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Denborough M A, Forster J F A, Lovell R R H, Maplestone P A & Villiers J D.
Anaesthetic deaths in a family. *Brit. J. Anaesth.* 34:395-6, 1962.
[Royal Melbourne Hospital, Victoria, Australia]

A dominantly inherited abnormality was described that predisposed to 10 deaths in one family from anaesthesia. The details of a hyperpyrexial response to halothane in one member of this family were recorded, together with the safe use of spinal anaesthesia in a subsequent operation. [The SCJ® indicates that this paper has been cited in over 185 publications.]

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The events that are described in this commentary began dramatically on April 8, 1960, two months after I had started a research fellowship at the Royal Melbourne Hospital. A 21-year-old student was brought up to the Casualty Department with a compound fracture of his leg. Both he and his mother, who accompanied him, were less concerned about his leg than by the fact that he was threatened with an anaesthetic, because they said that 10 of his close relatives had died after anaesthesia with ether. Because ether was incriminated, it was decided to give him halothane instead, but within 10 minutes he was noted to be acutely ill and very hot. The anaesthetic was stopped, the patient was packed in ice, and he survived. Jim Villiers and Pat Maplestone were the anaesthetists involved.

Next day, the patient was referred to the Department of Medicine, and the head, R.R.H. Lovell, asked me to see him because of my interest in genetics. It soon became clear to me

that the patient suffered from a previously unrecognised inborn error of metabolism that was of considerable clinical importance. Later study of the records of his relatives who had died showed that the abnormality was inherited as a dominant, and I wrote a letter to *Lancet* about the reaction.¹

Almost a year later, the same young man needed another anaesthetic for a stone impacted in the left ureter. John Forster was charged with giving the anaesthetic, and he seemed ideally suited for this terrifying task as he had won the Croix de Guerre as a parachutist in France in World War II. After considerable discussion, the patient was wired up from every possible orifice to every possible monitor and given a spinal anaesthetic, which he tolerated uneventfully. The knowledge that local anaesthesia could be used safely in affected individuals was of great practical help to us subsequently, because not only did the patient come from a very large family, but also from one that was very prone to accidents and operations.

The paper has been highly cited because it is the first description of malignant hyperpyrexia (MH), a syndrome that is now widely recognised to be an important complication of general anaesthesia,² and because it stimulated research into this condition. It is known now that there are several nonanaesthetic triggers of MH, and that there is an association between MH and cot (crib) death.³ A specific diagnostic test and treatment for MH have been found. Individuals who are susceptible to MH have an underlying disorder of the muscle-cell membrane⁴ involving the excitation-contraction coupling mechanism, so MH has stimulated research not only by anaesthetists, but also by neurologists, pharmacologists, biochemists, and physiologists.

For my work on MH, I was awarded the Eric Susman Prize from the Royal Australian College of Physicians in 1972, a DSc from Melbourne University in 1977, and a medal at the Fifth International Congress on Neuromuscular Diseases in Marseilles in 1982.

1. Denborough M A & Lovell R R H. Letter to editor. (Anaesthetic deaths in a family.) *Lancet* 2:45, 1960. (Cited 120 times.)
2. Denborough M A. Malignant hyperpyrexia. *Clin. Anesthesiol.* 2:669-75, 1984. (Cited 2 times.)
3. Denborough M A, Galloway G J & Hopkinson K C. Malignant hyperpyrexia and sudden infant death. *Lancet* 2:1068-9, 1982. (Cited 15 times.)
4. Denborough M A, Ebeling P, King J O & Zapf P. Myopathy and malignant hyperpyrexia. *Lancet* 1:1138-40, 1970. (Cited 105 times.)