Editorial: Neovascularisation

A simple algorithm (‘rule for solving a mathematical problem in a finite number of steps’—Chambers Twentieth Century Dictionary) for disease might run something like this: Attack→Response→Destruction→Repair→Outcome. If you were to try to fit neovascularisation neatly into this flow-chart, you would find that it could feature in more than one section: it might be part of the response, it may certainly be part of the repair, and it may undoubtedly (in the eye), by virtue of the fragility and hence tendency of the new vessels to bleed, profoundly affect the outcome. Yet it is strange that this absolutely basic component of pathology’s mechanism, which ought to rank with equal importance with the triad inflammation, neoplasm, and degeneration has hitherto not been recognised as being in the same league.

Understanding of the mechanisms of pathological neovascularisation has advanced rather slowly during the last 38 years, beginning with the observation of Michaelson in 1948 that a factor promoting vascularisation was probably present in the retina. Next in the historical sequence came retrolental fibroplasia (now retinopathy of prematurity), in which Ashton Ward and Serpell first demonstrated that the closure of retinal vasculature, paradoxically induced by the very element from which the retina was eventually to suffer lack, namely oxygen, initiated the later proliferative phase. This was followed soon afterwards, as the result of observation of the natural history of neovascularisation of the iris following central retinal vein occlusion, by the suggestion that neovascularisation on the iris was also the consequence of retinal anoxia and was mediated by a diffusible ‘metabolite which stimulates new vessel formation.’

The matter does not of course end here. Neovascularisation, by virtue of its accompanying fibrosis, causes retinal destruction in the posterior part of the eye and glaucoma in the anterior, but it also has another aspect which was not initially recognised but is now obvious. Neovascularisation in the eye leads to bleeding, and in this context we have two more major categories of ocular pathology where this fundamental mechanism is almost certainly involved—diabetic retinopathy and disciform macular degeneration.

It is difficult to be certain at what point in time it came to be realised that preretal and intravitreal haemorrhage, which eventually leads to retinal destruction in diabetes, was due specifically to the rupture of new-formed capillaries (as opposed to previous somewhat vague theories that bleeding came from ‘congested’ veins). It seems likely that it must have occurred some time in the late 1950s or early 1960s. So the sequence is retinal anoxia (or ischaemia), liberation of a diffusible substance, neovascularisation, either near the retinal lesion or at a remote site, and finally bleeding, with its consequences of fibrosis and ‘repair.’ This may be beneficial in a fracture or a skin wound but it spells disaster in the eye.

The various elements in the story have come to light gradually, first the initial theory in 1954, then the early evidence of benefit to rubecosis by destroying a wide area of retina by diathermy in 1961 and to diabetic retinopathy by light coagulation in 1965, though the authors of this paper were actually attempting to obliterate neovascular tissue itself. The first mention of light coagulation being used for its ‘indirect’ effect on neovascularisation (which is the mechanism widely accepted today) appears to have been in 1964 by Meyer Schwickerath just 10 years after the original retinal anoxia hypothesis. The next important step was the demonstration of retinal ischaemia following central vein occlusion by Laatikinen and Kohner in 1976 by means of fluorescein angiography.

Now a further link in the chain may have been forged. In a paper in this issue Taylor, Weiss, Kisson, and Garner produce evidence to suggest that they may have identified the ‘metabolite which stimulates new vessel formation’ in the eye, first postulated over 30 years ago. We congratulate the authors on their achievement and await with the greatest interest further studies which may confirm their important observations.

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References