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## **Autologous Cord Blood Transplantation in a Child With Acute Lymphoblastic Leukemia and Central Nervous System Relapse**

Christian Urban, Wolfgang Schwinger, Martin Benesch, Petra Sovinz, Guenter Henze and Hildegard Greinix

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*In Reply.*—

I am gratified that the group from British Columbia has expanded on my comment and pointed out the distressing hazards to child safety posed by both vehicles and the roadways they occupy, the design of which seldom shows much thought for pedestrians or cyclists. Long distance and parents' fear of crime are other notable barriers to walking or biking to school that they cite. Long distance is inherent in urban design subservient to automobiles, where the fabric must be stretched just to make room for cars, their storage, and the possibility that they can move at all.

Parents' fear of crime suggests another overarching issue precipitated by our automobile cities: the loss of social capital. Social capital can be defined as mutual trust, psychological sense of community, neighborhood cohesion, and community competence.<sup>1</sup> Jane Jacobs, an early influential scholar of American urban design, argued that the active pedestrian street life of older neighborhoods with shops, small streets, and mixed uses promoted safety. She coined the term "eyes on the street" and noted the sense of community in these neighborhoods. The concern of inhabitants for their fellows was in stark contrast to the high-rise projects and streets empty except for cars, which makes robbery and personal attack easier.<sup>2</sup>

Urban sprawl adds to the problem by segregating neighborhoods by income, taking good schools, jobs, and other resources to the periphery and leaving behind poverty and pollution in the inner city. Commentary on pollution generated by automobiles, profligate water and energy use, and global warming, all exacerbated by urban sprawl, is beyond the scope of this letter. However, one further issue might be mentioned as an example. Asthma remains a burdensome pediatric problem, and that burden is borne disproportionately by black children.<sup>3</sup> A study from Hartford, Connecticut, an urban minority community, used the health-field concept and studied factors that determine the health of communities: environment, human biology (genetics), personal behavior, and health care organization. The study concluded that "[i]mproved personal behaviors and medical care will have a limited sustained impact on childhood asthma until basic environmental issues are modified."<sup>4</sup>

Approaches to modifying environmental issues can be small or big. A neighborhood in Portland, Oregon, created a gathering place at a formerly busy intersection by painting a giant sunflower across the intersection, installing a fountain, an art wall, and an information kiosk. Walking and biking increased, as did measures of social capital and a neighborhood sense of well-being.<sup>5</sup>

The big approach is illustrated by the urban-design principles advocated by the New Urbanism,<sup>6</sup> including walkability, mixed use and diversity, mixed housing, traditional neighborhood structures, increased density, and smart pedestrian-friendly transportation. Big or little approaches to problems of the built environment could go a long way in mitigating a number of health issues, including obesity.

**James Fisk, MD**

Department of Pediatrics  
University of New Mexico  
Albuquerque, NM 87131

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## Autologous Cord Blood Transplantation in a Child With Acute Lymphoblastic Leukemia and Central Nervous System Relapse

*To the Editor.*—

We read with great interest "First Report of Autologous Cord Blood Transplantation in the Treatment of a Child With Leukemia" by Hayani et al.<sup>1</sup> The authors reported on the first successful autologous cord blood transplantation in a child with acute lymphoblastic leukemia of the B-precursor subtype with isolated central nervous system (CNS) relapse within 10 months from diagnosis. However, CNS and total-body irradiation (TBI) combined with high-dose conditioning and autologous stem cell transplantation can be considered an overtreatment in a 3-year-old child with acute lymphoblastic leukemia

and CNS relapse occurring within 18 months after initial diagnosis, because event-free survival is not superior in these patients compared with patients who are treated less intensively.<sup>2,3</sup> It is well known that umbilical cord blood (UCB) is associated with higher rates of engraftment failure compared with peripheral blood stem cells, which could have been used as well assuming that both sources are equally effective. Because TBI is myeloablative and UCB neither provides the opportunity to boost delayed engraftment nor to harvest stem cells for a second time in case of graft failure, at least autologous peripheral blood stem cells should have been harvested as a backup in case of nonengraftment of the UCB. In addition, the long-term adverse effects of TBI such as infertility, growth retardation, and an increased risk of secondary neoplasms should have been kept in mind. We consider it a severe conflict of interest that one of the authors employed at the commercial UCB bank where the autologous cord blood was stored advertises this case report on the company's homepage as proof of principle for treating relapsed leukemia. Furthermore, this case report is now being advertised uncritically in many other private UCB banks worldwide.

**Christian Urban, MD**  
**Wolfgang Schwinger, MD**  
**Martin Benesch, MD**  
**Petra Sovinz, MD**

Division of Pediatric Hematology and Oncology  
Department of Pediatrics and Adolescent Medicine  
Medical University of Graz  
A-8036 Graz, Austria

**Guenter Henze, MD**  
Division of Pediatric Hematology and Oncology  
Department of Pediatrics  
Charité Campus Virchow Klinikum  
13353 Berlin, Germany

**Hildegard Greinix, MD**  
Department of Internal Medicine I/BMT  
Medical University of Vienna  
A-1010 Vienna, Austria

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*In Reply.*—

In general, central nervous system relapse is not a clear and absolute indication for hematopoietic stem cell transplantation in children with acute lymphoblastic leukemia. However, early central nervous system relapse is associated with poor outcome when treated with conventional chemotherapy and radiation therapy. Although there have not been any randomized studies to establish an advantage of stem cell transplantation, such transplantation seems to provide better survival rates compared with conventional therapy (77% vs 46%).<sup>1,2</sup> In our patient, the very early onset of relapse (only 10 months) and the fact that she relapsed while receiving a more intensive chemotherapy regimen for high-risk leukemia put her at a high risk for treatment failure if she had been treated with conventional therapy. These factors led us to favor hematopoietic stem cell transplantation over conventional chemotherapy and radiotherapy.

Given the fact that the patient was still relatively young at the time of transplant and the viability of cord blood was excellent, we felt that the risk of graft failure was small, and collection of backup stem cells was not necessary. Autologous stem cells would have also had the possibility of being contaminated with residual leukemia cells.

We played no role in the family's decision to collect and save our patient's cord blood, and our report does not advocate private cord blood collection. One case report does not establish the efficacy or safety of autologous cord blood transplantation. It would be considered inappropriate for anyone to use this report as an argument in favor of private cord blood collection. Our main objective in writing the report was to discuss feasibility, safety, and uncertainties of autologous cord blood transplantation. We do believe that for children with high-risk relapsed leukemia in whom cord blood has been collected, the option of autologous cord blood transplantation should be considered and its risks and benefits should be weighed against conventional therapy and allogeneic stem cell transplantation.

**Ammar Hayani, MD**

Section of Pediatric Hematology/Oncology  
Advocate Hope Children's Hospital  
Oak Lawn, IL 60453

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