Editorial Response: Treatment of Cystic Echinococcosis—Improving but Still Limited

Despite efforts to educate persons at risk and the success of control programs in a few countries, cystic echinococcosis, or hydatid disease, caused by the larval form of the cestode *Echinococcus granulosus*, still constitutes a substantial health problem in most livestock-raising areas of the world [1]. In the United States and Canada, locally acquired cases of cystic echinococcosis are rare; in contrast, imported infections are diagnosed widely, most commonly in immigrants from Middle Eastern countries and, to a lesser extent, from South America and Europe [2]. Cystic echinococcosis is characterized by a slowly growing, fluid-filled cystic lesion (hydatid cyst) in the liver, lungs, or other organs; infection may be asymptomatic until cysts cause noticeable mass effect, and then signs and symptoms vary according to location, cyst size, and number. Until recently, surgery was the only option for treatment of echinococcal cysts; however, surgery has been associated with frequent recurrence and high rates of intra- and postoperative morbidity and mortality. Operative mortality in the first operation varies from 0.5% to 4% but increases with repeated interventions and under conditions of inexperience or inadequate facilities [3, 4].

In the past 20 years, benzimidazole compounds have been shown to have echinococcidal activity, and results of internationally coordinated clinical experiences document that approximately one-third of patients treated with albendazole or mebendazole have been cured of their disease (complete and permanent disappearance of cysts) and even higher proportions (30%–50%) have responded with significant regression of cyst size and alleviation of symptoms [5–8]. In this issue of *Clinical Infectious Diseases*, Franchi et al. [9] of the University of Rome report on the long-term follow-up of patients after treatment with albendazole or mebendazole; their findings further reveal the benefits and limitations of chemotherapy. Among 448 patients with 882 evaluable cysts, 74% of cysts showed degenerative changes on ultrasound or CT imaging after the patients received 3- to 6-months of continuous daily treatment with albendazole or mebendazole. Confirming previously reported experience [6, 7], these authors found that the efficacy of albendazole (82%) was superior to that of mebendazole (56%), presumably because of the former compound’s superior pharmacokinetic profile that favors intestinal absorption and penetration into the cyst(s).

Continued follow-up of the patients after cessation of treatment revealed progressive degeneration in 22% of the altered cysts; however, 25% showed evidence of regeneration, including increase in size or fluid volume, exogenous vesiculation, or reattachment of the membrane to the cyst wall. The rate of “relapse” was similar for patients treated with either albendazole or mebendazole but was more frequent for cysts with daughter cysts than for primary cysts, for cysts of the liver than for those in the lungs, and for cysts in patients <30 years of age than in those older; these different responses are presumably related to differences in permeabilities of the cyst membranes in these different types of cases, permitting greater or lesser diffusion of the drug into the cyst. More than three-fourths of relapses were noted within 2 years after the end of treatment and, very importantly, >90% of these cysts regressed on further treatment.

Side effects during chemotherapy were minimal and in all patients were reversible without discontinuing treatment: ~20% of patients showed transitory abdominal pain, headaches, alopecia, or elevated serum transaminases. Although not ideal, these findings support the view that chemotherapy alone offers a safe and effective alternative to surgery for the management of cystic echinococcosis in most locations. Future advances in chemotherapy may be achieved by using drugs with higher echinococcidal activity [10].

A third option for the treatment of hydatid cysts in the liver and some other locations is the PAIR procedure (percutaneous puncture with sonographic guidance, aspiration of substantial amounts of the liquid contents, injection of a protoscolicidal agent [e.g., 95% ethanol or hypertonic saline], followed by reaspiration, with concomitant chemotherapy) [11]. Although this procedure challenges a number of long-held concerns about management of cystic echinococcosis (e.g., risks of anaphylaxis and secondary recurrence), experiences among >1,000 patients have shown excellent results in terms of safety, efficacy, and cost [11–14]. This procedure, which can be done under conditions of minimal physical facilities, offers great promise for making treatment available in the often remote regions where echinococcosis is typically prevalent.

It has been observed that in echinococcosis it is easier to prove treatment failure than treatment success. The occult nature of the hydatid cyst confounds posttreatment evaluation. The reports by Franchi et al. [9] and others [7, 15] illustrate the necessity for extended posttreatment monitoring, because recurrence may not be observed until many years after treatment. Objective response to treatment is best assessed by repeated evaluation of cyst size...
and consistency at 3- to 6-month intervals with ultrasound, CT, or MRI. Since the time of appearance of recurrence is extremely variable, such monitoring should be continued for ≥5 years.

Although the consensus of experienced clinicians is that surgery remains the first choice for treatment for most cases of cystic echinococcosis because of the potential to totally remove the parasite and completely cure the patient [7], it is now clear that alternative approaches to treatment (surgery, chemotherapy, PAIR, or combinations of these) are available, safe, and effective. Depending on factors such as local professional experience and accessibility of adequate clinical facilities, different approaches may be chosen in different circumstances. Albendazole chemotherapy as primary treatment may be indicated for patients who are unfit for surgery, those with inoperable or recurrent cysts, and those who refuse surgery. PAIR may be the treatment of choice in some of those same situations or in cases of relapse after surgery. Factors limiting availability of the full range of choices include local traditions, resistance to change, and, in countries such as the United States where infection is rare, lack of a sufficient number of clinical cases for physicians to acquire adequate clinical expertise. Guidelines for current treatment of cystic echinococcosis have been published by the World Health Organization Informal Working Group on Echinococcosis [7], and expert consultation is available through the Internet (www.medicalweb.it/aumi/echinonet/).

Peter M. Schantz
Division of Parasitic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia

References