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CORRESPONDENCE

To the Editor: Since the introduction of cranial ultrasound for the detection of cerebral abnormalities in preterm neonates a vast amount of knowledge has been gathered concerning white matter echolucencies (1). Longitudinal ultrasound studies as well as sequential MRI studies have identified echolucencies as disease entities with a different pathological background. Porencephalic cysts following a parenchymal hemorrhage, usually referred to as a venous infarction, subependymal pseudocysts, cystic periventricular leukomalacia (PVL), and cysts after a focal ischemic infarction, for instance of the middle cerebral artery, can all be identified using sequential ultrasonography (2–5). Ultrasound machines using 7.5 MHz transducers, available at the time of enrollment of the patients studied by Dammann *et al*. (6) in 1991–1993, enable identification of these diseases, provided that the children were examined often enough and for a sufficient number of weeks (7). Mixed lesions consisting of venous infarctions and cystic PVL were seen in only 11% of cases in a recent study (8). This is similar to our experience (9). All aforementioned white matter echolucencies are a "hole in the brain," but have a totally different pathology, and a different long-term outcome (8, 9).

In this respect it is not surprising to see that Dammann *et al*. hardly found any association between low arterial $Paco_2$ values on day 1 and all white matter echolucencies combined. Others have demonstrated a close relationship between hypocarbia and cystic PVL (10–15). Associations of subependymal pseudocysts, venous infarction or neonatal stroke with hypocarbia, however, have never been reported. PVL is far less common at a gestational age ≤28 weeks than between 28 and 34 weeks, whereas major intracranial hemorrhages associated with a unilateral parenchymal hemorrhage are more common ≤28 weeks (personal observation). These observations are supported by the patterns of cerebral palsy that are observed in preterm neonates: hemiplegia seems to be more common in extremely preterm neonates, whereas spastic diplegia is seen more often in moderately preterm neonates (16). It is possible that some of the white matter echolucencies in the study by Dammann *et al*. were unilateral porencephalic cysts following a venous infarction. In our own clinical experience, substantial hypocarbia may also occur in preterm infants with a gestational age at birth ≤28 weeks when they are a few weeks old, *e.g.* during ventilation for septicemia or necrotizing enterocolitis, or following rapid pulmonary improvement after administration of corticosteroids. It is unclear whether these cases were identified with a maximum of three ultrasound scans, and whether they were eliminated from the control group. Of course, these white matter echolucencies related to so-called "late-onset PVL" can not be associated with hypocarbia during the 1st day of life. In addition to clinical studies, normoxic or hypoxic hypocarbia has been demonstrated to augment neonatal cerebral injury in different animal species underlining the potentially deleterious effects of hypocarbia (17, 18).

Which conclusions can be drawn from the study by Dammann *et al*.? Can hypocarbia on day 1 really be excluded as a risk factor for cystic PVL in preterm neonates with a gestational age ≤28 weeks? First, it is likely that the onset of periventricular leukomalacia is far less common than other white matter lesions at a gestational age ≤28 weeks, whatever happens to the brain. Second, it is possible that arterial blood vessels are less responsive to low $Paco_2$ values ≤ 28 weeks than at more advanced gestational ages. Although both arguments support Dammann's hypothesis, these conclusions cannot be drawn from their study as presented. Is it important to identify different white matter lesions? In our view it is. If not interpreted correctly, the study by Dammann *et al*. could be used to deny the risks of hypocarbia in ventilated preterm neonates (10–15).

Although the results of Dammann *et al*. are correct as presented, we feel that the term "white matter echolucencies" should no longer be used, as identification of different white matter lesions can easily be achieved with sequential ultrasound scans (9). In view of recent publications, hypocarbia remains a matter of concern for ventilated preterm neonates.

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REFERENCES

1. Volpe JJ 2001 Neurology of the Newborn. 4th Ed. W.B.Saunders, Philadelphia, pp 344–345 and 432—433.
2. Rademaker KJ, Groenendaal F, Jansen GH, Eken P, de Vries LS 1994 Unilateral haemorrhagic parenchymal lesions in the preterm infant: shape, site and prognosis. Acta Paediatr 83:602–608
3. Rademaker KJ, de Vries LS, Barth PG 1993 Subependymal pseudocysts: ultrasound diagnosis and findings at follow-up. Acta Paediatr 82:394–399
4. de Vries LS, Rademaker KJ, Groenendaal F, Eken P, van Haastert IC, Vandertop WP, Gooskens R, Meiners LC 1998 Correlation between neonatal cranial ultrasound, MRI in infancy and neurodevelopmental outcome in infants with a large intraventricular haemorrhage with or without unilateral parenchymal involvement. Neuropediatrics 29:180–188
5. de Vries LS, Groenendaal F, Eken P, van Haastert IC, Rademaker KJ, Meiners LC 1997 Infarcts in the vascular distribution of the middle cerebral artery in preterm and fullterm infants. Neuropediatrics 28:88–96
6. Dammann O, Allred EN, Kuban KC, Van Marter LJ, Stewart JE, Pagano M, Leviton A 2001 Hypocarbia during the first 24 postnatal hours and white matter echolucencies in newborns 28 weeks gestation. Pediatr Res 49:388–393
7. Pierrat V, Duquennoy C, van Haastert IC, Ernst M, Guilley N, de Vries LS 2001 Ultrasound diagnosis and neurodevelopmental outcome of localised and extensive cystic periventricular leucomalacia. Arch Dis Child Fetal Neonatal Ed 84:F151–F156
8. Bass WT, Jones MA, White LE, Montgomery TR, Aiello F, Karlowicz MG 1999 Ultrasonographic differential diagnosis and neurodevelopmental outcome of cerebral white matter lesions in premature infants. J Perinatol 19:330–336
9. Roelants-van Rijn AM, Groenendaal F, Eken P, de Vries LS 2001 Parenchymal brain injury in the preterm infant: comparison of cranial ultrasound, MRI and neurodevelopmental outcome. Neuopediatrics 32:80–89

10. Ikonen RS, Janas MO, Koivikko MJ, Laippala P, Kuusinen EJ 1992 Hyperbilirubinemia, hypocarbia and periventricular leukomalacia in preterm infants: relationship to cerebral palsy. Acta Paediatr 81:802–807
11. Kubota H, Ohsone Y, Oka F, Sueyoshi T, Takanashi J, Kohno Y 2001 Significance of clinical risk factors of cystic periventricular leukomalalcia in infants with different birthweights. Acta Paediatr 90:302–308
12. Greisen G, Vannucci RC 2001 Is periventricular leucomalacia a result of hypoxic-ischaemic injury? Hypocapnia and the preterm brain. Biol Neonate 79:194–200
13. Fujimoto S, Togari H, Yamaguchi N, Mizutani F, Suzuki S, Sobajima H 1994 Hypocarbia and cystic periventricular leukomalacia in premature infants. Arch Dis Child 71:F107–F110
14. Wiswell TE, Graziani LJ, Kornhauser MS, Stanley C, Merton DA, McKee L, Spitzer AR 1996 Effects of hypocarbia on the development of cystic periventricular leukomalacia in premature infants treated with high-frequency jet ventilation. Pediatrics 98:918–924
15. Okumura A, Hayakawa F, Kato T, Itomi K, Maruyama K, Ishihara N, Kubota T, Suzuki M, Sato Y, Kuno K, Watanabe K 2001 Hypocarbia in preterm infants with periventricular leukomalacia: the relation between hypocarbia and mechanical ventilation. Pediatrics 107:469–475
16. Stanley F, Blair E, Alberman E 2000 Pathways to cerebral palsy involving very preterm birth. In: Stanley F, Blair E, Alberman E (eds) Cerebral palsies: epidemiology and causal pathways. Clinics in Developmental Medicine 151. Cambridge University Press/Mac Keith Press, London, pp 60–82
17. Vannucci RC, Towfighi J, Heitjan DF, Brucklacher RM 1995 Carbon dioxide protects the perinatal brain from hypoxic- ischemic damage: an experimental study in the immature rat. Pediatrics 95:868–874
18. Tammela O, Pastuszko A, Lajevardi NS, Delivoria-Papadopoulos M, Wilson DF 1993 Activity of tyrosine hydroxylase in the striatum of newborn piglets in response to hypocapnic hypoxia. J Neurochem 60:1399–1406