ABSTRACT

Obesity and non-insulin dependent diabetes mellitus (NIDDM) are common diseases with multiple pathophysiological disturbances in glucose and lipid metabolism. These defects result from a complex interplay between one or more genetic loci and several environmental factors. Due to this complexity, it is difficult to estimate the relative importance of the individual components, or to assess the efficacy and determine the mode of action of potential new therapeutic agents. The application of various techniques allows to selectively perturb a complex *in vivo* system and to create selective physiological defects in order to determine their potential contribution to obesity and NIDDM. The main focus of this review is on current techniques for *in vivo* assessment of glucose and free fatty acid (FFA) metabolism. We discuss techniques for systemic measurement including clamp methods, isotope tracer methods, and indirect calorimetry. The outlined regional measurement techniques are: the arteriovenous differences, the microdialysis and the microperfusion for sampling interstitial fluid from muscle and adipose tissue, and the nuclear magnetic resonance (NMR) spectroscopy and the positron emission tomography (PET). Mathematical modeling approaches, like the minimal models for glucose utilization and deconvolution for reconstructing endogenous fluxes (hepatic glucose production and insulin secretion) are highlighted. The discussion of animal models includes the most common rodent models and transgenic approaches. Finally, the frequently used analytical techniques are briefly summarized. In summary, assessment of glucose and FFA metabolism is a scientific challenge, but with modern techniques, it is possible to further explore the cellular and molecular events involved in the regulation of these metabolic processes and develop therapeutic agents for the treatment of obesity and NIDDM.

KEY WORDS: non-insulin dependent diabetes mellitus, insulin resistance, clamp techniques, isotope tracer, microperfusion, mathematical modeling, animal models, analytical techniques.