

**Conclusions.** The present study demonstrated that streptozotocin-induced diabetes in rats is accompanied by a pronounced increase in serum neutral keto derivatives, serving as indicators of protein oxidative modification. The progressive elevation of these compounds from day 14 to day 70 of observation underscores the central role of oxidative stress in the pathogenesis of experimental diabetes. The most pronounced accumulation was documented at day 70, supporting the hypothesis that persistent hyperglycemia exacerbates protein oxidative injury over time. Monitoring neutral keto derivatives may thus represent a useful approach for evaluating the severity of oxidative stress in diabetes and for assessing the efficacy of potential antioxidant therapies.

**Keywords:** experimental diabetes mellitus, protein oxidative modification, oxidative stress, neutral keto derivatives

## ENDOCRINE EFFECTS OF COVID-19 VACCINATION

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**Introduction.** During the widespread use of vaccines against COVID-19, a number of negative effects were noted that may affect the functional state of the endocrine system.

**The aim** of this review was to summarize data on the possible physiological basis and clinical significance by analyzing information sources.

**Main part.** During the COVID-19 pandemic, several vaccines with varying efficacy and safety were developed.

1. Vaccines based on SARS-CoV-2 mRNA encoding the viral spike glycoprotein (glycoprotein S).

2. SARS-CoV-2 adenovirus-based vaccines carrying the genes for the complete SARS-CoV-2 S glycoprotein (viral vector).

3. Inactivated vaccine obtained by inactivating the SARS-CoV-2 virus with  $\beta$ -propiolactone and formulated with an adjuvant based on potassium aluminum salt.

Among the endocrine reactions associated with SARS-CoV-2 vaccination, the most common are changes in the thyroid, pituitary, and adrenal glands. Thyroid disorders were manifested by subacute thyroiditis (SAT), which was reported in more than a hundred cases. Among the 83 cases of thyroid abnormalities after vaccination against COVID-19, the most common was observed after mRNA vaccines (68.7%), followed by viral vectors (15.7%), and inactivated vaccines (14.5%). The most common disease was subacute thyroiditis (SAT, 60.2%), followed by Graves' disease - diffuse toxic goiter (GD, 25.3%), and other forms were less common. In most cases, symptoms of SAT (58.0%) and GD (61.9%) appeared after the first dose (median 10 days), the rest after the second dose (median 10–14 days).

Autoimmune thyroid disease has been reported in several cases of newly diagnosed or recurrent Graves' disease with manifestations of hyperthyroidism,

elevated thyroid hormone levels, thyrotropin suppression, and elevated antithyroid antibodies. A possible mechanism of development could be autoimmune inflammatory syndrome induced by adjuvants (ASIA), such as aluminum salts contained in vaccines. Exogenous factors such as silicon or aluminum can activate the immune system and induce the production of autoantibodies. They stimulate the differentiation of dendritic cells and phagocytic macrophages, independent of Toll-like receptors. Through activation of NLRP3 (part of the inflammasome that recognizes danger signals), macrophages secrete the pro-inflammatory cytokines IL-1 $\beta$  and IL-18, enhancing the immune response to the antigen. Lysosomal destabilization and cathepsin release have also been reported to be associated with NLRP3 activation under the influence of crystals, as well as some soluble adjuvants. Hyperstimulation of the immune system and molecular mimicry, which allows this virus to undermine the self-tolerance of the host's immune system, were noted as another pathophysiological mechanism for the development of autoimmune thyroiditis. It was determined that the sequence of thyroid peroxidase peptides in the tissue of the thyroid gland is similar to the sequence of the spike protein, nucleoprotein and membrane protein of SARS-CoV-2. Mutual recognition between the modified SARS-CoV-2 protein in the vaccine and the target protein of the thyroid gland (for example, the SARS-CoV-2 spike protein has structural homology) may contribute to the development of autoimmune thyroiditis.

COVID-19 vaccination has also caused severe hyperglycemic events, including diabetic ketoacidosis and hyperosmolar hyperglycemic syndrome (history of type 2 diabetes or prediabetes). Transient hyperglycemia after COVID-19 vaccination could be caused by both a systemic inflammatory response and an individual response to vaccine components (adenovirus vector, SARS-CoV-2 spike protein, vaccine adjuvants).

A case of hypopituitarism 3 days after a second vaccination with mRNA-1273 SARS-CoV-2 has also been described. Given that the headache began shortly after the second dose of the COVID-19 vaccine, this could have been a potential trigger for pituitary apoplexy. In cases of vaccine-associated apoplexy, pituitary hemorrhage can be caused by either vaccine-induced thrombophilia-thrombocytopenia syndrome (VITT) or ASIA. VITT is a rare, severe immunological reaction to non-replicating adenovirus-vectored vaccines. The main link in its pathogenesis is a high titer of IgG directed against platelet factor 4 (PF4), which activate platelets through Fc $\gamma$ IIa receptors, causing the formation of microthrombi and simultaneous thrombocytopenia, due to which vessels become vulnerable to bleeding.

**Conclusions.** In rare cases, adverse effects related to systemic immune activation have been observed after vaccination against COVID-19. Endocrine effects were mostly transient, and severe complications were rare, so vaccination remains safe for the majority of the population, and patients with existing endocrine diseases are recommended to consult a doctor before vaccination.