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This Week's Citation Classic

Nilsson I M & Olow B. Fibrinolysis induced by streptokinase in man.
Acta Chir. Scand. **123**:247-66, 1962.
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The authors administered various doses of streptokinase (SK), SK plus plasminogen, and SK plus EACA in a series of 67 surgical patients. SK produced a high fibrinolytic activity, but had a significant effect on the coagulation factors. It proved possible to counteract the coagulation defect by SK combined with EACA without affecting the lysis of the clot. [The *SCI*® indicates that this paper has been cited over 240 times since 1962.]

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"It was very gratifying to learn that our paper has been identified as one of the most cited articles in its field. If I ask myself why, I think it has been cited mainly because it contains detailed descriptions of various methods for assessing fibrinolysis, methods which were either not available at that time or not properly standardized. I had for some years been interested in haemophilia and von Willebrand's disease. The idea of the project was conceived at a dinner party with some colleagues in 1959. One of the guests was Bertil Olow, a skillful surgeon who had not yet received his MD. In the course of the evening it was suggested that it was about time that he thought of doing so, and I was asked to propose some suitable subject for his thesis. As he was a surgeon and I was a 'coagulationist' we thought that thrombosis would be the most suitable field.

"In 1958 Johnson and McCarty were the first to report that artificially induced thrombi in human volunteers could be lysed by infusion of purified SK preparation.[1] Such a preparation (Kabikinase) became available in Sweden in 1959. An investigation of thrombolysis by SK in man was therefore decided upon as the subject of the thesis. After some methodological studies we were able to publish methods for determining the fibrinolytic activity on fibrin plates, euglobulin clot lysis time, fibrinogen, fibrinogenolytic activity, plasminogen and the initial dose (TID) of SK. All together 93 infusions of SK were given to 67 patients. Infusion of one TID of SK produced only a brief and moderate increase of the fibrinolytic activity without any appreciable variation of the coagulation factors. The fourfold TID of SK caused an impressive rise of the fibrinolytic activity with a simultaneous clear decrease of fibrinogen, plasminogen, and factor V. Addition of plasminogen to the SK did not change the response. However, it proved possible to counteract the coagulation defect by supplementary administration of a fibrinolytic inhibitor, E-amino caproic acid (EACA), without undue depression of the thrombolytic effect. I do not think that the popularity of the article can be ascribed to the actual investigation of streptokinase, but rather to the descriptions of the methods. The results obtained hold good today. Despite the intensive research during the last ten years in this field, no agreement has been reached on the optimum dosage or duration of treatment.

"This investigation stimulated my interest in fibrinolysis, which besides von Wille-brand's disease is now one of the most important research fields at our laboratory. Olow published further articles on SK.[2] After having received his MD, Olow was appointed chief surgeon at a large general hospital (Angelholm). I myself have since become a professor in coagulation research and head of the coagulation laboratory at the General Hospital in Malmö and am working full-time with coagulation and fibrinolysis."

1. **Johnson A J & McCarty W R.** Lysis of artificially induced intravascular clots in man by intravenous infusions of streptokinase. *J. Clin. Invest.* **37**:905, 1958.
2. **Olow B, Johanson C, Andersson J & Ekelöf B.** Deep venous thrombosis treated with a standard dosage of streptokinase. *Acta Chir. Scand.* **136**:181-9. 1970.