Discussion and Final Conclusions

The early days of postnatal life in humans and animals have been extensively studied over the past few years by physiologists, paediatricians, neurologists and others. Whether the approach has been a biochemical or a physiological one, the enormous importance of the changes which take place during the first ten days of life have been widely recognized.

Much attention has been paid to the detection of early regulating mechanisms and their specific nature. Data on body temperature, circulation, respiration, biochemical levels such as blood sugar, minerals, blood gases etc., have been collected and analysed. It has been found that there is much variation in the biochemical and physiological values at this time but that this variability decreases during the first few days of life, and it may be concluded that this is due to the development of regulating mechanisms. This phenomenon is known as the postnatal adaptation of the infant to extra-uterine life.

The central nervous system clearly plays an important part in this adaptation process. Consequently the impairment of the nervous system would lead to delay and difficulty in the organization of homeostatic mechanisms. On the other hand, unfavourable conditions in the 'milieu interne' during birth may have specific effects on nervous functions and this may account for changes during the first days of life. More insight into the functional state of the central nervous system in this period is required, and this has been one of the aims of the present study.

As stated in the Introduction, the consistency of neurological signs in the newborn period is dependent on a number of different factors. Three basic questions were therefore asked:

1. What standardization procedures should the examiner introduce in order to get reliable information from the neurological examination?

This question is important, because previous studies have shown that ambient temperature (Brück et al. 1962), clothing (Lipton et al. 1960) and hunger (Richards 1936) influence the infant's nervous function. Therefore unless these variables have been strictly controlled, fluctuations in individual responses may be due to modifications of the external or internal environment. In the present study I attempted to minimize these effects by following various standardization procedures:

(a) the ambient temperature was kept constant and the infants were undressed before they were examined.

(b) the examinations were carried out only 2-3 hours after the last feed.

In addition the examination procedure itself was standardized as much as possible; for each test the infant was kept in an optimal position, the stimuli were applied in a constant sequence, etc. The state of the infant was also controlled for each test. Previous studies have shown that the intensity of many responses is dependent on the

159

Despite our attempt at standardization it is clear that it is practically impossible to control every variable which might influence the neurological signs. This limitation became apparent with the finding that the intensity of many responses was not only related to the short-term pre-stimulus state of the infant, but also to the infant's general motility (i.e. state cycle) throughout the examination. Thus, infants who are predominantly in state 4 (eyes open, gross movements, no crying) during the examination obtain higher scores for many items than other infants. On the first 2 or 3 days of life the state of many infants is unstable and difficult for the examiner to influence. These circumstances are important drawbacks for a neurological examination under standardized conditions at this early age.

2. What is the normal developmental course of neurological signs during the first days of life?

There are two aspects to this question:
(a) Are neurological signs dependent on the age of the infant?
(b) Does each baby develop a characteristic behaviour pattern which persists during the neonatal period?
(a) The relationship between the nature of neurological phenomena and age has been assumed for a long time, but it was based on studies of only a few individual reflexes and responses and most of the previous investigators did not re-examine the same infants. In the present study I attempted to investigate the relationship between neurological signs and neonatal age by longitudinal daily examinations.

Since for most of the signs only particular response-patterns were evaluated (and quantitatively assessed), no special consideration was given if a response was present but qualitatively different.

The development of each neurological sign was quantitatively assessed by comparing the individual scores at the final examination (usually on the 8th or 9th day) with the infants' scores for each of the former days. In order to find out whether these quantitative differences were purely accidental or reflected a general pattern, the differences in all individual babies were statistically analysed. The results of these computations are summarized in Table 1 (p.164). The symbols plus or minus indicate whether in the total sample of babies significantly high or low scores were obtained on each of the first eight days of life in comparison with the last examination. The picture which emerged showed three kinds of development of neurological signs:
(i) Many signs were weaker or more difficult to elicit on the first four days of life than on the next four or five days. This seems a neurologically meaningful finding and it is noticeable in all those responses in which motility is involved.
(ii) A second, smaller, group of signs showed the opposite developmental course. The scores were significantly higher on the first four days as compared with the next four. This result probably reflects the predominance of flexion postures in the limbs, which is very marked in the first days of life. Resistance against passive movements and recoil of the forearm at the elbow are examples.

(iii) A third, smaller group showed the opposite developmental course. The scores were significantly lower on the first four days as compared with the next four. This result probably reflects the predominance of flexion postures in the limbs, which is very marked in the first days of life. Resistance against passive movements and recoil of the forearm at the elbow are examples.

2. What is the normal developmental course of neurological signs during the first days of life?

There are two aspects to this question:
(a) Are neurological signs dependent on the age of the infant?
(b) Does each baby develop a characteristic behaviour pattern which persists during the neonatal period?
(a) The relationship between the nature of neurological phenomena and age has been assumed for a long time, but it was based on studies of only a few individual reflexes and responses and most of the previous investigators did not re-examine the same infants. In the present study I attempted to investigate the relationship between neurological signs and neonatal age by longitudinal daily examinations.

Since for most of the signs only particular response-patterns were evaluated (and quantitatively assessed), no special consideration was given if a response was present but qualitatively different.

The development of each neurological sign was quantitatively assessed by comparing the individual scores at the final examination (usually on the 8th or 9th day) with the infants' scores for each of the former days. In order to find out whether these quantitative differences were purely accidental or reflected a general pattern, the differences in all individual babies were statistically analysed. The results of these computations are summarized in Table 1 (p.164). The symbols plus or minus indicate whether in the total sample of babies significantly high or low scores were obtained on each of the first eight days of life in comparison with the last examination. The picture which emerged showed three kinds of development of neurological signs:
(i) Many signs were weaker or more difficult to elicit on the first four days of life than on the next four or five days. This seems a neurologically meaningful finding and it is noticeable in all those responses in which motility is involved.
(ii) A second, smaller, group of signs showed the opposite developmental course. The scores were significantly higher on the first four days as compared with the next four. This result probably reflects the predominance of flexion postures in the limbs, which is very marked in the first days of life. Resistance against passive movements and recoil of the forearm at the elbow are examples.

2. What is the normal developmental course of neurological signs during the first days of life?

There are two aspects to this question:
(a) Are neurological signs dependent on the age of the infant?
(b) Does each baby develop a characteristic behaviour pattern which persists during the neonatal period?
(a) The relationship between the nature of neurological phenomena and age has been assumed for a long time, but it was based on studies of only a few individual reflexes and responses and most of the previous investigators did not re-examine the same infants. In the present study I attempted to investigate the relationship between neurological signs and neonatal age by longitudinal daily examinations.

Since for most of the signs only particular response-patterns were evaluated (and quantitatively assessed), no special consideration was given if a response was present but qualitatively different.

The development of each neurological sign was quantitatively assessed by comparing the individual scores at the final examination (usually on the 8th or 9th day) with the infants' scores for each of the former days. In order to find out whether these quantitative differences were purely accidental or reflected a general pattern, the differences in all individual babies were statistically analysed. The results of these computations are summarized in Table 1 (p.164). The symbols plus or minus indicate whether in the total sample of babies significantly high or low scores were obtained on each of the first eight days of life in comparison with the last examination. The picture which emerged showed three kinds of development of neurological signs:
(i) Many signs were weaker or more difficult to elicit on the first four days of life than on the next four or five days. This seems a neurologically meaningful finding and it is noticeable in all those responses in which motility is involved.
(ii) A second, smaller, group of signs showed the opposite developmental course. The scores were significantly higher on the first four days as compared with the next four. This result probably reflects the predominance of flexion postures in the limbs, which is very marked in the first days of life. Resistance against passive movements and recoil of the forearm at the elbow are examples.

2. What is the normal developmental course of neurological signs during the first days of life?

There are two aspects to this question:
(a) Are neurological signs dependent on the age of the infant?
(b) Does each baby develop a characteristic behaviour pattern which persists during the neonatal period?
(a) The relationship between the nature of neurological phenomena and age has been assumed for a long time, but it was based on studies of only a few individual reflexes and responses and most of the previous investigators did not re-examine the same infants. In the present study I attempted to investigate the relationship between neurological signs and neonatal age by longitudinal daily examinations.

Since for most of the signs only particular response-patterns were evaluated (and quantitatively assessed), no special consideration was given if a response was present but qualitatively different.

The development of each neurological sign was quantitatively assessed by comparing the individual scores at the final examination (usually on the 8th or 9th day) with the infants' scores for each of the former days. In order to find out whether these quantitative differences were purely accidental or reflected a general pattern, the differences in all individual babies were statistically analysed. The results of these computations are summarized in Table 1 (p.164). The symbols plus or minus indicate whether in the total sample of babies significantly high or low scores were obtained on each of the first eight days of life in comparison with the last examination. The picture which emerged showed three kinds of development of neurological signs:
(i) Many signs were weaker or more difficult to elicit on the first four days of life than on the next four or five days. This seems a neurologically meaningful finding and it is noticeable in all those responses in which motility is involved.
(ii) A second, smaller, group of signs showed the opposite developmental course. The scores were significantly higher on the first four days as compared with the next four. This result probably reflects the predominance of flexion postures in the limbs, which is very marked in the first days of life. Resistance against passive movements and recoil of the forearm at the elbow are examples.
(iii) A third group of signs remains constant throughout the neonatal period. In this group there are a number of reflexes, such as the abdominal skin reflex, blink reflexes and tendon reflexes, which are often described in the current literature as being absent or weak in the newborn infant. In fact, these reflexes are easily elicited in the newborn infant provided the pre-stimulus state is optimal.

Question (a) can thus be confidently answered by 'yes'. In many examined neurological signs the intensity is dependent on the age of the newborn infant.

(b) This question refers to the consistency of neurological signs and clusters of signs in individual babies from day to day. It is important to study the consistency in order to clarify whether the results of a single neurological examination on a particular day are representative for the newborn period. In order to answer this question, we intercorrelated the daily scores for each item. In chapter VI the correlations between the first day examination and the examinations of the following days, as well as the correlations between the last day and the preceding days have been shown. These data are summarized in Tables II and III.

Although the findings on the first day are highly correlated with findings on the second day, only a few neurological signs on the first day are predictive for findings on later days. On the other hand, the correlations with the final examination show that from about the fourth day on, nearly all findings are representative for the rest of the neonatal period.

What has been pointed out for individual signs also holds true for clusters of signs. Four groups of such clusters of signs could be distinguished:

1. Signs which were significantly intercorrelated on practically every day of the neonatal period.
2. Signs which clustered only on the first and/or second day.
3. Signs which clustered on all but the first and/or second day.
4. Signs which were significantly intercorrelated only now and then.

The inconsistency of these interrelationships may be due to temporary influences.

While particular abnormal neurological signs remained present throughout the whole neonatal period (hypo- or hypertonia, hemisindrome), others were found to be less consistent. The hyper-excitability syndrome, for example, was rarely seen on the first two days; if it was found, however, it soon disappeared. From the fourth day on it is a consistent sign. On the other hand, the apathy syndrome was only diagnosed on the first six days. Three of the four infants who had a full-blown apathy syndrome on the first few days of life became hyperexcitable some days later.

The results of this study permit a conclusion of great practical significance to be drawn: neurological examinations carried out on the first two or three days of life give less valid results than those on later days of the neonatal period.

The reasons for this are:

1. The states of the infant are less stable and more difficult to influence on the first 2 or 3 days. Therefore a rigorous standardization of the examination is more difficult.
2. Many responses which are needed for the proper assessment of the function of the nervous system are weaker or even absent on the first 3 or 4 days. Therefore it is more difficult to detect hemis syndromes on these days.
Findings on the first 2 or 3 days are not representative for the whole neonatal period. The intensity of most of the responses tested in the neurological examination is characteristic for the individual only from the 4th day onwards. Many individual characteristics manifested by clusters of neurological signs are only consistent from the 3rd day onwards.

Although there are difficulties in carrying out a neurological examination in the first two or three days, it is evident that an early assessment of the functional state of the nervous system is essential for the early detection of severe brain damage. In these cases, however, careful and repeated observation of the infant’s respiration, colour, posture and spontaneous movements are valid parameters. In addition, cautious testing of the resistance against passive movements and responses such as palmar grasp and rooting may be helpful at this stage to get a global idea of the degree and nature of neurological abnormalities, but the extent of the damage should be assessed in a thorough neurological examination when the acute phase is past.

The instability of the state and the changes in intensity and threshold of many neurological items on the first few days are probably manifestations of the infant’s adaptation to extra-uterine life, as are the variations in biochemical and physiological values found at this time of life. Because inter-individual variations in this adaptation process have been described as being related to obstetrical complications, drugs given to the mother during labour, time and amount of the first feed, etc., the third question formulated in the Introduction was:

3. Do obstetrical and postnatal conditions affect the developmental course and the consistency of neurological signs throughout the neonatal period?

Reliable and standardized data on these obstetrical and postnatal conditions are very difficult to obtain and if these variables appear to correlate with certain neurological signs on certain days, one generally does not know their causal relationship.

(a) The possible effects of obstetrical conditions have been examined by correlating pre- and perinatal data with the daily scores of the neurological items. In addition we separated a ‘high risk’ group (of infants who had shown signs of foetal distress) and a ‘low risk’ group (of infants without apparent obstetrical complications in their history) from the total sample and compared the neurological signs of these two groups of babies with each other.

In this study umbilical cord loops around the neck and apnoea at birth (indicated by a delayed onset of breathing and a low Apgar-score) often resulted in the occurrence of the apathy syndrome, or some of its symptoms, on the first 3 or 4 days. The babies from the high risk group differed from those from the low risk group by a lower resistance against passive movements on the first day and by lower intensities for side-to-side movements of the head in prone position, crawling and stepping movements on the 3rd and/or 4th day. These findings give rise to the conclusion that infants who had suffered from perinatal complications often had a prolonged adaptation period. Obviously this ‘general depression’ of the nervous system on the first few days was also the reason why on these days neurological signs were significantly intercorrelated, but did not show any relationship to the results on later days.
Neurological phenomena during the first days of life can only be interpreted if the general postnatal condition of the infant is considered. Unfortunately only the serum bilirubin level of jaundiced infants was assessed systematically and the general condition of the baby was subjectively evaluated by signs such as gastro-intestinal upsets, poor turgor, etc.

Most of the infants who had a moderate resistance against passive movements on the first day and became hypotonic later on, appeared to be jaundiced and/or had persistent gastro-intestinal signs on these later days.

These findings stress the necessity for future correlative studies between neurological signs and thorough quantitative assessment of postnatal non-neurological factors. The relationships between these signs in the neonatal period and the later development of individual children is of course also of considerable interest, and studies of this relationship have been, and are, of continued interest to the workers in the Department of Developmental Neurology in Groningen.