Appendix I

Acetone Production in Children

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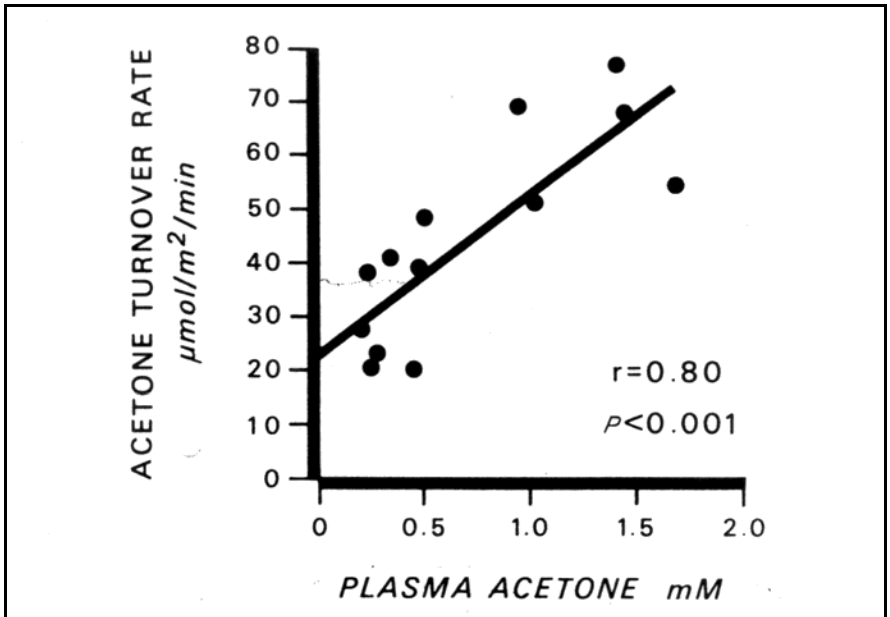
Acetone production in children was derived from the relationship of blood acetone levels and acetone "turnover rates" as reported by Reichard et al (1979) and Owen et al (1982). Because the Reichard et al studies and those by Owen et al (1982) showed a direct linear relationship between plasma acetone concentrations (when less than 5 mM) and rates of endogenous production, it is also believed to be an appropriate estimator of children's daily endogenous production. The range of acetone serum levels for normal children were reported by Peden (1964) and were used to estimate acetone turnover rates in children. Peden summarized the acetone serum ketone levels in normal infants and children as follows:

Table 1
Acetone Serum Ketone Levels in Normal Infants and Children

	Age							
	9 to 24 hrs	2 to 5 days	2 wks to 6 mos	6 mos to 1 yr	1 to 3 yrs	4 to 6 yrs	7 to 9 yrs	10 to 15 yrs
Number of patients	14	23	29	23	50	63	47	47
Mean (mg %)	1.2	2.7	1.3	1.2	1.2	1.5	1.5	0.9
Range (mg %)	0-3.0	0-14.0	0-3.0	0-3.0	0-3.7	0-3.7	0-3.5	0-3.4
Range (mM)	0-0.51	0-2.38	0-0.51	0-0.51	0.63	0-0.63	0-0.6	0-0.58

The acetone levels in children presented above were converted to acetone turnover rates using Figure 3 from Reichard et al (1979), as shown on the figure below.



Relationship between plasma acetone concentration and turnover rate. A significant correlation between concentration and turnover rate ($r = 0.80$, $P < 0.001$) was obtained.

Reichard et al. did not publish the regression equation relating turnover rates to plasma concentration; however, a significant correlation was reported ($r = 0.80$, $p<0.001$). Therefore, the values were estimated based on visual inspection of Figure 3. The age ranges presented correspond to those for which Peden reported serum acetone levels. Both the mean and maximum acetone production rates have been calculated from the average and maximum values presented in Peden (1964). A minimum has not been presented, as the minimum serum acetone value was reported as zero. It is not likely that this value is actually zero; rather an unknown analytical detection limit. The children's plasma concentration and acetone turnover rates are shown on Table 2 below.

Table 2
Acetone Turnover Rates for Children Derived from Figure 3 of Reichard et al, 1979

Age Group	Plasma Concentration[a] (mg/L)		Acetone Turnover Rate[c] (μmol/m^2/min)	
	Mean	Maximum	Mean	Maximum
0 to 12 Months	16	140	28	89
1 to 5 Years	14	37	27	38
6 to 13 Years	13	37	26	38
14 to 18 Years	9	34	24	37

a – Peden, 1964. Table 4.
b – Estimated from Figure 3 of Reichard *et al*, 1979.

Daily endogenous acetone production for children was calculated using the equation below and the information contained in Tables 2 and 3.

$$Acetone \cdot production(mg/kg/day) = \frac{TO \times SA \times MW \times 60\,\text{min}/hr \times 24hr/day}{BW \times 1000\mu g/mg}$$

where: TO = Acetone Turnover rate (endogenous dose) (μmol/lmin-m^2);
SA = surface area (m^2);
MW = molecular weight of acetone (58.08 μg/μmol); and
BW = body weight (kg).

Table 3
Physical Parameters for Children

Age Group	Body Weight[a] (kg)	Surface Area[a] (m^2)
0 to 12 Months	7.2	0.37
1 to 5 Years	15.4	0.65
6 to 13 Years	35.0	1.14
14 to 18 Years	61.0	1.65

a – Children's Exposure Factors Handbook (USEPA, 2002).

Based on the estimated turnover rates, the calculated children's daily average endogenous acetone production, ranged from 121 mg/kg-d for infants less than 1 year to

55 mg/kg-d for teenagers. The maximum daily production ranged from 387 mg/kg-d for infants to 83 mg/kg-d for teenagers. All of the results can be seen on Table 4.

Table 4
Results of Acetone Production Calculation in Children

Age Group	Acetone Production (mg/kg/day)	
	Mean	Maximum
0 to 12 Months	121	387
1 to 5 Years	94	135
6 to 13 Years	72	104
14 to 18 Years	55	83