Echinococcosis is caused by the ingestion of eggs of the dog tapeworm or fox tapeworm belonging to the genus Echinococcus. E. granulosus causes considerable human morbidity and mortality, with the highest prevalence in rural areas because of close co-habitation of humans, animal intermediate hosts, and final hosts. Oocytes migrate after ingestion to different organs and form cysts most commonly located in the liver (60–70%) and lungs (20%). Other localizations of cysts, including the kidney, spleen, muscles, bone, pancreas, central nervous system, and soft tissue, have been described but are less common.1–3

Treatment recommendations for E. granulosus cysts include long-term therapy with albendazole alone or in combination with praziquantel, percutaneous drainage, and surgical removal of the lesions.4–6 Albendazole is a benzimidazole derivative and is highly active against echinococcal protoscolecies. However, the in vivo therapeutic response is limited by its low and erratic bioavailability.7–10 Nevertheless albendazole is the most commonly used drug for pre- and post-operative anthelmintic treatment and continued suppressive therapy of inoperable hydatid cysts.11 On the background of its variable absorption, the penetration of albendazole and its active metabolite albendazole sulfoxide into cysts is of major importance for adequate in vivo activity. Whereas limited data are available for Echinococcus cysts of the liver, little is known about the intra-cystic concentrations of albendazole in patients treated for echinococcal cysts located in other organs than the liver. In this study, we aimed to assess the ability of albendazole sulfoxide—the active metabolite—to penetrate into E. granulosus cysts of two patients with non-liver cysts.

A 60-year-old woman of Turkish origin (Patient A) residing in Austria for > 5 years was diagnosed with a painless tumor on the left thigh, which became noticeable after voluntary weight loss of 25 kg. The second patient (Patient B), a 30-year-old Turkish citizen, presented at the hospital with progressive cough, night sweats, and dysnea. Inflammation markers were increased in both patients, with C-reactive protein at 8.7 and 2.4 mg/dL for Patients A and B, respectively (normal range, < 1 mg/dL). Marked eosinophilia was recorded (550 and 3,020/µL blood for Patients A and B, respectively) in differential blood count, and serologic investigation by enzyme-linked immunosorbent assay and Western blot confirmed the diagnosis of E. granulosus infection. Computer tomography and magnetic resonance imaging showed a cystic lesion in the proximal Musculus satorius of 7.5 cm diameter in Patient A. Patient B had a distinctive pleural effusion on the right side of the lung with transgression of the diaphragm. Following current treatment recommendations, patients were prescribed 400 mg albendazole to be taken twice daily with a fatty meal for 5 and 4 days before surgical removal, respectively.12 Histologic examination of cyst tissues confirmed diagnosis by visualization of typical protoscolecies. Patients continued anthelmintic treatment for 1 month after surgery and had no signs of recurrence of Echinococcus cysts.

Venous blood samples for drug analysis were taken in the morning of surgery before albendazole intake and during the intervention. Undiluted cyst fluid was obtained during operation and was subsequently stored at −80°C until further analysis. Concentrations of albendazole and albendazole sulfoxide in plasma and cyst fluid were measured by a validated high-performance liquid chromatographic (HPLC) method using an “UltiMate 3000” system ( Dionex, Sunnyvale, CA). Separation of albendazole sulfoxide was carried out using a Hypersil BDS-C18 column (Thermo Fisher Scientific, Waltham, MA) with an acetic acid/methanol mobile phase. The limit of quantification for albendazole and albendazole sulfoxide was 0.063 and 0.072 µg/mL, respectively. Coefficients of accuracy and precision for both compounds were < 8%.

HPLC measurement showed that, in all clinical samples, albendazole was below the limit of detection. However, albendazole sulfoxide—the active metabolite—was quantified in pre-operative and intra-operative samples in the range of 0.10 and 1.3 µg/mL in plasma. Furthermore, the analysis of cystic fluid samples also showed albendazole sulfoxide concentrations of 0.16 and 0.6 µg/mL, indicating a relative intra-cystic drug concentration of 48% and 156% compared with plasma, respectively (Table 1).

These data show—besides the known variability of plasma concentrations—good tissue penetration of albendazole sul-
phoxide into echinococcal cysts, with ~50% variation compared with plasma drug concentrations. In general, plasma concentrations of albendazole A previous report indicated maximum plasma levels for albendazole sulphoxide in the range of 0.45–2.96 µg/mL and intra-cystic drug concentrations between 0.06 and 0.42 µg/mL.12,13 Morris and others14 reported an ~20% intra-cystic concentration of albendazole sulphoxide in patients treated with 10 mg/kg albendazole for 1 month before surgery. Although these data are in line with our results for plasma drug concentrations, the relative intra-cystic drug concentration of albendazole sulphoxide was significantly higher in our patients. Interestingly, in a previous study, praziquantel, another anthelmintic drug with activity against tapeworms, led to a considerable increase in albendazole plasma levels.15 In that report, the activity against protoscolices was significantly higher in patients treated with a combination of albendazole and praziquantel.

Thus far, most data on target site drug concentrations derive from echinococcal cysts of the liver and information on intra-cystic drug penetration for other organs are scarce. Despite the limited number of patients in this study, our data indicate that drug penetration in cysts located in the pleural cavity and the skeletal muscle is comparable or potentially higher compared with previous data on liver cysts.

Albendazole has been used for the treatment of human echinococcosis since the 1980s and—depending on the stage of the disease—continuous long-term albendazole therapy shows cure rates between 30% and 80%. Although the oral bioavailability of albendazole is characterized by significant variation, intra-cystic drug penetration seems less variable and comparable to plasma drug levels. Although many questions about the optimal medical treatment of echinococcosis remain, the use of albendazole has been shown to allow safer manipulation of liver cysts during surgery, thus minimizing the chance of secondary recurrence. Based on our data, this may similarly be true for cysts localized in other organs.16,17 Further data on anthelmintic combination therapy and the development of novel anthelmintic drugs with improved oral bioavailability are desirable to further improve the management of echinococcosis.

Received May 4, 2009. Accepted for publication July 2, 2009.

Financial support: This work was supported by a grant of the independent Karl Landsteiner Gesellschaft, Austria.

Authors’ addresses: Meskure Capan, Department of Medicine I, Division of Infectious Diseases and Tropical Medicine, Medical University of Vienna, Währinger Gürtel 18-20, 1090 Vienna, Austria; and Institute of Tropical Medicine, University of Tübingen, Wilhelmstraße 27, 72074 Tübingen, Germany. Sebastian Keltner, Florian Thalhammer, and Stefan Winkler, Department of Medicine I, Division of Infectious Diseases and Tropical Medicine, Medical University of Vienna, Währinger Gürtel 18-20, 1090 Vienna, Austria. Walter Jäger, Department of Clinical Pharmacy and Diagnostics, Faculty of Life Sciences, University of Vienna, Althanstraße 14, 1090 Vienna, Austria. Markus Zeitlinger, Department of Clinical Pharmacology, Medical University of Vienna, Währinger Gürtel 18-20, 1090 Vienna, Austria. Michael Ramharter, Department of Medicine I, Division of Infectious Diseases and Tropical Medicine, Medical University of Vienna, Währinger Gürtel 18-20, 1090 Vienna, Austria; Institute of Tropical Medicine, University of Tübingen, Wilhelmstraße 27, 72074 Tübingen, Germany; and Karl Landsteiner Gesellschaft, Infektiologie, Julius Raab Promenade 7 3100 St. Pölten, Austria.