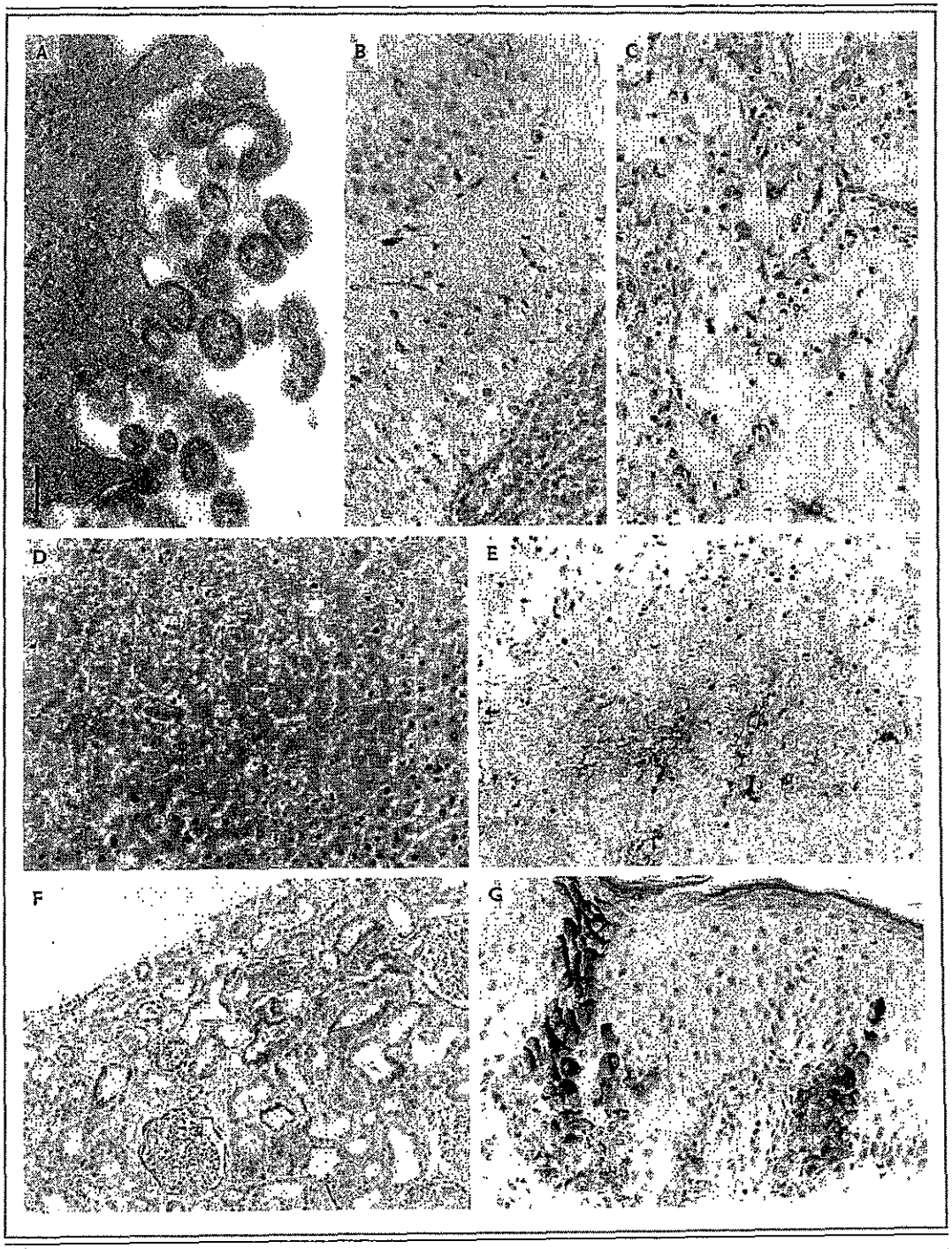

testing of multiple donor tissues by means of immunohistochemical analysis, cell culture, and RT-PCR revealed no evidence of LCMV. Neither IgM nor IgG antibodies against LCMV were detected in the donor's serum. Interviews with the donor's family revealed no known rodent exposures. Investigation of procedures, materials, and personnel in hospitals at which the donor and recipients had received care revealed no likely route of LCMV transmission.

INVESTIGATION OF THE 2005 CLUSTER

Results of testing in the 2005 cluster are summarized in Figure 4 and Table 2 (and Fig. 1 of the

Supplementary Appendix). LCMV was detected by immunohistochemical staining, cell culture, and quantitative real-time RT-PCR in multiple tissues from all four recipients. Both kidney recipients had IgM antibodies reactive to LCMV. Extensive testing of multiple donor tissues revealed no evidence of LCMV. No IgM or IgG antibodies against LCMV were detected in the serum of the donor.

The epidemiologic investigation revealed that a member of the donor's household had brought home a pet hamster three weeks before the donor died. Although the donor had not been the primary caretaker of the hamster, she had had contact with the rodent's environment on multiple occasions. Her home and work environment contained no evidence of active rodent infestation. Testing of multiple hamster tissues by immunohistochemical analysis, quantitative real-time RT-PCR, and viral culture detected evidence of LCMV infection (Fig. 4 and Table 2). The primary caretaker of the hamster was asymptomatic but had LCMV-reactive IgG and IgM antibodies present in the serum. Nucleotide analysis of PCR products identified that the viral isolates from all four organ recipients and the hamster were identical, but that they differed from the strain identified in the 2003 cluster and previously described LCMV strains (Fig. 1 of the Supplementary Appendix).

After identification of LCMV as the etiologic agent, intravenous ribavirin (a loading dose of 30 mg per kilogram of body weight, followed by 16 mg per kilogram every six hours for four days and then 8 mg per kilogram every eight hours) was initiated in Kidney Recipient A beginning on post-transplantation day 26 (Fig. 2 of the Supplementary Appendix).[14] The fever and diarrhea decreased; the pain, tenderness, and erythema in the area of the allograft diminished; and the hypoxemia, elevation of aminotransferase levels, thrombocytopenia, and coagulopathy decreased. After the patient's clinical condition had stabilized, ribavirin administration was changed to the oral route (400 mg every morning and 600 mg every evening), and it was discontinued after a renal-biopsy specimen was found to be LCMV-negative by RT-PCR and immunohistochemical staining and after serum IgM became detectable, 63 days after transplantation. During 37 days of ribavirin treatment, clinically significant hemolytic anemia developed and required the transfusion of 19 units of packed red cells. Three hundred eleven days after transplantation, the patient had stable graft function without evidence of infection, after he had restarted immunosuppressive therapy with tacrolimus, mycophenolate mofetil, and prednisolone.

Figure 4 (facing page). Immunohistochemical Staining for Lymphocytic Choriomeningitis Virus (LCMV) in Tissue Samples from the Donor, the Donor's Household Hamster, and Organ Recipients in the 2005 Cluster.

Red staining indicates the presence of LCMV antigens. The image in Panel A contains no immunohistochemical evidence of LCMV in choroid plexus from the donor. Panel B shows antigens in the kidney tubules of the donor's household hamster. Panel C shows LCMV antigens in lung tissue obtained at autopsy from the lung recipient; there are extensive hyaline-membrane formation and viral antigens in the interstitium. Panel D shows LCMV antigens in liver tissue obtained at autopsy from the liver recipient; viral antigens delineate the hepatocyte cytoplasmic membrane. Panel E shows LCMV antigens in a kidney specimen obtained at autopsy from Kidney Recipient B; viral antigens in endothelial cells are entering and exiting the glomerulus. Panel F shows LCMV antigens in a colon sample obtained at autopsy from Kidney Recipient B, with viral antigens in the muscularis mucosae and mucous cells of colonic glands. Panel G shows LCMV antigens in a kidney-biopsy specimen from Kidney Recipient A, who survived; viral antigens are in endothelial cells of the renal interstitium. (The studies shown in Panels A, B, E, and G used a rabbit anti-LCMV antibody, those in Panels C and D a mouse anti–Lassa virus antibody, and that in Panel F a mouse ascitic-fluid anti-LCMV antibody in an immunohistochemical assay with naphthol–fast red substrate and hematoxylin counterstain.) All micrographs are shown at low magnification.

TISSUE DISPOSITION

In the 2003 cluster, no additional tissues from the donor were transplanted. In the 2005 cluster, the corneas were transplanted into a 4-year-old girl and a 29-year-old woman in Algeria, neither of whom required systemic immunosuppression. Two hundred thirteen days after transplantation, neither patient had reported symptoms of infection or graft loss. The skin and liver-associated blood vessels were not transplanted.

DISCUSSION

We describe the transmission of LCMV by solid-organ transplantation. In both clusters, disseminated infection developed in the recipients of organs from a common donor who had no clini-