Th responses [3], as also noted in our article [4] and consistent with the observations of Dittmer and Hunsmann [1].

I agree that, although the hypothesis remains to be formally tested, it may be difficult to show that specifically augmenting lentivirus-specific Th responses in humans or macaques experiencing a pathogenic lentivirus infection is either possible or will provide a long-term benefit. Therapeutic HIV-1 vaccine trials have unfortunately so far shown little impact. Perhaps in the setting of effective antiretroviral therapy (attempting to turn the infection into a nonpathogenic one), a therapeutic benefit from augmented Th responses could be achieved. There have been recent concerns, however, about the durability of current antiretroviral therapies [5, 6].

The central, globally more important, question remains regarding whether preexisting vaccine-induced Th responses can facilitate turning exposure to an otherwise pathogenic lentivirus into a nonpathogenic or abortive infection. Data from a pathogenic SIV study suggest this may be possible in some situations, probably by providing T cell help for the generation of de novo cytotoxic T lymphocyte responses [7]. To date, however, this cannot be generalized to HIV-1 infection of previously vaccinated humans, perhaps particularly when the Th response is of a Th2 phenotype and there is poor antigenic cross-reactivity between the vaccine strain and the infecting isolate [8]. The chemokine and cytokine secretion profiles, antigen specificity, breadth, and quantity of vaccine-induced Th responses required to successfully prevent or control lentiviruses are not known but likely to be critical future HIV-1 vaccine issues. Careful studies of nonpathogenic infections can most definitely provide clues to the mechanisms of immunologic control of lentivirus infections in humans and macaques [3, 4, 9, 10], and such studies should ultimately improve HIV vaccine development.

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References


Maternal Enterovirus Infection

To the Editor—The research reported by Palmer et al. [1], demonstrating enterovirus infection of the placenta with significant abnormalities in the placentas and offspring of infected mice, should be read with caution when attempting to translate these findings to the human. The authors wisely raised this concern but did not refer to studies [2] that failed to demonstrate transplacental passage of human enteroviruses in the ex vivo human placental model. Even maternal viral inputs of 10^6 infectious doses failed to produce virus on the fetal side of the placenta. Electron microscopy also failed to demonstrate any placental virus. The mouse placenta differs too much from the human placenta to even consider similarities of infection. We are all looking for a better model.

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References


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The Journal of Infectious Diseases 1998;177:1771–2
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0022–1899/98/7706–0055$02.00

Reply

To the Editor—We appreciate and agree with Dr. Amstey’s comments [1] that our experimental findings should be translated to the human situation with caution. Nevertheless, there are parallels
between our findings and human data, including enterovirus isolation from human placentas (and, in some cases, fetuses) and pathologic changes (similar to those we observed) in enterovirus-infected human placentas [2–4]. It should be noted that the ex vivo model described demonstrated lack of transplacental transmission of enteroviruses in term human placentas [5].

We have previously shown in our murine model a placental barrier restricting transmission of Thielier’s murine encephalomyelitis virus during middle and late gestation [6, 7]. Our current study examined placental and fetal outcome following early gestation maternal infection. The effects of enterovirus infection on human placentas and embryos in early gestation require further study.

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The Journal of Infectious Diseases 1998; 177: 1772–3
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Nondiagnostic Bone Marrow in Parvovirus B19–Related Anemia in AIDS: Confounding Effect of Prior Transfusion?

To the Editor—Abkowitz et al. [1] describe 2 AIDS patients with proven parvovirus B19–related anemia who had nondiagnostic bone marrow morphology. On the basis of this finding, Abkowitz et al. [1] appear to suggest that bone marrow morphology may not be sensitive for the diagnosis of parvovirus B19–related anemia in human immunodefi ciency virus–infected patients. This may need reexamination in light of our experience described below.

In 3 AIDS patients admitted to Cook County Hospital with normocytic normochromic anemia, absent blood reticulocytes, and serum positive for parvovirus B19 DNA by polymerase chain reaction amplification, the bone marrow showed erythroid hyperplasia in 2 patients; in the third, the marrow showed abundant normal proerythroblasts and a complete absence of later forms. In all 3 patients, bone marrow aspiration was done 2–4 days after the transfusion of 4–6 units of packed erythrocytes.

In the 2 patients whose bone marrow showed erythroid hyperplasia, the pretransfusion hemoglobin levels were 3.2 and 1.6 g/dL. Neither patient received immunoglobulin therapy. Both patients were readmitted with symptomatic anemia within 2 months of discharge, and a repeat bone marrow biopsy showed pure red blood cell aplasia with giant proerythroblasts. They were treated with intravenous 1 g/kg immunoglobulin daily for 2 days and responded with complete resolution of their anemia. In the third patient, the bone marrow morphology was interpreted as being consistent with early recovery from parvovirus B19–related pure red blood cell aplasia; he was treated with intravenous immunoglobulin, which resulted in the normalization of his hemoglobin level.

The failure to demonstrate pure red blood cell aplasia in our patients during their initial evaluation may have been due to prior transfusion of several units of fresh packed erythrocytes. The presence of antibodies to parvovirus B19 in the plasma contained in the fresh packed erythrocyte transfusion may have resulted in virus neutralization and resumption of erythropoiesis, albeit short-lived.

Details of transfusion therapy prior to the bone marrow biopsy in the 2 patients reported by Abkowitz et al. [1] are thus of interest.

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Reference

1. Abkowitz JL, Brown KE, Wood RW, Kovach NL, Green SW, Young NS. Nondiagnostic Bone Marrow in Parvovirus B19– Related Anemia who had Nondiagnosis Bone Marrow Morphology. On the basis of this finding, Abkowitz et al. appear to suggest that bone marrow morphology may not be sensitive for the diagnosis of parvovirus B19–related anemia in human immunodeficiency virus–infected patients. This

Epidemiology of Invasive Streptococcal Infections

To the Editor—Kiska et al. recently provided important epidemiologic insights about group A streptococcal (GAS) strains that caused invasive disease in North Carolina during 1994 and 1995 [1]. These investigators indicated that, on the basis of published restriction fragment length polymorphism (RFLP) patterns, an M-3 streptococcal clone (designated pattern C) that caused invasive disease in North Carolina also caused a 1994 outbreak in Ohio [2]. On the basis of our interpretation of published RFLP patterns,