PREVENTATIVE PATHOLOGY - LEARNING FROM SUDDEN CARDIAC DEATH

APCSC

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PREVENTATIVE PATHOLOGY
LEARNING FROM SUDDEN CARDIAC DEATH

Outline

- Sudden cardiac death (SCD)
- Conditions associated with SCD
- Sudden death in young adults in WA
- Genetics in the mortuary
- Post mortem procedure
- Case example
- Conclusions

SUDDEN CARDIAC DEATH

SUDDEN CARDIAC DEATH

OVERVIEW

DEFINED AS

"the sudden, abrupt loss of heart function in a person who may or may not have diagnosed heart disease, whereby the time and mode of death are unexpected and the death occurs either instantly or shortly after symptoms appear"

American Heart Association

SUDDEN CARDIAC DEATH

OVERVIEW

- **Most common in the elderly**
- **Coronary artery disease**
- **Uncommon in the young**
- **Devastating complication of a number cardiovascular ds**
- **The death may be the first and only manifestation of a lethal familial disease**
- **Many cases remained unexplained**

SUDDEN CARDIAC DEATH

PAST AND CURRENT ISSUES

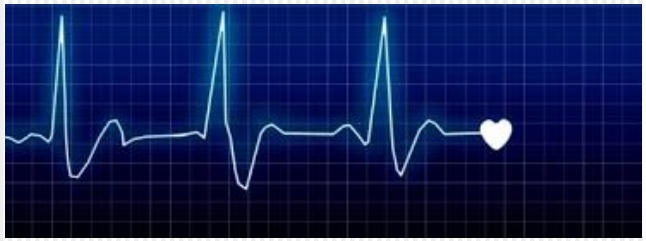
- **A diagnosis of exclusion (non-cardiac COD excluded)**
- **Have been inconsistencies in autopsy procedure, classification of COD and referral processes**
- **Potential for missing cases, incorrect COD, with no closure for families and no clinical follow up**
- **Delays in establishing COD**
- **Costs**

SUDDEN CARDIAC DEATH

OVERVIEW

- **2005 TRAGADY initiative (Trans-Tasman Response AGAinst Sudden Death in the Young) standard autopsy practices**
- **2008 RCPA endorsed SCD autopsy guidelines**
- **2011 Heart Rhythm society**
- **2011 European Heart Rhythm Association**
- **Association for European Cardiovascular Pathology**

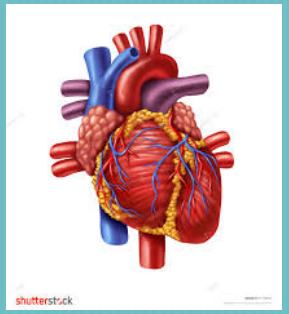
CAUSES OF SUDDEN CARDIAC DEATH



CONDITIONS ASSOCIATED WITH SUDDEN CARDIAC DEATH

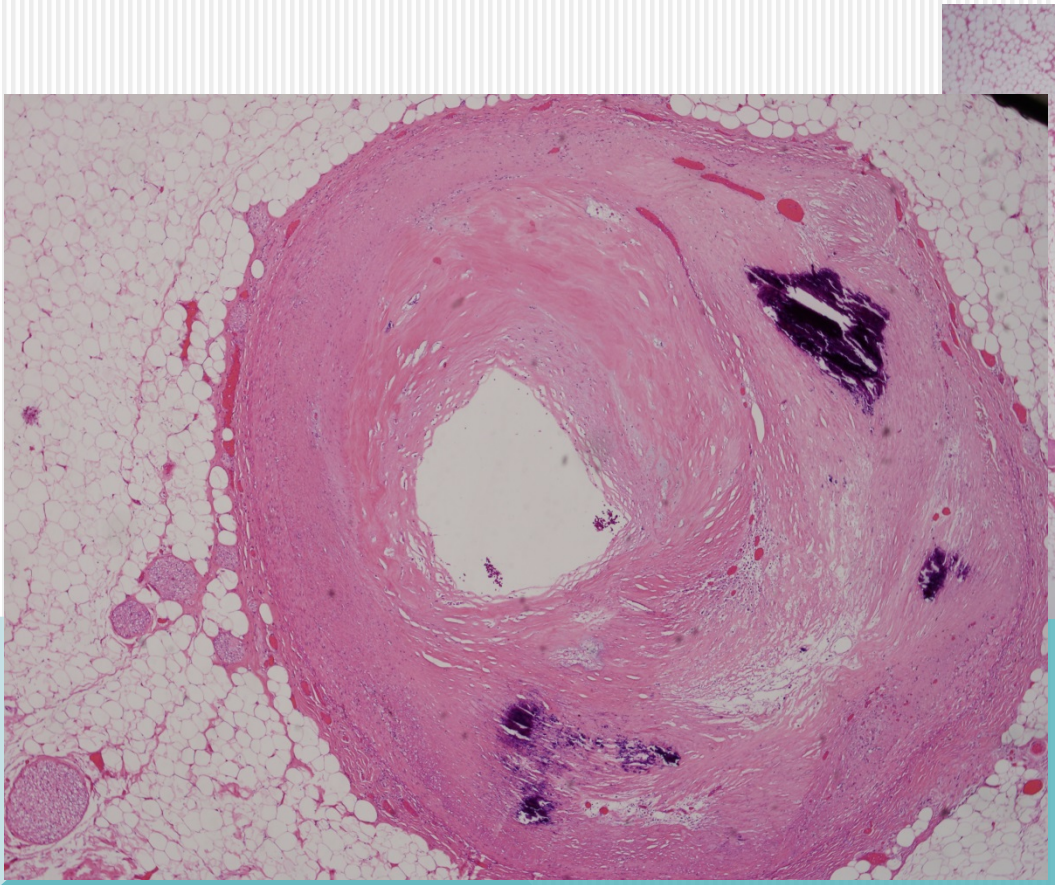
Structural abnormalities

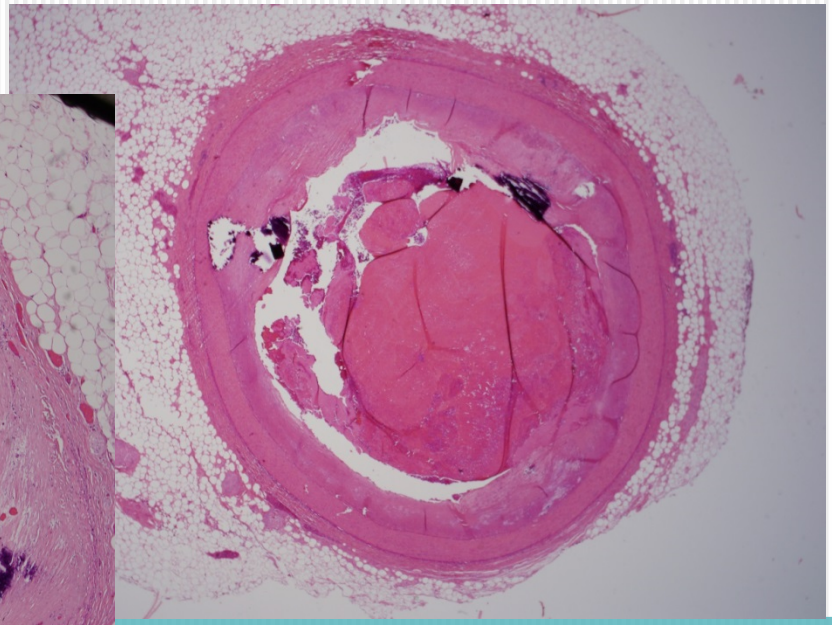
- **Genetic - mutations in genes encoding developmental components of the heart and vessels**
  - **Cardiomyopathies – dilated, hypertrophic, ARVD**
  - **Abnormalities of the coronary arteries**
  - **Connective tissue disorders – Marfan's**
  - **Valvular abnormalities**
- **Acquired - Coronary artery atherosclerosis**



CONDITIONS ASSOCIATED WITH SUDDEN CARDIAC DEATH

Coronary artery atherosclerosis and thrombosis





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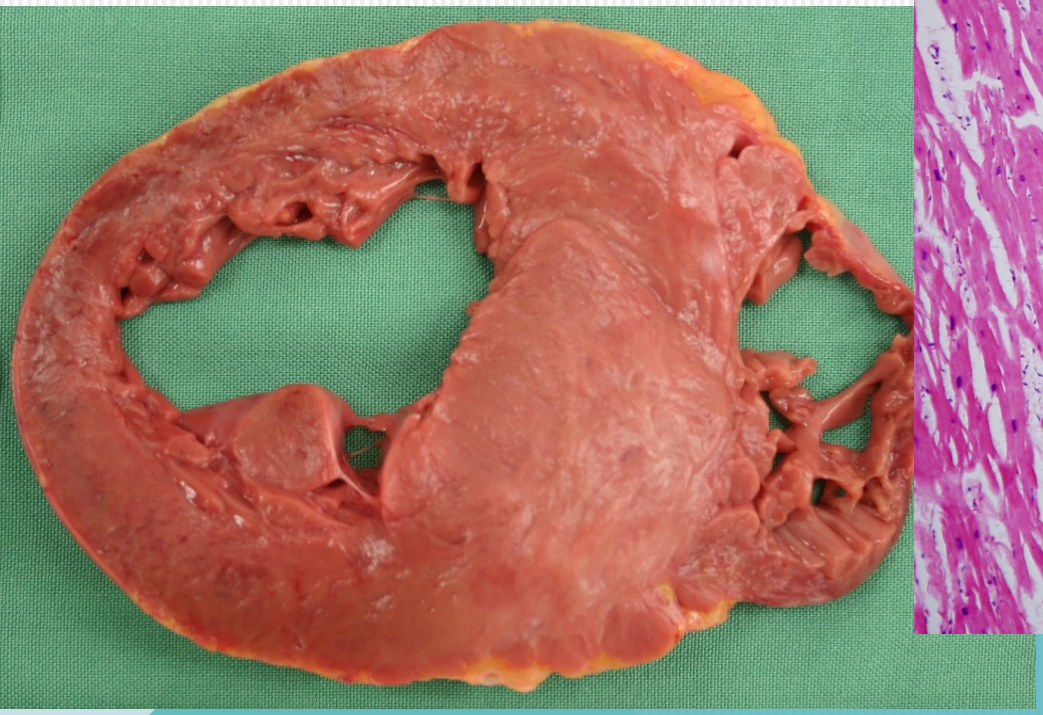
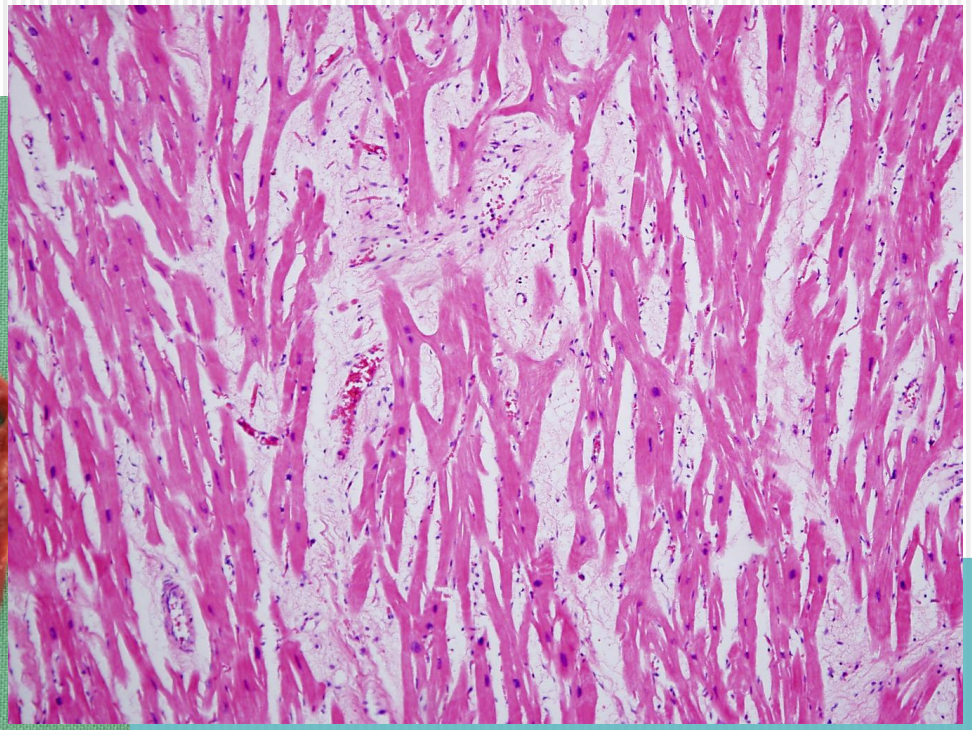
LABORATORY MEDICINE WA

CONDITIONS ASSOCIATED WITH SUDDEN CARDIAC DEATH

HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY (HOCM)





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CONDITIONS ASSOCIATED WITH SUDDEN CARDIAC DEATH

Non structural (grossly and histologically normal)

- *Inherited arrhythmogenic disorders*

Genetic mutations in genes encoding functional units in cardiac cells lead to problems in the generation and progression of the cardiac impulse.

Cardiac Channelopathies - Long QT syndrome,

Catecholaminergic polymorphic ventricular tachycardia,

Brugada syndrome

SUDDEN DEATH IN YOUNG ADULTS IN WESTERN AUSTRALIA

CORONIAL DEATHS IN WA

SUDDEN DEATH IN YOUNG ADULTS

2008-2012 period

- ***Av 2000 autopsies/year***
- **Young adults 17-35 years >1600 deaths**
- **Average >300 coronial autopsies/year (15%)**
- **Males 75% of cases**
- **Males over-represented in all types of death**

CORONIAL DEATHS IN WA

SUDDEN DEATH IN YOUNG ADULTS 17-35 YEARS

CAUSES OF DEATH

- **Trauma 30-35% (MVC, falls, industrial)**
- **Suicide 25-30%**
- **Drug related 15-20%**
- **Natural 5-10% (diabetes, malignancy, asthma, epilepsy, sepsis, PE)**
- **Homicide >5%**
- **Drowning 2-4% (some possibly cardiac related?)**
- **Unascertained 3-5% (some external, decomposed)**

CORONIAL DEATHS IN WA

Sudden death in young adults

Cardiac related **5% (80% male) – (some drug rel)**

Coronary atherosclerosis >50% cases

Cardiomyopathies >10%

Cardiac arrhythmia 10%

Myocarditis (6 cases)

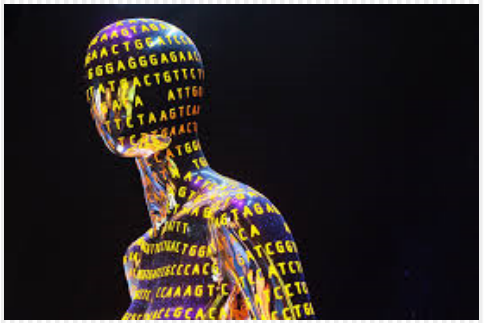
Aortic dissection (4 cases)

Heart failure (chronic illnesses diabetes, obesity)

Mitral valve prolapse

Congenital heart ds, and others (anom coronary arteries)

GENETICS IN THE MORTUARY



ATHLETES AND SUDDEN CARDIAC DEATH

- **Rare and highly visible, distressing event**
- **Increased incidence relating to greater risk with strenuous exercise**
- **Known or quiescent heart disease**
- **Many studies - have shown most often structural COD (HOCM and ARVD >50%, coronary atherosclerosis or anomalies, valve abnormalities, myocarditis)**
- **Structurally normal hearts in 3%**
- **Greatest numbers football codes/ basketball**
- **Increased risk for certain nationalities**
- **Led to protocols/regulations re player workup/review**

GENETICS IN THE MORTUARY

The molecular autopsy

- **Multiple uses in everyday clinical medicine**
- **Emerging role in the mortuary due to molecular advances**
- **Increasing molecular autopsy series supporting its use**
- **Autopsy negative sudden unexplained death in young adults 30% in most studies**
- **Establishing definitive pathogenic COD in some cases, confirmation of others**

GENETICS IN THE MORTUARY

The molecular autopsy

- **Forms part of a complete medico-legal examination in selected cases**
- **Suggested that genetic investigation of relatives can reveal an inherited heart disease in up to 30-40% cases**
- **The new standard of care - addressing community expectation**
- **Reduce the risk of additional SCD**
- **Generate new data that may uncover new mutations**

POST MORTEM PROCEDURE IN SUDDEN CARDIAC DEATH

POST MORTEM PROCEDURE IN SUDDEN CARDIAC DEATH

Thorough and detailed examination for determination of a COD

Closure for the family

Provide information and direction for the specialist follow-up and investigation of the family

POST MORTEM PROCEDURE
IN SUDDEN CARDIAC DEATH

Timely provision of comprehensive detailed information including:

- **Death – activity at time, witnessed, unwell prior to final event, drug use, resuscitation attempts, position when found**
- **Background history - habitual sport; medical (cardiac, diab, seizures); drug use including prescription meds - LQTS past 'episodes', allergies**
- **Family history – known cardiac, unexplained deaths**
- **Retrieval of any previous investigations**

POST MORTEM PROCEDURE IN SUDDEN CARDIAC DEATH

- **Post mortem – published guidelines (RCPA endorsed from TRAGADY group)**
- **Post mortem imaging**
- **Thorough external examination – general; drug use, stigmata of chronic disease (liver disease, diabetes, sepsis), syndromes (Marfans), medical intervention, seizure activity, injury (collapse type)**
- **Internal – detailed general examination for non-cardiac causes**
- **Detailed comprehensive examination of the heart to identify structural heart disease**
- **Further investigations**

POST MORTEM PROCEDURE IN SUDDEN CARDIAC DEATH

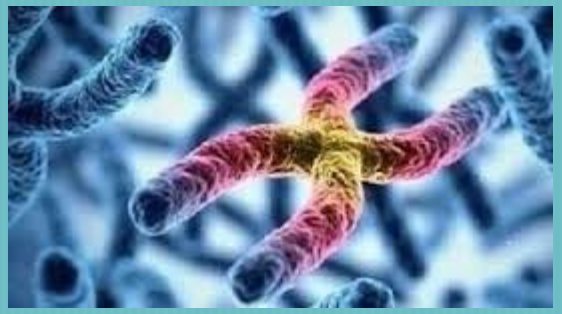
Guided Further investigations

- **Extensive histology (as per protocol)**
- **Referral if needed**
- **Biochemistry**
- **Microbiology/virology**
- **Neuropathology - seizures**

POST MORTEM PROCEDURE IN SUDDEN CARDIAC DEATH

Guided Further investigations

- **Toxicology – illicit drugs (amphetamines), synthetic drugs, anabolic steroids, alcohol**
- **Appropriate sampling of fresh tissue and blood samples for genetic studies**
- **DNA extraction/storage in definite/likely cases**
- **Storage in others**



POST MORTEM PROCEDURE IN SUDDEN CARDIAC DEATH

Determination of COD

- **SCD with cardiac structural abnormality,**
- **Undetermined - Exclusion of other COD**
- **SCD no structural abnormality or subtle changes – probable inherited channelopathy/unascertained**

Notification of coroner

Referral of family to genetic service, specialist review

POST MORTEM PROCEDURE IN SUDDEN CARDIAC DEATH

Some determined cases may also bear consideration

- **Drowning deaths**
- **Seizure related deaths**
- **Drug related deaths – ? vulnerable heart; new synthetic drugs**
- **Restraint deaths**
- **Age should not be a limiting factor**

POST MORTEM PROCEDURE IN SUDDEN CARDIAC DEATH

Drowning deaths

- **First report of PM molecular diagnosis SCD, LQT in 1999 after near drowning (Tester and Ackerman)**
- **Other case reports**
- **High index of suspicion - sample storage**
- **Don't exclude on circumstance or other positive results**

CASE STUDY

CASE STUDY 1

32 year old male

Tree surgeon, smoker

One child 7 years, mother and father, sister

At the casino with friends, drinking alcohol

Reported to be well

Suddenly collapsed and tried to stand, collapsing again to the ground

SJA resuscitation at tertiary hospital

PMH reported to have had an abnormal ECG 3 years previous

CASE STUDY 1

At post mortem –

- 185cm, 105kg
- Enlarged, soft and dilated heart 518g (range 241-481g)
- Thickened LV wall 15-18mm, prominent trabeculae
- Marked fatty tissue infiltration RV
- Normal coronary arteries
- Evident resuscitation
- **Toxicology alcohol 0.199%**

Cause of death

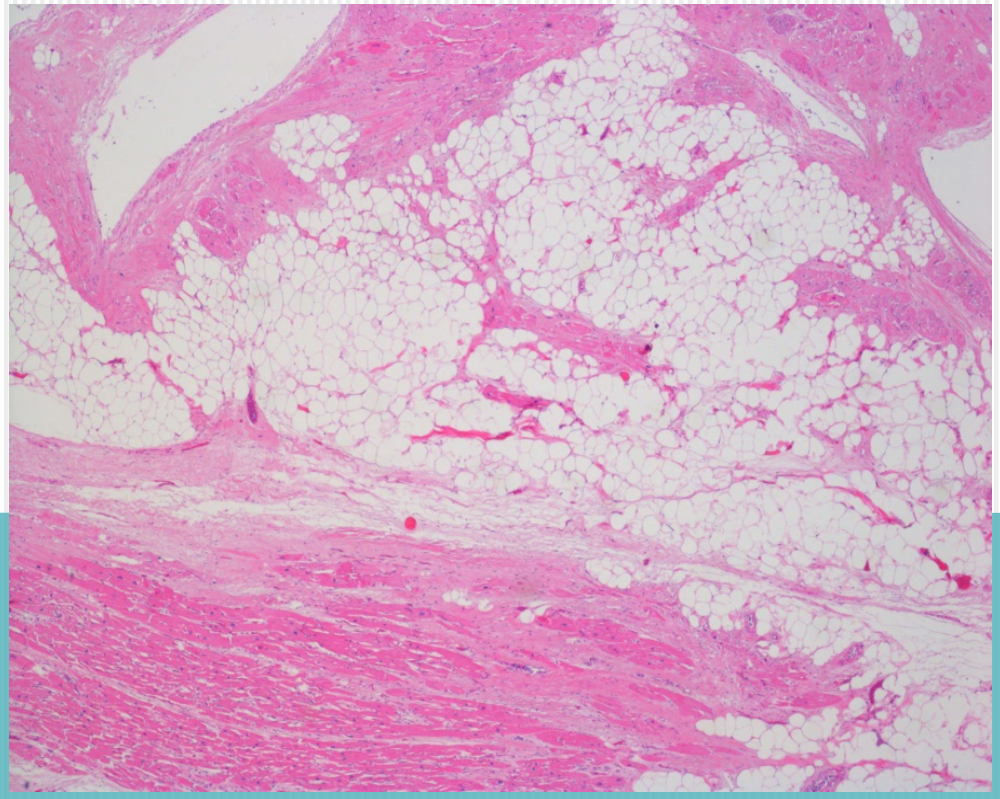
ARRHYTHMOGENIC RIGHT VENTRICULAR DYSPLASIA

ARRHYTHMOGENIC RIGHT VENTRICULAR DYSPLASIA

- An inherited myocardial disease, autosomal dominant
- Variable penetrance and expression
- Associated with abnormal heart rhythm (ventricular arrhythmias)
- Can first present as sudden cardiac death
- Progressive fibro-fatty tissue replacement of the heart muscle
- Most common in males, Mediterranean descent
- Diagnosis by combination of specific clinical, ECG and radiographical features
- Can be precipitated by exercise and medications/drugs
- Treatment determined by consideration of risk

CONDITIONS THAT MAY BE ASSOCIATED WITH SUDDEN CARDIAC DEATH

Arrhythmogenic right ventricular dysplasia/cardiomyopathy



PATHWAYS TO PREVENTION CONCLUSIONS

A devastating event for family and the community

Use of standardised pm practices

Establishment of coronial referral process for families

Targeted genetics is enabling us to accurately defining COD and provide answers

Implement preventative strategies to save lives

REFERENCES

Olivia A et al. State of the Art in Forensic Investigation of Sudden Cardiac Death. *Am J For Med Pathol.* 2011;32(1): 1-16

Michaud K et al. Molecular autopsy in sudden cardiac death and its implications for families: discussion of the practical, legal and ethical aspects of the multidisplinary collaboration. *Swiss Med Wkly* 2009;139(49-50): 712-718.

Basso C et al. Postmortem diagnosis in sudden cardiac death: macroscopic, microscopic and molecular findings. *Cardiovasc research* 2001;50:290-300.

Vohra J, Skinner J and Semsarian C. Cardiac genetic investigation of young sudden unexplained death and resuscitated out of hospital cardiac arrest. *Heart, Lung and Circ*. 2011;20:747-750

Tester DJ and Ackerman JA. The role of the molecular autopsy in unexplained sudden cardiac death. *Curr Opin Cardiol 2006; 21:166-172*

Semsarian C and Ingles J. Molecular autopsy in victims of inherited arrhythmias. *J Arrhythm*. 2016 Oct:32(5):359-365

Semsarian C, et al. A prospective Study of Sudden cardiac Death among Children and Young Adults. *N Engl J Med 2016;*374:2441-52.

www.rcpa.edu, RCPA Guidelines - "Post-mortem in sudden unexpected death in the young: Guidelines on Autopsy Practice", Prepared by the members of Trans-Tasman Response AGAinst sudden Death in the Young (TRAGADY)