum, issues of natal and postnatal oogenesis and histogenesis of primordial, secondary and tertiary follicles are insufficiently illuminated. the role of the connective tissue (mesenchymal) elements of the gonads in these processes, as well as in the maturation of follicles, the formation of corpus luteum, follicular and luteal cysts.

The duration of the functioning of the primary, secondary and tertiary follicles, the method of their movement into the deeper layers of the ovarian cortex, as well as the regularities of the extinction of these processes when the reproductive ability of animals ceases has not been clarified. Poorly studied and elucidated the issues of histofunctional, hormonal and biochemical changes in the ovaries, uterus, endocrine organs and the body of cows at various stages of the sexual cycle, during pregnancy, childbirth and in the postpartum period, both in norm and in pathology, as well as in functional disorders ovaries as in intact animals, the generalizations made it follows that one of the most mysterious and unknown organs in biology and, in particular, in reproduction are ovaries, on the study of which G.A. Cheremisinov has been working for many years. He discovered the phenomenon of the relationship of gametofolliculogenesis with the mesenchymal elements of the ovaries, which determine the formation, growth and development of follicles, their ovulation and the formation of corpus luteum. He found that the development and functioning of these structures is based on their specific reactivity to the effect of hypothalamic-pituitary hormones and biogenic amines, which determines the realization of the reproductive potential of the ovaries and their role in the regulation of the sexual function of females.

The slightest violation of this complex biological chain is manifested primarily by ovarian dysfunction and the cessation of reproduction of females. Therefore, the first task is to find methods and means to ensure the regulation of the resulting disorders in the ovaries. As stated above, this regulation is carried out by ensuring the proper trophic and plastic function of the mesenchymal elements determined in the tecal tissue of the follicles, thereby ensuring their growth, maturation and ovulation, or by excluding the persistence of the luteal structures of the ovaries and the subsequent endogenous restoration of ovarian function. If the folliculogenic function of the ovaries is regulated by endogenous or exogenous gonadotropic factors, then the luteolytic function in the gonads is performed by prostaglandins of the F-2 alpha group, the synthesis of which is being successfully worked by a team of scientists from the Institute of Chemistry of the BNTs URO of the Russian Academy of Sciences, headed by Academician of the Russian Academy of Sciences G.A. Tolstikov. In recent years, the Institute has created a whole group of prostanoids, including estufalan, clathraprostin, estufalan SF, clatraprostin SF, super-estufalan, superclatraprostin, A team of scientists from the Russian Research Institute of Non-communicable Animal Diseases headed by Professor G.A. Cheremisinov is working on the study of the biological properties of which, as well as on the development of optimal doses, indications and contraindications for the regulation of sexual function in farm animals.

In particular, if over the past years biological properties have been studied on cows and pigs, doses and indications for the use of estufalan and clathraprostin in obstetric and gynecological practice have been worked out, then in subsequent years the method of using these drugs in sheep breeding is being developed to synchronize sexual hunting in order to obtain broadtail and karakul, as well as for the restoration of dysfunctional disorders of the ovaries of sheep in Uzbekistan (G.A. Cheremisinov, B.M. Nurmukhamedov). indications and contraindications for the regulation of sexual function in farm animals is a team of scientists from the Russian Research Institute of Non-communicable Animal

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Chapter 1. STRUCTURAL AND FUNCTIONAL CHARACTERISTICS OF ANIMAL OVARIES

1.1. Modern understanding of the generative and endocrine function of the ovaries and hormonal regulation of the reproductive potential of animals

Before proceeding to the presentation of hormonal methods for increasing the fertility of cows and sheep, the development of which should be based on fundamental research on the structure and function of the gonads, it is necessary to dwell on the modern understanding of the role of specific cellular structures in the generative and endocrine function of the ovaries.

As evidenced by the literature data, few problems are the subject of such a lively discussion as the question of the origin of germ cells in mammals and the role of the primordial epithelium of the gonads in this. The question of oogenesis in the postnatal period remains especially controversial. GK Kuliev (1963) indicates that currently there are two views on oogenesis. According to one of them, the formation of germ cells occurs only during the fetal period, and according to the other, after birth.E.A. Pozhidaev (1967) notes that the primary germ cells are of extra genital origin.

In turn, when conducting a comparative study of postnatal oogenesis in carnivores (dog, tigress), rodents (rabbit), and ungulates (pig, sheep, cow), proliferation of the ovarian primordial epithelium among adult animals was observed only in dogs and rabbits. In pigs, sheep, cows and tigresses, the proliferation of the rudimentary epithelium and the formation of germ cells from it has not been established.

According to some researchers (E.A. Pozhidaev, 1967 and others), the role of the rudimentary epithelium is reduced to the formation of follicular epithelium.

Until now, the histogenesis of connective tissue and interstitial cells of the ovarian cortical substance, the formation of the connective tissue membrane of follicles and the way they move into deeper layers of the cortical substance have not been studied.

So A.A. Zavarzin (1954), I.F. Ivanov, P.A. Kovalsky (1962), Eliseev (1972) the connective tissue elements of the gonads are considered as supporting tissue, represented by collagen and elastic fibers with included spindle fibrocytes formed from interstitial cells, theca cells, granulosis or remnants of embryonic glandular tissue. In turn, the internal and external theca, according to A.P. Studentsov (1970), is formed from the ovarian stroma, and according to**G.A. Cheremisinov (1975)** from interstitial cells, and concludes that thecal cells exist as a reserve tissue from embryonic life until the termination of sexual function.

The question of what cellular structures of the ovary the corpus luteum is formed from cannot be considered finally resolved. **E. Nakama** (1969) indicates that for several decades, researchers have attached particular importance to three theories on the histogenesis of the corpus luteum: first, luteal cells originate from granulosa cells; the second is luteal cells from the cells of the internal theca; third, luteal cells are of dual origin, i.e. from granulosa and internal theca cells. With regard to the human ovaries, the third theory, according to the author, is generally accepted.

However, the majority of domestic and foreign authors (A.A. Zavarzin, 1954; I.F. Ivanov, I.A. Kovalsky, 1962; I.E. Eskin, 1968; V.T. Eliseev (1972); I.A. Wunder, 1973) believe that luteal cells are formed from granulosa cells by their glandular metamorphosis, while the inner follicle membrane forms the blood vessels and the connective tissue basis of the corpus luteum.

Opinions about the hormonal function of the ovarian cell structures are also very contradictory. EI Quater (1961) believe that interstitial cells and cells of the internal theca produce estrogens, and granulosis after its glandular metamorphosis into luteal cells - progesterone. According to I.E. Eskin (1968), both cells of the internal theca and granulosa cells are the source of estrogen formation.

In luteal cysts, in which granulosis is reduced, and the cells of the internal theca acquired the structure of luteal cells of the corpus luteum, progesterone was found, and in follicular cysts, where the internal theca undergoes atrophic changes with well-developed granulosis, estrogens. This gave the authors reason to conclude that estrogens are produced by the epithelium of the granular layer, and not by the cells of the inner layer of the follicle membrane, which produce progesterone. Insufficient attention was paid to the study of the timing of the manifestation of the sexual cycle in cows, fertilization and preservation of pregnancy, depending on the histofunctional state of the corpus luteum, the study of the histogenesis of the germ cells of primordial follicles, the state of the connective tissue and interstitial cells of the ovarian cortex, as well as changes in granulosis and internal flow during growth, development, atresia and ovulation of follicles at various stages of the sexual cycle and in early pregnancy. Research in this direction allows not only to reveal the morphological and functional characteristics of the ovaries of healthy animals, but also to correctly approach the assessment of their morphological and functional disorders in infertile cows. By the way, histofunctional changes in the gonads of cows during anovulatory reproductive cycles, hypofunction, persistent corpus luteum, follicular and luteal cysts, which are widespread and are a frequent cause of infertility, are also poorly studied. So to date, the reasons for the lack of ovulation of the follicles in these ovarian disorders have not been clarified,

An analysis of numerous works devoted to the use of gonadotropic drugs in the fight against infertility in cows indicates a lack of consensus on indications and contraindications, doses, frequency and intervals of their injections.

A.S. Lobodin (1982) indicates that the inconsistency of information about indications for use, doses of gonadotropic drugs is explained by the fact that researchers mainly took into account the biological properties of drugs and the clinical state of the body without determining the endocrine status, in particular, the level of ovarian hormones that play leading role in shaping, reproductive cycle, ovulation, implantation and pregnancy.

In fact, at present, science does not have sufficient information about the content of progesterone, total estrogen, estradiol-17 beta, cortisol, PF-2 alpha and other hormones and biogenic amines in the blood with a decrease in the functional activity of the ovaries and their hormonal regulation. Moreover, the relationship between the level of steroid hormones in the blood plasma and histofunctional changes in the ovaries has not been sufficiently studied. That is why the study of the effect of gonadotropic drugs on the endocrine and generative function of the ovaries will improve the methods of controlling the processes of reproduction, increasing fertility, preventing and treating infertility in animals.

The presence of conflicting conclusions on the biological and therapeutic efficacy of gonadotropic drugs indicates the need for further research to study their effect on the morphofunctional state of the ovaries, which are both in different stages of the sexual cycle and pregnancy, and in infertility due to hypofunction of the gonads, follicular and luteal cysts, and also anovulatory sex cycles. Elucidation of the reactivity of the cellular structures of the gonads, both in normal conditions and in pathology, to the effect of exogenous gonadotropins and PF-2 alpha will make it possible to determine the indications and contraindications, doses, frequency and intervals of their use and to give reasonable recommendations on the introduction of gonadotropic drugs and PF-2 alpha practice.

To restore reproductive capacity in cows with functional disorders of the ovaries, in recent years, prostaglandin F-2 alpha preparations have been widely used with a positive effect.

The use of PF-2 alpha preparations does not give the expected results, that after their introduction into the stage of excitation of the sexual cycle, 20% of animals exhibit anovulatory sexual cycles. The results of the use of PF-2 alpha preparations are especially contradictory when they are frontally administered (without taking into account the physiological state of the female reproductive apparatus) to infertile animals. In the available literature, we did not find reports on the effect of PF-2 alpha preparations on gametogenesis, folliculogenesis, luteal structures and connective tissue elements of the ovaries in normal and pathological cows with simultaneous determination of the level of ovarian hormones in the blood of cows.

The question of the effect of PF-2 alpha preparations on the endocrine function of the ovaries in cows also remains controversial. Most studies indicate a sharp decrease in the level of progesterone and an increase in the concentration of estrogen in the blood (cows), at the same time, a change in the level of sex steroids in the blood of cows after the administration of PF-2 alpha3-4 day after ovulation of the follicles.

In this regard, there is an urgent need to study the effect of PF-2 alpha on the generative and hormonal function of the ovaries (in cows) with different states of the reproductive system and functional disorders of the gonads in order to understand the patterns in the regulation of sexual function and improve methods for restoring the reproductive ability of animals.

1.2. New understanding of the relationship between gameto follicle luteogenesis and morphogenesis of the cortical substance of animal ovaries

1.2.1 Interaction of gameto-folliculogenesis with mesenchymal elements of animal ovaries

From the generalization of the literature data, it follows that, both in our country and abroad, the main regularities of the generative function of the ovaries, histogenesis and the genetic relationship of their specific cellular structures in the process of gametogenesis, formation, growth, maturation of follicles, their ovulation and the formation of corpus luteum have not been revealed. , as well as scientifically based methods of hormonal regulation of the reproductive function of cows have not been developed.

In this regard, we carried out experiments on a large number of laboratory animals (mice, rats, guinea pigs, rabbits), as well as on cows (1347 heads), sheep (97) Nurmukhamedov B.M. (1991), pigs (56) Cheremisinov G. A (1983) and mares (3) Podvaliuk D.V (2014) using obstetric-gynecological, histological, cytokaryometric, radioimmunological and biochemical research methods. They were performed on animals at various stages of the sexual cycle, during pregnancy, with functional disorders of the ovaries, extirpation of the rudimentary epithelium, thyroid gland and the introduction of various doses of gonadotropic, gestagenic hormones and PF-2 alpha.

It has been established that the germinal epithelium of the gonads is morphogenically active cellular structures, from which, during the life of the female and regardless of the state of sexual function and the effect of exogenous and endogenous gonadotropic hormones, in the process of proliferation, germ cells differentiate with their subsequent migration into the white membrane and the surface layer of the cortex ovary. Therefore, it can be concluded that gametogenesis in the studied animals is carried out from the rudimentary epithelium.

In mares, unlike other animal species, the primordial epithelium is located only in the ovulation fossa, from where proliferation and differentiation of germ cells occurs with the formation of primordial follicles. Podvaliuk D.V. (2014)

The regularities we have established in the histogenesis of germ cells and the role of other specific cellular structures of the ovary in this case open up wide possibilities for interfering in the process of oogenesis and directed improvement of gonocytes. Therefore, one cannot agree with the opinion of some authors that gametogenesis occurs only during the fetal period, the primary germ cells are of extragenital origin and the animal is born with a certain supply of these cells, which are consumed during the female's reproductive life (E.A. Pozhidaev, 1967).

It was found that primordial (primary) follicles are formed throughout the life of the female. This process is carried out in the more vascularized, superficial layer of the ovarian cortex by differentiation around the oocyte of 1-2 flat morphogenically active connective tissue (mesenchymal) cells. Their subsequent proliferation leads to the formation of a single-row layer of flat cells and the formation of primordial follicles. Then, in these cells, the nucleus increases in volume, acquires an oval shape, the cytoplasm is contoured, and as a result they acquire the structure of epithelial cells. The formed epithelial cells from connective tissue (mesenchymal) would be more correctly called epithelioid.

Metamorphosis of the surrounding cells of mesenchymal origin into epithelial cells, presumably, is based on the metabolic influence of germ cells, which creates an integral system that provides trophic function for the egg. This situation is confirmed by the following. After ovulation of the follicles, granulosis undergoes dystrophy and reduction, and typical follicular cells do not develop in the ovaries in the absence of gonocytes. The metabolic influence of oocytes or zygotes is also evidenced by the observed activation of reactivity and cellular structures of the endometrium, oviduct or peritoneum when they are nodded.

In this regard, there is a morphogenetic relationship between the reproductive and follicular cells, since the latter are reduced during oocyte dystrophy and typical follicular cells do not develop in the ovaries, which are devoid of oocytes. In cultivation***in vitro*** oocytes with granulosis were observed to maintain their structure and function, while without the oocyte follicular cells lost their granulosa-like appearance and underwent dystrophy.

It has been established that primordial follicles cannot persist for a long time in the surface layer of the ovarian cortex. Their further growth is associated with the formation of a well-vascularized, morphogenically active connective tissue membrane, basement membrane and movement with the proliferating connective tissue into the deeper layers of the ovarian cortex. During the formation of these structures, the morphogenic and secretory reaction in granulosis is enhanced, which ensures the rapid growth of primordial follicles and their transformation into secondary and tertiary ones. Around the oocyte, the radial differentiation of granulosis ends with the formation of a radiant crown and a transparent membrane. The latter are also called upon to perform a trophic function, ensuring the synthesis and transformation of nutrients into the egg, its growth and maturation.

In mares, due to the specificity of the structure of the ovaries, the migration of follicles from the ovulation fossa and their subsequent return to this area for ovulation occurs for a long time. As a result, the maturation of the follicles and the onset of ovulation are lengthened. Therefore, in mares, sexual hunting in comparison with other species of animals is longer.

At the heart of the manifestation of the generative function of the ovaries, characterized by the formation and movement of primordial follicles into the deeper layers of the ovarian cortex, their further growth and transformation into secondary and tertiary follicles, their ovulation and the formation of corpus luteum, is the ability of connective tissue elements to specifically respond to gonadotropic hormones and perform trophic, plastic and hormonal functions.

Connective tissue cells from the superficial zone of the ovaries differentiate around the oocytes, form primordial follicles and ensure their movement into the deeper layers of the cortical substance with subsequent transformation into secondary and tertiary follicles. The connective tissue cells differentiated around the follicles continue to be in a morphogenically active state, providing the formation of the inner and outer theca. After ovulation, obliterative atresia or follicular luteinization, these cellular elements enter a state of hyperplasia and hypertrophy, form yellow, atretic bodies or luteal cysts. Interstitial cells are also formed from such cellular structures.

Thus, these cellular elements should be considered as morphogenetically uniform structures, on which gonadotropin has a specific effect, and the connective tissue structures of the gonads as tissue performing trophic, plastic and hormonal functions. Therefore, these cellular structures of the ovaries, when activated, their function is more correctly called glanodulocytes.

Based on the radial proliferation of connective tissue elements from the superficial to the deeper layers of the ovarian cortex, primordial, secondary and small tertiary follicles cannot persist for a long time in the gonads. They are constantly, during the female's reproductive life, realized and formed again. There is an opinion among some scientists (A.A. Zavarzin, 1954; E.A. Pozhidaev, 1967; V.T, Eliseev, 1972) that primordial follicles are laid in the ovaries only during the fetal period or immediately after birth, and then are realized in throughout the reproductive period. This statement should be considered insufficiently substantiated, since it is not based on the disclosure of the morphogenic, trophic, plastic and hormonal functions of the connective tissue (mesenchymal) elements that determine the generative function of the ovaries.

Studies have shown that the development of hypoplastic or fibrotic processes in the connective tissue elements of the gonads lies at the heart of the age-related decline and termination of the generative function of the ovaries. This excludes the possibility of growth, maturation and ovulation of follicles, and therefore the manifestation of sexual cycles. However, after the termination of the reproductive ability of females, eggs, primordial, secondary and small tertiary follicles at various stages of dystrophy were detected in the ovaries, while maintaining the estrogenic background in the body. This phenomenon is possible due to the continuing gametogenic function of the primordial epithelium and the preservation of the morphogenic potency of the connective tissue elements in some areas of the surface layer of the ovarian cortex. With the predominance of fibrotic processes in the ovaries, the number of follicles is sharply reduced, although gametogenesis is still ongoing. Therefore, the age-related decrease in the number of primordial follicles is associated not with the consumption of the created supply during the fetal period, as is commonly believed (A.A. Zavarzin, 1954; I.F. Ivanov, 1962; V.T. Eliseev, 1972.), but with hypoplasia and fibrous (sclerotic) changes in the connective tissue elements of the ovarian cortex, which determine the folliculogenic function of the ovaries.

Thus, the gametogenic function of the rudimentary epithelium is practically manifested throughout the life of the females, while the generative function of the ovaries, and hence the reproductive ability of animals, is limited in time and is determined by the morphogenic potency of the connective tissue elements of the gonads. It follows from this how important is the role of connective tissue structures in the regulation of the generative function of the ovaries.

The presented new data on the patterns of histogenesis of the generative structures of the ovaries are confirmed by experiments on laboratory animals, and in the subsequent sections these patterns will be presented in the ovaries of heifers and cows.On sections of guinea pig ovaries taken at different stages of the sexual cycle, it was found **(Table 1)** that during the period of ovulation of follicles and the formation of corpus luteum, there is a decrease in the number of oocytes and follicles, respectively, by 18.1 and 17.2%, while during involution corpus luteum, the number of germ cells and follicles increases by 35% in comparison with the control. The observed decrease in follicles is associated with their ovulation and atresia, and the contraction of oocytes is due to their movement with the proliferating connective tissue into the deeper layers of the ovarian cortex and dystrophy. The increase in the number of germ cells and follicles during involution of the corpus luteum can be explained by the fact that proliferating oogonia from the rudimentary epithelium **(Fig.1a)**

Changes in the specific structures of the ovaries of guinea pigs depending on the state of sexual function

Table 1

Number of ovaries examined	The functional state of the ovaries	The number of active structures in the ovaries							
		oocytes and primary follicles	%	secondary and tertiary follicles	%	Yellow atretic	%	all structures	%
8	Follicle ovulation	59	81.9	29	82.8	sixteen	111.8	104.0	85.7
6	Functioning yellow bodies	72	100.0	35	100.0	fifteen	104.8	122.0	100.5
6	Yellow body involution	85	118.0	41	117.1	12	83.9	138.0	113.7
12	Control	72	100.0	35	100.0	14.3	100.0	121.3	100.0

X- is the number of structures in the ovaries per animal

The revealed changes in the quantitative composition of specific cellular structures of guinea pig ovaries are most demonstratively reproduced in experiments with the use of gonadotropic drugs (Table 2). So, on the 6th day after the introduction of gravohormone at a dose of 100 IU, the number of oocytes and follicles in comparison with the control decreased by 29.9 and 54.3%, respectively, while the number of corpus luteum and atretic bodies increased by 179.7%.

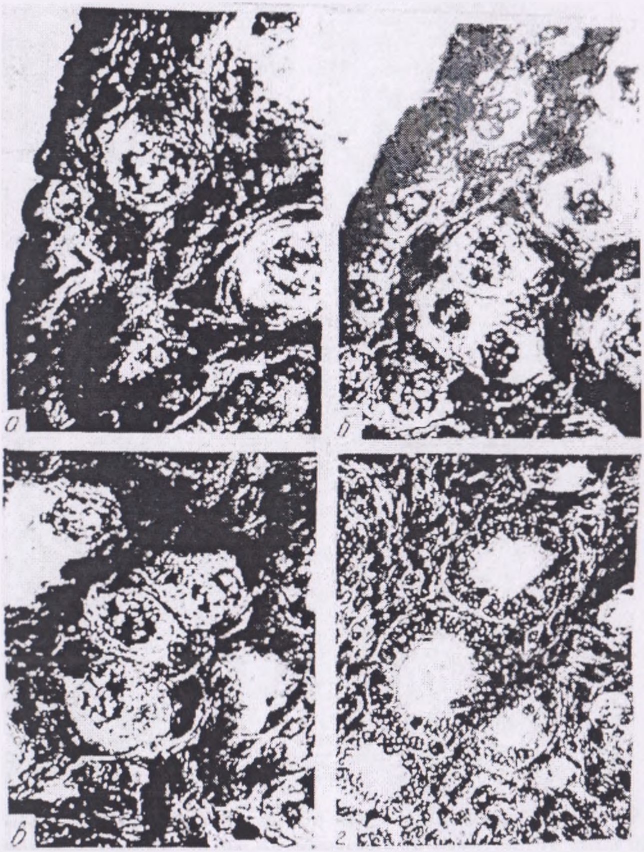


Fig. 1. Ovaries of intact guinea pigs. Proliferation and migration of germ cells from the rudimentary epithelium (a, b) with the formation of primordial (a, b, c) secondary and tertiary follicles (d). UV a, b, c-630, d-280

On histological sections prepared from the ovaries of these animals, the formation of the corpus luteum was completed, and the non-ovulated follicles underwent obliterative atresia. In this case, the eggs were subjected to degeneration. The connective tissue elements of the ovarian cortex entered a state of hypertrophy and hypersecretion. Proliferating cell strands emanated from the base of the tunica.

X-two injections of gravohormone with an interval of 6 days follicles

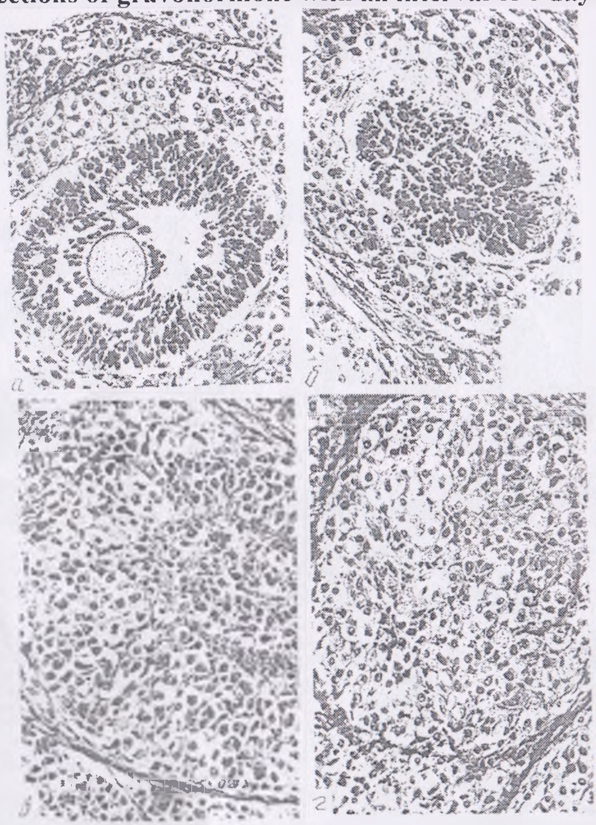


Fig. 2. Ovaries of guinea pigs on day 6 after administration of CZhK in a dose of 500 units. Hyperplasia and hypertrophy of the internal theca of follicles and interstitial cells of the ovary (a, b, c) with the formation of corpus luteum and atretic bodies (d) with reduction of granulosis and oocyte dystrophy (a, b), Uv. a, b, c, d – 280

Changes in the specific structures of the ovaries of guinea pigs after the administration of gravogormone

Table 2

A ovarian research	Long-body. experience in days	Dose of prepa-rata in the M.E..	Number of active structures in the ovaries							
			eggs and primary follicles	%	Secondary; And tertiary; f; Follicles	%	yellow and atrethes-3 bodies	%	всего структур	%
20	1-2	контрольных	72,0	100,0	35,0	100,0	14,3	100,0	121,0	100,0
12	6	100	50,5	70,1	16,0	45,7	40,0	279,7	106,5	87,7
12	6	500	34,0	47,2	7,0	20,0	71,0	496,5	112,0	92,3
10	12	100	77,0	106,9	44,0	125,7	29,0	181,8	150,0	123,6
10	12	500	45,0	62,5	28,0	80,0	69,0	482,5	142,0	117,0
8	20	100	53,0	73,6	19,0	54,3	25,0	174,8	97,0	79,9
8	20	500	97,0	134,7	53,0	151,4	21,0	146,8	171,0	140,9
4	6	100ˣ	22,0	30,5	7,0	20,0	57,0	398,6	86,0	70,8
4	6	500ˣ	16,0	22,2	3,0	8,5	92,0	643,3	111,0	91,5
2	12	100ˣ	51,0	70,8	17,0	48,6	44,0	307,6	112,0	92,3
2	12	500ˣ	39,0	54,1	12,0	34,3	85,0	694,4	136,0	112,1

An even more pronounced stimulating effect occurred after the use of large doses of gravogormone. So, 6 days after the introduction of this drug at a dose of 500 IU, the number of eggs decreased by 52.8%, and follicles by 80%, while the number of corpus luteum and atretic bodies increased to 396.5%, in comparison with the control ... Specific histofunctional changes in the ovaries of these animals include a pronounced activation of hyperplastic, hypertrophic and secretory reactions in the connective tissue elements of the ovarian cortex and follicle membranes. Together with the proliferating tissue, eggs and primordial follicles were carried deep into the ovary. As a result, sex cells were detected only in the primordial epithelium and its base, where there was no connective tissue structure.

As a result of the activation of proliferative processes in the connective tissue elements of the follicle membrane, a massive formation of corpus luteum and atretic bodies took place. In this regard, the cortical substance of the ovary acquired the structure of the parenchyma of the corpus luteum with large luteal cells, among which there were oolems and follicular epithelium in a state of dystrophy (Fig. 2 a, b, c, d). On the 6th day after two doses of gravogormone in a dose 100, and especially 500 IU, the number of oocytes and follicles, respectively, decreased by 77.8 and 91.5%, while atretic and corpus luteum increased to 543.3%. In some ovaries, eggs and follicles were not detected at all, and only yellow and atretic bodies and hypertrophic altered connective tissue cells were visible.

Moreover, both the latter and the luteal cells of the corpus luteum and atretic bodies under the influence of serum gonadotropin morphologically unified, acquiring large sizes (Fig. 2, a, b, c, d).

The described histofunctional changes indicate that the connective tissue cells of the ovarian cortex and follicle membrane are able to transform into typical luteal cells. In this regard, the corpus luteum and atretic bodies, as well as interstitial cells, should be considered as morphogenetically uniform cellular structures, the combined zone of which is embedded in the surface areas of the ovarian cortex. The transformation of the connective tissue elements of the ovarian cortical substance and follicle membranes into interstitial cells, yellow and atretic bodies, observed under the influence of gravogormone, indicates the specific reactivity of these cellular structures to serum gonadotropin. The latter, when used in optimal doses, provides vascularization and moderate stimulation of proliferative processes in the connective tissue membrane of the follicle, thereby creating trophic conditions for hyperfunction of granulosis, maturation of the egg and follicles, and after their ovulation, the formation of corpus luteum.

The morphogenetic and functional unity of the connective tissue elements of the gonads, which specifically respond to gonadotropic drugs, suggests the presence of a single gonadotropic hormone, which is necessary to activate the vascular and morphogenic reaction in the follicle membrane and ensure their maturation and ovulation. It is with the disclosure of the process of follicular growth and the formation of corpus luteum that the prevailing concept of the existence of supposedly two gonadotropic hormones: FSH, which ensures the growth of follicles, and LH, which causes their ovulation, is called into question.

Studying various gonadotropic hormones, theoretically containing FSH and LH, we came to the conclusion that their follicle-stimulating and luteinizing effect depends on the administered dose: in small doses, they stimulate only the growth of follicles, in their optimal maturation and ovulation, in large luteinization without their preliminary growth and ripening. However, the opinion of these authors until now has remained unrecognized, and this can be explained by the fact that, although they correctly noticed the general patterns in the action of the studied drugs, they were unable to reveal the specificity of their action on the connective tissue cellular structures of the gonads, which ensure the growth and maturation of follicles. their ovulation and the formation of corpus luteum.

At the same time, it was found that the rudimentary epithelium remains refractory to gonadotropin.

Therefore, on the 12th, and especially on the 20th day after the introduction of gravohormone, the quantitative composition of the sex cells and follicles is restored again and the generative function of the ovaries is resumed. So, on the 12th day after the introduction of this drug at a dose of 100 IU. the gametogenesis and histogenesis of follicles continue, the number of which, as compared with the 6th day of the experiment, increased by 135.8 and 180%, respectively. The histological picture and the quantitative composition of specific structures in this case are characteristic of the ovaries during the period of involution of the corpus luteum without exposure to exogenous gonadotropin.

20 days after the application of gravohormones at a dose of 100 IU, the ovarian sections showed changes characteristic of the gonads of intact animals during ovulation of follicles, i.e. the number of oocytes and follicles decreased with a significant increase in the corpus luteum and atretic bodies, which indicated the manifestation of an induced sexual cycle.

Even more pronounced changes in the quantitative composition of oocytes, follicles and corpus luteum were observed in the long term after the introduction of gravogormone at a dose of 500 IU. (Table 2). In particular, on the 12th and especially on the 20th day of the experiment, the number of eggs and follicles in comparison with the 6th day of the experiment, respectively, increased by 285.3 and 757.1%. At the same time, a mass number of oocytes and follicles was revealed on the ovarian sections (Fig. 3 a, b, c, d).

Histofunctional and quantitative changes in specific cellular structures of guinea pig ovaries are most demonstratively reproduced after the introduction of gravogormone at a dose of 1800 IU. (Table 3). Thus, one day after the injection of gravogormone at the indicated dose, the number of oocytes of the follicles in the ovaries sharply decreased, while on days 2-4 of the experiment they were not detected at all (Fig. 4 a, b).

The connective tissue elements of the superficial and deep zones of the ovarian cortical substance entered a state of hyperplasia, hypertrophy, acquiring the structure of typical luteal cells of the corpus luteum (Fig. 4 c, d). At the same time, hyperplastic and hypertrophic processes were activated in the connective tissue membrane of the follicles with the massive formation of corpus luteum and atretic bodies. Against this background, the basement membrane was reduced, and granulosis with pyknotically altered nuclei and lysed cytoplasm accumulated in the center of luteinized follicles (Fig. 4 a). Ultimately, interstitial cells, cells of atretic follicles and corpus luteum were unified in size and shape, and the secretory reaction was activated in them (Fig. 4 b, c, d).

Table 3

Changes in the number of active structures of the ovaries of guinea pigs after administration of gravogormone at a dose of 1800 IU

It's long. experience in days	Number of ovarian ovarian erssley-dovan	Number of active structures in the ovaries					
		eggs and primary follicles	%	secondary and tertiary follicles	%	corpora lutea and atretic bodies	%
1-40	30 x	64,0	100,0	33,0	100,0	13,0	100,0
1	4	27,0	42,1	22,0	66,6	36,0	276,9
2	6	9,0	14,0	-	-	127,0	976,9
3	4	3,0	4,6	-	-	158,0	1215,3
4	4	4,0	6,25	-	-	141,0	1084,6
7	4	11,0	17,1	3,0	9,0	139,0	1069,2
12	2	18,0	28,1	7,0	21,2	120,0	923,0
16	2	49,0	76,5	28,0	84,8	47,0	361,5
20	2	118,0	184,3	61,0	184,8	-	-
25	2	131,0	204,6	73,0	221,2	-	-
30	2	90,0	140,6	119,0	360,6	18,0	138,4
40	2	61,0	95,3	65,0	196,9	17,0	130,7

X-control animals

At the same time, starting from the 7th day after the administration of gravogormone, in the primordial epithelium and its base, single germ cells were found, as they migrated into the white membrane around them, a single-layer epithelium differentiated, which ended with the formation of primordial follicles.

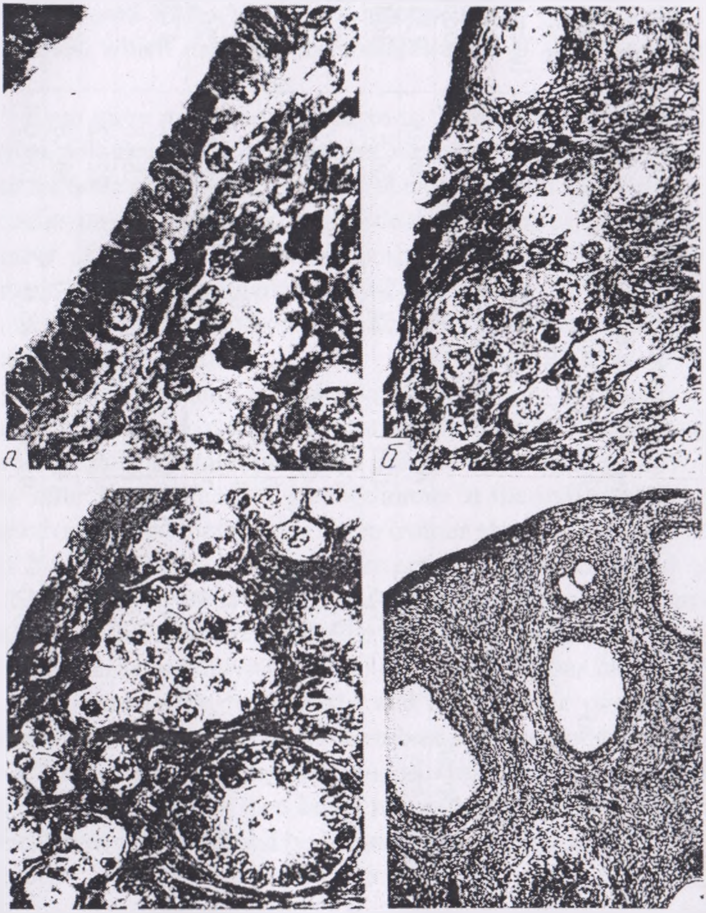


Fig. 3. Ovaries of guinea pigs on 12 (a, b, c) and 20 days after the introduction of FFA in a dose of 500 units. Differentiation of germ cells from the primordial epithelium (a, 6) with the formation of primordial (a, b), secondary and tertiary follicles (d). Uv. a, b, c - 280; g-63

On the 12-15th day after the administration of gravogormone, the number of oocytes and primordial follicles increased. At the same time, the appearance of single secondary and tertiary follicles was noted (Fig. 5 a, b). On the 20th and 25th days of the experiment, the number of oocytes, respectively, increased to 184.3 and 204.6% in comparison with the control.

An increase in secondary and tertiary follicles was observed in approximately the same quantitative ratio (Table 3). At the same time, the sections showed involution of atretic and yellow bodies, as well as interstitial cells of the cortex of the gonads by lysis of the cytoplasm and pycnosis of the nuclei.

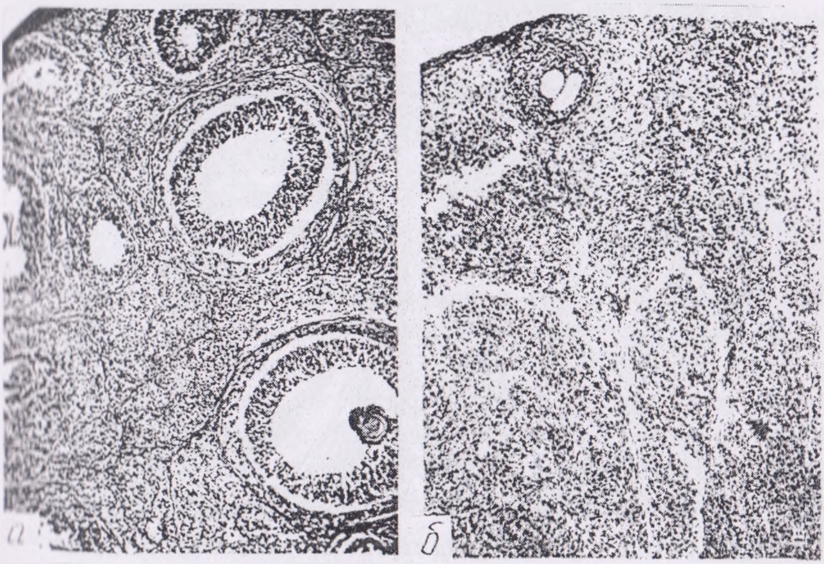
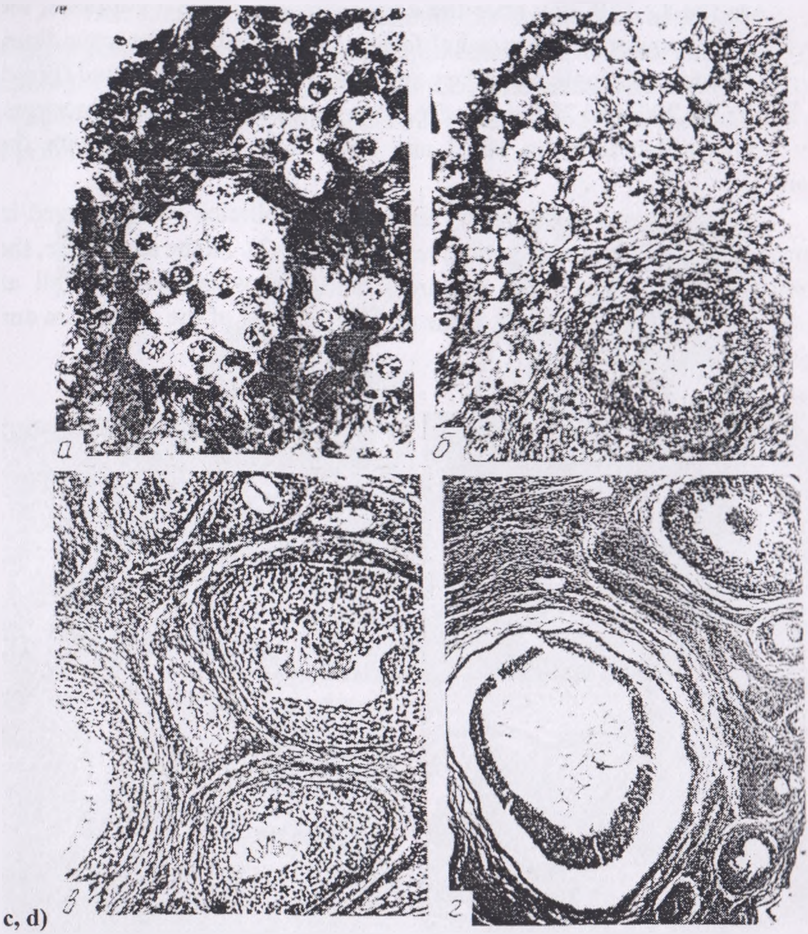


Fig. 4. Ovaries of guinea pigs on days 2 (a) 4 (b, c) and 7 (d) after the introduction of gravogoryun at a dose of 1800 units. Reduction of granulosis and dystrophy of oocytes (a, b, c) against the background of hyperplasia of thecal and interstitial cells and the formation of atretic and corpus luteum (b,



c, d)

Fig. 5. Ovaries of guinea pigs on days 20 (a, b) and 25 (c, d) after the administration of gravogormone at a dose of 1800 units. Gametogenesis and normalization of primordial follicles (a, b). Growth and cystic atresia of tertiary follicles (c, d). a, 6-280; c, g-83.

Against the background of involution of the corpus luteum, atretic bodies and interstitial cells, an increased growth of follicles was noted. At the same time, the development of follicles without a pronounced formation of a connective tissue membrane should be attributed to the characteristic features in the structure of the ovaries, which should be made dependent on the morphofunctional depletion of connective tissue cells in connection with their previous stimulation with large doses of gravogormone. As a result, the follicles did not ovulate, but underwent cystic atresia (Fig. 5 c, d).

By the end of the experiment (30-40 days), the function of the connective tissue elements of the ovarian cortex was restored, and in this regard, the growing follicles reached a high degree of differentiation and ovulated.

Summarizing the above material, we can conclude that the formation of germ cells occurs from the rudimentary epithelium. Their further fate, as well as the formation of follicles with migration into the deeper layers of the cortical substance, depends on the state of the connective tissue elements of the ovary, on which gonadotropin has a specific effect. In this regard, with a moderate reaction from the connective tissue cells, oogonia have time to go through the stages of prophase of meiosis, and primordial follicles with an egg cell develop into secondary and tertiary ones, as is observed with the manifestation of physiological sexual cycles and after the use of optimal doses of gonadotropic drugs.

The introduction of gonadotropin in large doses causes a rapid hyperplastic reaction in the connective tissue elements of the ovary, as a result of which the eggs and follicles, bypassing the stages of specific development, penetrate into the cortex and undergo dystrophy, and the previously formed follicles are obliterated atresia. It is these factors that determine the absence of eggs and follicles in the ovaries in the first days of the administration of large doses of gonadotropic drugs. From these data, it follows that the restoration of germ cells and follicles in the ovaries of guinea pigs is possible within 12-20 days.

To confirm the role of the primordial epithelium in gametogenesis, additional experiments with its removal were carried out. The results of these studies showed that on days 2-5 after treatment of the primordial epithelium with a 5% formalin solution or tincture of iodine, it is completely reduced. On the border of the tunica albuginea and the surface layer of the cortical substance, sex cells and follicles are found at various stages of development and atresia, as well as the corpus luteum. Expressed proliferation of connective tissue cells from the side of the surface layer into the depths of the ovarian cortex.

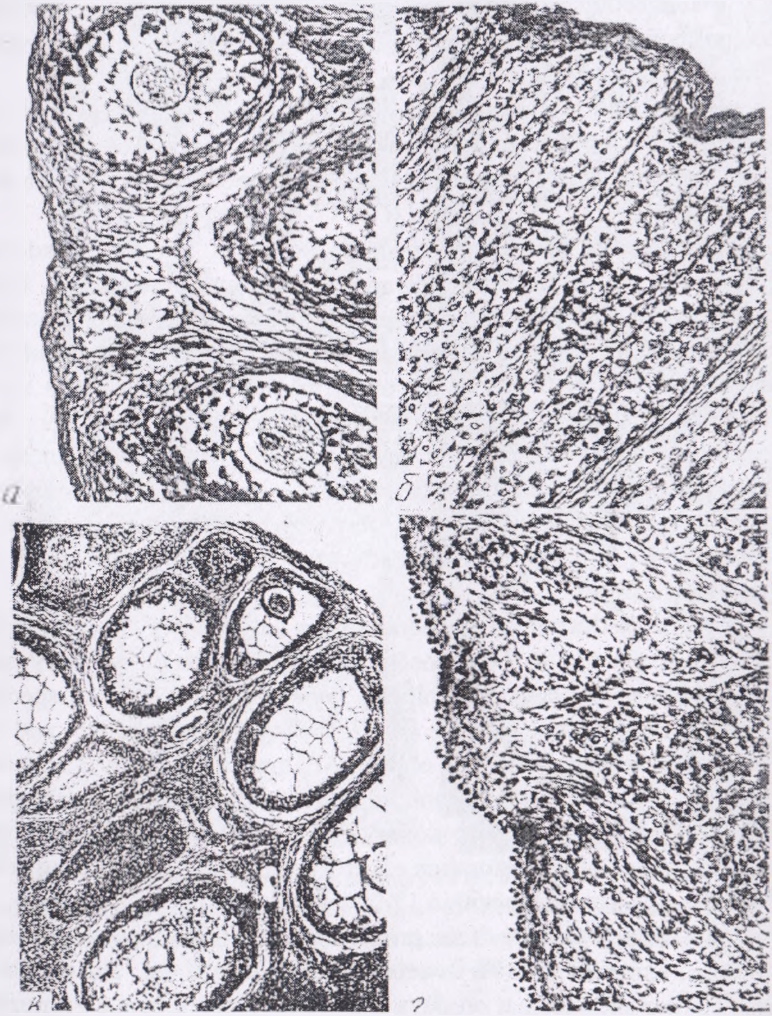


Fig. 6. Ovaries of guinea pigs after removal of the primordial epithelium (a, b), thyroidectomy (c, d) and the introduction of gravogormone at a dose of 500 units. (b, d), dystrophy of follicles and oocytes (a, 6), hyperplasia and hypertrophy of cortical cells (b, d). Cc a, b, c, d - 140.

On days 10-20, dystrophically altered eggs, primordial follicles were detected in the ovaries, as well as oolems and Graaf's vesicles, most of which were in a state of dystrophy (Fig. 6 a). After 30-40 days from the beginning of the experiment, the ovaries were deprived of eggs, follicles and yellow bodies.

The introduction against this background of gravohormone at a dose of 940 IU. activated proliferative processes in the connective tissue cells of the cortex, which hypertrophied, acquiring the structure of luteal cells of the corpus luteum and entered a state of hypersecretion (Fig. 6, b), while restoration of gametogenesis and follicular growth did not occur.

These experiments once again confirm the specificity of the action of gonadotropin on connective tissue cells, and with the transformation into luteal-morphogenetic unity. In turn, the formation of sex and follicular cells, and therefore follicles, is possible only with the preservation of the primordial epithelium, which is a plastic material for these cellular structures. Experiments with extirpation of the thyroid gland testify to the leading role of connective tissue elements in the regulation of the generative function of the ovaries (Table 4).

These studies have established that after thyroidectomy, connective tissue cells of the ovarian cortex and follicle membranes come to a state of hypoplasia. In this regard, a fibrillar structure is clearly visible, oriented from the surface layer of the cortical substance into the depths of the ovary, as well as atrophy of the cells of the connective tissue membrane of the follicles. This is accompanied by granulosa dystrophy and follicular cystic atresia (Fig. 6c). The introduction of gonadotropic drugs against this background restores hyperplastic processes in the connective tissue cells of the cortical substance of the ovaries and follicle membranes, however, due to the violation in these structures of morphogenetic processes and dystrophy of the oocytes, the phenomenon of ovulation is not observed. At the same time, there is a massive formation of atretic bodies with dystrophic changes in the oocytes and, ultimately, the entire connective tissue of the ovary acquires the structure of the corpus luteum (Fig. 6 d).

Table 4

Changes in the number of active structures of guinea pig ovaries after thyroidectomy and administration of gravogormone

The quantity	Long-bodyn; experience in days	Thyroid ectomy	Doses of grave hormone. E.	Nombre de structures actives dans les ovaires							
				eggs and primary. Follicles	%	secondary and tri-specific follicles	%	atret-tel	%	total construction tour	%
24	7-20		**(intactn)**	56	100	33	100	**17**	**100,0**	**106**	**100,0**
8	4	control thyroidect	-	18	32,1	19	57,5	**14**	**82,3**	**51**	**48,1**
6	7		-	-				**12**	**70,5**	**12**	**11,3**
6	10		-	-				**13**	**76,4**	**13**	**12,3**
6	20		-	-				-	-	-	-
4	7		140	-				**19**	**111,7**	**19**	**17,9**
4	7		250	-				**29**	**170,5**	**29**	**27,3**
4	7		560	-				**143**	**841,1**	**143**	**134,9**
4	7		1740	-				**157**	**923,5**	**157**	**148,1**

From the generalization of the above data, it follows that the generative function of the ovaries is defined as gametogenesis. Consequently, the state of the rudimentary epithelium and the function of the connective tissue elements, on which gonadotropin has a specific effect, stimulating their proliferation, differentiation around the follicles and transformation into corpus luteum and atretic bodies. After removal of the primordial epithelium, the formation of germ cells and follicles stops, and extirpation of the thyroid gland leads to the development of atrophic processes in the connective tissue elements of the ovaries, and therefore the follicles undergo atresia, and the egg cells undergo dystrophy. Both in the first and in the second case, the generative function of the ovaries stops. In this regard, the function of the thyroid gland belongs to an important role in the regulation of morphogenetic processes in the ovaries.

Chapter 2. STRUCTURE AND ENDOCRINE CHARACTERISTICS OF OVARIES OF COWS IN RHYTHMIC STATE OF SEXUAL FUNCTION

The correct organization of animal reproduction, ensuring a high level of their reproduction is largely determined by the level of our knowledge about the physiological mechanisms of regulation of sexual function. According to modern concepts A.P. Studentsov (1970), V.S. Shipilov (1977) and others, O.N. Savchenko, G.S. Stepanov (1977); M.I. Prokofiev (1983); V.A. Pavlov, 1984.

The reproductive function of animals is regulated by a complex neurohumoral system, consisting of five main links: the cerebral cortex, hypothalamus, pituitary gland, ovaries and uterus. The hypothalamus is the highest subcortical autonomic center, where the integration of information coming from the peripheral endocrine glands, parts of the nervous system and the switching of nerve impulses to hormonal ones. The nuclei of the hypothalamus have a specific secretory function; they produce neurosecrets that are capable of stimulating (releasing factors) or inhibiting (inhibiting factors) the secretion of adenohypophyseal hormones (V.V. Aleshin, 1971).

One of the main neurosecrets that regulate sexual function is the gonadotropin-releasing hormone gonadoliberin, which is formed in the preoptic region of the hypothalamus. Gonadoliberin along the axons of neurosecretory cells, capillaries and the portal venous system enters the adenohypophysis, providing incretion, and possibly the synthesis of gonadotropic hormones in it (V.V. Aleshin, 1971; A.I. Akayevsky, 1975; O.N. Savchenko, G.S. Stepanov, 1977), who play the main role in the regulation of sexual function.

The change in the concentration of gonadotropic hormones in the blood determines the endocrine and generative function of the target organs, the ovaries. Gametogenesis and the formation of primordial follicles in the ovary occurs constantly (G.A. Cheremisinov, 1974, 1984) and the early stages of their growth and development can be carried out outside the control of the anterior lobe of the pituitary gland (I.A.Eskin, 1968). However, to activate the growth of follicles to an ovulatory state, a gonadotropic stimulus is required, the mechanism of action of which in the ovary is carried out through adenylcyclase, monoaminophosphoric acid and prostaglandins (N.A. Yudaev et al., 1972 V.A. Pavlov, 1977). The influence of gonadotropic hormones on the function of the ovaries is that they prepare morphological structures for the biosynthesis of sex hormones and stimulate the growth of follicles, affect the activity of steroidogenesis in the ovaries by activating the processes of converting cholesterol into pregnenolone. Their biological effect consists in the implementation of ovulation, the release of an egg, followed by its fertilization, advancement and implantation of the zygote, in the formation and stimulation of the functional activity of the corpus luteum and interstitial tissue of the ovaries (MI Prokofiev, 1983).

The generative function of the ovaries is characterized by the maturation of the follicles and their ovulation. In the ovarian follicle, a number of processes occur, characterized by an increase in the synthesis of estrogens in granulosa cells, an increase in receptors for gonadotropic hormones. The presence of a large amount of estrogen through a feedback mechanism through the pituitary-hypothalamus system inhibits the secretion of FSH and stimulates the cyclic release of LH, which leads to ovulation. However, in this process, great importance is also attached to a decrease in the synthesis of sex hormones under the influence of the ovulatory peak of LH and a decrease in the number of LH receptors. and FSH, as well as prostaglandins, which contribute to the rupture of the follicle, causing a contraction of its wall and the entire ovary as a whole. At the site of follicle rupture, a corpus luteum is formed from interna theca cells, which produces progesterone (G.A. Cheremisinov, 1972; T.E. Ponomareva, 1981; A.S. Lobodin, 1982).A large number of sex hormones secreted by the ovaries, through negative feedback through the estrogen-progesterone receptors of the hypothalamus and pituitary gland, inhibits the release of gonadotropins, which, in turn, leads to a change in the nature of the secretion of sex hormones N.A. Yudaev et al. 1978. That is, the activity of the adenohypophysis is determined by the estrogen-progesterone ratio ON Savchenko, GS Stepanov, 1977.

For the development of biotechnology of intensive reproduction, the study of the generative and hormonal functions of the ovaries is of particular scientific and practical importance.

Summarizing the vast literature, it is noted that the maturation of follicles in cows occurs mainly during estrus. By the time of ovulation, the diameter of the follicle is 16-19 mm. After rupture of the follicle, the diameter of the cavity is reduced to 6-7 mm due to the formation of folds of the granular and inner layer of the follicle shell.

Hemorrhage, as a rule, is observed at the site of rupture of the follicle and without the formation of bloody clots in its cavity.

According to A.P. Studentsov (1970), after ovulation, the follicle is filled with blood, and a layer of new cells grows from the remaining peripheral cells of the follicular epithelium, gradually replacing the blood clot within several days. As a result of the proliferation of connective tissue cells of the follicle membrane, the corpus luteum acquires a lobular structure. In the cytoplasm of cells, the pigment lutein is deposited, which gives the entire formation a yellow color. The formation of the corpus luteum ends by the 7th day.

Before ovulation, mitotic activity increases in granulosa and internal theca cells. In 24-48 hours after ovulation, the basement membrane disappears, granulosa and theca cells fuse. In this case, the bulk of the corpus luteum is formed from the follicular epithelium, consisting of large luteal cells, along the periphery of which there is a layer of small luteal cells derived from the internal theca. In the latter, mitoses are also detected on the 7th day after ovulation. During these periods, the size of the corpus luteum increases sharply. On days 9-11, mitosis in the cells of the corpus luteum disappears and signs of dystrophy appear. It is characterized by vacuolization, wrinkling of the cytoplasm and obliteration of blood vessels. It is noted that on the second day after ovulation, a corpus luteum forms at the site of the bursting follicle, which reaches full development on days 9-12, after which it undergoes dystrophy. However, the decrease in the function of the corpus luteum only on the 19th day.

Non-ovulated follicles are reported to undergo atresia. This process can be observed in all stages of the reproductive cycle. In contrast, atresia and luteinization of the follicles were observed only shortly before ovulation. There were no normal follicles in the luteal phase larger than 5 mm in diameter, while follicles in a state of atresia larger than 5 mm were observed in all stages of the reproductive cycle. The growth of follicles in the ovaries of cows was observed both during estrus and in the middle of the sexual cycle. Two waves of follicular growth have been reported, occurring on days 3-4 and 12-14 of the sexual cycle. Moreover, the mitotic activity of follicular cells ceased as soon as the diameter of the follicles reached 3-5 mm. Mitotic activity in granulosis both before and after ovulation.

From the above data, it follows that the histofunctional changes in the ovaries at various stages of the reproductive cycle and during pregnancy have been poorly studied. In particular, the histogenesis of germ cells and primordial follicles has not been studied, there is no data on the formation of follicle membranes during their growth and maturation, on the way they move into the depths of the ovary, as well as on changes in connective tissue and interstitial cells. Opinions about the development of follicles, their atresia and luteinization, as well as the formation and functioning of the corpus luteum in these states of sexual function are very contradictory. Of particular interest are the literature data on morpho-functional disorders in the ovaries of cows. The most common of them is ovarian hypofunction, as a result of adverse effects on the body of alimentary, climatic, operational and other factors (A.P. Studentsov, 1970). However, the literature data on histofunctional changes in the ovaries during their hypofunction are very limited. A.S. Bibilashvili (1971) reports that with hypofunction in the ovaries, yellow bodies are constantly absent, there are regressive changes in oocytes, follicular atresia, obliteration of blood vessels, hypoplasia of connective tissue cells and an increase in the number of stroma. An increase in the number of atretic follicles in the ovaries of cows in the absence and irregular reproductive cycles was established.

With a high milk productivity of animals, a violation in feeding and keeping, with the sucking method of raising calves, as well as endometritis in the ovaries of cows, the retention of yellow bodies is possible (E. Kuldac, 1968; A.P. Studentsov, 1970).

Common morphological and functional disorders in the ovaries include cysts, which are a common cause of infertility in cows. A.P. Studentsov (1970) notes that ovarian cysts are formed from follicles or corpus luteum due to degeneration of their cellular elements. Luteal cysts differ histologically from follicular cysts only in that their wall is formed by 15-20 rows of luteal cells. The development of cysts is associated with a violation of the relationship between the ovaries, the pituitary gland and the nervous system due to alimentary, climatic and other factors, that in the early stage of follicular cysts development, when the granular layer remains, estrogens are determined in their contents, while in cysts larger than 2 , 5 cm in diameter, the contents lose hormonal activity. Progesterone is detected in luteal cysts.

As for what cellular structures cysts are formed from, the state of connective tissue and other specific cellular structures of the ovaries, these issues have not been sufficiently studied and poorly covered in the literature.

The ovaries perform both generative, providing gametofolliculogenesis, the formation of the corpus luteum of the sexual cycle and pregnancy, and hormonal, producing estrogens and progesterone. The main biological property of ovarian hormones boils down to activating the growth of tissues of the reproductive system of the endometrium, myometrium, vagina and external genital organs, as well as creating a certain functional state during the period of manifestation of sexual cycles, implantation, pregnancy and childbirth. In addition, they, acting on the hypothalamic-pituitary system, are involved in the regulation of sexual function. At the same time, as indicated by A.P. Studentsov (1970), ovarian hormones act on the ventromedial centers of the hypothalamus, providing the manifestation of sexual arousal.

Researchers differ on which ovarian cell structures synthesize estrogens and progesterone. Some authors believe that the synthesis of estrogens is carried out by the follicular epithelium, and others by the cells of the internal theca, while I.E. Eskin (1968), come to the conclusion that both granulosa cells and thecal cells are involved in the synthesis. Some researchers attribute the steroid-synthesizing function to the interstitial cells of the ovarian stroma, as well as to atresizing follicles. In contrast to these data, progesterone was found in luteal cysts, in which granulosis was reduced, and the cells of the internal theca acquired the structure of luteal cells of the corpus luteum, and estrogens were found in follicular cysts, where the internal theca undergoes atrophic changes with well-developed granulosis. This gave the authors reason to conclude that estrogens are produced by the epithelium of the granular layer, and not by the cells of the inner layer of the follicle membrane, which produce progesterone.

Using gonadotropic drugs, studying enzymatic activity, extirpating individual cellular structures of the ovaries and determining progesterone and pregnandiol, they come to the conclusion that interstitial cells and cells of the internal theca, like the corpus luteum and luteal cysts, produce progesterone. The change in progesterone concentration reflects the function of these structures.

In case of violation of reproductive ability in animals, changes in the endocrine system are noted (O. Agthe, 1973). According to the data, in cows with ovarian cysts in the blood with prolonged estrus contains 38.8 ± 4.9 estrone; estradiol-17 beta 125 ± 3.4; estriol 23.6 ± 3.2 pg / ml. With irregular estrus, respectively, 4.9 ± 2.3; 48.5 ± 3.0 and 4.5 ± 6.1, and in animals in anestrus 10.7 ± 4.5; 17.4 and 3.6 ± 5.2 pg / ml. J. Derivaux (1970) reports that during functional anestrus, the content of estradiol in the peripheral blood is less (0.8-2.5 pg / ml) than during postpartum anestrus, when its concentration is 1.3-5.04 pg / ml.

The literature also contains data on the content of progesterone in animals with impaired reproductive function. In a radioimmunological study of the blood of cows, the minimum content of progesterone was in animals with ovarian atrophy and amounted to 0.57 pg / ml, respectively. Similar results were obtained in the study of functional and postpartum diestrus in cattle. It was found that during anestrus the level of progesterone was unchanged low and corresponded to the baseline value during the normal cycle.

A direct relationship was found between the concentration of progesterone and the function of the corpus luteum, as well as the volume of luteal cells and their lipoid inclusions.

From the above data, it follows that sex hormones play an important role in the regulation of the reproductive function of animals. However, the available information on the localization of steroid-producing structures, the dynamics of steroid hormones in the peripheral blood of cows during the sexual cycle, during pregnancy and with functional disorders of the ovaries are few and contradictory.

To study morphofunctional changes in the ovaries and ovarian hormones in the blood plasma at different stages of the sexual cycle, at different periods of pregnancy, with hypofunction of the gonads, persistence of the corpus luteum, follicular and luteal cysts, multiple anovulatory sexual cycles, 203 Simmental cows of the age were included in the experiment. from 4 to 10 years old, weighing 500-650 kg, average and above average body condition.

To study changes in the ovaries at various stages of the reproductive cycle, material was obtained from 98 cows on the 1st, 2, 3, 4, 5, 7, 9, 12, 16, 18, 19, 20, 21, 23 and 24 days from the beginning of the sexual detection. hunting, after slaughter or ovariectomy, in each case, 5-7 animals.

In order to study morphological and functional changes in these organs in pregnant cows, 40 animals were included in the experiment, of which 10 had a gestation period of 10-30 days, 5 - from 1 to 2 months, 5 - from two to three, 5 - from three up to four, 3 from four to five, 2 from five to six, 2 from six to seven, and 8 from eight months to calving. Morphofunctional changes in the ovaries were also studied in 17 cows with ovarian hypofunction, 10 with persistent yellow bodies, 39 with follicular and luteal cysts, and 5 cows with multiple (3-5) anovulatory sexual cycles. Animals with functional disorders in the ovaries were killed or extirpated after diagnosis.

After slaughter or ovariectomy, the ovaries were subjected to macroscopic and histological examination. Macroscopic examination of the ovaries determined their weight, size, as well as the number and size of follicles, corpus luteum, follicular and luteal cysts, hemorrhagic and luteinized follicles and atretic bodies. For histological examination, the fragments of organs were fixed in a 10% solution of neutral formalin and embedded in paraffin. The staining of serial sections with a thickness of 7 microns was carried out with hematoxylin-eosin according to Van Gieson, Heidenhain, Frenkel, and Foote. Sections prepared on a freezing microtome were stained with Sudan III + IV and Sudan black. In total, 12 thousand sections and more than 2 thousand micrographs were prepared.

When analyzing histological preparations of the ovaries, gametogenesis, changes in the specific cellular structures of the gonads during the growth and maturation of primary, secondary and tertiary follicles, their ovulation, formation, functioning and involution of corpus luteum and atretic bodies, follicular and luteal cysts were determined.

In order to elucidate the dynamics of the formation, functioning and involution of the corpus luteum of the reproductive cycle in intact animals and after the use of gravogormone, as well as at various stages of pregnancy and with luteal cysts, the diameter of luteal cells and the volume of their nuclei from 61 animals were measured using an eyepiece micrometer. The average data for these indicators was derived from 200 measurements. Statistical and graphical methods were used to analyze the measurement results.

To study the dynamics of sex hormones during the sexual cycle, there were 59 cows in the experiment. For them, clinical control was established with rectal examinations and blood sampling for the study of sex hormones on the day of ovulation, on days 2-3, 6-7, 10-12, 14-15, 17-18, 19-21 days of the sexual cycle. For the histological examination of the ovaries, material was taken from 24 cows killed in the same period of 3-5 animals in each case.

In order to find out the content of ovarian hormones in the blood with ovarian hypofunction, studies were carried out on 21 animals.
Blood was taken from 5 cows for 3 weeks with an interval of 2-3 days, and from 16 cows once, at the time of the experiment. Blood for analysis in an amount of 5-10 ml was taken in tubes with heparin in the period from 9 to 11 hours. The resulting plasma was frozen and stored until the study at a temperature of -15 ° C. Progesterone, total estrogens, estradiol-17 beta were determined by radioimmunoassay. Radioactivity was measured on a Beckman liquid scintillation counter with a tritium counting efficiency of about 57%. The dynamics of the content of sex hormones in the blood in the early stages of pregnancy was studied in seven cows on the day of insemination, at 6-7, 9-10, 12-14, 20-21, 23-30, 42-45, 60-62 day after insemination. 47 animals were included in the experiment on the study of hormonal changes in the body of cows during fruiting, during childbirth and in the early postpartum period. Blood for the determination of hormones was also taken from the jugular vein at 3, 4, 5, 6, 7, 8, 9 months of pregnancy, 1-3 days before childbirth, during childbirth, as well as 6, 12, 24 and 48 hours after birth of a calf. Hormones were also determined by radioimmunoassay.

In addition, in 16 and 3 cows, respectively, with luteal and follicular cysts in the blood plasma, progesterone and estradiol-17 beta were also different periods of pregnancy, with hypofunction of the gonads, persistence of the corpus luteum, follicular and luteal cysts, multiple anovulatory sexual cycles, 203 Simmental cows of the age were included in the experiment. from 4 to 10 years old, weighing 500-650 kg, average and above average body condition.

To study changes in the ovaries at various stages of the reproductive cycle, material was obtained from 98 cows on the 1st, 2, 3, 4, 5, 7, 9, 12, 16, 18, 19, 20, 21, 23 and 24 days from the beginning of the sexual detection. hunting, after slaughter or ovariectomy, in each case, 5-7 animals.

In order to study morphological and functional changes in these organs in pregnant cows, 40 animals were included in the experiment, of which 10 had a gestation period of 10-30 days, 5 - from 1 to 2 months, 5 - from two to three, 5 - from three up to four, 3 from four to five, 2 from five to six, 2 from six to seven, and 8 from eight months to calving.
Morphofunctional changes in the ovaries were also studied in 17 cows with ovarian hypofunction, 10 with persistent yellow bodies, 39 with follicular and luteal cysts, and 5 cows with multiple (3-5) anovulatory sexual cycles. Animals with functional disorders in the ovaries were killed or extirpated after diagnosis.

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In addition, in 16 and 3 cows, respectively, with luteal and follicular cysts in the blood plasma, progesterone and estradiol-17 beta were also

determined by the radioimmunological method when a clinical diagnosis was made and after 12, 24, 48, 96 and 142 hours from the beginning of the experiment, followed by extirpation of the ovaries.
The animals were fed according to the VIZH standards. Before setting and during the period of the experiment, the state of the body was monitored according to the biochemical parameters of blood, in which total protein, albumin, alpha, beta, gamma globulins, calcium, phosphorus, glucose, vitamins A, C, magnesium, ketone bodies, alkaline reserve were determined , alkaline phosphatase, cholesterol, carotene, sodium and potassium. Chemical analysis of feed was carried out.

2.1. The structure of changes in the ovaries and the dynamics of ovarian hormones in the blood of cows during the sexual cycle Morphologically, the ovaries of cows are represented by the cortex and medulla.

From the surface, the gonads are covered with the primordial epithelium, then the tunica albuginea follows. The parenchyma of the cortex, in addition to the morphologically very variable connective tissue cells, includes follicles at various stages of development and atresia, as well as corpus luteum and atretic bodies. The nature of macroscopic changes in the ovaries during the sexual cycle is reflected in table 5. From the analysis of the table it follows that the number of large and medium-sized follicles increases with the onset of sexual heat, then there is a slight decrease with a simultaneous increase in the number of corpus luteum and atretic bodies. No noticeable changes in the composition of small follicles throughout the entire sexual cycle have been established. The formation of the corpus luteum ends 5-6 days after ovulation. At the same time, it acquires an elastic-elastic consistency, a yellow color with a violet tint, and many injected vessels are visible on its surface. The corpus luteum reaches its largest size 7-8 days after ovulation and is in this state in most animals up to 15-18 days. Subsequently, mainly on days 20-21, the corpus luteum of the reproductive cycle decreases in size, acquires a denser consistency and a grayish-yellow color. The final involution of the corpus luteum, with the acquisition of a fibrous structure and light color (white boobserved 28-30 days after ovulation.

Table 5

Changes in the ovaries of cows during the sexual cycle

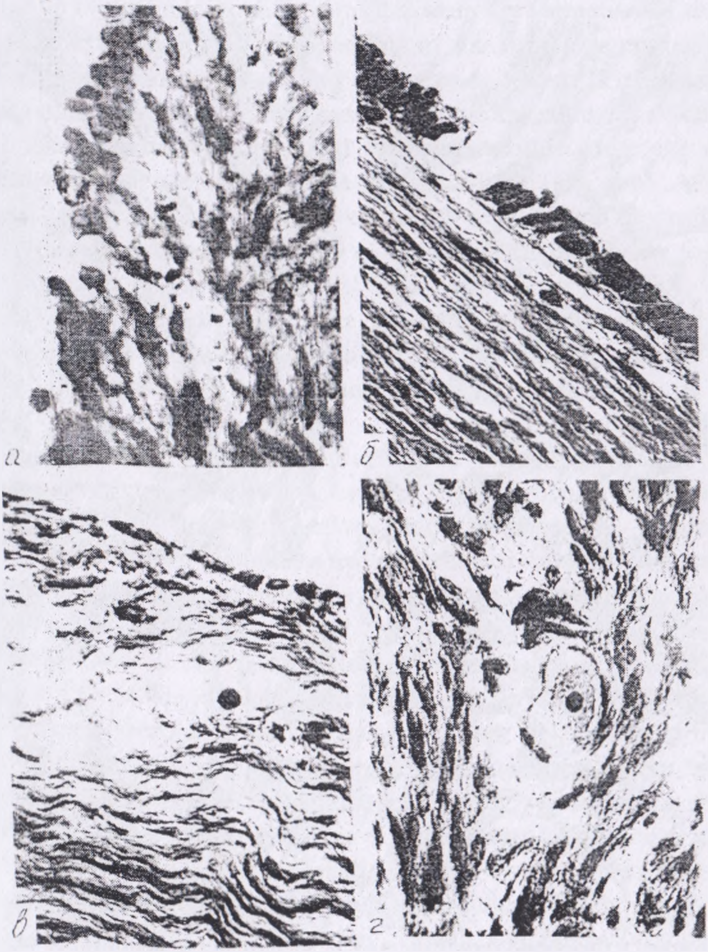
The quantity	The days of the sexes of the cycle from the beginning	Follicles (see)			Yellow bodies			Atretic bodies
		1-1,5	0,5-09	0,2-0,4	Developing	Functioning	Involution	
4	1	6,0/1,5	6,0/1,5	68,0/17,0	-	-	3,0/0,7	3,0/0,7
4	2	1,0/0,2	6,0/1,5	75,0/18,7	4,0/1,0	-	4,0/1,0	14,0/3,5
4	3	1,0/0,2	7,0/1,7	50,0/12,2	4,0/1,0	-	6,0/1,5	10,0/2,5
2	4	1,0/0,5	3,0/1,5	35,0/17,5	2,0/1,0	-	2,0/1,0	6,0/3,0
2	5	1,0/0,5	4,0/2,0	26,0/13,0	-	2,0/1,0	5,0/2,5	4,0/2,0
2	7	1,0/0,5	2,0/1,0	33,0/16,5	-	2,0/1,0	2,0/1,0	3,0/1,5
2	9	2,0/1,0	-	22,0/11,0	-	2,0/2,0	2,0/1,0	3,0/1,5
2	12	-	6,0/3,0	30,0/15,0		1,0/0,5	1,0/0,5	3,0/1,5
2	16	1,0/0,5	3,0/1,5	20,0/10,0	-	2,0/1,0	-	3,0/1,5
2	18	4,0/2,0	4,0/2,0	34,0/17,0	-	1,0/0,5	1,0/0,5	4,0/2,0
3	19	5,0/1,7	6,0/2,0	49,0/16,3	-	-	3,0/1,0	3,0/3,0
2	20	3,0/1,5	4,0/2,0	40,0/20,0	2,0/1,0	-	3,0/1,5	3,0/3,0
2	21	1,0/0,5	5,0/2,5	39,0/19,5	2,0/1,0	-	3,0/1,5	2,0/1,0
2	23	1,0/0,5	6,0/3,0	14,0/7,0	2,0/1,0	-	2,0/1,0	3,0/1,5
3	24	2,0/0,7	2,0/0,7	30,0/10,0	-	2,0/0,7	5,0/1,7	6,0/2,0

Note: the numerator is total structures in the ovaries
denominator - number of structures per animal

When studying histological changes in the ovaries, it was revealed that in some cellular structures of these organs, pronounced changes are observed during the sexual cycle, while in others a similar phenomenon has not been established. In particular, in the primordial epithelium, regardless of the stage of the sexual cycle, there is a constant differentiation of large cells and their migration to its base and tunica albuginea (Fig. 7 a, b, c, d). In this case, the cells increase in volume, the nuclei become chromophilic, and the cytoplasm is light-basophilic. Sometimes in such cells it is possible to trace changes in the structure of the nucleus, characteristic of the prophase stage of meiosis (Fig. 8 a, b). This gives grounds to suggest that gametogenesis occurs from the rudimentary epithelium and this process occurs throughout the entire reproductive period of cows. In the process of moving oocytes around them, 1-2 and smaller cells differentiate, the proliferation of which leads to the completion of the formation of primordial follicles (Fig. 7 d, Fig. 8 c, d, Fig. 9 a). In this regard, the cells formed around the oocyte should be considered as follicular, which originate from the surrounding connective tissue elements of the ovary. That is why one cannot agree with the opinion of some authors (E.N. Pozhidaev, 1967), who believe that the germ cells are of extragenital origin, are laid in the fetal period in the cortex of the ovary in the form of primordial follicles and are realized during the reproductive life of the female. In contrast to these authors, A.P. Studentsov (1970), do not exclude the possibility of postnatal oogenesis from the rudimentary epithelium, while in the ovaries of mice, rats, guinea pigs, cats, monkeys and humans, many researchers observed postnatal oogenesis, then in cows this not clarified.

Our studies have shown that in the ovaries of both laboratory animals and cows, sheep, pigs and mares, regardless of the state of sexual function, gametogenesis and the formation of primordial follicles are constantly carried out B.M. Nurmukhamedov, A.G. Cheremisinov, D.V. Podvalyuk ... (1991)

It has been established that primordial follicles cannot persist for a long time in the surface layer of the cortex, but they constantly move into the depths of the ovary. This is carried out due to the proliferation of connective tissue cells from the cambial zone, laid down at the base tunica albuginea, in the direction of the medulla. In the process of moving primordial follicles deep into the ovary, some of them undergo dystrophy, while others, when a vascularized connective tissue membrane and basement membrane are formed around them, pass into secondary and tertiary (Fig. 9b, c, d).



Rice.7. Cow ovaries. Migration of sex cells from rudimentary epithelium (a,b) White shell (B) with differentiation. flat cells (g). A,b-280; V,g - 140.

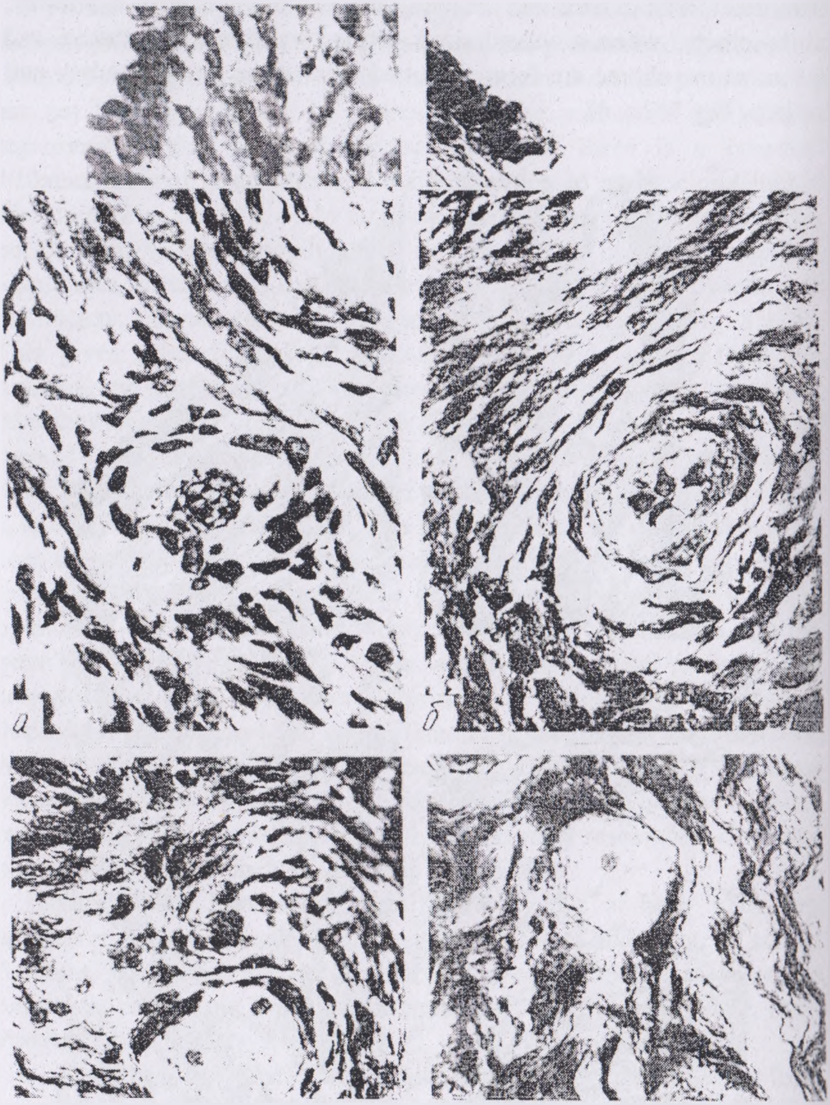


Figure.8.Ovichnikikors. Processes of meiosis in the genital cells (a,b) primordial follicles (v,g). Uv (a,b, w)-630

At the same time, there is an increase in the volume of epithelial cells and their proliferation. In this regard, a well-vascularized connective tissue membrane should be considered as a tissue that performs a trophic function, and the basement membrane as a structure that provides the transport of necessary nutrients from the vascular layer of the follicle membrane to the granulosis and ovum. It is with the formation of these structures that the morphogenic reaction in the follicular epithelium intensifies and its transition from single-layer to multilayer is carried out. At the same time, the egg cell increases in volume and occupies a central position. The presence of a stratified epithelium with a large egg cell characterizes the development of a secondary follicle (Fig. 9 b). At the same time, radial differentiation of epithelial cells, called the radiant crown, ends around the oocyte (Fig. 9 c). A transparent membrane forms between the radially located epithelial cells and the egg (Fig. 9c). The latter, like the basement membrane, ensures the transformation of nutrients from the granulosis into the egg, and therefore creates the necessary conditions for its growth and maturation.

The results of our studies are consistent with the data on the participation of the follicular epithelium in the formation of the transparent membrane, the oocyte, and on the presence of an organic connection between the reproductive and follicular cells, which is disrupted by the time of maturation and ovulation of the follicle. In turn, the oocyte developing in the follicle is separated from the circulatory system by means of a numerous membrane-cell barrier, and the follicular cells transfer into it all the substances necessary for growth and maturation. That is why the germ cell and accompanying follicular cells form an integral morphological and functional unit, well separated from the rest of the cellular elements. However, the statement of the latter authors cannot be considered complete, because the function of the germ and follicular cells, which form an integral morphofunctional unit, depends, as our data indicate, mainly on the formation of a well-vascularized connective tissue membrane around them, which in this case performs a trophic function, providing growth and the maturation of follicles, and after their ovulation and the formation of the corpus luteum (plastic role). The continuing proliferation of epithelial cells and the activation of hypersecretion in them should be attributed to a further stage in the development of secondary follicles. As a result, drops of secretion appear in the intercellular areas, which, when combined, form follicular fluid. The concentration of the follicular fluid and the differentiation of the epithelium along the follicle wall characterizes the development of the tertiary follicle. The peculiarities in the structure of the tertiary follicles include the formation of an ovarian tubercle and a more pronounced proliferation and vascularization of the cells of the connective tissue membrane **(Fig. 9 d)**.

It should be noted that gametogenesis, as well as the growth of primary, secondary and small tertiary follicles, can be observed in the ovaries of cows at all stages of the reproductive cycle, while maturing large tertiary follicles are found only shortly before the onset of estrus and sexual heat. At the same time, characteristic changes develop in the granulosis and connective tissue membrane of the follicles. In particular, if in growing tertiary follicles granulosis retains radial differentiation (Fig. 10 a), then in maturing graaf vesicles epithelial cells undergo dystrophy. This process intensifies shortly before ovulation of the follicles and is characterized by a violation of the structure of the basement membrane and desquamation of follicular cells (Fig. 10 b). As a result of these changes, the necessary conditions are created for the rejection of the germ cell from the follicle wall and its free exit into the follicular fluid, together with which, after rupture of the follicle, the oocyte membrane and granulosis, which created trophic conditions for the growth and maturation of the egg and the necessary estrogenic background in the body for manifestations of the phenomena of the stage of arousal of the sexual cycle.

In maturing follicles, the cessation of the mitotic activity of granulosis, intense pycnosis of the nuclei and the decay of the cells of the egg-bearing tubercle were observed. This was accompanied by inhibition of enzymatic activity in the follicular epithelium and an increase in the latter in the internal theca with the activation of progesterone synthesis in it.

In contrast, in the cells of the connective tissue membrane of maturing follicles, morphogenic, secretory and vascular reactions are activated with the formation of large thecalutein cells, represented by oval and rounded nuclei and vacuolated cytoplasm **(Fig. 10 c).** Similar phenomena indicate that luteinization of preovulatory follicles begins shortly before ovulation. Progesterone is first secreted by luteinized cells of theca, then by the corpus luteum, and an increase in progesterone concentration is an indicator of follicular luteinization. During this period, A.G. Nezhdanov (1983) notes the appearance of the first signs of endometrial transformation, which intensifies after ovulation of the follicles. This once again confirms that the corpus luteum is formed from the cells of the connective tissue membrane, which, even before ovulation, begin to transform into luteal cells that provide the synthesis of progesterone, whereas, according to the opinion of supporters of the formation of the corpus luteum from granulosis, "the phenomenon of metamorphosis into luteal cells ".

Due to increased vascularization and increased hyperplastic and hypertrophic processes in the cells of the connective tissue membrane, it increases in volume. A similar circumstance, apparently, leads to an increase in intrafollicular pressure, and in this regard, a condition is created for rupture of the wall of the Graafian bubble and the release of an egg from it. 2 to 4 large and medium-sized follicles, however, one, rarely two Graafian vesicles undergo ovulation, and the rest undergo obliteration **(Fig. 11 a, b, c)** or cyst atresia **(Fig. 11 d)**. Such cystic changes in follicles, according to the data of B.M. Khvatov (1955), should be considered as a physiological phenomenon characterized by the growth of the majority of follicles without their subsequent ovulation. At the same time, the phenomena of vacuolization and lysis develop in the cytoplasm of the cells of the connective tissue membrane, and the nuclei acquire a flat shape.

Subsequently, on the 5-7th day of the sexual cycle, the connective tissue membrane acquires a fibrous structure, and granulosis is reduced (Fig. 11 d). Such cystic follicles are observed in the ovaries of cows at all stages of the reproductive cycle. The prevalence of the number of growing follicles over their ovulation observed in the stage of excitation of the sexual cycle can be explained by the physiological need to create the proper hormonal (estrogenic) background in the body for the manifestation of estrus, general reaction and sexual desire. It is during this period that the highest level of total estrogens in the blood plasma is observed (108.1 ± 28.9 pg / ml). The disclosure of this pattern makes it possible to explain the observed anestral, alibid and areactive sexual cycles with insufficient folliculogenesis at the stage of excitation of the sexual cycle. The continuing proliferation of epithelial cells and the activation of hypersecretion in them should be attributed to a further stage in the development of secondary follicles. As a result, drops of secretion appear in the intercellular areas, which, when combined, form follicular fluid. The concentration of the follicular fluid and the differentiation of the epithelium along the follicle wall characterizes the development of the tertiary follicle. The peculiarities in the structure of the tertiary follicles include the formation of an ovarian tubercle and a more pronounced proliferation and vascularization of the cells of the connective tissue membrane **(Fig. 9 d)**.

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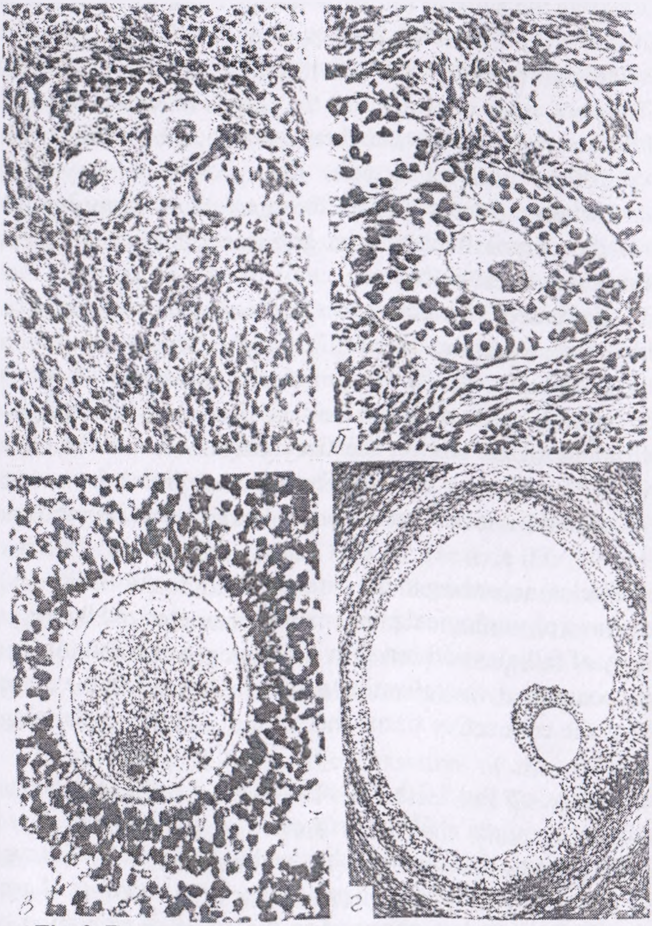

Fig. 9. Formation of primordial (a) secondary (b) and tertiary (c.d.) falicules in the ovaries of cows. Magnification a,b-140; c - 280; d – 63;

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It was found that in the process of ovulation of the follicles, their wall collapses, forming corrugated invaginations due to the proliferating cells of the internal theca. At the same time, the contours of the basement membrane and dystrophically altered granulosa cells are revealed on the surface of the hyperplastically altered thecal cells **(Fig.10c,d).**

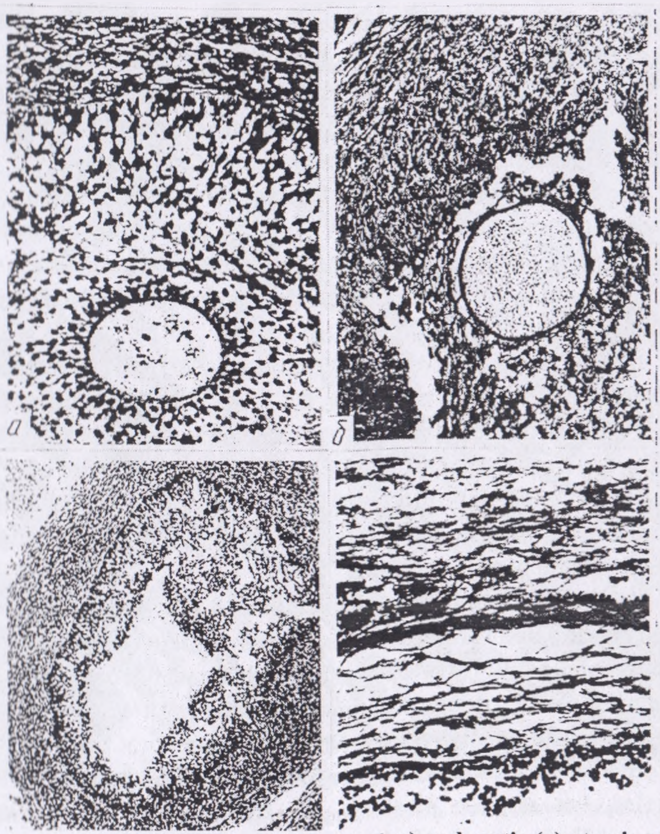


Figure.10. Ovaries of cows. Obliterative (a,b,c) and cystic (g) atresia of follicles. Cv. b 63; a,v,g – 140

Together with the connective tissue membrane, the blood vessels move into the cavity of the burst follicle. If the integrity of the latter is violated, a large number of blood cells are seen on the sections, which, together with the regenerating capillary network, creates a favorable trophic environment for the proliferation of connective tissue cells of the ovulated follicle membrane. In this case, follicular cells are found in the form of separate islets with lysed cytoplasm and pycnotically altered nuclei, surrounded by proliferating cells of the inner theca **(Fig. 10d).** At the same time, the cells of the outer theca retain their typical connective tissue structure. It is these changes that are observed on the first day of ovulation of the follicle. In subsequent periods, the formation of luteal cells of the corpus luteum also occurs from these structures.

So, on the second day after ovulation, in addition to the continuing proliferation of cells of the inner layer of theca, the plastic reaction in the corrugated invaginations of the outer theca is enhanced.

From the side of these structures, powerful proliferating radially located cords emanate, the cells of which, as they move towards the center of the forming corpus luteum, change from typical connective tissue with flat nuclei to luteal with oval and rounded nuclei and well-defined cytoplasm.

On the third day after ovulation, the cells of the internal theca differentiate into luteal cells **(Fig. 12 a, b),** most of which pass into the stage of secretion **(Fig. 12 c).** At the same time, the cells of the outer theca and the adjacent tissue of the ovarian cortex are in a state of proliferative activity and enhanced differentiation into luteal cells. It is due to these connective tissue cells that the corpus luteum is formed on the 4-5th day from the moment of ovulation.

At the same time, from the previously well-pronounced connective tissue corrugated protuberances, there remain insignificant radially located bundles, represented by elastic fibers, which determine the lobular structures of the corpus luteum. In this regard, the connective tissue membrane of the follicles should be considered not only as a tissue that performs a trophic function, ensuring the growth and maturation of follicles, but also as plastic - the formation of corpus luteum and homonopoietic - the production of progesterone. In turn, the inner and outer theca are formed from the connective tissue elements of the ovarian cortex, and therefore these structures, like the corpus luteum, are morphogenetically uniform.

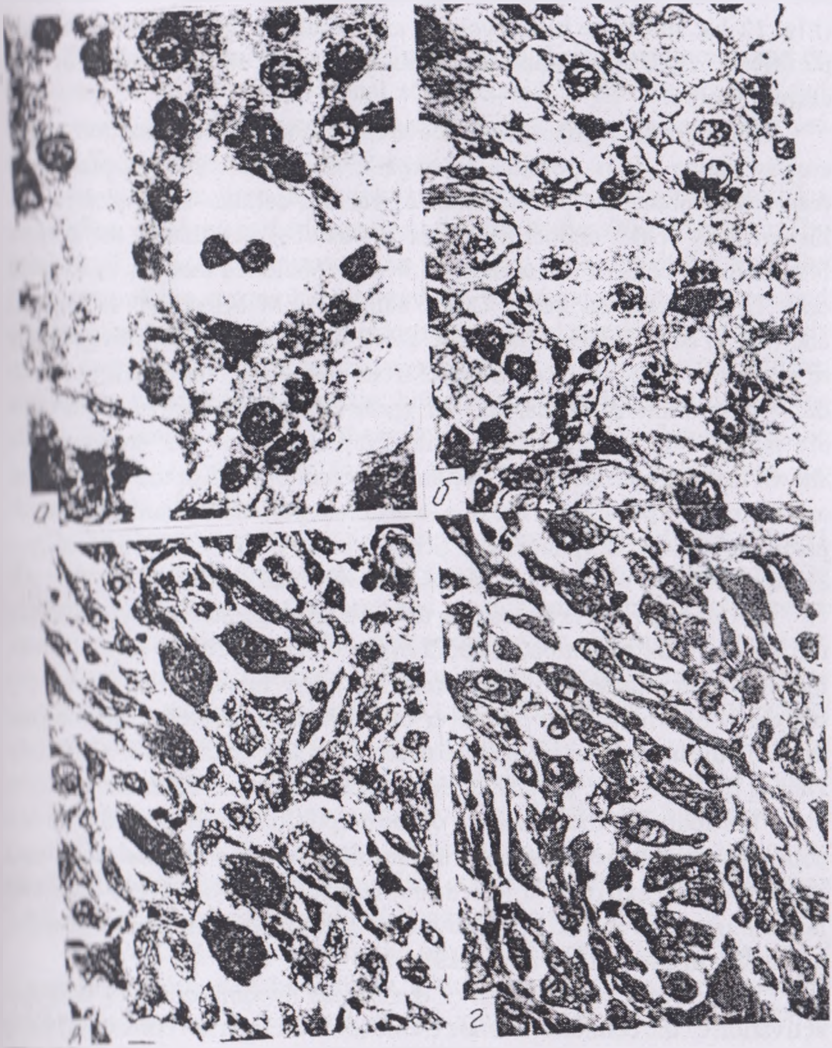


Fig. 12. Ovaries of cows. Formation (a), functioning (b, c) and involution (d) of the corpus luteum of the reproductive cycle. Uv (a, b, c, d) -280.

On the 6-7th day after ovulation, the corpus luteum is presented, besides single small cells in a state of proliferation, by a multitude of large one or two-nucleated luteal cells surrounded by a dense capillary network **(Fig. 12 b),** and large blood vessels are visible in the connective tissue partitions ... All this indicates the completion of the formation of the corpus luteum.

Based on the regularities we have established in the formation of the corpus luteum, it is possible to explain the contradictory opinion of researchers about the participation of various cellular structures in the histogenesis of this endocrine organ. It was observed that in the corpus luteum luteal cells of the same size, it was concluded that it was formed only from granulosa cells. Other authors (BM Khvatov, 1955.), in addition to large luteal cells, found small ones. This gave them grounds to assert that large cells are derived from granulosis, and small cells are derived from internal theca, i.e. both epithelial and connective tissue cells are involved in the formation of the corpus luteum. Our studies have shown that differences in the size and structure of cells in the developing and formed corpus luteum are due to different periods of manifestation of proliferative and morphogenetic processes observed in the internal and external flow, as well as the state of their vascularization.

In this regard, it is interesting to cite a message that indicates that on the 4th day after ovulation, the bulk of the corpus luteum is formed from the follicular epithelium, consisting of large luteal cells, along the periphery of which there is a layer of small cells derived from internal theca. In the latter, mitoses are also detected on the 7th day after ovulation. During these periods, the size of the corpus luteum increases sharply.

The timing of the formation of the corpus luteum coincides with our data, however, large luteal cells are formed from the internal flow, and small from the external, in which proliferative processes occur later and last a longer time and do not always end with the formation of large cells, especially in connective tissue trabeculus

The process of formation of the corpus luteum coincides with the activation of the connective tissue elements of the ovarian cortex and their differentiation into interstitial cells. In most of these cells, as well as in the connective tissue cells of the membranes of non-ovulated follicles, vacuolization of the cytoplasm is expressed with the manifestation of a light substance in the intercellular spaces. The latter circumstance indicates that during the period of functioning of the corpus luteum, the connective tissue elements of the ovaries also come into a state of hyperfunction.

The fact that the process of formation of the corpus luteum and its transition to an active functional state coincides with hyperplasia and hypersecretion of the connective tissue elements of the ovarian cortex and their differentiation into interstitial cells.

At the same time, the luteinizing reaction in the tertiary follicles intensifies, resulting in the formation of atretic bodies **(Fig. 11a, b, c).** The process of follicle luteinization, in principle, does not differ from the formation of the corpus luteum, and the pronounced morphogenic and secretory reactions both in the corpus luteum and atretic, and in the cells of the cortex and connective tissue membranes of non-ovulated follicles indicate not only morphogenetic, but also the functional unity of these structures, aimed at creating the proper progesterone background in the body, which is necessary for the formation of the zygote and the development of embryos.

The observed obliterative and cystic atresia of the follicles **(Fig. 11 d),** coinciding with the ovulation of Graaf vesicles and the formation of corpus luteum, suggests that large and medium-sized tertiary follicles are capable of functioning within one sexual cycle. In contrast, primary, secondary and small tertiary follicles, in which the connective tissue membrane is poorly developed and vascularization is not sufficiently expressed in it, do not undergo atresia, and therefore, regardless of the stage of the reproductive cycle, continue their development to the state of visible tertiary follicles. However, if we consider that the histogenesis of connective tissue cells is carried out only constantly from the side of the tunica albuginea in the direction of the ovarian medulla, then the duration of the existence of primordial follicles is also very limited.

The described changes in the ovaries of cows relate to the first 7 days after ovulation of the follicles. In the following terms, the assessment of further changes in the functioning corpus luteum and specific cellular structures of the ovaries deserves attention.

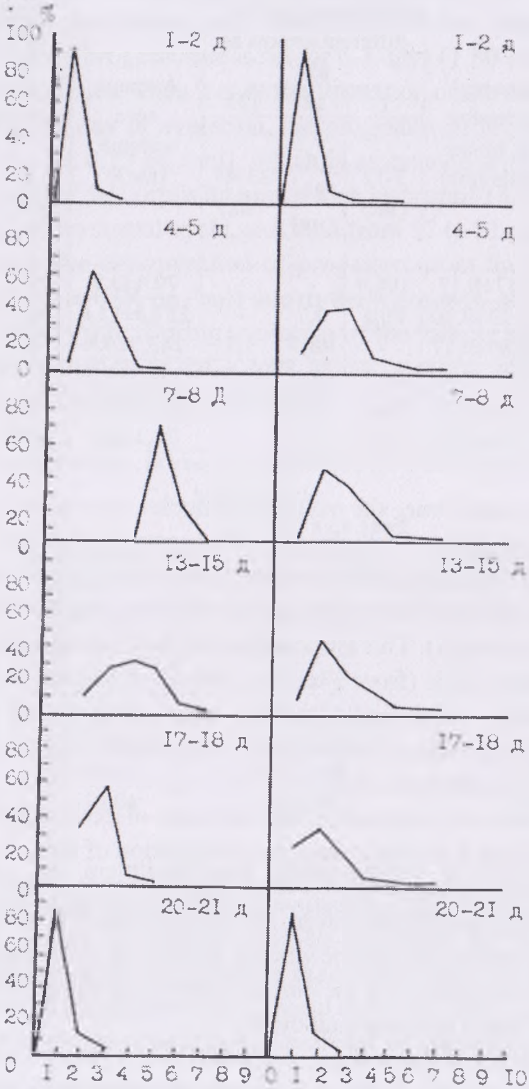
So, on the 8-9th day after ovulation, the most characteristic changes in the functioning cyclical corpus luteum were reduced to hypersecretion of luteal cells. This was manifested by an increase in the volume of nuclei, vacuolization of the cytoplasm, lysis of its marginal participants and the accumulation of light substance in the intercellular spaces. The interstitial cells of the cortex were also in a secretory-active state.

It should be noted that starting from the 10th day after ovulation, in some areas of the corpus luteum, single luteal cells with partial or complete oxyphilization of the cytoplasm appeared **(Fig. 12 c).** Subsequently, similar cells from oval passed into triangular, cubic, fusiform and flat. At the same time, the nuclei decreased in volume, underwent pyknosis, and the phenomenon of lysis developed in the cytoplasm (Fig. 12 d). Due to this, individual areas or whole lobes of the parenchyma of the corpus luteum acquired a fibrous structure.For a more complete understanding of functional shifts in the corpus luteum of the reproductive cycle.

From the analysis of the data presented **(Table 6, Graph 1),** it follows that changes in luteal structures depend on the development and functional state of the corpus luteum. Thus, the smallest diameter of luteal cells (5.47 ± 0.17 microns) and the volume of their nuclei (70.6 ± 3.9 microns) are observed in the first two days after ovulation, when young, poorly differentiated cells predominate. The variation curve of cell diameter and nucleus volume is located on the left side of the coordinate system. Starting from the 4th day after ovulation, the cell diameter increases to 11.23 ± 0.30 microns, and the volume of the nuclei increases to 227.3 ± 11.6 microns. These indicators reach a maximum value on days 7-8, when the cell diameter is 25.30 ± 0.27 microns and the volume of nuclei is 243.7 ± 9.8 microns. Moreover, most of the luteal cells (98.7%) have a diameter of 18 to 32 microns and contain 27.7% of nuclei with a volume of 310 to 612 microns. This leads to a sharp shift of the variation curve to the right. On the 12-14th day of the functioning of the corpus luteum, the morphometric indicators are somewhat stabilized with a slight decrease in the diameter of the cells (19.73 ± 0.50 μ) and the volume of the nuclei (233.3 ± 8.3 $\mu 3$) 17-18 days after ovulation, the variation curve shifts noticeably to the left. At the same time, the cell diameter decreases to 13.50 ± 0.35 microns, 94.0% of which are located in the first group.

VARIATION CURVES OF CELL DIAMETER AND VOLUME OF YELLOW BODY NUCLEI OF COW'S GENITAL CYCLE

Schedule 1



Cyto- and karyometric characteristics of the luteal cells of the corpus luteum of the reproductive cycle of cows (n = 3)

Table 6

The timing of the cows' ovectomy from the beginning of ovulation (days)	Average diameter of lutein cells (mc)	Number of cells of different groups as a%			Average core volume (mc3)	Number of cores of different groups as %		
		1	11	111		1	11	111
		3-17 (мк)	18-32 (мк)	33-47 (мк)		7-309 (мк^3)	310-612 (мк^3)	613-1016 (мк^3)
1-2	5,47±0,17	**100,0**	-	-	**70,6±3,9**	**99,0**	1,0	-
4-5	11,23±0,30	**99,3**	**0,7**	-	**227,3±11,6**	**81,3**	**17,7**	1,0
7-8	25,80±0,27	-	**98,7**	1,3	**243,7±9,8**	**76,0**	**23,7**	**0,3**
12-14	19,73±0,50	**36,7**	**62,0**	1,3	**233,3±8,3**	77,7	**21,3**	**1,0**
17-18	13,50±0,35	**94,0**	**6,0**	-	**173,0±9,1**	**93,0**	**6,5**	**0,5**
20-21	5,93±0,20	**99,0**	**1,0**	-	**72,3±3,3**	**100,0**	-	-

At the same time, the volume of nuclei decreases to 173.0 ± 9.1 microns, the number of which in the first group (from 7 to 309 microns) is 93.0%. On days 20-21 after ovulation, there is a significant decrease in the diameter of luteal cells (5.93 ± 0.20 microns) and the volume of their nuclei (72.3 microns). This is accompanied by an increase to 100% of the number of small cells (from 3 to 17 microns) with lysed and pyknotically altered nuclei, which indicates the most pronounced processes of involution of the corpus luteum of the reproductive cycle. The variation curve shifts sharply to the left.

The observed increase in the diameter of cells and the volume of their nuclei from 4 to 8 days and the stabilization of these indicators up to 14 days after ovulation indicates the highest functional state of the corpus luteum during this period. From 17-18 days, there is a decrease in the diameter of luteal cells and the volume of their nuclei, which indicates the processes of involution of the corpus luteum, which are most noticeable on the 20-21 days of the sexual cycle.

The results of the content of sex hormones in the blood of cows are summarized in Table 7, the comparison of which with histological and cytokaryometric studies allows you to create a fairly complete picture of the function of the ovaries during the sexual cycle.

From the analysis of **Table 7,** it follows that the most clear dynamics during the sexual cycle is seen in progesterone, which is associated with the development, functioning and involution of the corpus luteum. Moreover, the rise in progesterone is set for 6-7 days (1.80 ± 0.08 ng / ml) ovulation of the follicles, when it ends the formation of the corpus luteum, then on the 10-12th day of ovulation, the progesterone level reaches the highest limit (2.43 ± 0.19 pg / ml), which is associated with the greatest functional activity of the corpus luteum, which lasts until 14-15 days (2.17 ± 0.31 pg / ml) of the sexual cycle, and then from 17 to 21 days there is a sharp decrease in the concentration of progesterone in the blood (from 1.02 ± 0.14 to 0.25 ± 0.04 pg / ml) due to the regression of yellow body of the reproductive cycle. During ovulation of the follicle and in the first 2-3 days of the formation of the corpus luteum, progesterone rises from 0.39 ± 0.07 pg / ml to 0.52 ± 0.05 pg / ml.

Table 7

The level of progesterone, estrogen in the blood plasma of cows during the sexual cycle

days	N o to a t e l and		
	Progesterone ng/ml	Total estrogens	Estradiol-17 beta
		PG/ml	
овуляция	0,39±0,07	69,7±16,0	14,9±3,8 -
2-3	0,52±0,05	79,1±11,8	12,1±4,5
6-7	1,80±0,08	85,1±7,1	9,8±2,5
10-12	2,43±0,19	88,8±9,9	14,1±2,6
14-15	2,17±0,31	74,3±19,0	7,1±2,6
17-18	1,02±0,14	108, Lr28,9	7,9±1,6
19-21	0,25±0,04	85,0±9,5	16,8±5,2

Based on the histofunctional characteristics of the ovaries, the observed rise in progesterone during ovulation of the follicles, when the corpus luteum is not yet formed, can be explained by the hormone-producing function of secretory-active theca-luteal cells in preovulatory follicles, as well as hypersecretion of thecal cells obliterating follicles and interstitial tissue. Progesterone is first secreted by luteinized theca cells, and then by the corpus luteum, and an increase in progesterone concentration is an indicator of follicle luteinization.

Considering that during the sexual cycle there is a continuous growth of follicles and their luteinization, due to this, a certain level of progesterone is constantly maintained in the body, including during involution of the corpus luteum, when its hormone-producing function stops. This feature of steroidogenesis will be shown when applying material with functional disorders of the ovaries, when they lack the corpus luteum.

As for the dynamics of estrogens during the sexual cycle, as can be seen from Table 7, the greatest rise in total estrogens (108.1 ± 28.9 pg / ml) is observed at the beginning of the involution of the corpus luteum, which coincides with the greatest activation of the growth and maturation of follicles , the hormone-producing function of which is aimed at creating certain physiological and morphological changes in the genitals and the body in order to ensure the manifestation of the female's specific reaction to the male, insemination and fertilization. After ovulation and atresia of non-ovulated follicles, the level of total estrogen decreases to 69.7 ± 16.0 pg / ml.

During the period of the highest functional activity of the corpus luteum, the concentration of total estrogens increases to 88.8 ± 9.9 pg / ml.

At the same time, in most growing large follicles, granulosis and the basement membrane are reduced, and the contents of the follicles are resorbed, which creates conditions for an increased amount of estrogen to enter the body. This can explain the increase in the level of estrogen both with the onset of the stage of excitation of the sexual cycle, and at the highest functional state of the corpus luteum, which is due to changes in the hypothalamic-pituitary regulation of ovarian function. A similar pattern is observed during the sexual cycle and in the dynamics of estradiol-17 beta. The highest concentration of this hormone in the blood was established in the pre-ovulatory state of the follicles and during ovulation (16.8 ± 5.2 and 14.9 ± 3.8 pg / ml), as well as at the highest functional state of the corpus luteum (14 , 1 ± 2.6 pg / ml). In the rest of the sexual cycle, when the luteolytic and reactionary-dystrophic processes in the growing follicles decrease, the level of total estrogens and estradiol-

17 beta in the blood falls. In these cases, it is more correct to talk not about the wave-like growth of follicles during the sexual cycle, as many authors believe (MI Prokofiev, 1983), but about changes in the neuro-endocrine regulation of ovarian function and the response of their specific structures to the effects of gonadotropic factors that regulate the level of sex hormones entering the body.

Gametogenesis, as well as the growth of follicles in the ovaries, as we have established, occurs at any age and state of sexual function, and their ovulation or the development of obliterative and cystic processes in them depends, as indicated above, on the initial state of the cellular structures of the gonads, specifically reacting to gonadotropin, which determines the level of production of ovarian hormones and their resorption into the body. This pattern will be confirmed when presenting the material obtained during pregnancy, functional disorders of the ovaries and when exposed to gonadotropic drugs and PF-2 alpha on the ovaries of cows.

2.2. Morphological changes in the ovaries with violations of their function and the dynamics of ovarian hormones in the blood of cows.

Out of more than 20 thousand obstetric and gynecological cows examinedin farms of the Central Black Earth Zone Russian Federation at 1530% established infertility from 2 months or more due to ovarian hypofunction (25-40%), follicular and luteal cysts (15-25%), persistent corpus luteum (5-7%), anovulatory reproductive cycles (8-11%) and other functional disorders of the genital organs (15-25%) (G.A. Cheremisinov, 1975). In this regard, the disclosure of the patterns of morphofunctional disorders in the ovaries and the dynamics of ovarian hormones in the blood, as well as metabolic processes in the body in order to elucidate the etiology and pathogenesis of gonadal disorders and develop methods for their diagnosis, treatment and prevention is a necessary condition for the biotechnology of intensive reproduction of cattle.

At the same time, the literature data concerning the simultaneous study of histofunctional changes, in particular, with hypofunction of the ovaries and the dynamics of sex hormones in the blood of cows, are very limited and do not reveal the essence of gameto-follicle and hormonogenesis, as well as the reasons for the absence of maturation and ovulation of follicles.

Among the functional disorders of the ovaries, as mentioned above, their hypofunction is the most common. Rectally and macroscopically, such ovaries are somewhat reduced in size, mainly due to the absence of yellow bodies in them, single large and medium-sized and many small follicles are determined on their surface, yellow bodies are absent or sometimes remnants of white and atretic bodies are visible. Clinically, such animals, as a rule, do not have sexual cycles or they appear in the form of anestral, alibid, areactive and anovulatory.

Biochemical blood tests of cows with ovarian hypofunction in comparison with animals at the stage of balancing the sexual cycle, carried out by an employee of our laboratory S.V. Bykova, showed that cows with ovarian hypofunction have significantly lower glucose levels (41.33 ± 1.03 mg%, P <0.001), inorganic phosphorus (5.04 ± 0.15 mg%, P <0.02), beta-carotene (371.77 ± 20.89, P <0.001). The concentration of total calcium was at the lower limit of the norm (9.51 ± 0.13 mg%, P <0.01). There was no significant difference in total protein levels. In turn, cows with ovarian hypofunction had the highest concentration of vitamin A (73.03 ± 5.03 mg%, P <0.02), vitamin E (1.40 ± 0.07, P <0.001) 9 vitamin C (0.91 ± 0.07) and total cholesterol (172.70 ± 9.92, P <0.01).

With this level of metabolic processes, animals remain sterile for 5-6 months or more. Moreover, the study of the dynamics of these biochemical indicators during this period of infertility did not show significant changes, although there were some shifts towards the improvement or deterioration of metabolic parameters with a stable low level of glucose, inorganic phosphorus, beta-carotene and total calcium. If we consider the occurrence of ovarian hypofunction from the point of view of metabolic disorders in the body, then the regulation of these missing indicators should be given priority attention. At the same time, an excess of certain vitamins (A, C,-E)and cholesterol, which are directly related to the regulation of morphological and hormonal processes in sexual function, indicates their insufficient implementation in case of ovarian hypofunction in cows. In these cases, it is quite reasonable, of course, provided that the missing biologically active substances are replenished, the regulation of sexual function with hormonal agents that activate the generative and hormonal function of the ovaries and the implementation of excess accumulated substances during maturation, ovulation of follicles, the functioning of the corpus luteum and their hormonogenesis, about which in detail will be described below.

Concerning the issue of the histofunctional and hormonal characteristics of the ovaries during their hypofunction, it should be noted that with hypofunction of the ovaries, as well as at various stages of the reproductive cycle and during pregnancy, the differentiation of germ cells from the rudimentary epithelium and the formation of primordial follicles does not stop **(Fig. 15 a, b, c).** At the same time, changes are also observed in the nuclei of germ cells, characteristic of the prophase of meiosis **(Fig. 15 b)**.

However, in connection with the hypoplasia of the connective tissue elements of the ovarian cortex, the possibility of the formation of morphogenic, well-vascularized tecal tissue around the follicles is excluded. Therefore, most follicles undergo dystrophy at the stages of their primary and secondary development **(Fig. 15 c, d).** This is accompanied by wrinkling of the cytoplasm and a change in the configuration of the nuclei of germ cells against the background of hypoplasia of the surrounding tissue **(Fig. 15 c).** As a result of this phenomenon, from 10 tofifteen ool, surrounded by dystrophic altered granulosis and poorly vascularized connective tissue in a state of hypoplasia **(Fig. 15 d).** At the same time, further growth of secondary and tertiary medium and large follicles is observed. At the same time, in the follicles, there is a highly differentiated, radially located granulosis in a state of hypersecretion and an internal theca with hyperplastic and hypertrophic altered thecalutein cells in a state of hypersecretion. However, such follicles do not reach ovulation maturity and in some cases undergo obliterative atresia by proliferation of thecal tissue against the background of egg cell dystrophy and granulosis, in other cases - cystic atresia with obliteration of blood vessels and the development of fibrotic changes in the internal flow. At the same time, granulosis and egg cells undergo dystrophy.

From the analysis of table 8, it follows that in the blood of cows with ovarian hypofunction, accompanied by impaired growth and lack of ovulation of follicles, there is a low level of progesterone. As can be seen from table 8, the concentration of progesterone is on average 0.24 ± 0.02

ng / ml, which is significantly ($P < 0.05$) lower than the content of this hormone in the blood of cows at various stages of the reproductive cycle, which are given in the first section of this chapters,

In another experiment, when studying the dynamics of progesterone in the blood of cows with ovarian hypofunction for 21 days, it was found that in all animals the level of this hormone is not constantly recorded and for 9-17 days of the experiment was beyond the sensitivity of the method. Progesterone levels observed on individual study days ranged from 0.03 to 0.68 ng / ml.

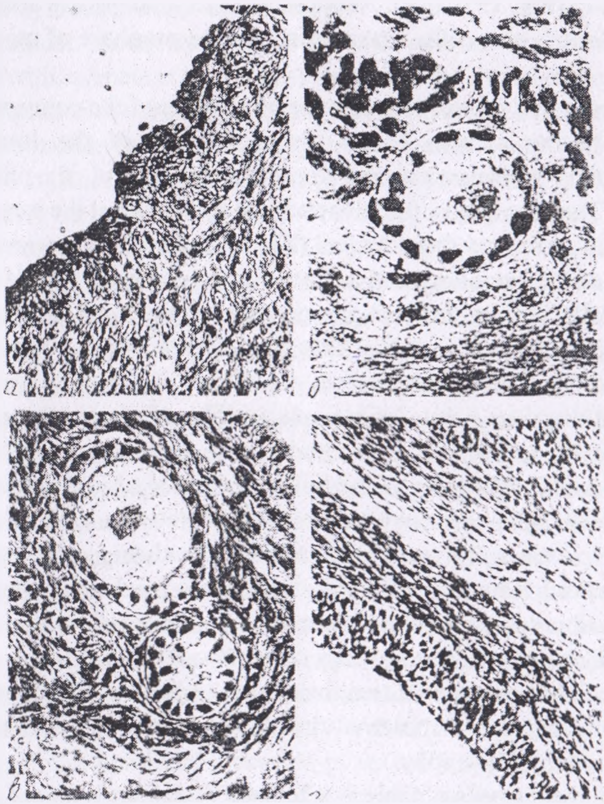
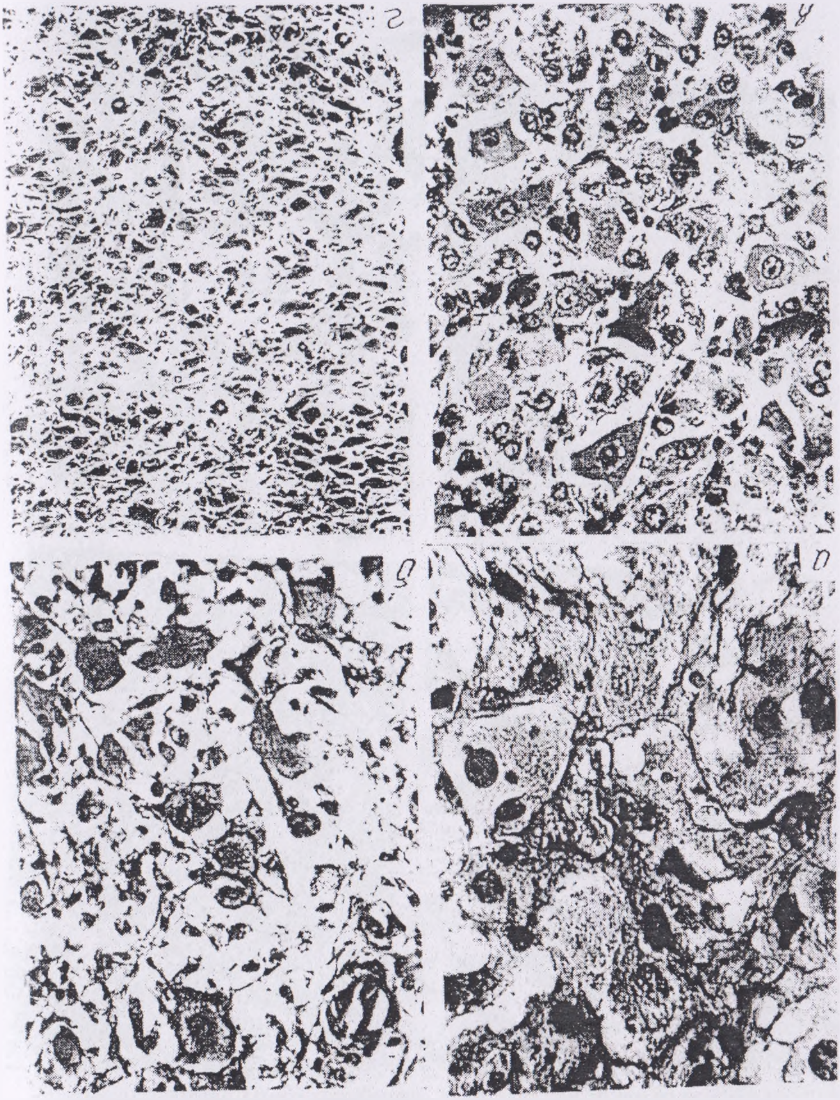
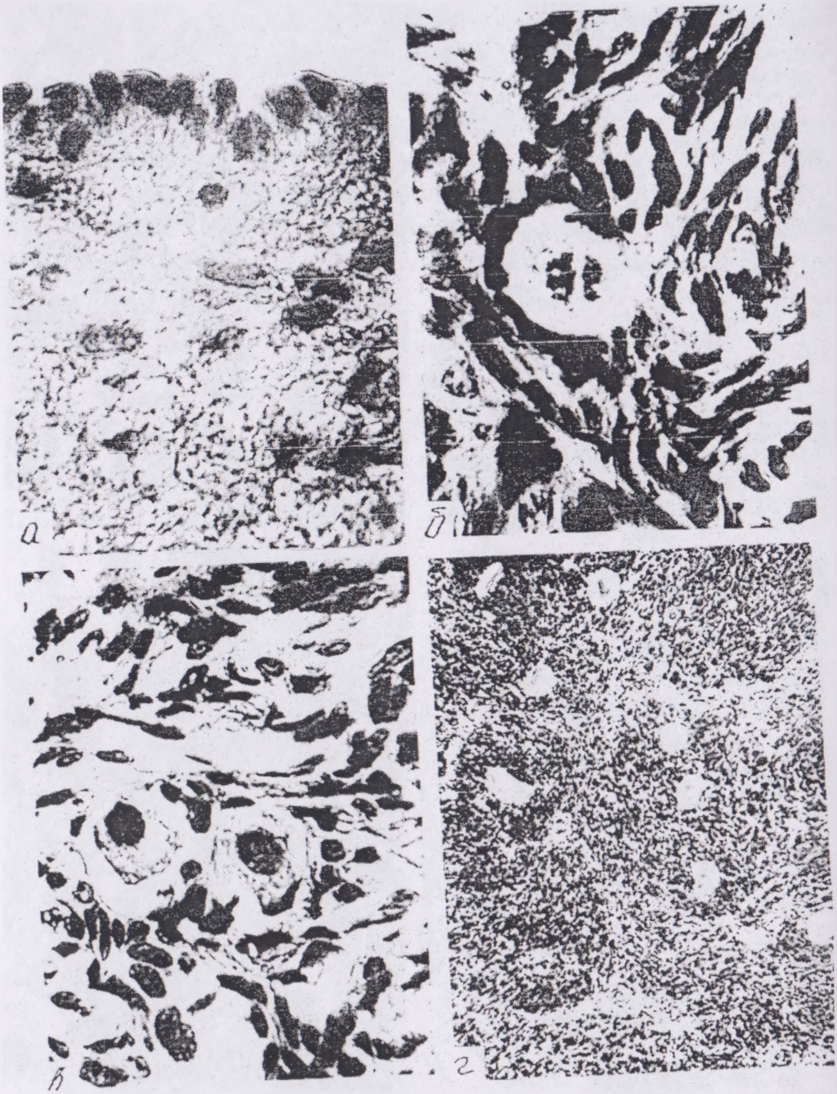


Fig. 13... Gamay*togenesis in the rudimentary epithelium* (a), formingprimordial (b), secondary (c) and tertiary (d) follicles in the ovaries of pregnant cows. sw. but- 630; b,c-280 g-140.



Rice. 14. Histostructure of the corpus luteum in 20-day, three-six and nine-month pregnancy of cows Uv a-630b,in-280; g-140.



Rice.15. Gametogenesis from the rudimentary epithelium (a) with the formation of primordial follicles (b, c) and their dystrophy (d) with hypofunction of cow ovaries. Uv a, b, c-280; g-140

Table 8

The content of ovarian hormones in the blood with hypofunction of the ovaries of cows

Animal number	Progesterone (ng / ml)	Total estrogens (pg / ml)	Estrodiol-17 beta (pg / ml)
158	0.23	24.7	· 16.2
197	0.08	39.3	5.8
205	0.07	12.9	-
212	0.36	87.9	6.2
93	0.13	20.7	4.5
201	0.60	26.9	14.1
202	0.46	38.6	6.8
228	0.20	22.1	11.2
7	0.37	36.6	do not investigate.
241	0.29	47.1	-
240	0.04	55.8	6.9
27	0.12	19.6	13.0
232	0.32	64.2	3.9
31	0.24	31.7	-
35	0.15	23.0	4.3
231	do not investigate.	do not investigate.	19.8
M ± m	0.24 ± 0.02	36.7 ± 2.57	7.5 ± 0.52

Comparing the histofunctional changes in the ovaries with the dynamics of progesterone, it should be noted that despite the absence of corpus luteum in the gonads, progesterone in most animals **(Table 8)** is determined in the blood of cows, albeit at the lowest level, which we associate with the presence of hormone-synthesizing cellular cells in the ovaries. cultures. These structures, based on the morphogenetic unity of the interstitial cells of the cortical substance, thecal cells of the follicles, as well as the atretic and corpus luteum, should also include the functioning theca-luteal cells in separate growing follicles and formed by the proliferation of the internal theca of the atretic bodies. Different levels of follicle and atretic body formation in animals determine different concentrations of progesterone in the blood of cows with ovarian hypofunction (0.08-0.60 ng / ml).

The results of studying changes in total estrogens in the peripheral blood of cows with ovarian hypofunction indicate that their level is significantly lower in comparison with the content in healthy animals during the sexual cycle (Table 7). The determined absolute values of hormones (36.7 ± 2.5 pg / ml) were significantly (P <6 0.01-0.05) lower than the total estrogens in healthy cows by 23.6-7, 10-12, 17-18 and 19-21 days after ovulation, i.e. during the formation, functioning and involution of the corpus luteum of the reproductive cycle. At the same time, the range of total estrogens in cows with ovarian hypofunction is very wide and is in the range of 12.9-87.9 pg / ml. This indicates that the level of estrogen in some sick animals reaches the levels of healthy cows, which is explained by the presence of single large animals in the ovaries of such animals,

When studying the dynamics of total estrogens in the blood of cows with ovarian hypofunction (Table 9) during 21 days of the experiment, no stability in the level of hormones was established, but a periodicity in their rise and fall was observed. Approximately the same pattern was observed in the dynamics of estradiol-17 beta **(Table 10).**

At the same time, in 80.0% of cows, the maximum content of estradiode-17 beta in the blood coincided with one of the periods of increase in total estrogens. On some days of the experiment (39.4%), the level of estradiol was beyond the sensitivity of the method. Consequently, with hypofunction of the ovaries in cows gametogenesis, the formation of primordial, the growth of secondary and tertiary follicles does not stop, however, with hypoplasia of the trophic and plastic function of the connective tissue (mesenchymal) structures of the gonads, they do not reach ovulation maturity, but undergo cystic and obliterative atresia. At the same time, according to the growth and atresia of follicles, the dynamics of the content of progesterone and estrogen in the blood of cows also changes in the direction of decrease. Therefore, ovarian hypofunction should be understood as the insufficiency of the trophic and plastic function of the connective tissue (mesenchymal) structures of the gonads, in connection with which folliculogenesis is disturbed, cystic and obliterative atresia of the follicles develops, the level of ovarian hormones decreases,

Table 9

THE LEVEL OF TOTAL ESTROGENS IN THE PERIPHERAL BLOOD PLASMA OF COWS WITH OVARIAN HYPOFUNCTION IN THE DYNAMICS OF THE EXPERIMENT (PG / ML)

Animal number	Days of experience						
	one	3	7	12	fifteen	eighteen	21
255	12.9	23.8	14.2	65.7	12.6	23.6	57.4
259	115.4	9,7	47.9	20.1	not later	... 42.9	35.8
262	24.6	not researched	21.8	4.4	7.5	62.5	40.6
263	21.5	20.4	52.7	21.1	14.4	96.3	49.7
264	16.1	3.7	37.4	51.6	9.9	not researched	not researched

Table 10

The content of estradiol-17 beta in the peripheral blood plasma of cows with ovarian hypofunction (pg / ml)

Animal number	Days of experience						
	one	3	7	12	fifteen	eighteen	21
255	0.5	-	1.5	7.5	-	-	19.2
259	five, 3	4.7	21.9		-	0.8	6.6
262	five,0	not explored	4.6	-	-	14.2	17.7
263	3.4	6,7	1.6	-	-	9.8	18.5
264	-	4	-	-	-	9.2	not explored

I considered the issue of ovarian cysts, one cannot but dwell on their functional and structural differences. Based on the morphofunctional specificity of the ovarian cell structures, cysts, as functioning formations, can be of two types: luteal, formed from proliferating connective tissue cells of the follicle membrane, and follicular, with secretory active granulosis.

Luteal cysts are rectally defined as spherical formations with a dense wall and tight fluctuation. In the presence of such cysts in animals, sexual cycles stop. Macroscopically, luteal cysts are represented by a powerful wall, the inner layer of which resembles the parenchyma of a functioning corpus luteum in color and consistency.

We (G.A. Cheremisinov, V.N. Karymov, 1986), through a clinical (rectal) study of 17246 cows in 18 farms in the Voronezh and two farms in the Tambov region, found from 5 to 15% of animals with luteal ovarian cysts with a duration of infertility from 6 months and more than a year, which on average is 226 days of infertility and causes economic damage only from the lack of offspring and milk in the amount of 758.5 thousand rubles (period 1986-1990).

Concerning the question of the causes of ovarian cysts, they are mainly associated with metabolic disorders in the body due to biologically unjustified, mainly unilateral feeding, hypodynamia and widespread postpartum pathology (retention of the afterbirth, subinvolution of the uterus, endometritis), which disrupts the luteolytic function of the uterus. In general, these reasons disrupt the neuroendocrine regulation of the generative function of the gonads, and in particular, lead to the development of cysts in the ovaries.

So, in the state farm "2nd Five-Year Plan" of the Liskinsky District of the Voronezh Region, as shown by the results of the analysis of the diet during the winter period, animals receive 4-5 kg of concentrated feed. Chemical analysis of the diet, carried out in the laboratory of zoohygiene of feed and premixes of the All-Union Research Institute of Non-communicable Animal Diseases (L.A. Matyushevsky), found that with such a diet the calcium-phosphorus ratio of 2.75: 1 is disturbed, there is a 2.5-fold lack of carotene, an excess protein on*41%* ***(Table 11).***

From the results of a biochemical blood test carried out in the laboratory of metabolic pathology in cattle of the All-Union Research Institute of Non-communicable Animal Diseases (P.E. Petrov), it was found that acidosis was observed in the body of cows, the total number of ketone bodies reaches 7.52 (at a rate of 6 , 0), and some animals contain up to 46.8. There was a low level of glucose (23.68 mg% with a norm of 45-55 mg%).

In addition, during the last 15 years, active exercise has been absent both during stall and spring-summer keeping of animals.

When conducting clinical studies of cows on this farm during 1981-1983. luteal ovarian cysts were diagnosed in 8-10% of the total number of animals. This pathology occurred both in the autumn-winter and spring-summer periods.

Table 11

The ration of feeding in cows during the winter stall period in the state farm "2nd five-year plan" of the Liskinsky district of the Voronezh region

Stern	Kg	because ed	Digestion. protein	Ca	R	Carotene
Feed flour (mixture)	four	5.36	427.6	7.52	7.04	-
Herbal flour	one	0.56	102.1	9.86	0.10	74.88
Corn silage	25	5.0	345.0	47.50	13.00	31.00
Hay (alfalfa ± bonfire)	2	1.28	87.0	17.70	4.65	2.88
Barley straw	2	0.82	25.4	7.28	1.32	-
Premixes	0.1	-	-	7.0	9.6	
Is given		13.02	987.1	35.9	97.9	108.8
Required		7.0	700.0	30.0	50.0	260.0
+ or -		+6.02	+287.1	+5.9	+47.9	-151.2

Clinically, morphologically and radioimmunologically, luteal (75%) and less often (25%) follicular cysts are diagnosed in the ovaries of cows. In the presence of luteal cysts, animals are in a state of anaphradisia for a long time. This condition and the formation of luteal cysts is preceded by the manifestation after childbirth 2-4, mainly anovulatory sexual cycles.

In the state farm "2nd Five-Year Plan" of the Liskinsky District of the Voronezh Region, based on the data of a triple clinical examination with an interval of 10 days, anamnesis and the results of accounting for artificial insemination of animals in 19 cows in the ovaries, cystic degeneration of follicles was established, of which 16 had luteal cysts , in 3 - follicular. The validity of clinical methods for diagnosing luteal cysts was confirmed by radioimmunoassay of peripheral blood plasma from these animals (Table 12).

From the analysis of Table 12 it follows that of the 16 cows in which luteal cysts were clinically diagnosed, 12 animals had a high level of progesterone (2020-4050 pg / ml) and a low content of estradiol-17 beta (5.50-24.50 pg / ml), which indicates a high functional state of luteal cysts. Such cysts had a diameter of 1 to 6 cm.In comparison with the above 12 animals, in four cows the level of progesterone in blood plasma was much lower (1500-1700 pg / ml) with a simultaneous significant increase in estradiol-17 beta (25.50-35, 00 pg / ml). Such cysts, as a rule, had a smaller diameter (2.5-4.0 cm) and were in a state of formation by proliferation and differentiation of thecal cells into lutein cells or at the initial stage of involution.

Table 12

The content of steroid hormones in the blood plasma of cows with luteal ovarian cysts

Animal number	*Content*(pg / ml)	
	progesterone (pg / ml)	estradiol-17 beta
14	3300	13.00
1	2020	24.50
2	2680	17.50
3	1700	35,00
22	1580	26.50
8	2600	11.50
6	2200	22.25
1152	1650	30,00
3386	3400	5.50
0412	2600	7.50
0339	2000	14.50
9118	2650	12.50
1108	4050	7.50
2186	1600	30,00
2086	2750	9.50
2406	3020	14.50

The observed rather high level of estradiol-17 beta in most animals indicates a constant growth of follicles in the ovaries with luteal cysts. The content of cysts has a yellowish gelatinous mass. The size of the cysts is highly variable and ranges from 1 to 6 cm in diameter **(Fig. 16 a, b).**

On histological sections, the walls of functioning luteal cysts consist of a thick layer (0.2-0.8 cm) of hyperplastic and hypertrophic altered cells of the internal theca **(Fig. 16 c).** The cellular structures in such cysts are similar to the luteal cells of a functioning corpus luteum **(Fig. 16 c, d),** the granulosis is reduced. And only sometimes it is necessary to observe the preserved follicular cells in a state of dystrophy.

In ovaries with functioning luteal cysts, gametogenesis and follicular growth do not stop, however, as the latter increase, granulosis loses radial differentiation and undergoes desquamation. In this case, the cytoplasm of the cells of the connective tissue membrane is lysed with the formation of a fibrous structure, which excludes the possibility of follicle maturation and the manifestation of the stage of excitation of the sexual cycle. Sometimes in growing follicles, thecal tissue undergoes hyperplasia and hypertrophy with the formation of large luteal cells. This leads to the formation of multiple luteal cysts in the ovaries.

It should be noted that with luteal cysts, the connective tissue membrane of the ovarian cortex is in a state of proliferation and secretion. This is evidenced by the presence of radially located proliferating areas or cords emanating from the surface layer of the ovarian cortex. This proliferating mass contains cells with large vacuolated cytoplasm in a state of marginal lysis.

A light substance in the form of vacuoles and lacunae is constantly found between the interstitial cells.

Along with functioning luteal cysts, there are cystic formations, the luteal tissue of which undergoes involution with the formation of a powerful fibrous layer **(Fig. 17 a)**. The process of involution of luteal cysts is similar to the changes established during the involution of the corpus luteum of the reproductive cycle.

From the comparison of histological studies with morphometric data **(Table 13 and Graph 2),** it follows that during the formation of luteal cysts, as well as the development of the corpus luteum of the reproductive cycle **(Table 6, Graph 1),** the smallest diameter of luteal cells is noted (7.60 ± 0, 15 μ) and the volume of nuclei (135.5 ± 8.3 μ3), which are located in the first group. The variation curve is located on the left side of the coordinate system **(Graph 2).** On days 4-5 of the functioning of luteal cysts, the cell diameter increases to 16.70 ± 0.30 microns, and the volume of their nuclei increases to 418.0 ± 9.8 microns. In this case, 37.0% of nuclei with a volume of 310 to 612 μ3 are moved to the second group. The variation curve shifts sharply to the right. This is the largest volume of nuclei in comparison with the nuclei of the luteal cells of the corpus luteum of the sexual cycle and pregnancy **(Table 1).6, eight)**. On days 7-8 of follicle luteinization, in comparison with days 4-5, a decrease in the diameter of luteal cells (13.90 ± 0.25 μ) and the volume of nuclei (195.5 ± 9.7 μ3) was established. Approximately the same morphometric data were obtained on days 13-14 of the functioning of luteal cysts, whereas on days 17-18 after follicle luteinization, the diameter of luteal cells and the volume of nuclei approached the indicators established in the first 2 days of cyst formation. However, if in the early days the small diameter of luteal cells and the volume of their nuclei were associated with the proliferation of the internal theca and the beginning of its differentiation into luteal cells, then on the 17-18th day of the experiment the decrease in morphometric parameters was due to the lysis of the cytoplasm and pycnosis of the nuclei, which characterized the process of involution. luteal cysts.

Table 13

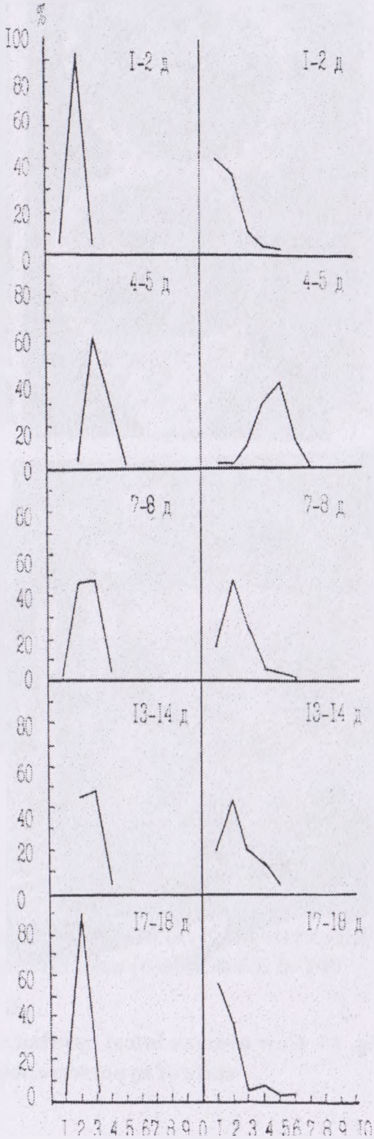
Cyto- and karyometric changes in cells: luteal cysts of cows

Timing of ova-rioectomy of cows from the beginning of luteinization of follicles (days)	Number of women	Average diameter of luteal cells (mk)	The number of cells of various groups in %			Average core volume	The number of nuclei of various groups in %		
			one	eleven	111		one	eleven	111
1-2	3	7.60 ± 0.15	100.0	-	-	135.5 ± 8.3	95.5	4.5	
4-5	3	16.70 ± 0.30	65.0	35.0	-	418.0 ± 9.8	12.0	87.0	1.0
7-8	3	13.90 ± 0.25	93.0	7.0	-	195.5 ± 9.7	88.0	12.0	-
13-14	3	12.20 ± 0.30	95.0	5.0	-	195.0 ± 10.4	83.0	17.0	-
17-18	3	9.90 ± 0.20	100.0	-	-	120.0 ± 9.3	93.0	7.0	-

Schedule2

VARIATION CURVES OF CELL DIAMETER AND VOLUME OF LUTHEIN CYSTAL CYSTES IN COVES

No. cl	cell class boundaries
one	3-7
2	8-12
3	13 - 17
four	18 - 22
five	23 - 27
b	28 - 32
7	33 - 37
eight	38 - 42
nine	43 - 47
No. cl	kernel class boundaries
one	7 - 107
2	108 - 208
3	209 - 309
four	310 - 410
five	411 - 511
6	512 - 612
7	613 - 713
eight	714 - 814
nine	815 - 915
10	916 - 1016



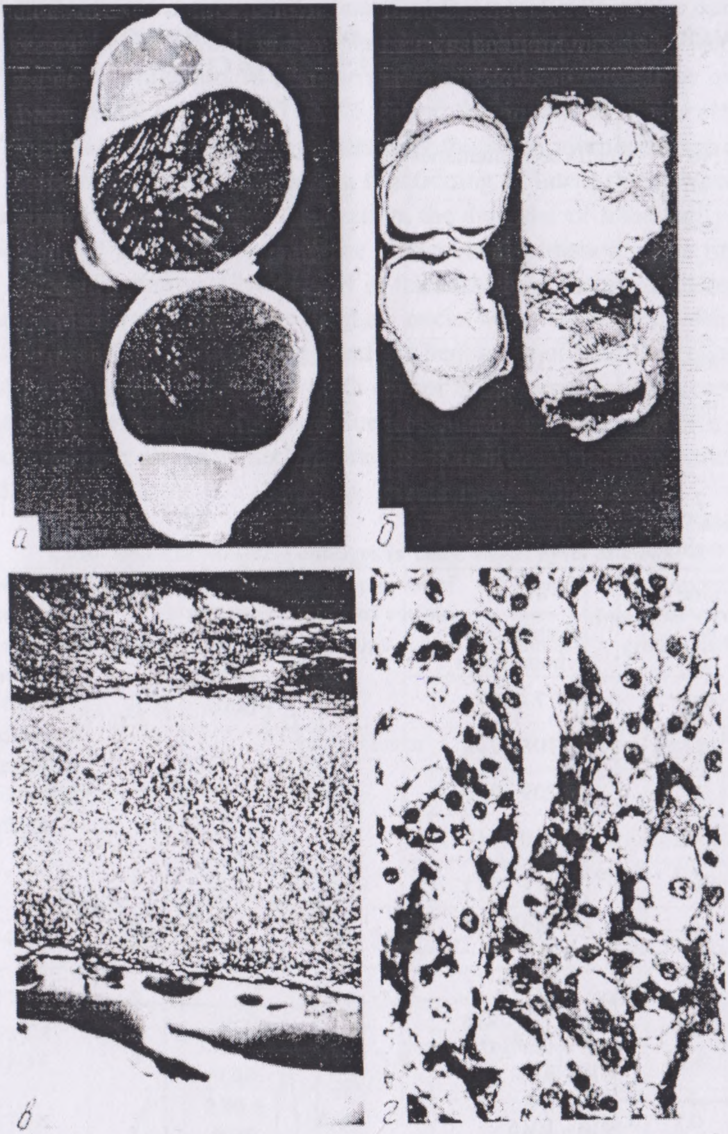
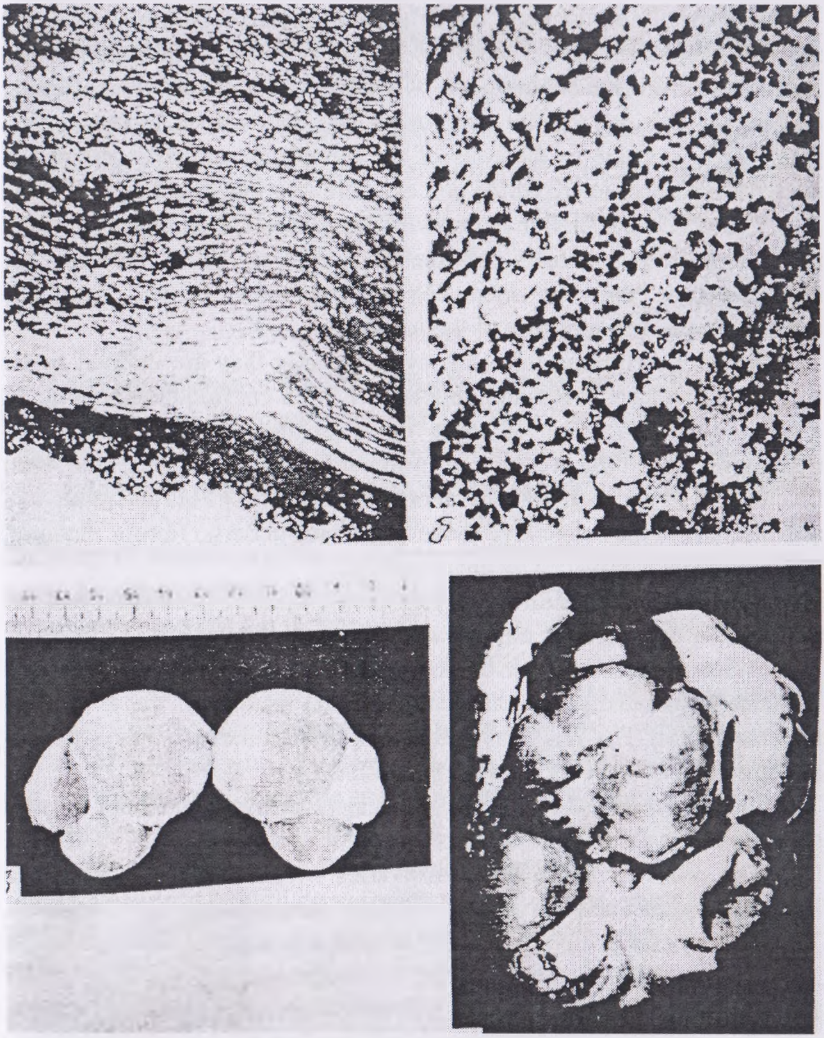


Fig. 16. Cow ovarian luteal cyst(but,b) with hypertrophied luteal cells in a state of hypersecretion (c, d). Uv. v-63, g-280



Rice.17. Fibrous wall changes liuthosedifferentcysts (a) Follicular cysts(b c d) with granulosis c state of hypersecretion (b). Uv. a-63; b- 140

However, if in the early days the small diameter of luteal cells and the volume of their nuclei were associated with the proliferation of the internal theca and the beginning of its differentiation into luteal cells, then on the 17-18th day of the experiment the decrease in morphometric parameters was due to the lysis of the cytoplasm and pycnosis of the nuclei, which characterized the process of involution. luteal cysts.

The observed similar patterns of morphometric changes in luteal cysts and corpus luteum of the reproductive cycle indicate the morphogenetic unity of their cellular structures, formed from the connective tissue membrane of the follicles.

As for functioning follicular cysts, rectally they are defined in the form of thin-walled fluctuating bubbles, 1.5-5.5 cm in diameter **(Fig. 17 c, d).** Clinically, most of these cows exhibit the phenomenon of nymphomania. In the presence of cysts ranging in size from 2.5 to 4 cm in diameter, in which granulosis enters a state of hypoplasia and reduction, and the cells of the connective tissue membrane undergo fibrotic changes, nymphomania is replaced by anaphrodisia.

Macroscopically follicular cysts have a thinned membrane and are represented by single or numerous cystic formations **(Fig. 17 c, d).** In nymphomania, sections from the walls of follicular cysts are characterized by undifferentiated, hyperplastically altered granulosis in a state of hypersecretion. The inner layer of theca is vascularized, has a fibrous structure and single oval cells **(Fig. 17 6).**

The outer shell of the cyst wall is in a state of hypoplasia and forms a single whole with the surrounding ovarian tissue.

The characteristic features in ovaries with follicular cysts include low morphogenic activity of the connective tissue elements of the cortex. That is why the growing follicles do not ovulate, but undergo cystic atresia. This once again confirms the important trophic and plastic function of the connective tissue cells of the gonads in the growth, ovulation of follicles and the formation of the corpus luteum.

Hormonal changes in the blood plasma of cows with ovarian follicular cysts are presented in **Table 14.**

Table 14

The content of steroid hormones in the blood plasma of cows with follicular cysts

Animal number	Progesterone (pg / ml)	Estradiol-17 beta pg / ml)
3205	370	112.50
0207	740	79,00
3715	300	66.50

From the analysis of the table it can be seen that with follicular cysts, there is a low level of progesterone (0.30-0.74 pg / ml) and high levels of estradiol-17 beta (61.50-116.50 pg / ml). Moreover, in animal No. 3205, in which the level of estradiol-17 beta was the highest (112.50 pg / ml) in comparison with cows with similar functional disorders of the ovaries and in the stage of excitation of the sexual cycle, nymphomania was observed.

A high level of estradiol-17 beta in follicular cysts is created both due to the hypersecretion of granulosis in them and the secretory-active state of these cellular structures in constantly growing follicles. The presence of a small amount of progesterone in the blood plasma can be associated with the formation of single lutein cells in constantly growing follicles. In contrast, with luteal cysts, the parenchymal tissue of which is in an active secretory state, the observed obliterative atresia of growing follicles creates a high background of progesterone and a low concentration of estradiol-17 beta in the blood plasma.

As a result, it should be noted that ovarian cysts create a different hormonal background in the body, and therefore it seems possible to clearly differentiate them and, depending on the diagnosis, carry out specific treatment aimed at normalizing the generative function of the ovaries and restoring the reproductive function of cows.

Macroscopically and histologically, it was established that the functionally active delayed corpus luteum does not differ from the functioning corpus luteum of the reproductive cycle. They are well vascularized, have large luteal cells with basophilic cytoplasm and rounded nuclei. At the same time, diagnosed rectally persistent corpus luteum during histological examination sometimes turns out to be in a state of involution.

At the same time, the number of luteal cells decreases, their configuration is disturbed, the cytoplasm is lysed, the volume of nuclei decreases, blood vessels are obliterated and the amount of fibrous structure increases. They have the size of a normal corpus luteum, but a denser texture, light yellow color, and poor vascularization.

As for the histogenesis of primary and secondary follicles, this process continues regardless of the functional state of the corpus luteum, and they, together with the proliferating connective tissue, move from the superficial to the deeper layers of the ovarian cortex, transforming into tertiary follicles. In the latter, in the presence of a functioning persistent corpus luteum, granulosis loses radial differentiation and is reduced, and the previously observed initial signs of activation of proliferating processes in the connective tissue membrane end in its fibrous degeneration. This excludes the possibility of follicle maturation, and in this regard, the manifestation of stages of arousal of the reproductive cycle. In this case, large and small interstitial cells with cytoplasm in a state of hypersecretion are determined in the cortical substance of the ovary.

With involution of the lingering corpus luteum in most of the growing follicles, granulosis and the cells of the inner layer of theca reach a high degree of differentiation, specific for follicles, close to ovulation.

With multiple sexual cycles, as many yellow and white bodies are found in the ovaries as there were ovulations. Macroscopically, in addition to the corpus luteum, follicles in a state of development and atresia are determined in the ovaries, which depends, as mentioned earlier, on the stages of the reproductive cycle. At the same time, it was found that in most animals, multiple sexual cycles lead to a decrease in plastic processes in the connective tissue elements of the ovarian cortex and follicle membranes. In this case, the cortical substance is characterized by the presence of small flat cores located in the fibrous structure. From the side of the superficial zone of the cortex, small cell proliferates emanate, which, although they differentiate around the follicles, do not ensure the formation of a well vascularized morphogenically active connective tissue membrane. Therefore, growing follicles mostly undergo cystic atresia.

That is why some animals, after the manifestation of 3-5 sexual cycles, comein state of anaphrodysia. For the same reason, many cows have anovulatory sex cycles or develop small yellow bodies that quickly undergo involution. It follows from this how important is the role of connective tissue elements in the regulation of the generative function of the ovaries.

Chapter 3. IMPROVEMENT OF METHODS OF HORMONAL REGULATION OF THE REPRODUCTIVE FUNCTION OF COWS AND COLORS

Currently, there are no experimental studies reflecting the effect of various doses of gonadotropic drugs and prostaglandins F-2 alpha on ovarian function and the relationship of structural transformations in the gonads with the level of sex hormones in the blood at various states of sexual function and its functional disorders.

At the same time, the study of the patterns of histofunctional changes occurring in the ovaries and the dynamics of ovarian hormones in the blood of cows under the influence of gonadotropins and PF-2 alpha is necessary to determine the biological properties of drugs, assess their effect on ovarian function and develop biotechnology for rational methods of hormonal regulation of the reproductive system. animals.

To study the effect of gravohormone at different stages of the reproductive cycle on the dynamics of sex hormones in the blood and morphofunctional changes in the ovaries, 166 cows were included in the experiment. Of these, from 106 cows on the day of drug administration, as well as on days 1-2, 3-4, 5-7 after injection, blood was obtained to determine plasma progesterone, total estrogens and estradiol-17 beta. On 3-4 and 9-12 days of the experiment, in all groups, animals were slaughtered, 3-16 cows for each dose, followed by extirpation of the ovaries and their macroscopic and histological examination according to the above method.

Progesterone, estradiol-17 beta and total estrogens were determined by radioimmunoassay. Gravogormone was administered in doses of 4, 6, 8, 10 and 12 IU. per kg of body weight.

A comparative study of the biological properties of gravohormone and FFA was carried out on 36 cows with ovarian hypofunction. The drugs were administered in doses of 4, 6, 8, 10, 12 IU. per kg of body weight. In the blood plasma of cows that were injected with drugs in doses of 6-8 IU. per kg of body weight, progesterone and estradiol 17 beta were determined with an interval of 3-5 days.

Along with this, in order to determine the biological properties of gonadotropic efficacy, indications and contraindications, optimal doses, frequency and intervals of gravohormone administration, 189 cows were included in the experiment, which were divided into 5 groups (Table 15). 161 cows were injected subcutaneously in the upper third of the neck with gravohormone at a dose of 2 to 11 thousand IU, and 38 animals did not use the drug, they served as control.

For a comparative assessment of the gonadotropic efficacy of gravogormone, experiments were carried out in parallel on 272 cows to study changes in the ovaries and thyroid gland under the influence of FFA. FFA were administered to 201 cows once, subcutaneously in the upper third of the neck in doses from 1 to 12 thousand IU,
71 animals were not given the drug, and they served as control.

Observations of experimental animals after administration of gravogormone and FFA were carried out for 2-26 days. During this time, the timing of the onset of the stage of arousal of the sexual cycle and changes in the ovaries, which were established during rectal examination, were taken into account. For a more detailed study of the dynamics of macroscopic and histofunational changes in the ovaries and thyroid gland, animals were slaughtered at the Voronezh meat-packing plant 2, 3, 5, 10, 15, 20, 26 days after the administration of gonadotropic drugs.

Table 15

The effect of gravohormone on cow ovaries

Groups	Functional .; condition: ovaries	Of	Doses of pre-pairs thousand m.u.	The timing of the floors has come. hunting days	Active ovarian structures			
					Follecules		Yellow bodies	
					Total	On the 1st	Total	On f
one	Ovarian hypofunction	10	2	-	23	2,3	-	-
		fifteen	3	13	48	3.2	eleven	0.7
		7	four	10	31	4.4	7	1.0
		eight	five	four	27	3.4	nine	1.1
		10	6	3	25	2.5	25	2.5
		eight	7	2	nineteen	2.4	25	3.1
		3	eight	2	7	2,3	10	3.3
		one	nine	-	-	-	four	4.0

Control.	-"-	five	not input.		four	0.8	-	
2	Involution of yellow bodies	2	2	6	6	3.0	2	1.0
		2	3	five	five	2.5	3	1.5
		four	four	four	23	5.7	7	1.7
		2	five	3	four	2.0	five	2.5
		6	6	2	fifteen	2.5	sixteen	2.7
		2	7	2	-	-	nine	4.5
		one	eleven	2	-	-	29	29.0
Control.	-"-	five	not input.	6	10	2.0	five	1.0
3	Yellow bodies sexual cycle	3	2		7	2,3		-
		2	3	-	five	2.5	-	-
		five	four	-	eighteen	3.6	-	-
		four	five	-	twenty	5.0	-	-
		3	6	-	17	5.7	-	-
		3	7	-	24	8.0	-	-
		2	eight	-	nineteen	9.5	-	-
		2	eleven	-	one	0.5		-
Control.	-"-	five	not input.		7	1.4	-	-
four	Yellow bodies of pregnancy	five	3	-	22	4.4	-	-
		eleven	four	-	45	4.1	-	-
		five	five	-	27	5.4	-	-
		five	b	-	36	7.2	-	-
		6	7	-	45	7.5	-	-
		2	b	-	twenty	10.0	-	-
		five	eleven	-	3	0.6	-	-
Control.	-"-	eight	not input.		four	1.7	-	-
five	Persistent yellow bodies	2	2		five	2.5		
		five	3	26	24	4.8	one	0.2
		four	four	25	32	8.0	one	0.25
		3	five	-	36	12.0	-	
		3	7	12	58	16.0	one	0.33
Control.	-"-	five	not input.		7	1.4	-	-

In connection with the synthesis in our country of the domestic prostaglandin F-2 alpha-estufalan by the institutes of chemistry of the Estonian Academy of Sciences and the Bashkir branch of the Academy of Sciences, we studied its biological properties, determined the optimal doses, indications and contraindications for obstetric-gynecological pathology of cows. In particular, morphofunctional changes in the ovaries were studied on 165 cows under the influence of various doses (250, 500, 750, 1000 and 2000 μg) of this drug, introduced at different stages of the sexual cycle (3-4, 10-12, 18 days of the sexual cycle and after ovulation of the follicles) and during pregnancy. Before the introduction and before the extirpation of the ovaries, which was carried out after 2, 3, 4, 6 and 9 days from the beginning of the experiment, both in experimental and control animals, blood was taken from the jugular vein for radioimmunoassay for the content of progesterone and estradiol-17 beta. The extirpated ovaries were subjected to macroscopic and histological examination. Estufalan was tested on 42 mature heifers in doses of 200, 300, 400 and 600 μg.

In addition, optimal doses of estufalan were worked out to restore fertility in cows with luteal ovarian cysts, either alone or in combination with gonadotropin FFA. The experiment included 29 cows with luteal ovarian cysts, of which 6 were controls. Before the administration of the drugs and before the extirpation of the ovaries in both experimental and control animals, which was carried out two and four days before the start of the experiment, blood was taken from the jugular vein for radioimmunoassay for the content of progesterone and estradiol-17 beta. Estirpated ovaries were subjected to macroscopic and histological examination according to the above method. The role of progesterone, estradiol-17 beta and PF-2 alpha in the pathogenesis of postpartum pathology in cows was also studied.

3.1. The effect of gravohormone on the ovaries and thyroid gland of cows with involution of the corpus luteum of the reproductive cycle

Studies have shown that after the introduction of gravogormone against the background of involution of the corpus luteum, changes in the ovaries and thyroid gland depend on the dose of the drug **(Table 15).** So, 4 days after the injection of the drug at a dose of 2 thousand m.u. in the ovaries of two cows, yellow bodies in a state of involution are installed, 1-2 large or medium-sized and single small follicles. Some of the follicles have well-differentiated, secretory active granulosis and hyperplatic altered connective tissue membrane, while in other follicles the granulosis is reduced, and the membrane cells are fibrously changed. The sections contain many primary and secondary follicles at various stages of development and dystrophy. Single germ cells are observed, differentiating from the primordial epithelium and moving to its base and tunica albuginea. In the thyroid glands of these animals, oxyphilization of the intra- and interfollicular colloid predominates. There is an increase in the height of the epithelium and a change in the cytoplase from basophilic to light, fine-grained.

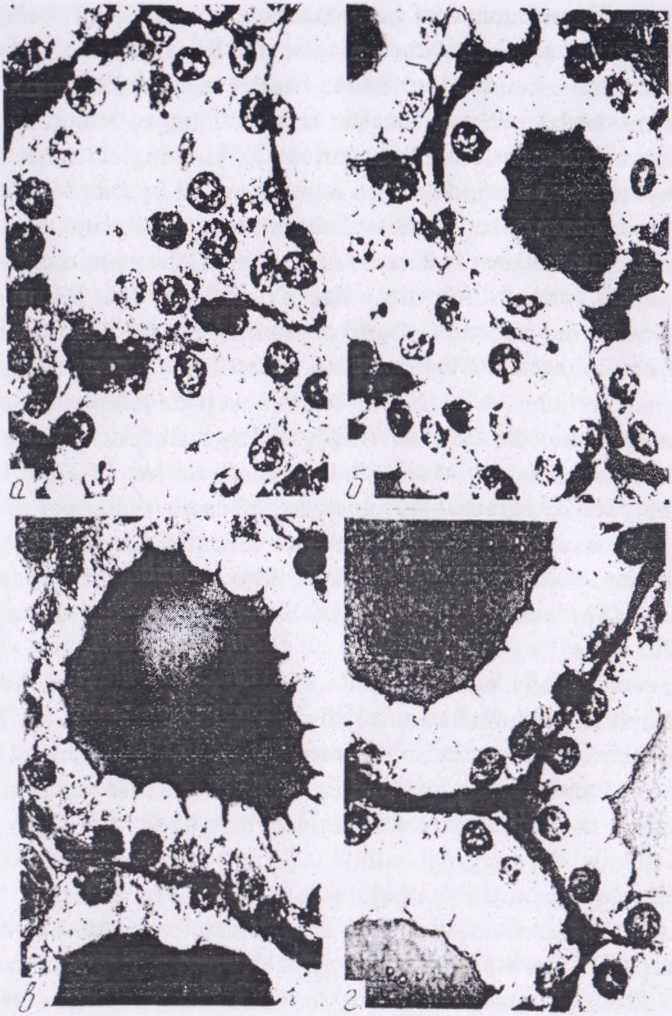
Under the influence of gravohormone at a dose of 3 thousand m.u. the stage of excitation of the sexual cycle in animals began on the 4th and 5th days. In the ovaries of cow No. 07437, killed on the 12th day of the experiment, one small yellow body in a state of involution and one large, newly formed, as well as one large, 2 - medium-sized and 31 small follicles. The thyroid gland of this animal is in a state of hypersecretion. In animal No. 07409, killed on the 25th day of the experiment or 20 days after the onset of the onset of the stage of excitation of the sexual cycle, a yellow and white body, 2 large, 1 medium-sized and 23 small follicles were found in the ovaries. In the thyroid gland, oxyphilization of the marginal colloid predominates and proliferating foci in the interfollicular epithelium are visible.

The use of gravohormone at a dose of 4 thousand IU ensured the manifestation of the stage of arousal of the sexual cycle in all cows on days 2-4. After the slaughter of two cows on the 12th day of the experiment, from one to two yellow bodies were formed in the ovaries. In most thyroid follicles in a state of secretion, the marginal colloid is dissolved and resorbed. Two cows killed on the 26th day and on the 23rd day of the experiment had a repeated sexual cycle. In their ovaries, from one to two yellow bodies from the first sexual cycle in a state of involution and one ovulating follicle were found. The thyroid glands are in a state of hyperfunction.

Under the influence of gravohormone at a dose of 5 thousand IU. the stage of arousal of the sexual cycle began on the 3rd day of the experiment. Animal No. 07445, killed on the 12th day of the experiment, had 2 yellow, 5 atretic bodies, 1 large, 3 medium-sized and many small follicles in the ovaries. On histological sections, the parenchyma of the corpus luteum is represented by large luteal cells surrounded by a dense capillary network. In the thyroid gland, the marginal colloid is deeply dissolved, resorbed, the epithelium is low cubic, and in some follicles it is flat. Cow No. 07413, killed on the 25th day after the injection of gravohormone, had 2 corpus luteum in the ovaries, 5 luteinized follicles in a state of involution, 1 large and many small follicles. A large follicle has a well-developed connective tissue membrane, the cells of which undergo fibrotic changes, and granulosis is reduced. Most of the small tertiary follicles have secretory active granulosis and hyperplastic changes in the connective tissue membrane. There are lobes of the thyroid gland, where in the follicles the marginal colloid is resorbed, the epithelium is thinned. The remaining light and basophilic colloid acquires an oxyphilic color.

Gravogormone, administered to 6 cows at a dose of 6 thousand IU, ensured the manifestation of the stage of arousal of the sexual cycle in all animals on day 3. Their ovaries were characterized by the presence of 2 to 5 yellow bodies **(Fig. 18 a),** mass luteinization of the tertiary and the appearance of single hemorrhagic follicles. In the thyroid glands, the marginal colloid is dissolved and resorbed into the interfollicular space, the epithelium is thinned **(Fig. 18 b).**

After the introduction of gravohormone to two cows at a dose of 7 thousand IU. the stage of excitement of the sexual cycle came on days 2 and 3. In animal No. 07405, on the 23rd day of the experiment, a repeated stage of excitation of the sexual cycle was established. After slaughterthis cows on day 25 in the ovaries: 2 yellow bodies were found, one of which is in a state of involution, and the second is in the initial stage of development, as well as 1 large, 5 medium-sized and small follicles in a state of luteinization.



Pic.18. Differentiation of thyrocytes around the secretion secreted by them and the formation of follicles in the thyroid gland of the fruits of the sea siblings- (a, 6), Start (c) and end (d) secretion thyrocytes of the apocrine type during the period of activation of sexual function in guinea pigs. Uv.a B C D-630.

In addition, many small atretic bodies are revealed. In the ovaries of cow No. 07434, which was also killed on the 25th day, 4 yellow bodies in a state of involution, 1 large, 2 medium-sized and many small follicles were found. The sections contain many hyalinized atretic bodies, as well as developing primordial and secondary follicles. From the primordial epithelium, germ cells are differentiated, moving to its base and tunica albuginea. The thyroid gland has a low epithelium, a polymorphic colloid with marginal oxyphilization. Small proliferating foci are seen in the interfollicular epithelium.

Under the influence of gravohormone at a dose of 11 thousand IU. 29 follicles underwent luteinization. At the same time, no signs of manifestation of the stage of arousal of the sexual cycle were observed. In the thyroid gland, deep dissolution of the marginal colloid, thinning of the epithelium with rejection of its apical sections and desquamation of single cells into the marginal colloid were noted. Such changes indicate that the drug in a large dose leads to hypersecretion of the thyroid epithelium.

Consequently, during the involution of the corpus luteum, gravogormone in a dose of 3 thousand m.u. provides activation of sexual function and ovulation, as a rule, of one follicle. INthisconnection, the drug can be recommended as an effective remedy for anovulatory reproductive cycles caused by hypoplasia of the connective tissue cells of the follicle membrane. Under the influence of the drug in dose4 thousand m.u. the timing of the onset of the stage of arousal of the sexual cycle is reduced and the ovulation of two follicles predominates. This gives grounds to recommend gravohormone in the indicated dose to stimulate multiple pregnancy in beef cows. With increasing doses of gravogormone up to 5-6-11 thousand IU. in the ovaries, the phenomena of poliovulation, mass luteinization and the formation of hemorrhagic follicles develop. The processes of hypersecretion and functional exhaustion develop in the thyroid gland. All this testifies to the inexpediency of using gravogormone in doses over 4 thousand IU. with involution of the corpus luteum.

Along with this, we (G.A. Cheremisinov, A.S. Lobodin, 1982) studied the dynamics of sex hormones in the blood and morphological changes in the ovaries of cows under the influence of gravogormone during involution of the corpus luteum or at the stage of excitation of the sexual cycle.

The results of a study on the change in the concentration of progesterone in the blood of cows under the influence of gravogormone are presented in Table 16. As can be seen from the table, in intact animals, due to the involution of the corpus luteum, the level of progesterone in the first 1-2 days decreases 3.6 times (P <0, 05) and is 0.25 ± 0.04 ng / ml. After ovulation of the follicle and the formation of corpus luteum, the steroid concentration gradually increases again and on days 9-12 of the experiment reaches 1.79 ± 0.12 ng / ml, which is 2 times higher than the initial data (0.89 ± 0.21 ng / ml) (P <0.05).

After the introduction of gonadotropin at a dose of 2 thousand IU. on days 17-18 of the sexual cycle, the progesterone concentration decreases from 0.46 ± 0.09 ng / ml at the beginning of the experiment to 0.21 ± 0.05 ng / ml (P <0.05) on days 1-2. From 3-4 days of observation, as in the control animals, the level of the corpus luteum hormone begins to rise and by 9-12 days of research exceeds the initial data by 1.4 times.

Changes in the concentration of progesterone in the peripheral blood plasma of cows after the administration of gravogormone with involution of the corpus luteum

Table 16

Drug dose (thousand m.u.)	Number of animals	Days of experience				
		before drug administration	1-2	3-4	5-7	9-12
-	nine	0.89 ± 0.21	0.25 ± 0.04	0.3 6 ± 0.08	0.56 ± 0.08	1.79 ± 0.12
2	nine	0.46 ± 0.09	0.21 ± 0.05	0.35 ± 0.08	0.43 ± 0.06	0.66 ± 0.27
3	3	0.46 ± 0.09	0.34 ± 0.12	0.49 ± 0.33	-	-
four	five	1.06 ± 0.19	-	0.28 ± 0.10	0.44 ± 0.05	1.34 ± 0.14
5-6	10	0.57 ± 0.11	0.28 ± 0.03	0.43 ± 0.07	1.02 ± 0.34	2.02 ± 0.37

The content of progesterone after the introduction of gonadotropin at a dose of 3 thousand IU in the first 3-4 days, the concentration of steroid in the blood of cows in the control and previous groups was similar.

At the same time, in the first 1-2 days of research, the level of the hormone decreases by 26.1% and is 0.34 ± 0.12 ng / ml. On day 3-4, the amount of progesterone increases to 0.49 ± 0.33 ng / ml.

In the group of cows treated with the drug at a dose of 4 thousand m , 6% (P <0.05). In the future, the level of the hormone gradually increases and on days 9-12 reaches 1.34 ± 0.14 ng / ml. After the introduction of gonadotropin at a dose of 5-6 thousand m.u. the concentration of progesterone in the first 1-2 days of the experiment decreases by 50.9% (P <0.05) and reaches 0.28 ± 0.03 ng / ml. From 3-4 days of observation, its content begins to grow rapidly and by the end of the study (9-12 days) the steroid level exceeds the initial data (0.57 ± 0.11 ng / ml) by 3.5 times and is 2.02 ± 0.37 ng / ml.

Dynamics of total estrogens in the peripheral blood plasma of cows after the administration of gonadotropin with involution of the corpus luteum (M ± m, pg / ml)

Table 17

Drug dose (thousand m.u.)	Number of animals	Days of experience				
		day of drug administration	1-2	3-4	5-7	9-12
-	98.2 ± 17.2	85.0 ± 9.5	71.6 ± 17.3	78.7 ± 13.3	84.8 ± 11.7	98.2 ± 17.2
four	55.0 ± 7.9	45.2 ± 12.1	58.6 ± 9.1	31.6 ± 13.1	42.8 ± 26.9	55.0 ± 7.9
6	40.2 ± 17.7	62.8 ± 17.1	53.1 ± 31.9	24.1 ±	41.5	40.2 ± 17.7
cight	70.2 ± 30.2	-	70.5 ± 2.4	63.2 ± 3.4	54.8 ± 5.0	70.2 ± 30.2
10-12	10	52.5 ± 9.1	43.4 ± 12.5	67.9 ± 9.8	106.3 ± 43.7	69.1 ± 12.2

The results of experiments on studying the effect of gravogormone on the level of total estrogens are presented in Table 17, from the data of which it follows that in intact animals in the first 3-4 days of observation, the level of estrogen in the blood gradually decreases by 27.1% and reaches 71.6 ± 17, 3 pg / ml. Subsequently, the concentration of hormones rises again and on days 9-12 of the experiment is 84.8 ± 11.7 pg / ml, which is still 13.7% lower than the initial data.

After the introduction of gonadotropin at a dose of 2 thousand m.u. on the 3-4th day of the experiment, there is a slight increase in total estrogens (from 55.0 ± 7.9 pg / ml at the beginning of the study to 58.6 ± 9.1 pg / ml). Subsequently, the level of hormones again decreases by 22.2-42.6%.

In the blood of cows treated with the drug at a dose of 3 thousand m.u., in the first 3-4 days of research, the content of total estrogens exceeds the initial data by 32.1-56.2%. Moreover, the highest level of steroids is observed on days 1-2 and is 62.8 ± 17.1 pg / ml versus 40.2 ± 17.7 pg / ml at the beginning of the experiment.

After a significant decrease in estrogens on the 5-7th day of observation, by the 9-12th day, the estrogen content increases and is 41.5 pg / ml, which is almost the same as the initial data.

Table 17 shows that after administration of the drug at a dose of 4 thousand m.u. the concentration of total estrogen in the blood of cows on the 3-4th day of the experiment does not differ from the initial data. In intact animals during this period, a pronounced (27.1%) drop in the level of steroids is observed. By days 9-12, when the hormone level in the control cows increased, the experimental animals showed a decrease in the concentration of total estrogens by 21.8% compared to the beginning of the experiment.

In the blood plasma of cows that received gonadotropin at a dose of 5-6 thousand m.u., there was a decrease in the level of total estrogens on the 2nd day of the experiment by 17.3% (from 52.5 ± 9.1 pg / ml to 43.4 ± 12.5 pg / ml). By 3-4 and 5-7 days, in contrast to intact animals, the concentration of hormones rapidly rises to 67.9 ± 9.8 pg / ml and 106.3 ± 43.7 pg / ml, respectively, and exceeds the initial values
1.3 and 2.0 times. By the end of observations (9-12 days), the level of total estrogens is 69.1 ± 12.2 pg / ml, which is 31.6% more than at the beginning of the experiment.

With the introduction of different doses of gravogormone at the stage of arousal of the sexual cycle, the content of estradiol-17 beta also changes

(Table 18). It can be seen from the table that in control animals the highest hormone content in the blood is noted the day before ovulation (after 1-2 days from the beginning of the experiment) and is 16.8 ± 5.2 pg / ml, which is 1.6 times higher than the initial data. Subsequently, the level of estradiol decreases and on days 9-12 of observation reaches 9.2 ± 3.5 pg / ml.

The concentration of the steroid in the blood of cows under the influence of the drug in a dose of 2 thousand m.u. throughout the entire experiment, it gradually increases by 8.5-125.6% and reaches 39.7 ± 24.1 pg / ml by days 9-12 of the study (versus 17.6 ± 2.4 pg / ml at the beginning of the experiment).

After the introduction of gonadotropin at a dose of 3 thousand m.u. the level of estradiol-17 beta changes insignificantly over 5-7 days of research and exceeds the initial data (16.4 ± 7.1 pg / ml) by only 4.0-18.3%. On days 9-12 of the experiment, the hormone content decreases by 60.9% and is 6.4 pg / ml.

Under the influence of the drug at a dose of 5-6 thousand m.u. there is a gradual increase in the concentration of estradiol-17 beta, which by 5-7 days increases from 15.8 ± 3.2 pg / ml to 67.6 ± 30.1 pg / ml, or increases by 3.3 times. However, on days 9-12, there is a sharp decrease in the level of the hormone to 7.9 ± 2.3 pg / ml. As shown by morphological studies of the ovaries of experimental animals (Table 19), the introduction of gonadotropin at a dose of 2 thousand m.u. provides the formation of 3-5 follicles, of which one, less often two ovulate, and the rest undergo atresia. Change in the content of estradiol-17 beta in the peripheral blood plasma of cows after the administration of gravogormone with involution of the corpus luteum (M ± m, pg / ml)

Table 18

Drug dose (thousand m.u.)	Number of animals	Days of experience				
		Day drug administ-ration	1-2	3-4	5-7	9-12
-	nine	10.6 ±	16.8 ± 5.2	15.2 ± 3.2	11.5 ± 7.2	9.2 ± 3.5
2	nine	17.6 ± 2.4	19.1 ± 4.4	20.1 ± 2.9	28.0 ± 21.3	39.7 ± 24.1
3	3	16.4 ± 7.1	17.1 ± 0.9	19.2 ± 2.4	19.4	6.4
5-6	10	15.8 ± 3.2	22.5 ± 4.7	31.1 ± 6.4	67.6 ± 30.1	7.9 ± 2.3

Table 19

The number of active structures in the ovaries of cows after the administration of gonadotropin with involution of the corpus luteum

Dose of the drug, thousand IU	Number of animals	Active ovarian structures			
		yellow bodies		follicles	
		Total	per animal	Total	per animal
-	6	6	1.0	11	1.8
2	7	8	1.1	19	2.7
3	5	11	1.7	13	2.6
4	3	5	2.2	9	3.0
5-6	8	34	3.3	84	10.5

Histologically, on the 3-4th day of research in the yellow bodies of the previous sexual cycle, deep involutional processes are revealed, characterized by obliteration of blood vessels, lysis of the cytoplasm and pycnosis of nuclei with the formation of a delicate fibrous structure. In the newly formed corpus luteum, there is an increased proliferation of thecal cells and a reduction of granulosis. Closer to the center, cells with a well-defined cytoplasm appear, some of which pass into a state of secretion.

Secondary and small tertiary follicles undergo obliterative atresia. In large follicles, along with pycnosis of nuclei and lysis of the cytoplasm of epithelial cells, their desquamation is noted. The theca is well vascularized, secretory and proliferatively active, forms powerful corrugated invaginations, which acquire a fibrous structure by the end of the experiment. On days 9-12 of observation, the formed corpus luteum is well vascularized, large luteal cells are in a state of hypersecretion. In some animals, the first signs of involution of the corpus luteum appear, which is manifested by oxyphilization, marginal or complete vacuolization of the cytoplasm and pycnosis of the nuclei.

After the introduction of gonadotropin at a dose of 3 thousand m.u. in the ovaries of cows, as a rule, one or two yellow bodies and 2-4 large follicles are determined (2.2 and 2.6, respectively, per animal). On day 3-4, the forming experimental yellow bodies are represented by hyperplastic and hypertrophic luteal cells in a state of hypersecretion. In non-ovulated follicles, granulosis undergoes lysis and desquamation, and the internal theca is well vascularized, proliferatively active, and forms areas of corrugated invaginations.

On days 9-12 of observations, large luteal cells with vacuolated cytoplasm are detected in the corpus luteum. The growth of secondary and small tertiary follicles is noted. In previously formed large follicles, epithelial cells undergo lysis and desquamation, and fibrotic changes prevail in the formed corrugated invaginations of non-proliferating thecal cells.

Higher doses of gonadotropin (4 thousand IU and higher) cause ovulation of two follicles in the ovaries of most animals. After applying 5-6 thousand m.u. the drug in the ovaries is formed by 3.6 yellow bodies and 10.5 large follicles per animal. Histological changes in the corpus luteum are similar to those found in cows of the previous groups.
On the 3-4th day of the experiment, non-ovulated follicles are represented by a powerful tecal layer, in which the formed single luteal cells were in a state of hypersecretion, and granulosis lost differentiation and lysed.

When examining the ovaries on days 9-12 of the experiment, non-ovulated follicles underwent cystic atresia. At the same time, granulosis was completely reduced, and thecal cells were lysed with the formation of a delicate fibrous structure.

Thus, the dynamics of progesterone in the blood of animals after the administration of gonadotropin at a dose of 2-6 thousand IU. similar to the change in this steroid in control cows, especially in the pre- and post-ovulation period. The concentration of progesterone in all groups in the first two days of the experiment decreases by 51.2-71.8% ($P < 0.02-0.05$). However, the rate of decrease in the steroid content in the first 1-2 days of observation in experimental cows is 24.9-53.5%, while in intact animals during this period, the concentration of the hormone decreases by 71.7%. The absence of a pronounced luteotropic action of gonadotropin is probably associated with the involution of the corpus luteum and a sharp decrease in the number of secretory active luteal cells. Secretion of progesterone by the remaining cells, as well as other structures (interstitial tissue,

In turn, if on the 5-7th day of research after the introduction of 2-4 thousand m.u of gonadotropin, the ovaries of experimental cows secrete the same amount of progesterone as the ovaries of control animals (0.43-0.44 ng / ml versus 0, 56 ng / ml), then in the blood of cows to which the drug was administered at a dose of 5-6 thousand IU, the concentration of the steroid was more than two times higher and amounted to 1.02 ± 0.34 ng / ml. Subsequently, in animals to which gonadotropin was injected at a dose of 2-4 thousand m.u, the concentration of progesterone rises and on days 9-12 of the study exceeds the initial data by 1.4 times, and the administration of the drug at a dose of 5-6 thousand m e. helps to increase the level of the corpus luteum hormone by 3.5 times. Consequently, with multiple ovulation of follicles, a faster increase in the concentration of progesterone occurs and a higher level of it in the blood plasma is observed in comparison with animals,

In addition, gravogormone, activating the growth and maturation of follicles, causes significant changes in the dynamics of estrogenic hormones. In this case, the nature of the changes is determined by the dose of the drug. Under the influence of gonadotropin at a dose of 2, 3 and 4 thousand IU. there is an increase in the level of total estrogens and estradiol-17 beta within the normal range or slightly higher, while higher doses of the drug, overstimulating the growth of follicles, increase the amount of estrogen in the blood to a level significantly higher than the norm. In this case, the resulting hormonal dysfunction can adversely affect metabolic processes in the body and the fertility of animals. Therefore, these doses of gonadotropin cannot be recommended for the regulation of the reproductive function of cows. The most optimal doses of the drug, ensuring growth, ovulation of follicles and hormonal changes in the body within the physiological norm, when introduced into the stage of excitation of the sexual cycle, 3 thousand IU should be recognized. In this case, gonadotropin at a dose of 3 thousand IU. can be used for the prevention of anovulatory reproductive cycles, and 4 thousand IU. - to stimulate multiple pregnancies.

3.2. The effect of gravohormone on the ovaries and thyroid gland of cows with functioning corpus luteum of the reproductive cycle

With functioning corpus luteum of the reproductive cycle in experimental animals, after the administration of gravogormone, an increase in follicular growth is observed, however, the manifestation of the stage of excitation of the sexual cycle and ovulation of graaf bubbles is not observed **(Table 15).**

So, after the introduction of gonadotropin in a dose of 2 thousand IU to three cows. and their slaughter on the 4th day of the experiment, one large yellow body was established in the ovaries, the parenchyma of which is represented by luteal cells with basophilic cytoplasm and oval nuclei, surrounded by a dense capillary network. In some cells, vacuolization and lysis of the edge sections of the cytoplasm are noted with the formation of a light substance in the intercellular spaces. Along with this, there are single cells with an oxyphilic cytoplasm that have an irregular shape. In addition, the ovaries contain 1-2 large, 2-3 medium-sized and many (21-40) small follicles. In large follicles, granulosis undergoes desquamation, and the connective membrane undergoes fibrotic changes. In medium-sized follicles, granulosa is secretory active, and the cells of the connective tissue membrane are in a state of proliferation and lysis with the formation of a fibrous structure. Ultimately, these follicles also undergo cystic atresia with the formation of a fibrous membrane. At the same time, granulosis is reduced. Sections reveal the proliferation of germ cells from the primordial epithelium with the formation of primordial, secondary and small tertiary follicles. The activation of connective tissue cells from the side of the tunica albuginea and the movement of the growing follicles with it into the depths of the ovarian cortex are expressed. The thyroid gland of these animals is in a secretory active state. Sections reveal the proliferation of germ cells from the primordial epithelium with the formation of primordial, secondary and small tertiary follicles. The activation of connective tissue cells from the side of the tunica albuginea and the movement of the growing follicles with it into the depths of the ovarian cortex are expressed. The thyroid gland of these animals is in a secretory active state. Sections reveal the proliferation of germ cells from the primordial epithelium with the formation of primordial, secondary and small tertiary follicles. The activation of connective tissue cells from the side of the tunica albuginea and the movement of the growing follicles with it into the depths of the ovarian cortex are expressed. The thyroid gland of these animals is in a secretory active state.

Under the influence of gravohormone at a dose of 3 thousand IU. in the ovaries of cow No. 07512, extirpated on the 7th day of the experiment, a corpus luteum, 7 large, 1 medium-sized, and 36 small follicles were established. In animal no. 07515, also killed during this period, a yellow body, 2 large, 3 medium-sized and 35 small follicles were found in the ovaries. On sections in large and medium-sized follicles, granulosis is reduced, and the connective tissue membrane undergoes fibrotic changes. In small follicles, the connective tissue membrane is represented by a thick layer of hyperplastically modified cells and a well-developed secretory active granulosis. The corpus luteum is characterized by lysis of the cytoplasm, pycnosis of the nuclei, obliteration of blood vessels, and an increase in the amount of fibrous structure.

The thyroid glands of these animals are dominated by squamous epithelium and follicles with a polymorphic colloid of light, basophilic, oxyphilic color and, accordingly, a fibrous, coarse-grained and homogeneous structure. Marginal oxyphilization of the colloid is noted. There are proliferatively active sites with the formation of small follicles.

Out of five animals, which were injected with gravohormone at a dose of 4 thousand IU, in two, the ovaries were extirpated on the 4th day of the experiment. In the gonads of these cows 7-9 large and medium-sized, as well as many (up to 80) small follicles were found. ... On histological sections from large and medium-sized follicles, lysis of cells of the connective tissue membrane, obliteration of blood vessels and desquamation of granulosis is noted. Most of the small follicles are in the initial stage of obliterative atresia. The corpus luteum is represented by large luteal cells with vacuolated and lysed marginal areas of the cytoplasm. The thyroid gland of cow No. 0188 is in a state of hypersecretion.

In three cows killed on the 7th day after the injection of gravohormone, there were from 2 to 4 large, 3-5 medium-sized and many small follicles in the ovaries. In large and medium-sized follicles, granulosis is in a state of desquamation, and the connective tissue membrane is fibrously degenerated. Expressed proliferation of connective tissue cells from the side of the tunica albuginea. In the luteal cells of the corpus luteum, lysis of the cytoplasm and pycnosis of the nuclei predominate, which indicates the onset of their involution. In the thyroid glands, the marginal colloid is resorbed, the epithelium is thinned, proliferating foci are visible.

After the introduction of gravogormone to 4 cows at a dose of 5 thousand IU. in the ovaries of each of these animals, there were 5-9 large, 4-7 medium-sized and many small follicles, as well as a functioning corpus luteum of the reproductive cycle (Fig. 18c). With increasing doses of gravogormone (6, 7, 8, 11 thousand IU), the number of large and medium-sized follicles that underwent obliterative or cystic atresia naturally increased in the experimental cows. The phenomena of ovulation and the manifestation of other phenomena of the stage of arousal of the sexual cycle, as in previous cases, were not observed. In this case, the cytoplasm of the luteal cells of the corpus luteum and connective tissue cells of the ovarian cortex was vacuolized and lysed. Hemorrhages in the follicles and ovarian cortex were observed, as well as the formation of Exner bodies. Increased proliferation of connective tissue cells from the side of the tunica albuginea and the movement of primary and secondary follicles with them into the depths of the ovarian cortex. Under the influence of high doses of gravogormone, the thyroid gland entered a state of hypersecretion, and the colloid acquires a polymorphic color from oxyphilic, basophilic to light **(Fig. 18d).**

Consequently, with functioning corpus luteum of the sexual cycle, gravogormone at a dose of 3-4 thousand IU. provides activation of the growth of follicles that do not ovulate, but undergo obliteration and cystic atresia. This is accompanied by a reduction of granulosis and fibrous degeneration of the cells of the connective tissue membrane of the follicles. With increasing doses of gravogormone, in addition to more pronounced activation of follicular growth and their luteinization, hemorrhages are noted in the ovaries. The secretory function of interstitial, luteal and thyroid cells is enhanced.

At the same time, we studied the dynamics of sex hormones in the blood and morphological changes in the ovaries of cows under the influence of gravogormone with functioning corpus lutcum. Data on the dynamics of the progesterone content in the blood plasma of cows after the introduction of equal doses of gravogormone at the stage of balancing the sexual cycle are presented in Table 20. Studies have established that in intact cows the level of the corpus luteum hormone decreases from 2.36 ± 0 within 3-4 days of the experiment, 25 ng / ml up to 1.46 ± 0.16 ng /

ml or by 38.2% (P <0.01), and in the next 6-8 days up to 0.25 ± 0.04 ng / ml or almost in 10 times (P <0.001).

When cows are injected with gonadotropin at a dose of 2 thousand IU. the steroid content in the first 1-2 days of observation increases from 2.73 ± 0.14 ng / ml to 4.24 ± 0.04 ng / ml, or 1.6 times (P <0.01). However, already from 3-4 days of the experiment, a sharp decrease in the concentration of the corpus luteum hormone is revealed, and the rate and time of the drop in its amount in the blood plasma significantly exceeds these indicators in control animals. If on the 3-4th day of research in the blood of experimental cows 1.39 ± 0.53 ng / ml of progesterone is recorded, then on the 5-7th day the concentration of the hormone is 0.40 ng / ml, which is 85.4% less than the initial level. Subsequently, in connection with the onset of the next sexual cycle, ovulation of follicles and the formation of corpus luteum in individual animals, the concentration of progesterone increases again and on days 9-12 of the experiment is equal to 1.41 ng / ml.

Concentration of progesterone in the peripheral blood plasma of cows after administration of gravogormone with functioning corpus luteum of the sexual cycle (M ± m, ng / ml)

Table 20

Drug dose (thousand m.u.)	Number of animals	Days of experience				
		day of drug administration	1-2	3-4	5-7	9-12
-	9	2.36 ± 0.25	-	1.46 ± 0.16	0.89 ± 0.21	0.25 ± 0.04
2	3	2.73 ± 0.14	4.24 ± 0.04	1.39 ± 0.53	0.40	1.41
3	8	2.35 ± 0.37	-	2.50 ± 0.79	2.15 ± 0.73	0.79
4	12	2.13 ± 0.17	3.60 ± 0.38	4.21 ± 0.57	1.40 ± 0.64	2.91 ± 0.78
5-6	17	2.22 ± 0.16	5.31 ± 0.21	3.72 ± 0.55	1.82 ± 0.24	2.77 ± 0.66

In animals that were injected with gonadotropin at a dose of 3 thousand IU on days 10-12 of the sexual cycle, by 3-4 days the amount of steroid in the blood increases by 6.4% compared to the initial data, while in control cows during this period there is a significant decrease in the content of the corpus luteum hormone by 38.1%. A high level of progesterone (2.15 ± 0.73 ng / ml) in experimental cows is maintained until 5-7 days of the experiment. Subsequently, its amount decreases by 66.4% and is 0.79 ng / ml.

The use of the drug in a dose of 4 thousand IU. in the stage of balancing the sexual cycle contributes to a significant ($P < 0.01$) increase in progesterone in the first 3-4 days of the study from 2.13 ± 0.17 ng / ml to 4.21 ± 0.57 ng / ml. On days 5-7 of the study, the steroid level begins to decrease and is 1.40 ± 0.64 ng / ml, which is 34.1% less than the initial level. The subsequent luteinization or ovulation of the follicles and the formation of the corpus luteum contribute to a new rise in the concentration of the hormone to 2.91 ± 0.78 ng / ml on days 9-12 of observation.

In cows of the experimental group, which were injected with gonadotropin at a dose of 5-6 thousand IU, there is also a statistically significant increase in the concentration of the corpus luteum hormone during the first 3-4 days of the experiment by 67.9-139.7% ($P < 0.01$-0.02). On days 3-4, 3.72 ± 0.55 ng / ml of progesterone is recorded in the blood compared to 2.22 ± 0.16 ng / ml at the beginning of the study. Subsequently, after a slight (by 18.0%) decrease in the steroid level, its content on days 9-12 again rises to 2.79 ± 0.66 ng / ml, which is due to follicle luteinization by the formation of corpus luteum induced by the administration of gonadotropin.

Significant changes under the influence of gravogormone also occur in the dynamics of estrogen (Table 21). From the data in the table it can be seen that in the control animals the maximum content of total estrogens (98.2 ± 17.2 pg / ml) is observed at5-7 days of research and exceeds the initial data by 13%.

Under the influence of 2 thousand m.u. of the drug, the level of total estrogens increases by 12.3% by 3-4 days and is 38.4 ± 9.2 pg-ml, while in intact animals during this period there is a decrease in the level of hormones by 10.6%. On the 9-12th day of research in experimental cows, the content of total estrogens exceeds the initial data (34.2 ± 1.1 pg / ml) by 33.9% and reaches 45.8 pg / ml, while in animals of the control group the concentration steroid is almost unchanged.

Table 21

Change in the content of total estrogens in the blood plasma of cows after the introduction of gonadotropin at the stage of balancing the sexual cycle (M ± m, pg / ml)

Drug dose (thousand m.u.)	Number of animals	Days of experience				
		Day drug administration	1-2	3-4	5-7	9-12
-	9	86.4 ± 14.0	-	77.2 ± 26.4	98.2 ± 17.2	85.0 ± 9.5
2	3	34.2 ± 1.1	26.1 ± 0.2	38.4 ± 9.2	28.5	45.8
3	8	44.6 ± 7.1	64.9 ± 12.4	55.9 ± 6.9	43.2 ± 8.4	29.7
4	12	51.5 ± 7.4	57.7 ± 11.2	68.9 ± 8.7	46.3 ± 11.4	64.7 ± 7.7
5-6	17	69.1 ± 5.6	66.8 ± 32.5	117.5 ± 13.9	83.5 ± 15.2	69.3 ± 8.4

More significant shifts in the level of total estrogens in the blood of cows are observed with the introduction of gonadotropin at a dose of 3 thousand IU. On days 1-2, 3-4 of the experiment, when a decrease in the concentration of hormones is recorded in intact animals, an increase in the content of total estrogens is observed in the experimental cows from 44.6 ± 7.1 pg-ml to 64.9 ± 12.4 pg / ml (by 45.5%) and 55.9 ± 6.9 pg / ml (by 25.3%), respectively. Subsequently, the level of hormones decreases and by 9-12 days of research reaches 29.7 pg / ml.

After using the drug at a dose of 4 thousand IU in the blood of animals, as in the previous group, the maximum content of steroids is recorded on day 3-4 and is 68.0 ± 7.5 pg / ml. On the 5-7th day, when the beginning of the pre-ovulation rise in estrogens is noted in the control cows, the steroid level in experimental animals decreases by 10.1% compared to the initial content and rises only by 9-12 days to 64.7 ± 7.7 pg / ml.

The introduction of gravohormone at a dose of 5-6 thousand m.u. in the stage of balancing the sexual cycle in the first 1-2 days causes a slight decrease in the level of estrogen (by 3.3%). Subsequently, for 3-7 days, the concentration of hormones exceeds the initial data (69.1 ± 5.6 pg / ml) by 20.8-70.0%, and an increase in the steroid content in the blood to 117.5 ± 13.9 pg / ml on 3-4 days of the study is statistically significant (P <0.01). On days 9-12 of the experiment, quantitative differences in the content of total estrogens compared with the beginning of the experiment were not expressed. In the blood during this period, 69.3 ± 8.4 pg / ml of estrogenic hormones are recorded.

The dynamics of total estrogen in the blood plasma of cows does not always coincide with the change in the level of estradiol-17 beta. As can be seen from table 22, in control animals, the concentration of estradiol decreases by 80% by 3-4 days of research. Subsequently, due to the growth and maturation of follicles, the content of hormones begins to rise and on days 9-12 of the experiment exceeds the initial data (13.5 ± 4.5 pg / ml) by 1.2 times.

Under the influence of the drug at a dose of 2 thousand IU. the concentration of estradiol, after a slight decrease by 1-2 days by 3-4 days, increases by 239.1% and is 7.8 ± 1.3 pg / ml versus 2.3 ± 0.05 pg / ml at the beginning of the experiment.

After the introduction of gonadotropin at a dose of 3 thousand IU e0, the content of estradiol-17 beta by 3-4 days increases by 2.4 times (P <0.05) and reaches 25.4 ± 4.4 pg / ml 0 At 5-7 day of the experiment, the level of steroid in the blood decreases to 13.0 ± 1.8 pg / ml.

Table 22

Dynamics of estradiol-17 beta in the peripheral blood plasma of cows after the introduction of gravogormone in the stage of balancing the sexual cycle (M ± m, pg / ml)

Drug dose (thousand m.u.)	Number of animals	Days of experience				
		Day of drug administration	1-2	3-4	5-7	9-12
-	nine	13.5 ± 4.5		2.7 ± 0.6	10.6 ± 3.8	16.8 ± 5.2
2	3	2.3 ± 0.05	-	7.8 ± 1.3	-	-
3	eight	10.7 ± 1.8	19.7 ± 4.3	25.4 ± 4.4	13.0 ± 1.8	-
four	12	7.6 ± 1.0	11.7 ± 1.6	17.9 ± 2.9	27.1 ± 15.0	16.7 ± 3.7
5-6	17	13.9 ± 2.1	8.2 ± 4.1	31.5 ± 17.5	53.8 ± 18.9	15.6 ± 3.4

Under the influence of gravohormone at a dose of 4 thousand. m ethe concentration of the hormone in the first 3-4 days of research significantly (P <0.05) increases and by 5-7 days exceeds the initial level (7.6 ± 1.0 pg / ml) by 3.6 times. On the 9-12th day after the administration of the drug, its amount slightly decreases and is 16.7 ± 3.7 pg / ml, which is 2.2 times lower than the initial level.

When applying 5-6 thousand m.u. gonadotropin content of estradiol-17 beta after a slight decrease in the first 1-2 days increases significantly in the next 3-7 days of the experiment. At the same time, the concentration peak (52.2 ± 18.3 pg / ml), as in the cows of the previous group, is recorded on the 5-7th day of the experiment and exceeds the initial data (13.9 ± 2.1 pg / ml) in 3, 9 times (P <0.01). On days 9-12 of observation, the steroid level sharply decreases and is 15.6 ± 3.4 pg / ml.

The noted changes in the dynamics of sex hormones under the influence of gravogormone are the result of complex structural transformations in the ovaries of cows (Table 23).

From the data in the table, it follows that after the use of gonadotropin at a dose of 2 thousand IU. on the 3-4th day of observations in the ovaries, as in the control animals, an average of 1 corpus luteum and 2 large follicles are recorded. In the corpus luteum, the bulk of luteal cells undergo oxyphilization, and a few are in a state of hypersecretion and lysis. Follicle luteinization is also detected. Moreover, in large and medium-sized tertiary follicles, granulosis is secretory active, and proliferative processes develop with the formation of corrugated invaginations in the internal flow. On days 9-12 of research, there are 3-5 follicles in the gonads and one old or newly formed corpus luteum.

In animals that were injected with gonadotropin at a dose of 3 thousand IU, on day 3-4 of observations, the number of large follicles in the ovaries increased to 3.3 per animal. In well-vascularized corpus luteum, involutional processes prevail, expressed in lysis and disruption of the configuration of luteal cells. Single cells undergo oxyphilization. In follicles hypersecretion, lysis and reduction of granulosis, hypersecretion and proliferation of cells of the connective tissue membrane with the formation of corrugated invaginations are noted. On the 9-12th day of the experiment in the gonads, an average of one yellow body and 3, 8 large follicles are recorded.

Table 23

Change in the number of active structures of the ovaries of cows after the introduction of gravogormone in the stage of balancing the sexual cycle

Dose of the drug, thousand IU	Duration of experience in days	Number of animals	Active ovarian structures			
			yellow bodies		follicles	
			Total	per animal	Total	per animal
1	3-4	3	3	1.0	6	2.0
	9-12	3	3	1.0	12	4.0
2	3-4	3	3	1.0	6	2.0
	9-12	3	3	1.0	12	4.0
3	3-4	4	4	1.0	13	3.3
	9-12	4	4	1.0	15	3.8
4	3-4	4	4	1.0	12	3.0
	9-12	4	16	1.0	35	4.4
5-6	3-4	7	8	1.1	44	6.2
	9-12	9	19	1.1	95	10.6

Somewhat different results were obtained under the influence of gravohormone administered at a dose of 4 thousand m.u. On the 3-4th day of the experiment, the corpus luteum is well vascularized, the luteal cells lose their configuration, undergo oxyphilization and lysis. In the connective tissue membrane of the follicles, proliferation, secretion and minor lysis are noted. Granulosa undergoes desquamation and lysis. In large follicles, the theca is well vascularized, proliferatively active, and forms powerful corrugated outgrowths.

On the 9-12th day of observation, due to the activation of follicle growth and their subsequent ovulation, from 1 to 7 large follicles are noted in the ovaries of the experimental cows. On sections of old corpus luteum, cells are noted in a state of oxyphilization, lysis and dystrophy. In small tertiary follicles, the connective tissue membrane is well vascularized, proliferatively active, the follicular epithelium is in a state of proliferation and hypersecretion. Along with this, in the ovaries there are not only small, but also large follicles, the granulosis of which is subjected to lysis and desquamation, and the theca is proliferative and secretory active, well vascularized, and forms corrugated invaginations.

Under the influence of gonadotropin at a dose of 5-6 thousand IU. the number of large follicles increases by 3-4 days of the experiment. In small tertiary follicles, theca formation is observed, as well as proliferation and secretion of follicular epithelium. In follicles of medium and large size, the connective tissue membranes are in a state of proliferation, and granulosis is in a state of hypersecretion, lysis and dystrophy.

On days 9-12 of observation, the number of follicles per animal increases to 10.6. Histological examination of old corpus luteum reveals obliteration of blood vessels, lysis of luteal cells with the formation of a fibrous structure. In small tertiary follicles, granulosis is in a state of hypersecretion, lysis and desquamation. The connective tissue membrane is moderately vascularized, in a state of proliferation. In follicles of medium and large size, the theca is proliferatively active, the formation of corrugated invaginations is noted, in which intensive processes of lysis and fibrous replacement take place.

From the above data, it follows that the change in the level of sex hormones under the influence of gonadotropin FFA depends on the nature of morphofunctional transformations in the ovaries.

It should be noted that gonadotropin has a specific luteotropic effect, activating the hormone-producing function of the corpus luteum, thereby increasing the level of progesterone in the blood of cows. At the same time, under the influence of small doses of the drug (2 thousand IU), an increase in the level of progesterone occurs due to an increase in the secretion of luteal cells unaffected by involution. A high level of the hormone for 5-7 days of observation, noted after an injection of 3 thousand IU. gonadotropin, due to increased vascularization and secretion of cells of the corpus luteum.

Higher doses of the hormone (4-6 thousand IU) have a luteotropic effect in the first 3-4 days of observation by activating the processes of secretion and lysis of luteal cells, as well as increasing vascularization of the corpus luteum tissue. At the same time, by the end of the experiment, the change in the concentration of progesterone in the blood is determined both by the number and functional state of the corpus luteum and by the number of large follicles formed with secretory active thecalutein cells.

The introduction of gonadotropin on days 10-12 of the sexual cycle, along with an increase in the concentration of progesterone, reflecting the luteotrophic activity of gravoghormone, causes a change in the level of total estrogens and estradiol-17 beta. In this case, the dynamics of estrogen in the blood of cows is determined by the dose of the drug.

Gravogormone in a dose of 2-3 thousand IU. in the first days of the experiment, it causes an increase in proliferative and secretory processes in the epithelial cells of large follicles, which causes an increase in the concentration of total estrogens and estradiol-17 beta in the blood plasma of cows. With an increase in the dose of the drug to 4 thousand IU. the increase in the concentration of estrogens in the first days of observation occurs against the background of the intensification of plastic and trophic processes in the connective tissue membrane of large and activation of the growth and maturation of small follicles. A decrease in the level of estrogen on days 9-12 of research is associated with cystic and obliterative follicular atresia.

Comparing the data of radioimmunological, histological and macroscopic studies, it should be noted that gravohormone administered to cows on days 10-12 of the sexual cycle in small doses (no more than 3 thousand IU) moderately stimulates the secretory function of luteal cells, enhances vascularization of the corpus luteum. In this regard, gonadotropin in the indicated dose can be recommended to increase the function of the corpus luteum and prevent early embryonic mortality.

Higher doses of the drug (4-6 thousand IU) cause massive development of follicles in the ovaries, which undergo obliterative or cystic atresia. Therefore, the introduction of gonadotropin FFA in these doses against the background of functioning corpus luteum cannot be recommended to increase the fertility of cows.

The dynamics of sex hormones in the blood and morphological changes in the ovaries of cows under the influence of gravohormone introduced during the formation of the corpus luteum, a radioimmunological study of the blood plasma of cows for the content of progesterone after the introduction of gravohormone into the stage of inhibition of the sexual cycle, showed (Table 24) that already under the influence of the drug in dose of 2 thousand m.u. stimulation of the synthesis of this hormone is noted, although the dynamics of its concentration during the experiment is similar to the changes in the hormone in intact cows. Thus, in control animals, 7 days after the beginning of the experiment, the level of progesterone in the blood increased by 4 times (from 0.56 ± 0.08 ng / ml to 2.36 ± 0.12 ng / ml, P <0.001), while in cows treated with gonadotropin, the progesterone content by this time increased 5 times (from 0.68 ± 0.13 ng / ml to 3.42 ± 0.21 ng / ml, P <0, 001) and exceeded the level of control animals by 44% P <0.001. These differences persisted on days 9-12 of the experiment.

An even more significant effect on the dynamics of the corpus luteum hormone in the blood of cows is exerted by the introduction of 3 thousand IU. drug. At the same time, the amount of progesterone by 3-4 and 5-7 days of research increases 10-14 times (P <0.01-0.001) and exceeds the steroid level in intact animals by 2.3-2.5 times (P <0, 02-0.01) On days 9-12 of the experiment, when the processes of oxyphilization and lysis are intensified in the luteal cells of control animals, and the level of progesterone decreases to 1.46 ± 0.16 ng / ml, the amount of the hormone in experimental cows remains at a high level and is 4.05 ± 1.75 ng / ml.

Table 24

Change in the concentration of progesterone in the peripheral blood plasma of cows after the introduction of gravogormone in the stage of inhibition of the sexual cycle (M ± m, ng / ml)

Drug dose (thousand m.u.)	Number of animals	Days of experience				
		day of drug administration	1-2	3-4	5-7	9-12
1	9	0.56 ± 0.08	one	1.79 ± 0.12	2.36 ± 0.25	1.46 ± 0.16
2	4	0.68 ± 0.13	1.15 ± 0.23	1.93 ± 0.42	3.42 ± 0.21	2.35 ± 0.48
3	6	0.41 ± 0.08	0.89 ± 0.25	4.30 ± 0.86	5.86 ± 1.08	4.05 ± 1.75
4	3	0.55 ± 0.20	0.76 ± 0.11	1.22 ± 0.34	-	0.27
5-6	6	0.49 ± 0.09	1.43 ± 0.34	1.60 ± 0.23	-	2.22 ± 0.76

An even more significant effect on the dynamics of the corpus luteum hormone in the blood of cows is exerted by the introduction of 3 thousand IU. The amount of progesterone in this case, by 3-4 and 5-7 days of research, increases 10-14 times (P <0.01-0.001) and exceeds the steroid level in intact animals by 2.3-2.5 times (P <0 On days 9-12 of the experiment, when the processes of oxyphilization and lysis are intensified in the luteal cells of control cows, and the level of progesterone decreases to 1.46 ± 0.16 ng / ml, in the experimental cows the amount of the hormone remains at high level and is 4.06 ± 1.75 ng / ml

The introduction of gonadotropin in higher doses, as can be seen from table 24, caused, on the contrary, some inhibition of progesterone synthesis by the corpus luteum. So, under the influence of the drug at a dose of 4 thousand IU. the level of steroid increases on the 3-4th day of research only 2.2 times and was lower than the control animals by 46.7%. On the 12th day of the experiment, this difference reached more than 500%.

The use of gravohormone at a dose of 5-6 thousand, IU provides a rapid increase in the concentration of progesterone in the blood plasma of cows in the first two days (from 0.49 ± 0.09 ng / ml to 1.43 ± 0.34 ng / ml, P <0.05). In subsequent periods, the synthesis of the hormone by the corpus luteum in these animals slows down.

The nature of the change in the concentration of total estrogens in the blood of cows under the influence of the drug is presented in table 25. As follows from the table, in intact animals in the first 5-7 days of the experiment, the content of total estrogens increased by 9, and returned to the initial data by 9-12 days. The introduction of gonadotropin at a dose of 2 thousand m.u. somewhat inhibits the synthesis of estrogenic hormones. So, their content by the 5-7th day of the experiment decreased by 16%, and by the 12th day by 86%.

After administration of the drug at a dose of 3 thousand IU. the level of hormones increases by 42.5% only in the first 3-4 days of the experiment, and then decreases and by 9-12 days it turned out to be 19.7% lower than the initial data.

Increasing the dose of gonadotropin to 4 thousand, IU. causes a more pronounced rise in total estrogen compared with the control and the previous group. So, already on the second day of the experiment, the level of hormones increases from 37.5 ± 14.0 pg / ml to 57.3 ± 10.9 pg / ml, or by 52.8%, and on 3-4 days to 75.4 ± 7.1 pg / ml or more than 2 times the baseline level.

When the drug is administered at a dose of 5-6 thousand m.u. the concentration of total estrogens by the 5-7th day of the experiment exceeds the initial data by 4 times (314.1 pg / ml versus 77.6 pg / ml). However, after 4-5 days, their content decreased to 52.1 pg / ml.

Table 25

The content of total estrogens in the plasma of the peripheral blood of cows after the introduction of gravogormone in the stage of inhibition of the sexual cycle (M ± m, pg / ml)

Drug dose (thousand m.u.)	Number of animals	Days of experience				
		Day of drug administration	1-2	3-4	5-7	9-12
-	9	78.7 ± 13.3	-	84.8 ± 11.7	86.4 ± 14.0	77.2 ± 26.4
2	4	49.2 ± 10.3	-	43.8 ± 4.8	41.2 ± 6.0	26.4 ± 2.4
3	6	54.3 ± 10.2	59.1 ± 13.6	77.4 ± 16.5	52.5 ± 11.4	43.6 ± 19.0
4	3	37.5 ± 14.6	57.3 ± 9.8	75.4 ± 5.9	-	-
5-6	6	77.6 ± 27.8	59.7 ± 15.8	82.8 ± 18.4	314.1	52.1

Data on the effect of gonadotropin on the level of estradiol-17 beta in the blood of cows are presented in Table 26. In control animals, the maximum content of the hormone is observed on days 5-7 of observation and is 13.5 ± 4.5 pg / ml, which exceeds the initial data (11 , 5 ± 7.2 pg / ml) by 17.3%.

Change in steroid concentration under the influence of 2 thousand IU. the drug in the first 3-4 days slightly differs from the dynamics of this hormone in intact cows. The estradiol level decreases from 27.5 ± 10.8 pg / ml to 19.5 ± 6.5 pg / ml, or by 29.1%. Subsequently, in contrast to the control cows, the steroid content continues to decrease and on days 5-7, 9-12 of observation, its concentration ranges from 11.5 to 12.5 pg / ml, which is 54-58% less than at the beginning of the experiment. ...

After the application of 3 thousand m.u. gonadotropin for 3-4 days in the blood of experimental cows there is an increase in the concentration of mountainsmona from 5.1 ± 0.9 pg / ml to 21.4 ± 5.9 pg / ml or more than 4 times (P <0.05). On days 9-12, the concentration of estradiol-17 beta remains at a high level and amounts to 27.7 ± 18.3 pg / ml.

Table 26

The level of estradiol-17 beta in the blood plasma of cows after the introduction of gonadotropin FFA in the stage of inhibition of the sexual cycle(M ± m, pg / ml)

Drug dose (thousand m.u.)	Number of animals	Days of experience				
		day of drug administration	1-2	3-4	5-7	9-12
-	9	11.5 ± 7.2	-	9.2 ± 3.5	13.5 ± 4.5	2.7 ± 0.6
2	4	27.5 ± 10.8	-	19.5 ± 6.5	11.5	12.5
3	6	5.1 ± 0.9	8.3 ± 3.8	21.4 ± 5.9	6.9	27.6 ± 18.3
4	3	13.0 ± 5.8	12.3 ± 2.1	18.8 ± 8.8	-	10.9
5-6	6	9.4 ± 1.7	10.0 ± 3.2	18.1 ± 2.7	278.7	14.3 ± 4.6

Under the influence of 4 thousand m.u. gonadotropin, the content of estradiol-17 beta, after a slight decrease on days 1-2 of the experiment to 12.3 ± 2.1 pg / ml, by 3-4 days increases by 1.4 times and reaches 18.8 ± 8.8 pg / ml. However, on days 9-12, the concentration of the hormone falls and is equal to 10.9 pg / ml.

Administration of the drug to cows at a dose of 5-6 thousand m2. increased the level of estradiol-17 beta in blood plasma by 3-4 days by 92.6% (from 9.4 ± 1.7 pg / ml to 18.1 ± 2.7 pg / ml, P <0.05). However, on days 9-12, the hormone content again decreases to 14.3 ± 4.6 pg / ml, which is 52.1% more than the initial data.

Pronounced hormonal changes occurring under the influence of gonadotropic drugs develop against the background of complex transformations of cellular structures; ovaries **(Table 27).**

So, after the introduction of gonadotropin to cows at a dose of 2 thousand IU. the number of large follicles increases 1.5 times. In the inner membrane of such follicles, the proliferation of secretions is noted, the formation of corrugated invaginations begins, and granulosis undergoes lysis.

Under the influence of 3 thousand m.u. the drug, the number of corpus luteum remains unchanged, and the content of follicles in the ovaries increased to 4 per animal. Histological examination on the 3-4th day of the experiment showed that the drug in this dose, along with the activation of secretory processes in the luteal cells of the corpus luteum, enhances the functional activity of thecal and follicular cells. In tertiary follicles, the inner membrane is moderately developed, granulosis is differentiated, cells are rounded, secretory active.

Table 27

Effect of gravohormone, introduced at the stage of inhibition of the reproductive cycle, on the ovaries of cows

Dose of the drug at a.m. e.	Number of cows	Active ovarian structures			
		Yellow bodies		follicles	
		Total	per animal	Total	per animal
-	6	6	1.0	12	2.0
2	3	3	1.0	9	3.0
3	3	3	1.0	12	4.0
4	8	8	1.0	43	7.1
5-6	7	7	1.0	64	9.1

On the 9-12th day after the administration of the drug, the number of corpus luteum remained unchanged, and the number of large follicles doubled. Moreover, if in experimental cows the vast majority of luteal cells are in a state of increased secretory activity, then in intact animals the cells of the corpus luteum undergo oxyphilization and lysis. In cows of the experimental group, as in intact animals, follicular atresia is noted. In secondary and tertiary follicles, granulosis is in a state of hypersecretion, turning into lysis. Thecal cells are well vascularized, proliferative and secretory active, lysed in some areas. In large tertiary follicles, epithelial cells are secretory active, partially lysed. In the flow of such follicles, either lysis processes with the formation of a fibrous structure predominate,

A more pronounced reaction from the gonads is observed after the application of gonadotropin to animals at a dose of 4 thousand m.u .. The number of secretory active follicles increases sharply and averages 7.1 per animal. On the 3-4th day of the study, when intact cows have only separate areas of proliferative active tissue, and the bulk of the corpus luteum is represented by large single and binuclear cells, most of which are in a state of hypersecretion, in experimental animals in proliferatively active areas, predominantly medium size is formed luteal cells, which pass into an active secretory state. The nuclei of such cells are round, clear, with well-defined nucleoli. On the large surface of the corpus luteum section, increased vascularization and lysis of luteal cells are noted. Single cells undergo oxyphilization. The number of follicles in comparison with control animals increases 2 times and is 4.0 per head. Microscopic examination revealed that granulosis in secondary and tertiary follicles is in a state of hypersecretion, lysis and desquamation. The inner connective tissue membrane is proliferatively active, has separate areas of lysed cells.

By the 9-12th day of observation, the number of corpus luteum remains unchanged, and luteal cells undergo further degeneration and lysis. In the resulting tertiary follicles, cystic atresia is noted. Thecal cells of such follicles are proliferatively active in places, while most of them acquire a fibrous structure. The follicular epithelium is in a state of hypersecretion and lysis.

Under the influence of gravohormone at a dose of 5-6 thousand m.u. significant morphological changes occur in the ovaries. The number of large follicles reaches an average of 9.1 per animal. At the same time, on the 3-4th day of the experiment, pronounced processes of lysis and oxyphilization of luteal cells are revealed in the corpus luteum. It should be noted that small cells are more susceptible to dystrophic changes, and in large and medium cells, oxyphilization, vacuolization and lysis are more often observed. At the same time, along the periphery of the corpus luteum, there are areas of large, secretory active luteal cells. A histological examination of large follicles revealed that the cytoplasm of granulosa is in a state of hypersecretion and lysis, and the nuclei undergo pycnosis. Theca is proliferatively active, forms corrugated outgrowths, most cells are luteinized.

In the ovaries of cows killed on days 9-12 of the experiment, one corpus luteum in a state of involution and from 3 to 38 large follicles (on average, 14.5 per animal) were found. The bulk of the corpus luteum during this period is made up of polygonal cells in a state of oxyphilization and fragments of lysed luteal cells. In some areas, there is a small number of medium and small luteal cells in a state of hypersecretion and lysis. In all follicles, granulosis is in a state of hypersecretion, lysis, degeneration and desquamation. Theca is well vascularized, proliferatively active, forms powerful (especially in large tertiary follicles) corrugated invaginations. There is a massive appearance of secretory, but active theca-luteal cells, most of which undergo vacuolization and lysis.

Analysis of the data obtained shows that the effect of gonadotropin on morphofunctional changes in the ovaries and the content of steroid hormones in the blood plasma of cows when administered at the stage of inhibition of the sexual cycle depends on the dose of the drug.

It turned out that the drug has not only follicle-stimulating and luteinizing, but also luteotropic action, and already in a dose of 2-3 thousand IU. activates the function of the corpus luteum. Moreover, an increase in its hormonal activity provides morphofunctional restructuring, which causes an increase in secretory processes in luteal cells. Higher doses of the drug (4-6 thousand IU) lead to the formation of smaller luteal cells in the corpus luteum, in which involutional processes begin faster. The synthesis and secretion of progesterone on days 9-12 of the experiment is provided by theca-luteal cells of the inner lining of the follicles.

The change in the level of estrogen occurs due to an increase in the functional activity of medium and large follicles present in the ovaries of cows during this period, as well as in connection with the secretion of steroids by follicles formed under the action of gonadotropin. At the same time, an increase in the secretory activity of thecal and epithelial cells under the influence of 3 thousand m.u. the drug indicates that an increase in the level of estrogen on 3-4 days after the use of gravohormone is associated with the stimulation of steroidogenesis in the follicles present in the ovaries. An increase in the concentration of estradiol-17 beta on days 9-12 after administration of 2-3 thousand, IU. the drug is due to an increase in the number of large follicles, the growth of which was activated by gonadotropin.

Mass appearance of large follicles in the first 3-4 days after the application of 4 thousand IU. gravogormone indicates that the level of estrogen during this period is influenced by large follicles, the growth and maturation of which was accelerated by the drug. Subsequently, these follicles undergo atresia.

Under the influence of a high dose of gravogormone (5-6 thousand m.u.), large follicles undergo luteinization and the concentration of total estrogens decreases for a short time. The subsequent increase in the content of estrogens, in our opinion, reflects the growth of small follicles unaffected by luteinization, which reach the peak of their secretory activity on days 5-7 of the study. However, in this case, they do not ovulate, but undergo atresia.

Thus, gravohormone in a dose of 2-3 thousand IU. has a luteotropic effect, causes a pronounced increase in the concentration of progesterone without pathological changes in the follicles and hormonal disorders in the blood. From the data obtained, it can be concluded that gravogormone in a dose of 2-3 thousand IU. can be used in the stage of inhibition of the sexual cycle in order to activate proliferative and secretory processes in the forming corpus luteum.

3.3. Influence of gravohormone on the thyroid and gonads during ovarian hypofunction in cows

The results of the study showed that in case of hypofunction of the ovaries of cows, the introduction of gravogormone provides a gonado and a thyroid-stimulating effect. In this case, the nature of morphofunctional changes in the studied organs and the manifestation of the sexual cycle were determined by the administered dose of the drug **(Table 15).**

So, after the introduction of 10 cows gravogormone in a dose of 2 thousand IU. the number of follicles in comparison with the control increased almost 3 times (2.3 per animal versus 0.8 in the control), however, the restoration of sexual function was not observed. The histological study of follicles showed that gravogormone in this dose provides in the first 4-7 days of the experiment the formation of a vascularized hyperplastically altered connective tissue membrane and secretory active granulosis. However, on the 12th day after the application of the drug, the connective tissue cells of the membrane of large and medium-sized follicles underwent a fibrotic change, and granulosis with an oocyte underwent dystrophy.

Under the influence of gravohormone in this dose, a slight increase in the height of the follicular epithelium with the transformation of the cytoplasm into a light substance was noted in some areas of the thyroid gland. At the same time, single vacuoles appeared in the marginal colloid.

Under the influence of gravohormone at a dose of 3 thousand IU. a more pronounced reaction from the ovaries and thyroid gland was established. In this subgroup, in contrast to the previous one, out of 15 in 8 cows within 3-6 days the stage of excitement of the sexual cycle began. The ovaries of five of these cows, extirpated on day 4 after the administration of gravogormone, contained 1-2 large follicles close to ovulation, or one ovulated graafian vesicle, as well as 2-4 medium-sized ones, and many small tertiary follicles with hyperplastically altered connective tissue. shell. Cow # 0166 was ovariectomyroaned on the 7th day after administration of the drug. Her ovaries contain a large follicle (1.3 cm in diameter), 3 medium-sized and many small follicles. Cow No. 97363, ovariectomized on the 26th day of the experiment, had 2 yellow bodies in the ovaries, one of which was in a state of involution, and the second was in the initial stage of formation. Animal No. 07423 was killed on the 21st day of the experiment. Its ovaries contain a corpus luteum in a state of involution, one large, two medium-sized and many small follicles.

Of the remaining 7 cows, three of the stages of arousal of the sexual cycle began on the 11-13th day with the formation of one corpus luteum in the ovaries. In the gonads of these animals, extirpated on day 26, that is, 12-14 days after ovulation of the follicles, yellow bodies with large luteal cells and vacuolated cytoplasm are installed. At the same time, luteal cells of a smaller size, irregular shape with oxyphilization or lysed cytoplasm appeared, which indicates the development of the initial processes of involution of the corpus luteum.

In four cows, the stage of arousal of the sexual cycle did not occur, although the activation of follicular growth followed by their atresia was determined. Moreover, obliterative atresia developed in small follicles, and cystic atresia in large follicles. Under the influence of gravogormone in this dose, changes in the thyroid gland are most pronounced in animals during ovulation of follicles and functioning of the corpus luteum. This was characterized by an increase in vascularization, an increase in the thyroid epithelium and its abundant secretion by the beginning of involution of the corpus luteum, the secretion of thyroid cells ceases, and the colloid acquires an oxyphilic color and a homogeneous structure. In this subgroup of animals, as in the previous one, there are cows with cystic changes in the thyroid glands.

Thus, the gravohormone in a dose of 3 thousand IU, although it stimulates the growth of follicles, does not in all cases ensure their maturation and ovulation. As a result, not all animals exhibit sexual cycles in the first 6 days of the experiment. At the same time, due to the use of the drug in these doses, there is a manifestation of sexual cycles at a later date. Both in the first and in the second case, changes in the specific cellular structures of the ovaries are similar to the transformations previously described in intact animals during the period of follicle ovulation, formation, functioning and involution of the corpus luteum.

With the introduction of gravohormone at a dose of 4 thousand IU. more significant functional and morphological changes occurred in the ovaries in the thyroid gland. Of the 7 experimental cows in the first three days, the stage of arousal of the sexual cycle occurred in four, on the sixth in two, and on the twelfth day in one cow.

In three animals, ovariectomized on the 4th day after administration of the drug, development of one yellow body was observed in the ovaries, and also contained 1-2 large, 2-4 medium-sized and many small follicles. In non-ovulated follicles, the cells of the connective tissue membrane were in a state of proliferation, and granulosis lost radial differentiation and underwent desquamation. The proliferation of connective tissue cells from the tunica albuginea and their differentiation around primordial and secondary follicles were activated. In the thyroid glands of these animals, the follicular epithelium passed into a state of hypersecretion, and the colloid underwent deep dissolution, which indicates an increase in the function of this endocrine organ.

In one animal No. 07441, killed on the 12th day of the experiment (6 days after the onset of the stage of excitement of the sexual cycle), a formed corpus luteum with large luteal cells was found in the right ovary, one cystic follicle (1.4 cm in diameter) with reduced granulosis and a fibrous connective tissue sheath, and in the left ovary there are 2 large, 1 medium-sized and many small follicles. The thyroid gland was in a state of hypersecretion. In the second animal (No. 07440), the stage of excitation of the sexual cycle was established on the day of slaughter (on the 12th day after the introduction of gravogormone). Visually, there are 2 large, 3 medium-sized and many small follicles in the ovaries. On sections, large and medium-sized follicles are represented by a hyperplastically altered connective tissue membrane and granulosis in a state of desquamation.

Cow No. 07427, killed on day 21 of the experiment (14 days after ovulation), had a yellow body in the initial stage of involution and 12 small follicles in the right ovary, and 1 large, 2 medium-sized and 14 small follicles in the left ovary. the thyroid gland epithelium is low, cubic, colloid oxyphilization is expressed.

In animal No. 07371, the stage of excitation of the sexual cycle occurred on the 4th and 26th days after the administration of gravogormone. Macroscopically, a corpus luteum in a state of involution, a large follicle 1.8 cm in diameter and 8 small follicles were found in the right ovary. The left ovary revealed 2 atretic bodies, 3 medium-sized and 19 small follicles. In sections, the corpus luteum is represented by luteal cells with lysed cytoplasm and pycnostically altered nuclei. Blood vessels in a state of obliteration and desolation. A large follicle is characterized by a hyperplastic and hypertrophic altered connective tissue membrane, while granulosa loses radial differentiation and undergoes desquamation. Of the three medium-sized follicles, two have a differentiated secretory active granulosis and a proliferating, well-vascularized flow, and one - reduced granulosis and fibro-degenerated connective tissue membrane. The sections showed many primordial, secondary and tertiary follicles at various stages of development. The thyroid gland is dominated by a polymorphic colloid with pronounced marginal oxyphilization, the epithelium is cubic and cylindrical.

Thus, gravohormone at a dose of 4 thousand IU. has a more pronounced gonadotropic effect, providing in most animals in the near future the growth and maturation of follicles, their ovulation and the development of the corpus luteum. Under the influence of the drug at this dose, the manifestation and induction of sexual cycles is observed.

Under the influence of gravohormone, administered at a dose of 5 thousand IU, the stage of excitation of the sexual cycle in all 8 cows began on the 3rd-6th day. In four animals killed on the 21st day from the beginning of the experiment or on the 14-16th day after ovulation of the follicles, macroscopically one corpus luteum, 1-2 large, 2-3 medium-sized and many small follicles were established in the ovaries. On sections, the corpus luteum is well vascularized, the luteal cells are large with rounded nuclei, and the cytoplasm is vacuolated. In the intercellular spaces, gaps of the light substance are visible. There are areas of the corpus luteum with initial signs of involution.

In most large and medium-sized follicles, granulosis is reduced, and the connective tissue membrane is fibrously changed. Proliferation of germ cells from the primordial epithelium with the formation of primary, secondary and tertiary follicles is noted.

The thyroid gland is represented by large and small follicles. In the first, the epithelium is low cubic, in the second, it is high cubic or cylindrical. The marginal colloid in many follicles or in some of its parts is vacuolated, lagging behind the thyroid epithelium. There are follicles with a completely dissolved colloid, which has a light-basophilic color, fibrous or coarse-grained structure. In the interfollicular space, large lacunae of light or basophilic substance are visible.

In the remaining four animals, on days 19-25 after the administration of gravogormone, a repeated manifestation of the stage of arousal of the sexual cycle was established. In the ovaries of cow No. 07429, extirpated on the 21st day from the beginning of the experiment, 2 corpus luteum in a state of involution, the formation of which occurred in the first sexual cycle, and one in a state of development, were revealed. On histological sections, the parenchyma of the corpus luteum from the first sexual cycle is represented by small, irregularly shaped luteal cells with oxyphilic or lysed cytoplasm and pyknotic nuclei. The young corpus luteum is formed from the proliferating cells of the connective tissue membrane and the surrounding ovarian tissue. This process is accompanied by increased vascularization. In small tertiary follicles obliterative atresia prevails with the formation of atretic bodies,

In the ovaries of cow No. 07414, extirpated on the 5th day after the manifestation of the repeated stage of arousal of the sexual cycle, a developing corpus luteum was found, as well as a corpus luteum in a state of involution, 1 large, 7 medium-sized and 32 small follicles. In large and medium-sized follicles, granulosis undergoes desquamation, and the cells of the connective tissue membrane undergo lysis and fibrous replacement.

In most follicles of the thyroid gland of these animals, the marginal colloid is dissolved, resorbed, the thyroid epithelium is in a state of hypersecretion. In the ovaries of two cows killed on the day of the manifestation of the repeated stage of excitation of the sexual cycle, one corpus luteum in a state of involution, 1-2 large and medium-sized ones, as well as many small follicles were found. In the thyroid glands, an increase in the height of the epithelium is noted with the transformation of the apical sections of the cytoplasm into a light substance and their rejection into the marginal colloid. In this regard, single vacuoles appear in the latter. Revealed proliferating foci in the follicular and interfollicular epithelium.

Consequently, under the influence of gravohormone at a dose of 5 thousand IU. in the first 6 days of the experiment, the stage of excitation of the sexual cycle with the formation of one, and in some animals two, yellow bodies is restored in all animals. This is accompanied by an activation of the thyroid gland function. It is also characteristic that the drug in this dose provides the manifestation of full repetitive sexual cycles.

After administration of the drug at a dose of 6 thousand IU. the first sexual cycle in all 10 experimental animals began on day 3-4. Of the five cows killed on days 4-7 of the experiment, four ovulated from 2 to 7 follicles, and one had 9 large, 5 medium-sized and 50 small follicles.

On histological sections from fragments of ovulated follicles, proliferation of connective tissue cells with their differentiation into luteal cells is noted. Remnants of granulosis are visible between the forming lobes of the corpus luteum. In non-ovulated, both large and small follicles, the connective tissue membrane is in a state of proliferation, resulting in the formation of atretic bodies and luteal cysts. Granulosis is reduced. Proliferation of connective tissue cells from the side of the tunica albuginea and movement of primordial and secondary follicles deep into the cortical substance of the ovary are expressed. In the thyroid glands of these animals, the thyroid epithelium is in a state of hypersecretion, there is a deep dissolution of the colloid and its resorption into the interfollicular lymphatic bed.

In the ovaries of animal No. 07433, killed 21 days after the injection of gravogormone, two luteal brushes are installed. On sections, cyst cells have a flat shape, the cytoplasm is lysed, and the nuclei undergo pyknosis and are located in the fibrous structure. The vessels are obliterated. Such histological changes indicate the involution of luteal cysts. In most follicles of the thyroid gland, the marginal colloid is resorbed, the epithelium is thinned, proliferation of the thyroid epithelium and the formation of small follicles are noted.

Cow No. 7417 had a second sexual cycle on the 22nd day after the administration of gravogormone. After her slaughter on the 25th day of the experiment, two yellow bodies in a state of involution were found in the right ovary, and a forming corpus luteum and many atretic bodies in the left ovary. The thyroid gland is predominantly represented by large follicles with low cubic epithelium. In many follicles, the marginal colloid is resorbed and lags behind the epithelial cells. There are small follicles with secretory active epithelium and vacuolated colloid.

All 8 cows, which were injected with gravohormone at a dose of 7 thousand m, that is, on the 2-3rd day, began the stage of excitement of the sexual cycle. In two of these animals, killed on day 4 of the experiment, five follicles ovulated in the ovaries, and the rest underwent luteinization. The ovaries of cows are characterized by increased proliferation of connective tissue cells from the side of the tunica albuginea and the movement of dystrophically altered primordial follicles deep into the cortex. The thyroid glands of these cows were characterized by a hyperfunctional state, which was manifested by abundant secretion of cells and deep dissolution of the colloid.

In the ovaries of two animals killed on the 12th day of the experiment, 3-4 yellow bodies, 1-2 large luteinized follicles and many atretic bodies were established. In large luteinized follicles, the connective tissue membrane has acquired a fibrous structure. In most follicles of the thyroid gland, the marginal colloid is dissolved and resorbed, the epithelium is thinned.

After the slaughter of two cows on the 21st and 25th day of the experiment, 2-3 yellow, 5-7 atretic bodies, as well as 1-2 large, 2-3 medium-sized and up to 22 small follicles were found in the ovaries. The corpus luteum in a state of involution. In large follicles, granulosis is reduced, and the connective tissue membrane has acquired a fibrous structure. Follicles of medium and small size with well-developed secretory active granulosis and hyperplastically altered connective tissue membrane. Primary and secondary follicles are observed, as well as single oocytes migrating from the primordial epithelium to its base and tunica albuginea. The thyroid glands of these animals are represented by follicles of irregular shape, made by oxyphilic and basophilic colloids. Moreover, colloid oxyphilization begins from its marginal areas adjacent to the follicle wall.

In cow No. 07406, on the 22nd day after the administration of gravogormone, a repeated stage of excitation of the sexual cycle was established. In her ovaries, extirpated on the 26th day of the experiment, 3 corpus luteum from the first sexual cycle in a state of involution, a new corpus luteum was forming, as well as 8 atretic bodies, 3 large, 1 medium-sized and 14 small follicles were found. Small and medium-sized follicles were in a state of luteinization, and large follicles were cystically altered with reduced granulosis and fibrously altered connective tissue sheath. The follicles of the thyroid gland for the most part have an irregular shape, in which the marginal colloid is resorbed, and the rest is characterized by polymorphic color and structure, the epithelium is low cubic. In small follicles, the thyroid epithelium is in a state of hypersecretion.

Gravohormone in a dose of 8 thousand IU, administered to three cows, in all animals caused the manifestation of the stage of excitation of the sexual cycle on days 2-3 of the experiment. After their slaughter on the 4th day of drug administration, significant pathological changes were established in the ovaries, characterized by hemorrhage into the follicles, continuous luteinization and massive formation of luteal cysts. The connective tissue elements of the ovarian cortex are in a state of proliferation. At the same time, the hyperplasia of these cellular structures from the side of the tunica is especially enhanced with a reduction of oocytes and primordial follicles, and only the rudimentary epithelium retained the ability to differentiate germ cells with their subsequent migration into the tunica albuginea.

The established pathological changes in the ovaries were intensified even more under the influence of gravogormone in a dose of 9 thousand IU. Thus, animal No. 97506, killed on the 7th day of the experiment, had 14 small yellow bodies and 5 luteinized hemorrhagic follicles in the ovaries (Fig. 21 a). Moreover, the manifestation of the stage of arousal of the sexual cycle was not observed. The thyroid gland of this animal was in a state of hyperfunction, which was characterized by rejection of the apical portions of the cytoplasm in thyroid cells, deep dissolution of the marginal colloid and desquamation of thyrocytes **(Fig. 21 b).**

Thus, for all animals that were injected with gravoghormone at a dose of 6 thousand mf. and above, excessive growth stimulation, ovulation and luteinization of follicles, the formation of luteal cysts, and hemorrhage into the follicles are characteristic. Under the influence of gravohormone in these doses, proliferative processes in the connective tissue elements of the ovarian cortex are strongly activated, and luteinization of the tertiary and reduction of primary and secondary follicles is also noted. It is the insufficient maturity of tertiary follicles and their rapid luteinization that can explain the absence of the stage of excitation of the sexual cycle in cows after administration of the drug at a dose of 9 thousand IU. Such a reaction on the part of specific cellular structures of the ovaries to large doses of gravogormone leads to the complete disappearance of follicles.

However, subsequently, due to the cytogenesis of germ cells from the rudimentary epithelium and the formation of new follicles, the generative function of the ovaries is restored. Under the influence of these doses of gravogormone, the process of hypersecretion develops in the epithelium of the thyroid gland, giving way to functional depletion of the thyroid structures. All this testifies to the inexpediency of using the drug in a dose of 6 thousand IU. and higher with hypofunction of the ovaries of cows. Based on the studies carried out, it can be concluded that the optimal dose of gravogormone for hypofunction of the ovaries of cows is 4 thousand IU, which provides a moderate activation of follicular growth and their ovulation, the manifestation of direct and induced reproductive cycles with physiologically normal stimulation of the thyroid gland function. This dose of the drug provides not only growth,

The table shows that in the first two days of the formation of the corpus luteum, the smallest diameter of luteal cells (7.57 ± 0.30 μ) and the volume of nuclei (179.3 ± 10.2 μ3) are observed when the variation curve is located on the left side of the coordinate system (Graph 3). On the 4-5th day after ovulation, there is a significant increase in the diameter of luteal cells (21.4 ± 0.73 microns) and the volume of their nuclei (377.0 ± 20.0 microns). Moreover, 66.3% of luteal cells and 57.4% of nuclei are located in the second and third groups, and the variation curve shifts to the right. The largest size of luteal cells (21.20 ± 0.60 μ) and the volume of nuclei (461.7

±14.3 microns) was set on the 7-8th day of ovulation, when 97.7% of the cells had a diameter from 18 to 47 microns and 81.3% of nuclei - from 310 to 1016 micr

Schedule 3

VARIATION CURVES OF THE DIAMETER OF LUTHEIN CELLS AND THE VOLUME OF THEIR NUCLEI AFTER INJECTION OF GRAVOHORMONE (5 thousand units) IN HYPOFUNCTION OF THE OVARIES OF COVES

No. qu.	cell class boundaries
one	3-7
2	8-12
3	13-17
four	18-22
five	23-27
6	28-32
7	33-37
eight	38-42
nine	43-47
No. qu.	kernel class boundaries
one	7 - 107
2	108-208
3	209-309
four	310-410
five	411-511
6	512-612
7	613-713
eight	714-814
nine	815-915
10	916-1016

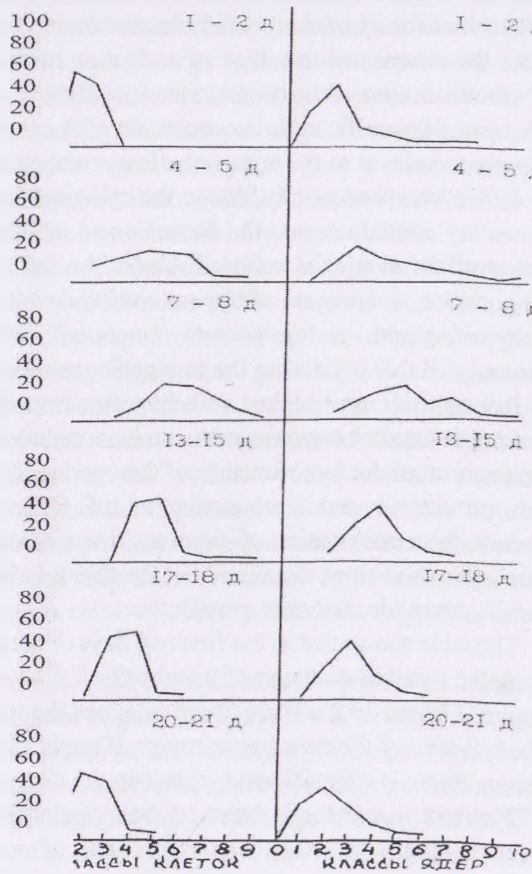


Table 28

Cyto- and cariometric characteristic of lutein cells of yellow bodies formed under the influence of gravogormona, introduced during hypofunction

Timing of cow ovario-tomi from the beginning of ovulation	Medium-diametry (m)	Number of cells of different groups as a%			Average core volume (mc3)	Group cores%		
		I	II	III		I	II	III
		3-17 (мс^3)	18-32 (мс^3)	33-47 (мс^3)		7-309 (мс^3)	310-612 (мс^3)	613-1016 (мс^3)
1-2	7,57±0,30	100,0	-	-	179,3±10,2	86,0	13,0	1,0
4-5	21,40±0,73	33,7	60,3	6,0	377,0±20,0	42,7	44,7	12,7
7-8	29,20±0,60	2,3	68,0	29,7	461,7±14,3	18,7	60,0	21,3
13-15	23,60±0,33	3,3	96,0	0,7	355,3±10,8	32,7	65,7	1,7
17-18	18,20±0,37	46,0	54,0	-	272,3±7,9	69,7	30,3	-
20-21	12,33±0,27	94,7	5,3	-	188,3±8,7	86,7	13,3	-

In subsequent time, the studied morphometric indicators are somewhat stabilized with a minor decrease in the diameter of lutein cells (23.60 ± 0.33) and their nuclei (355.3 ± 10.8 Mc3) for 13-15 days compared with 7-8 Day of the functioning of the yellow body. After 17-18 days after ovulation, the diameter of lutein cells decreases to 18.20 ± 0.37 MK, and their nuclei to 272.3 ± 7.9 μ3. On 20-21, the ovulation day is observed a significant decrease in the size of the cells (12.33 ± 0.27 MK) and the volume of nuclei (188.3 ± 8.7 MK). At the same time, 94.7% of cells have a diameter from 3 to 17 MK and 86.7% of the nuclei are represented by a volume of from 7 to 309 MK3, and the variation curve moves to the left part of the coordinate system, which is associated with the involution of the yellow tel.

Special scientific interest is a comparison of the resulting morphometric changes in the yellow bodies arising under the influence of the gravogormon (Table 28) with changes in the lutein cells of yellow bodies of the sexual cycle of intact animals (Table 6). It is characteristic of the fact that the largest diameter of lutein cells and their nuclei are observed in yellow bodies formed after the administration of the gravogormon.

Higher morphometric indicators indicate the more active functional state of these yellow bodies in comparison with the yellow bodies of the sexual cycle of intact animals. In this regard, gravogormon is a highly efficient biological gonadotropic drug that provides both growth, ripening and ovulation of follicles and the active functioning of the yellow body, which gives the basis to recommend its use as a therapeutic agent in the hypofunction of cows in dose of 4 thousand meters. Under the influence of this dose-magormon (Table.29), the cows with the ovarian hypofunction cows uve-incompass the content of an inorganic iodine by 1.90 μg% (7.00 ± 0.73 versus 5.10 ± 0.49 μg%), the level of SB to 1.10 μg% (5.50 ± 0.73 versus 4.40 ± 0.31 μg%), and also 3 times the content of iodine in milk increases (from 33.0 ± 1.23 to 91.0 ± 7.87 μg / l; p <0.001), which should be addicted to the dependence on the activation of the function of the thyroid gland.

Table 29

Effect of gravogormmon on iodine and protein levels in the blood and milk of cows with ovarian hypofunction (M ±m)

Reveals	Before the introduction	On the 6th day after the introduction
Blood serum		
Inorganic iodine (MCG%)	5,10±0,49	7,00±0,73
SB (MCG%)	4,10±0,31	5,50±0,73
Common protein (%)	7,33±0,10	8,02±0,09ˣ
Albumin (%)	3,74±0,08	3,74±0,14
Alpha Globulins (%)	1,11±0,05	1,26±0,06
Beta globulins (%)	1,19±0,16	1,37±0,21
Gamma Globulin (%)	1,29±0,04	1,65±0,01ˣ
Coefficient a / g	1,05±0,05	0,88±0,09
Milk		
Inorganic iodine (μg / l)	33,0±1,23	91,0±7,87ˣ
note:x - P< 0, 01-0,001		

This is regulated by protein organism. In particular, the protein level of 0.69% increases (8.02 ± 0.09 opposite to 0.01 ± 0.10; p <0.01) mainly due to globulin fractions, namely, the content of gamma globulins (on 0 , 36%, p <0.001) and alpha globulins (0.15%).

Consequently, when the ovarian hypofunction is gravogormon in a dose of 4 thousand meters. Adjusts the function of the thyroid gland and normalizes protein metabolism, which is accompanied by the restoration of the generative and hormonal function of the ovaries and the manifestation of the full-fledged stage of excitation of the sexual cycle.

In addition, we studied the dynamics of the concentration of genital hormones in the blood and morphological changes in the ovaries under the influence of the gravogormon introduced by cows with gonad hypofunction. The results of radioimmunological studies of the blood of cows with the pitipofunction of ovaries after the introduction of the gravogormon on the content of progesterone are presented in Table 30.

These data indicate that with the introduction of 2 thousand m. The drug is already 3-4 days. The level of progesterone increases by 2 times (from 0.31 ± 0.09 ng / ml to 0.61 ± 0.03 ng / ml, p <0.05), and to 9-12 days 2.3 times (up to 0.72 ± 0.19 ng / ml).

A more pronounced activation of the progesterone secretion is observed after the administration of gonadotropin in a dose of 3 thousand meters. The hormone concentration increased from 0.19 ± 0.07 ng / ml at the beginning of the experience to 0.48 ± 0.20 ng / ml (152 , 6%) for 1-2 day and 0.49 ± 0.11 ng / ml (157.9%) for 3-4 days of observation. By 5-7 days, due to the ovulation of follicles and the formation of yellow bodies in individual animals, the concentration of the steroid rises by 5.7 times and reaches 1.09 ± 0.45 ng / ml.

After applying the drug at a dose of 4 thousand meters In the blood of animals, after 1-2 days, an increase in the concentration of progesterone was observed by 1.7 times (from 0.42 ± 0.08 ng / ml to 0.73 ± 0.02 ng / ml). In the future, due to ovulation, the formation and development of yellow bodies, the concentration of this steroid continues to rise to 9-12 observation day of 1.88 ± 0.11 ng / ml. This indicator is above the initial data by 4.7 times (p <0.001).

Introduction of gonadotropin at a dose of 5-6 thousand IU. provides a sharp increase in progesterone levels. Moreover, if on days 3-4, 5-7 of the experiment, the steroid content increases 4-8 times (P <0.05), then on days 9-12 of the study, in connection with polio, the level of the hormone exceeds the initial values (0 , 19 ± 0.05 ng / ml) 55 times and is 10.38 ± 3.48 ng / ml (P <0.02).

Table 30

Change in progesterone concentration in peripheral blood plasma after the introduction of gravogormone to cows with ovarian hypofunction (M±m, ng/ml)

Dose of the drug, thousand m.e.	Number of animals	Days of experience				
		day of the drug administration	1-2	3-4	5-7	9-12
2	5	0,31±0,09	0,43±0,09	0,61±0,08	0,54±0,11	0,72±0,19
3	4	0,19±0,07	0,48±0,20	0,49±0,11	1,09±0,45	-
4	4	0,42±0,08	0,73±0,02	0,94±0,29	1,11±0,75	1,88±0,11
5-6	7	0,19±0,05	0,79±0,42	0,62±0,14	1,55±0,37	10,38±3,48

The results of studies on the change in the content of total estrogens in the blood plasma of cows after the use of gonadotropin are presented in Table 31. It was found that the introduction of 2 thousand IU. the drug causes a decrease in the concentration of steroids within 1-2 days by 24%. However, starting from 3-4 days, the concentration of hormones increases again and reaches 54.0 ± 10.29 pg / ml on days 5-7 of observations, which is 49 more than the initial data (36.15 ± 7.0 pg / ml), 37%.

Under the influence of gonadotropin at a dose of 3 thousand IU. in the blood of experimental cows, the maximum content of hormones (75.7 ± 17.7 pg / ml) is recorded on the 3-4th day of research. By days 5-7, the amount of steroid decreases slightly and is 58.3 ± 0.5 pg / ml, but remains higher than the initial level by 41.5%.

Activation of follicular growth after the introduction of 4 thousand IU. the drug causes a change in estrogen secretion, similar to the changes in the previous group.

Table 31

Dynamics of total estrogens in the peripheral blood of cows with ovarian hypofunction after the introduction of gravogormong (M±m, pg/ml) The dynamics of total estrogens in the peripheral blood of cows with ovarian hypofunction after the introduction of gravogormmon (M±m, pg/ml)

Dose of the drug, thousand m.e.	Number of animals	Days of experience				
		day of the drug administration	1-2	3-4	5-7	9-12
2	5	36,2±7,0	27,5±6,9	34,7±11,9	54,0±10,3	36,9±7,6
3	4	42,1±17,6	48,6±13,7	75,7±17,7	58,3±0,5	-
4	4	36,9±6,7	-	41,4±9,8	54,1±26,3	54,7±6,7
5-6	7	29,6±4,6	73,5±18,6	51,2±7,8	95,7±54,3	54,6±8,5

The concentration of hormones gradually increases from 36.9 ± 6.7 pg / ml at the beginning of the experiment to 54.1 ± 26.3 pg / ml on days 5-7 of the study. Subsequently, the level of steroids remains at the same level and is 54.7 ± 6.7 pg / ml on days 9-12 of observations, which is 48% higher than the initial data.

When applying 5-6 thousand m.u. gonadotropin, the amount of total estrogens in the blood of cows increases sharply and is kept at a high level throughout the entire period of research. In this case, the maximum content of hormones is recorded on days 1-2 and 5-7 of observation, when their concentration is 73.5 ± 18.6 pg / ml and 95.7 ± 54.3 pg / ml, respectively. Although on days 3-4 and 9-12 of the experiment, the level of total estrogens is slightly lower, it is also 1.7 and 1.8 times ($P <0.05$) higher than the initial data (29.6 ± 4.6 pg / ml).

Gonadotropin also has a pronounced effect on the dynamics of estradiol-17 beta (Table 32). After the introduction of gonadotropin at a dose of 2 thousand IU. in the blood of animals, after 1-2 days, there is an increase in the concentration of estradiol-17 beta by 1.7 times (from 9.3 ± 4.8 pg / ml to 15.8 ± 2.3 pg / ml), which reaches maximum values on days 9-12 of the experiment (39.3 pg / ml). The hormone level during this period is 4.2 times higher than the initial data.The content of estradiol-17 beta in the first 1-2 days after application of 3 thousand IU the drug is reduced by 58.6%. Then the level of the hormone begins to increase gradually and is 10.2 ± 6.1 pg / ml by 3-4; 15.4 pg / ml on days 5-7, exceeding the initial concentration (9.4 ± 3.2 pg / ml) by 10.9 and 63.8%, respectively.

Table 32

Change in estradiol-17 beta in the plasma of peripheral blood of cows with ovarian hypofunction after the introduction of gravogormong (M±m, pg/ml)

Dose of the drug, thousand m.e.	Number of animals	Days of experience				
		day of the drug administration	1-2	3-4	5-7	9-12
2	5	9,3±4,8	15,8±2,3	15,9±4,4	20,1	39,3
3	4	9,1±3,9	3,9±2,2	10,2±6,1	15,4	-
4	4	9,0±2,6	-	12,9	63,3±5,6	24,4±9,6
5-6	7	6,8*1,1	15,3±2,8	26,8±6,5	8,1±2,0	10,6±2,3

Under the influence of gonadotropin at a dose of 4 thousand IU. there is an increase in the content of estradiol-17 beta up to 5-7 days of research. During this period, the level of the hormone in the blood is 63.3 ± 8.6 pg / ml, which is 7 times (P <0.05) more than at the beginning of the experiment. Subsequently concentration. The steroid decreases slightly and on days 9-12 is 24.4 ± 9.6 pg / ml, which is 170.6% higher than the initial data.

Introduction of gonadotropin at a dose of 5-6 thousand IU. causes an increase in the content of estradiol-17 beta in the blood of experimental cows up to 3-4 days of research, inclusive. At this time, the level of the hormone increases from 9.6 ± 3.1 pg / ml at the beginning of the experiment to 15.3 ± 2.8 pg / ml for 1-2 and 26.8 ± 6.5 pg / ml for 3-4 days , which is 59.4% and 179.2% (P <0.05), respectively. On days 5-7 and 9-12, the amount of the hormone in the blood of cows sharply decreases and equals 8.1 ± 2.0 and 10.6 ± 2.3 pg / ml.

These changes in the dynamics of ovarian hormones are in direct proportion to the structural transformations occurring in the ovaries under the influence of gonadotropin

Table 33

Effect of gravogormmon on active gonad structures in the hypofunction of the ovaries of cows

Dose of the drug, thousand m.e.	Duration of opita in days	To live	Active ovarian structures			
			yellow bodies		Follicles	
			altogether	for 1 alive	altogether	1 alive.;
2	3-4	2			6	3,0
	9-12	3	1	0,3	8	2,7
3	3-4	3	2	0,7	8	2,7
	9-12	4	1	0,25	14	3,5
4	3-4	3	3	1,0	6	2,0
	9-12	6	7	1,1	19	3,2
5-6	3-4	1	1	1,0	3	3,0
	9-12	8	26	3,3	26	3,3
control	-	7	-	-	12	1,7

So, gonadotropic drugs in a dose of 2-3 thousand IU. cause a moderate stimulation of follicle growth, as a result of which, already on the 3-4th day of the experiment, their number increases and averages 2.7-3.0 per animal against 1.7 in the control. A histological examination of the ovaries found that on the 3-4th day of observations, when an increase in the content of progesterone and estrogen is recorded in the blood, vascularization, proliferation and hypersecretion increase in the internal flow of large and medium-sized follicles, with simultaneous proliferation and hypersecretion of granulosis. This activates the growth of secondary and small tertiary follicles. By 9-12 observations, the number of medium-sized and large follicles increases to 2.7-3.5 per animal, but most of them do not reach ovulation maturity. That is why the number of corpus luteum in the ovaries remains low.

A more pronounced follicle-stimulating effect is observed after the use of gonadotropin at a dose of 4 thousand IU. Under the influence of this dose, on the 6th day of the experiment, macroscopically in the ovaries of cows, an average of one ovulating and two large follicles were established. The formation of the corpus luteum was histologically confirmed. Large and medium-sized follicles were in a state of obliterative atresia. At the same time, gonadotropin in this dose ensures not only the maturation and ovulation of large follicles present in the ovary, but also causes a moderate growth of small follicles, which leads to the formation of up to 3.2 large follicles per day on the 9-12th day of the experiment. animal.

When the drug is administered at a dose of 5-6 thousand IU. in the ovaries of cows, the number of corpus luteum and large follicles increased sharply. However, if on 3-4 days in some animals ovulation of one and the formation of up to three large follicles was noted, then on days 9-12 of the experiment the phenomenon of superovulation was observed in most other cows and the formation of an average of 3.3 yellow body and 3.3 large follicles. It was found that structural changes in single and multiple corpus luteum indicate two periods of their formation. The corpus luteum formed in the first period, which falls on the beginning of the experiment (up to 3-4 days inclusive), is characterized by hyperplasia and lysis of most luteal cells, while in the corpus luteum, which appeared 5-7 days after the administration of the drug, the bulk of well-vascularized tissue is represented by large single and binuclear cells, most of which are in a state of hypersecretion. It should be noted that animals whose follicles ovulated in the first period have one, at most two yellow bodies, while in cows in which ovulation occurred in the second period, the formation of 4 to 26 yellow bodies is recorded. Secondary and small tertiary follicles undergo obliterative atresia. In follicles of medium and large sizes, hypersecretion, lysis and desquamation of granulosis are noted. The connective tissue membrane is well developed, the cells are proliferative and secretory active, most of them undergo luteinization.

Thus, the administration of gonadotropin FFA to cows with ovarian hypo-function has a pronounced effect on morphofunctional changes in the gonads and the state of secretion of sex steroids.

At the same time, gonadotropin in a dose of 2-6 thousand IU, activating the specific cellular structures of the gonads (interstitial cells of the cortex, thecaluteal cells of large atretic follicles), causes an increase in the level of progesterone in the first days of research. Subsequent vacuolization and lysis of thekaluteal cells cause a decrease in the content of the steroid, however, due to ovulation of follicles and the formation of corpus luteum, the concentration of progesterone rises again on days 9-12 of observation.

The level of estrogen under the influence of 2-4 thousand m.u. the drug depends on the restructuring of steroid-producing structures of both large and small follicles, the growth of which is activated by gonadotropin. The introduction of the drug at this dose enhances the proliferative and secretory processes in the follicles, increases their number and causes ovulation in individual animals by the 3-4th day of research. The resulting change in the level of sex hormones is probably associated mainly with structural changes in large follicles, where during this period there is a slowdown or even prevention of atresia. Along with this, the activation of the growth of secondary and small tertiary follicles, which contributes to an increase in the number of large follicles by days 9-12 of the study, by more than 2 times, apparently affects the level of estrogenic hormones from 3-4 to 9- 12 days of experience.

It should be noted that the dose of gonadotropin is 2-3 thousand IU. causes maturation and ovulation of follicles in individual animals, while under the influence of 4 thousand IU. ovulation and the formation of corpus luteum are observed in all animals.

After the introduction of gonadotropin at a dose of 5-6 thousand IU. in the ovaries of cows there is an increase in the luteinization of large, as well as the activation of row.

A clear regularity is observed in the exchange of inorganic magnesium, which is manifested in a significant increase in its content in the blood in the first days of the experiment, followed by a sharp decrease in it in the middle of the experiment and a steep rise towards the end of the study. Moreover, in cows with ovarian hypofunction, fluctuations in the level of magnesium are more pronounced (41.2%, 37.5%, 104.8%) than in animals with functioning corpus luteum (5.6%, 22.2 and 4.5%).

The administration of gonadotropin to cows with ovarian hypofunction provides them with a significant increase in cholesterol levels (61.2, 39.7 and 45.0%, respectively, over the days of the experiment) in comparison with animals with involution of the corpus luteum (18.1, 17.1, 13.5%) In this regard, the tested dose of gonadotropin during involution of the corpus luteum should be considered somewhat overestimated.The level of beta-lipoproteins in all series of the experiment increased in the first days of the experiment to 67.0%, followed by a decrease in their content by the end of the experiment to 5.5%.

Changes in carbohydrate metabolism are quite natural, especially in animals with ovarian hypofunction, manifested in the first days of the experiment by an increase in glucose levels to 86.4%, followed by a decrease to 3.3% and an increase to 15.2% by the end. experience.As a result, it should be noted that gravogormone exerts both direct and through hormones of organs of smisheny an induced effect on metabolic processes, the nature of which depends on the initial state of sexual function. In this regard, when using gonadotropic drugs to regulate sexual function, it is necessary to take into account both its initial state and the initial background of metabolic processes, and if necessary, regulate it, bringing it to a physiological state.Due to the fact that in pregnant animals and with persistent yellow bodies in the ovaries, the changes are similar to the functioning yellow bodies of the reproductive cycle, this material is not analyzed, but will be limited to the data in **Table 15.**Considering that changes in the ovaries and thyroid gland under the influence of FFA turned out to be very similar to the previously described regularities after the introduction of gravogormone, in order to reduce the volume of material, these data are summarized .

Table 34.

Effect of SIC on cow's ovaries

Group	Functional state of the ovaries	Cow	A dose of pre-para-ta thous.	The timing came of the water-hunting in the day.	Active ovarian structures			
					yellow bodies		Follicles	
					altogether	1 live	altogether	1 live
1	Hypofunction of the ovaries	6	1	21	41	6,8	3	0,5
		3	2	18	44	5,5	4	0,5
		14	2,4	9	51	3,6	22	1,6
		24		5	87	3,6	39	1,6
		9	4	8	32	3,5	25	2,8
		7	5	2	23	3,3	36	5,1
		10	7	2	15	1,5	83	8,3
		3	12	-	-	-	4	8,3
control		7	no put	-	6	0,8	-	-
2	Involution-yellow bodies	3	2	4	213		5	1,66
		9	3	4	74	8,2	17	1,88
		9	4	3	40.5	4,5	22	2,5
control		9	no put		37	4,4	4	0,44
3	Yellow bodies of the sex cycle	4	2	-	17	4,2	-	-
		23	3	-	127	5,5	-	-
		4	4	-	125	31,2	-	-
		3	10	-	63	31,0	-	-
control		22	no put	-	84	3,8	-	-
4	Yellow Bodies of Pregnancy	4	2	мм	10	2,5	-	-
		11	3	-	89	8,1	-	-
		14	4	-	149	10.6	-	-
control		21	no put	-	76	3,6	-	-
5	Persistent yellow bodies	2	2	-	9	4,5	-	-
		6	3	18	29	4,8	1	0,1
		4	4	21	50	12,5	1	0,2
		7	5	13	97	13,8	3	0,4
		4	7	26	72	18,0	2	0,5
control		6	no put		26	4,3	-	-
6	Ovarian follicular cysts	4	4	мм	77	19,2	-	-
		2	5	-	45	22,5	-	-
		-	10	4	35	17,5	3	1,5
control		6	no put	71	11,8	-	-	-
7	Lutein-ovarian cysts	1	3	-	5	5	-	-
		1	5	5	11	11	1	1
		1	6	5	15	15	-	-
		1	7	-	21	21	-	-
		1	8	-	18	18	-	-

Conducting a comparative assessment of gravoghormone and FFA, it should be noted that the common thing for these drugs is the similarity of the mechanism of action, which manifests itself in the activation of proliferative processes in the connective tissue cells of the follicle membrane and the ovarian cortex, in the movement of follicles with proliferating tissue into the deeper cortical zone. gonadal substance, their growth and maturation with the phenomenon of ovulation and the formation of the corpus luteum, as well as in stimulating the function of the thyroid gland. In addition, gonadotropic drugs on the basis of a negative and positive relationship restore the gonadotropic and thyroid-stimulating function of the hypothalamic-pituitary system, which provides the manifestations of induced sexual cycles in 2-3 weeks from the beginning of the injection of hormones. In this regard, the interval between the first and second administration of gonadotropin should be at least three weeks. Gravohormone with an equivalent follicle-stimulating and ovulation effect differs from FFA in significantly smaller side effects on the ovaries, the absence of ballast proteins, is easily transported, persists for a long time and does not have anaphylactic properties, and therefore should take the lead in the practice of combating infertility and increasing the multiplicity of animals a place.

Thus, gravohormone and FFA deserve to be used for ovarian hypofunction, anovulatory reproductive cycles, follicular cysts and stimulation of multiple pregnancy in beef cows, and in combination with PGF-2 alpha for persistent corpus luteum, luteal cysts, as well as for synchronization of sexual heat in cows and heifers, which will be discussed below.

3.4. Morphofunctional changes in the ovaries and the dynamics of ovarian hormones in the blood of cows and heifers under the influence of PGF-2alfa

In experimental studies carried out by us (G.A. Cheremisinov, A.G. Nezhdanov, V.N.Karymov, 1983) on 165 animals at various stages of the sexual cycle, during pregnancy, with functional disorders of the ovaries, the effect of various doses of one PGF-2 alpha (estufalan) and in combination with gonadotropin FFA on the reactivity of ovarian cellular structures, the dynamics of sex hormones in the blood and the manifestation of the sexual cycle in order to develop indications and contraindications for the use of these agents for the regulation of sexual function.

At the first stage of work, PGF-2 alpha was used in doses of 500, 1000 and 2000 μg at the beginning of the stage of arousal of the sexual cycle, during ovulation and on 3-4 and 10-12 days from the moment of ovulation, as well as at different periods of pregnancy with subsequent material during the setting of the experiment and in the next 2, 3, 4, 6 and 9 days from its beginning with a constant clinical study. The dynamics of sex hormones in all experiments was studied in at least 8 animals.

It was found that injections of PGF-2alpha at the onset of the stage of excitation of the sexual cycle, when involution processes develop in the corpus luteum, additionally activate lysis in luteal cells, and therefore the level of progesterone in the blood plasma in the first 2-3 days of the experiment sharply falls. Lytic processes in the cells of the corpus luteum of the reproductive cycle are especially enhanced under the influence of PGF-2alpha at a dose of 2000 μg, which leads, after two days of the experiment, to a drop in the concentration of progesterone to 0.46 ± 0.07 ng / mp **(Table 35).** Under the influence of this dose of the drug, the level of estradiol-17 beta was significantly lower compared to both control and experimental animals that were injected with lower doses of PGF-2 alpha (Table 35). This is due to the fact that overestimated doses of the drug not only activate the lytic processes in the corpus luteum, but also cause lysis of thekaluteal cells in the formed follicles, in connection with which they undergo cystic atresia. This leads to the manifestation of defective sexual cycles, mainly anovulatory.

At the same time, PGF-2 alpha at a dose of 500 μg, reducing the time of involution of the corpus luteum and indirectly activating the growth of follicles, provides ovulation of follicles and the formation of corpus luteum in comparison with the control at an earlier date. Therefore, in such experimental animals, already on the 4th day of the experiment, the level of progesterone increases (0.71 ± 0.15 ng / ml) in comparison with the control (0.57 ± 0.19 ng / mp). On the 6-9th day of the experiment, both in the experimental after the introduction of PGF-2 alpha at a dose of 500 μg, and in the control animals, formed yellow bodies are determined in the ovaries.

Table 35

The dynamics of sex hormones in the blood plasma of cows under the influence of PGF-2 alpha, introduced at the beginning of the stage of sexual cycle arousal

Dose of the drug, mcg	Sex hormones	Day of experience					
		before the v-den. prepar	2	3	4	6	9
500	Progesterone ng / mp)	1,20±1,10	0,60±0,08 0 P 0,5	0,54±0,15 P 0,5	0,71±0,15 P 0,5	1,39±0,36 P 0,5	2,18±0,52 P 0,2
	Estradiol-17 beta (pg / ml)	34,50±11,7	49,5±9,25 P 0,2	32,5±12,5 P 0,5	41,8±12,5 P 0,5	21,3±16,0 P 0,5	23,75±11,5 P 0,5
1000	Progesterone (ng / ml)	1,3±0,2	0,58±0,25 P		0,6±0,18 P 0,02		
	Estradiol-17 beta (pg / ml)	30,75±13,25	0,05 43,75±10,0 P 0,5		46,5±11,25 P 0,5		
2000	Progesterone ng / ml	1,28±0,28	0,48±0,07		0,58±0,17P 0,02		
	Estradiol-17 beta (pg / ml)	31,25±12,75	0.02 39,0±8,75 P 0,5		0,02 37,25±18,5 P 0,5		
control	Progesterone (ng / ml)	1,23±0,1	0,85±0.11 P 0,01	0,58±0,12 - 0,01 P- 0,5	0,57±0,19 P 0,01	1,30±0.25 P 0,5	2,25±0,6 P - 0,2
	Estradiol-17 beta (pg / ml)	32,75±14,5	41,85±12,75P 0,5	43,5±12 P 0,5	46,25±16.7 P5	25,5±7,75 P 0,5	22,75±8,5 P 0,5

In the ovaries of experimental cows, which were injected with PGF-2 alpha at a dose of 1000 μg, and especially 2000 μg against the background of cysticated large and medium-sized follicles, the growth of new graaf vesicles was observed, and therefore, by the end of the experiment, most of these animals showed full inductions. -induced sexual cycles.

Considering that PGF-2 alpha accelerates the involution of the corpus luteum of the reproductive cycle, this drug deserves the use of elongated reproductive cycles, due to the slower involution of luteal structures. A special place should be given to the use of PGF-2 alpha, even in overestimated doses, for the prevention of postpartum pathology (retention of the placenta, subinvolution of the uterus, endometritis) caused by insufficient involution of the corpus luteum of pregnancy or the formation of new functioning luteal structures in the ovaries of cows after calving. In this case, PGF-2 alpha ensures the removal of the progesterone block from the uterus and, activating folliculogenesis in the ovaries,increaseits contractile function and resistance.

It was found that the use of PGF-2 alpha during follicle ovulation delays the formation of corpus luteum for a certain period, as evidenced by the slow growth of progesterone in the first four days of the experiment in comparison with the control **(Table 36).**

This phenomenon is due to the fact that even before ovulation, as well as in the process of ovulation of follicles and at the beginning of the formation of corpus luteum, differentiation of large luteal cells with well-defined cytoplasm and large nuclei occurs, on which PGF-2 alpha has a specific effect, causing their lysis, which excludes the possibility of progesterone production. At the same time, this drug has no effect on the proliferating tecal tissue, which is devoid of a formed capillary system. Therefore, after the cessation of the action of the drug, the formation of new luteal cells of the corpus luteum continues, which causes the synthesis of progesterone and an increase in its concentration in the blood plasma by the end of the experiment, although it does not reach the level of control animals **(Table 36).**

Table 36

Dynamics of sex hormones in the blood plasma of cows under the influence of PGF-2 alpha, introduced 4-8 hours after ovulation (p-6)

Dose of the drug, mcg	Sex hormones	Day of experience					
		before the v-den. prepar	2	3	4	6	9
500	Progesterone tng / mp)	0,59±0,11	0,62±0,09 P 0,5	0,64±0,10 P 0,5	0,68±0.12P 0,	0,89±0.10 P 0,2	1,52±0,76 P 0,2
	Estradiol-17 beta (pg / ml)	44,25±11,25	46,5±14,75 P 0,5	36,0±8,5 P 0,5	32,25±9,5 P “0,5	34,75±11,5 P 0,5	28,64±12.41 P 0,5
1000	Progesterone (ng / ml)	0,65±0,12	0,62±0,10 P 0,5		0,72±0,12 P 0,5		
	Estradiol-17 beta (pg / ml)	42,75±9,5	45,7±12,5 P 0,5		30,5±5,75 P 0,5		
2000	Progesterone tng / ml	0,55±0,11	0,58±0,08 P 0,5		0,60±0,13 P 0,5		
	Estradiol-17 beta (pg / ml)	40,75±10,75	48,5±15,25 P 0,5		34,25±10,0 P 0,5		
control	Progesterone (ng / ml)	0,63±0,23	0,85±0,13 P 0,5	1,38±0,25 P “0,5	1,30±0,25 P 0,1	1,80±0,63 P “0,1	2,05±0.73 P 0,5
	Estradiol-17 beta (pg/ml)	45,75±17,5	38,25±8.2P 0,5	29,1±9,75 P 0,5	26,5±7,75 P 0,5	20,00±6,25 P 0,2	21,75±7,00 P 0,2

The low functional activity of the corpus luteum in experimental animals, especially after the introduction of PGF-2 alpha at a dose of 2000 μg, does not provide a proper inhibition of the growth of new follicles, and therefore the level of estradiol-17 beta in the first two days of the experiment not only does not decrease, as in the control animals, and even increases. And only towards the end of the experiment, when the function of the corpus luteum increases, and the growth of follicles is inhibited, the level of estradiol-17 beta approaches the control **(Table 36).**

Considering that PGF-2 alpha causes lysis of the forming luteal cells, and in this regard, the function of the corpus luteum decreases and the threat of implantation of the zygote is created, this drug cannot be used after ovulation and during the development of the corpus luteum. However, with anovulatory reproductive cycles and in order to prevent the formation of luteal cysts, this drug deserves to be used in gynecological practice for the indicated functional disorders of the ovaries of cows.It was found that the introduction of PGF-2 alpha at a dose of 500 μg on 3-4 days after ovulation in the first 4 days of the experiment reduces the level of progesterone by more than 2 times, in comparison with the control, with its subsequent restoration on the 6-9 day of the experiment **(Table 37).** Against the background of a decrease in the level of progesterone, the amount of estradiol-17 beta increased, and only by the end of the experiment, when the function of the corpus luteum was restored, the concentration of estradiol-17 beta, in comparison with the initial data, as well as with the control, in some periods decreased by more than 2 times **(Table 37)**.Hormonal changes in the body clearly correlated with histofunctional changes in the ovaries. In particular, hemostasis and partial obliteration of large trabecular vessels with inhibition of proliferation and differentiation of luteal cells prevailed on sections prepared from the corpus luteum, taken on days 2-3 of the experiment.

In these areas (lobes), lysis, cytoplasm and nuclear pycnosis prevailed. At the same time, on the 4th, and especially on the 6th and 9th Day of experience, when the level of progesterone in the blood plasma sharply increased, the corpus luteum were represented by large luteal cells surrounded by a dense capillary network. At the same time, the structure of the parenchyma of the corpus luteum, as well as its size and color in the experimental cows did not differ from the control.

Table 37

Dynamics of sex hormones in the plasma of peripheral blood under the influence of PGF-2 alpha, introduced on 3-4 days after ovulation (pq6)

Dose of the drug, mcg	Sex hormones	Day of experience					
		before the y-den. prepar	2	3	4	6	9
500	Progesterone (ng / mp)	1,32±0,13	0,63±0,21 P "0,01	0,56±0,36 P 0,05	0,96±0,35 P 0.5	1,17±0,25 P 0,5	2,42±0,12 P o,001
	Estradiol-17 beta (pg / ml)	28,75±10,25	30,0±9,25 P "0,5	22,33±10,0 P 075	29,0±7,25 P 0,5	27,33±11,75 P 0,5	12,75±6,25 P~0,2
1000	Progesterone (ng / ml)	1,28±0,16	0,58±0,19 P 0,02		0,91±0,26 P 0,5		
	Estradiol-17 beta (pg / ml)	25,5±8,75	26,75±6,25 P 0,5		24,2±8,5 P 0,5		
2000	Progesterone ng / ml	1,20±0,10	0,49±0,23 P 0,02		0,83±0,30 P "0,2		
	Estradiol-17 beta (pg / ml)	27,1±11,25	26,25±12,00 P 0,5		25,0±9,25 P 0,5		
Control	Progesterone (ng / ml)	1,38±0,25	1,59±0.45 P 0,5	1,80±0,63 P 0,5	2,25±0,47 P 0,2	2,05±0,73 P 0,5	2,95±0,10 P 0,001
	Estradiol-17 beta (pg / ml)	29,1±9,75	25.75±8,2 P 0,5	20,0±6,25 P 0,5	26,0±7,75 P 0,5	21,75±7,0 P 0,5	20,75±7,75 P 0,5

Regarding the state of follicles in experimental animals, it should be noted that during the period of inhibition of the formation of the corpus luteum, the growth of tertiary follicles was activated, some of which reached 0.7-1.2 cm in diameter on the 3-4th day of the experiment. granulosis is radially differentiated, and the internal theca is represented by a thick layer of well-vascularized proliferatively active tissue. However, subsequently, on Day 6-9 of experience, with the restoration of the corpus luteum function, such follicles underwent cystic atresia, which was characterized by dystrophy and reduction of granulosis and the development of atrophic processes in the tecal tissue of the follicles.

During the period of the highest rise in the estrogenic function of the ovaries in some experimental animals, the release of light mucus from the vaginas was noted without the manifestation of other phenomena of the stage of arousal of the sexual cycle.

Under the influence of PGF-2alpha, introduced at the same time of the sexual cycle at a dose of both 1000 and 2000 μg, the same regularities remain as in the previous experiment. However, luteolytic processes intensified even more. In particular, there was a 3-fold decrease in progesterone levels in comparison with controls. Subsequently, 4 days after the administration of the drug, the concentration of progesterone in the blood plasma increased. In parallel, there was a sharper decrease in the level of estradiol-17 beta **(Table 37).**

Against such a hormonal background, a more pronounced reaction was observed on the part of specific cellular structures of the ovaries. So, already 2 days after the administration of the drug in a dose of 1000, and especially 2000 μg, in most differentiated luteal cells of the corpus luteum, lysis of the cytoplasm and pycnosis of nuclei were observed against the background of hemostasis and vascular obliteration. This was evidenced by the paler color of the corpus luteum in comparison with the control animals. At the same time, the proliferation of thecal cells continued, mainly from the corrugated invaginations of the forming lobes of the corpus luteum. On the 4th day of the experiment, foci of luteal cells in a state of deep involution with the formation of a fibrous structure were observed in the corpus luteum. The bulk of the corpus luteum had well-vascularized large luteal cells. Proliferative processes were also observed from the trabecular tissue. At the same time, the forming luteal cells were smaller, which should be attributed to the incompleteness of the formation of the corpus luteum 7-9 days after ovulation.

The characteristic features in this group of animals should include specific reactivity from the tecal tissue of tertiary follicles, manifested by lysis of differentiated theca-luteal cells against the background of hemostasis and vascular obliteration with simultaneous desquamation of granulosa, which ends with cystic atresia of the follicles. At the same time, PGF-2 alpha, even in high doses, has no effect on the poorly differentiated tecal tissue of growing follicles, and therefore the further growth of follicles does not stop.

Summing up this experience, it should be noted that PGF-2 alpha, administered at a dose of 500 µg on 3-4 days after ovulation of follicles, inhibits the formation of the corpus luteum, and in large doses (1000-2000 µg), in addition, it causes premature cystic atresia of follicles , and therefore excludes the possibility of its use without taking into account the initial state of the sexual function. In turn, a decrease in the function of the corpus luteum can lead to the deprivation of the possibility of implantation of the zygote or embryonic mortality.

The introduction of PGF-2 alpha on days 10-12 of the sexual cycle at a dose of 500, and especially 1000 and 2000 mcg, led to a sharp shift both in the hormonal background of the body **(Table 38)** and in the morpho-functional changes in the ovaries of cows.

From the analysis of **table 38** it follows that already 2 days after the administration of PGF-2 alpha, the level of progesterone compared with the initial data and control decreased within six times with a simultaneous sharp rise in the concentration of estradiol-17 beta in the blood plasma. In the next 3-4 days of the experiment, the digital values of progesterone did not change, while estradiol-17 beta continued to increase, reaching the indicators during the manifestation of the sex cycle in intact animals. At this level of estradiol, in most animals, on the 3-4th day of the experiment, the stage of excitation of the sexual cycle begins with ovulation of follicles and the formation of corpus luteum. In this regard, on the 6th, and especially on the 9th day of the experiment, the level of estradiol decreased within two times, and progesterone increased.

It should be especially noted that with increasing doses of PGF-2 alpha, the level of progesterone significantly decreases compared to the optimal dose (500 mg), which is associated with an increase in lytic processes in the luteal cells of the corpus luteum, which are characterized by vacuolization and lysis of the cytoplasm, pycnosis of the nuclei **(Fig. 23 a, b, c),** obliteration of large blood vessels and complete reduction of the capillary system. These processes are completed within 2-4 days, and the corpus luteum acquires a fibrous structure, decreasing in volume by 4-5 times.

Table 39

Dynamics of sex hormones in peripheral blood plasma under the influence of PGF-2alpha entered on 10-12 days of a sex cycle (P = 6)

Dose preparation ta, mcg	Sexual hormones	Days of experience					
		before the introduction den. preparation	2	3	four	6	nine
500	Progesterone ng / mp)	3.25 ± 1.13	0.56 ± 0.10x	0.61 ± 0.10x	0.62 ± 0.15 x	1.42 ± 0.29	1.78 ± 0.45
	Estradiol-17bet (pg / ml)	21.75 ± 5.55	30.25 ± 11.7 5x	42.75 ± 11.5 x	38.2 ± 9.55 x	28.25 ± 6.0 x	21.0 ± 5.75 x
1000	Progesterone (ng / ml)	3.05 ± 1.13	0.53 ± 0.09x		0.57 ± 0.12		
	Estradiol-17bet (pg / ml)	22.75 ± 7.5	29.5 ± 11.75 x		39.25 ± 8.2 five		
2000	Progesterone ng / ml	2.85 ± 0.65	0.5 ± 0.13x		0.53 ± 0.09		
	Estradiol-17 beta (pg / ml)	23.25 ± 8.5	36.25 ± 11.7 5x		40.25 ± 9.5		
Control b	Progesterone(ng / ml)	3.01 ± 1.21	2.95 ± 1.03 3.15 ± 0.82	2.98 ± 0.95	1.25 ± 0.43 x	0.6 ± 0.19x	3.01 ± 1.21
	Estradiol-17bet (pg / ml)	22.25 ± 8.5	20.75 ± 7.75 20.0 ± 8.5	21.5 ± 9.75	31.75 ± 6.5 x	43.5 ± 11.7 5x	22.25 ± 8.5

Note: $P < 0.05-0.001$

experiments on the study of biological properties, as well as indications and contraindications for the use of PGF-2 alpha, it should be noted that common to all groups of experimental animals is specificity the luteolytic effect of this drug on functioning luteal structures of the ovaries, including luteal cells of the corpus luteum and atretic bodies, thecaluteal cells of maturing follicles and functioning interstitial cells of the ovarian cortex. In turn, PGF-2 alpha, regardless of the dose administered, does not have a specific effect on the primordial epithelium and poorly differentiated proliferating connective tissue elements of the ovaries, which ensures constant hemetogenesis from the primordial epithelium and the formation of new primordial follicles with their subsequent transformation into secondary and tertiary. That is why the negative effect of PGF-2 alpha on the generative function of the ovaries is excluded and this drug deserves widespread introduction into obstetric and gynecological practice.

Table 40

Dynamics of sex hormones in the plasma of peripheral blood under the influence of PGF-2alpha with luteal cysts of ovaries (n = 6)

Dose of the drug, mcg	Sex hormones	Days of experience		
		forward in the future-den. prepar	2	4
500	Progesterone (ng / mp)	2,85±0,56	0,72±0,13 P 0,01	0,48±0.10 P 0,01
	Estradiol-17 beta (pg / ml)	29,00±10,40	34,75±9,25 P 0,5	36,50±12,75 P "0,5
1000	Progesterone (ng / ml)	3,08±0,37	0,60±0,15 P 0,001	0,62±0,15 P 0.001
	Estradiol-17 beta (pg / ml)	3,08±0,37	29,75±11,00 P 0,1	33,50±9,75 P 0,5
2000	Progesterone tng / ml	2,75±0,42	0,63±0,09 P 0.001	0,56±0,13 P 0,001
	Estradiol-17 beta (pg / ml)	25,50±6,75	33,00±9,25 P 0,5	35,75±11,00 P 0,5
control	Progesterone (ng / ml)	2,80±0,64	2,85±0,53 P "0,5	2,79±0,73 P "0,5
	Estradiol-17 beta (pg / ml)	19,00±12,0	21,75±10,00 p 0, 5	24,25±8,25

As a result, it should be noted that PGF-2 alpha can be used to synchronize sexual function, induce premature birth in cows, with anovulatory and prolonged reproductive cycles, luteal cysts and persistent corpus luteum, as well as for the prevention and treatment of postpartum pathology in cows.

In addition to studying biological properties, as well as indications and contraindications for the use of PGF-2 alpha in obstetric

In particular, the walls of such luteal cysts are represented by a thick layer (0.2 - 0.6 cm in radius) of parenchymal tissue, similar in color and consistency to the functioning corpus luteum of the reproductive cycle and pregnancy. The content of such cysts is of a gelatinous consistency and yellow in color, close to their parenchymal tissue, which indicates an active metabolism of these structures and the accumulation of a large amount of progesterone in them. On histological sections, parenchymal tissue is represented by large luteal cells abundantly vascularized in a state of hypersecretion, often larger than similar cells of functioning yellow cellbodies of the sexual cycle. All this creates a high progesterone background in the body, as evidenced by the results of radioimmunoassay (Table 40) and leads to prolonged anaphrodisia.In addition, the body continues to maintain a low estrogenic background for a long time, which does not provide for the activation of the luteolytic function of the uterus. All this leads to long-term persistence of luteal cysts.

A low estrogenic background in the body is associated with the deprivation of the possibility of growth of large follicles, although the formation primordial, the growth of secondary and small tertiary follicles does not stop. However, as they increase, they undergo obliterative atresia by filling the follicular cavity proliferating thecal tissue with simultaneous degeneration and reduction of granulosis. This excludes the creation of the proper estrogenic background in the body, which is necessary for the regular manifestation of sexual cycles.

Proceeding from theoretical assumptions about the low luteolytic function of the uterus in this functional disorder of the ovaries, we decided to take the path of exogenous regulation of the reproductive capacity of animals with the help of PGF-2 alpha.

The results of experimental studies showed that under the influence of PGF-2 alpha at a dose of 500, as well as 1000 and 2000 μg on the second, and especially on the fourth day of the experiment, the level of progesterone in the blood plasma of cows sharply decreases and the concentration of estradiol-17 beta increases (table.40). So, after two days, there is a decrease in progesterone to 0.60 ± 0.15 - 0.72 ± 0.13 hg / mland continued to decrease to 0.48 ± 0.10 -

0.62 ± 0.15 ng / ml by the end of the fourth day. The content of estradiol-17 beta increased by the end of the experiment to 33.50 ± 9.75 - 36.50 ± 12.7p/ml.

However, if the dynamics of hormones, regardless of the doses administered, PGF-2 alpha and manifests itself synchronously, then the results of clinical studies and histofunctional changes in the ovaries of cows with luteal cysts make it possible to differentiate the difference in the reactivity of the gonads to the administered dose of the drug. So, two days after the injection of PGF-2 alpha at a dose of 500 μg, no noticeable clinical and macroscopic changes in the ovarian cysts were found. On sections of the parenchyma of luteal cysts, luteal cells with vascularized and in a state of lysis cytoplasm are visible. Four days after the administration of the drug at this dose, in addition to the intensification of lytic processes, pycnosis of the nuclei is also observed in the cytoplasm, in connection with which the luteal cells change their configuration from oval to flat with streaks of fibrous structure. In this case, obliteration of the vessels is noted. Along with this, there are also luteal cells in a high functional state with differentiated cytoplasm and large oval nuclei. Against this background, the walls of luteal cysts become thinner and acquire a more gentle fluctuation, however, by this time, the restoration of sexual function is not observed. Under the influence of 1000, and especially 2000 μg of PGF-2 alpha, two days later, noticeable clinical and macroscopic changes were noted, which were characterized by thinning of the walls of the luteal cysts and their clearly expressed fluctuation. On the 3-4th day of the experiment, most animals (75%) experienced resorption of cysts. At the same time, the ovaries decreased 2-3 times. In a histological study of fragments of the walls of luteal cysts under the influence of PGF-2 alpha at a dose of 1000 μg, two days after the beginning of the experiment, the processes of vacuolization and lysis with simultaneous pycnosis of nuclei developed in the cytoplasm of most luteal cells. The wall of luteal cysts acquired a fibrous structure. In this case, obliteration of not only small, but also larger blood vessels occurred. By this time, in the ovaries of most animals, luteal cysts acquired a gently fluctuating consistency and at the slightest pressure, the cyst wall ruptured. The processes of luteolysis of cysts intensified by the end of the fourth day. So, after the injection of 1000 μg of PGF-2 alpha, the wall of luteal cysts acquired a fibrous structure with singly included luteal cells of a fusiform and flat shape. These processes in the walls of luteal cysts were enhanced under the influence of PGF-2 alpha at a dose of 2000 μg. In the cortical layer of the ovary, both under the influence of PGF-2 alpha at a dose of 500, as well as 1000 and 2000 μg, the migration of germ cells into the tunica albuginea, the formation of primordial ones, as well as the growth of secondary and small tertiary follicles, which reached the average in two days, were noted, and by the end of the large-scale experiment. In some large follicles, there was cystic, and in the middle size, obliterative atresia. Based on the experience, it is necessary to conclude that the decrease in the level of progesterone in the blood plasma of cows with luteal ovarian cysts does not depend on the dose of the administered drug. Based on clinical data and confirmed by morphological studies, a dose of 500 μg of PGF-2 alpha for the treatment of cows with luteal ovarian cysts is insufficient, since it does not cause complete luteal cell lysis of the cyst wall within 2 days. PGF-2 alpha in doses 1000, and especially 2000 mcg has a strong lytic effect not only on luteal, but also on differentiated thecal cells of large follicles. However, at the same time, the growth of small tertiary follicles continues, due to which the induced reproductive cycles are manifested, and therefore the dose of PGF-2 alpha in 1000 μg is the most optimal for the treatment of cows with luteal ovarian cysts. However, the dose of 500 mcg of PGF-2 alpha is more physiological and therefore can also be recommended for the treatment of luteal cysts of the ovaries of cows. Considering that when treating cows with luteal ovarian cysts PGF-2 alpha at a dose of 1000 mcg, only induced manifestation of sexual cycles occurs, we have established the experience of combined use of PGF-2 alpha at a dose of 1000 mcg and gonadotropin FFA (gravogormone) at a dose of 2000 IU. At the same time, it was found that the level of progesterone in the peripheral blood plasma decreased from 2.66 ± 0.27 ng / ml to 0.70 ± 0.10 ng / ml and continued to decrease by the end of the experiment to 0.48 ± 0.10 ng / ml. Along with this, the content of estradiol-17 beta during this period increased from 13.90 ± 5.80 pg / ml to 42.79 ± 19.40 pg / ml, and then its gradual decrease by the end of the experiment to 31.00 ± 16.20 pg / ml was observed (Table 41).

The data of the radioimmunological study allow us to conclude that by the end of the first day after the use of the drugs, the function of the luteal cyst is sharply inhibited and the growth of follicles is activated. At the same time, by the end of the second day of the experiment, the wall of the cyst becomes thinner, acquiring a delicate consistency and ruptures on palpation. From the surface of the ovaries, many small, medium-sized and large follicles are visible. In the cytoplasm of the luteal cells of the cyst wall, deep processes of vacuolization and lysis developed, pycnosis of the nuclei was noted against the background of pronounced obliteration of the blood vessels. Follicles with differentiated thecal cells underwent obliteration and cystic atresia. Migration of germ cells from the rudimentary epithelium into the tunica albuginea with the formation of primordial follicles was noted. Selected large follicles with well-vascularized thecal cells and developed grazulosa were in a pre-ovulatory state.

Table41

Dynamics of sex hormones in the plasma of peripheral blood of cows with saluteal cysts of the ovaries under the influence of PGF-2alphaigonadotropin FFA (n = 6)

Sex hormones	Before the introduction of the drug	clock			
		12	24	48	96
Progesterone (ng / ml)	2,66±0,27	0,70±0,16ˣ	0,51±0,09ˣ	0,82±0,21ˣ	0,48±0,10ˣ
Estradiol-17 beta (pg / ml)	13,94±5,80	42,79±19,40	42,24±3,60ˣ	28,30±14,30	31,00±16,20

After four days, lytic processes in the cells of the luteal cyst intensified, their cytoplasm was completely lysed and replaced by a fibrous structure. In most animals, follicles ovulated, followed by the formation of corpus luteum.

The restoration of sexual function was accompanied by certain changes in the biochemical parameters of the blood. In particular, already 96 hours after the use of PGF-2 alpha and gonadotropin FFA, the concentration of glucose in the blood increased by 9.1%, inorganic phosphorus by 15.1%, total cholesterol by 23.6%, beta-lipoproteins by 5.0 %, vitamin A on 72.6%, vitamin E by 115.1%, vitamin C by 45.1%. By the end of the experiment (after 192 hours), the level of total protein in the blood decreased by 6.1%, inorganic phosphorus by 16.3%, beta-lipoproteins by 9.9%, total calcium by 3.4%, ionized calcium by 22, 2%, carotene by 54.5%, vitamin A by 34.1%, vitamin E by 40.5%, vitamin C by 28.7%.

As a result, the combined use of PGF-2 alpha at a dose of 1000 μg and gonadotropin FFA at a dose of 2500 IU. ensures the involution of luteal cysts, activation of the growth and maturation of follicles with their subsequent ovulation in the first 3-5 days of the experiment in more than 50% of animals. In this regard, this combined use of the two drugs deserves testing in the treatment of luteal cysts of the ovaries of cow. (G.A. Cheremisinov, S.P. Eremen, 1985) worked out the optimal doses, indications and contraindications for the use of domestic PGF-2 alpha estufalan on heifers. The experiment included 42 heifers of 16-18 months of age with functioning corpus luteum of the sexual cycle, on which a comparative study of the dynamics of progesterone in the blood and morphofunctional changes in the ovaries under the influence of 200, 300, 400 and 600 μg of estufalan and estrophan was carried out. In addition, 10 heifers with hypofunction and 12 animals with involution of the corpus luteum of the sexual cycle, the efficacy of estufalan alone at a dose of 300 μg and in combination with gonadotropin FFA at a dose of 1.5 thousand m.u. was tested.

It was found that the nature of the histofunctional changes in the ovaries and progesterone in the blood of heifers with functioning corpus luteum after the administration of the same doses of estufalan and estrophan are similar, and therefore the material, depending on the doses of PGF-2 alpha, should be analyzed together **(Table 42).** From the analysis of the material it follows that both under the influence of estufalan and estrophan, in the first three days of the experiment, the level of progesterone in the blood of heifers decreases by 4-10 times. Moreover, with increasing doses of drugs, the concentration of progesterone in the blood in the first three days of the experiment decreases from 3.99 ± 0.79 to 0.36 ± 0.04 ng / ml. 5 days after the administration of drugs, the level of progesterone in the blood of heifers begins to increase. At the same time, the nature of changes in the concentration of progesterone in the blood of calves also depends on the doses of drugs administered, i.e. with increasing doses of PGF-2 alpha (400-600 mcg), the rise in progesterone levels is less pronounced in comparison with injections of lower doses (200-300 mcg). At the heart of this phenomenon, as shown by the results of the study histofunctional changes in the ovaries of heifers, there is a different degree of reactivity of specific cellular structures of the gonads.

Table 42

Dynamics of progesterone (ng / ml) in the blood plasma of heifers under the influence of estufalan and estrophan, administered on the 8-10th day of the sexual cycle

Number: animals	The name of the drug	Dose (mcg)	Before the introduction of the drug	Days of experience	
				3	5
6	Estufalan	200	2,89±0,43	0,78±0,36ˣ	1,12±0,53
3	Estufalan	300	2,57±0,32	0,67±0,08ˣ	0,88±0,03
6	Estufalan	400	2,26±0,12	0,49±0,09ˣ	0,83±0,24
5	Estufalan	600	2,98±0,34	0,45±0,09ˣ	0,79±0,10
6	Estufalan	200	2,56±0,29	0,72±0,32ˣ	0,86±0,43
3	Estufalan	300	3,18±0,38	0,56±0,07ˣ.	0,96±0,40
6	Estufalan	400	3,99±0,79	0,36±0,04ˣ	0,81±0,02
4	Estufalan	600	3,66±0,58	0,45±0,09ˣ	0,61±0,17
3	Control	-	2,75±0,40	-	2,28±0,36

It was found that 3 days after the administration of PGF-2 alpha at a dose of 200 μg, involutional processes develop in the corpus luteum, which are characterized by vacuolization and lysis of the cytoplasm and pycnosis of luteal cell nuclei. This process occurs against the background of vascular obliteration and hemostasis of the blood cells in them. At the same time, under the influence of this dose of drugs, most luteal cells do not lose duringfrom impairing their configuration during involution of the corpus luteum, and in some lobes single luteal cells of a round and oval shape, characteristic of a functioning corpus luteum, are preserved. However, against this background, there is an activation of the growth of follicles, in which granulosis comes to state hypersecretion, but in internal teke intensify proliferative processes with the formation of single theca-luteal cells.5 days after the administration of PGF-2 alpha at the test dose in the ovaries of heifers, 2-3 large follicles are determined, some of which are in a pre-ovulatory state or ovulate, which is accompanied by an increase in the level of progesterone in the blood from 0.78 ± 0.36 to1.12 ± 0.53 ng / ml. At the same time, the functioning yellow bodies undergo deep involutional processes, which is characterized by the loss of cell configuration, the formation of a fibrous structure and obliteration of blood vessels.

Under the influence of PGF-2 alpha, after 3 days the involutional processes in the corpus luteum intensify. In this case, the cells acquire a polygonal, cubic or flat shape, the nuclei undergo pyknosis, and a fibrous structure is formed in the intercellular spaces against the background of vascular obliteration. After 5 days, the corpus luteum acquires the size of small yellowish-gray bodies of a fibrous structure with singly included flat nuclei. The vessels are obliterated.

Against this background, the growth of follicles is activated. Moreover, in the ovaries of each animal, after 3 days, 2-3 large and medium-sized follicles with secretory active granulosis and internal fluid in a state of proliferation and differentiation of single thecalutein cells are determined. After 5 days, most heifers ovulate mainly in one follicle, which is accompanied by an increase in the level of progesterone in the blood plasma. In other animals, the follicles are in a pre-ovulatory state, as evidenced by the reduction of granulosis against the background of increased vascularization and proliferation of cells of the internal theca. In separate non-ovulated follicles, thecal tissue protrudes into the follicular cavity, forming corrugated invaginations. These processes are even more pronounced in the ovarian follicles animals that have ovulated.

With increasing doses of PGF-2 alpha to 400-600 μg on day 3 of the experiment, the level of progesterone in the blood sharply decreases, which is accompanied by pronounced lysis of the cytoplasm and pycnosis of the nuclei against the background of obliteration of blood vessels and reduction of the capillary system. Against this background, the development of lytic processes in the tecal tissue of follicles and interstitial cells of the ovarian cortex is noted in follicles activated to growth. In this regard, especially under the influence of 600 μg of PGF-2 alpha, growing follicles undergo cystic atresia by reducing granulosis and fibrous replacement of the internal theca. Therefore, the phenomenon of ovulation on the 5th day of the experiment after the introduction of 600 μg of PGF-2 alpha is not observed, and therefore the level of progesterone in the blood remains much lower in comparison with animals that were injected with PGF-2 alpha at a dose of 200-300 μg, although in comparison with the 3rd day of the experiment, there is a slight rise in this hormone. This is due to the activation of new follicular growth and the formation of thecalutein cells, which have the ability to produce progesterone even before the ovulation of the follicles.

Therefore, the most optimal dose of estufalan and estrophan for heifers is 200-300 mcg. These doses provide in physiological terms the involution of the corpus luteum and the maturation of follicles with their subsequent ovulation. An increase in the dose of the studied drugs from 400 to 600 μg, in addition to shortening the time of involution of the corpus luteum, enhances lytic processes in the thecal cells of growing follicles, which excludes the possibility of their ovulation during the immediate sexual cycle. Therefore, the use of PGF-2 alpha in doses of 400-600 mcg should be recognized as economically and physiologically inexpedient.

Considering that PGF-2 alpha in the established optimal doses ensures lysis of luteal cells and activates the growth of follicles with their subsequent ovulation against the background of manifestation of other phenomena of the sexual cycle, it is quite advisable to use this drug as one and in combination with gonadotropin FFA for persistent corpus luteum and luteal cysts of the ovaries of heifers.

Considering that in heifers, during the development of sexual function, violations of the rhythm of the reproductive cycles are often observed in the form of their shortened or lengthened manifestation, which is associated with hypofunction or delayed corpus luteum, it is quite reasonable to raise the question of using PGF-2 alpha alone or in combination with gonadotropin FFA to improve the biotechnology of their intensive and rhythmic reproduction.

It was found that after the introduction of estufalan at a dose of 300 μg on days 15-17 of the sexual cycle, the progesterone content in the blood plasma of heifers within 3 days of the experiment decreases from 1.11 ± 0.21 ng / ml to 0.52 ± 0.04 ng / ml. At the same time, the level of estradiol-17 beta increases from 20.44 ± 0.73 to 28.17 ± 3.74 pg / ml. Joint injection of estufalan at a dose of 300 μg with gonadotropin FFA at a dose of 2 thousand IU, along with a decrease in progesterone, as in the previous experiment, provided a sharp increase in the level of estradiol-17 beta in the blood plasma, which reached 79.76 ± 7, 29 pg / ml, which was accompanied by the growth of large follicles with radially differentiated granulosis in a state of hypersecretion and proliferatively active and well vascularized internal fluid. Against this background, by the end of the experiment, the phenomena of estrus and general excitement were determined in some animals. The corpus luteum of the sexual cycle underwent involution after 3 days of the experiment. At the same time, in some animals of the control group, there was a slight decrease in the level of progesterone and a slight increase in the concentration of estradiol-17 beta in the blood plasma (from 22.11 ± 7.78 to 24.27 ± 5.53 pg / ml), while in other heifers these indicators remained stable for 3 days of the experiment. The manifestation of the stage of arousal of the sexual cycle was not established in any of the animals of the control group during the period of the experiment. On sections of the ovaries, luteal cells with lysed cytoplasm and pyknotically altered nuclei were seen in separate lobes of the corpus luteum. 53 pg / ml), while in other heifers these parameters remained stable for 3 days of the experiment. The manifestation of the stage of arousal of the sexual cycle was not established in any of the animals of the control group during the period of the experiment. On sections of the ovaries, luteal cells with lysed cytoplasm and pyknotically altered nuclei were seen in separate lobes of the corpus luteum. 53 pg / ml), while in other heifers these parameters remained stable for 3 days of the experiment. The manifestation of the stage of arousal of the sexual cycle was not established in any of the animals of the control group during the period of the experiment. On sections of the ovaries, luteal cells with lysed cytoplasm and pyknotically altered nuclei were seen in separate lobes of the corpus luteum.

Most of the lobes of the corpus luteum contained large luteal cells with vacuolated cytoplasm in a state of hypersecretion and oval nuclei. Single large and medium-sized follicles were noted.

Consequently, in case of irregular reproductive cycles or their disorders, the use of PGF-2 alpha in combination with FFA gonadotropin deserves attention, which will ensure the regulation and synchronization of the sexual cycles and timely fertilize heifers when they reach physiological maturity.

Upon reaching physiological maturity and the required body weight, some heifers sometimes lack sexual cycles, which is associated with ovarian hypofunction. In these cases, for timely insemination and fertilization of heifers, it is necessary to resort to hormonal regulation of sexual function.

The results of the study showed that when estufalan was used at a dose of 300 μg to heifers with ovarian hypofunction, a slight decrease in progesterone plasma was observed in the first 5 days of the experiment (from 0.39 ± 0.13 to 0.26 ± 0.09 ng / ml) with a slight increase in the level of estradiol-17 beta (with12.86 $\pm$ 1.60 to 15.67 $\pm$ 3.57 pg / ml). At the same time, on histological sections prepared from the ovaries of experimental animals, atretic bodies were observed at various stages of development, functioning and fibrous replacement, as well as follicles in the initial stage of obliterative atresia with proliferating thecal cells, on which estufalan has a lytic effect. In this regard, the observed slight decrease in the level of progesterone in the blood plasma of experimental animals should be associated with luteolysis of functioning cells of obliterating follicles and atretic bodies, which in turn leads to some activation of the growth of new follicles and an increase in the level of estradiol in the blood.

The combined use of PGF-2 alpha with gonadotropin FFA, respectively, in doses of 300 μg and 2 thousand m.u., in addition to causing lytic processes in functioning luteal structures, provides active growth and maturation of follicles with an increase in the level of estradiol17 beta by 3-4 times and restoration of sexual function in non-cycling cows. In this regard, the joint use of these drugs for the restoration of sexual function and timely fertilization of heifers with ovarian hypofunction has been scientifically substantiated. At the same time, it was found that after administration of the studied drugs, some heifers do not show signs of sexual heat, although luteal structures are formed in the ovaries either after ovulation or by follicle luteinization. In this case, heifers that did not come into heat and were not inseminated within 10-12 days after the use of the drugs should be re-administered estufalan at a dose of 300 µg. In the presence of functioning luteal structures in the ovaries, they undergo regression and on the 3-5th day there is a recovery of sexual function with the manifestation of full-fledged sexual cycles. Subsequent studies in the form of the use of gravohormone (300 µg estufalan + 1000 IU of gravogormone) gave a high therapeutic effect, and therefore drugs in these doses should be recognized as optimal for the regulation of functional disorders of the ovaries of heifers.

3.5. Dynamics of ovarian hormones and PGF-2 alpha and development methods of hormonal therapy of obstetric and gynecological pathology cows

To implement this working hypothesis, we carried out special experimental and research and production experiments on the use of PGF-2 alpha for the prevention and treatment of postpartum endometritis and subinvolution of the uterus in cows.

In order to study the preventive effect of PGF-2 alpha in postpartum endometritis and uterine subinvolution in cows, studies were carried out on 30 experimental and 20 control cows. For this purpose, No.-2 alpha was administered to animals intramuscularly once in a dose of 500 µg for no more than 12 hours after calving. Control animals at the same time were injected with 40-50 units of oxytocin (baseline).Clinical obstetric and gynecological studies in experimental animals were carried out within 100 days after calving. The number of animals with a normal and pathological course of the postpartum period, the time of manifestation of the stage of arousal of the sexual cycle and fruitful insemination, the fertility rate, and the number of days of infertility were taken into account. As a result of the studies, the pathological course of the postpartum period was established in 7 cows in the experimental (23.9%) and 9 (45.0%) in the control groups (Table 45).

As can be seen from the above table, the normal course of the postpartum period was recorded in 23 experimental and 11 control subjects, who at various times came into the hunt and fruitfully inseminated 76.7% and 55.0%, respectively. On average, the number of days of infertility in the group was 71.90 in the experimental group and 91.75 in the control group. The data obtained indicate that PGF-2 alpha prevents uterine subinvolution and postpartum endometritis by 21.7% and reduces the number of days of infertility by 19.9 days compared to the control.

One of the most common diseases of the genital organs in cows is chronic subinvolution of the uterus. During a gynecological examination of 5.5 thousand cows for 4 years in a number of farms, chronic subinvolution of the uterus was established in 827 animals or in 15%.Previously, cows with such a diagnosis were treated without taking into account the initial state of the ovaries or their possible functional disorders. With the disclosure of the luteolytic function of the uterus, a new understanding of the role of the uterus in the regulation of the reproductive function of cows and its close relationship with the function of the ovaries was created. Of the cows examined, ovarian hypofunction was found in

53.2%, corpus luteum - in 37.7% and luteal ovarian cysts - in 9.1%. In cows with hypofunction and luteal ovarian cysts, anaphrodisia was noted. The duration of infertility in them was 57.6 ± 6.12 days. In the presence of corpus luteum in the ovaries, animals were observed to have multiple sexual cycles, their insemination (4.3 ± 0.28) did not give a result, the number of sterile days was 78.1 ± 8.14.

Therefore, in order to improve the diagnosis of chronic subinvolution of the uterus, 20 sick animals were slaughtered, followed by a macroscopic and histological assessment of the state of the uterus and ovaries. Clinical and gynecological results, macroscopic andhistological studies have allowed us to subdivide the chronic subinvolution of the uterus in cows into 3 degrees.

At the first degree of chronic subinvolution, the uterus in cows to the middle of the horns is located in the pelvic cavity, somewhat (1.2-1.4 times) increased in size, weakly responds to massage. In the area of the bifurcation, a slight flattening of the horns was noted (when they were squeezed from the sides). At autopsy, a thickening of the wall of the uterine horns and an increase in its lumen were observed.

Table 43

Indicators of prevention of postpartum endometritis and uterine subinvolution in cows

Groups of animals x	Number alive	Sick of animals		With normal postpartum period		The Sly		coeff.fertiliser-creation	Days of Unspothed Dia	
		All (goal)	%	Total (goal)	%	Total (goal)	%		Total (goal)	%
Experienced	30	7	23,3	23	76,5	23	76,5	1,69	71,9	52,4
Cont-no	20	9	45,0	11	55,0	11	55,0	1,90	91,75	51,9

On the surface of the endometrium, there were remnants of caruncles in the form papillae up to 3-4 mm high. In the subepithelial layer of the endometrium, moderate cellular infiltration and the development of destructive processes in the uterine glands were observed. With the second degree of chronic involution, the horns of the uterus hang by 2/3 into the abdominal cavity, are enlarged (1.4-1.6 times), and do not respond to massage. The flattening of the horns is well expressed throughout. At autopsy, an uneven thickening of the horn wall was observed, an increase in their cavity up to 1.5-2.0 cm. The papillae of their uterine mucosa reached 5-6 mm. In the stroma of the endometrium, pronounced cellular infiltration and obliteration of blood vessels were observed. In the uterine glands, an increase in destructive processes was noted, which characterized dystrophy and reduction of epithelial cells and their partial replacement with connective tissue elements.

At the third degree of chronic involution, the horns of the uterus hang over the pubic fusion, are increased in size (1.7-2.5 times), do not respond to massage, their flattening is sharply expressed. At autopsy, a pronounced longitudinal and transverse folding of the uterine horns, uneven thickening of its wall were observed. The cavity of the uterine horns reached 2.5-3.0 cm in diameter, the size of the papillae on the surface of the endometrium in some animals was 7-8 mm. Histological examination revealed diffuse cellular infiltration of the endometrial stroma and pronounced dystrophic changes in the integumentary epithelium and epithelium of the uterine glands, obliteration of blood vessels.

In clinically healthy cows, 25-30 days after calving, the uterus is in the pelvic cavity, it can be freely grasped by hand. Horns of the uterus are relatively symmetrical, elastic-elastic consistency, respond well to massage. In cross section, the lumen of the horns of the uterus has the shape of a stellate slit. The subepithelial layer of the endometrium is represented by a delicate, fibrous structure, in which a small number of cellular elements are visible. The uterine glands have different configuration with varying degrees of secretory activity, in the ovaries ripening, mature follicles or corpus luteum of the reproductive cycle.

With hypofunction of the ovaries, the growing follicles undergo atresia. The parenchyma of functioning corpus luteum in the ovaries is represented by large oval luteal cells with varying degrees of secretion. Luteal ovarian cysts have a rounded or round shape, up to 3-4 cm in diameter, the contents are gelatinous, light yellow in color. The cyst wall reaches 2-4 mm, its cells are similar to the tissues of a functioning corpus luteum.

The content of sex hormones progesterone and estradiol-17 beta in blood samples of cows (n = 17) with chronic subinvolution was determined by the radnoimmunological method **(Table 44).**

Table 44

The content of progesterone and estradiol in blood samples from cows with chronic subinvolution of the uterus (M ± m)

Hormones	Ovarian condition		
	hypofunction	corpus luteum, cycle	luteal cysts
Progesterone (ng / ml)	0.5 ± p, 12	3.23 ± 0.54	3.08 ± 0.48
Estradiol (pg / ml)	11.96 ± 1.77	14.40 ± 3.87	12.21 ± 1.18

From the data in the table it follows that that in the ovaries of cows with chronic luteal structures function by subinvolution of the uterus, the degree of endocrine activity of which is different. The highest concentration of progesterone was found in cows with functioning corpus luteum and luteal cysts in the ovaries (respectively, in4.04 and 3.85 times (P <0.002) higher than ovarian hypofunction). The estradiol content in blood samples from all animals was low. After the introduction of estufalan to cows, in all cases there was a significant decrease in the blood concentration of progesterone and an increase in the level of estradiol. So, after 6 hours, the content of progesterone in the samples blood of animals with functioning corpus luteum, luteal cysts and ovarian hypofunction decreased by 4.25, 3.5 and 1.5 times, respectively, and after 4 days by 11.96, 8.8 and 4.46 times. At the same time, the concentration of estradiol 1 la in the blood increased after 4 days, respectively, in 2.34,3.27 and 2.94 times.

Histological examination of ovaries from 8 cows with functioning corpus luteum (removed 48, 72 and 96 hours after estufalan injection) revealed the luteolytic effect of this drug, characterized by vacuolization and lysis of the cytoplasm, pycnosis of luteal cell nuclei against the background of severe obliteration of blood vessels. 96 hours after the administration of estufalan, the corpus luteum completely regresses and is represented by a fibrous structure with single small nuclei. Against this background, follicles grow and mature in the ovaries, which explains the increase in the level of estradiol in the blood.

Research results have shown that the treatment of cows with chronic subinvolution of the uterus should be comprehensive and aimed at restoring the function of not only the uterus, but also the ovaries. In addition, it is known that a decrease in the level of progesterone and an increase in the concentration of estradiol in blood samples of cows are accompanied by an increase in the tone of the uterus, an increase in its contractile function and sensitivity to drugs of uterine action. Therefore, in the treatment of cows with chronic subinvolution of the uterus, it is necessary to include one of the preparations of prostaglandin F2-alpha find more effective methods of treating cows with chronic subinvolution of the uterus, 2 experiments were carried out without taking into account and taking into account the initial state of the ovaries.

In the first experiment, 136 cows were used without taking into account the initial state of the ovaries. The animals were divided into 6 groups of 20-26 animals each. The cows of the first group were once injected intramuscularly with estufalan in dose of 2 ml (500 μg), the second animals were given a single dose of estufalan and ichthyol therapy was carried out (ichthyol of 7% concentration, prepared sterile in 0.85% sodium chloride solution, was injected subcutaneously in the upper third of the neck in the following doses: 20, 25, 30, 35, 30 and 25 ml with a 48-hour interval). The cows of the third group were injected with estufalan, ichthyol and oxytocin (8 units per 100 kg of body weight, 3 times with a 24 hour interval), starting the next day after the administration of estufalan. The animals of the fourth group received estufalan, ichthyol, and oxytocin. On the 11th day of the course of treatment, estufalan was re-administered to those who did not come into the hunt. Cows of the fifth group were injected with a solution of ichthyol and oxytocin (baseline), the sixth the drugs were not injected (negative control). In order to normalize the metabolism of vitamins, all animals were given vitamins A, D, and E twice (with a weekly interval). **Table 45** shows that in the negative control group, fertilization occurred only in 4 (16%) cows over a 3-month period. The greatest therapeutic efficacy was achieved in animals that were twice injected with estufalan in combination with ichthyolotherapy and oxytocin injections (fourth group).

Table 45

The effectiveness of various therapies for cows with chronic subinvolution of the uterus

group	Number of belly-thring	Fertilized, %		The period of fertilization, the day	Remained barren, %	Days of infertility per cow group
		IN 1 months.	For 3 months.			
I	22	36,4	68,2	39,8±4,83	31,8	51,0±4,75^{xx}
П	20	40,0	80,0	33,7±3,92^{x}	20,0	42,2±4,42^{xx}
Ш	26	42,3	84,6	34,1±3,29^{x}	15,4	40,8±3,19^{xx}
IV	20	55,0	90,0	28,1±3,41^{xx}	10,0	32,4±4, 21^{xx}
V	23	26,1	69,6	49,3±4,48	30,4	68,1±4,87^{xx}
VI	25	-	16,0	67,6±9,87	84,0	86,4±2,02

Note: 1. X - P <0.01; XX -P <0.001;

2. The reliability of the cow fertilization period is given in comparison with the baseline option (column V), and days of infertility - with negative control (column VI) Within 2 weeks, 60% clinically recovered, in 20 days - 90% of cows. Their fertilization occurred on average after 28.1 ± 3.41 days. One cow in this group has the smallest number of days of infertility (32.4 ± 4.21). A relatively high efficiency of therapy was also obtained in animals of the third group. It should be noted that out of 43 cows, the stage of arousal of the sexual cycle in which occurred in the first 20 days from the start of treatment, only 5 (11.6%) animals were fertilized.

In the second experiment, 130 cows with chronic subinvolution of the uterus, depending on the initial state of the ovaries (hypofunction, luteal cysts, functioning yellow bodies), were divided into 3 groups of 41-47 animals, and each group into two subgroups: experimental and control. The cows of the experimental subgroups with the presence of corpus luteum and luteal cysts in the ovaries were injected with estufalan in combination with ichthyolotherapy and oxytocin injections. On day 11 ± 3 of the course of treatment, cows were additionally injected with estufalan in combination with gravohormone (6 IU / kg body weight). The animals of the control subgroup were not injected with drugs. To normalize vitamin metabolism, all cows were given vitamins A, D, and E twice with feed.

Table 48 shows that 80.0-88.9% of untreated cows remained sterile. At the same time, the course of complex therapy of cows, taking into account the initial state of the ovaries, provided rapid recovery and fertilization of 91.3-96.3% of animals after 22.5 ± 1.63 - 24.4 ± 2.76 days from the start of treatmen.It should be noted that of the cows treated and remained infertile, 85.7% are animals with the third degree of chronic subinvolution of the uterus and 14.3% - with the second

Table 46

The effectiveness of the treatment of cows with chronic subinvolution of the uterus, taking into account the initial state of the varies

Ovarian condition	Subgroups	The qui/is alive - goal	Fertilization, %		The period of fertilization (days)	Remaining infertile, %	Days of infertility per cow group
			В 1 мес.	За 3 мес			
Corpus luteum of the reproductive cycle	Experienced	27	59,3	96,3	22,5±1,63 xx	3,7	25,0±3,23
	It's in control.	20	-	20,0	65,0±10,57	80,0	85,0±2,70
Hypofunction	Experienced	25	56,0	96,0	24,4±2,76 xx	4,0	27,1±3,91 xx
	Control	17	5,9	17,6	67,3±3,93	82,4	85,9±3,55
Lutein cysts	Experienced	23	52,2	91,3	23,9±1,19 xx	8,7	28,3±3,86 xx
	Control	18	-	11,1	80,0±6,03	88,9	88,9±0,99

The economic efficiency of treatment of cows with chronic subinvolution of the uterus in the presence of functioning corpus luteum, luteal cysts and their hypofunction is 68.92.61.20 and 66.20 rubles, respectively. for one animal.

Studies have shown that chronic subinvolution of the uterus in cows is widespread and is one of the reasons for their symptomatic infertility. Depending on the severity of the pathological process, one should distinguish between chronic subinvolution of the uterus in cows of the first, second and third degree.

Treatment of cows with chronic subinvolution of the uterus should be aimed at restoring the function of not only the uterus, but also the ovaries.An effective way of treating cows with chronic subinvolution of the uterus is the use of ichthyolotherapy in combination with injections of oxytocin, estufalan and one of the gonadotropic drugs, which should be administered at half the optimal dose.

Chapter4.SEASONAL CHANGES IN OVARIES AND IMPROVEMENT OF METHODS OF HORMONAL REGULATION OF REPRODUCTIVE FUNCTION IN CARACUL SHEEP

Improving the methods of hormonal regulation of reproductive function in sheep should be based on the knowledge of the laws of gametofolliculo and luteogenesis in the ovaries and their functional disorders, taking into account the season of the year, manifestations of the stage of the sexual cycle and during pregnancy. In this regard, we first studied the morphofunctional changes in the ovaries of sheep in different seasons of the year, at different stages of the sexual cycle and periods of pregnancy, and then worked out the method of hormonal regulation of the sexual function of sheep. In total, 1839 karakul ewes were used in the experiments.

Experimental studies included the slaughter of experimental ewes with ovarian extirpation and determination of their weight, size, the presence of corpus luteum and atretic bodies, follicles, as well as follicular and luteal cysts.

The prepared histological sections were used to study the structures of the primordial epithelium, the patterns of oogenesis, the formation of primordial follicles, their transformation into secondary and tertiary ones, the development of lytic processes in the corpus luteum under the influence of the tested doses of drugs, as well as the growth of follicles. Histo-functional changes in the ovaries were compared with the dynamics of sex hormones. For histological examination, the ovaries were fixed in a 12% solution of neutral formalin and embedded in paraffin. Serial sections with a thickness of 6-7 microns were stained with hematoxylin-eosin, according to Van Gieson, Frenkel, and Foote. Sections prepared on a freezing microtome were stained with Sudan black and III ± IV.

Morphofunctional changes in the ovaries of sheep in the seasonal aspect (July, October, April) were studied in 36 animals.

4.1. Seasonal morphological characteristics of ovaries in Karakul sheep

It has been established that the common for the ovaries of animals, regardless of the season of the year, the state of sexual function and pregnancy, is constant gametogenesis from the rudimentary epithelium and the formation of primordial, secondary and tertiary follicles (Fig. 19). The further fate of these follicles is determined by the season of the year and the state of sexual function. In particular, in the summer period, from 1-3 large, 3-6 medium-sized and 12-25 small follicles are determined in the ovaries. The corpus luteum and atretic bodies are absent.

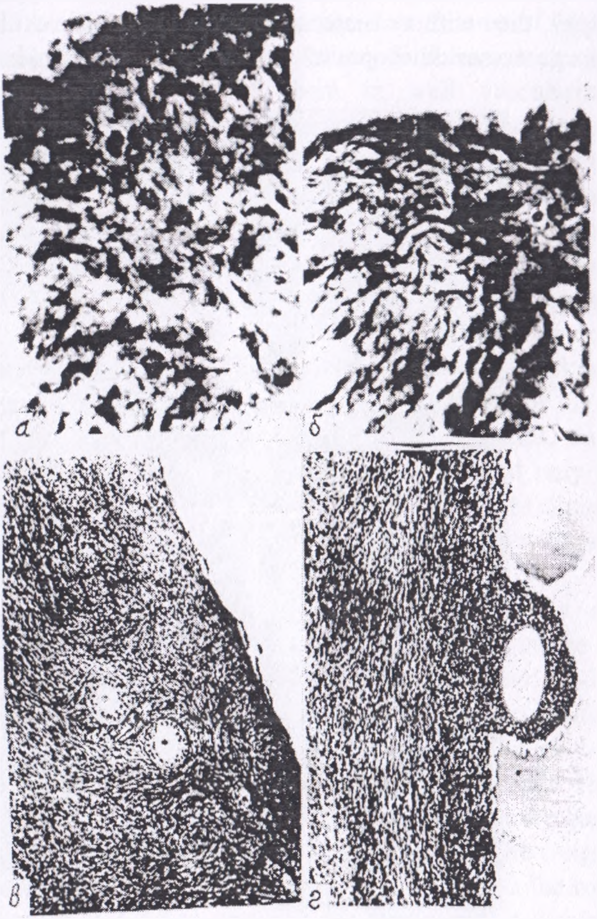


Fig. 19. Sheep ovaries. Gametogenesis from the rudimentary epithelium (a, b) the formation of primordial, condary and tertiary follicles (c, d). Coloring, hematoxylin-eosin. Uv. a, b-1000, c, d-70.

A histological examination of the ovaries showed that in the summer season, the growing follicles do not reach ovulation maturity, but undergo cystic atresia. This phenomenon is based on the development of dystrophic processes in the tecal tissue of the follicles with the subsequent reduction of granulosis and ovum (Fig. 20). The mechanism of this process is that if, with the growth of secondary and small tertiary follicles, well-vascularized thecal tissue enters a state of hyperplasia and hypertrophy, then with an increase in the size of follicles in thecaluteal cells, lytic processes develop with the formation of a fibrous structure.

Figure.20. Sheep's ovaries. Primordial dystrophy (a) secondary and tertiary follicles (b,v,g). Coloration of hematoxyline-eosine. Cv. a-280; 6-70; v,g-24.5.

These processes occur against the background of a decrease in the vascularization of thecal tissue. In this case, large vessels are obliterated.

That is why large follicles determined in the summer season in the ovaries are at different stages of cystic atresia. Fibrosis and replacement of the surrounding tissue of the cortical layer of the gonads, which excludes the possibility of their maturation and the manifestation of the phenomena of the stage of excitation of the sexual cycle.

It should be noted that in the summer season, most of the forming primordial and growing secondary and tertiary follicles come to a state of dystrophy, and only a few of them in well vascularized and morphogenically active areas of the ovarian cortex continue to grow and develop, reaching large sizes. In this regard, one of the factors of seasonal inhibition of sexual function in sheep in summer is morphogenic insufficiency of the mesenchymal elements of the cortex and, as a consequence, of the tecal tissue of the follicles. This excludes the possibility of follicle maturation, their ovulation, the formation of corpus luteum or atretic bodies and the manifestation of other phenomena of the stage of arousal of the sexual cycle. Therefore, against the background of low morphogenic potency of the mesenchymal elements of the ovarian cortical substance and the tecal tissue of growing follicles, the use of gonadotropic and prostanoid drugs is inappropriate. And only this can explain the failed attempts of A.I. Lopyrin (1947) and M.M. Zavadovsky (1963) to cause the activation of sexual function in sheep with hormonal drugs in the summer season.

The ovaries of Karakul sheep are in a completely different generative state, with the restoration of pilaf function in the autumn season. Macroscopically, 1-3 large, 3-5 medium-sized and 15-20 small follicles are visible in the ovaries. In the presence of corpus luteum and atretic bodies, the number of large and medium-sized follicles decreases. The number of small follicles remains within the same range. However, in an ovary with a corpus luteum, as a rule, large follicles are absent, the number of small and medium-sized follicles decreases. The weight of the ovaries does not change significantly in comparison with the ovaries in the summer season (1.7-2.8 g), however, the ovaries with a corpus luteum are always larger in weight and size of the gonads in the summer season and the ovaries in the autumn period and are 2.5-3, respectively. , 1 and 1.6-2.8 g. The size of the ovaries is within 1.9-2.8 cm in diameter.

A histological study of sheep ovaries showed that the phenomenon of gametogenesis from the primordial epithelium with the formation of primordial follicles and their transition to secondary and small tertiary follicles is observed constantly and regardless of the state of the reproductive function and the presence or absence of corpus luteum in the gonads.

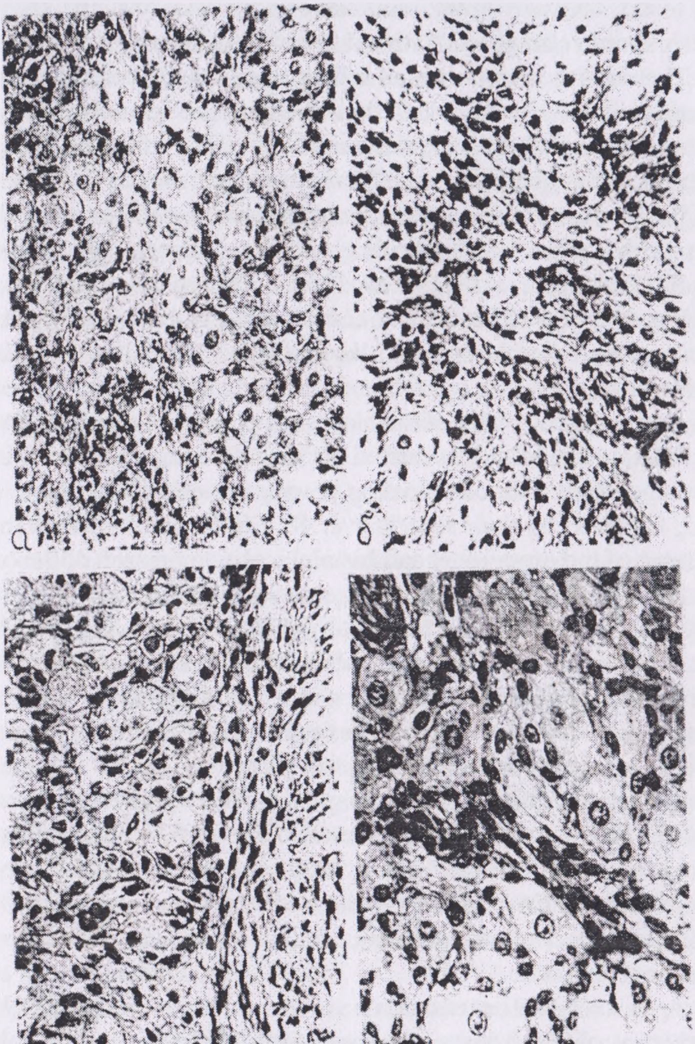
Maturation and ovulation of follicles occur only with a certain state of sexual function. In particular, with ovarian hypo-function, despite the growth of primary, secondary and small tertiary follicles, their complete maturation and ovulation does not occur, which is associated with hypoplasia of the connective tissue elements of the ovarian cortex and follicle membranes.

With the activation of the sexual function of sheep, which has been observed since the second half of September, as well as with involution of the corpus luteum of the sexual cycle, vascularization and proliferation of cells of the internal theca increase, which creates trophic conditions for hyperplasia and hypersecretion of granulosis **(Fig. 21).**

In this regard, the growing follicles reach large sizes, then ovulation and the formation of the corpus luteum occur.

It should be noted that corpus luteum and atretic bodies are formed from proliferating cells of the internal theca, while granulosis undergoes dystrophy (Fig. 21). In this regard, well-vascularized functionally active connective tissue elements of the membranes of graaf vesicles should be considered as a tissue that performs a trophic function (ensuring the growth and maturation of follicles), plastic (transformation into corpus luteum) and hormonal (production of progesterone) functions.

With functioning yellow bodies of the sexual cycle, the growth of follicles does not stop, however, they do not reach ovulation maturity, but undergo atresia. Consequently, the maturation of follicles and the realization of the ovulation effect are determined by the potential of the connective tissue elements of the ovaries.



21. Sheep's ovaries. Formation of yellow bodies. Cv. a, b, 280 g-400.

4.2. Improving the methods of hormonal and pro-stanoid synchronization of sexual function in Karakul sheep

To reveal the regularities of folliculo and luteogenesis in the ovaries of sheep and to clarify the role of the mesenchymal elements of the gonads and thecal tissue of follicles, the specificity of the effect on the cellular structures of the gonads of gonadotropic and prostanoid drugs and their biological properties, special experiments were carried out on 97 Karakul sheep, which were injected with gonadotropic drugs (gravogormone, FFA, FSH) at a dose of 900, 1200, 1250, 1600, 2400 units on 7-8, 13-14 days from the start of heat detection and with ovarian hypofunction. The animals were slaughtered on the 5th day after the injection of gonadotropins.

A comparative study of the biological properties of gravoghormone, FFA, FSH, LH and CG was carried out on 320 mice, which were injected with drugs alone or in combination (augmentation test) at a dose of 3 to 35 IU, followed by their slaughter at 48, 66, 74 and 96 hours from the beginning of the experiment and histological examination of the ovaries.

It has been established that gametogenesis and the formation of primordial follicles are constantly carried out in sheep and mice **(Fig. 21)** Their further growth and transformation into secondary and tertiary follicles are associated with migration into the deeper layers of the ovarian cortex and the differentiation of a well vascularized morphogenically active connective tissue membrane around them.

In experiments with the use of gonadotropic drugs, it was found that with hypofunction of the ovaries and involution of the corpus luteum, the number of ovulating follicles increased with increasing doses of gravogormone, FFA and FSH, while with functioning corpus luteum of the sexual cycle, only the growth of follicles was activated without their subsequent ovulation.

A histological examination of the ovaries revealed that the introduction of these drugs in a dose of 900 IU. sheep with involutional yellow bodies and 1200 IU. with hypofunction of the ovaries, it stimulates morphogenic processes in the connective tissue structures of the gonads, as a result of which 2-3 follicles undergo ovulation.

With an increase in doses of FSH (1250 IU), gravogormone and FFA (1600, 2400 IU), in addition to an increase in the number of ovulated follicles (3-6), the plastic reaction in the connective tissue elements of the cortex and follicle membranes increases. In this regard, non-ovulated small and medium follicles undergo luteonization, and primordial and secondary ones, being carried deep into the ovarian cortex, undergo dystrophy. Therefore, after the introduction of large doses of gonadotropic drugs, the number of follicles in the ovaries sharply decreases or they are not detected, while the connective tissue cells of the cortex, undergoing hyperplasia and hypertrophy, acquire the structure of interstitial cells. Consequently, the use of large doses of gonadotropic drugs is inappropriate, although they do not cause biological castration due to the preservation of the gametogenic function of the ovaries.

After the introduction of gonadotropic drugs on sections of ovaries with functioning yellow bodies, an activation of vascularization and proliferation of the vascular layer of the follicle membrane was observed, followed by lysis of the cytoplasm, pycnosis of the nuclei and the formation of a fibrous structure.

The established regularity of the action of the tested gonadotropic drugs on sheep was confirmed also on infantile mice. In particular, the introduction of gravohormone, FFA, FSH, LH and CG to mice at a dose of 3-12 IU. each individually or in different versions (augmentation test) provided superovulation, an increase in the mass of the uterus and ovaries. At the same time, vascular and morphogenic reactions in the connective tissue elements of the cortical substance of the ovaries and follicle membranes were activated, which ensured the growth, maturation and ovulation of follicles. Under the influence of higher doses (24-35 IU) of drugs, hyperplasia and hypertrophy of the connective tissue elements of the cortex of follicle membranes occurred with the formation of atretic, yellow bodies and interstitial cells. The granulosis was reduced (Fig. 21). It follows from this that both FSH, LH, CG, and FFA and gravogormone have a specific effect on the connective tissue elements of the ovary and, depending on the doses administered, can provide follicle growth and luteinization without pre-maturation, which was observed in the last experiment. This is the reason for the lack of reaction from the uterus (loss of estrous effect).

It should be noted that gametogenesis and the formation of primordial follicles occur throughout the female's reproductive life.

Further growth of follicles is associated with the differentiation around them of the morphogenically active connective tissue membrane, from the cells of which the corpus luteum is formed. This was confirmed by enzymatic-histochemical research methods. In this regard, one cannot agree with the prevailing opinion about the participation in the formation of the corpus luteum of the follicular epithelium and the production of their progesterone after its glandular metamorphosis into luteal cells. It follows that estrogens are synthesized by the follicular epithelium.

Based on the fact that gonadotropic hormones (FSH, LH, hCG) and drugs (FFA, gravogormone) regulate the function of the ovaries through their connective tissue

Based on the revealed patterns in the generative function of the ovaries and taking into account the influence of gonadotropic factors on sexual function, experiments were carried out on 1794 ewes of the Karakul breed to work out the optimal doses of estufalan, clathraprostin and gravoprost, synchronize their sexual activity and in the fight against infertility, as well as for the purpose of terminating pregnancy to obtain broadtail.

The experiments were carried out in September October and February March 1990. Estufalan was tested on 60 ewes at doses of 0.25 ml (62.5 μg), 0.5 ml (125 μg), 1 ml (250 μg) and 2 ml (500 μg) based on the active ingredient (cloprostenol) in 1 ml 250 mcg. Clathraprostin was administered to the same number of animals at doses of 0.25, 0.5, 1.0 and 2.0 ml based on the active principle (cloprostenol) in 1 ml 50 μg. The tested drugs were administered against the background of a functioning corpus luteum sexual cycle (6-8 days). In experimental animals, using ram probes, sexual heat was detected, morphofunctional changes in the ovaries and the dynamics of sex hormones (progesterone and estradiol-17 beta) were studied 12, 24, 48, 72 and 96 hours after the administration of various doses of the above-mentioned preparations. Each series of experiments consisted of 12 animals. A total of 120 animals were used in the experiments. In addition, on 288 ewes, the optimal doses of gravogormone (1000, 750 and 500 IU) were worked out in combination with estufalan and clathraprostin in the established optimal doses (0.5 ml or 125 and 25 μg, respectively) for the synchronization of sexual heat and in case of dysfunctions. ovaries of sheep.

For 160 pregnant (128-132 days of pregnancy) ewes, the above optimal doses were worked out for termination of pregnancy in order to obtain broadtail.
Along with this, production experiments were carried out on 1200 ewes, respectively, in an equal number (600 heads) for testing estufalan and clathraprostin alone and in combination with gravogormone.

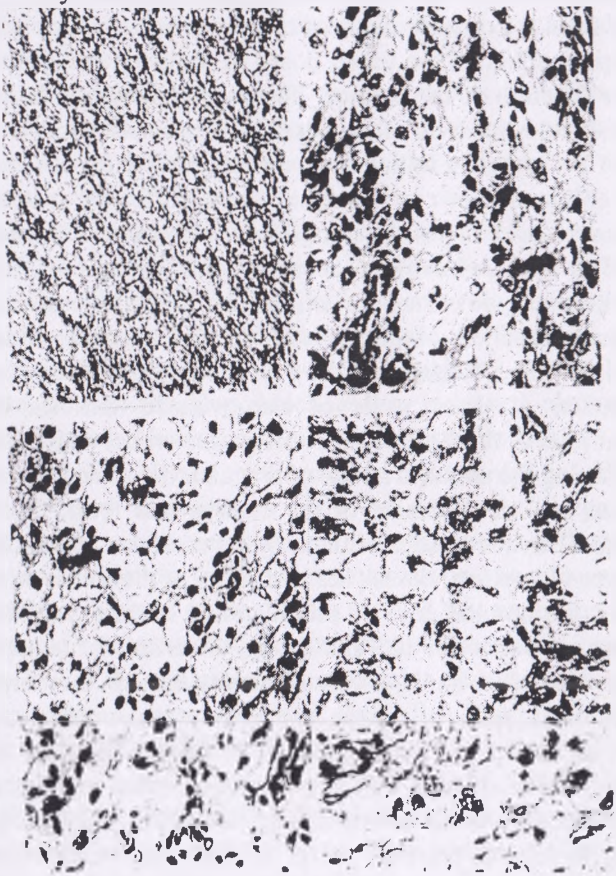
The characteristics of this material showed that the weight of the ovaries of the control animals is in the range of 1.5-2.0 g, the size is 1.7-2.4 cm, the weight of the ovaries with a corpus luteum somewhat exceeds the ovaries without a corpus luteum (0.2-0.4 g), the size of the corpus luteum was 1.0-0.6 cm in diameter. On the ovaries, mainly small follicles were seen, and only in a few animals can one find medium-sized follicles. Under the influence of the tested drugs, complex morphological and hormonal changes in the ovaries are observed, and these changes are reduced to a decrease in the size of the corpus luteum and the appearance of large and medium-sized follicles in the ovaries.
It was found that common to all ovaries of control and experimental animals is constant gametogenesis from the rudimentary epithelium and the formation of primordial, secondary and tertiary follicles (Fig. 19a, b). Moreover, in the process of histogenesis of these structures, some of them are transformed from primordial to secondary and tertiary, while others undergo dystrophy at different stations. In this regard, the sections show both functionally active structures and in a state of dystrophy. Moreover, tertiary follicles, in addition to the development of dystrophic processes in them, undergo atresia by reduction of granulosis and proliferation of the internal theca with the formation of atretic bodies. The corpus luteum of control animals was characterized by the development of destructive processes, namely: due to the development of lytic processes in the cytoplasm and pycnosis of the nuclei, as well as the reduction of the capillary network, the connection between the cells was disrupted, they acquired a cubic, elongated or flat shape. These processes intensified on 3-4 days and on 5-6 days ended with large oval luteal cells with rounded nuclei covered with a capillary system. In the trabeculae that divide the corpus luteum into lobes, there are large blood vessels. Outside, the corpus luteum is covered with a fibrous layer.

In ovaries with a corpus luteum, gametogenesis and the formation of primordial follicles do not stop, however, tertiary follicles are found much less in comparison with an ovary free of the corpus luteum.

Considering that morphological changes in the ovaries and hormonal changes in the blood of experimental animals under the influence of doses of estufalan and clathraprostin equal in terms of the active principles are very similar, in order to reduce the presentation of the material, the data obtained in series of experiments similar in doses will be presented together.

It was found that the nature of morphological changes in the ovaries is determined by the administered dose of the tested drugs, the initial state of sexual function and the duration of the experiments.

So, out of 12 ewes, which were injected estufalan and clathraprostin at a dose of 0.25 ml (62.5 and 12.5 μg of the active principle) on the 7-8 day after insemination, 4 of them showed sexual intercourse 48 hours after the administration of the drug. hunting, and in the ovaries, against the background of involution of the corpus luteum, ovulation occurred in one follicle. In 4 animals, sexual heat was not detected, however, ovulation occurred in one follicle in the ovaries. In the remaining 4 animals, sexual heat was not revealed and yellow bodies were preserved in the ovaries. Histologically, involutional processes in the corpus luteum on the second day after the injection of protenoids at a dose of 0.5 ml were characterized by the development of destructive processes, namely: due to the development of lytic processes in the cytoplasm and pycnosis of the nuclei, as well as the reduction of the capillary network, the connection between the cells was disrupted, they acquired cubic, elongated or flat. These processes intensified on days 3-4 and ended on days 5-6. At the same time, obliterating vessels and single cells with vacuolated (lysed) cytoplasm and small nuclei included in the connective tissue stroma were seen in place of the corpus luteum (Fig. 22). In the process of luteolysis of the corpus luteum, gametogenesis continued, the formation of primordial follicles, and the growth of secondary and tertiary follicles. Against this background, follicles maturation, their ovulation with the manifestation of other phenomena of the stage of arousal of the sexual cycle took place. Ovulation of follicles occurred on the third, less often on the fourth day of the experiment. The ovulation process was preceded by the development of hyperplastic and hypertrophic processes in the tecal tissue of the follicles, an increase in its vascularization, as well as a reduction (together with the ovum) of the surface layers of granulosis. In the process of ovulation, a hypertrophically altered and well-vascularized internal body protrudes into the vacated cavity of the bursting follicle. In this case, there is a rupture of blood vessels and hemorrhage into the cavity, which creates trophic conditions for the proliferation of morphogenically active thecal tissue.



Rice.22. Sheep's ovaries.Difference in the degree of involution of yellow bodies with lysis of cytoplasm and pictorosis of nuclei. Coloration of hematoxyline-eosine. Cv. 280

Along with the proliferation of thecal cells, they differentiate into luteocytes with the formation of a capillary system around them. These processes ended 3-4 days after ovulation and the corpus luteum was already presented as a formed endocrine organ. On the 5-6th day after ovulation, the corpus luteum acquired large sizes, an elastic elastic consistency, and well-injected vessels were traced on their surface, which indicated the completion of their formation.

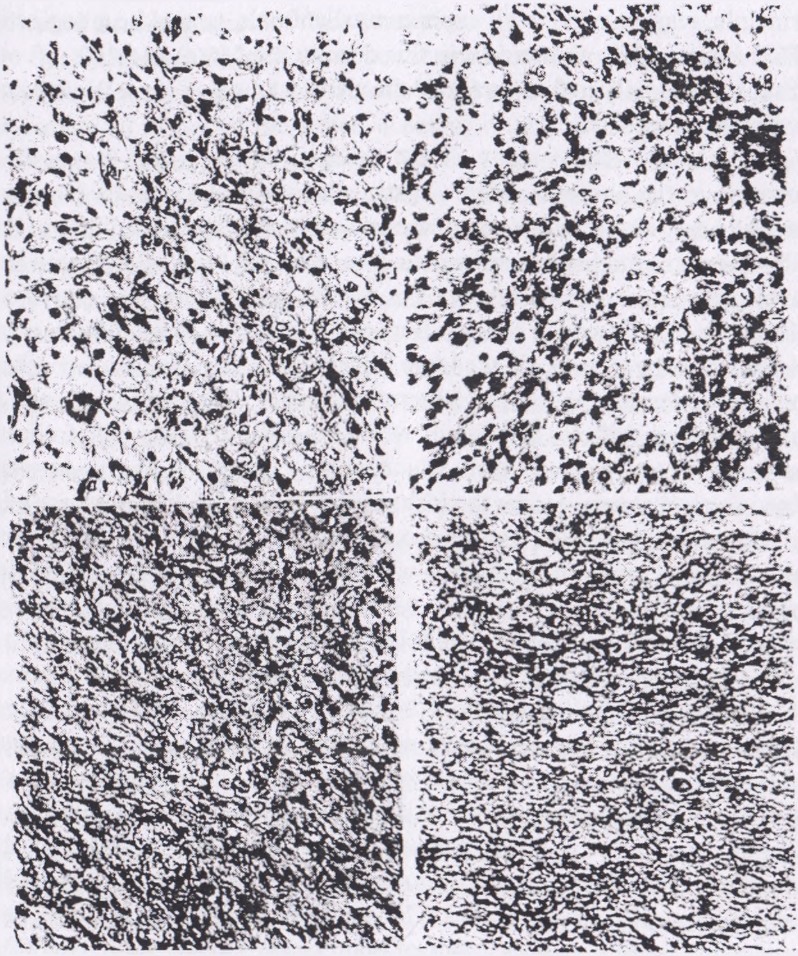
It should be noted that the structure and size of the corpus luteum did not differ from the corpus luteum of control animals, which indicates the physiological effect of the tested doses of drugs on the generative and endocrine function of the ovaries. This is evidenced by the continuing gameto-follicular function of the ovaries. At the same time, it was found that out of 2-4 maturing follicles one ovulates, less often two, and the rest undergo obliterative or cystic atresia. The need for the maturation of a large number of follicles in comparison with their ovulation can be explained by the creation of a proper estrogenic background in the body, which is necessary to ensure the activation of the proliferative, secretory and protenoid functions of the uterus and the manifestation of the female's sexual dominance. Obliteration by proliferation, differentiation and hyperfunction of thecal cells of non-ovulated follicles creates an additional reserve for the production of progesterone, which is necessary for transferring the uterus to a state of pregnancy, ensuring the nidation of the zygote, and development of the embryo and fetus. These are the physiological characteristics of the subjects estufalan and clathraprostin, administered in optimal doses (125 and 25 μg of the active principle).

Thus, the optimal dose of estufalan and clathraprostine should be considered, respectively, 125 and 25 μg, under the influence of which, within physiological limits, involutional processes in the corpus luteum are carried out, follicles mature and ovulate, new corpus luteum are formed and, therefore, the regulation of sexual function inherent in generative and endocrine function of the ovaries of intact animals. Therefore, drugs in this dose can be recommended for the synchronization of sexual hunting in Karakul sheep. At the same time, comparing the minimum and optimal doses of drugs and observing in the first case luteolytic and folliculogenic effects in some animals, it becomes necessary to conduct additional studies in order to work out a more optimal dose.

With increasing doses of the tested drugs, the luteolytic effect in the ovaries increases with a simultaneous decrease in the manifestation of sexual desire and ovulation of the follicles. So, if after the introduction of estufalan and clathraprostine in a dose of 1 ml (250 and 50 μg of the active principle, respectively) in all experimental animals, sexual heat begins in 48-72 hours, while an increase in this dose to 2 ml (500 and 100 μg) out of six animals only in four provided the manifestation of sexual desire and ovulation of follicles.

In a macroscopic study of the ovaries, it was found that with a decrease in the ovulation effect, cystic changes in the ovaries increase, which is associated with an increase in the dose of the tested drugs. So, after the introduction of protenoids in a dose of 1 ml, along with the involution of the corpus luteum, the growth of follicles was activated. Moreover, 12-13 small, 5-6 medium-sized and 3-4 large follicles are identified in the ovaries. Of the large follicles, as a rule, one ovulated, and the rest underwent cystic or obliterative atresia. Obliterative atresia of medium-sized follicles prevailed, while the majority of small follicles continued to grow and develop, which, as they increased, also underwent physiological atresia. Under the influence of prostaglandins in a dose of 2 ml, the number of small and medium-sized follicles did not differ from the previous group of animals, while the number of large follicles increased and their size increased. Moreover, in animals without signs of sexual heat and ovulation, the follicles underwent cystic changes.

A histological study of the ovaries showed that under the influence of estufalan and clathraprostine, administered at doses of 250 and 50 μg, if after one day of the experiment no noticeable changes in the structure of the corpus luteum were observed, then after 2 days the cytoplasm underwent vacuolization and lysis, the intercellular communication was disrupted and they lost configuration. After 3 days of the experiment, the parenchyma of the corpus luteum is represented by elongated and flat cells with pyknotically altered nuclei. The capillary system was reduced, and large blood vessels came to a state of obliteration. On the 3-4th day of the experiment, the corpus luteum decreased to a pea or millet grain, and on the sections fibrous structures with single included flat nuclei and obliterating vessels were observed, around which single intercellular proliferates were observed (Fig. 23).Against the background of the involution of the corpus luteum, the growth of follicles was activated. This process mainly concerned secondary and tertiary follicles with a differentiated and well-vascularized flow.



Ovich sheep. Involutionary processes in yellow bodies under the influence of prostaglandin F-2 alpha. Coloration of hematoxyline-eosine. Cv. 280.

At the same time, with the proliferation and vascularization of thecal tissue, the proliferative processes in granulosis intensified, which acquired a multilayer radial structure and were characterized by a hypersecretory state, ensuring the accumulation and content of follicles. an increase in their volume. As a result of the activation of the folliculogenic function of the ovaries, on the 2-3rd day of the experiment, up to 3-4 large and 12-15 small tertiary follicles were identified in them. A feature of the effect of the tested drugs at a dose of 1 ml .

At the same time, granulosis undergoes dystrophy and reduction, and the follicle cavity is filled with thecal cells with high morphogenic potency, forming a corpus luteum. The same processes are observed during obliteration of non-ovulated smaller follicles. However, under the influence of these doses of prostaglandins, in contrast to the lower and optimal doses, cystic atresia of the follicles predominates. This is due to more pronounced lytic processes in thecaluteal cells with their subsequent fibrous replacement. These processes intensify with increasing doses of prostaglandins.The introduction of estufalan and clathraprostine in a dose of 2 ml or, respectively, 500 and 100 μg of the active principle causes a more pronounced lytic and follicle-stimulating effect with symptoms of cystic dystrophy of the follicles. At the same time, out of 12 experimental animals, only 8 showed ovulation and ovulation of follicles, in 4 ewes, ovulation and ovulation did not appear.Analyzing the material obtained at the histological level, it should be noted that already a day after the injection of drugs in certain areas of the parenchyma of the corpus luteum, especially with its pronounced vascularization, the cytoplasm of luteal cells undergoes vacuolization and lysis with the accumulation of light substance in the intercellular spaces. After two days, these processes intensify and luteocytes from oval pass into elongated and flat ones with pyknotically altered nuclei. Against the background of destruction of luteal cells, the capillary system is reduced, and large blood vessels are obliterated. On the 3-4th day of the experiment, the corpus luteum acquired a fibrous structure with obliterating vessels (Fig. 23).Along with the development of lytic processes in the corpus luteum, the phenomenon of lysis is observed in large tertiary follicles with differentiated thecalutein cells (Fig. 23).Moreover, in animals without signs of sexual heat and ovulation, the ovaries acquire a cystic structure, the follicles of which are characterized by reduced granulosis and fibrous changes in the internal flow. In sheep with revealed heat and ovulation, differentiated thecaluteal cells also underwent a lytic process, but the rest of the well-vascularized tissue provided maturation and ovulation, as a rule, of one follicle, and the remaining large follicles underwent cystic atresia. It should be especially noted that in this group of experimental animals there is a slow development of experimental yellow bodies, which, as a rule, do not fill the entire strip of the ovulated follicle, as a result of which cysts of the living bodies are formed. This indicates a negative effect of overestimated doses of the tested prostaglandins on the morphogenic function of the corpus luteum. At the same time, the gametogenic function of the ovaries with the formation of primordial follicles and their transformation into secondary and tertiary follicles is preserved, which excludes the possibility of a sterilizing effect of protenoids on the gonads. Therefore, these drugs, even in overestimated doses, cannot adversely affect the reproductive potential of females.From a comparison of morphological changes in the ovaries with the dynamics of sex hormones in the blood of experimental animals, it follows **(Table 47)** that if in control ewes the level of progesterone and estradiol-17 beta in the blood is quite stable and is, respectively, in the range of 2096.8-2897.4 and 27.6-21.9 ng / ml with a slight increase in progesterone and a drop in the level of estradiol-17 beta as the histofunctional determination of luteocytes in the corpus luteum proceeds, then after the introduction of estufalan, the function of the corpus luteum drops sharply.

Moreover, the level of progesterone in the blood decreases with increasing doses of estufalan. So, under the influence of estufalan at doses of 500, 250 and 125 mkg, the level of progesterone on 2-3 days of the experiment decreases 3-5 times with a simultaneous increase in the level of estradiol-17 beta, while the introduction of this drug at a dose of 62.5 mkg does not provided sharp changes in the dynamics of sex hormones in the blood (although in some animals the level of progesterone approached the values after the injection of 125 mkg of es-tufalan), which should be attributed to the insufficient dose of the drug.

Table47

Dynamics of sex hormones in the blood plasma of sheep with functioning yellow bodies under the influence of estuphalan (pg/ml, p-6)

group	Hormones under study	Doses of estuphalan	Before introduced, the drug	After the introduction of the drug				
				12 hour	24 hour	48 hour	72 hour	96 hour
1	Progesterone	2 ml(500мkg)	2850,0±173,27	1975,0±120,15	718,6±84,12	62,3±12,18	98,2±21,03	303,1±35,12
	Estradiol-17 beta	-"-	21,1±3,08	23,5±4,51	24,1±2,11	31,5±3,09	29,4±2,08	45,5±3,55
2	Progesterone	1 ml (250 мkg	1984,0±133,05	1566,1±97,04	1114.4±151,12	77,1±15,11	872,4±20,51	441,9±32,15
	Estradiol-17 beta	-"-	29,7±5,02	28,4±3,51	26,1±2,08	35,4±3,22	28,8±2,77	39,7±3,65
3	Progesterone	0.5 (125 мkg)	2085,0±161,15	1864,4±119,11	827.4±97,24	86,5±27,51	365,1±18,13	899,7±31,7
	Estradiol-17 beta	-"-	20,1±3,15	22,5±4,19	29,5±3,35	36,4±4,07	25,4±3,15	21,5±2,11
4	Progesterone	0.25 (62.5 мkg)	2975,4±160,12	2834,1±181,4	2019,7±164,1	1215,3±219,4	1419,6±384,7	1645,4±219,6
	Estradiol-17 beta	-"-	27,5±4,19	29,4±4,19	32,1±5,21	33,4±6,17	26,4±7,12	25,6±6,19
5	Progesterone	-	2096,8±145,14	2109,4±139,19	2197,2±149,14	2088,5±141,11	2304,1±149,09	2897,4±157,12
	Estradiol -17 beta	-	27,6±1,98	26,9±1,07	28,6±2,09	27,1±1,91	24,7±1,09	21,9±0,45

At the same time, after the introduction of estufalan in doses of 500 and 250 mkg, by the end of the experiment, there was a sharp rise in estradiol-17 beta and a slight increase in progesterone in the blood, which is associated with excessive activation of follicle growth and their cystic dystrophy. Therefore, these doses of the drug should be attributed to overestimated and they cannot be recommended for production.

The optimal dose of estufalan should be recognized as 0.5 ml (125 mkg), under the influence of which there is a pronounced involution of the corpus luteum with a drop in the level of progesterone from 2085.0 ± 161.15 mkg to 86.5 ± 27.56 ng / ml after 48 hours of experience with simultaneous growth, maturation and ovulation of follicles in the background of an increase in the level of estradiol-17 beta from 20.1 ± 3.15 to 36.4 ± 4.07 ng / ml. With ovulation and the formation of corpus luteum, the level of progesterone in the blood on the 5th day of the experiment increases from 86.5 ± 56.0 to 899.7 ± 31.7 ng / ml with a simultaneous decrease in the blood levels of estradiol-17 beta to 21.5 ± 2, 11 ng / ml.

A similar pattern in the dynamics of sex hormones in the blood is observed after the administration of different doses of clathraprostine **(Table 50).** However, this drug, even in high doses (100 and 50 mkg), unlike estufalan, does not cause a sharp increase in estradiol-17 beta in the blood and provides a moderate increase in the level of progesterone in the blood by the end of the experiment, which is associated with ovulation and the formation of new yellow bodies against the background of exclusion or reduction of follicular cystic dystrophy. This gives grounds to conclude about a more physiological effect of clathraprostine in comparison with estufalan and to recommend it for production.

Table48

Dynamics of sex hormones in the blood plasma of sheep with functioning yellow bodies under the influence of clatraprostin (ng/ml p)6

groupe	Investigated hormones	Doses d'estuphalan	Avant d'introduire, le médicament	Après l'introduction du médicament				
				12 hour	24 hour	48 hour	72 hour	96 hour
1	Progesterone	2 ml (100мkg)	3105+1+198,15	2008,4+175,13	945,4+29,15	95,9+47,4	275,1+29,7	894,9+109,17
	Estradiol-17 beta	-"-	26,7+3,14	28,4+4,07	31,5+3,04	39,1+2,15	29,7+3,04	39,4+2,18
2	Progesterone	1 ml (50 мkg)	2574,2+145,12	1975,3+157,21	847,1+37,12	82,4+39,7	347,4+24,9	795,4+27,12
	Estradiol-17 beta	-"-	29,5+3,12	31,4+2,81	34,4+4,11	42,3+3,09	30,1+2,31	32,9+3,19
3	Progesterone	0.5 (25 мkg)	1996,5+157,12	1281,4+117,2	695,3+42,15	91,4+17,24	298,1+19,8	839,9+31,15
	Estradiol-17 beta	-"-	38,5+4,19	37,4+6,18	42,9+4,19	46,5+3,17	32,4+2,18	26,7+3,16
4	Progesterone	0.25 (12.5 мkg)	2106,8+119,7	1929,1+49,7	1278,8+47,5	1021,5+81,2	1271,1+91,56	1525,3+86,12
	Estradiol-17 beta	-"-	26,9+4,11	29,5+4,07	31,4+8,12	34,1+7,15	28,7+3,11	26,5+4,02
5	Progesterone	-	2096,8+145,14	2109,4+139,19	2197,2+149,14	2088,5+141,11	2304,1+149,09	2897,4+157,12
	Estradiol-17 beta	-	27,6+1,98	26,9+1,07	24,6+2,09	27,1+1,91	24,7+1,09	21,9+0,45

4.3. Development of hormone therapy methods for ovarian dysfunction in Karakul sheep

In addition to studying the biological properties and determining the optimal doses of estuphalan and clathraprostin, our task was to find out the possibility of complex use of prostanoids with gonadotropin FFA, which have luteolytic and follicle-regulating effects, and therefore provide-prevention and treatment of ovarian functional disorders insheep. Various doses of gravohormone alone (1000, 750, and 500 iu) were used, or in combination with estuphalan and clathraprostine at the established optimal doses (125, 25 mcg, or 0.5 ml). Experimental schemes are presented in table 51. So, out of 7 groups of experimental animals, sexual hunting did not occur in 2, 4 and 6 groups of animals that were administered one gravohormone. All experimental ewes of groups 1 and 7 who were treated with estuphalan alone and in combination with gravohormone at a dose of 500 m. e., developed sexual hunting after 48-72 hours and wereartificially inseminated. In groups 3-5 ewes treated with gravohormon at a dose of 1000 and 750 m. e. in combination with estuphalan, 3 and 4 ewes started hunting and were inseminated, respectively.

Analysis of morphohistological changes in the ovaries andthe dynamics of hormones in sheep blood plasma showed that under the influence of one gravohormone in the ovaries, the growth of follicles that do not ovulate, but undergo cystic or obliterative atresia, is activated. In this regard, the level of estradiol-17 beta in the blood plasma increases by 1.5-3 times on day 2-3 of the experiment, with a simultaneous increase in the concentration of progesterone in the blood.By the end of the experiment, these indicators reach the initial level or slightly exceed it in terms of progesterone, which should be explained not only by the ongoing hyperfunction of the corpus luteum, but also by the production of progesterone by obliteratingfollicles. Comparing the follicle-stimulating effect of different doses of gravohormone against the background of functioning yellow bodies, we shouldnote the most physiological effect of gravohormone at a dose of 500 m. e., under the influence of which the progesteroneand estrogen function of the ovaries is moderately activated with maturation and obliteration of 1-3 large follicles. With ovarian hypofunction, a similar effect, as noted above, is achieved by doubling this dose.

Table49

Dynamics of sex hormones in the blood plasma of sheep with functioning yellow bodies under the influence of gravohormone (G) and estuphalan (E)

gravoprost (pg / ml, n=6)

Group	Hormones under study	Doses of estuphalan	Before introduced, the drug	After the introduction of the drug				
				12 час	24 hour	48 hour	72 hour	96 hour
1	Progesterone	E-125 mcg	2985,6±161,15	1864,4±119,11	827,4±97,24	86,5±27,55	365,0±18,13	899,7±31,7
	Estradiol-17 beta	-"-	20,1±3,15	22,5±4,19	79,5±3,75	36,4±4,67	25,4±3,15	25,1±2,11
2	Progesterone	G-1000	24,05±127,41	2486,1±149,39	2509,7±169,95	2985,4±149,13	3798,9±158,92	3596,8±132,17
	Estradiol-17 beta	-"-	26,8±2,19	31, 9±2,96	52,7±3,68	89,6±4,17	94,1±4,87	25,9±1,11
3	Progesterone	G-1000	1898,1± 135,15	1454,2± 49,71	587,9± 31,91	91,5± 18,15	621,4± 22,t5	1250,1± 34,19
	Estradiol-17 beta	-"-	21,7±1,18	35,4±4,19	41,9±4,21	52,4±3,15	14,2±1,13	7,5±0,12
4	Progesterone	G-750	2314,9±164,12	2601,2±151,17	2709,6±139,39	3089,6±149,69	3468,8±149,67	3179,5±144,89
	Estradiol-17 beta	-"-	28,91±3,01	32,6±2,81	41,9±3,04	84,7±4,95	91,8±4,1	29,2±1,11
5	Progesterone	G-750 - 125 mkg	2495,9±139,16	1634,9± 56,17	399.4± 39,60	101,2± 24, 17	549,1± 19, 17	1309,2± 24,18
	Estradiol-17 beta	-	25,4±1,09	31,5±1,11	39,7±2,01	46,9±3,11	13,9±1,09	8,1±0,15
6	Progesterone	G-500 n	2575,4± 131,92	2604,3± 149,12	2696,7± 136,91	2895 1± 124,67	3129,7± 130,96	2915,3± 119,27
	Estradiol-17 beta	-"-	24,7±1,69	27,9±1,87	39,6±2,98	45,7±4,12	52,1±3,96	39,5±2,69
7	Progesterone	G-500 ед. E-125 mcg	3001,5± 146,17	1619,9± 59,16	600,9± 43,17	119,6± 12,19	314,6± 17,12	802,4± 17,02
	Estradiol-17 beta	-"-	29,6	35,9	37,6	38,1	27,9	25,6
8	Progesterone	-	2096,8± 145,14	2109,4± 139 ,19	2197,2± 149,14	2088,5± 141,11	2309,1± 149,69	2897,4± 157,12
	Estradiol-17 beta	-	27,6±1,98	26,9±1,07	24,7±2,09	27,1±1,91	24,7±1,09	21,9±0,45

Table50

Dynamics of sex hormones in the blood plasma of sheep with functioning yellow bodies after administration of gravohormone (G), clathraprostin (K) - gravoclatran (ng / ml, n=6)

Group	Test hormones	Estuphalan doses	Prior to the introduction of the drug	After drug administration				
				12 hours	24 hours	48 hours	72 hours	96 hours
1	Progesterone	G-1000, K-25 mcg	2465,4±150,85	1956.3±115,12	529,1±47,15	89,2±19,64	497,17±29,13	835,9±37,14
	Estradiol-17 beta	-"-	28,5±6,15	29,4±4,17	32,3±3,11	31,5±2,18	18,1±2,17	8,1±0,19
2	Progesterone	G-750, K-25 mcg	1998,4±171,15	1015,8±87,14	429,2 39,12	79,4±18,12	395,4±37,12	915,4±42,11
	Estradiol-17 beta	-"-	26,7±3,12	39,1±3,19	41,4±4,04	35,1±3,01	21,2±2,91	13,5±2,40
3	Progesterone	G-500, K-25 mcg	2125,4±147,12	1719,9±192,12"	609.9± 47,9 G	90,7±19,15	219,4±29,17"	649,9±39,11
	Estradiol-17 beta	-"-	29,4±3,09	30,4±3,11	47,1±3,91	31,1±2,01	24,2±2,02	26,1±3,11
4	Progesterone	-	2096,8±145,14"	2109,4±139,19	2197,2±149,14	2088,5±141,11	2309,1±149,09	2897,4±157,12
	Estradiol-17 beta	-	27,6±1,98	26,4±1,07	24,6±2,09	27,1±1,91	24,7±1,09	21,9±0,45

Introduction one Astypalea or concomitant use with grogoryan at a dose of 500 M. E. ensured the development involuinnovative processes in the yellow bodies and the decrease in the concentration aboutgesterone in the blood after 48 hours of experience with 2955,6-3001,5 to 86.5 is 119.6 ng/ml, while increasing the level of estradiol-17 beta from 20.1-29.6 to 36,4 to 38.1. Ovulation and the development of yellow bodies led to a drop in the blood concentrationof estradiol-17 beta to 21.5-25.6 ng / ml and an increase inthe blood level of progesterone to 899.7-802.4 ng / ml on day 5 of the experiment.

The combined use astutely with higher doses of grogoryan (1000 and 750 E. M.), along with the development of political processes in the yellow bodies and fall in the blood level progesteRon, caused a more pronounced and its EFfect, in which the ovaries develop on 3-8 large and medium-sized follicles, most of which are not ovuleravelo, and has undergone cystic and obliteration atresia. This was accompanied in some animals by the manifestation of alibid anovulatory sexual cycles. In this connection, out of 12 experimental ewes, sexual hunting was detected only in 7. Therefore, these doses of gravohormone cannot be recommended in the practice of sheep breeding.

Therefore, the optimal dose of gravohormone should be considered 500 m. e., and estufalan-125 mcg. The combined use of these drugs ensures the development of involutional processes in the yellow bodies, and the inductionof endogenous gonadotropin of the pituitary gland and exogenous gonadotropin complete the growth, maturation and ovulation of follicles with the manifestation of other phenomena of the stage of sexual arousal of the sexual cycle. It is the summation of exogenous and endogenous gonadotropic effectsagainst the background of yellow body involution that ensures the manifestationof exogenous gonadotropic drugs in lower doses.Analysis **Table 50** in comparison with morphohistologicalmi changes in the ovaries and the identification of sexual hunting after applying latrepirdine in the dose of 25 µg in combinationTanya with different doses of grogoryan (1000, 750 and 500 M. E.) forshows that in the second and third groups of animals all the timewhether in hunting and artificially inseminated, whereas in the first groupPE animals, which introduced 1000 M. E. grogoryan and 25 µg latrepirdine, one sheep showed rut. Itwas found that under the influence of clathraprostin and gravohormone during the first two days, the level of progesterone in the blooddecreases 2.5-3 times with a simultaneous increase in the level of esradiol- 17 beta **(Table 50).** At the same time, lytic processes develop morphologically in luteocytes, culminating in the-involution of yellow bodies, and

the folliculogenic function inthe ovaries increases. Moreover, under the influence of 750 and, especially, 1000 mg of gravohormone, the number of large and medium-sized follicles increasesby 2-3 times in comparison with the use ofgonadotropin at a dose of 500 mg.By the end of the experiment, as a result of ovulation of folliclesand the formation of yellow bodies, the level of estradiol in the blood decreases, and progesterone increases. Moreover, under the influence of high doses of gravohormone (1000 iu), the level of estradiol-17 beta reaches a lower limit (8.1±0.19 ng / ml), which is associated with luteinization of follicles. For this reason, one animaldid not enter the stage of arousal of the sexual cycle

Группа	Progesterone Estradiol -17 beta	Doses of estufalan	Before the drug is administered	After the introduction of the drug				
				12 o'clock	24 o'clock	48 o'clock	72 o'clock	96 o'clock
1	Progesterone	8 ml (2000mkg)	6680,4±218,13	2147,4±125,11	471.5±43,09	80,1±18,91	178,9±15,11	496,4±34,16
	Estradiol -17 beta	-"-	61,5±5,15	64,7±3,19	70,7±4,01	79,08±8,12	65,1±3,01	41,5±2,09
2	Progesterone	6 ml (1500mkg)	5801,7± 195,18"	1995,4± 149,01"	521.4± 39,	82,4± 13, 17	204.5± 17,04"	394,7± 21,5Г
	Estradiol -17 beta	-"-	57,4±3,95	69,5±3,17	72,5±4,01	76,5±4,95	49,4±4,07	44,7±3,19
3	Progesterone	4 ml (1000mkg)	5600,1±195,12	2445.1± 139,01"	625,1± 34,11	95,4± 17,22	295,1± 23,14	495,7± 26,15
	Estradiol -17 beta	-"-	48,1±5,12	49,9±3,09	53,5±3,04	59,4±4,17	47,1±3,14	39,9±2,01
4	Progesterone	2 мд (500mkg)	6100,0± 149,5 -	2257,4± 147,14"	815.4± 31,95"	96,3± 16,95	151,5± 15,76"	501,5± 21,17
	Estradiol -17 beta	-"-	49,0±3,15	50,4±2,14	59,3±2,91	61,5±3,97	54,5±4,61	49,5±4,91

5	Progesterone	1 мд (250mkg)	4000,8±167, 01	1825.4±121,65	945,1±41,74	112,5±19,49	522.9±19,75	1295,7±43,15
	Estradiol -17 beta	-	52,5±2,17	54,1±2,97	59,3±3,44	64,1±4,93	50,4±2,47	48,9±2,98
6	Progesterone	0,5 мд (125mkg)	. 4800.4±147,09	2445,9±149,99	1229,8±135,^6"	216.5±41,25	399,6±29,6	578,1±19,14
	Estradiol -17 beta	-"-	64,7±3,11	62,6±4,75	65,7±3,15	69,9±3,96	56,7±2,29	42,4±3,01
7	Progesterone	0,25 мд (62,5 mkg)	4500,7±193,10	3944,5±151,19	3054.1±162,69	2804,8±169,14	3014.1±125,04	3221,5±134,18
	Estradiol -17 beta	-"-	53,4±3,99	54,1±2,47	53,9±2,91	56,7±4,85	59,6±3,16	52,5±2,05
8	Progesterone	-	4899.5±147,01	4268.6±149,68	4204.4±139,96	3985,5±149,94	4304,1±139,18	4109,4±131,15
	Estradiol -17 beta	-	55,7±3,07	62,5±4,08	58,2±3,96	56,8±4,19	59,7±3,85	51,8±4,15

Table51

Dynamics of sex hormones in the blood plasma of pregnant sheep (128-132 days) after administration of estuphalan (pg/ml, n=51)

group	Investigated hormones	Investigated hormones	Before introduced, the drug	After the introduction of the drug				
				12 hour	24 hour	48 hour	72 hour	96hour
1	Progesterone	8ml(2000 mkg)	6680,4±218,13	2147,4±125,11	471.5±43,09	80,1±18,91	178,9±15,11	496,4±34,16
	Estradiol -17 beta	-"-	61,5±5,15	64,7±3,19	70,7±4,01	79,08±8,12	65,1±3,01	41,5±2,09
2	Progesterone	6 ml (1500mkg)	5801,7±195,18"	1995,4±149,01"	521.4±39,	82,4±13, 17	204.5±17,04"	394,7±21,5Г
	Estradiol -17 beta	-"-	57,4±3,95	69,5±3,17	72,5±4,01	76,5±4,95	49,4±4,07	44,7±3,19
3	Progesterone	4 ml (1000mkg)	5600,1±195,12	2445.1±139,01"	625,1±34,11	95,4±17,22	295,1±23,14	495,7±26,15
	Estradiol -17 beta	-"-	48,1±5,12	49,9±3,09	53,5±3,04	59,4±4,17	47,1±3,14	39,9±2,01

4	Progeste rone	2 ml (500mkg)	6100,0± 149,5 -	2257,4± 147,14"	815.4± 31,95"	96,3± 16,95	151,5± 15,76"	501,5± 21,17
	Estradiol -17 beta	-"-	49,0±3,15	50,4±2,14	59,3±2,9 1	61,5±3, 97	54,5±4,6 1	49,5±4,9 1
5	Progeste rone	1 ml (250mkg)	4000,8±1 67, 01	1825.4± 121,65	945,1± 41,74	112,5± 19,49	522.9± 19,75	1295,7± 43,15
	Estradiol -17 beta	-	52,5±2,17	54,1±2,97	59,3±3,4 4	64,1±4, 93	50,4±2,4 7	48,9±2,9 8
6	Progeste rone	0,5 ml (125mkg)	4800.4± 147,09	2445,9± 149,99	1229,8± 135,^6"	216.5± 41,25	399,6± 29,6	578,1± 19,14
	Estradiol -17 beta	-"-	64,7±3,11	62,6±4,75	65,7±3,1 5	69,9±3, 96	56,7±2,2 9	42,4±3,0 1
7	Progeste rone	0,25 ml (62,5 mkg)	4500,7± 193,10	3944,5± 151,19	3054.1± 162,69	2804,8 ± 169,14	3014.1± 125,04	3221,5± 134,18
	Estradiol -17 beta	-"-	53,4±3,99	54,1±2,47	53,9±2,9 1	56,7±4, 85	59,6±3,1 6	52,5±2,0 5
8	Progeste rone	-	4899.5± 147,01	4268.6± 149,68	4204.4± 139,96	3985,5 ± 149,94	4304,1± 139,18	4109,4± 131,15
	Estradiol -17 beta	-	55,7±3,07	62,5±4,08	58,2±3,9 6	56,8±4, 19	59,7±3,8 5	51,8±4,1 5

AnalysisTable 50 in comparison with morphohistologicalmi changes in the ovaries and the identification of sexual hunting after applying latrepirdine in the dose of 25 µg in combinationTanya with different doses of grogoryan (1000, 750 and 500 mü. E.) forshows that in the second and third groups of animals all the timewhether in hunting and artificially inseminated, whereas in the first groupPE animals, which introduced 1000 M. E. grogoryan and 25 µg latrepirdine, one sheep showed rut. Itwas found that under the influence of clathraprostin and gravohormone during the first two days, the level of progesterone in the blooddecreases 2.5-3 times with a simultaneous increase in the level of esradiol- 17 beta (Table 50). At the same time, lytic processes develop morphologically in luteocytes, culminating in theinvolution of yellow bodies, and the folliculogenic function inthe ovaries increases. Moreover, under the influence of 750 and, especially, 1000 mg of gravohormone, the number of large and medium-sized follicles increasesby 2-3 times in comparison with the use ofgonadotropin at a dose of 500 mg.By the end of the experiment, as a result of ovulation of folliclesand the formation of yellow bodies, the level of estradiol in the blood decreases, and progesterone increases. Moreover, under the influence of high doses of gravohormone (1000 iu), the level of estradiol-17 beta reaches a lower limit (8.1±0.19 ng / ml), which is associated with luteinization of follicles. For this reason, one animaldid not enter the stage of arousal of the sexual cycle.

Comparing the combined use of estuphalan and clathraprostinewith gravogomone, we should note a more physiological effect of clathraprostine and gravogormone even in higherdoses, which is manifested by a decrease in the number of animals with the phenomenon of anaphrodisia and more physiological changes in the structure and hormonal function of the ovaries. In this regard, when addressing the issue of widespread use of the developed method in sheep breeding, clathraprostin with gravohormone should be preferred. Moreover, the most optimal dosesthat provide moderate development of lytic processes in the yellow bodies, activation of follicle growth, and their ovulation against the background of other phenomena of the sexual cycle arousal stageare gravohormon at a dose of 500 mg and clathraprostin at a dose of 25 mcg.

In addition to determining the optimal doses of estuphalan and clathraprostine, our task was to develop a technique for using themto synchronize sexual hunting in order to organize tour lambs and get cuttlefish, as well as testing alone or in combination with gonadotropin SJK (gravohormon) for the prevention and treatment of infertility in sheepdue to ovarian dysfunction. Experiments were conducted in the random season (September-October) of 1990 on 70 sheep, which were divided into 7 groups of 10 animals each.

Animals of the first group were injected estupinan at a dose of 0.5 ml (125 mg) of the current, the ewes of the second group were injected intramuscularly chatrapati at a dose of 0.5 ml (25 μg), the third group of ewes was used one gravoormon at a dose of 1000 M. E., the fourth group of animals was injected underthe skin gravothermal at a dose of 1000 M. E. and intramuscular klatreprostin at a dose of 0.5 ml, sheep fifth group was used gravohormone at a dose of 750 M. E. and chatrapati at a dose of 0.5 ml the sixth group of ewes injected grogorov the dose of 500 M. E.

and chatrapati at a dose of 0.5 ml and the seventh group of animals drugs are introduced, they were used as control. Sexual hunting in experimental animals was detected by test rams twice, in the morning and in the evening. The sheep that came to sexual hunting weresubjected to artificial insemination. After 10-11 days, unseeded sheep were reinjected with clathraprostin at a dose of 0.5 ml, followed by detection of sexual hunting and artificial insemination.

It was found that sexual hunting after the use of prostaglandins alone or in combination with gravohormone occurred within 48-72 hours of the experiment, and after the introduction of one gravohormone for 4-6 days. Artificially inseminated in the first days of the experiment, respectively, by groups 6, 7, 5, 6, 8, 10 and 2 sheeputerus. From the analysis of the data obtained, it follows that the best, 100% effect was obtained from the combined use of clathraprostin at a dose of 0.5 ml and gravohormon at a dose of 500 m. e. Satisfactory results with 80% inseminationof sheep were obtained after the combined use of gravohormon at a dose of 750 m.e and clatraprostin 0.5 ml: Relatively low sheep hunting activity (60%) was observed after injection of gravohormone 1000 m. e. and clatraprostin 0.5 ml, which is associated with luteinization of immature follicles due to the combinedendogenous and exogenous effects of large dosesof gonadotropin. This is confirmed by macroscopic and histological examination of the ovaries. In particular,pre-ovulatory follicles with proliferating thecal tissue and reduced granulosa and egg cells in the state of dystrophy were examined on ovarian sections. The administration of one gravohormone at a dose of 1000 m. e. also gave a low effect (50%), which is associated with the use of the drug in 50% of sheep against the background of functioning yellow bodies, in the remaining sheep ovaries were observed in a state of hypofunction. In the first case, follicle growth followed by cystic atresia was observed against the background of functioning yellow bodies. In the second case, in case of ovarian hypofunction, the introduced gravohormone provided active follicle growth, maturation and ovulation with the manifestation of other phenomenaof the sexual cycle arousal stage. Positive results from the use of prostaglandins alone were obtained in sheep thathad functioning yellow bodies in their ovaries. With ovarian hypofunction,the recovery of sexual cycles under the influence of the test prostanoids did not occur.

Repeated, after 10-11 days, administration of clathraprostin to sheep that did not come to the hunt in the first days of the experiment, ensured insemination of all sheep that were injected with gravohormone, while out of 7 unseminated animals that were injected with prostaglandins alone, only 3 ovs came to the hunt andinseminated. Ovarian estirpation in these unseeded ewesmade it possible to diagnose ovarian hypofunction.

Therefore, the best synchronization of sexual hunting in sheep with ovarian dysfunction was obtained from the combined useof gravohormone at a dose of 500 iu and clathraprostine (estuphalan) at a dose of 0.5 ml or 25 (125) mcg. The use of pro-stanoids alone to synchronize sexual hunting is effective in thepresence of yellow bodies in sheep ovaries. With ovarian hypofunction, the syncing effect of prostaglandins is reduced.

4.4. Development of methods of termination of pregnancy in Karakul sheep in Iorder to obtain karakul feeding

In addition, for testing the optimal doses astutely and latrepirdine of abortion with the aim of obtainingniya at Karakul Karakul breed of sheep into an experience was to includeChenoa 160 animals with a pregnancy 128-132 day (FebRAL-March 1990). Astutely was tested in doses of 0.25 ml (62,5 g), 0.5 ml (125 mg), 1.0 ml (250 mcg), 2.0 ml (500 mcg), 4.0 ml (1,000 mcg), 6 ml (1500 mg) and 8.0 ml (2000 mcg) at the rate of active substances (cloprostenol) in 1 ml of 250 µg. Clathraprostin was administered in doses of 0.25, 0.5.1, 2 and 4 ml at the rate of the active substance (cloprostenol) in 1 ml-50 mcg or 12.5, 25,100 and 200 mcg, respectively. Morphofunctionalchanges in the ovaries and the dynamics of sex hormones (progesterone and estradiol-17 beta) were studied in experimental animals 12, 24, 48, 72, and 96 hours after administration of various doses of the above drugs. There were 5 animals in each series of experiments **(Table 51,52)** After slaughtering the animals, the weight of the ovaries, the weight ofthe ovary with a yellow body and their size were determined, and thenumber of yellow bodies of large, medium-sized and small folliclesand atretic bodies, as well as follicular and lutealcysts, was calculated. When estuphalan and clathraprostin were administered at a dose of 0.25 ml (62.5; 12.5 mcg of the active start), noticeable changes in the ovaries were observed only on the fourth day after administration of the drugs and were characterized by the appearance of lytic processes in the marginal areas of the cytoplasm of luteocytes, as well as in the voc-nuclei.

Table52

Dynamics of sex hormones in the blood plasma of pregnant sheep (128-132 days) after clathraprostine administration (ng / ml, N=5)

Group	Test hormones	Estuphalan doses	Prior to the introduction of the drug	After drug administration				
				12 hours	24 hours	48 hours	72 hours	96 hours
1	Progesterone	4 ml (200 mcg)	5450,8± 175,44	3545,1± 139,14	1252,9± 101,16	105,4± 19,13	194,3±18 ,11	415,7±29,54
	Estradiol-17 beta	-"-	82,1±2,19	74,5±4,18	86,2±5,94	94,8±4,95	81,4±3,17	71,5±3,45 1
2	Progesterone	2 ml (100 mcg)	4510,2± 102,18	3195,6± 119,74	1477,8± 102,95	116,7± 12,17	202,9± 17,15	517,8± 22,13
	Estradiol-17 beta	-"-	78,9±3,44	83,6±4,09	88,9±5,11	92,4±4,15	80,6±3,46	75,4±4,01
3	Progesterone	1 ml (50 mcg)	4825.4± 161,94"	3056.0± 144,01	1351.4± 120,00	251,8± 41,5	345.6± 16,04	647.9± 29,81
	Estradiol-17 beta		84,3±4,28	89,1±3,98	91,9±4,19	105,0±5,46	84,5±4,90	79,1±5,61
4	Progesterone	0.5 ml (25 mcg)	7005.6±224, 67	4091,6± 196,15	1495,1± 58,94	246.3± 18,07	456.4± 24,01	549,7± 28,34
	Estradiol-17 beta	-"-	91,7±6,19	87,9±5,04	98,6±6,01	111,9±7,46	88,4±5,14	74,5±4,18
5	Progesterone	0.25 ml (12.5 mcg)	4025,1± 242,56	3895,9± 196,14	3561.1± 17 6,95	2912.6± 145,09	3115,4± 162,18	3480,4± 169,95
	Estradiol-17 beta	-"-	75,1±7,27	78,5±6,11	84,1±5,09	81,9±4,19	76,7±3,95	75,9±4,15
6	Progesterone	-	4899.5± 147,01	4268.6± 149,68	4204.4± 139,96"	3985.5± 149,94	4304,1±139,18	4109,4±131,15
	Estradiol-17 beta	-	55,7±3,07	62,5±4.08	58,2±3,96	56,8±4,19	59,7±3,85	51,8±4,15

Moreover, these processes are most pronounced along theperiphery of the parenchyma of the yellow bodies and in the most vascularized zones. In these zones, a decrease in the volume of nuclei was also observed with their transition from a rounded to a flatter shape, andtheir movement from the center to the periphery of the cytoplasm. In the ovaries of both experimental and control animals, gametogenesis from the rudimentary epithelium and the formation of primordial follicles with their transition to secondary and tertiary ones were observed. Moreover, a noticeable increase in tertiary follicles in comparison with the control was not observed.

As a result, these doses of drugs, although they cause minor lytic processes in the yellow body by the endof the experiment, do not provide complete involution of yellow bodies andactivation of follicle growth, and therefore they should be consideredinsufficient.

Under the influence of estuphalan and clathraprostine, administered at a dose of 0.5 ml (125 and 25 mcg), more pronounced changes occurin the ovaries. Moreover, the nature of these changes depends on the duration of the experiments. So, 24 hours after the administration of drugs, the yellow body visually did not differ from the control and had a size within 1 cm in diameter, mushroom-shaped rising above the surface of the ovary. The yellow body is gray-cinnamon in color, and the injected vessels are visible on its surface. On the surface of the ovaries, on average,there were 23 small, 2 medium-sized follicles and 2 atretic bodies. On histological sections, the corpus luteum is represented by differentiated, oval-shaped luteocytes covered with a capillary system. The kernels are large, rounded, and well contoured. There are binucleated luteocytes. Cellswith vacuolated cytoplasm are rarely encountered. Moreover,vacuolization is observed both in the cell periphery and in the vox-nuclei. In such cells, the nuclei lose their configuration, acquirea denser chromophobic color and peripheral location.

In the surface layer of the ovarian cortex, from 2 to 10 primordial follicles are visible in the field of vision, around which morphogenically active cellularelements are differentiated, the proliferation of which deep into the ovarian cortex provides migration and transformation of primary to secondary and tertiary follicles. There are follicles at various stages of dystrophy, cystic and obliterative atresia, as well as developing tertiary follicles with secretory active granulosa and proliferatively active and well-vascularized internal theca, of whichup to 5 medium-sized and 4 small follicles with a diameter of 0.2 to 0.6 cm are counted on sections.48 hours after the administration of drugs, the yellow body decreases in size (0.8 cm in diameter), becomes more gray in color. There are 2 medium-sized and 16 small follicles on the surface of the ovaries.

On histological sections, luteocytes retain an oval shape with a contoured shell, but their cytoplasm is vacuolated, the nuclei acquire a marginal position, changefrom rounded to oval and flat, and are chromophobic in color. Proliferative foci are seen in the septa of the parenchyma of the yellow body and in the endothelium of capillaries, in connection with which the yellow body acquires small cell proliferation, which increases in the following days of the experiment. At the same time, the proliferation of cellular elements at the base of the protein envelope and their migration deep into the ovarian cortex are activated, dragging primordial follicles with their transformation into secondary and tertiary ones. At the same time, the numberof tertiary follicles increases to 5-8 per slice. Such tertiary follicles are in an active morphogenic and secretory state, as evidenced by an increase in the volume of follicular fluid and the diameter of the proliferatively active and vascularized internal flow.

72 hours after the administration of the test drugs in a dose of 0.5 ml, the characteristic changes in the uterus andovaries include the opening of the cervical canal and pronounced involutionalprocesses in the yellow bodies with the activation of follicle growth.

In this regard, yellow bodies had a size of 0.1-0.4 cm in diameter, pale color and dense structure. In the ovaries,there are 1 large, 2 medium-sized and 7 small follicles.

On ovarian sections, the parenchyma of yellow bodies is represented by obliterating blood vessels, and the capillary systemis restored. Luteocytes acquire formulas from oval to triangular, cubic and flat. In this case, the cytoplasmis transformed into elastic and collagen fibers, in whichflat nuclei are seen. Eventually,fibrous tissue forms on the site of the corpus luteum, which is mainlyobserved on the 4th day of the experiment. However, during this period, in the middle lobe of the corpus luteum parenchyma, oval-shaped luteocytes with a contoured shell and traces of cytoplasm are still found, in which small, mostly flat nuclei are visible.

Regarding the folliculogenic function of the ovaries, it shouldbe noted that against the background of involution of the corpus luteum, the growth of tertiary follicles is activated, which are represented by hypersecretory granulosa and powerful vascularized thecal tissue. Moreover, in some follicles, the surface layers of granulosa are desquamated, and theca-luteal cells appear in the thecal tissue. Such changes in the follicles indicate thecompletion of their development and the arrival in the pre-ovulatory state. Due to the activation of the morphogenic functionof ovarian cortical cells and their differentiation around primordial follicles, the number of secondary ones increasesand their transition to tertiary follicles increases. Consequently, against the background of involution of yellow bodies, the folliculogenic function of the ovaries is activated.

96 hours after the administration of drugs in a dose of 0.5 ml, the cervical canal remains open, and against the background of the completion of lytic processes in the yellow body, the growth of folliclesis activated. Atthe same time, a pale gray fibrous formation the size of a grain of grass is visually visible on the site of the corpus luteum, whilethe rest of the ovarian tissue is represented by a multitude of small to large follicles. In particular, in the ovaries there are from 1 to *2* large, 3-5 medium-sized and from 10 to 14 small follicles. Characteristic of thisis that the transformation of secondary to tertiary follicles occurs against the background of the formation and activation of proliferativeprocesses in the thecal tissue, which is intensively vascularized.

Comparing the histological changes in the ovaries under the influence of estuphalan and clathraprostin, it is necessary to notesome differences in their effect. In particular, the effectof clathrastin is more labile, which is manifested on 3-4 days of experience by the development of more moderatelytic processes in the yellow body and more physiological development and growth of follicles. Moreover, follicles with a well-developed and radially located granulosa are in a state of hypersecretion, and the internalflow is in an active proliferative state against the background of pronounced vascularization.

Under the influence of estuphalan and clathraprostine, respectively, administered in doses of 250 and 50 mcg, lytic and follicle-stimulating processes in the ovaries increase asthe experiment continues. Moreover,

if luteocytes retain their shape one day after the administration ofdrugs, and rounded nuclei and nucleoli are visible in the cytoplasm, then after 2 days the phenomenon of vacuolization and lysis develops in the marginal areas of the cytoplasm and in the areas of contact with the nucleus, the nucleoli are reduced, and the nuclei acquire a peripheral location and lose-their rounded shape. 72 hours after the administration of drugs, these processes are intensified. In particular, luteocytes acquire an oval-elongated shape, the nuclei become flat, the parenchyma vessels are obliterated, and the capillary system is reduced.
Proliferation of connective tissue elements is expressed in the trabeculae of the corpus luteum parenchyma and in the areas of vascular obliteration. In this regard, fibrous tissue with millet grain remains in place of the yellow body. In parallel with these processes, the growth of tertiary and secondary follicles is activated, the proliferation of connective tissue cells from the protein envelope and the migration of primordial follicles deep into the ovarian cortex with their transformation into secondary follicles increases. Due tothe activation of the ovarian folliculogenic function, 1-2 large, 3-5 medium-sized, and 6-15 small follicles are found in them. The cervix is open and a light heavy mucus is released from it.

On the 4th day of the experiment, a dense gray fibrous area the size of a millet grain remains in place of the yellow body. The ovary contains 2-3 large, 4-6 medium-sized and 8-17 small follicles. On sections of large follicles, granulosa is reduced, the internal theca is in a state of proliferation and differentiation into theca-luteal cells with the formation of corrugated protrusions into the follicle. At the same time, thecalutein cells are mostly lysed, forming a fibrillar structure with flat nuclei, which creates conditions for cystic atresia of follicles. The cervical canal is open and a light mucus cord is released from it.

An even more pronounced luteolytic and follicle-stimulating effect with the phenomenon of cystic dystrophy of the follicles is observed after administration of estuphalan and clathraprostine in doses of 500 and 100 mcg, respectively.

In particular, if 24 hours after the administration of these drugs only lytic processes develop in single luteocytes, then after two days the cytoplasm of luteal cells undergoes vacuolization and lysis, the nuclei acquire a flat shape, and the luteocytes pass from oval to elongated and flat. At the same time, light substance and obliterating vessels are visible in the intercellular spaces against the background of reduction of the capillary network. As a result, on the second day of the experiment, the yellow body decreases in size from 0.7-0.5 to 0.6-0.4 cm in diameter, and after three days it was 0.2-0.1 cm in diameter and is viewed as a millet grain. On the section, such a corpus luteum had a fibrillar structure with small flat nuclei and obliterating vessels.

Against the background of involution of luteal structures, the folliculogenic function of the ovaries increases. So, if after 24 hours of the experiment 2-4 medium-sized and 5-9 small follicles were detected in the ovaries, then after 48 hours 3-4 large, 2-6 medium-sized and 12-20 small follicles were counted in the gonads. On day 3-4 of the experiment, lytic processes developed in the thecal tissue of tertiary follicles with simultaneous development of dystrophic processes in granulosa and its desquamation into follicular fluid. At the same time, the egg was rejected and its dystrophy occurred.

Consequently, under the influence of estuphalan and clathraprostine, respectively, at doses of 250, 50 and 500, 100 mcg, along with the strengtheningof lytic processes in the yellow body, the growth of follicles that do not reach ovulatory maturity and undergo dystrophy is also activated, and the flow of these doses of drugs should be considered overestimated. At the same time, the transformation of primary to secondary follicles and their growth continues, which ensures the preservation of the generative function of the ovaries. Therefore, these drugs, even in excessive doses, do not lead to a loss of reproductive ability of animals.

With increasing doses of the tested drugs (estuphalan at a dose of 1000, 1500 and 2000 and clathraprostin at doses of 200, 300 and 400 mcg), the lytic and follicle-stimulating effect in the ovariesincreases. Thus, macroscopically, on 3-4 days of the experiment, only traces of pregnancy yellow bodies are detected in the ovaries, while thenumber of follicles increases 3-4 times. Atthe same time, up to 3-6 large, 4-8 medium-sized and up to 18-25 small follicles are formed in the ovaries. Moreover, the yellow bodies at the end of the experiment are represented by a fibrous structure with obliterating vessels, the walls of which also undergo lytic processes. The former parenchyma of the corpus luteum is replaced by cellular structures of the ovarian cortex, and therefore cell proliferates are visible on the surface and in the depth of the corpus luteum, which provide lysis and replacement of these invol-lating structures.

Regarding the folliculogenic function of the ovaries, it should be noted that as the follicles grow, lytic *processes develop in the internal theca,* and the granulosa along with the egg cell undergoes dystrophy. In this regard, by the end of the experiment, large follicles are characterized by the presence of fibrous internal flow and reduced granulosa, traces of which, together with the egg, arevisible in the follicular fluid, which-indicates cystic dystrophy of large follicles. At the same time, small tertiary follicles continue to grow and develop. In this regard, both follicles at various stages of cystic dystrophy and developing graaf vesicles with radially differentiated granulosa in a state of hypersecretion and a strong layer of well-vascularized cells of the internal flow are detected in the ovaries. At the same time, there is a process of differentiation of primordial follicles into secondary and small tertiary ones, which eliminates the possibility of inhibiting the generative, and therefore folliculogenic, function of the ovaries.

Thus, the optimal dose of estuphalan and clathraprostine should be considered 125 and 25 micrograms or 0.5 ml, respectively.Smaller doses (0.25 ml) do not provide an involutional andstimulating effect, while large doses (2-8 ml), along with excessive lytic and follicle-stimulating effect, cause cystic dystrophy of follicles. At the same time,the tested drugs, causing luteolytic and follicle-stimulating effects, as well as cervical dilatation,do not ensure termination of pregnancy. Therefore, thereis a need to find new methods and meansof aborting pregnancy in order to obtain doodle.

On the basis of experimental research laid the experiments on the production test of the efficacy of drugs 1200 ewes, of which 200 ewes were injected estupinan at a dose of 0.5 ml (125 mg), and the same number chatrapati were injected a single dose of 0.5 ml (25 μg) and in complex with grogoryan at a dose of 500 M. E., 600 ewes served as controlLEM that the drug was not administered. The results of these experiments are summarized and final conclusions will be made afterthe offspring is born.

CONCLUSION

On the basis of experimental investigations carried out on laboratory animals, cows, sheep, pigs and mares at different state of sexual function and its disorders, POSLe exposure to different doses of hormones, extirpation Zacatecoluca epithelium of the gonads and the thyroid gland, clampingLeno that gametogenesis is of zakatkow-go epithelium with subsequent formation of a primordial foulMikulov and this process does not depend on the function function, and consequently, from the effects of endogenous and exogenous gonadotropins.

It was found that the process of formation of primordialfollicles is carried out by differentiation around the genitalcell of connective tissue (mesenchymal) elements, which in the process of hyperplasia and hypertrophy acquire the structure of epithelial(follicular) cells. The phenomenon of metamorphosisof mesenchymal elements of the surface layer of the testicular cortexinto epithelial cells is due to the metabolic influenceof the germ cell on this process, which is biologically quite justified. In this regard, both gametogenesis and the formation of primordial follicles in the postnatal period shouldbe considered as a promising study, which, with the developmentof appropriate methods, will solve the problemof obtaining and long-term storage of the necessary number of germ cells (by analogy with sperm) fromhighly productive animals during breeding work, etc.Very important General biological patterns in the gene for the-operational functions of the ovaries should be attributed installed phention of proliferation of connective tissue cells of the cambial zone, founded in the surface areas of the cortical substance of the gonads, in the direction of the brain substance, due to which predis provided the opportunity to explain a previously unknown process of moving into the deeper layers of the cortical substance of the ovary primordial, secondary and tertiary follicles are small and fast reduction atresias follicles and invaliduser yellow bodies in connection with their lysis in most vascularizedbath layer of the gonads. This feature in ovarian function, in turn, indicates that primordial follicles, as well as secondary and small tertiary follicles, cannot persist in the ovaries for a long time. In this regard, the established concept in science about the alleged simultaneous laying-of primordial follicles in the ovaries of fetuses with their subsequent implementation during the reproductive life of the female disappears.

In connection with the establishment of permanent gametogenesis due tocellular epithelium, which turned out to be refractory to endogenousand exogenous gonadotropin and PGF-2 alpha, and in connection with this permanent histogenesis of primordial follicles, it is very important for science and practice to exclude the possibility of biological castration under the influence of these biologically activesubstances. Therefore, the previously established notion thatgonadotropic drugs can supposedly cause biologicalcastration of females by completely expending a certain supply of follicles should be recognized as scientifically unfounded.-This opens up a broad prospect for the use of hormonal drugs for the intensification of reproduction, as well as for the restoration of functional disorders of the gonads. This is one of the most important features of our material, the implementation of the theoretical basis of which will ensure proper economic profit in the national economy.

Using versatile research methods, wefound that connective tissue elements of the ovarian cortex and follicular membranes, specifically reacting to endogenous and exogenous gonadotropin, create trophic conditions for the egg cell, as well as for the maturation of follicles. Insweat, after ovulation of the follicles,yellow bodies are formed from the connective tissue structures of the shell. Based on this, we put forward a new position that the connectivetissue elements of the ovary should be considered as a tissue that performs a trophic function, ensuring the growth and maturation of follicles, plastic formation of yellow, atretic bodies and luteal cysts, and hormonal -- progesterone production. Therefore, connective tissue elementsthat proliferate from the protein envelope and differentiateinto interstitial cells of the follicle envelope, and then into luteal cells, should be considered not only morphogenetically, but also functionally as unified structures.

In turn, based on the proposed theoretical provisions concerning follicle growth, new gerantological and pathogenetic concepts of the dependence and duration of female reproductive function or its-disruption due to the termination of follicle histogenesis due to morphofunctional depletion or fibrouschange in the elements of the ovarian cortex and follicular membranes are revealed. The established regularity is importantnot only for veterinary and medical gynecology in the prevention of disorders of the reproductive function of females, but also for gerantology in the disclosure of certain phenomena of aging of the body in general and the terminationof reproductive function in particular.

The above material allows us to conclude that the established complex and multifaceted phenomena of interaction of the gametogenic function of the rudimentary epithelium with the trophic, plastic function of the connective tissue elementsof the ovaries are decisive in the generative function of the gonads and the duration of the reproductive capacity of females.

The established regularities allow us to characterize the state of the sex glands at various stages of the sexual cycle, during pregnancy, with persistent yellow, corpus luteum,follicular and luteal cysts, anovulatory sexual cycles and gonadal hypofunction, while assigning a leading role to connectivetissue (mesenchymal) elements in the generative functionof the ovaries. Thanks to the study of these structures, it was possible for the first time to decipher thephenomena of lack of ovulation of follicles in hypo-ovarian function, functioning yellow bodies, follicular and luteal cysts, as well as to explain the pathogenesisof anovulatory sexual cycles.

Based on the morphogenetic and functional unity of connective tissue elements, it is quite reasonable to speak about the coincidence of ovulation processes with luteinization of non-ovulated follicles and activation of morphogenic andsecretive processes in interstitial cells-of the ovarian cortex, aimed at creating the proper phoof progesterone in the body, necessary for zygote nidationand embryo development. These studies allow us to clearly determine which cellular structures produce progesterone. In turn, the follicular epithelium is characterized by the production of estrogens.

The cystic and obliterative atresia of the follicles observed during ovulation and the functioning of the corpus luteum, as well as their complete reduction after the introduction of gonadotropins with their restoration after 3-4 weeks, gave us reason to conclude that the period of follicle existence is veryshort. At the same time, the absence of a direct effectof gonadotropic drugs and PGF-2 alpha on the oogenic function of the rudimentary epithelium excludes the possibility of depletion of potentialreserves of germ cells and follicles, which biologically justifiesthe expediency of widespread useof gonadotropic drugs and PGF-2 alpha for regulating the sexual function of animals.

Based on the established specificity of the action of gonadotropicdrugs on the connective tissue elements of the ovaryand depending on their initial morphofunctionalstate, the reaction to gonadotropin also manifests itself differently. Thus, with functioning yellow bodies of the sexual cycle, pregnancy, their persistence, as well as luteal cysts, when the connective tissue elements of the ovary experience highfunctional tension, gonadotropic drugs do notprovide an ovulatory effect. In hypoplasia of connective tissue cells of the ovarian cortex and follicle membranes, gonadotropic drugs activate the js function, andconsequently, ensure the growth, maturation and ovulation of follicles. That is why gonadotropin provides the proper therapeutic effect for ovarian hypofunction, anovulatory sexual cycles, and follicular cysts. A similar effectis observed in persistent yellow bodies and luteal cysts, if gonadotropin is used against the background of preliminary injections of progesterone and PGF-2 alpha.

Given that the existing gonadotropins (FSH, LH, XP) and drugs (FLC, graphogame, etc.) carry out regulatorytion of ovarian function through their connective structure and in connection with the disclosure patterns of folliculogenesis, you can speak for the presence of a single isotropic beginning, therapeuticand regulatory effect of which is not determined by the relationstion of FSH and LH, as is commonly believed, with the administered dose goof nototropis, the initial state of the trophic and plastic functions of connective tissue elements of the gonads.

If gonadotropic drugs and hormones activate Prooperativnye and secretory processes in morphogenetics EDItion of the cellular structures of the ovaries, the specific effect of PGF-2 alpha is manifested in luteolysis differentiated, funkrationally active luteal cell structures and atleticheskij yellow bodies, luteal cysts, theca luteal cells of maturing follicles and interstitial cells of the cortical substance of the gonads and the decrease in the level of progesterone in the blood plasma of cows. At the same time, the rudimentary epithelium and poorlydifferentiated proliferating connective tissue cells of the ovaries remain refractory to the action of PGF-2 alpha, and the flow of gametogenesis, formation of primordial, growth of secondary and smalltertiary follicles with their subsequent maturation,ovulation and formation of yellow bodies after the use of this drug continues. These studies made itpossible to determine the doses of PGF-2 alpha for heifers and cows, the indications and contraindicationsfor their use, and to develop a method for the preventionand therapeutic effectiveness of estuphalan in postpartum pathologyand functional disorders of the ovaries of cows. The materials of these studies were included in the "Interim Manual onthe use of estuphalan in animal husbandry and veterinary medicine", approved by the State Department of the State Agroprom of the USSR in 1986.

The function of the ovaries is in a certain correlation with the function of the thyroid gland. Its greatest activation is observedduring ovulation of the follicles, the functioning of the yellow bodies of the sexual cycle and in the first half of pregnancy. A decrease in thyroid function is noted in hypofunction and follicular cysts of the ovaries, anovulatory genitalcycles and insufficient development of yellow bodies, while in persistentyellow bodies and luteal cysts, the thyroid gland is in an active functional state.

Ovariectomy is accompanied in the first 10 daysby an increase in the functional activity of the thyroid gland and a decrease in its function in the longer term. Functional insufficiency of the thyroid gland or its extirpation leads to hypoplasia of the connective tissue elements of the ovaries, their hypofunction, the appearance of anovulatory sexual cycles and the formation of follicular cysts, which indicates the important role of thyroid hormones in the regulation of sexual function and the pathogenesis of morphofunctional disorders of the gonads.

Due to the fact that the thyroid glandhas the highest functional activity after calving, and the function ofthe thyroid gland and connective tissue elements of the ovaries decreases during sexual cycles and their repeated manifestations, the first month after calving should be considered the most favorable physiologicalstate for fertilization. This is what should be the main focus of the development of a complex of therapeutic and preventivemeasures in the fight against infertility and cow and sheep dairiness.

In the end, it should be noted that the study of the formation of a Polohowl function in heifers, uncover patterns in generative and hormonal function of the ovaries, the relationship of sexual and tireo-IGNOU functions, as well as the elucidation of the etiology and pathogenesis aftergeneric pathology and functional disorders of the gonads with .the development ofprocessing methods of hormonal regulation of reproductive function in cows, heifers and sheep is the basis of excellencetion of biotechnology intensive reproduction of animals.

Generalizing materials of our research, which are of practical significance, are reflected in the " Guidelines forthe use of gravohormone (gonadotropin from the blood and serumof foaled mares) to increase fertility and regulatesexual function in animals,"Recommendations on hormonalstimulation of the reproductive function of cows and heifers, " Recommendations for the prevention and treatment of the most common non-infectious diseases of farm animals."

LITERATURE

1. Aleshin B. V. Histophysiology of the hypothalamic-pituitary system-Medicine 1971-493 p

2. Akaevsky A. I Anatomiya domashnykh zhivotnykh “Kolos” (Anatomy of domestic animals "Kolos") 1975-590 p.

3. Babilashvili A. S. Some histological features of the genitals in case of ovarian hypofunction in cows Collection of works of the Leningrad vet.institute. - L., 1971.

4. BerezovskiyA.V., Kharenkom. I., Podvalyukd. V., HarutaG. G., Khomins. P., KalinovskiyG. M., StefanikV. Yu., Chekano. M., Kornichenkol. E., Galatyuko. E., FedorovV. P., Ordinyu. M.physiologiyapathologiyrazprostraneniya koney. Uchebnikukraina, 2014.

5. Vunder P. A. Endocrinology of reproductive sex, Moscow, 1973.

6. Eliseev V. T. Histologiya [Histology], Moscow, 1972

7. Zavadovsky M. M. Teoriya i praktika hormonalnogo metoda stimuliatsii mnogoplodiya sel'skikh zhivotnykh [Theory and practice of hormonal method of stimulation of multiple fertility of farm animals].

8. Zavarzin A. A. Guide to histology, L., 1954

9. Zvereva G. V. Prevention of animal infertility - on a scientific basis.Veterinary medicine. - 1969.- № 3.

10. Ivanov I. F. Histology with the basics of pet embryology, Moscow, 1962.

11. Kvater E. I. Hormonal diagnostics and therapy in obstetrics and gynecology, Moscow, 1961.

12. Kuliev G. K. K voprosu razvitiya ovarikov i formirovanie ovogeneza zverytayushchikh zhivotnykh [On the question of ovarian development and the formation of ovogenesis of experiencing animals]. Izv.AN AzerC. SSR.- Ser. biol. and med. sciences. - 1963.- № 6.

13. Lapyrin A. I Biologiya razmozheniya ovets [Biology of sheep breeding], Moscow, 1947

14. Litvinova L. D. Ovarian development in cattle in the uterine period. Tr. inst. eksperimental'noi biologii I KazSSR. - 1954.

14. Lobodin A. S. Influence of gonadotropin FFA on ovarian function and its application to stimulate the reproductive ability of cows: Dis. kand. vet. nauk. Voronezh ,1982-234 p. (in Russian)

15. Nezhdanov A. G. Cheremisinov G. A.Steroid hormones in the blood of cows // Veterinary Medicine-1979-No. 12. p. 46-47
16. Nezhdanov A. G. / / Biochemical changes in the blood of cows during childbirth and the postpartum period / / Sb. trudov VNIINBZH.- Problems of increasing animal resistance .1983
17. Nurmukhamedov B. M. Seasonal characteristics of ovaries of Karakul sheep. Abstracts of the conference of young scientists. - Voronezh, 1990.
18. Nurmukhamedov B. M. Reaction of sheep ovarian generative function to prostaglandins F-2 alpha Abstracts of the conference of young scientists.- Voronezh, 1990.
19. Nurmukhamedov B. M. Seasonal characteristics of the ovaries of Karakul sheep Voronezh 1990. p. 28 (Russia).
20. Nurmukhamedov B. M. Reaction of sheep ovarian generative function to prostaglandins f-2 alpha abstracts of the conference of young scientists
Voronezh 1990 yil (Russia) With .28 abstracts of the conference of young scientists p. 29-30.
21. Nurmukhamedov B. M. Biological assessment of ovaries and hormonal regulation of reproductive function in Karakul sheep . Tashkent 1990 Prevention and treatment of non-infectious animal diseases in Uzbekistan pp. 64-67
22. Nurmukhamedov B. M. Cheremisinov G. A. Pulatov G. S. Temporary adjustment for the use of estuphalan and clathraprostin in veterinary medicine and sheep breeding 1991 10 July. Tashkent Main Veterinary Department of the Ministry of Agriculture of the Republic of Uzbekistan.
23. Nurmukhamedov B. M. Cheremisinov . Improvement of methods of hormonal regulation of sexual function in sheep. Gorki 1991 June 27-26 (Belarus) abstracts of scientific and practical conference reports pp. 60-61.
24. Nurmukhamedov B. M.. Nurmukhamedov M. N. Cheremisinov. G. A Biological assessment of ovaries and hormonal regulation of reproductive function in Karakul sheep. Moscow 1992 (Russia) Problemy Morfologii i Parasitologii nauchnyy trudy Moskovskoy

meditsinskoy akademii Imeni I. I. Sechenov [Problems of Morphology and Parasitology].
25. Nurmukhamedov B. M. Nurmukhamedov N. M. Recommendation on the use of estuphalan and clathraprostin in sheep and goat breeding. Tashkent Main Veterinary Department of the Ministry of Agriculture of the Republic of Uzbekistan 1994 December 20.
26. Nurmukhamedov B. M. Khaitov R. H. Biological features of generative ovarian function and application of methods of hormonal regulation of sexual function.Moscow October 17-19, 1996 (Russia) - Russian Congress on Pathophysiology S-336.
27. Nurmukhamedov B. M. Tuguzov Yu. M.Seasonal characteristics of goat ovaries.Tashkent, 1997 ,No. 2 Journal of Veterinary Medicine. P-8.
28. Nurmukhamedov B. M. Khaitov R. H. Development of indications for the use of PGF-2 alpha in goat breeding. Moscow, 1997 (Russia) Problems of Morphology and Parasitology . Scientific works of the I. M. Moscow Medical AcademySechenova S. 169-171.
29. Nurmukhamedov B. M. Khaitov R. H. Seasonal characteristics of goat ovaries in the conditions of Uzbekistan Moscow 1997 (Russia) Problems of Morphology and parasitology . Scientific works of the I. M. Sechenov Moscow Medical Academy, pp. 169-171.
30. Nurmukhamedov B. M., U. A. Rakhmonov., T. E. Kurtametov.Seasonal characteristics of goat ovaries in Central Asia. Samarkand 2015 scientific conference collection 1 part
31. Nurmukhamedov B. M., Eshburiev S. B., Tagaeva M. F. [In Russian]. Biological assessment of ovaries and hormonal correction of reproductive functions in Karakul sheep. Samarkand 2015 scientific conference collection 1 part
32. Nurmukhamedov B. M., Eshburiev S. B., Velikanova A. A. [In Russian]. Biological assessment of ovaries and hormonal correction of reproductive functions in female goats. Samarkand 2015 scientific conference collection 1 part.
32. Nurmukhamedov B. M. S. B. Eshburiev.I. Leshchinskaya. Application of prostaglandins F-2 alpha for termination of pregnancy in Karakul sheep
Samarkand 2015 scientific conference collection 1 part.

33 Nurmukhamedov B. M., Meliboev N. K., Abdumazhitov V. B. Comparative effectiveness of prostanoids in the treatment of cows with functional ovarian disorders . Collection of proceedings of the Republican Scientific Conference Part-2 P. 52-53. Samarkand 2015.
33. Nurmukhamedov B. M., Abdumazhitov V. B., Kurbonov F. M. Hormonal correction of reproductive function of ovaries in goats. Collection of scientific articles of the faculty Part-2 21-22 April P. 49-52 Samarkand 2016.
34. Pozhidaev *E. A.*Oogenesis of mammals, L., 1967.
35. Pavlov V. A. Prostoglandins and prospects of their application in animal husbandry. - Moscow, 1977, p. 65.
36. Prakof'ev M. I. Regulation of reproduction of impulsive animals. L:nauka 1983-264s
37. Savchenko O. N., Stepanov G. S. Hormonal regulation of the function of the genital glands. Hormones in animal husbandry / Tr. VASHNIL. - M.: Kolos, 1977.
38. Savchenko O. N. Sexual glands / / Physiology of the endocrine system .Moscow: Nauka Publ., 1979, pp. 341-371
39. Studentsov A. P. Veterinary obstetrics and gynecology. Kolos Publishing House.- M 1970 S519.
40.Studentsov A. A., Shipilov V. S., Subbotin L. T., Preobrazhenskaya O. N. Veterinary obstetrics and gynecology.Agropromizdat-Moscow, 1986. P479.
41. Khvatov B. M. Structure and physiological changes in the sexual system of female domestic animals.
42. Cheremisinov G. A. Razrabotka i sovershenstvovaniya hormonalnykh metodov regulyatsii i stemulyatsii reproducitel'noy funktsii korov [Development and improvement of hormonal methods of regulation and stemulation of the reproductive function of cows].- Voronezh, 1975. 338C
43. Cheremisinov G. A., Karymov V. N. , Sovershenstvovanie metodov hormonalnal'noi regulyatsii polovotsitskoi funktsii korov [Improvement of methods of hormonal regulation of the sexual function of cows].- Persiyanovka,1983 P52-57.

44. Cheremisinov G. A. Regularities in the generative function of the ovaries and hormonal methods for increasing the fertility of animals// Bulletin of Agricultural Sciences.- 1984.- № 6.
45. Shipilov V. S. Physiological bases of prevention of infertility of cows. Moscow, 1977.
46.Khvatov B. P. Stroenie i fiziologicheskie polovoi sistemy samok domashnykh zhivotnykh [Structure and physiological sexual systems of female domestic animals].
47 Yudaev N. A. Etikhina Z. F.. Sovremennye predstavleniya o hypothalomicheskikh releyingfaktrov [Modern concepts of hypothalomic releasing factors]. Sovremennye voprsy endocrinologii, Moscow: Meditsina Publ., 1972, pp. 8-20
48. Eskin I. A. Fundamentals of endocrine gland physiology.Moscow, 1968.
49. Agthe O.Die Endocrine regulation der Geburt bei Rind , Schof and Ziege.// D.T.W. 1973 V.89.N.2 P64-68
50.Derivaux J. Phisiopatholohie de I'ovaire et ses aspects clinigues // Annales med. Veter .1970.-144(5).- P287-304
51.Kuldac.E.,Arendarcik J. The excretion of pituitary gonadotropine in urine of cows during normal and synchronized cycles.Inst.Nat.Rech.Agron.Paris.1986.

CONTENT

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IMPROVEMENT OF METHODS IN HORMONAL REGULATION OF REPRODUCTIVE FUNCTION IN COWS AND SHEEP

MONOGRAPH

In order to carry out publishing and printing activities, the Agency for Information and Mass Communications under the Administration of the President of the Republic of Uzbekistan of 10.05.2024 №. 273109 and 24.05.2024 №. 283607 issued a confirmation

Director	J. Shukurov
Editor	L. Khoshimov
Those. editor	A.Umarov

ISBN: 978-9910-8946-3-3

8172

04.12.2024 printing allowed.
Paper sheet 60x84 1/16.
Times New Roman headset.
Conditional account – 13,7. Publishing account – 15,0
Circulation 30 copies. Order № 11

Samarkand State Veterinary Medicine,
University of Animal Husbandry and Biotechnology
The publication was published in the printing center.
77 Mirzo Ulugbek str., Samarkand
Tel. 93 359 70 98

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ISBN 978-9910-8946-3-3

9 789910 894633