

# Serum Immunoglobulin G Levels in Small-for-Dates Newborn Babies

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**Papadatos, C., Papaevangelou, G. J., Alexiou, D., and Mendris, J. (1970).** *Archives of Disease in Childhood*, **45**, 570. **Serum immunoglobulin G levels in small-for-dates newborn babies.** Immunoglobulin G levels have been studied in 47 small-for-dates (SFD) and 197 singleton babies of normal birthweight for their gestational age.

The IgG values in the SFD babies were below those expected for the normal newborn of an equivalent gestational age, but above those of the normally growing baby of equivalent birthweight. There is a statistically significant difference in the slopes of the regression lines in the two groups whether IgG is plotted against birthweight or gestational age.

Under normal conditions the human fetus produces immunoglobulins in minute amounts (Stiehm and Fudenberg, 1966; Johansson and Berg, 1967). However, levels of IgG at birth approach and even surpass adult serum concentrations; nearly all this IgG in the newborn is of maternal origin (Bridges *et al.*, 1959).

Low concentrations of IgG have been reported in obviously premature infants (Hobbs and Davis, 1967; Papadatos *et al.*, 1969). With advancing gestational age these levels tend to rise and a linear relation has been shown to exist between IgG concentration and gestational age (Yeung and Hobbs, 1968; Papadatos *et al.*, 1969).

While findings in post-mature babies are contradictory (Yeung and Hobbs, 1968; Papadatos *et al.*, 1969; Ackerman, Taylor, and O'Loughlin, 1969), results in small-for-dates (SFD) newborn babies, though based on a small number of observations (Yeung and Hobbs, 1968), show that IgG levels remain below the corresponding mean values for their gestational age.

In this report we provide additional information on immunoglobulin G in the SFD baby.

## Material and Methods

Our material consisted of 197 normal singleton newborns, with a gestational age of 24 to 48 weeks, and 47

SFD babies with a gestational age of 36 to 44 weeks, born at the Alexandra Maternity Hospital from January 1968 to July 1969. Newborns with congenital malformations were excluded from the study. Their gestational age was estimated from the first day of the mother's last menstrual period, and was considered accurate if the mother stated that she was sure of her dates. An attempt was made to correlate the gestational age to neurological examination. Specific tests that have been described by different authors (Brett, 1965; Farr, 1968; Koenigsberger, 1966; Robinson, 1966; Saint-Anne-Dargassies, 1955) as well as morphological criteria described by Usher, McLean, and Scott (1966) and Farr *et al.* (1966) have been used in all our babies.

The SFD group had birthweights 2 SD or more below the mean for their gestational age according to the developmental curves of the British Perinatal Mortality Survey (Butler and Alberman, 1969).

The umbilical cords were clamped immediately—within 10 seconds after delivery. Placental studies were not done. Blood samples were obtained by venepuncture under aseptic conditions within the first 24 hours after birth, and the serum was maintained after separation at  $-20^{\circ}\text{C}$ . The determination of all serum IgG levels was done by using the quantitative gel diffusion technique with antibody incorporated into the agar in appropriate dilution as described by Mancini, Carbonara, and Heremans (1965).

## Results

As previously shown, a linear relation exists between serum log IgG (mg./100 ml.) levels and gestational age from the 24th up to the 42nd week

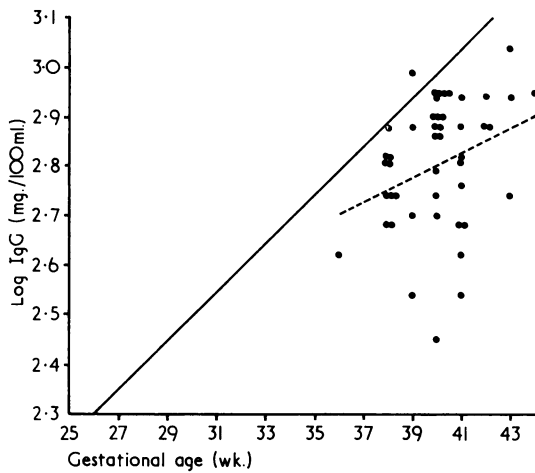


FIG. 1.—Correlation of log serum IgG levels to gestational age (weeks) in normal newborns (—) and small-for-dates (-----) babies. The circles (•) represent the individual values of IgG in the SFD babies.

(Yeung and Hobbs, 1968; Papadatos *et al.*, 1969). Complete data, including 95% confidence limits on the 197 normal newborns have already been published (Papadatos *et al.*, 1969). The best fitting regression line for mean IgG values at each gestational age is shown in Fig. 1. All except one of the 47 SFD babies had IgG levels below the mean for their gestational age.

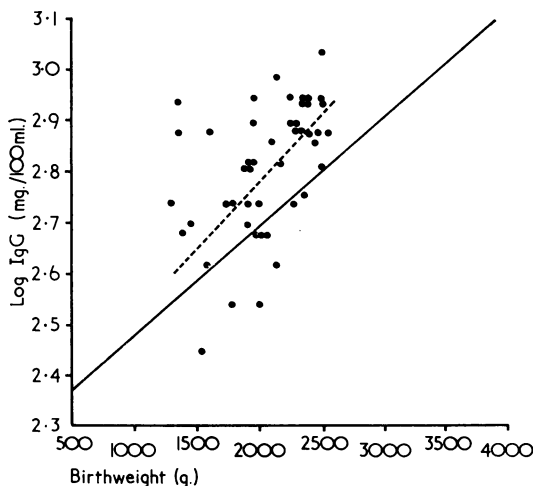


FIG. 2.—Correlation of log IgG level to birthweight (g.) in normal newborns (—) and small-for-dates (-----) babies. The circles (•) represent the individual values of IgG in SFD babies.

In the study of the relation between length of pregnancy and IgG concentration, gestational age may be difficult to estimate in some individual cases. We approached the problem by trying to correlate the date of the first day of the last menstrual period of the mother with the neurological evaluation of the newborn as described by different authors (Brett, 1965; Farr, 1968; Robinson, 1966; Koenigsberger, 1966; Saint-Anne-Dargassies, 1955) and the morphological criteria described by Usher *et al.* (1966) and Farr *et al.* (1966). We found the babies' responses very variable, and did not feel confident in the use of any of the proposed methods. We therefore relied on maternal information.

Further statistical analysis of our results shows that the log IgG levels in the SFD babies are directly correlated to their gestational age. The correlation coefficient is found to be 0.31 (0.01 < p < 0.05). The best fitting regression line of Y on X is shown in Fig. 1 (dashed line) and its equation is:  $\log \text{IgG} = 1.8043 + 0.0250 \times \text{gestation in weeks}$ .

Though the number of SFD babies studied is small, the analysis of variance appears to justify the assumption that the relation is linear ( $F = 0.99$ ,  $p < 0.05$ ). The comparison of the two regression lines shows that their slopes differ significantly ( $t = 9.45$ ,  $p < 0.001$ ).

Fig. 2 shows the correlation between log IgG levels and birthweight. We used logarithmic rather than arithmetic values of IgG levels because the log values gave a better fit to a straight line relation. In the 197 babies of normal birthweight for their gestational age, the correlation coefficient was 0.78 ( $p < 0.01$ ) and the equation for the regression line through the means was:

$$\log \text{IgG} = 0.000215 \times \text{birthweight in g.} + 2.26478.$$

At a given birthweight the SFD babies had slightly higher IgG levels than the babies of normal birthweight for their gestation (Fig. 2). Only 9 of them (19%) had IgG values below the corresponding mean for normal newborns of equivalent birthweight. Our results on the SFD babies also show that there is a smaller ( $r = 0.62$ ) but significant ( $p < 0.01$ ) correlation. The regression line (dashed) is shown in Fig. 2. The slopes of the two regression lines differ significantly ( $t = 3.9$ ;  $p < 0.05$ ).

### Discussion

The few previous studies on IgG levels in SFD babies have shown values below the mean for the corresponding gestational age (Yeung and Hobbs, 1968; Papadatos *et al.*, 1969). It should be stressed, however, that SFD babies do not represent a homogeneous population (Wigglesworth, 1967), for

limitation of fetal growth support, loosely considered as 'placental' insufficiency, has not been fully elucidated.

In the present study we compared IgG levels in two groups of babies. The first included 197 newborns with a birthweight within the mean  $\pm 2$  SD for their gestational age, while in the second group we studied 47 SFD babies. A dependence of IgG levels on gestational age was found in both groups. With one exception SFD babies had levels below the mean for their gestational age. The regression coefficient in the two groups measures the average amount by which IgG increases for each week's increase in gestational age. The statistically significant difference between the two regression coefficients denotes that this increase is slower in SFD newborns, which is in good agreement with the general pattern of growth in these babies.

The IgG level of the newborn is not the result of a passive but rather of an active placental transport from mother to fetus. It is reasonable to suppose that the relatively slow increase of IgG in the SFD fetus, like the slow fetal growth, indicates inadequate placental function.

Our results show that for the normally growing babies there is also a significant correlation between birthweight and IgG. In the SFD newborns this correlation is smaller but nevertheless significant. In the SFD babies the average increase in IgG is significantly greater than in babies with normal growth, and therefore SFD babies have greater amounts of IgG than normally growing newborns with similar birthweights.

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