Dr. N. Gilboa comments:

Thank you for allowing me to comment on the letter from Dr. Wharton. We performed the study of CPK levels in randomly selected normal newborns for the following reasons. (1) The increased interest in the subject due to the possibility of using CPK in newborn screening for Duchenne muscular dystrophy (DMD) (Zellweger and Antonik, 1975). (2) Although several previous investigations dealt with CPK in normal newborns, only a few, as noted by Wharton et al. (1971), have given sufficient clinical correlation. (3) The inconclusiveness of the findings regarding the effect of the perinatal factors on the CPK activity (Ballario and Pavesio, 1969; Bodensteiner and Zellweger, 1971; Rudolph and Gross, 1966). (4) Lack of consistent data regarding the difference of CPK activity in simultaneously obtained cord, venous, and capillary blood in newborns (Bodensteiner and Zellweger, 1970). (5) The large number of laboratory techniques with widely varying degrees of reliability used in the previous works. This poses a significant problem in standardization of CPK. Our study was preformed using the Rosalki (1967) method which is one of the most widely used and most reliable methods (Dubowitz, 1976a).

With the exception of 2 cases reported by Heyck et al. (1966) and Dubowitz (1976b), the CPK level in newborns affected or carriers of DMD is unknown. Some of the normal newborns have CPK levels up to 10 times the upper limit of normal (Gilboa and Swanson, 1976). These levels are not significantly different from the CPK level found by Dubowitz (1976b) in the affected male on the third day of life. We also showed that while the mean CPK level was still raised after 4 days of life, it was well within the normal range in all infants examined at age 6 to 10 weeks. Thus, unless proved to the contrary, it is very possible that the CPK of an affected male, and particularly of a carrier, may be lost in the upper limits of normal if obtained within the first few days of life.

I agree with Dr. Wharton that a prospective study of CPK in newborns from families with a known history of DMD is very important and should be performed to investigation of a newborn screening programme. However, if such a programme is initiated the study of CPK should be delayed for a few weeks, and certainly for at least one week after birth, in order to minimize the risk of false-positive results.

Finally, I would like to note that according to the Rosalki method (Rosalki, 1967) used in our study, the determination of the CPK was performed in serum and not in plasma, as referred to by Dr. Wharton.

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REFERENCES


Rapid assessment of gestational age at birth

Sir,

We read with interest the article of Parkin, Hey, and Clowes (1976) on this subject based on four superficial criteria, in which they obtained 95% confidence limits of ± 15 days on a curvilinear regression. Since a comprehensive computer analysis of our original data (Dubowitz, Dubowitz, and Goldberg, 1970) was unable to yield any smaller combination of criteria approaching the reliability of the total group (L. M. S. Dubowitz, and R. A. Dixon, unpublished observations, 1973), their results were somewhat surprising to us. We thought that one possible reason for the discrepancy might have been a difference in our respective samples. Theirs had a fairly normal distribution with 36 of their 314 term infants (11%) being small-for-dates, whereas in our total series of 166 infants 49 were small-for-dates (about 30%). Moreover, there were only 46 preterm infants in their total series of 392 (11%) whereas in ours there were 53 (about 30%).

We have accordingly reanalysed our original data for the four criteria selected by Parkin et al. with particular reference to the error of prediction in the small-for-dates and appropriate-for-dates groups. On a linear regres-
sion our original 95% confidence limits for the whole sample (using all 21 criteria) was ±14 days. When separated now into appropriate-for-dates and small-for-dates subgroups, the corresponding 95% confidence limits were ±14·3 and ±13 days respectively. With Parkin et al.'s criteria, the 95% confidence limits for our whole sample was ±21 days (on a curvilinear regression), for the appropriate-for-dates infants ±18·5 days, and for the small-for-dates infants 23·8 days (with a linear regression fitting the data better).

One other possible difference for these discrepancies may be that all Parkin's babies were examined between 12 and 36 hours whereas our data were collected within the first 5 days after birth. We think the skin colour is likely to be most affected by this difference in time of examination. We therefore did a further analysis on our data substituting planter skin creases (which also had good predictive value in Parkin's analysis) for skin colour, with the following results: 95% confidence limits for the whole sample ±18 days: for appropriate-for-dates infants ±16·6 days, and for small-for-dates infants 21 days. A curvilinear regression best fitted the data for all three of these groups.

As originally pointed out by Farr and Mitchell (1967), the superficial criteria which they recommended (which are the ones on which Parkin et al., and our assessments were based) are influenced by birthweight, giving a lower score in small-for-dates infants. We obtained similar results but have also observed that neurological criteria tended to be influenced in the other direction in small-for-dates infants thus giving better overall correlation with a combination of neurological and superficial criteria (Dubowitz and Dubowitz, 1977).

This suggests that Parkin's selected criteria are satisfactory for term infants of appropriate weight, but give a poorer correlation for small-for-dates infants, and might also be less reliable for preterm infants.

Once the accuracy of a method drops to ±21 days it is approaching the relative unreliability of using criteria such as birthweight or x-ray of the epiphyses.

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Dr. J. M. Parkin comments:

To suggest that a method of assessing gestational age is of practical value only in term and infants of appropriate weight is, in effect, to suggest that the technique is useless. We therefore are pleased to have the opportunity of replying to the letter of L. M. S. Dubowitz and her colleagues, and agree that there is a need to explain our differences.

The widening of the 95% confidence limits in the reanalyses of their original data to 21 days using our four external characteristics or to 18 days when skin colour is replaced by planter skin creases, may have occurred by chance. It is well known that the accuracy of a predictor is usually not as good in a new sample as in the original (Gardner, 1972). However, the findings in the two groups of babies studied by us at an interval of 2 years were very similar. This fact gives us confidence in the robustness of our conclusions and suggests that there is some other explanation for the differences in the results of the two studies.

We agree that the difference in ages of the babies at examination may be relevant; the assessment of skin colour may be affected by postnatal age, though we found no evidence of this during the first 48 hours of life. The fact that the earlier assessment appears to increase the accuracy of any gestational assessment is, of course, reassuring.

We deliberately avoided any assumption about there being any mathematical relation between gestational age and total score, and simply recorded the range of gestational age for each score. We lack sufficient data to analyse the accuracy of the score in very small babies, but, contrary to the assertion in the letter of Dubowitz et al., the predicted accuracy of the score did not decrease with decreasing gestational age in babies of more than 30 weeks' gestation. In our data the accuracy of the score was only marginally affected by weight for gestational age at birth. Breast bud and ear cartilage development are both slightly retarded in babies who are light-for-dates at birth, but, nevertheless, the total score underestimated gestational age by an average of only 1·5 days in a group of babies of birthweight below the 10th centile and overestimated gestational age by 1·1 days in babies with birthweight above the 90th centile (Parkin, 1970).

We believe that the avoidance of any assumption regarding an underlying mathematical relation between gestational age and total score is the most important reason for the differences high-lighted by Dr. Dubowitz. We see no evidence that these differences are due to differences in the composition of the population studied and we remain confident that our method is valid in babies of short gestation and in babies of abnormal weight for gestational age at birth.

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Rapid assessment of gestational age at birth.

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Updated information and services can be found at:
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