

exceeded 10%. With an inspiratory time of 0.2 seconds, a mean fall of 22% was seen in tidal volume with a greater than 10% drop in nine of 13 studies.

Discussion

The results show that tidal volume is well maintained with inspiratory times down to and including 0.4 seconds. With an inspiratory time of 0.3 seconds, there is a small decrease in tidal volume but reduction of inspiratory time to 0.2 seconds is associated with a 22% fall in tidal volume. We ensured in the studies presented here that expiratory time was always at least equal to inspiratory time. At the highest ventilator rates, however, the short expiratory time may have contributed to the loss of tidal volume. An inspiratory time of 0.4 seconds or less, used in conjunction with a rapid ventilator rate, will produce a minute volume which is apparently more than satisfactory for the infant's requirement. Dead space, however, remains constant during ven-

tilation and any reduction in tidal volume cannot always be compensated for by an increased ventilator rate.

The relation between fast ventilator rates and blood gas status is a complex one and does not depend entirely on tidal volume.² It would seem appropriate to recommend that care be taken when using intermittent positive pressure ventilation with inspiratory times less than 0.3 seconds.

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Reference ranges for serum α_1 antitrypsin

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SUMMARY Reference ranges for serum α_1 antitrypsin at various ages have been constructed using specific protein calibration material (SPS-01). Median values and 5th-95th centile ranges for α_1 antitrypsin in cord blood are equivalent to those of the adult. The median concentration falls during the first 6 months of age to rise again to adult values by 12 months. Concentrations in early school age are higher than in normal adults.

The estimation of serum α_1 antitrypsin is of value in the assessment of liver disease in childhood¹ as well as in chronic obstructive airway disease.² The comparison of results between centres has been hampered to an extent by the lack of correlation between various available standards of calibrants. This problem has not been alleviated to any great degree by the availability of an international refer-

ence preparation because of the general reluctance to change from familiar mass concentrations to the more anonymous units. This variability of calibrants was a major factor in the desire to produce a national working calibrant for specific protein assays within UK laboratories.³

This report details reference ranges for serum α_1 antitrypsin for various ages throughout childhood in relation to the specific protein calibration material (SPS-01). Because of the known influence of the PI genetic system on serum concentrations of α_1 antitrypsin⁴ all samples have been subjected to PI phenotype evaluation.

Materials and methods

Blood samples were obtained from 590 normal healthy children between the ages of 6 months and 15 years as part of a study of IgE values in the offspring of asthmatic parents. Consent for vene-

Table Reference ranges for serum α_1 antitrypsin
(All values in g/l with SPS-01 as calibrant)

Age	No	Centiles				
		2.5th	5th	50th	95th	97.5th
Birth	331	0.8	0.9	1.6	2.2	2.4
6-8 months	87	0.7	0.8	1.2	1.8	2.0
9-10 months	107	0.9	1.0	1.4	2.0	2.2
1-2 years	107	1.0	1.1	1.5	2.0	2.2
3-5 years	113	1.0	1.1	1.5	2.2	2.3
6-10 years	70	1.2	1.4	1.7	2.3	2.4
11-15 years	106	1.1	1.2	1.6	2.0	2.2
Adult		0.9	1.1	1.6	2.1	2.3

puncture was given by the parents and the study was approved by the ethical committee. An additional 331 cord blood samples were obtained after delivery of normal term infants. The blood samples were allowed to clot at ambient temperature and the separated serum was stored at -30°C until analysis. Residual sera remaining after completion of the primary study were assayed for α_1 antitrypsin by single radial immunodiffusion using antiserum obtained from Atlantic Antibodies, USA, and SPS-01 as calibrant.

PI phenotypes were characterised by isoelectric focussing in polyacrylamide gels at pH 4-5.

Results

The reference ranges for serum α_1 antitrypsin at various ages during childhood from birth to 15 years are shown in the Table.

Cord blood concentrations equate with the normal adult value.⁵ There is a slight but significant fall during the first six months of life followed by a steady rise to essentially adult levels by 1 year of age. Children of school age (5-15 years) show values slightly higher than the adult norm with a return to adult values after the age of 15 years.

The distribution of PI phenotypes found in this population sample did not differ significantly from that expected in a UK population.⁴ The small numbers of the non-MM phenotypes in any one age group makes formal presentation of mean values and centiles inappropriate. Eighty per cent of the PI*MS and all of the PI*MZ, FZ, and SS showed values below the age related median and the PI*SZ below the age related 2.5th centile value.

Discussion

Alpha₁ antitrypsin values in various commercial calibrants have been shown to vary widely in their antigenic potency. The introduction of SPS-01 as a

national working calibrant for specific protein assays³ has caused a major revision of adult reference ranges for α_1 antitrypsin.⁵ Because of the considerable clinical interest in α_1 antitrypsin in childhood it was also necessary to construct reference ranges for children of various ages in terms of this new currency.

The reported ranges confirm the modest fall in serum concentrations seen with many serum proteins during the first six months of life. They also show a slight increase above the adult norms during early school age consistent with the acute phase nature of this protein. This increase, together with the slightly skewed distribution in the 9 month to 10 year cohorts, reflects the high incidence of minor infective conditions at this age.

Serum concentrations of α_1 antitrypsin are influenced by the genetic status of the subject. Those who are heterozygous for PI*S, PI*P, PI*Mmalton, PI*Mduarte, PI*Z, or PI*null show serum values below the normal median, and the homozygous or combination heterozygous subjects will show concentrations well below the 5th centile. These values will increase in the acute phase so that most heterozygotes exceed the population median.

In general terms, however, for children over 1 year of age a serum α_1 antitrypsin concentration of less than 1.4 g/l, the 20th centile for the normal adult population, should be considered for formal investigation of the PI genetic status. For children of less than 12 months of age, the relevant discriminant value should be 1.1 g/l. These recommended values will allow detection of all the deficiency states of clinical importance and most of the PI*MS and PI*MZ heterozygotes.

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