mild inflammation. IF samples extracted on day 1 using greater negative pressure had lower protein concentrations than those extracted at a lower pressure, indicating an increased water fraction and an intact sieve function of the vascular wall. The differences were less pronounced on days 2 to 5. Extraction volumes were dependent on the extraction pressure on all days. The findings indicate the usefulness of the technique for clinical experimental purposes.

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Antihistamines in the Treatment of Mosquito-bite Allergy

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Dr. Ari Karppinen *(right)* defended his thesis on October 26, 2001 at the University of Tampere. Opponent was Docent Ilkka Harvima *(left)* from University of Kuopio, and Chairman Professor Timo Reunala.

Mosquitoes are important vectors of many diseases and, in addition, cause much nuisance by attacking man in many areas in the world. Skin reacts to the bites by whealing and also with delayed bite papules accompanied by pruritus. No efficient drug therapies have earlier been known for people seeking medical advice for their disturbing mosquito-bite reactions. Because whealing is mediated by mosquito antisaliva IgE antibodies, we wanted to study the effect of different antihistamines on the size of the mosquito-bite reactions and on pruritus in mosquito-bite sensitive adults and children (studies I-IV). The stud-

ies were placebo-controlled, cross-over type and included a total of 113 subjects challenged with *Aedes communis* mosquitoes in the field or *A. aegypti* mosquitoes in the laboratory. In addition, the effect of cetirizine 20 mg on inflammatory cells was examined from biopsy specimens taken from the lesions at 2, 6 and 24 h after the *A. aegypti* bites (study V). This study included 26 subjects who got either cetirizine or placebo in a parallel fashion.

The clinical study (I) performed in the field showed that cetirizine 10 mg decreased significantly the size of whealing and delayed bite papules, and also had a profound effect on accompanying pruritus. The second field study (II) performed with ebastine 20 mg showed a similar decrease in the size of whealing and accompanying pruritus than that found with cetirizine 10 mg. Ebastine decreased also pruritus at 24 h but did not show any significant effect on the size of the delayed bite papules. Study III was a placebo-controlled, cross-over study with *A. aegypti* laboratory mosquitoes in 25 mosquito-bite-sensitive children. The results showed that loratadine 0.3 mg/kg decreased significantly the size of wheals and also the size of the delayed 24 h bite papules. Pruritus could be evaluated at 15 min in 12 children and it also decreased significantly. In study IV the effects of the three antihistamines (cetirizine 10mg, ebastine 10 mg, loratadine 10 mg) were compared to each other and to placebo in 27 mosquito-bite-sensitive adults. This study showed that cetirizine 10 mg and ebastine 10 mg reduced significantly the size of wheals and pruritus caused by *A. aegypti* laboratory mosquitoes. A finding that cetirizine and ebastine seemed to have a more profound effect on the bigger than the smaller wheals could be of clinical importance, i.e. these antihistamines work best on subjects with intense bite reactions. Though loratadine 10 mg is the recommended dose in the treatment of pollen allergy and urticaria in adults, it seems obvious that a higher dose, e.g. 20 mg of loratadine, is needed to control effectively immediate mosquito-bite symptoms. Cetirizine caused more sedation than the other antihistamines but the difference was not significant.

The biopsy study (V) showed that the inflammatory cell response in the delayed mosquito-bite lesions is characterized by an early influx of eosinophils and neutrophils with a subsequent increase in the numbers of CD4+ lymphocytes. An unexpected finding was the effect of cetirizine on the inflammatory cell response. Overall, the median numbers of eosinophils and CD4+ cells were significantly increased in the cetirizine-treated subjects compared with the placebo-treated subjects. From this observation it was concluded that cetirizine does not inhibit cellular influx in the delayed mosquito-bite lesions but could possibly modulate eosinophils and CD4+ lymphocytes to become as inactive bystanders in the dermis.

The results of these placebo-controlled clinical studies clearly show that for mosquito-bite sensitive adults can be recommend prophylactically taken cetirizine 10 mg or ebastine 10 mg (20 mg) and for children loratadine (0.3 mg/kg). In Finland intense mosquito-bite allergy is now an official indication for treatment with second generation antihistamines.

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