Section of Pædiatrics

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The Neurology of Early Childhood [*Abridged*]

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The Neuro-respiratory Distress Syndrome

It is now established that neurological and respiratory symptoms are frequently associated in cases of distress in the premature infant, but in no case can this association be easily related to a precise cause.

Associated Pulmonary and Central Nervous System Lesions

The best way to evaluate the problems raised by this association is to consider a certain number of fatal cases which have shown both kinds of involvement at autopsy.

Table 1 summarizes work carried out at our laboratory by Amiel & Larroche (1965), and shows that out of 80 cases of intraventricular hæmorrhage 52 were associated with pulmonary lesions, including hyaline membrane, idiopathic respiratory distress syndrome, pulmonary atelectasis, infection, massive aspiration of amniotic fluid or massive pulmonary hæmorrhage. During life, 7 of these infants had no apparent respiratory difficulties; the most frequent pulmonary symptom has been apnœa which occurred often in intraventricular hæmorrhage alone, with pulmonary lesions alone (unspecified) and in the association of both.

Primary Pulmonary Involvement Acting Secondarily on the Central Nervous System

Amiel & Larroche have shown (Table 2) by their control series that out of 40 cases of pulmonary lesions alone, confirmed at post-mortem examination, clinical neurological findings have been very frequent (*see also* Table 1, col. 3).

Possible mechanisms: (1) One of the main causes of secondary brain involvement is probably hypoventilation which might be caused in various ways, e.g. hyaline membrane, primary anectasis in premature infants of less than 28 weeks. Also, excess CO_2 retention might depress the respiratory centre in the brain stem, as recently demonstrated by Proudhon & Nelson (1964). (2) Banker & Larroche (1962) have demonstrated that, in premature infants, periventricular leukomalacia is present in one-third of the fatal cases associated with a clinical picture of asphyxia during life: a finding recently confirmed experimentally.

Table 1
Association of intraventricular hæmorrhage with pulmonary lesions

	Intraventricular hæmorrhages alone	*IVH with pulmonary lesions*	*Control without IVH*
Total number	28	52	40
Respiratory distress syndrome with chest retraction	10 (10 28 wks)	23 (7 28 wks)	16 (5 28 wks)
Respiratory difficulty without retraction	9	22	15
No respiratory difficulty	7	9	9
Apnœic episodes	21	38	32
Convulsions	9	8	6
Hyperexcitability	17	24	24
Abnormal tone	15	29	25
Abnormal primary reflex	13	18	13

From Amiel & Larroche (1965)

Table 2
Control (pulmonary alone)

Hyaline membrane (total or partial)	17
Atelectasis	11
Pulmonary infection	7
Aspiration of amniotic fluid	5

Primary CNS Involvement Affecting Respiration
This is clear from the clinical picture shown by Amiel & Larroche in Table 1, where in 28 cases of intraventricular hæmorrhage alone 7 patients had no respiratory difficulty while 21 had apnœic spells.

Apnœic spells can occur in what is purely a CNS involvement. We must elucidate how much of this could be due to raised intracranial pressure, and to the pressure cone in the foramen magnum.

From autopsy findings we know that the blood runs from the ventricles towards the posterior fossa and collects around the medulla. It is possible that this exerts direct pressure on the respiratory centre of the medulla; however, this pressure might be applied indirectly by the pressure cone to the foramen magnum or even by an obstruction from the perimedullary clot, thus preventing free circulation of CSF from the posterior fossa to the spinal canal.

We can now, with extreme caution, attempt to demonstrate an indirect proof of this process. We have been impressed by the experience of neurosurgeons who, in order to counteract the effect of raised intracranial pressure which among other symptoms causes respiratory difficulty, have placed the patient in a head-down position. Sometimes we have placed in a head-down position premature infants exhibiting severe neurological symptoms associated with repeated apnœic spells, intracranial hæmorrhage being controlled by spinal tap (Minkowski 1952). In 5 cases we have observed a complete reversal of the situation with a rapid return to normal respiration. This manœuvre should be restricted to desperate cases only. It associates blood flow change and bronchial drainage.

Comments
We now require accurate data on the flow of cerebrospinal fluid in premature infants, on how its high pressure might affect respiration and on the use of spinal drainage of CSF.

Metabolic Neuro-respiratory Distress
A purely metabolic disturbance can produce neurological and respiratory symptoms (excess CO_2, excess lactate, &c.). One condition that can combine convulsions and apnœic episodes is related to neonatal hypoglycæmia. Brown & Wallis (1963) and Neligan *et al.* (1963), following observations first made by Cornblath *et al.* (1959), have presented evidence that both neurological and respiratory symptoms might be related to persistent or recurrent hypoglycæmia in the neonatal period which can lead to death or permanent brain damage.

We think, however, that caution is advisable before definitely relating this condition to hypoglycæmia alone: (1) The effect of an intravenous infusion of 30% glucose might sometimes be due to the reduction of the raised intracranial pressure by the non-specific action of a hypertonic solution. (2) At autopsy there are mixed findings, either pulmonary or intracranial, severe enough to cause death (Tynan & Haas 1963). (3) In 19 of our 'small for dates' babies we found hypernatræmia associated with hypoglycæmia. The following case is an example:

Case 1
An infant weighing 1,100 g was born at 37 weeks. Forty-five minutes after birth the blood glucose was 9 mg/100 ml, and plasma sodium 180 mEq/l. During the next forty-eight hours he had both convulsions and apnœic episodes. He was on continuous intravenous 10% glucose but died at three days, the glucose remaining at 10 mg/100 ml, and the sodium rising to 195 mEq/l. (potassium 3 mEq/l.). Autopsy showed cerebral œdema only. The lungs were normal. *Comment:* In this case hypernatræmia rather than hypoglycæmia would account for death.

In a recent review of our 'dysmature' infants, born to toxæmic mothers, we found 19 cases with an initial plasma sodium over 160 mEq/l.; only 7 of these infants had a blood glucose below 20 mg/100 ml. All the 19 had at some time either twitched, had convulsions or apnœa, or all these symptoms. In 5 the urinary sodium output was investigated. During five to seven days on breast milk, it was 1 mEq/24 h or less. The plasma sodium and urinary sodium output only returned to normal with a salt-free diet. In 5 cases a lumbar puncture produced a jet-like flow of CSF.

In this condition, therefore, we are dealing with respiratory and neurological symptoms related only to sodium retention with or without hypoglycæmia. This has led us to a combined study of electrolytes in the plasma and CSF, and also to the estimation of cell potassium as an indirect index of brain cell osmolarity.

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