Introduction

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Microcirculation and Leg Ulcers

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Venous diseases of the lower limb are very common, with a prevalence of 10-20% of the adult population, and in Europe drugs are widely used to treat these. Many of these drugs were developed and used without detailed knowledge of their mechanisms of action. Recent research has uncovered many details of the biological processes at work in blood vessels. This has led to a revolution in the understanding of ischaemia and atheroma formation. It has been found that many of the mechanisms responsible for ischaemia reperfusion injury are also involved in the development of skin damage and ulceration in patients with chronic venous disease of the leg. The symposium included in the pages that follow was originally presented to the VIth World Microcirculation Congress in Munich on 29th August 1996. The articles in it review the effect of a widely used phlebotropic drug, Daflon® 500 mg, on several models of tissue ischaemia. The animal models selected are well known and widely used in the study of ischaemia as well as in testing various interventions to protect against ischaemia reperfusion injury. The data show that there is a substantial, easily measurable effect of Daflon 500 on endothelial-leucocyte interactions caused by ischaemia reperfusion injury. These are similar to the effects of some well-known methods of preventing endothelial injury, such as the use of antibodies to the leucocyte ligand CD11b. These are certainly interesting and unexpected findings. The severity of ischaemia reperfusion injury is generally very great and important cellular mechanisms must be inhibited to modify this process. It is fascinating to see that Daflon 500 has the ability to achieve measurable effects in such models. Tissue damage caused by venous disease is usually more insidious, slowly destroying the endothelium of the skin microcirculation in the leg over a number of years. How-

ever, it is now clear that many of the same processes are at work in patients with ambulatory venous hypertension to produce damage in the skin microcirculation. It would be very interesting to discover whether Daflon 500 could modify the same mechanisms in patients with venous disease. Clearly different methods of investigation would be required, but such studies would confirm the reasons for the efficacy of Daflon 500 in the management of venous disease.

The last two papers in this symposium discuss the results of treatment in 2 different groups of patients. In neither group has the leucocyte response been assessed in detail, although a number of rheological factors have been measured by Dr. Le Dévéhat. He investigated a group of patients with mild venous symptoms and recorded a small influence of Daflon 500 on the parameters he investigated. In contrast Prof. Nicolaidis reports the efficacy of Daflon 500 on venous ulcer healing. Despite the fact that only a small group of patients was studied, large differences in the rate of ulcer healing between the placebo- and Daflon 500-treated groups were observed. Although this pilot study was only of 8 weeks duration, the preliminary data from this

work suggests that Daflon 500 may result in improved venous ulcer healing. Clearly, further work must be done to confirm that Daflon 500 also modifies leucocyte-endothelial cell interaction in patients with severe venous disease and that this is the explanation for more rapid ulcer healing. The observations in the leg ulcer study should be confirmed in a larger trial with longer patient follow-up.

This symposium reports important new data concerning the mode of action of Daflon 500. These data suggest new mechanisms by which this drug is helpful in the management of venous diseases.

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