

- 6 Weldhagen GF. Integrons and beta-lactamases—a novel perspective on resistance. *Int J Antimicrob Agents* 2004; **23**: 556–62.
- 7 Poirel P, Héritier C, Tolün V, Nordmann P. Emergence of oxacillinase-mediated resistance to imipenem in *Klebsiella pneumoniae*. *Antimicrob Agents Chemother* 2004; **48**: 15–22.
- 8 Yang Y, Bush K. Biochemical characterization of the carbapenem-hydrolyzing beta-lactamase AsbM1 from *Aeromonas sobria* AER 14M: a member of a novel subgroup of metallo-beta-lactamases. *FEMS Microbiol Lett* 1996; **137**: 193–200.
- 9 Yigit H, Queenan AM, Anderson GJ, et al. Novel carbapenem-hydrolyzing beta-lactamase, KPC-1, from a carbapenem-resistant strain of *Klebsiella pneumoniae*. *Antimicrob Agents Chemother* 2001; **45**: 1151–61.
- 10 Lee SH, Jeong SH, Park Y-M. Characterization of *bla*<sub>TEM-10</sub>, a novel, plasmid-encoded AmpC-type beta-lactamase gene in a clinical isolate of *Enterobacter aerogenes*. *J Appl Microbiol* 2003; **95**: 744–52.
- 11 Jacoby G, Bush K. Amino acid sequences for TEM, SHV and OXA extended-spectrum and inhibitor resistant beta-lactamases. <http://www.lahey.org/studies/webt.asp> (accessed Sept 15, 2006).
- 12 Walther-Rasmussen J, Høiby N. OXA-type carbapenemases. *J Antimicrob Chemother* 2006; **57**: 373–83.
- 13 Grimm V, Ezaki S, Susa M, Knabbe C, Schmid RD, Bachmann TT. Use of DNA microarrays for rapid genotyping of TEM beta-lactamases that confer resistance. *J Clin Microbiol* 2004; **42**: 3766–74.

## Albendazole for mass drug administration to eliminate lymphatic filariasis



Sunish and colleagues<sup>1</sup> discussed advances in the treatment of lymphatic filariasis, particularly the effectiveness of single-dose diethylcarbamazine in reducing microfilaraemia, and its enhanced effectiveness when co-administered with a single dose of albendazole. WHO currently recommends that in large-scale control and elimination programmes, albendazole should be administered in a single-dose regimen, in conjunction with either diethylcarbamazine or ivermectin.<sup>1</sup>

Whether albendazole enhances treatment with diethylcarbamazine in mass drug administration for lymphatic filariasis elimination is a question debated around the world, especially in India, which alone contributes to about 38% of the global burden of the disease.<sup>2–4</sup> India is the single largest country under the lymphatic filariasis elimination programme that was hesitating until recently to use the two-drug regimen over its entire endemic region because of the lack of evidence regarding albendazole's beneficial effects. A common observation in most of the recent studies is that there is a substantial reduction in the microfilariae prevalence and intensity following mass drug administration (three to five rounds) with diethylcarbamazine alone, and also a substantial reduction with diethylcarbamazine plus albendazole.<sup>1,2,4</sup> The rate of reduction is more pronounced in the two-drug regimen compared with the single-drug regimen; however, the difference between the two arms is not always significant. This reduction is more visible in children and young adults.

In most lymphatic filariasis endemic regions, children and young adults are more infective (microfilaraemic), and also vulnerable to intestinal geohelminth/soil-

transmitted helminth infections (mainly roundworm [*Ascaris lumbricoides*], whipworm [*Trichuris trichiura*], and hookworm [*Ancylostoma duodenale*]).<sup>5</sup> The gastrointestinal tract of a child living in poverty in a developing country is likely to be parasitised with at least one—and in many cases all three—soil-transmitted helminths, with resultant impairments in physical, intellectual, and cognitive development. Some of the major ailments caused by soil-transmitted helminths include intestinal discomfort and malabsorption.<sup>5</sup> The potential benefits of albendazole in treatment against the geohelminths have been well documented.<sup>5–7</sup>

Bethony and colleagues have expressed concern about the sustainability of periodic deworming with anthelmintics.<sup>6</sup> Although it has not been resolved whether albendazole should be used as a microfilaricide or macrofilaricide for treating individual patients with lymphatic filarial infections,<sup>2,8</sup> albendazole's use as an adjunct to diethylcarbamazine for mass drug administration in the lymphatic filariasis elimination programme is likely to ensure periodical deworming. A study on deworming programmes for school children also ruled out any possible clinical allergy associated with albendazole treatment.<sup>9</sup>

Although diethylcarbamazine is mainly a microfilaricide drug, it also has some macrofilaricidal action.<sup>7,10</sup> The effect of diethylcarbamazine against microfilariae depends on the host immune status and the level of absorption of the drug (from the intestine to the bloodstream).<sup>10</sup> In cases of co-infections caused by lymphatic filariasis (harbouring microfilariae) and soil-transmitted helminths, it is very likely that the absorption of diethylcarbamazine was enhanced by the

addition of albendazole, since the intestinal obstruction was cleared simultaneously. A greater reduction of microfilariae prevalence, intensity, and antigenaemia was reported in children and young adults following the two-drug regimen,<sup>1</sup> and this might be caused by a higher proportion of co-infection in this group. Similar findings from different geographical areas could add strength to this view.

At present, the drug(s) are given to the individuals and it is their option to consume the drug(s) any time after taking food. In the two-drug mass drug administration strategy, it might be ideal to advocate that the individuals are asked to take albendazole on the first day (as it takes a day or two for the worms to clear), and diethylcarbamazine on the subsequent day. This strategy would facilitate better absorption of diethylcarbamazine and thereby ensure the enhanced effect of mass drug administration.

*Shanmugavelu Sabesan*

Vector Control Research Centre, Medical Complex, Indira Nagar,  
Pondicherry – 605 006, India

I thank the Director, Vector Control Research Centre, Pondicherry for his continued support and facilities provided to address the issues related to the Lymphatic Filariasis Elimination. I declare that I have no conflicts of interest.

- 1 Sunish IP, Rajendran R, Mani TR, Dash AP, Tyagi BK. Evidence for the use of albendazole for the elimination of lymphatic filariasis. *Lancet Infect Dis* 2006; **6**: 125–26.
- 2 Tisch DJ, Michael E, Kazura JW. Mass chemotherapy options to control lymphatic filariasis: a systematic review. *Lancet Infect Dis* 2005; **5**: 514–23.
- 3 Sabesan S, Ravi R, Das PK. Elimination of lymphatic filariasis in India. *Lancet Infect Dis* 2005; **5**: 4–5.
- 4 Ramzy RM, El Setouhy M, Helmy H, et al. Effect of yearly mass drug administration with diethylcarbamazine and albendazole on bancroftian filariasis in Egypt: a comprehensive assessment. *Lancet* 2006; **367**: 992–99.
- 5 Manson-Bahr PEC, Bell DR. Soil-transmitted helminths. In: Manson's tropical diseases, 19th edn. London, UK: Bailliere Tindall, 1987: 407–46.
- 6 Bethony J, Brooker S, Albonico M, et al. Soil-transmitted helminth infections: ascariasis, trichuriasis, and hookworm. *Lancet* 2006; **367**: 1521–32.
- 7 Ottesen EA, Duke BO, Karam M, Behbehani K. Strategies and tools for the control/elimination of lymphatic filariasis. *Bull World Health Organ* 1997; **75**: 491–503.
- 8 Ottesen EA, Ismail MM, Horton J. The role of albendazole in programmes to eliminate lymphatic filariasis. *Parasitol Today* 1999; **15**: 382–86.
- 9 Cooper PJ, Chico ME, Vaca MG, et al. Effect of albendazole treatments on the prevalence of atopy in children living in communities endemic for geohelminth parasites: a cluster-randomised trial. *Lancet* 2006; **367**: 1598–603.
- 10 World Health Organization. Lymphatic filariasis. Fourth report of the WHO Expert Committee on Filariasis. *World Health Organ Tech Rep Ser* 1984; **702**: 3–112.