

the true nature of this cell line had become known), rendering some of the conclusions irrelevant to the biology of multiple myeloma.¹⁰ Unless Anderson et al and other investigators wish to assign Burkitt lymphoma to the entity of multiple myeloma and related diseases, cell line HS-Sultan should not be employed any longer as a model system for multiple myeloma.

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To the editor:

Traumatic lumbar puncture at diagnosis and outcome in childhood acute lymphoblastic leukemia

The recent report by Gajjar et al¹ demonstrates impressively the adverse effect of a traumatic lumbar puncture (defined as more than 10 red blood cells per microliter of cerebrospinal fluid [CSF]) at the time of diagnosis on treatment outcome of children with acute lymphoblastic leukemia (ALL). The inferior prognosis can be predominantly observed in a subgroup of patients with 2 consecutive traumatic lumbar punctures and the detection of leukemic cells in the CSF. The authors conclude that the iatrogenic introduction of leukemic cells into the CSF may be one reason for the reduced outcome.

In the treatment protocols XI² and XII³ of the St Jude's Children's Research Hospital, the patients received the first intrathecal therapy with methotrexate, hydrocortisone, and cytarabine at day 2. Thus they had a period of at least 24 hours without sufficient central nervous system (CNS)-directed treatment. In contrast, in ALL-Berlin-Frankfurt-Munich (BFM) frontline protocols, the first intrathecal methotrexate is immediately administered during the diagnostic lumbar puncture. Consecutive lumbar punctures (at diagnosis and for CNS-directed treatment), which may increase the risk of contamination of the CSF with blast cells, are not necessary. Furthermore, Gajjar et al's data show a surprisingly high percentage of traumatic punctures (21%), in more than half of the cases with detection of leukemic blasts in the CSF after cytocentrifugation.¹

From 88 children with initial ALL treated in our institution between November 1995 and January 2001, 56 CSF preparations of the diagnostic lumbar puncture had been preserved and the CNS status could be reevaluated. A traumatic lumbar puncture according

to the above classification groups occurred in 4 out of 56 cases (7%), and in only 1 sample could 1 single leukemic cell be observed. Hitherto, 5 children suffered a leukemic relapse (3 isolated and 2 combined bone marrow/testis relapses). No CNS relapse occurred within this group.

These data emphasize the importance of a properly performed lumbar puncture particularly at time point of diagnosis when higher numbers of blast cells are circulating in the peripheral blood. Diagnostic lumbar punctures should only be done by an experienced physician. Furthermore, early administration of CNS-directed therapy might help to reduce the risk of blast cell microdissemination in the case of iatrogenic inoculation of blood during the procedure.

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Response:

Traumatic lumbar puncture at diagnosis of childhood acute lymphoblastic leukemia

We agree with the recommendations of Kebelmann-Betzing et al that initial lumbar puncture should be performed by an experienced clinician and followed immediately by intrathecal therapy. As also stated in our article,¹ we now routinely perform this procedure with patients under short-acting general anesthesia. When the diagnosis of leukemia is uncertain because of the lack of circulating leukemic cells, we postpone lumbar puncture and intrathecal therapy until the diagnosis is established by bone marrow examination.

It is difficult to compare the frequency of traumatic lumbar puncture in the series of Kebelmann-Betzing et al with that of ours because the status of their patients was determined retrospectively on the basis of "preserved" cerebrospinal fluid; in contrast, we used fresh samples of cerebrospinal fluid. The integrity of the erythrocytes and the morphology of the leukocytes are expected to be altered in preserved samples. Since we first implemented steps to reduce this iatrogenic complication, we have substantially reduced the frequency of traumatic lumbar punctures with blast cells from 11% to 5% and that of traumatic lumbar punctures without blast cells from 10% to 7%. It should be noted that we stringently define traumatic lumbar puncture as at least 10 erythrocytes per microliter.

As shown by Total Therapy Study XIII,² early intensive intrathecal and systemic therapy is now more successful in treating and preventing central nervous system (CNS) leukemia, even in patients whose leukemic blast cells are iatrogenically introduced into the cerebrospinal fluid by traumatic lumbar

puncture. Therefore, cranial irradiation is seldom necessary in contemporary treatment programs. But others have reported neuropsychologic deficits in children who received CNS-directed therapy consisting solely of approximately 20 intrathecal treatments of methotrexate, hydrocortisone, and cytarabine over 3 years.³ The challenge now is to optimize intrathecal and systemic therapy to maximize efficacy and minimize toxicity. Developing appropriate measures to avoid traumatic lumbar puncture and hence the need of extra intrathecal therapy is but one step toward this goal.

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To the editor:

Transcobalamin polymorphism and homocysteine

Namour et al¹ suggest that codon 259 of the transcobalamin (TC) gene is a major determinant of TC polymorphism in Caucasians and that heterozygous individuals have higher plasma homocysteine. Total serum homocysteine (tHcy) is increased in patients with Alzheimer disease (AD) and may be a risk factor for cognitive decline.²⁻⁵ Furthermore, TC saturation declines with age in AD.⁶

We therefore determined nonfasting tHcy, TC phenotype, and codon 259 polymorphism in 144 (93 female, 51 male) healthy elderly volunteers (73) and dementia patients (71) recruited to a study of tHcy and cognition (the COBALZ II project) after ethical committee approval. Phenotypes were identified by polyacrylamide gel electrophoresis (PAGE) of neuraminidase-treated radiolabeled serum samples (Figure 1) and genotypes by solid-phase minisequencing (Figure 2).^{7,8} Nonfasting tHcy was assayed with the Drew Scientific DS30 Hcy Analyser (Barrow in Furness, England); Vitamin B₁₂ and folate were assayed with the Bayer ACS 180 Automated Chemiluminescence System (Newbury, England).

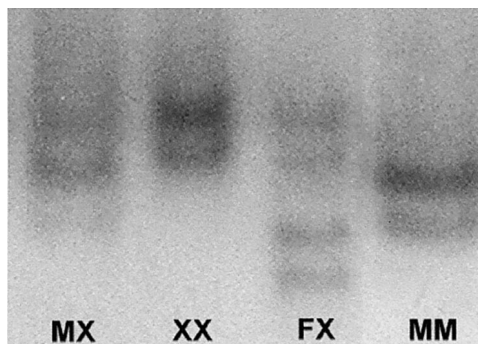


Figure 1. TC phenotypes revealed by PAGE. Serum (25 μ L) saturated with 10 μ L of radioactive B₁₂ (⁵⁷Co-B₁₂; 200mCi/mg, 1 μ Ci/mL [7.4 GBq/mg, 37 kBq/mL]; Amersham Pharmacia Biotech "CT2" diluted 1:5 N-saline) was incubated with 25 μ L of neuraminidase (0.2 IU/mL) in 25 μ L of buffer (0.05 M sodium acetate, 0.1% CaCl₂, and 0.95% NaCl, pH 5.5) at 37°C for 30 minutes. Twenty-five μ L was replaced with buffer (65% [wt/vol] sucrose) and bromophenol blue as an albumin- and front-marker. PAGE was performed in a 10% polyacrylamide gel (1.5 mm \times 7.0 cm \times 12.5 cm) with 3.5% concentrating top gel (1.5 cm high) and Tris-glycine electrode buffer at pH 8.3 and electrophoresed at 250 V.