Myocardiocyte loss due to apoptosis

The findings presented by Dispersyn et al. (June 2002 issue) on dedifferentiation and apoptosis of myocardiocytes late after AMI were extremely interesting. The presence of both myocardiocytes with metabolic rearrangement (‘dedifferentiated’ or ‘hibernated’) and cells committed to programmed death (apoptotic) in this experimental model of post-infarction left ventricular remodelling in sheep suggests that both these mechanisms are possible cellular responses to ischaemia.

However, a major issue is the effective myocardiocyte loss due to apoptosis. The data presented by the authors on myocardial apoptosis substantially confirm results presented earlier in a similar model of multiple AMI in dogs (0·12% of apoptosis in the former and 0·53% in the latter), while they appear strikingly different from our recent data in post-mortem human hearts. We have recently shown that the apoptotic rate is as high as 25% in the infarcted area of the hearts of human subjects who died 12 to 62 days after an AMI. A comparison of the two studies reveals a nearly 200-fold increase in our samples compared to the data by Dispersyn et al. Could these differences be due to selection biases in both studies? Perhaps yes.

We believe that estimates of apoptotic rates may show quite different results in hearts of individuals dying spontaneously compared to animals surviving and being killed. In facts, our results may have been biased by the selection of a population with a significantly poor prognosis (median time to death 23 days), who may have been associated with extremely elevated rates of apoptosis. On the other hand, Dispersyn et al. may have selected individuals who were relatively protected from apoptosis with a more favourable prognosis (the sheep with a 50% reduction in left ventricular ejection fraction were allowed to survive longer after AMI and showed significantly lower apoptotic rates at sites of infarction).

An accurate definition of the factors promoting death or survival should lead to a more complete understanding of the variability observed in experimental animal models and human observational studies. Indeed it is possible that some individuals are relatively protected from apoptosis, surviving longer after AMI and showing only low grade apoptosis and a very low rate of transition from metabolic rearrangements to commitment to death, as in the cases presented by Dispersyn et al.

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Danesh and colleagues have examined the relationship between markers of chronic infection and incidence of heart disease in a number of studies. They report in a March 2002 issue a further analysis of data from the British regional heart study[1]. I wonder whether it may be a little misleading to subtitle this as a ‘prospective study’. The ‘24 towns’ study, set up by Gerry Shaper and colleagues, was a prospective study of risk factors for heart disease in men and the original investigators had the foresight to store blood for later analysis to test new hypothesis[2–3]. The present paper describes a ‘nested case-control study’ undertaken retrospectively on a proportion of the men, included in the original and for whom stored blood was available for analysis. It is not clear what proportion of incident heart disease ‘cases’ was analysed and hence whether there was possibility of bias.

I wonder also whether it may be misleading to summarize the findings as ‘Neither IgA nor IgG titles are strongly predictive in a general population’ (conclusion and abstract). The present paper reports on IgA, and Fig. 1 pools studies that have reported on IgA. While it may be true that the present pooled ‘odds ratio (1:25 for IgA) is compatible with the previously reported pooled odds ratio of 1:15 for IgG and not significant’ (my parentheses), the analysis reported here derives a highly significant odds ratio of 1:76–1:85 depending on degree of adjustment, or 2:21 in men, without evidence of CHD at baseline, from the ‘24 towns’ study (Table 3) and presents a statistically significant pooled odds ratio of 1:25 in the meta-analysis. Furthermore the three studies that contribute almost all the weight to the pooling were of men.

There would appear to be some inconsistency between the significant association with IgA observed in 502 cases vs 1005 controls in this paper and some non-significant relationships (after similar adjustments) with IgG reported previously in nearly the same material from the 24 towns study (496 cases vs 989 controls, Table 3 in BMJ article[4]).

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References