Mass treatment with ivermectin: an underutilized public health strategy

Rick Speare[1] & David Durrheim[1]

Ivermectin was a revolutionary drug in the 1980s, the forerunner of a new group of antiparasitic agents with activity against both parasitic nematodes and arthropods. Initially it was marketed for veterinary use by Merck & Co. Inc.; it was used largely for nematode control in cattle, horses, pigs and dogs and became the standard for control of the ectoparasitic disease, scabies. The injectable cattle formulation, Ivomec, became the world's most profitable veterinary drug (*1*).

Merck recognized Ivermectin's potential for human use, particularly in the control of filariasis and most notably onchocerciasis, the cause of river blindness in West Africa, in the early 1980s. In collaboration with WHO, nongovernmental organizations and affected national governments, the company initiated a drug donation programme for onchocerciasis control that subsequently became the global model for philanthropic partnerships between pharmaceutical companies and countries unable to afford the drug. Profits from the veterinary use of ivermectin supported this programme (*1*).

Merck's patent on ivermectin expired in 1996, though it was extended for different periods in various countries. Thus, other companies' ivermectin preparations are now commercially available. Bioavailability of drugs depends on formulation and manufacturing processes, so the results obtained with the ivermectin manufactured by Merck may not apply to the new products. It is thus encouraging to see clinical trials evaluating new formulations of this valuable drug.

Heukelbach et al. (pp.563–579) report a study that investigates changes in parasitological parameters and the occurrence of side-effects after treatment with ivermectin in a Brazilian community heavily parasitized with intestinal helminths and ectoparasites. The trial was unblinded and uncontrolled, but provided valuable information. Community members, ineligible for ivermectin, were treated with mebendazole, albendazole or deltamethrin to achieve a high level of coverage. Of particular importance was the finding that ivermectin was highly effective against *Strongyloides stercoralis*, with a 94% reduction in prevalence that was sustained for nine months. This provided field evidence for a paper that predicted that strongyloidiasis in heavily endemic communities could be successfully controlled with a highly effective drug, owing to its low transmission potential (*2*). The evidence presented by Heukelbach et al. adds considerably to evidence from smaller-scale controlled trials (*3–6*).

Ivermectin has valuable public health applications for controlling strongyloidiasis and scabies (by breaking the infection cycle through its therapeutic effect) and filariasis, through its effect on transmission. Ivermectin also acts against other intestinal nematodes, but it is not the most effective drug available. In control programmes for filariasis, ivermectin is the drug of choice in areas with onchocerciasis, but can be replaced by diethylcarbamazine for control of other filarial diseases.

Since ivermectin's use in the human field, adverse reactions occurred in 50% or more of the population (*7*) and ivermectin was "tainted" with a high adverse reaction profile, despite evidence that the majority of such reactions were attributable to the interaction between the drug and the disease, not to the drug itself (*8*). A number of follow-up studies have found that inadvertent filariasis mass campaign use of ivermectin during pregnancy has not been associated with adverse pregnancy outcomes or negative effects on pregnant women or their offspring (*9*). The lack of serious adverse events found in the study reported by Heukelbach et al. is reassuring, as the low incidence of minor adverse events fell from 14% after the initial treatment to 5% 10 days later.

It is time to capitalize on the full public health potential of ivermectin. Carefully designed studies to evaluate the efficacy of community-wide ivermectin-based control programmes for strongyloidiasis and scabies in developing countries are indicated, as are similar studies in marginalized communities in developed countries with high prevalences of these two diseases, including indigenous communities in Australia (*10*). ■

1. Collins K. Profitable gifts: a history of the Merck Mectivan donation program and its implications for international health. *Perspectives in Biology and Medicine* 2004;47:100-9.
2. Conway DJ, Lindo JF, Robinson RD, Bundy DAP. Towards effective control of *Strongyloides stercoralis*. *Parasitology Today* 1995;11:421-4.
3. Datry A, Hilmarsdottir I, Mayorga-Sagastume R, Lyagoubi M, Gaxotte P, Biligui S, et al. Treatment of *Strongyloides stercoralis* infection with ivermectin compared with albendazole: results of an open study of 60 cases. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1994;88:344-5.
4. Gann PH, Neva FA, Gam AA. A randomized trial of single- and two-dose ivermectin versus thiabendazole for treatment of strongyloidiasis. *Journal of Infectious Diseases* 1994;169:1076-9.
5. Toma H, Sato Y, Shiroma Y, Kobayashi J, Shimabukuro I, Takara M. Comparative studies on the efficacy of three anthelminthics on treatment of human strongyloidiasis in Okinawa, Japan. *Southeast Asian Journal of Tropical Medicine and Public Health* 2000;31:147-51.
6. Adenusi AA, Oke AO, Adenusi AO. Comparison of ivermectin and thiabendazole in the treatment of uncomplicated human *Strongyloides stercoralis* infection. *African Journal of Biotechnology* 2003;2:465-9.
7. Kipp W, Bamhuhiiga J, Rubaale T, Buttner DW. Adverse reactions to ivermectin treatment in *Simulium naevei*-transmitted onchocerciasis. *American Journal of Tropical Medicine and Hygiene* 2003;69:621-3.
8. Awadzi K. Clinical picture and outcome of serious adverse events in the treatment of onchocerciasis. *Filaria Journal* 2003;2 Suppl:S6. Available from: http://filariajournal.com/content/2/S1/S6
9. Gyapong JO, Chinbuah MA, Gyapong M. Inadvertent exposure of pregnant women to ivermectin and albendazole during mass drug administration for lymphatic filariasis. *Tropical Medicine and International Health* 2003;8:1093-101.
10. McCarthy JS, Garrow SC. Parasite elimination programs: at home and away. *Medical Journal of Australia* 2002;176:456-7.

[1] School of Public Health and Tropical Medicine, James Cook University, Townsville, Queensland 4811, Australia. Correspondence should be sent to Dr Speare (email: richard.speare@jcu.edu.au).

Ref. No. **04-015214**