Reducing sudden death in young people in Australia and New Zealand: The TRAGADY initiative

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Reducing sudden death in young people in Australia and New Zealand: the TRAGADY initiative

Jon R Skinner, Johan A Duflou and Christopher Semsarian

Best-practice guidelines mandate a full postmortem examination in these deaths to identify genetic causes and allow potentially life-saving interventions in the victim's relatives

The sudden and unexpected death of an apparently fit, healthy young person has a devastating effect on the family and community. If there is no adequate explanation for the death, the desperate sadness is usually compounded by frustration and fear that another family member may be struck. Yet, there is no uniform process in place in Australia and New Zealand to obtain a proper medical history of the victim, or to examine and investigate the victim's family. Such a process could provide clues to the diagnosis and also identify previously undiagnosed genetic diseases.

The lack of a consistent definition for sudden unexpected death in young people means there are few prevalence data. The best studies of incidence and causes of sudden natural death in 1–40-year-olds have been conducted by two forensic pathology centres in New South Wales.[1,2] These suggest an annual incidence of around 20 per million — about 400 deaths per year in Australia. A striking feature was that the postmortem examination identified no specific cause of death in a third. This suggests an arrhythmic death caused by an underlying cardiac channelopathy, such as long-QT syndrome, Brugada syndrome or catecholaminergic polymorphic ventricular tachycardia.[3] Clinical and genetic studies have confirmed the presence of these conditions in the Australian and New Zealand populations.[4] They are the consequence of inherited dysfunction of cardiac cell channels (for potassium, sodium and calcium), which are involved in generating the cardiac action potential. The mode of death is ventricular tachycardia or fibrillation. The results of the two NSW pathology studies[1,2] were surprising, as previous studies on sudden death in young athletes found that the most prominent causes were the structural heart diseases, hypertrophic cardiomyopathy (HCM) and arrhythmogenic right ventricular cardiomyopathy (ARVC).

Cardiac channelopathies, HCM and ARVC are all familial, with over 90% of cases inherited in an autosomal dominant fashion, meaning that 50% of first-degree relatives are potentially at risk. There is now good evidence that people with these conditions can benefit from interventions such as β-blockade and cardioverter defibrillators,[5] so that identification of affected family members is potentially life-saving. Cardiological and genetic investigation of the relatives of young victims of sudden death can reveal an inherited heart disease in 40% of cases.[6,7]

To achieve this outcome, there is a need for a coordinated multidisciplinary team approach to the postmortem investigation of sudden deaths, including expert pathology, cardiology, clinical and molecular genetic assessment.[8] The TRAGADY (Trans-Tasman Response Against Sudden Death in the Young) initiative was established in 2005, and comprises a group of over 50 highly motivated Australian and New Zealand health professionals, scientists and patient advocates who share the aim of reducing sudden death in the young caused by inherited heart diseases.

Key points of best-practice guidelines on postmortem investigation of sudden death of a young person*

- A full postmortem examination should be completed in all cases of sudden unexpected death in young people (0–40 years).
- The investigation, ideally led by a pathologist, involves a team approach, including as a minimum:
  - A person designated to liaise with the family;
  - Specialist cardiology involvement with the family when non-cardiac causes are excluded; and
  - Laboratories with molecular genetics, toxicology and metabolic expertise.
- A detailed antecedent clinical history must be obtained.
- A detailed and relevant family history must be obtained.
- Liaison with the family should be established early and be ongoing until a cause of death is ascertained.
- Skilled macroscopic and microscopic examination of the organs is required, particularly of the heart (especially right ventricular muscle), and the brain. This may require some specimens to be examined by other specialists.
- Adequate histological material must be obtained for review or, if necessary, referral.
- Tissue or blood suitable for DNA extraction must be obtained (paraffin-embedded tissue blocks are *not* suitable).

* Devised by TRAGADY (Trans-Tasman Response Against Sudden Death in the Young) and endorsed by the Royal College of Pathologists of Australasia. ◆

The group has formulated a mission statement[9] and, recognising the inconsistencies in postmortem practice across Australia and New Zealand, its first aim was to create a best-practice guideline for the postmortem investigation of sudden unexpected death in the young. This guideline has now been completed and formally approved by the Royal College of Pathologists of Australasia, and is available on the College website.[10]

A key message for the general practitioner is that a skilled postmortem examination is imperative after such deaths. There may be pressure from the family to avoid an autopsy, but ascribing such deaths to "heart attack", for example, when there was some previous chest pain, misses the opportunity to make a proper diagnosis and potentially save the lives of other family members. Similarly, arrhythmic syndromes such as long-QT syndrome have been falsely diagnosed as epilepsy, and the death of any young person with epilepsy should be investigated in detail. Many families have suffered several sudden deaths because of a failure to investigate completely, as described on support group websites, such as that of the Australian Sudden Arrhythmia Death Syndromes Foundation (http://www.sads.org.au).

Key points of the TRAGADY best-practice guidelines are summarised in the Box.

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