Do leukocytes have a role in the cerebral no-reflow phenomenon?

Aspey et al. failed to demonstrate any difference in either the incidence or severity of the no-reflow phenomenon induced by severe cerebral ischaemia in gerbils rendered leucopenic by pretreatment with cyclophosphamide as compared to controls. The authors have suggested that the absolute number of leukocytes is of limited value in the no-reflow phenomenon. We would like to make the following points: first, it may be invalid to compare data derived from humans suffering from focal ischaemia, and probably having coexistent atherosclerotic disease, to that obtained from an experimental model of bilateral hemispheric ischaemia in gerbils with an intact cerebral circulation. Secondly the results do not take into consideration the qualitative role of leukocytes in ischaemia, that is, ischaemic related no-reflow phenomenon induced by activation of blood cells and the role of the individual leukocyte subpopulations during ischaemia. Furthermore, comments on the subtype of blood cell responsible for plugging of capillaries are not valid given the method used.

Our own interest in leukocytes and cerebral ischaemia led us to study the rheological behaviour of blood cell subpopulations, that is, red blood cell, granulocyte and mononuclear leukocytes, in 20 males suffering from acute cerebral infarction compared to 20 age-matched healthy controls. The filterability of blood cells, separated using Ficoll-Hypaque density gradient after centrifugation, were determined following the technique of Lennie et al. This method enables investigation of blood cell subpopulations under similar conditions and above all, results are unaffected by the number of cells, platelet contamination, or plasma protein interactions. Filterability is expressed as a pressure ratio of cell suspension to buffer after six minutes filtration. Our results suggested that mononuclear leukocyte and granulocyte filterability was impaired in cerebral infarction [7-26 (SD) 2 and 5.75 (SD) 0.87 respectively] compared to controls [5.55 (SD) 1.23 and 4.19 (SD) 0.43], while no differences existed in red blood cells. Furthermore we have obtained similar results in a human model of treadmill-induced, controlled ischaemia in stage II peripheral artery disease and coronary artery disease (unpublished material). These studies provide evidence that leukocytes are functionally altered under ischaemic conditions.

The mechanism leading to the altered filterability of leukocytes during ischaemia is not fully understood. It has, however, been suggested that leukocyte activation may occur as a consequence of ischaemia and may contribute to the ischaemia by releasing vasoactive substances and mechanically obstructing capillaries. Furthermore, activation of the cells impairs their filterability.

This hypothesis concurs with our results since the filtration procedure measures the ability of cells to pass through the pore-filter, whose diameter of 5 microns approximates the diameter of capillaries. We feel an important issue is the nature of leukocyte activation in the pathogenesis of the no-reflow phenomenon. While Aspey et al. have studied the role of the absolute leucocyte count, they have not considered leucocyte behaviour. It would be important to assess the filterability or the percentage of activated cells in the neutrophilic compared to the control group. It may be that only a small number of activated leukocytes are required to contribute to the no-reflow phenomenon.

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Dr. Aspey et al. reply: We were interested to see the in vitro results of reduced leukocyte filterability following stroke reported by Mercuri et al. We accept that our results do not address the issue of leukocyte activation during cerebral ischaemia. What we have shown is that a behavioural change in any subpopulation of leukocytes is of pathological significance in the brain. Only interventional studies are likely to achieve this as has been attempted in the case of experimental myocardial ischaemia where reducing total leukocyte number improves post-ischaemic perfusion. Our failure to show a parallel change in the brain is possibly due to the microcirculations of brain and heart differ in their responses to ischaemia.

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The escalating number of medical negligence claims and the delays, costs and uncertainties of the present legal process have led the four editors, two surgeons and two lawyers, all from Kansas, to put forward their proposals to replace the current legal process with the Model Medical Accident Compensation Act. They are assisted by eleven other contributors, four doctors, five lawyers and two in the field of finance and insurance. The solution to the problem is proposed in the setting of United States law but richard smith (Senior Assistant Editor of the British Medical Journal) describes the present situation in Great Britain, Diana Braham (legal correspondent of The Lancet), describes the Swedish and Finnish patient insurance schemes, and Sir Owen Woodhouse (Chairman of the Royal Commission on Compensation and Rehabilitation for Personal Injury in New Zealand) describes the experiences in that country.

The first four chapters deal with the history and development of the law of tort and of the tort that this has had upon medical care in the United States and in this country. The second part of the book deals with other proposals which involve a greater or lesser degree of reform of the existing legal system or its replacement by arbitration. Part three deals with the systems of arbitration which exist in New Zealand, Sweden and Finland, and also the workers compensation statutes in which the claimants’ rights to access to courts and the courts’ liability has been laid aside in favour of prompt, equitable and certain compensation.

The details of the Model Medical Accident Compensation Act are then set out in some detail but with reasonable clarity and are followed by expert speculation on the financial consequences of the proposal. The concluding chapter returns to the important question of the constitutionality of the proposals, and the “trade-off” of the constitutional right of the individual to seek redress in the courts, against the greater speed and certainty of the proposed Model Act.

For the reader not well versed in law the text is not easy going but it is by no means insuperable, thanks to the layout of the chapters and their clear division under sub-headings, together with conclusions and, in some cases, a brief introduction from the editors. There are numerous references mainly to American legal literature, and the index is comprehensive.

John Evans


This volume provides a workman-like compendium to every detail of the techniques of...