

BÖLÜM 7



KETOZİS VE İNFERTİLİTE

Gökhan DOĞRUER¹

Ahmet GÖZER²

Onur BAHAN³

GİRİŞ VE TANIM

Ketozis, sütçü ineklerde erken laktasyon döneminde kan, süt ve idrarda keton cisimciklerin konsantrasyonunun yükselmesi ile karakterize metabolik bir hastalıktır. Reprodüktif kayıplara ve verim azalmasına neden olur, şiddetli olgular ise sürüden erken çıkışma ve ölümle sonlanabilmektedir (1, 2). Süt ineklerinde postpartum dönemde ketozisin oldukça yaygın olduğu bilinmektedir (3). Loiklung ve ark. (4) yaptıkları meta-analiz çalışmalarında küresel olarak subklinik ketozis prevalansının %22,7 seviyelerinde olduğunu ifade etmektedirler.

Ketozis nedeniyle süt üretiminin dolayısıyla süt inegi işletmelerinin karlılığının ve sürdürülebilirliğinin olumsuz etkilendiği bildirilmektedir (5). Dohoo ve Martin (6) ketozisin süt verimi üzerindeki etkilerini inceledikleri çalışmalarında günlük süt veriminde 1-1,4 kg düzeyinde bir azalma olduğunu saptamışlardır. McArt ve ark. (7) subklinik ketozisli ineklerin postpartum ilk 30 günde süt verimlerinin sağlıklı ineklere göre 2,2 kg/gün daha az olduğunu

¹ Prof.Dr., Hatay Mustafa Kemal Üniversitesi Veteriner Fakültesi Doğum ve Jinekoloji AD.,
gdogruer73@yahoo.com

² Arş. Gör. Dr., Hatay Mustafa Kemal Üniversitesi Veteriner Fakültesi Doğum ve Jinekoloji AD.,
ahmetgozer@gmail.com

³ Arş.Gör. Yozgat Bozok Üniversitesi Veteriner Fakültesi Doğum ve Jinekoloji AD.,
onurbahan@gmail.com

larını ve yağ metabolizmasını düzenler (127). Kolin yağ asidi metabolizmasında ve transportunda görev almaktadır. Karaciğerden yağların VLDL olarak dolaşma verilmesinde görevlidir (131). Prepartum kolin uygulamasının postpartum kuru madde tüketimini, süt verimini, süt yağ ve protein oranını artttırdığı ifade edilmektedir (132).

Tedavide genel prensip propilen glikol, dekstroz, insülin, Vitamin B12/fosfor ve dekzametazon uygulamalarının olduğu görülmektedir. 300 ml %100'luk propilen glikolün 5 gün boyunca günde 1 defa uygulanmasının tedavide yeterli olduğu ifade edilmektedir. Dekstroz (500 ml %50'lik) uygulamaları ise sınırsel bulguların eşlik ettiği hipoglisemi ile seyreden şiddetli ketozis olgularında kullanılmaktadır. Tedaviye cevap vermeyen ketozis olgularında hepatik lipidozis şekillenmiş olabileceği ifade edilmektedir. Bu tür olgularda insulin direncinin şekillenebileceği dolayısıyla da insulin uygulamalarının tedaviye eklenebileceği belirtilmektedir. Ancak insulin enjeksiyonlarının maliyetinin yüksek olması insulin uygulamalarının tedavide yaygınlaşmasını önüne geçmektedir. Geçmişten bu yana ketozis tedavisinde kortikosteroidlerin kullanımının gerçekeleştiriliği görülse de yağ ve protein yıkımını artttırması ve insülinin etkilerini engellemesi nedeniyle ketozis tedavisinde kullanımı önerilmemektedir. Vitamin B12 ve fosfor kullanımının ise ketozis tedavisinde glukoneogenezisi desteklemesi açısından yaygın olarak kullanılmaktadır (28).

KAYNAKLAR

1. McArt JAA, Nydam DV, Overton MW. Hyperketonemia in early lactation dairy cattle: A deterministic estimate of component and total cost per case. *Journal of Dairy Science*. 2015;98: 2043–2054.
2. Mostert PF, Bokkers EAM, van Middelaar CE, et al. Estimating the economic impact of subclinical ketosis in dairy cattle using a dynamic stochastic simulation model. *Animal*. 2018;12: 145–154.
3. Oetzel GR. Monitoring and testing dairy herds for metabolic disease. *Veterinary Clinics of North America: Food Animal Practice*. 2004;20: 651-674.
4. Loiklungs C, Sukon P, Thamrongyoswittayakul C. Global prevalence of subclinical ketosis in dairy cows: A systematic review and meta-analysis. *Research in Veterinary Science*. 2022;144: 66-76.
5. Miettinen PV, Setälä JJ. Relationships between subclinical ketosis, milk production and fertility in Finnish dairy cattle. *Preventive Veterinary Medicine*. 1993;17(1-2): 1-8.
6. Dohoo IR, Martin SW. Subclinical ketosis: prevalence and associations with production and disease. *Canadian Journal of Comparative Medicine*. 1984;48: 1–5.
7. McArt JAA, Nydam DV, Oetzel GR. Epidemiology of subclinical ketosis in early lactation dairy cattle. *Journal of Dairy Science*. 2012;95(9): 5056-5066.

8. Nikkhah A, RezaGholivand A, Khabbazan MH. Milk yield depression and its economic loss due to production diseases: Iran's large dairy herds. *Iranian Journal of Veterinary Research*. 2021;22(2): 136.
9. Yang W, Zhang B, Xu C, et al. Effects of ketosis in dairy cows on blood biochemical parameters, milk yield and composition, and digestive capacity. *Journal of Veterinary Research*. 2019;63(4): 555-560.
10. Raboisson D, Mounié M, Khenifar E, et al. The economic impact of subclinical ketosis at the farm level: Tackling the challenge of over-estimation due to multiple interactions. *Preventive Veterinary Medicine*. 2015;122: 417-425.
11. Liang D, Arnold LM, Stowe CJ, et al. Estimating US dairy clinical disease costs with a stochastic simulation model. *Journal of Dairy Science*. 2017;100: 1472-1486.
12. Melendez P, Risco CA. Management of transition cows to optimize reproductive efficiency in dairy herds. *Veterinary Clinics: Food Animal Practice*. 2005;21(2): 485-501.
13. Bell AW. Regulation of organic nutrient metabolism during transition from late pregnancy to early lactation. *Journal of Animal Science*. 1995;73: 2804-2819.
14. Herdt TH. Ruminant adaptation to negative energy balance-Influences on the etiology of ketosis and fatty liver. *Veterinary Clinical of North America Food Animal Practice*. 2000;16: 215-230.
15. Ingvartsen KL. Feeding-and management-related diseases in the transition cow: Physiological adaptations around calving and strategies to reduce feeding-related diseases. *Animal Feed Science Technology*. 2006;126: 175-213.
16. Grummer RR, Mashek DG, Hayirli A. Dry matter intake and energy balance in the transition period. *Veterinary Clinical of North America Food Animal Practice*. 2004;20(3): 447-470.
17. Lean IJ, Van Saun R, DeGaris PJ. Energy and protein nutrition management of transition dairy cows. *Veterinary Clinics: Food Animal Practice*. 2013; 29(2): 337-366.
18. Zhang G, Ametaj BN. Ketosis an old story under a new approach. *Dairy*. 2020;1(1): 5.
19. Furken C, Nakao T, Hoedemaker M. Energy balance in transition cows and its association with health, reproduction and milk production. *Tierarztliche Praxis Ausgabe Grosstiere Nutztiere*. 2015;43: 341-349.
20. White HM. The role of TCA cycle anaplerosis in ketosis and fatty liver in periparturient dairy cows. *Animals*. 2015; 5: 793-802.
21. Cooper R. Ketosis in dairy cattle. *Livestock*. 2014;19(2): 74-82.
22. Adewuyi AA, Gruys E, Van Eerdenburg FJCM. Non esterified fatty acids (NEFA) in dairy cattle. A review. *Veterinary quarterly*. 2005;27(3): 117-126.
23. Goff JP, Horst RL. Physiological changes at parturition and their relationship to metabolic disorders. *Journal of Dairy Science*. 1997;80: 1260-1268.
24. Grummer RR. Nutritional and management strategies for the prevention of fatty liver in dairy cattle. *Veterinary Journal*. 2008;176: 10-20.
25. Lei Mariana Alves Caipira, João Simões. "Invited review: ketosis diagnosis and monitoring in high-producing dairy cows." *Dairy*. 2021;303-325.
26. Holtenius P, Holtenius K. New aspects of ketone bodies in energy metabolism of dairy cows: A review. *Journal of Veterinary Medicine*. 1996;43: 579-587.
27. Oetzel GR. Herd-level ketosis-diagnosis and risk factors. American Association of Bovine Practitioners. In: *Proceedings of the 40th Annual Conference*, 3-6 January 2007, Vancouver, Canada.
28. Gordon JL, LeBlanc SJ, Duffield TF. Ketosis treatment in lactating dairy cattle. *Veterinary Clinics: Food Animal Practice*. 2013;29(2): 433-445.
29. Brunner N, Groeger S, Raposo JC, et al. Prevalence of subclinical ketosis and production diseases in dairy cows in Central and South America, Africa, Asia, Australia, New Zealand, and Eastern Europe. *Translational Animal Science*. 2018;3: 84-92.

30. Työppönen J, Kauppinen K. The stability and automatic determination of ketone bodies in blood samples taken in field conditions. *Acta Veterinaria Scandinavica*. 1980;21: 55–61.
31. Đoković R, Ilić Z, Kurćubić V, et al. Diagnosis of subclinical ketosis in dairy cows. *Biotechnology in Animal Husbandry*. 2019;35(2): 111-125.
32. Zhang Z, Liu G, Wang H, et al. Detection of subclinical ketosis in dairy cows. *Pakistan Veterinary Journal*. 2012;32: 156-160.
33. Ospina PA, McArt JA, Overton TR, et al. Using nonesterified fatty acids and β -hydroxybutyrate concentrations during the transition period for herd-level monitoring of increased risk of disease and decreased reproductive and milking performance. *Veterinary Clinical Food Animal*. 2013;29: 387–412.
34. Iwersen M, Falkenberg U, Voigtsberger R, et al. Evaluation of an electronic cowside test to detect subclinical ketosis in dairy cows. *Journal of Dairy Science*. 2009; 92(6):2618–24.
35. Konkol K, Godden P, Rapnicki P, et al. Validation of a rapid cow-side test for the measurement of blood beta-hydroxybutyrate in fresh cows. In: *42nd Annual Conference of American Association of Bovine Practitioners*. 2009, p. 190.
36. Gruber S, Mansfeld, R. Herd health monitoring in dairy farms-discover metabolic diseases. An overview. *Tierarztliche Praxis Ausgabe Grossstiere Nutztiere*. 2019;47: 246–255.
37. Duffield T. Subclinical ketosis in lactating dairy cattle. *Veterinary Clinics of North America: Food Animal Practice*. 2000;16(2), 231-253.
38. Jenkins NT, Peña G, Risco C, et al. Utility of inline milk fat and protein ratio to diagnose subclinical ketosis and to assign propylene glycol treatment in lactating dairy cows. *Canadian Veterinary Journal*. 2015;56: 850–854.
39. Toni F, Vincenti L, Grigoletto L, et al. Early lactation ratio of fat and protein percentage in milk is associated with health, milk production, and survival. *Journal of Dairy Science*. 2011;94(4):1772–83.
40. Allen MS, Bradford BJ, Oba M. The hepatic oxidation theory of the control of feed intake and its application to ruminants. *Journal of Animal Science*. 2009;87: 3317–3334.
41. Leblanc S. Monitoring metabolic health of dairy cattle in the transition period. *Journal of Reproduction Development*. 2010;56: 29–35.
42. Shin EK, Jeong JK, Choi IS, et al. Relationships among ketosis, serum metabolites, body condition, and reproductive outcomes in dairy cows. *Theriogenology*. 2015;84(2): 252-260.
43. Cao Y, Zhang J, Yang W, et al. Predictive value of plasma parameters in the risk of postpartum ketosis in dairy cows. *Journal of Veterinary Research*. 2017;61: 91–95.
44. Ospina PA, Nydam DV, Stokol T, et al. Association between the proportion of sampled transition cows with increased nonesterified fatty acids and β -hydroxybutyrate and disease incidence, pregnancy rate, and milk production at the herd level. *Journal of Dairy Science*. 2010;93(8): 3595-3601.
45. Cameron REB, Dyk PB, Herdt TH, et al. Dry cow diet, management, and energy balance as risk factors for displaced abomasum in high producing dairy herds. *Journal of Dairy Science*. 1998; 81: 132-139.
46. Quiroz-Rocha GF, LeBlanc SJ, Duffield T, et al. Evaluation of prepartum serum cholesterol and fatty acids concentrations as predictors of postpartum retention of the placenta in dairy cows. *Journal of American Veterinary Medicine Association*. 2009; 234: 790–793.
47. Duffield T, LeBlanc S, Leslie K. Impact of subclinical metabolic disease on risk of early lactation culling. *Journal of Dairy Science*. 2005; 88(1): 199 (abstr.).
48. Arthur GH, Noakes DE, Pearson H (1989) *Veterinary Reproduction and Obstetrics (Theriogenology)*. 6th ed. Tindall, London: Baillière; 1989.
49. Plaizier JC, Lissemore KD, Kelton D, et al. Evaluation of overall reproductive performance of dairy herds. *Journal of Dairy Science*. 1998;81: 1848-1854.

50. Walsh SW, Williams EJ, Evans AC. A review of the causes of poor fertility in high milk producing dairy cows. *Animal Reproduction Science*. 2011;123: 127-138.
51. Abraham F. An overview on functional causes of infertility in cows. *Journal of Fertilisation Reproduction Medicine, Genetic and Stem Cell*. 2017;5(2): 203.
52. Pryce JE, Coffey MP, Simm G. The relationship between body condition score and reproductive performance. *Journal of Dairy Science*. 2001;84:1508–15.
53. Taylor VJ, Beever DE, Wathes DC. Physiological adaptations to milk production that affect fertility in high yielding dairy cows. In: Dairying, using science to meet consumer needs. Br. Soc. Anim. Sci. Occasional Publication No. 29. Nottingham University Press; 2003. p. 37–71.
54. Wathes DC, Bourne N, Cheng Z, et al. Multiple correlation analyses of metabolic and endocrine profiles with fertility in primiparous and multiparous cows. *Journal of Dairy Science*. 2007a;90: 1310–25.
55. Beam SW, Butler WR. Effects of energy balance on follicular development and first ovulation in postpartum dairy cows. *Journal of Reproduction and Fertility*. 1999;54: 411–24.
56. Wathes DC, Taylor VJ, Cheng Z, Mann GE. Follicle growth, corpus luteum function and their effects on embryo development in the post partum cow. *Reproduction*. 2003;61: 219–37.
57. Leroy JLMR, Opsomer G, Van Soom A, et al. Reduced fertility in High-yielding dairy cows: Are the oocyte and embryo in danger? Part I the importance of negative energy balance and altered corpus luteum function to the reduction of oocyte and embryo quality in High-yielding dairy cows. *Reproduction in Domestic Animals*. 2008; 43(5), 612-622.
58. Missio D, Fritzen A, Vieira CC, et al. Increased β -hydroxybutyrate (BHBA) concentration affect follicular growth in cattle. *Animal Reproduction Science*. 2022;243, 107033.
59. Vanholder T, Leroy JLMR, Van Soom A, et al. Effects of β -OH Butyrate on bovine granulosa and theca cell function in vitro. *Reproduction in Domestic Animals*. 2006; 41(1), 39-40.
60. Leroy JL, Vanholder T, Delanghe JR, et al. Metabolic changes in follicular fluid of the dominant follicle in high-yielding dairy cows early post partum. *Theriogenology*. 2004;62: 1131–43.
61. Leroy JL, Vanholder T, Mateusen B, et al. Non-esterified fatty acids in follicular fluid of dairy cows and their effect on developmental capacity of bovine oocytes in vitro. *Reproduction*. 2005;130:485–95.
62. Roche JF. The effect of nutritional management of the dairy cow on reproductive efficiency. *Animal Reproduction Science*. 2006; 96: 282–96.
63. Lucy MC, Jiang H, Kobayashi Y. Changes in the somatotrophic axis associated with the initiation of lactation. *Journal of Dairy Science*. 2001;84: E113–9.
64. Wathes DC, Fenwick M, Cheng Z, et al. Influence of negative energy balance on cyclicity and fertility in the high producing dairy cow. *Theriogenology*. 2007;68: 232-241.
65. Butler WR. Relationships of negative energy balance with fertility. *Advances in Dairy Technology*. 2005;17: 35-46.
66. Lucy MC. Functional differences in the growth hormone and insulin-like growth factor axis in cattle and pigs: implications for post-partum nutrition and reproduction. *Reproduction in Domestic Animals*. 2008; 43 (2): 31–9.
67. Fenwick MA, Llewellyn S, Fitzpatrick R, et al. Negative energy balance in dairy cows is associated with specific changes in IGF-binding protein expression in the oviduct. *Reproduction*. 2008;135(1): 63.
68. Diskin MG, Mackey DR, Roche JF, et al. Effects of nutrition and metabolic status on circulating hormones and ovarian follicle development in cattle. *Animal Reproduction Science*. 2003; 78: 345–70.

69. Crowe MA. Fertility in dairy cows – the conference in perspective. *Fertility in Dairy Cows-Bridging the Gaps*, Liverpool Hope University, Liverpool, UK. *British Society for Animal Science*. 2008; 175–9.
70. Terqui M, D Chupin, D Gauthier et al. Influence of management and nutrition on postpartum endocrine function and ovarian activity in cows. Factors influencing fertility in the postpartum cow. In: *Current Topics Veterinary Medicine Animals Science*. H Kard, E.Schallenger, (eds.) 1982;20: 384
71. Butler WR. Energy balance relationships with follicular development, ovulation and fertility in postpartum dairy cows. *Livestock Production Science*. 2003;83: 211-218.
72. Jorritsma R, Wensing T, Kruip TAM, et al. Metabolic changes in early lactation and impaired reproductive performance in dairy cows. *Veterinary Research*. 2003;34: 11-26.
73. Harrison LM, Randel RD. Influence of insulin and energy intake on ovulation rate, luteinizing hormone and progesterone in beef heifers. *Journal of Animal Science*. 1986;63: 1228-1235.
74. McCann JP, Hansel W. Relationships between insulin and glucose metabolism and pituitary-ovarian functions in fasted heifers. *Biology of Reproduction*. 1986;34: 630.
75. Canfield RW, Butler WR. Energy balance, first ovulation and the effects of naloxone on LH secretion in early postpartum dairy cows. *Journal of Animal Science*. 1991;69: 740-783.
76. Miyoshi S, Pate JL, Palmquist DL. Effects of propylene glycol drenching on energy balance, plasma glucose, plasma insulin, ovarian function and conception in dairy cows. *Animal Reproduction Science*. 2001;68(1-2): 29-43.
77. Imakawa KML, Day DD, Zalesky A, et al. Effects of 17beta-estradiol and diets varying in energy on secretion of luteinizing hormone in beef heifers. *Journal of Animal Science*. 1987;64: 805.
78. Rutter LM, Manns JG. Hypoglycemia alters pulsatile luteinizing hormone secretion in the postpartum beef cow. *Journal of Animal Science*. 1987;64: 479-488.
79. Van Houten M, Posner BI, Kopriwa BM, et al. Insulin-binding sites in the rat brain: in vivo localization to the circumventricular organs by quantitative radiography. *Endocrinology*. 1979;105: 666.
80. Hawkins RA, Biebuyck JF. Ketone bodies are selectively used by individual brain regions. *Science*. 1979;205: 325.
81. Butler WR, Smith RD. Interrelationships between energy balance and postpartum reproductive function in dairy cattle. *Journal of Dairy Science*. 1989;72(3): 767-783.
82. Tamminga S. The effect of the supply of rumen degradable protein and metabolisable protein on negative energy balance and fertility in dairy cows. *Animal Reproduction Science*. 2006;96: 227-239.
83. Hoeben D, Heyneman R, Burvenich C. Elevated levels of β -hydroxybutyric acid in periparturient cows and in vitro effect on respiratory burst activity of bovine neutrophils. *Veterinary Immunology and Immunopathology*. 1997;58(2): 165-170.
84. Song Y, Li N, Gu J, et al. β -Hydroxybutyrate induces bovine hepatocyte apoptosis via an ROS-p38 signaling pathway. *Journal of Dairy Science*. 2016;99: 9184-9198.
85. Suthar VS, Canelas-Raposo J, Deniz A, et al. Prevalence of subclinical ketosis and relationships with postpartum diseases in European dairy cows. *Journal of Dairy Science*. 2013;96(5): 2925-2938.
86. Suriyasathaporn W, Heuer C, Noordhuizen-Stassen EN, et al. Hyperketonemia and udder defense: a review. *Veterinary Research*. 2000;31: 397-412.
87. Albaaj A, Foucras G, Raboisson D. Changes in milk urea around insemination are negatively associated with conception success in dairy cows. *Journal of Dairy Science*. 2017;100: 3257-3265.

88. Pedroza GH, Lanzon LF, Rabaglino MB, et al. Exposure to non-esterified fatty acids in vitro results in changes in the ovarian and follicular environment in cattle. *Animal Reproduction Science*. 2022;238: 106937.
89. Ferst JG, Missio D, Bertolin K, et al. Intrafollicular injection of nonesterified fatty acids impaired dominant follicle growth in cattle. *Animal Reproduction Science*. 2020;219: 106536.
90. Marei WF, De Bie J, Xhonneux I, et al. Metabolic and antioxidant status during transition is associated with changes in the granulosa cell transcriptome in the preovulatory follicle in high-producing dairy cows at the time of breeding. *Journal of Dairy Science*. 2022;105(8): 6956-6972.
91. Yung MC, VandeHaar MJ, Fogwell RL, et al. Effect of energy balance and somatotropin on insulin-like growth factor I in serum and on weight and progesterone of corpus luteum in heifers. *Journal of Animal Science*. 1996;74(9): 2239-2244.
92. Geishauser T, Leslie K, Kelton D, et al. Monitoring for subclinical ketosis in dairy herds. *Compendium*. 2001;23(8): p65-71.
93. Walsh RB, Kelton DF, Duffield TF, et al. Prevalence and risk factors for postpartum anovulatory condition in dairy cows. *Journal of Dairy Science*. 2007;90: 315-324.
94. Duffield TF, Lissemore KD, McBride BW, et al. Impact of hyperketonemia in early lactation dairy cows on health and production. *Journal of Dairy Science*. 2009;92: 571-580.
95. Roberts T, Chapinal N, LeBlanc SJ, et al. Metabolic parameters in transition cows as indicators for early-lactation culling risk. *Journal of Dairy Science*. 2012;95: 3057-3063.
96. Chankeaw W, Guo YZ, Båge R, et al. Elevated non-esterified fatty acids impair survival and promote lipid accumulation and pro-inflammatory cytokine production in bovine endometrial epithelial cells. *Reproduction, Fertility and Development*. 2018;30(12): 1770-1784.
97. Li P, Li L, Zhang C, et al. Palmitic acid and β -hydroxybutyrate induce inflammatory responses in bovine endometrial cells by activating oxidative stress-mediated NF- κ B signaling. *Molecules*. 2019;24(13): 2421.
98. Niringiyumukiza JD, Cai H, Xiang W. Prostaglandin E2 involvement in mammalian female fertility: ovulation, fertilization, embryo development and early implantation. *Reproductive Biology and Endocrinology*. 2018;16(1): 1-10.
99. Qin X, Yang S, Zhang Y, et al. Effects of non-esterified fatty acids on relative abundance of prostaglandin E2 and F2 α synthesis-related mRNA transcripts and protein in endometrial cells of cattle in vitro. *Animal Reproduction Science*. 2020;221: 106549.
100. Smits A, Leroy JL, Bols PE, et al. Rescue potential of supportive embryo culture conditions on bovine embryos derived from metabolically compromised oocytes. *International Journal of Molecular Sciences*. 2020;21(21): 8206.
101. Ribeiro ES, Gomes G, Greco LF, et al. Carryover effect of postpartum inflammatory diseases on developmental biology and fertility in lactating dairy cows. *Journal of Dairy Science*. 2016;99(3): 2201-2220.
102. Furukawa E, Chen Z, Ueshiba H, et al. Postpartum cows showed high oocyte triacylglycerols concurrently with high plasma free fatty acids. *Theriogenology*. 2021;176: 174-182.
103. Kim IH, Na KJ, Yang MP. Immune responses during the peripartum period in dairy cows with postpartum endometritis. *Journal of Reproduction and Development*. 2005; 0510050026-0510050026.
104. Hammon DS, Evjen IM, Dhiman TR, et al. Neutrophil function and energy status in Holstein cows with uterine health disorders. *Veterinary Immunology and Immunopathology*. 2006;113: 21-29.
105. Wathes DC, Cheng Z, Chowdhury W, et al. Negative energy balance alters global gene expression and immune responses in the uterus of postpartum dairy cows. *Physiological Genomics*. 2009;39(1): 1-13.

106. Sheldon IM, Cronin JG, Pospiech M, et al. Symposium review: Mechanisms linking metabolic stress with innate immunity in the endometrium. *Journal of Dairy Science*. 2018;101(4): 3655-3664.
107. Eslami M. Alterations of non-esterified fatty acids, β -hydroxybutyric acid, urea, and bilirubin traits in clinical endometritis cows following treatment. *Comparative Clinical Pathology*. 2018;27(1): 173-179.
108. Cheong SH, Nydam DV, Galvao KN, et al. Cow-level and herd-level risk factors for subclinical endometritis in lactating Holstein cows. *Journal of Dairy Science*. 2011;94: 762-770.
109. Gautam G, Nakao T, Koike K, et al. Spontaneous recovery or persistence of postpartum endometritis and risk factors for its persistence in Holstein cows. *Theriogenology*. 2010;73: 168-179.
110. Van Mourik MS, Macklon NS, Heijnen CJ. Embryonic implantation: cytokines, adhesion molecules, and immune cells in establishing an implantation environment. *Journal of Leukocyte Biology*. 2009;85(1): 4-19.
111. Campanile G, Baruselli PS, Limone A, et al. Local action of cytokines and immune cells in communication between the conceptus and uterus during the critical period of early embryo development, attachment and implantation—Implications for embryo survival in cattle: A review. *Theriogenology*. 2021;167: 1-12.
112. Wegmann TG, Lin H, Guilbert L, et al. Bidirectional cytokine interactions in the maternal-fetal relationship: is successful pregnancy a TH2 phenomenon? *Immunology Today*. 1993;14(7): 353-356.
113. Hill JA, Choi BC. Maternal immunological aspects of pregnancy success and failure. *Journal of Reproduction and Fertility*. Supplement. 2000;55: 91-97.
114. Hotamisligil GS, Erbay E. Nutrient sensing and inflammation in metabolic diseases. *Nature Reviews Immunology*. 2008;8: 923-934.
115. Tilg H, Moschen AR. Inflammatory mechanisms in the regulation of insulin resistance. *Molecular Medicine*. 2008;14: 222-231.
116. Ohtsu A, Tanaka H, Seno K, et al. Palmitic acid stimulates interleukin-8 via the TLR4/NF- κ B/ROS pathway and induces mitochondrial dysfunction in bovine oviduct epithelial cells. *American Journal of Reproductive Immunology*. 2017;77(6): e12642.
117. Leroy JLMR, Van Soom A, Opsomer G, et al. The consequences of metabolic changes in high-yielding dairy cows on oocyte and embryo quality. *Animal*. 2008b;2(8): 1120-1127.
118. Pascottini OB, LeBlanc SJ. Modulation of immune function in the bovine uterus peripartum. *Theriogenology*. 2020;150: 193-200.
119. Hayırlı A, Çolak A. İneklerin Kuru ve Geçiş Dönemlerinde Sevk-İdare ve Besleme Stratejileri: Postpartum Süreçte Metabolik Profil, Sağlık Durumu ve Fertiliteye Etkisi. *Turkiye Klinikleri Journal of Veterinary Sciences*. 2011;2(1): 1-35.
120. Busato A, Faissler D, Küpfer U. Body condition scores in dairy cows: associations with metabolic and endocrine changes in healthy dairy cows. *Journal of Veterinary Medicine Series A*. 2002;49(9): 455-460.
121. Gillund P, Reksen O, Gröhn YT, et al. Body condition related to ketosis and reproductive performance in Norwegian dairy cows. *Journal of Dairy Science*. 2001;84: 1390-1396.
122. Studer VA, Grummer RR, Bertics SJ. Effect of prepartum propylene glycol administration on periparturient fatty liver in dairy cows. *Journal of Dairy Science*. 1993;76(10): 2931-2939.
123. Juchem SO, Santos FAP, Imaizumi H, et al. Production and blood parameters of Holstein cows treated prepartum with sodium monensin or propylene glycol. *Journal of Dairy Science*. 2004;87(3): 680-689.

124. Zhang F, Nan X, Wang H, et al. Effects of propylene glycol on negative energy balance of postpartum dairy cows. *Animals*. 2020;10(9): 1526.
125. Nielsen NI, Ingvarseten KL. Propylene glycol for dairy cows: A review of the metabolism of propylene glycol and its effects on physiological parameters, feed intake, milk production and risk of ketosis. *Animal Feed Science and Technology*. 2004;115(3-4): 191-213.
126. Burhans WS, Briggs EA, Rathmacher JA, et al. Glucogenic supplementation does not reduce body tissue protein degradation in periparturient dairy cows. *Journal of Dairy Science*. 1997;80(1): 167.
127. Manning A. Clinical and subclinical ketosis in dairy cattle. *Livestock*. 2019;24(1): 13-17.
128. Duffield TF, Rabiee AR, Lean IJ. A meta-analysis of the impact of monensin in lactating dairy cattle. Part 1. Metabolic effects. *Journal of Dairy Science*. 2008;91(4): 1334–1346.
129. Duffield TF, Rabiee AR, Lean IJ. A meta-analysis of the impact of monensin in lactating dairy cattle. Part 2. Production effects. *Journal of Dairy Science*. 2008b;91(4): 1347-1360.
130. Duffield TF, Rabiee AR, Lean IJ. A meta-analysis of the impact of monensin in lactating dairy cattle. Part 3. Health and reproduction. *Journal of Dairy Science*. 2008c;91(6): 2328-2341.
131. Shahsavari A, Michael JD, Al Jassim R. The role of rumen-protected choline in hepatic function and performance of transition dairy cows. *British Journal of Nutrition*. 2016;116(1): 35-44.
132. Humer E, Bruggeman G, Zebeli Q. A meta-analysis on the impact of the supplementation of rumen-protected choline on the metabolic health and performance of dairy cattle. *Animals*. 2019;9(8): 566.