STUDIES ON MATURITY IN NEWBORN INFANTS

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This summary is based on the following six papers, which will be referred to in the text by their Roman numerals:

- I. Finnström, O.: Studies on maturity. I. Birth weight, crown-heel length, head circumference and skull diameters in relation to gestational age. Acta Paediat Scand, in press.
- II. Finnström, O.: Studies on maturity in newborn infants. II. External characteristics. Acta Paediat Scand, in press.
- III. Finnström, O.: Studies on maturity in newborn infants. III. Neurological examination. Neuropädiatrie, in press.
- IV. Finnström, O.: Studies on maturity in newborn infants. IV. Postnatal radiological examination of epiphyseal centers. Neuropädiatrie, in press.
- V. Blom, S. and Finnström, O.: Studies on maturity in newborn infants. V. Motor conduction velocity. Neuropädiatrie, in press.
- VI. Finnström, O.: Studies on maturity in newborn infants. VI. Comparison between different methods for maturity estimation. Acta Paediat Scand, in press.

Introduction

During recent years it has become evident that the estimation of maturity and thus of the gestational age of newborn infants is of considerable value. It is of practical importance for the correct management of the individual infant, since clinical problems depend not only on the size but also on the gestational age of an infant (c. f. the IRDS syndrome in pre-term infants and hypoglycemia in small-for-gestational-age infants). Furthermore, materials on which neonatal physiological studies are to be carried out must be controlled with respect to gestational age (Casaer and Akiyama 1970). Thirdly, knowledge of true gestational age is important in developmental testing of pre-term infants (Parmelee and Schulte 1970).

Birth weight is an unreliable index of gestational age (Gruenwald 1963 and others). This has led to the search for methods for maturity estimation in which the investigated parameter is better correlated to gestational age than is birth weight.

Important studies of neurological maturation in newborn infants have been performed by Saint-Anne Dargassies (1966), who described neurological maturation in infants from 28 weeks gestational age up to term. Other methods described for maturity studies are e. g. EEG sleep studies (Dreyfus-Brisac 1966), measurement of fetal hemoglobin (Brody 1960), scoring of external characteristics (Farr et al. 1966) and measurement of motor conduction velocity (Schulte et al. 1968, Blom and Finnström 1968 and others). For a review of different methods for maturity estimation, see Casaer and Akiyama (1970).

For various reasons to be discussed, it is difficult to evaluate the results of most of these studies. Certainly there has been a tendency in much work to overestimate the precision of estimating gestational age.

The author therefore believed it would be valuable to further study and compare some methods and combinations of methods for maturity assessment in newborn infants.

The aims of the present study

1. To investigate and compare the value of five different methods as well as combinations of these methods in the estimation of gestational age in newborn infants.
2. To study these methods in small-for-gestational-age infants and in certain perinatal complications.
3. To give prediction models for practical use in the newborn period.
4. To compare the results obtained with those in the literature, and to discuss the evaluation of methods for maturity assessment.

Materials

The investigated material consisted of 174 newborn infants of various birth weights and gestational ages. Only infants whose mothers gave a reliable menstrual history were included in the study. Details about the material and its selection are given in paper I. Not all these infants could be investigated without the author's knowing their gestational age. A second material of 28 infants (see II or III) was investigated in order to test the prediction models constructed from the results obtained from the examination of the first 174 infants. The age of these infants was unknown to the author at the time of examination.

Methods

The methods used in the studies were:

measurement of birth weight, crown-heel length, head circumference and skull diameters (I).

scoring of external characteristics (II).

scoring of neurological tests (III).

radiological examination of epiphyseal centers (IV).

measurement of motor conduction velocity (V).

Details are given in the respective papers.

Statistical methods are described in paper I.

Abbreviations:

SGA: small-for-gestational-age.

AGA: appropriate-for-gestational-age.

MCV: motor conduction velocity.

LMP: last menstrual period.

Results and conclusions

I. Birth weight, crown-heel length, head circumference and skull diameters in relation to gestational age

The five measurements were correlated to the gestational age at birth in linear regression analysis. Head circumference showed the highest degree of correlation to gestational age. Birth weight and crown-heel length had the same degree of correlation to gestational age. The two skull diameters showed the lowest degree of correlation to gestational age. Measurement of head circumference is of some value for estimating the gestational age of newborn infants, especially in combination with other methods (see VI), giving a better estimation of gestational age than birth weight.

In analysing all five measurements together in stepwise multiple regression analysis with gestational age as dependent variable, only head circumference entered the multiple regression at a significant ($p < 0.05$) F-value. Thus, using other anthropometric measurements in addition to head circumference did not improve the estimation of gestational age.

In small-for-gestational-age infants, defined as infants with birth weight below - 2 S. D. in the relation between birth weight and gestational age according to Swedish standard curves (Engström and Sterky 1966, Sterky 1970), crown-heel length and head circumference were not significantly greater than in pre-term infants of the same mean birth weight.

II. External characteristics

A total of 12 external characteristics were investigated. Each characteristic was scored according to 2-4 different response alternatives, supposed to represent different degrees of maturation. The separate characteristics were individually correlated to gestational age. Nine of them showed a good to fairly good correlation to age. Eight of these (excluding one that showed differences between boys and girls at the same gestational age) were summed to a total maturity score as earlier suggested by Farr et al. (1966). This maturity score was correlated to gestational age at birth in linear regression analysis. The formula for estimating gestational age from this score is given. It was shown that the maturity score estimated gestational age considerably better than did birth weight, as was earlier shown by Farr et al. (1966). This method is recommended for routine use during the first postnatal week. It is simple to perform and the reproducibility is probably sufficiently high. The method is not suitable after the first week of life.

Small-for-gestational-age infants, as defined above, had lower mean scores than AGA infants of the same mean age but higher scores than AGA pre-term infants of the same mean birth weight. Infants with external signs of dysmaturity probably have lower scores than expected for their gestational age.

It is pointed out that maturity estimations based on external characteristics must be based on a number of characteristics, since for individual characteristics there was a smooth change in distribution from low to high scores with advancing gestational age.

The prediction model given was tested with the second material and was shown to be useful, giving a correct estimation of gestational age to within 3 weeks for 26 of 28 infants.

III. Neurological tests

A total of 28 neurological tests were investigated under well-defined conditions, usually 4 to 5 days after birth and in a certain behavioural state as defined by Prechtl and Beintema (1964). These tests were mainly based on work by Saint-Anne Dargassies (1966). Each test was scored according to 2-4 response alternatives, supposed to represent different degrees of maturation. The separate tests were individually correlated to gestational age. 10 of them that showed a good to fairly good correlation to gestational age were summed to a total maturity score. This maturity score was correlated to gestational age at birth in linear regression analysis. The formula for estimating gestational age from this score is given. This total score estimated gestational age considerably better than did birth weight. Prediction models using more tests than the 10 gave a poorer estimation of gestational age. Repeated examinations on some of the infants indicated that this type of maturity estimation can also be used later than during the first postnatal week in pre-term infants. The performance and evaluation of the neurological tests requires a certain amount of experience.

Small-for-gestational-age infants had lower mean scores than AGA infants of the same mean age but higher scores than AGA pre-term infants of the same mean birth weight.

Infants who had had transitory fetal bradycardia, transitory post-natal asphyxia, hyperbilirubinaemia, jitteriness (hyperexcitability) or lethargy seemed to have scores appropriate for their gestational age.

For the individual tests, there was a smooth change in distribution from low to high scores with advancing gestational age. This indicates

that an evaluation of maturity cannot be based on only one or a few neurological tests. It was found that both tests based on "tone" (French concept, see André-Thomas et al. 1960) and on reflexes are of value in maturity estimation.

The prediction model given was tested with the second material and was shown to be useful, giving a correct estimation of gestational age to within 3 weeks for all infants but one.

IV. Postnatal radiological examination of epiphyseal centers

The presence and size of epiphyseal centers in the distal femur, proximal tibia, calcaneus and talus were studied by postnatal radiological examination. There is great variation in the time at which the centers can be visualized radiologically.

The size of the centers (largest diameter) was correlated to gestational age at birth in linear regression analysis. Even when the size of the centers, and not only their presence, was considered, the method gave no better estimation of gestational age than did birth weight.

The centers were analysed together in stepwise multiple regression analysis. Two centers entered the multiple regression at significant ($p < 0.05$) F-values. The improvement in the estimation of gestational age was small.

Small-for-gestational-age infants had delayed ossification of epiphyseal centers. The sizes of the centers in the SGA infants did not differ significantly from those in pre-term AGA infants of the same mean birth weight.

Thus, radiological examination of epiphyseal centers is of limited value both in pre- and postnatal assessment of maturity. This opinion is at variance with the views of some earlier authors (Hartley 1957, Russell 1969 and others).

V. Motor conduction velocity

Motor conduction velocity was measured in the ulnar nerve and, in a little more than half of the infants, in the peroneal nerve as well.

The mean values and S.D. 's for different age groups are in accord with previous studies (Blom and Finnström 1968, Schulte et al. 1968 and others).

The range in results at a given gestational age was fairly wide.

MCV was correlated to gestational age at birth in linear regression analysis. MCV is of limited value in estimating the gestational age of individual infants. This should be pointed out, since the value of MCV in this context has been overestimated earlier (Dubowitz et al. 1968).

MCV seems to be appropriate for the gestational age in SGA infants, as earlier pointed out (Schulte et al. 1968). It also seems to be appropriate for the gestational age in infants with signs of fetal bradycardia, postnatal asphyxia, hyperbilirubinaemia, jitteriness (hyperexcitability) and lethargy. Schulte et al. (1969) also found the MCV to be unaffected in some perinatal complications.

Therefore, MCV is a suitable method to use when groups of infants are to be compared and controlled with respect to gestational age, e.g. for physiological studies.

Pre-term infants reaching the time for expected delivery outside the uterus seem to have mean motor conduction velocities comparable to those of full-term newborn infants.

VI. Comparison between different methods for maturity estimation

In addition to prediction models based on single methods, models based on combinations of methods are given in this paper. The models were compared by comparing the calculated 95% confidence limits for estimating gestational age at mean values of the examined parameter or combinations of parameters. It was possible to do this, since all examinations and calculations were done on the same material of newborn infants.

The best single methods tested by the author were scoring of external characteristics and neurological tests. For routine work during the first postnatal week, the former is the more suitable, since it is not dependent on the condition of the infant, the time after birth or the time from the last meal. The method is probably also easier for the inexperienced doctor to learn.

The use of a combination of methods substantially increases the precision of estimating gestational age. Useful combinations are two or all of the following: external characteristics, neurological tests and head circumference.

The prediction models were tested with the second material of 28 infants not included in the construction of the models. The results indicate that it is possible to obtain a precision in estimating gestational age of $\pm 2\frac{1}{2}$ weeks for about 95% of the infants (27 of 28) using a combination of methods. It is probably not possible to obtain greater precision with methods used to day, although Saint-Anne Dargassies (1966), Dubowitz et al. (1968), Dubowitz et al. (1970) and others claim to be able to estimate gestational age to within 2 weeks or less.

The factors limiting the precision of estimating gestational age have rarely been discussed and evaluated. These factors are the time variation between LMP and conception, the degree of reproducibility of the methods used and the biological variation in maturity among infants of the same gestational age. It is important to bear these limiting factors in mind when discussing the precision of methods for maturity estimation.

Various difficulties in evaluating the results of maturity studies are discussed with reference to the pertinent literature. It is pointed out that new methods must be compared with a simple and precise reference method, e.g. the estimation of gestational age from birth weight. Comparison between different methods applied to different materials of newborn infants must be made with caution and the commonly used 95% confidence limits are not suitable for these comparisons. This depends

on the fact that the breadth of the confidence limits is determined not only by the degree of correlation between gestational age and the investigated parameter, but also by the age distribution within the sample, the proportion of SGA infants and other factors.

Summary

1. Studies on maturity, with a view to estimate gestational age, have been performed on 174 newborn infants of various gestational ages. Only infants whose mothers gave a reliable menstrual history were included in the study.
2. The methods used were based on anthropometric measurements, scoring of external characteristics, scoring of neurological tests, radiological examination of epiphyseal centers and the measurement of motor conduction velocity.
3. Prediction models for estimating gestational age from single methods or combinations of methods are given.
4. The best single methods were scoring of external characteristics and neurological tests, the former being simpler for routine work.
5. The use of combinations of methods increases the precision of estimating gestational age. Suitable combinations are two or all of the following: external characteristics, neurological tests and head circumference.
6. The prediction models constructed were tested with a second material of 28 infants. The results of this study indicate that it is possible to obtain a precision in estimating gestational age of $\pm 2\frac{1}{2}$ weeks, using a combination of methods.
7. Further increase in precision is probably not possible with current methods. There are factors that limit the precision of all methods used for maturity studies, i. e. the variation in time between the last menstrual period and conception, the degree of reproducibility of the methods, and the biological variation among infants of the same gestational age.

8. The difficulty of evaluating results from other maturity studies is pointed out and discussed. The importance of comparing a new method with a simple and precise reference method applied to the same material is stressed.

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