

Serum creatine kinase levels in normal females

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SUMMARY Serum creatine kinase levels were determined in 75 girls (age range, one month to 15 years) and 200 normal adult women (age range, 18 to 50 years). The values ranged from 12.5 to 80 IU/l in girls and 19 to 155 IU/l in adult females. The SCK level appeared to increase with age from 1 to 15 years, after which the level remained fairly constant. These data should be helpful in the detection of carriers of X-linked forms of muscular dystrophy.

Determination of serum creatine kinase (SCK) levels has been accepted as the most reliable single test for detecting female carriers of X-linked Duchenne and Becker muscular dystrophies (Emery, 1969). One drawback to this method is that it yields about 25% false negatives (Walton and Gardner-Medwin, 1974). The carrier detection rate may be better in younger women, because in carriers the level of the enzyme decreases with increasing age (Dreyfus *et al.*, 1970; Moser and Vogt, 1974; Skinner *et al.*, 1975; Dubowitz, 1976; McCormick and Allen, 1976). Zellweger and Hanson (1970) reported that even in normal people the SCK level decreases with increasing age, but Griffiths (1964) and Wilson *et al.* (1965) did not find any significant age effect in normal controls. It has been suggested (Thompson *et al.*, 1967; Moser and Vogt, 1974) that the number of false negative results could be minimised if carrier status were determined during childhood. It is therefore important to establish the range of SCK levels in normal females, both children and adults.

Materials and methods

Venous blood was collected from 75 girls aged between one month and 15 years. All these children were attending the Royal Hospital for Sick Children, Edinburgh, for treatment of disorders other than ones known to affect the SCK levels. None of the subjects had any family history of nervous or muscular disorders. Blood samples were also collected from 200 healthy females (age range, 18 to 50 years). Within 2 hours of collection of the blood the serum was removed and stored at -20°C . SCK levels were determined within 7 days by the method of Rosalki (1967). The assays were performed at 30°C

and the results expressed as International Units (IU) per litre.

All chemicals were supplied by Calbiochem Ltd.

Results and discussion

SCK levels in normal female children ranged between 12.5 to 80 IU/l with a mean of 39.09 ± 18.12 . There was a small but non-significant tendency for SCK level to decrease in the first year of life, after which the level appeared to increase with age into adulthood. Though newborns have not been included in this series, Bodensteiner and Zellweger (1971) and Gilboa and Swanson (1976) reported very high levels of SCK during that period. According to Gilboa and Swanson (1976), the levels decreased to the normal range found in adults and older children 6 to 10 weeks after birth, whereas Zellweger and Hanson (1970) noted a gradual decline throughout the first year of life. The cause of high SCK level during the newborn period is not clearly understood. Bodensteiner and Zellweger (1971) attributed it to birth trauma, but Gilboa and Swanson (1976) have questioned this interpretation.

The present childhood results have been compared with SCK levels of 200 healthy adult females aged between 18 and 50 years previously estimated in this Department. When the individual results of the subjects between 1 and 50 years of age were plotted, and the best fit curve drawn through them, it appeared that the SCK level increased with age until about 15 years of age after which it seemed to remain fairly constant (Table 1, Fig.). The increase of SCK level with age could possibly be attributed to a positive correlation between SCK level and lean body mass, which was suggested by Hughes (1962), and later confirmed by Gracia (1974). Allen *et al.* (1960) showed that a crude but direct relationship exists

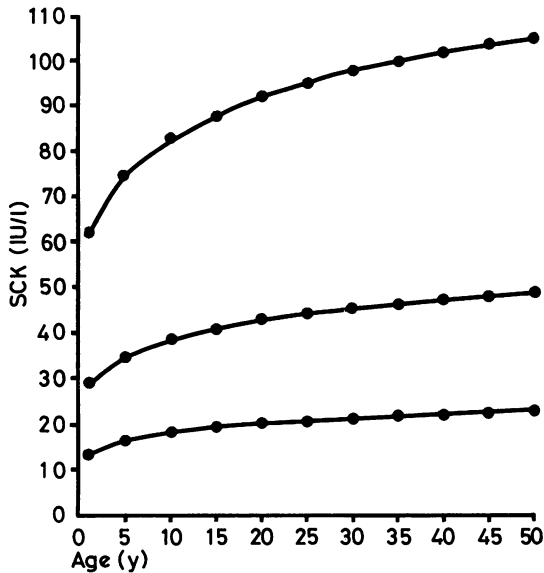


Fig. SCK level vs. age. Best fitting line with 95% confidence limits.

between total body potassium and the fat free mass of growing females. They also showed an increase in potassium levels up to the age of 17 years, followed by an almost constant level up to 40 years of age. Later, Forbes and Hursh (1963), studying lean body mass in females from 7 to 32 years of age, showed an increase in lean body mass up to 15 years followed by an almost constant level thereafter.

Since the SCK level increases with age during childhood in normal females and decreases in carriers, it is likely that the difference in SCK levels in normal and carrier females would be greatest during the younger ages. The upper 95th centile for female children from 1 to 15 years of age was 75 IU/l and in the present series there was no case above 80 IU/l (Table 2).

Table 1 SCK values in different age groups in normal females

Age range (y)	No.	SCK (IU/l)		
		Mean	SD	Range
Less than 1	17	41.14	16.99	14.0- 72.0
1-2	7	26.28	11.52	12.5- 43.0
3-4	12	40.91	21.76	13.0- 70.5
5-6	5	30.50	13.72	15.5- 51.0
7-8	13	45.69	21.60	15.0- 75.0
9-10	6	38.00	7.75	24.5- 45.5
11-12	7	42.14	23.06	20.5- 80.0
13-14	4	37.37	17.52	18.5- 60.5
15-20	68	46.58	17.04	21.0-130.0
21-30	75	47.97	20.79	19.0-134.0
31-40	38	45.45	16.43	27.0-119.0
41-50	23	50.61	29.27	21.0-155.0

Table 2 Distribution of SCK values in girls ($n = 75$) and women ($n = 200$)

Range of SCK values (IU/l)	Girls (<15 years)		Women (>15 years)	
	No.	%	No.	%
11-30	27	36	26	13
31-50	30	40	112	56
51-70	12	16	47	23.5
71-90	6	8	6	3
91-110	0	0	3	1.5
111-130	0	0	4	2
131-150	0	0	1	0.5
151-170	0	0	1	0.5
>170	0	0	0	0

Thus, the determination of carrier status should preferably be carried out after infancy but certainly during childhood, since it would seem likely that during this period the test is most informative. Ideally, in calculating the likelihood of heterozygosity, the distribution of SCK levels in known carriers during childhood should also be taken into account (Emery, 1976). However, even with prospective studies, this may be difficult to determine because until an accurate prenatal test for Duchenne muscular dystrophy becomes available, potential carriers are unlikely to risk having any affected sons which might confirm their carrier status.

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