

Jorfeldt L, Löfström B, Pernow B, Persson B, Wahren J & Widman B. The effect of local anaesthetics on the central circulation and respiration in man and dog.

Acta Anaesthesiol. Scand. 12:153-69, 1968.

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In this study, subconvulsive (in man and dog) and convulsive (in dog) infusions of the local anaesthetics mepivacaine, bupivacaine, and lidocaine were administered, and the effects on central circulation and respiration studied. We failed to demonstrate a depressive action of the local anaesthetics and instead saw a slight stimulatory one. [The *SCI*® indicates that this paper has been cited in over 120 publications.]

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Early in the 1960s, Widman and I discussed a research project to elucidate the circulatory and respiratory effects of local anaesthetics, a project intended to provoke Widman to write a doctoral thesis. The general idea was to infuse IV local anaesthetics in man (subconvulsive dose) and dog (subconvulsive and convulsive dose) while taking repeated measurements of circulatory and respiratory parameters. We realized that to obtain the best possible results it was of extreme importance to have professional clinical physiologists in our team. So Pernow and Wahren joined in and appointed Jorfeldt to be our "slave." Jorfeldt, undergoing training to become a clinical physiologist, also had the merit of some training in anaesthesiology.

However, two more problems remained to be solved. The crossover studies on dogs had to be done without the assistance of sedatives or anaesthesia, as we had strong suspicions that the de-

pressive effects ascribed to local anaesthetics were caused more by the sedation than by the local anaesthetic itself. We found Persson, a PhD at the Veterinary University of Stockholm, who had four dogs trained to take part unpremedicated in all kinds of experiments. Finally, as a site for our work, we were allowed to carry out the dog experiments at the Serafimer Hospital.

What were the important results? The study failed to show any circulatory or respiratory depression, even in the dogs who convulsed during the infusions of mepivacaine and bupivacaine. Signs of brain stimulation and, to some extent, stimulation of the circulation were the earliest toxic symptoms. We also obtained a rough idea of toxic plasma levels for the three drugs studied and learned an important lesson about species differences, as the dog's plasma level at the end of the subconvulsive infusion was only half that of man.

What was good about the study? It was professionally carried out. Jorfeldt *et al.* continued as a group for years and no longer stuck to the Scandinavian physiologist's most sacred rule that authors should be placed in alphabetic order. In a subsequent paper,¹ we obtained results indicating that local anaesthetic stimulates vascular smooth muscles producing a decrease in volume and compliance of the venous system as well as a peripheral arterial constriction when infused intra-arterially. The general circulatory effect described seems to lead to an increased muscle blood flow,² one of several likely explanations of the anti-thrombotic effect today correlated to extradural blockade.

Widman defended his medical thesis early in the 1970s with the highest marks.³

1. Jorfeldt L, Löfström B, Pernow B & Wahren J. The effect of mepivacaine and lidocaine on forearm resistance and capacitance vessels in man. *Acta Anaesthesiol. Scand.* 14:183-201, 1970.
2. Löfström J B, Thorborg P & Lund N. Direct and indirect effect of some local anaesthetics on muscle blood flow-tissue oxygen pressure. *Regional Anesthesia* 2:82-7, 1985.
3. Widman B. *Clinical and experimental studies on local anaesthetics with special reference to bupivacaine.* PhD dissertation. Linköping, Sweden: Linköping University, 1973. 44 p.