SUMMARY

Obesity is a most common metabolic disorder worldwide. Prevalence of obesity is consistently growing in all continents during last years. Primarily the increase of incidence of obesity in children is alarming. Obesity is linked to elevated risk of type 2 diabetes, hyperlipidemia, cardiovascular diseases, some cancers and disorders of musculoskeletal system. The cost of the treatment of diseases linked to obesity is annually increasing and obesity represents very important part of costs of health system in developed – and recently also developing – countries. This fact shows the necessity of research in the area of preventive and therapeutic procedures.

The development of metabolic disturbances linked to obesity is associated with dysfunction of adipose tissue. Its two main features are: 1) altered secretion of specific substance with hormonal or paracrinne charakter (called adipokines) and 2) elevated mobilization of non-esterified fatty acids (NEMK) from adipose tissue and subsequently their increased release into the circulation (1). In our studies we paid attention to the study of lipolysis. The rate of lipolysis is the primary factor that determines the release of NEFA from adipose tissue. We focused to a role of adiponectin and natriuretic peptid type B (BNP) in the regulation of lipolysis in two pathological states with disorder of lipolysis – obesity and chronic heart failure (HF).

In the first two studies we show that adiponectin, hormon produced in adipocytes of adipose tissue, influences the lipolysis in adipocytes by autocrine respectively paracrine manner. In study No. 1 we showed that adiponectin inhibits spontaneous and catecholamine-induced lipolysis in non-obese but not in obese subjects. Adiponectin is secreted from adipocyte in several polymeric forms with different biological effect: therefore, in study No. 2 we investigated the role of polymeric forms in regulation of lipolysis in subcutaneous and visceral adipose tissue (SAT and VAT, respectively). We showed that globular adiponectin inhibited lipolysis in SAT and trimeric adiponectin inhibited lipolysis in VAT in obese women. We explored the mechanisms underlying these lipolytic actions and showed that globular adiponectin induces an activity of AMP-activated protein kinase (AMPK) in SAT.

In the next study (study No. 3) we present original findings on disturbances of lipolysis regulation in patiens with HF. The enhanced lipolysis in advanced HF can contribute to the overload of myocardium with the flow of non-esterified fatty acids and to the whole-body insulin resistance and cardiac cachexia. Mechanisms of increased adipose tissue lipolysis in

HF patients are incompletely understood. We investigated the effects of natriuretic peptides in adipose tissue and showed that BNP_{1-32} contributes to lipolysis in SAT and that induction of lipolysis by bioactive form of BNP is enhanced in HF patiens in comparison with healthy control group. This suggests that BNP is a hormone that contributes to the enhanced lipolysis in HF patiens. It is, presumably, more important than catecholamines (in physiological conditions the most important stimulators of lipolysis).

In study No. 4 we examined secretion of adiponectin isoforms from adipocytes in SAT and VAT. We found that total adiponectin quantity secreted from adipose tissue explants was higher in SAT than in VAT. When compared to non-obese, the adiponectin secretion was reduced in obese subjects, the reduction being more significant in SAT than in VAT. According to our results, SAT seems to be more important – when compared with VAT – determinant of the altered adiponectin production in obesity.

The above mentioned findings contribute to the understanding of pathogenesis of metabolic complications of obesity and HF and can contribute to the development of preventive and therapeutic measures influencing metabolic and cardiovascular complications of obesity.