

stand the pharmacokinetics of several corticosteroids in this age group, and then we should design trials that use the lowest possible effective doses for the shortest period. Neurodevelopmental complications on follow-up constitute the essential safety issue. Since clinicians will not stop using corticosteroids, we need to understand how to use them safely, if that is possible.

From the Division of Pulmonary Biology and Neonatology, Cincinnati Children's Hospital Medical Center, Cincinnati.

1. Liggins GC, Howie RN. A controlled trial of antepartum glucocorticoid treatment for prevention of respiratory distress syndrome in premature infants. *Pediatrics* 1972;50:515-25.
2. Crowley P. Prophylactic corticosteroids for preterm birth. *Cochrane Database Syst Rev* 2000;2:CD000065.
3. Halliday HL, Ehrenkranz RA, Doyle LW. Moderately early (7-14 days) postnatal corticosteroids for preventing chronic lung disease in preterm infants. *Cochrane Database Syst Rev* 2003;1:CD001144.
4. *Idem*. Delayed (>3 weeks) postnatal corticosteroids for chronic lung disease in preterm infants. *Cochrane Database Syst Rev* 2003;1:CD001145.
5. *Idem*. Early postnatal (<96 hours) corticosteroids for preventing

chronic lung disease in preterm infants. *Cochrane Database Syst Rev* 2003;1:CD001146.

6. Baud O, Foix-L'Helias L, Kaminski M, et al. Antenatal glucocorticoid treatment and cystic periventricular leukomalacia in very premature infants. *N Engl J Med* 1999;341:1190-6.
7. Watterberg KL. Adrenocortical function and dysfunction in the fetus and neonate. *Semin Neonatol* 2004;9:13-21.
8. Committee on Fetus and Newborn. Postnatal corticosteroids to treat or prevent chronic lung disease in preterm infants. *Pediatrics* 2002;109:330-8.
9. Yeh TF, Lin YJ, Lin HC, et al. Outcomes at school age after postnatal dexamethasone therapy for lung disease of prematurity. *N Engl J Med* 2004;350:1304-13.
10. Barrington KJ. The adverse neuro-developmental effects of postnatal steroids in the preterm infant: a systematic review of RCTs. *BMC Pediatr* 2001;1:1.
11. Stark AR, Carlo WA, Tyson JE, et al. Adverse effects of early dexamethasone treatment in extremely-low-birth-weight infants. *N Engl J Med* 2001;344:95-101.
12. Stark AR, Carlo W, Vohr BR, et al. Neurodevelopmental outcome and growth at 18-22 months in infants treated with early dexamethasone. *Pediatr Res* 2001;49:Suppl:388A. abstract.
13. Watterberg KL, Gerdes JS, Gifford KL, Lin HM. Prophylaxis against early adrenal insufficiency to prevent chronic lung disease in premature infants. *Pediatrics* 1999;104:1258-63.

Copyright © 2004 Massachusetts Medical Society.

Two Fillips for Human Embryonic Stem Cells

Elizabeth G. Phimister, Ph.D., and Jeffrey M. Drazen, M.D.

Although there has been a lot of debate about the use of human embryonic stem cells, there has been little action until very recently, when a group from South Korea described the derivation of human embryonic stem cells obtained from a cloned blastocyst.¹ This represents a significant step toward the cure of diseases that involve the loss of a particular cell type — diseases such as type 1 diabetes and Parkinson's disease.

Such a cure would entail transplanting differentiated embryonic stem cells derived from a cloned blastocyst, itself derived from the somatic nucleus of the patient's cell. This approach has attractive features. The chance of tissue rejection would be small, because the transplant would be derived from the patient. The proliferation of stem cells over a long period of time increases the odds that there will be enough cells for treatment. And the pluripotent nature of embryonic stem cells makes it possible to tailor the transplant according to the tissue type required.

The South Korean study is a step in a long journey. There are still many hurdles to clear before embryonic stem cells can be used therapeutically. For example, because undifferentiated embryonic stem cells can form tumors after transplantation in his-

tocompatible animals, it is important to determine an appropriate stage of differentiation before transplantation. Differentiation protocols for many cell types have yet to be established. Targeting the differentiated cells to the appropriate organ and the appropriate part of the organ is also a challenge. Although these challenges are daunting, none are beyond theoretical reach.

Embryonic stem-cell lines are required to clear the hurdles between concept and practice. However, federal regulations limit their use because of the concern, as cited by President George W. Bush in 2001, that blastocysts "have at least the potential for life" and that therefore destroying them would cross "a fundamental moral line" (see <http://whitehouse.gov/news/releases/2001/08/20010809-2.html>). There are human embryonic stem-cell lines available for research involving the use of federal funds, but they are limited to lines established before 2001, when the "life and death decision" (as Bush put it) had already been made. At the moment, 15 such cell lines are available, and they are reportedly difficult to obtain, difficult to maintain, or poorly characterized.

It therefore comes as welcome news that a group led by Douglas Melton, a stem-cell researcher and

father of children with type 1 diabetes, has derived, characterized, and prepared for dissemination 17 new human embryonic stem-cell lines. A description of the cell lines and their derivation is provided in the Special Report in this issue of the *Journal*.² The report is notable in that it sets a standard for the characterization of embryonic stem-cell lines, and the cell lines described are easy to culture in vivo. Moreover, they are available to scientists with a Material Transfer Agreement, for noncommercial research purposes, albeit only those whose research on the cell lines will not make use of federal funds. It is not surprising that this resource comes from those in a position to recognize the therapeutic potential of stem-cell therapy.

These advances are the first steps in a path toward substantial progress in our ability to improve the health of patients, especially those with

chronic debilitating diseases. In our opinion, the cell lines described by Melton and colleagues and the others that will follow should become part of the National Institutes of Health (NIH) Human Embryonic Stem Cell Registry (<http://stemcells.nih.gov/registry/index.asp>) for researchers funded by the NIH. There is too much suffering that may be remediable through the therapeutic application of this new approach to place the new cell lines off limits to many North American research scientists.

This editorial was published at www.nejm.org on March 3, 2004.

1. Hwang WS, Ryu YJ, Park JH, et al. Evidence of a pluripotent human embryonic stem cell line derived from a cloned blastocyst. *Science* (in press).
2. Cowan CA, Klimanskaya I, McMahon J, et al. Derivation of embryonic stem-cell lines from human blastocysts. *N Engl J Med* 2004;350:1353-6.

Copyright © 2004 Massachusetts Medical Society.

Editor's Note: The scientific report by Hwang et al.¹ that is described in this article was retracted by *Science* on January 12, 2006. See Snyder and Loring (*N Engl J Med* 2006; 354:321-4) for further information.