



FIGURE 6.2 — Mitochondrial Fatty Acid Metabolism Markers

In all tissues except brain, most ATP generation is derived from oxidation of fatty acids. The process is initiated by entry of the fatty acid into the matrix of mitochondria. The rate limiting step for entry is the formation of fatty acyl carnitine by one of three enzyme systems that operate on medium, long or very long chain fatty acids. Even a slight interruption of this dynamic pathway causes increased amounts of fatty acids to be processed via omega oxidation occurring in peroxisomes. The lower efficiency of peroxisomal processing allows intermediates to escape and be lost when the blood is filtered in the kidneys. Adipate and suberate are biochemical markers that reflect the degree to which mitochondrial entry is impaired due to insufficiency of carnitine or other genotrophic factors. See Figure 5.4 (Fatty Acids) for carnitine shuttle details.

of fatty acyl-carnitine, and this reaction is governed by carnitine concentration. The extreme importance of fatty acid oxidation to provide cellular energy is indicated by the redundancy of systems. Both β - and ω -oxidation systems are contained in peroxisomes. When the mitochondrial system fails to meet demands, peroxisomes can take over to a limited degree, but lack of the

double membrane containment of the mitochondrion means that the system is less efficient because substrates may escape and be lost as renal excretory products. Examples of human mitochondrial β -oxidation deficiency are well known to produce infant death, though some individuals exhibit normal development for a few weeks or months.³⁶ As usual, the severe manifestations of such