The key enzyme in the peripheral metabolism of glucocorticoids is 11β-hydroxysteroid dehydrogenase (11β-HSD), which catalyzes the conversion of glucocorticoids into their less active 11-oxo derivatives and vice versa, thus potentially influencing the concentration of these hormones directly in tissues. There are two isoenzymes of 11β-HSD. 11β-HSD2 is only capable of decreasing glucocorticoid levels and is expressed not only in mineralocorticoid target tissues but also, for example, in the placenta. In contrast, 11β-HSD1 predominantly increases the local concentration of glucocorticoids in vivo and is expressed in various tissues. The presence of these isoenzymes in tissues is highly significant for mediating both mineralocorticoid and glucocorticoid signaling. It is known that mineralocorticoids (aldosterone) and glucocorticoids (cortisol, corticosterone) have approximately the same affinity for the mineralocorticoid receptor (MR) in vitro, and additionally, the plasma concentration of glucocorticoids is about 1000 times higher than that of mineralocorticoids. However, in vivo, there is specific binding of aldosterone to MR. This selective binding is enabled by 11β-HSD2, which converts glucocorticoids into less active 11-oxo derivatives. Insufficient function of this isoenzyme leads to excessive activation of MR by glucocorticoids, resulting in the development of hypertension. Recently, it has been considered that in the heart and brain, where MR is expressed and to a lesser extent 11β-HSD2, MR may form an inactive complex with glucocorticoids. One possibility to ensure activation of the receptor by mineralocorticoids is to convert the glucocorticoid into a less active 11-oxo derivative using 11β-HSD2. On the other hand, 11β-HSD1 may increase the local concentration of glucocorticoids and help form an inactive complex between MR and glucocorticoids. Both dehydrogenases, by altering the local concentration of glucocorticoids, can also influence glucocorticoid signaling mediated by the glucocorticoid receptor or potentially affect the action of other hormones. This is because the permissive effect of glucocorticoids on the action of vasoconstrictor substances, such as norepinephrine and angiotensin II, is well known.