

CORRESPONDENCE

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ANTENATAL TREATMENT OF HYDROCEPHALUS

To the Editor: The article by Birnholz and Frigoletto in the April 23 issue demonstrates a technical achievement in perinatal medicine and the use of diagnostic ultrasound imaging.¹ I fear, however, that it also represents unwarranted meddling without adequate information.

As the authors point out, early-onset hydrocephalus in most cases reflects one aspect of a severe defect in the morphogenesis and development of the central nervous system. This was confirmed in the child in their case report by both prenatal and postnatal imaging, which demonstrated agenesis of the corpus callosum and a "midline cyst" (apparently a cavum vergae). That these were gross markers of a defect in cellular organization was shown by the child's early neurologic abnormalities, Developmental Quotient of 38, and seizure disorder. Such problems could have been anticipated, and they serve to emphasize that simple reduction of ventricular size to allow "growth of the cerebral mantle" is an inadequate measure for the prevention of future problems.

Throughout the article there is little evidence to support the efficacy of the entire series of procedures. Although the scan immediately after aspiration — i.e., Figure 2 in their article — shows a decrease in ventricular size, there is nothing to indicate the rate of accumulation of spinal fluid or the rate of ventricular enlargement. The only information given is that when taps were performed at intervals of seven to 10 days, the pressure was high and the ventricles were again enlarged. At birth, the child's head circumference was above the 95th percentile for the gestational age. Since serial lumbar punctures for hydrocephalus after neonatal intracranial hemorrhage must usually be performed daily (at times, twice daily) to control ventricular size, and since an infant's daily production of spinal fluid is five times the total volume of spinal fluid — i.e., approximately 25 ml — the schedule of taps at the intervals mentioned (with the removal of 40 ml) seems hardly adequate to achieve the result claimed. It is likely that the hydrocephalus was already partially compensated. Furthermore, tapping a cavum vergae at any time is a useless procedure.

Of greatest interest is the association of an apparent X-linked muscular disorder (if this child is a boy) with a cerebral malformation that may occur in an X-linked inheritance pattern.² Although Becker's dystrophy only rarely begins at this age, associated mental changes are rarer, and cerebral malformations have not been reported previously. Further follow-up evaluations and more extensive genetic studies of this family are certainly warranted.

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Birnholz JC, Frigoletto FD. Antenatal treatment of hydrocephalus. *N Engl J Med*. 1981; 304:1021-3.

O'Connor P, Wright FS, Hosfield WB. Laboratory examination. In: Swaiman KP, Wright FS, eds. *The practice of pediatric neurology*. St Louis: CV Mosby, 1975:51.

Menkes JH, Philippon M, Clark DB. Hereditary partial agenesis of the corpus callosum. *Arch Neurol*. 1964; 11:198-201.

The above letter was referred to the authors of the article in question who offer the following reply:

To the Editor: Like Dr. Sunder, we are concerned by the dearth of

pathophysiologic data on fetal hydrocephalus. We were able to develop a means of estimating changes in cranial volume ultrasonically (by correlating biparietal and occipitofrontal diameters before and after each tap) in order to study the rate of accumulation of fluid, which was approximately 4 ml per day at 25 weeks, 12 ml per day at 28 weeks, and 19 ml per day at 31 weeks. It has been our hope that additional data on the volumes, obtained in conjunction with measurements of intracranial pressure, may indicate specific needs for shunting in future cases.

Serial cephalocentesis does not provide definitive treatment for hydrocephalus. The object of our report was to show that the distended ventricles of a third-trimester fetus could be entered percutaneously without infection, adverse cardiovascular effect, intracranial hemorrhage, or apparent cerebral damage. More thorough treatment options may be developed from this procedural capability.

The assumption that increased intracranial pressure during fetal life retards cerebral development, and the converse proposition that relieving that pressure will ameliorate the process are unproved extrapolations from observations in newborns. Until more specific data become available, we suggest that any possible steps should be taken to lessen the ultimate cerebral deficit both in patients with correctable lesions and in patients with dysmorphic brain development who will suffer certain handicap.

Improvements in antenatal diagnosis have led to an abundance of ethical and judgmental issues. We believe that research studies into potential methods for antenatal treatment should be pursued vigorously, despite the clinical pessimism that often attends detection of fetal malady. Work in this area should conform to the Hippocratic injunction: first, to help, and second, to do no harm — or perhaps to a modern amendment: to help while minimizing risk of harm.

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POST-TRANSFUSION HEPATITIS AND SERUM ALANINE AMINOTRANSFERASE IN BLOOD DONORS

To the Editor: Aach and his colleagues have performed a thorough and useful study of levels of alanine aminotransferase (ALT) in blood donors and post-transfusion hepatitis (April 23 issue).¹ They believe that there is a compelling argument for the measurement of ALT to reduce the incidence of this illness. However, the test is insensitive and nonspecific, the illness is incompletely understood, and the morbidity and mortality have not yet been determined in full. It also remains to be proved that removal of blood donations with elevated ALT reduces the incidence of post-transfusion hepatitis.

The cost of the proposed testing could exceed \$10 million per year nationally. The cost and morbidity of evaluating donor "transaminitis" are unknown. This money might better be applied to basic and clinical research on the problem and to reducing the use of paid blood donors.

The recommendation for screening is premature.

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*Aach RD, Szmuness W, Mosley JW, et al. Serum alanine aminotransferase of donors in relation to the risk of non-A, non-B hepatitis in recipients: the Transfusion-Transmitted Viruses Study. *N Engl J Med*. 1981; 304:989-94.

To the Editor: The finding of a positive correlation between increased ALT and the attack rate of post-transfusion non-A, non-B hepatitis, as reported by Aach et al., gives strong support to their suggestion of using screening of donor-blood ALT to decrease the incidence of this disease. Holland et al., however, draw attention to a number of problems of routine screening.¹

Although we agree that such screening for a nonspecific marker might alleviate the problem in regions where a positive correlation between increased levels of ALT in donor blood and the incidence in post-transfusion hepatitis has been demonstrated, we would like to draw attention to the somewhat different results of our study on the incidence of post-transfusion non-A,non-B hepatitis in the Netherlands.² In this prospective follow-up study of 380 recipients of blood (negative for HBsAg), we observed an attack rate of 3.4 per cent, with no correlation with ALT levels in donor blood. The highest ALT level in our donors implicated in cases of this hepatitis was 21 IU. If the epidemiologic situation in our part of the world is similar to that in the United States, one would expect from the results of Aach et al. that the attack rate in our group of recipients would be between 9 per cent and 13 per cent. In view of the epidemiology of hepatitis B, quantitative differences should not be surprising. We believe, however, that there are also qualitative differences: our patients with hepatitis were all asymptomatic; the disturbances of ALT were of short duration; and the disease did not directly progress to chronic liver disease in any of the 13 patients whom we observed. In 1965 Brandt et al. studied post-transfusion hepatitis in the same region that we did; they found that 2.8 per cent of blood donors had increased serum levels of aspartate aminotransferase and ALT, and that the incidence of icteric post-transfusion hepatitis was 0.3 per cent.³

It appears, therefore, that although screening of blood donors for HBsAg is of universal value in blood transfusion, the introduction of screening of blood donors for ALT should be considered on a regional basis — at best. On the basis of our results, we have chosen to refrain from its introduction, awaiting the development of a specific test (or tests) for markers for non-A,non-B hepatitis.

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- Holland PV, Bancroft W, Zimmerman H. Post-transfusion viral hepatitis and the TTVS. *N Engl J Med*. 1981; 304:1033-5.
- Katchaki JN, Siem TH, Brouwer R, van Loon AM, van der Logt JTHM. Post-transfusion non-A,non-B hepatitis in the Netherlands. *Br Med J*. 1981; 282:107-8.
- Brandt K-H, Meulendijk PN, Poulie NJ, et al. Data on the determination of SGOT and SGPT activity in donor blood for the possible prevention of post-transfusion hepatitis. *Acta Med Scand*. 1965; 177:321-5.

The above letters were referred to Dr. Aach, who offers the following reply:

To the Editor: The Transfusion Transmitted Viruses Study (TTVS) Group did not recommend that routine screening of blood-donor ALT be initiated immediately on the basis of their findings presented in this article. A number of questions that we believed should be answered first were listed in the Discussion section of the paper, including many of those raised in Dr. Blumberg's letter. The TTVS paper stressed the nonspecificity and relative insensitivity of ALT screening as compared with the potential of a specific serologic assay for a non-A,non-B virus (or viruses). A serologic assay is clearly preferable if and when it becomes available. However, despite more than five years of intensive effort by many investigators, a confirmed, reproducible serologic test is not available, and even if it were developed in a research laboratory in the very near future, three to five years would be needed to adapt the test to large-scale screening. Until that time, screening of donor ALT might provide an interim means to reduce the incidence of non-A,non-B post-transfusion hepatitis in the United States, on the basis of the observations of the TTVS group and the investigations of Alter et al.¹ In both these studies, the evidence was predictive rather than absolute — the same type of evidence that served as a basis for adoption of routine testing of donors for HBsAg in order to reduce Type B hepatitis transmission by transfusion.

The findings of Katchaki et al.² are of interest and suggest that the relation between the level of donor ALT and the risk of

non-A,non-B hepatitis may not exist in all populations. My colleagues and I agree that there may be regional differences in the prevalence of non-A,non-B carriers and donors with an elevated ALT level that are similar to differences in the prevalence of HBsAg positivity. The low incidence and the very mild and self-limited nature of the hepatitis acquired by the recipients in the Netherlands study raises the possibility that the non-A,non-B agent (or agents) in the donor population is different from that observed in the four participating centers of the Transfusion-Transmitted Viruses Study. The infrequent sequelae of chronic hepatitis and presumably a chronic carrier state may explain the apparent lack of correlation. However, the conclusions of Katchaki et al. are relevant only if they are able to show no correlation between the administration of blood with an elevated ALT level and the development of non-A,non-B hepatitis. The numbers of donors and cases of hepatitis among recipients studied by these investigators are small as compared with those of our study, and a different trend may be observed with greater numbers. Thus, Alter et al. initially were not able to confirm the correlation between donor ALT and risk of non-A,non-B post-transfusion hepatitis³ until the study population increased substantially in size.⁴

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- Alter HJ, Purcell RH, Holland PV, Alving DW, Kozlowski DE. The relationship of donor transaminase (ALT) to recipient hepatitis: impact on blood transfusion services. *JAMA*. (in press).
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- Alter HJ, Purcell RH, Feinstone SM, Holland PV, Morrow AG. Non-A,non-B hepatitis: a review and interim report on an ongoing prospective study. In: Vyas GN, Cohen SN, Schmid R, eds. *Viral hepatitis*. Philadelphia: Franklin Institute Press, 1978:359-69.

VASOPRESSIN AND BLOOD PRESSURE

To the Editor: In the April 30 issue Padfield et al. report information suggesting that vasopressin does not participate in an important way in the regulation of blood pressure.¹ In the accompanying editorial, Bartter further discusses the seeming paradox: why an apparently pressor substance does not appear to be a pressor hormone in conscious human beings.²

Bartter raises but then rejects as unlikely the possibility of "a cross-reacting, nonpressor form of antidiuretic hormone." Both the rejection of this possibility in the editorial and the discussion in the paper suggest a lack of familiarity with a recent report from this laboratory. This paper demonstrates that the prevalent forms of arginine vasopressin in bovine neurohypophyses are Ala-Gly-[Arg⁸] vasopressin and Val-Asp-[Arg⁸] vasopressin rather than [Arg⁸] vasopressin.³ The most conspicuous difference between the biologic activities of these recently identified vasopressin peptides and that of synthetic [Arg⁸] vasopressin is the former's diminished pressor activity.

It is not known whether these peptides are strictly storage forms or may be the secreted forms of antidiuretic hormone. This information awaits the development of a radioimmunoassay technique that will distinguish between [Arg⁸] vasopressin and either of these compounds. However, the absence of a correlation between blood pressure and immunoassayable levels of [Arg⁸] vasopressin increases the likelihood that the secreted form of antidiuretic hormone may be one or both of these new peptides with diminished pressor activity.

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- Padfield PL, Brown JJ, Lever AF, Morton JJ, Robertson JIS. Blood pressure in acute and chronic vasopressin excess: studies of malignant hypertension and the syndrome of inappropriate antidiuretic hormone secretion. *N Engl J Med*. 1981; 304:1067-70.

- Bartter FC. 304:1097-8.
- Gitelman HJ, Val-Asp-[Arg⁸] vasopressin with natri

The above letter, in which the author offers

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