4 Tissue Specific and Subcellular Distribution of Creatine Kinase Isoenzymes

4.1 Tissue Specific Distribution of Creatine Kinase Isoenzymes

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Because of its central role in cellular energy metabolism the enzyme creatine kinase can be found in all tissues. Accordingly the highest activity can be measured in the contractile system and in the brain.

While investigating skeletal muscle and brain of chickens, Eppenberger et al. [189] observed for the first time heterogeneity of creatine kinase and a disproportionate activity in different organs. This led to the discovery of the CK isoenzyme system. Three CK isoenzymes were described in skeletal muscle, brain and heart homogenates of several vertebrates including man, after electrophoretic separation. These were designated, according to where they occurred most frequently, as skeletal, brain and myocardial forms. These results were independently confirmed by Sjövall et al. [743], who, for the first time, indicated the possible significance of CK isoenzymes for the diagnosis of muscular and myocardial diseases.

The dimeric structure of CK was proved by Dawson et al. [149]. These authors then named the CK isoenzymes: CK-MM (muscle type), CK-BB (brain type), and CK-MB (hybrid type). The reviewer has tried to compile in this chapter a summary of present knowledge concerning the organ distribution of these creatine kinase isoenzymes. However, considering the
continuing publication of new results it is questionable, how long this re­view will be current.

In the original investigations only electrophoretic, chromatographic, and fluorescence kinetic differentiation methods were used. These results are set forth in the first part of the review. More recently immunological methodology was also introduced into CK isoenzyme differentiation. The results obtained by this method by several groups including our own, will be presented in the review's second part.

4.1.1 Investigations with Non Immunological Methods

While the principal pattern of organ distribution, as described in the first publications, is continually confirmed, a wide diversity of results and opinions – especially in questions of diagnostic significance – is found in the literature. This is not surprising in view of the different types of specimens used, some obtained from autopsies, others from surgical operations or biopsies. The comparison of results is also greatly imped by use of different methods for homogenization, storage and activity measurement (substrates, activators, temperature, etc.).

Extensive investigations were published by Allard et al. [11], van der Veen et al. [826], Goto et al. [259], Tsung [815], Jockers-Wretou et al. [340], and Roberts et al. [649, 655]. In Table 1 the essential data are summarized and arranged according to the level of CK activity in specific tissues. In each case the particular methodology is given. The most important results of these investigations will be discussed in detail in the following sections of this chapter.

4.1.1.1 Skeletal Muscle

All investigators agree that the highest relative CK activity is always found in skeletal muscle. Depending on muscle, type, sex, and methodology used the total CK activity measured is between 225 and 12,000 U/g fresh tissue. The significance of the CK isoenzyme pattern, however, has recently come under discussion with regard to its diagnostic application. Is it increased CK-MM activity alone that is diagnostically important, or is a measurable CK-MB and/or CK-BB activity also significant?

Early investigators, using electrophoretic separation, always reported a weak CK-MB band. Rosalki [675] noticed for the first time a different electrophoretic pattern in red and in white musculature: the obligate CK-MB band in red muscles is absent in white muscles. Later investigations of skeletal muscle yielded equivocal results, some authors were not able to find a CK-MB band at all [399, 572, 647], whereas the majority of authors confirmed the presence of the CK-MB band [11, 93, 593, 743, 812, 826, 864]. CK-MB activity in some muscles can account for up to 31% of total CK activity (Goto [259], Thorstensson [808]). In some cases an