Intraventricular and Periventricular Haemorrhage in the Newborn —

A Frequent Early Complication in the Low Birth Weight Infant

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Intraventricular Haemorrhage (IVH) is the most important single event in the early neonatal period which imparts such a catastrophic effect on the prognosis of the ill preterm, both as regards mortality as well as morbidity. A number of aetiological factors are concerned in the causation of this complication; a few, at least, are preventable to a certain extent. Various workers in the field have over the past few years thrown new light on the pathogenesis and diagnosis of this problem, to a degree which begs a reappraisal of the concept.

The increase incidence of subependymal and intraventricular haemorrhage in preterm infants has been related by pathologists to the structure of the immature periventricular subependymal area and its vascular system, particularly the distinctive anatomy of the subependymal germinal matrix, the maturation-dependent vascular supply to the region, the structure of the periventricular capillaries, the regulation of cerebral blood flow, systemic haemodynamic events and fibrinolytic factors within periventricular cerebral tissue. (Volpe, 1982). The contribution of parturition events were studied by Bejar et al (1981) who utilised serial realtime ultrasound scanning of the brain through the anterior fontanelle; uterine contractions were shown to cause sufficient deformations of the preterm pliable skull to cause an increase in intravascular pressure resulting in peri/intraventricular haemorrhage. Further support has been rendered by Horbar et al (1981) who reported on the decrease in incidence of haemorrhage in infants of mothers who received tocolytic agents.

Dykes et al (1980) analysed 151 preterms under 35 weeks of gestation and who required intensive care for more than 24 hours; diagnosis of haemorrhage was confirmed by CT scan, ventricular tap or autopsy. Intracerebral haemorrhage was noted to be positively correlated with a number of factors. 42% of the 151 infants developed an IVH, and the associated factors of importance have been tabulated below.

Alveolar rupture associated with a	74%
incidence of IVH PaO_2 under 30 Torr	69%
PaO_2 under 50 Torr	48%
$PaCO_2$ over 50 Torr	49%
Intermittent mandatory ventilation	52%
Peak Insp. Pressure over 25 cm H_2O	70%
I:E ratio more than 1:1	66%
Severe Hyaline membrane disease	59%
Patent ductus arteriosus	62%
$NaHCO_3$: after 24 hours of age	60%
Volume expansion: under 24 hrs of age	54%
Mean arterial pressure under 25 mmHg.	59%
Light for gestational age	50%

(I Inspiratory E Expiratory)

The *single* most important associated factor was alveolar rupture which occurred in 26% of the infants studied; Hyaline Membrane Disease (HMD) occurred in 85% of the infants with alveolar rupture, and the incidence of bleeding in this group rose to 82%, so that the onset of alveolar rupture in HMD would contribute heavily towards the likelihood of the development of an intracerebral and a much poorer prognosis.

Among the factors which Bejar et al could not positively correlate with an increase in incidence of IVH were actual birthweight and gestatioal age, male sex, low Apgar score (below 5), osmolality exceeding 300 mmol/l, sodium exceeding 150 mEq/l, CVP over 6 cm H_2O, and PEEP over 5 cm of water, unattended delivery, hypothermia, obstetric trauma and coagulopathy; the converse is true, however, with the last-mentioned factor, in so fas as IVH/PVH is an important aetiological factor in triggering off the coagulation cascade in Disseminated Intravascular

Coagulopathy (Cockburn & Drillien, 1974).

Although other workers suchs as Lipscomb et al (1981) and Hill et al (1982) have also correlated pneumothorax with PVH/IVH Cooke et al (1981) were not able to confirm this association, and have alternatively suggested that endotracheal tube blockage is the important aetiological factor by causing hypoventilation and consequent hypoxia and hypercapnoea with resulting cerebral vasodilation this with a relief of the tube obstruction and consequent improved ventilation, the increased cardiac output would rupture the dilated cerebral vascular bed and cause an IVH/PVH. Recent work has demonstrated the pathogenic importance of impaired vascular autoregulation in the human premature. (Volpe, 1979).

Present data in fact suggest that sharp increases in blood flow are dangerous because of the pressure passivity of cerebral blood flow regulation in the sick preterm.

Lou et al, 1979; Goddard et al, 1980; Fujimara et al, 1979). Goldberg (1980) had also demonstrated the importance of rapid volume expansion in the pathogenisis of IVH, whilst Milligan (1980), using jugular venous occlusion plethysmography, has shown that transfusion-induced elevations of blood pressure resulted in striking increases in cerebral blood flow causing an IVH with 12 hours. Severe pulse waves to the premature brain may also be produced by a patent ductus arteriosus (Periman, 1981; Lipman, 1982); such changes would play a major role in the pathogenesis of IVH.

The Doppler technique has recently been adopted in IVH/PVH to confirm the increase in cerebral blood flow velocity associated with a rise of blood pressure soon after alveolar rupture and pneumothorax (Hill, 1982). Other conditions associated with temporary elevation of blood pressure in the preterm include simple motor activity, handling, seizures and apnoeic attacks; prophylactic measures to offset these occurrences may present some difficulties, but the importance of a minimum of handling, blood sampling and other investigations and interventions, needs to be particularly stressed to enthusiastic medical staff. *Primum non nocere* is particularly applicable in this case.

Diagnosis of IVH/PVH is based first of all on the identification of the clinical setting, i.e. essentially any preterm infant in a special care baby unit; lumbar puncture initially reveals the presence of large numbers of RBCs and elevated protein, and later this is followed by xanthochromia and diminished glucose. Confirmation is made by CT scan or ultrasonography. (Volpe, 1979).

The study of Tsiantos (1974) on autopsied infants had timed the occurrence of PVH/IVH to the second day of life. The more wide-spread use of realtime ultrasound scanning of preterms in Special Care Baby Units has recently disclosed the very high percentage of bleeds which occur in preterms in the first day of life, with an average age of 6 hours; whereas CT scan had yielded a 45% incidence of this complication in preterms, ultrasound scan has detected a bleed on 90% of infants under 34 weeks of gestation. (Bejar et al, 1980). 49% of these haemorrhages are large, and some bleeds are detected as early as 15 minutes of age; resolution may take as long as three months. CT scanning, however, still remains the choice investigation for parenchymatous lesions, subdural haemorrhages or collection and lesions in the posterior fossa.

Since most haemorrhages originate at the level of the head of the caudate nucleus, which is nearly directly below the anterior fontanelle, a coronal view with the linear array ultrasound transducer is particularly useful for the detection of haemorrhages within the the germinal matrix at this site. Sagittal views are useful for the demonstration of the extent of the bleed; whilst both views complement each other in the estimation of ventricular size.

A recent study by de Crespigny (1982) has yielded results similar to those of Bejar et al (1980); 65% of infants weighing less than 1500g who developed an IVH/PVH did so in the first 5 hours of life, thereby enhancing the probable aetiological role of labour events in pathogenesis. Parturition events themselves are the topics of current research in the investigation of the sequence of events leading to these haemorrhages in low birth weight infants, and, in particular, the hypothesis is being studied that a bleed may already be present at or very soon after birth, whilst postnatal events such as alveolar rupture would actually cause an extension rather than the initiation of such a bleed (Hill, 1982). Ultrasound scanning assumes great importance in these instances by detecting small bleeds very early on and alerting the neonatalogist to the risk of extension. With an established haemorrhage, serial scans and OFC (Occipito-frontal circumference) measurements are invaluable in diagnosing and following the progress of complicating hydrocephalus and the effectiveness of therapeutic lumbar punctures and ventricular taps through the assessment of the cerebral mantel and ventricular size. Volpe (1979) shown that the initial presentation of posthaemorrhagic hydrocephalus is progressive ventricular dilatation with normal intracranial pressure. Fifty per cent of these resolve, without treatment, withing a month, on average. With the remaining cases of normal pressure hydrocephalus who continue to manifest ventricular dilation the treatment of choice at present is serial lumbar punctures or drugs which decrease CSF production, i.e. acetazolamide, frusemide or glycerol. If there exists no adequate patent communication between

the lateral ventricles and the lumbar suberachnoid space, or if there is raised intracranial pressure, ventricular drainage is required if irreversible brain damage is to be prevented. A temporary external ventriculostomy can be left for a week, but may later be repeated, and allows the infant to grow and attain better health to withstand a more permanent ventriculo-peritoneal shunt.

Donn et al (1981) have utilised US scanning to monitor the effectiveness of phenobaritone in the prophylactic measurement of IVH/PVH, and a beneficial effect has been demonstrated on a dose of 5mg/kg/day for seven days, after a 10mg/kg bolus on admission. An incidence of 13% of haemorrhages in the treated group contrasted remarkably with the 47% incidence in the untreated infants. This effect has been confirmed clinically in our SCBU where phenobarbitone is routinely administered to preterm infants in the first week of life, with the added advantage of enhancing hepatic glucuronation which is immature in these infants. We have also observed a decreased incidence or attenuation of apnoeic attacks in these infants on phenobarbitone and a study is under way to establish a possible relationship between intracerebral haemorrhage and apnoeic attacks, particularly in preterms under 34 weeks of gestation. Morgan et al (1981) have failed to confirm Donn's findings when they used intramuscular phenobarbitone as a bolus (20mg/kg) in the first few hours of life; neither have they been able to obtain significant prophylactic benefit from Etamsylate which is thought to reduce capillary bleeding by polymerising hyaluronic acid, thereby reinforcing the basement membrane of the capillary; it is also thought to increase platelet adhesiveness.

The field still provides very fertile soil for further research, but these recent developments in the pathogenesis and diagnosis of IVH/PVH must of necessity modify the lines of its management, and the preventive aspect in particular needs to be stressed. Protection of the perterm's pliable skull against excessive uterine contraction, prevention of premature delivery, the acquisition of a good L:S ratio prior to delivery and the careful prophylactic use of betamethasone are primarily the concern of the obstetrician, but further postnatal responsibility needs to be extended to the neonatologist who should avoid therapies which can cause sudden increases in cerebral perfusion; he should also utilise minimal mean airway pressure to achieve normal tidal volumes and optimal lung compliance in ventilated infants, and ensure a correct I:E ratio. Volume expanders and sodium bicarbonate are to be used with great caution and within the desired recommendations, particularly in the first two days of life. Serial blood gas analysis is required to monitor oxygen and carbon dioxide tension in order to avoid hypoxia and hypercapnia. The maintenance of an adequate mean arterial pressure and the use of prostaglandin synthetase inhibitors in the management of PDA (Patent Ductus Arteriosus) present special problems to the neonatal team, who should not at the same time forget to keep handling to a minimum. The prophylactic use of phenobarbitone is recommended.

The gravity of this complication places the affected infant at great risk of developing psychomotor retardation, so that follow up of survivors extends well beyond the neonatal period.

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