

Sampling from a Suction-induced Mini-erosion in Human Skin

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Sampling from the interstitium is of interest as a complement, and in some cases as an alternative, to taking blood samples. In clinical medicine there is a need for non-invasive and painless ways to sample freely diffusible solutes such as glucose, which have to be measured frequently in subjects with diabetes and in newborns. In experimental medicine, sampling of interstitial fluid (IF) is of interest as it represents the fluid that actually surrounds the cells in the tissues. With the blister suction technique a blister is formed with the split between epidermis and dermis. Thus the roof of the blister consists of epidermis. The dermal IF is accessed by collecting the content of the blister. The safety of this method is already established, based on widespread experimental use. The sampling technique, used in the thesis, uses the suction blister erosion as sampling site. The epidermal barrier is replaced by an occlusive film to prevent dehydration, allowing samples to be extracted serially from the site by suctioning.

In the thesis, the feasibility of using IF extraction by suction for serial measurement of glucose and for monitoring metabolites in IF during



Christer Svedman (*right*) defended his thesis on May 21st, 2001 at Malmö University Hospital, Sweden. Faculty Opponent was Ass. Prof. Urpo Kiistala (*left*), University of Helsinki, who described the suction blister technique in 1967. Chairman was Prof. B. Jepsson, Dept. of Surgery, Malmö University Hospital. Prof. B. Rippe, Dept. of Nephrology, Lund University Hospital, Ass. Prof. S. Polberger, Dept. of Pediatrics, Lund University Hospital, Ass. Prof. B. Alsbjörn, Dept. of Plastic and Reconstructive Surgery, Rigshospitalet, Denmark were faculty reviewer.

an oral glucose tolerance test (OGTT) was assessed. The changes in IF composition with regard to a number of plasma proteins in a wide size range (6–720 kDa) were studied over several days and finally, the effects of varying the sample extraction pressure were determined.

IF was extracted serially and painlessly for as long as 6 days. Sample volumes exceeded those required for measuring a wide range of biological substances. Epidermal regeneration was rapid. There was no scar formation, but a transient hyperpigmentation could be seen at the sampling site for several weeks.

Glucose concentrations in IF and plasma, measured in diabetic and non-diabetic subjects for as long as 6

days, were closely correlated over a wide range of values. During oral glucose tolerance tests on days 1 and 3 after forming the erosion, the OGTT curves for glucose, 3-hydroxybutyrate and glycerol were similar to plasma. IF lactate curves were higher than those in plasma, reflecting glycolytic activity, whereas insulin curves were lower, reflecting the vascular permeability. A potential is suggested for clinical sampling of glucose in subjects with diabetes mellitus, and for experimental monitoring of dermal metabolism.

The IF concentration of plasma proteins (size 6–720 kDa) measured in IF on day 1 in healthy volunteers was consistent with findings obtained with other techniques. From day 2 to 5, sample fluid reflected a steady state of increased permeability induced by

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 in-

dicate the usefulness of the technique for clinical experimental purposes.

List of original publications

- I. Svedman P, Svedman Ch. Skin mini-erosion sampling technique: feasibility with regard to serial glucose measurement. *Pharm Res* 1998; 15: 883-888.
- II. Svedman Ch, Samra JS, Clark ML, Levy JC, Frayn KN. Skin mini-erosion technique for monitoring metabolites in interstitial fluid: its feasibility demonstrated by OGTT results in diabetic and non-diabetic subjects. *Scand J Clin Lab Invest* 1999; 59: 115-123.
- III. Svedman Ch, Yu BB, Ryan TJ, Svensson H. Plasma proteins in a standardized skin mini-erosion (I): permeability changes as a function of time. Submitted to *Dermatology*, 2001.
- IV. Svedman Ch, Yu BB, Ryan TJ, Svensson H. Plasma proteins in a standardized skin mini-erosion (II): effects of extraction pressure. Submitted to *Dermatology*, 2001.

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Antihistamines in the Treatment of Mosquito-bite Allergy

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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 mos-



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.

quito 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-