reported since then. The first, reported by Dewar, Horler, and Cassells-Smith, in 1961, where the treatment was always given within 12 hours and on average in about six, gave wholly negative results. Two more in 1963 (Dewar, Stephenson, Horler, Cassells-Smith, and Ellis) and in 1966 (Menon and Dewar) in which treatment was begun later also gave negative results. Details are now given of another trial, organized internationally by Professor Verstraete and his colleagues, in which we took part, where treatment was begun up to 72 hours after onset and was controlled very carefully for both potency and safety. The two groups of carefully randomized patients comprising 84 treated and 83 controls proved to be fully comparable in all important respects. The treated group unfortunately developed significant side effects from the drug, notably fever, back pain, and bleeding, and the mortality figures were no better than in the controls. The only trials which have given convincing evidence of beneficial effect from a streptokinase preparation have been those of Poliwoda, Diederich, Schneider, Rodenburg, Heckner, Körtge, van de Loo, Pezold, Praetorins, Schmutzler, and Zekorn (1966). They can be accused of unsatisfactory randomization, but do nevertheless suggest that where treatment can be so organized as to begin within three and a half hours a definite beneficial effect can be expected, but not during the first 24 hours of treatment.

Evidence was presented as to why it is difficult to institute treatment early and of how large is the initial and hitherto unavoidable mortality. It is suggested therefore that the thrombolytic approach to coronary thrombosis may prove to be more successful when based on the prophylactic enhancement of the fibrinolytic activity of the blood of susceptible persons.

REFERENCES

- Dewar, H. A., Horler, A. R., and Cassells-Smith, A. J. (1961). *Brit. med. J.*, 2, 671.
 —, Stephenson, P., Horler, A. R., Cassells-Smith, A. J., and Ellis, P. A. (1963). *Ibid.*, 1, 915.
 Menon, I. S., and Dewar, H. A. (1966). As part of an international trial organized by Professor Verstraete, Universiteitsklinieken, Leuven, Belgium.
 Poliwoda, H., Diederich, K. W., Schneider, B., Rodenburg, R., Heckner, F., Körtge, P., van de Loo, J., Pezold, F. A., Praetorins, F., Schmutzler, R., and Zekorn, D. (1966). *Dtsch. med. Wschr.*, 21, 978.
 Rueggsegger, P., Nydick, I., Hutter, R. V., Freiman, A., Bang, N. H., Clifton, E. E., and LaDue, J. S. (1959). *Circulation*, 19, 7.

EXPERIENCES WITH INTRAARTERIAL STREPTOKINASE PERFUSSION IN THE TREATMENT OF ACUTE ARTERIAL THROMBOSIS

A. BOSE, S. S. BROSE, AND G. HARTLEY (*Departments of Surgery and Radiology, Withington Hospital, Manchester*) This paper describes our experiences over the past 18 months with streptokinase in the treatment of the severely ischaemic limb.

Initially, we used thrombolytic therapy in 11 cases of poor risk advanced atherosclerotics who presented with severe pain at rest and incipient gangrene. Many had been treated unsuccessfully or successfully for a time with direct arterial surgery, lumbar sympathectomy *etc.*, and were presenting with the end result of a long battle to

preserve their peripheral circulation. Four were given intravenous streptokinase, 1.2 million units over a 24-hour period; the other seven were given a continuous intraarterial perfusion for 48 hours during which they received a total dose of streptokinase of between 0.25 to 0.75 million units. In this first series of 11 cases, our results were uniformly disappointing: we had two deaths, five major amputations, and the remaining four cases initially showed slight improvement but relapsed within six weeks.

The twelfth patient was a 47-year-old obese woman who had undergone a pelvic operation and had post-operatively developed a massive collapse of the left lung with peripheral circulatory collapse. She was hypotensive and lay on her side for a considerable period of time. Twelve hours after operation she was found to have an ischaemic painful left hand with ascending oedema of the arm and absent radial and brachial pulses. A stellate ganglion block and anticoagulants did not improve her condition over the next eight hours. A long Teflon catheter was threaded in retrograde fashion via the right femoral artery into the aortic arch and its tip engaged in the origin of the left subclavian artery. Two million units of Kabikinase in 2 litres of normal saline to which 2,400 mg of lincomycin was added was infused over 18 hours. Ten hours later a faint radial pulse appeared and by 15 hours the colour of her hand improved considerably, the acute pain was diminished, and the radial pulse was full and bounding. Her subsequent recovery was uneventful and with physiotherapy she regained the full use of her hand by the end of three weeks.

Thereafter we tried to standardize our regimen of thrombolytic therapy in arterial thrombosis. First we restricted streptokinase perfusion to the cases of acute or acute-on-chronic thrombotic episodes. Secondly, in the acute cases, we gave a continuous intraarterial perfusion over 24 to 48 hours of a litre of normal saline containing 1.2 million units of Kabikinase and 1,200 mg of lincomycin every 12 hours. Thirdly, in the less urgent acute-on-chronic episodes, we gave a continuous intraarterial perfusion for 48 to 72 hours during which thrombolytic therapy was given intermittently by alternating, each 12 hours, a litre of normal saline containing streptokinase and lincomycin with a litre of Lomodox (low molecular weight dextran 40,000) containing thymoxamine (Opilon) 160 mg and lincomycin 1,200 mg.

Initially we used hydrocortisone systemically before and during perfusion but subsequently found this was not necessary. We did not use any laboratory control.

Of the last 36 cases, 11 showed side reactions of variable degree but none warranted discontinuation of perfusion. The complications broadly fell into two main groups. Firstly, bleeding at the site of arterial puncture (six cases) ranging from ecchymosis (two cases), persistent ooze (two cases), subcutaneous extravasation (one case), to haematoma (one case). Secondly, pyrexia over 100°F in five cases which persisted during perfusion only; this was not troublesome except in one patient who had rigors, arthralgia, and pain in the back which lasted during perfusion.

As assessed clinically and observed by peripheral circulatory studies, all 36 cases showed improvement, a few very dramatically. There have been no deaths, no major amputations, and six months after the last perfusion, all have remained well although one case required a minor foot amputation.

ADDENDUM

D. R. BANGHAM (*Division of Biological Standards, National Institute for Medical Research, London*) The biological activity of several of the substances mentioned in these discussions is estimated in terms of, *ie*, by direct

comparison with, a reference material. The use of a common reference preparation, or at least the unit defined by it, will do a lot to make valid the comparison of results from different laboratories and from time to time in the same laboratory.

Participants may be interested to know that an international reference preparation of urokinase was recently established. It will thus be possible to describe the potency of a preparation of urokinase in international units as it is done already for streptokinase in terms of the international standard for streptokinase. Unofficial research reference materials for other components of the fibrinolytic and clotting systems are under preparation.

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