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### Introduction

Intrauterine growth restriction and embryonic death in dairy cows at the early stages of their gestation is one of the most significant problems in the biology of reproduction and modern dairy cattle breeding. The frequency of manifestation of these pathologies reaches 20-40% or more and increases with rising level of dairy productivity. In the mechanisms of establishment and

formation of gestation, implantation and embryo development in ruminants, ovarian progesterone (P4), trophoblastic interferontype I, interferon-tau (INFT) and cytokines, polypeptide mediators of the immune system controlled by them, play a key role.

### Materials and methods

The studies were conducted on Black-Motley Holstein-Friesian cows during the physiological formation of the embryo (n = 9), intrauterine growth restriction (n = 9) and embryonic death (n = 9)= 8). Blood was obtained from cows on the day of artificial insemination (0), during implantation of the embryo (days 15-16) and formation of primary genital organs (days 32-33). The dynamics of the concentration of progesterone (P4) in the blood serum was studied using IEA (immune-enzyme analysis)test systems of "NVO Immunotech" CJSC (Russia) and cytokines: INFT, interleukin IL-2, tumor necrosis factor (TNF $\alpha$ ), interferon- $\gamma$  (INF- $\gamma$ ) using species-specific IEA test systems Bovine Elisa Kit Cloud-Clone Corp (USA).

# Interferon-Tau in the Pathogenesis and Prevention of **Intrauterine Growth Restriction and Embryonic Death** in Dairy Cows

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Fig. 1. The indicators of progesterone concentration in the blood of cows during the early stages of gestation, nmol/L

Days after insemination	Norm	Intrauterine growth restriction	Embryonic death
Interleukin-2, IL-2			
8-9	58.3±4.65	60.6±3.37	59.4±2.94
15-16	46.7±3.21	49.2±2.19	77.9±4.12
32-33	27.5±1.95	40.3±2.64	85.4±6.47
Tumor necrosis factor alpha, TNFα			
8-9	254.2±12.4	233.6±11.8	267.8±15.7
15-16	294.6±14.1	329.1±16.6	401.2±19.8
32-33	237.1±10.4	278.1±12.4	309.7±18.3
Interferon-y, INF-y			
8-9	883.5±44.2	1248.1±69.7	1272.4±81.9
15-16	518.2±31.8	819.1±61.7	876.9±50.5
32-33	389.5±23.7	693.±37.4	1153.4±66.9

Fig. 3. The content of cytokines in the blood serum of cows during the early stages of gestation, pg/ml

Fig. 2. The concentration of interferon-tau in the blood serum of cows during the early stages of gestation, pg/ml



Fig. 4. Embryo size on days 30-32 of gestation when using bovine recombinant interferon-tau, mm





## **Results**

It was detected that the concentration of progesterone in the blood serum of fertilized cows with a subsequent intrauterine growth restriction and embryonic death even on the day of insemination was lower than in animals with the physiological formation of the embryo by 22.1-24.4% (Fig. 1), during blastogenesis -by 15 times, 2-28.0%, and during implantation - by 14.0-30.1%.

The concentration of interferon-tau normally from 364.0 pg/ml on days 8-9 (Fig. 2) increased by the implantation period up to 1403.2 pg/ml or by 3.85 times and decreased by 42.0% by days 32-33 in comparison with the maximum level. The level of interferon-tau concentration in cows with the symptoms of intrauterine growth restriction during all periods of the studies was significantly lower by 22.0-25.3%, and at embryonic death - by 22.6-37.7%.

In cows with intrauterine growth restriction and embryonic death, serum concentration of interleukin 2 (Fig. 2) was higher by 46.5-310.5%, tumor necrosis factor alpha - by 11.7-36.2%, interferon-gamma - by 58.0-296.0% in comparison with cows with the physiological formation of the embryo.

Replenishment of the deficit of interferon-tau in the body of cows by three injections of bovine recombinant interferon-tau resulted in an increase in their blood concentration of progesterone in comparison with the intact animals, during implantation - by 21.5%, and during placentation by 35.7%, which had a beneficial effect on the development of the embryo, the average size of which at days 30-32 of gestation exceeded those in intact animals, by 30.3-34.8%, respectively (Fig. 4).

# Conclusion

Disruption of interferon-tau production by the developing embryo is a universal pathogenetic mechanism for the formation of early embryopathies and embryonicdeath. Parenteral administration of a bovine recombinant INFT preparation during the pre- and implantation period ensures the formation of a comfortable communication network between the mother's body and the embryo, its physiological development and preservation of gestation.