ventricular septal defect is therefore required. Moreover, longitudinal follow-up of these patients will have to clarify the time course within which this lesion is formed and eventually progresses. Finally, it remains to be demonstrated that the ridges described can give rise to significant outflow tract obstruction with important pressure gradients.

The observations by Özkutlu et al. are very important for the clinical follow-up of patients with a doubly committed ventricular septal defect. A careful echocardiographic examination with special attention to the outflow tracts is required. Moreover, when surgical ventricular septal defect closure is considered, special attention should be given to the presence of subarterial ridges which need to be removed at the time of surgery. Pre-operative colour Doppler examination should thereby focus on the origin of flow turbulence in outflow tracts (e.g. the presence of hypertrophiied muscle bundles), so that they can be resected at the time of surgery.

For vascular biologists it remains challenging to unravel the link between haemodynamics and cardiovascular response. The surge of endothelial biology with identification of a vast array of different vaso-active and growth factors will probably provide new means for therapeutic intervention.

References


The report of Wesslén et al.\(^1\) is of great interest because the unexplained deaths of young and presumably healthy persons is extremely dramatic and arouses the concern of the medical community. Nevertheless, several issues have to be addressed. As we know from other studies, an organic disorder constitutes the basis for the pathogenesis of aborted sudden death or sudden death in most cases of previously apparently healthy young people. Electrical instability due to ventricular tachyarrhythmia is the cause of cardiac arrest in most instances\(^2\)\(^–\)\(^4\). Myocarditis is one of the potential causes of sudden cardiac death in the young. In previous studies, an incidence of up to 22\% has been demonstrated\(^3\). This is somewhat lower than that in the population reported by Wesslén et al. Besides an infection of the myocardium by \textit{Chlamydia pneumoniae}, other exogenic factors may also account for this increased incidence of myocardial inflammatory reaction in the study population. For example, the use of cocaine has been identified as an agent which can precipitate cardiac disorders, including myocardial infarction, life-threatening ventricular arrhythmias and myocarditis\(^3\). Additionally, methodological aspects have to be considered. The inter-observer variability in assessing histopathological samples for active and especially in cases of ‘healed’ or ‘probably healed’ myocarditis makes a reliable comparison between the incidence in different studies difficult.

The presented study population represents a heterogeneous cohort with respect to their previously reported clinical symptoms and other cardiovascular abnormalities, giving rise to further speculation on the individual causes for the fatal events. The athlete with previously diagnosed Wolff–Parkinson–White syndrome may well have experienced sudden cardiac death due to atrial fibrillation with rapid anterograde conduction via an overt accessory pathway and subsequent degeneration into ventricular fibrillation\(^3\). This is a rare but well known mechanism of cardiac arrest in these patients. In one case, arrhythmogenic right ventricular dysplasia was the substrate for recurrent ventricular tachycardia. This subject, who already had the clinical manifestation of right ventricular disease, as well as three others with only histopathological features consistent with arrhythmogenic right ventricular dysplasia, had an increased risk of dying suddenly\(^5\). Furthermore, five other athletes had ECG abnormalities during the repolarization phase with or without previous syncope during exercise. These findings may be suggestive of ‘athlete’s heart’ but may also be consistent with hypertrophic cardiomyopathy, probably the most common cause of cardiac death in young athletes\(^4\), or arrhythmogenic right ventricular disease\(^5\).

Although \textit{Chlamydia pneumoniae}-associated infection of the heart\(^7\) has been reported previously, the authors could not prove a link between serological and histopathological findings. So far it has not been possible directly to reveal the presence of the organism within the diseased myocardial cells, but it may be possible to achieve this by immunocytochemistry or in situ hybridization. Another option is the use of polymerase chain reaction which was apparently performed in two persons with a primer set directed to the rRNA gene of \textit{Chlamydia pneumoniae}. However, the result was inconsistent because only one primer was positive. To our knowledge these techniques have not been used so far to identify \textit{Chlamydia pneumoniae} within a biopsy specimen of myocardial cells. The significance of these tests is of course limited by the autolytic process and simply the time interval between death and microbiological investigation. However, it seems to be worthwhile performing these kinds of investigations in order eventually to verify myocardial infection with this organism, especially because there is no doubt that all subjects in whom serological tests were performed had had previous contact with \textit{Chlamydia pneumoniae}. This organism is known to be responsible for widespread epidemics in Scandinavian countries\(^7\). Nevertheless, the difference between orienteers who die suddenly and asymptomatic athletes with IgG antibodies directed against \textit{Chlamydia pneumoniae}, who served as a control group, remain unclear. Furthermore, the striking incidence of \textit{Chlamydia pneumoniae}-exposed orienteers as compared to other endurance athletes in the same geographic region has to be further elucidated.

Several individual independent factors predisposed to an increased risk of sudden cardiac death were present in the study population. Nonetheless, one has to keep in mind the important histological and serological findings of the study. Further attempts are urgently warranted to demonstrate the association between sudden cardiac death, inflammatory reaction of myocardial cells and a potential \textit{Chlamydia pneumoniae} infection of the myocardium. Therefore, the authors should be encouraged to continue their investigations to prove their important hypothesis. Whatever the reason for the increased sudden death rate, the result of the advice given by the national committee retrospectively confirmed the prudence of the decision. The results of this study and the lessons we have learned from previous reports of sudden deaths among ambitious prominent elite athletes\(^6\) strongly suggest that careful screening and strict withdrawal from high-performance exercise in case of a potentially hazardous underlying cardiovascular disorder may be the only preventive tool.
Coronary angioplasty as a model of ischaemic preconditioning: fact or fancy?

See page 846 for the article to which this Editorial refers

It is well established in the laboratory that brief periods of myocardial ischaemia can markedly reduce necrotic damage and arrhythmias during a subsequent period of ischaemia. This remarkable manifestation of adaptation to ischaemic stress, ischaemic preconditioning, has been investigated extensively in various animal species. The idea that preconditioning is mediated by endogenous protective substances has proved attractive to investigators, possibly because definable paracrine mediators could provide the chemical templates for the development of new therapeutical entities. So far, the vast research effort to unravel the cellular mechanisms of this powerful response has resulted in a picture of Daedalean complexity. In part, this complexity may be ascribed to major differences in the endpoints of ischaemic damage used to assess the preconditioning response in different laboratories. A further source of complication resides in species differences: even when the same endpoint is used (e.g. necrosis) there are marked differences in the apparent mechanism of preconditioning between one animal species and another. In view of these species differences, the need for elucidation of the mechanisms in man is pressing.

Examination of preconditioning has been extended to human myocardium in a variety of ways which ingeniously circumvent the obvious ethical issues associated with the experimental application of ischaemia in situ in human myocardium. For example, preconditioning of human myocardial tissue has been examined in vitro using isolated atrial trabeculae and human isolated cardiac myocytes. There have also been studies examining the potential for preconditioning human myocardium in situ during elective procedures in which ischaemia is induced routinely. These studies have been conducted during coronary artery by-pass grafting using the cross-clamp fibrillation technique in which the heart is subjected to repeated ischaemic arrest, and during percutaneous transluminal coronary angioplasty where repeated balloon inflation induces sequential brief periods of myocardial ischaemia. An example of this latter approach to investigating preconditioning is reported by Tomai and colleagues in the current issue.

In this study, two sequential angioplasty balloon inflations were performed in patients undergoing elective angioplasty for stable angina. The authors determined three endpoints of ischaemic severity — intracoronary electrocardiographic ST segment elevation, surface electrocardiographic ST segment elevation and subjective pain score — and compared these during the first 2 min balloon inflation and the second balloon inflation. During the second inflation, ST shifts were attenuated, as was the pain score, suggesting that the severity of ischaemia was less during the second inflation. This apparently