

## Potential for Expansion of the Donor Pool Using Liver Allografts From Donors With Bacterial Meningitis

The use of liver grafts from donors with bacterial meningitis. *Satoi S, Bramhall SR, Solomon M, Hastings M, Mayer AD, de Goyet JV, et al.* Transplantation 2001;72(6):1108-1113. (Reprinted with permission.)

### Abstract

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### Comments

The shortage of organs is the single most important limitation to organ transplantation today. The demand created by the number of patients who are now regarded as candidates for organ transplantation is not matched by the supply of suitable donor organs. The number of cadaveric organ donors is declining because of multiple factors, including improved motor vehicle safety and infectious diseases affecting potential donors. This has resulted in an increase in living organ donation. According to preliminary data from the United Network for Organ Sharing, in the United States, the number of living organ donors surpassed the number of cadaveric donors for the first time in 2001. It is cur-

rently estimated that 80,000 patients in the US are on the waiting list for organ transplantation. Of these, 16 patients die every day.<sup>1</sup>

The article by Satoi et al<sup>2</sup> is a retrospective case control study performed between 1989 and 1999 at two hospitals in Birmingham, United Kingdom. In this study the investigators examined the hospital records of 34 patients who received orthotopic liver transplants from 33 donors with bacterial meningitis. These 34 patients were compared with matched recipients from cadaveric donors who died of causes other than meningitis. The meningitis organisms isolated from the donors were *Neisseria meningitidis* (n = 14), *Streptococcus pneumoniae* (n = 4), *Haemophilus influenzae* (n = 1), *Streptococcus* species (n = 2), and unknown (n = 12). It is concerning that the infecting microorganism was not known in so many cases. The antimicrobial susceptibility results of the pathogenic microorganisms were, unfortunately, not reported. Donors received antimicrobial therapy for a mean duration of 3 days (range, 1 to 6) before organ procurement. The mean duration of antimicrobial therapy in recipients was 6 days (range, 1 to 18). The mean posttransplantation follow-up was 37 months (range, 1 day to 106 months). The investigators did not observe a difference in recipient and graft survival rates between the study and the recipient-matched groups. In particular, no infections caused by the meningeal pathogens were observed in the study group. The investigators concluded that organ procurement from donors with bacterial meningitis is a safe procedure provided both donors and recipients receive adequate antimicrobial therapy. What can be learned from this study?

Transplantation centers have traditionally adhered to strict selection criteria because of the concern of transmitting an infection to an immunosuppressed recipient. The need to increase the donor pool has prompted some transplant centers to accept organs from donors previously considered marginal. Donor-transmitted infection can be caused by viruses<sup>3</sup> (e.g., HIV, cytomegalovirus, herpes simplex virus, Epstein-Barr virus, hepatitis B virus, hepatitis C virus, human herpes virus 8), prions (e.g., Creutzfeldt-Jakob disease), bacteria<sup>4</sup> (e.g., *Staphylococcus aureus*, *Streptococcus* species, *Pseudomonas* species, *Escherichia coli*, *Bacteroides fragilis*, *Treponema pallidum*, *Mycobacterium tuberculosis*), fungi<sup>5</sup> (e.g., *Histoplasma capsulatum*, *Candida* species, *Aspergillus fumigatus*), or parasites (e.g., *Plasmodium* spp, *Toxoplasma gondii*, *Trypanosoma cruzi*).

Some centers have published guidelines regarding bacterial infections in general suggesting that a potential donor infected or colonized with a multiresistant bacterium, with a disseminated infection causing septic shock and death or with a mycobacterial infection,

constitutes an absolute contraindication for organ retrieval.<sup>6</sup> Cautious consideration of the use of infected donors has been suggested to be acceptable under the following circumstances. (1) Bacteremia with a relatively nonvirulent organism or with an organism that is rapidly cleared from the bloodstream with effective bactericidal therapy, or (2) bacteremia caused by *Staphylococcus aureus* or *Pseudomonas aeruginosa* provided that at least 2 weeks of bactericidal therapy have been administered and that subsequent blood cultures over 1 week off of antibiotics have been negative.<sup>7</sup> The same investigators suggest that a potential donor with an invasive tissue infection or an infection with a difficult-to-treat organism (e.g., *Streptococcus pyogenes*, vancomycin-resistant enterococcus, *S. milleri*, *Salmonella* sp., *Mycobacterium* sp., or *Nocardia* sp.) should be eliminated from consideration for organ retrieval.<sup>7</sup> It has also been suggested that although an infection confined to an organ contraindicates its retrieval, the retrieval of other potentially transplantable organs may be acceptable. Lopez-Navidad et al.<sup>8</sup> for example, reported a prevalence of pneumonia of 15% among their donors that did not prevent the retrieval of other transplantable organs without subsequent infectious complications in recipients.

The presence of bacterial meningitis in potential donors has historically been considered an absolute contraindication for organ retrieval.<sup>4,9,10</sup> However, the findings of Sato et al.<sup>2</sup> together with prior smaller reports of successful transplantation of organs from donors with bacterial meningitis,<sup>8,11-13</sup> suggest that some patients with bacterial meningitis may be acceptable liver donors. The use of such donors may expand the potential liver donor pool.

Bacterial meningitis is responsible for 3.4% to 8% of intensive care unit brain-dead adult patients<sup>10</sup> and between 13% to 15% of brain-dead pediatric patients.<sup>14,15</sup> Use of such patients as donors could increase the pool of organ donors by more than 5%.<sup>12</sup> The organisms that most commonly cause bacterial meningitis (*S. pneumoniae*, *H. influenzae*, *N. meningitidis*) are extremely susceptible to unfavorable environmental changes, including the low temperatures attained during perfusion and storage of organs at 4°C before transplantation. This, along with the use of adequate antimicrobial therapy (discussed below) in donors and recipients, may explain why transmission of infection from brain-dead donors with bacterial meningitis to recipients has not been reported.

Factors that bear consideration in evaluating potential liver donors with meningitis include the organism(s), the time course of infection, and the duration and type of antimicrobial therapy.

### The Organism(s)

Bacterial meningitis caused by *Listeria monocytogenes* has a high risk of relapse.<sup>16</sup> Thus, it is inadvisable to consider organ donation from a patient with listerial meningitis.<sup>8</sup> Transmission of *M. tuberculosis* from a donor with unrecognized tuberculous meningitis to two recipients, one of whom died, has been reported.<sup>17</sup> Neither recipient received antituberculous therapy.<sup>17</sup> Tuberculous meningitis is a contraindication to organ donation. Although distinct from bacterial meningitis, fungal meningitis (e.g., caused by *Candida* species, *C. neoformans*, *Blastomyces dermatidis*, *Coccidioides immitis*, or *H. capsulatum*) is also a contraindication to organ donation because of the requirement for far more extensive therapy than bacterial meningitis and the limited opportunity for adequate donor treatment. Meningitis caused by organisms that are generally a rare cause of meningitis but that are notable for establishing metastatic infection, adherence to endothelial surfaces, or possession of other markers of virulence (e.g., *Staphylococcus* sp., *P. aeruginosa*, *Salmonella* sp.) is likewise a contraindication to organ donation, as is viral (e.g., West Nile virus) central nervous system infection.

In our opinion, the study by Sato et al applies only to potential liver donors with bacterial meningitis caused by penicillin-susceptible *S. pneumoniae*, *N. meningitidis*, and *H. influenzae*. An additional single case report of successful transplantation of organs retrieved from a donor with postneurosurgical *E. coli* meningitis suggests that some cases of postneurosurgical meningitis caused by *E. coli* (or similar organisms) may also bear consideration.<sup>8</sup> A word of caution is warranted regarding gram-negative bacillary meningitis in general; if the meningitis is not clearly related to a neurosurgical procedure, a thorough search to exclude an extrameningeal focus of infection affecting the potentially transplantable organs is indicated.<sup>8</sup>

### Time Course of Infection

Patients with sustained bacteremia caused by any organism are not suitable candidates for liver donation because of the concern of metastatic infection. In contrast, donors with acute meningococcal or pneumococcal meningitis, in whom the bloodstream infection is typically rapidly cleared and metastatic infection is unusual, may be considered for liver retrieval.

### Antimicrobial Therapy

The definition of adequate antimicrobial therapy of donors and recipients in the context of liver transplantation from a donor with bacterial meningitis is not well

established. Sato et al suggest in their study that high-dose antimicrobial therapy for at least 24 to 48 hours before procurement is adequate. Rubin and Fishman<sup>7</sup> note that antimicrobial therapy for 4 to 5 days would clear the bloodstream of bacteria in donors with pneumococcal or meningococcal meningitis. Lopez-Navidad et al<sup>8</sup> reported five cases of successful transplantation of organs retrieved from donors with bacterial meningitis. In their study, donors received antimicrobial therapy for 24 to 48 hours before organ procurement and the duration of antimicrobial therapy in recipients ranged between 1 week and 10 days. Caballero et al<sup>18</sup> reported successful transplantation of organs retrieved from a donor with enterococcal endocarditis. In this report, the donor received just 4 days of antimicrobial therapy before organ retrieval, and the recipients were treated with antimicrobial therapy for 10 days. In general, antimicrobial therapy should be adequate if bactericidal therapy has been administered long enough to clear any concomitant bloodstream infection and any potential metastatic infection of the allograft.

In summary, liver retrieval from donors with bacterial meningitis caused by *S. pneumoniae*, *H. influenzae*, or *N. meningitidis* may be cautiously considered as a way to expand the donor pool, provided that bloodstream and metastatic infection are absent (or controlled), the infectious agent and susceptibilities are known, and both the donor and recipient receive adequate bactericidal antimicrobial therapy, before procurement and after transplantation, respectively. The definition of adequate antimicrobial therapy is not well established. Several studies<sup>2,8,12</sup> suggest that antimicrobial therapy for 24 to 48 hours before liver retrieval in the donor and 1 week in the recipient may be adequate. The creation of a registry in which both successes and failures are collected would be helpful to establish more definitive guidelines to help guide the selection of potential donors with bacterial meningitis and other infectious processes.

Nicolas C. Issa, MD  
Division of Infectious Diseases  
Department of Internal Medicine

Robin Patel, MD  
Division of Infectious Diseases  
Department of Internal Medicine  
Division of Clinical Microbiology  
Department of Laboratory Medicine and Pathology  
Mayo Clinic  
Rochester, MN

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