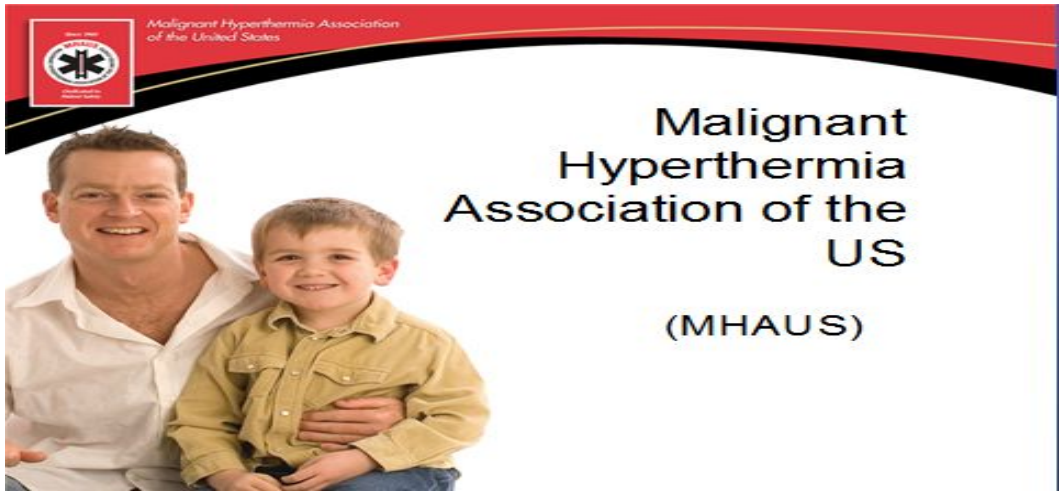
Malignant Hyperthermia Syndrome What Clinicians Need to Know in Order to Save a Life



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GOAL AND OBJECTIVES

- Describe the pathophysiology of MH
- Describe typical presentations of MH
- Acute treatment of MH in the OR
- Describe the Diagnostic Tests for MH susceptibility
- How to manage the MH susceptible patient
- Describe the Epidemiology of MH
- Value of genetic testing for MH

SUMMARY OF IMPORTANT ITEMS

- MH IS AN AUTOSOMAL DOMINANT DISORDER
- THREE GENES ASSOCIATED: **RYR1**,CACNA1S, STAC3
- OVER 200 VARIANTS ASSOCIATED WITH MH
- OVER 50 ARE PATHOGENIC OR LIKELY PATHOGENIC
- ONE IN ~850 PEOPLE CARRY THE P OR LP VARIANT
- THEREFORE ABOUT 400,00 IN THE USA CARRY A CAUSATIVE VARIANT
- BASED ON 30 MILLION ANESTHETICS/YEAR 350-1000 MH CASES EXPECTED PER YEAR.
- CAFFEINE-HALOTHANE CONTRACTURE TEST DISAPPEARING
- ONLY FOUR CENTERS IN NORTH AMERICA

- DEATH FROM MH IN USA, EUROPE IS ABOUT 10%
- WITHOUT DANTROLENE (E.G. CHINA) MORTALITY OVER 50%
- GENETIC TEST FOR MH IS FIRST DIAGNOSTIC TEST IN EUROPE, CANADA, NEW ZEALAND, AUSTRALIA AND SOUTH AFRICA
- GENETIC TEST AVAILABLE THROUGH MANY COMMERCIAL LABS
- 60-80% PATIENTS WITH POSITIVE HISTORY OR CONTRACTURE TEST CARRY PATHOGENIC/LIKELY PATHOGENIC MH VARIANT
- GENETIC TESTING IS NON INVASIVE AND NO LONGER VERY EXPENSIVE ($250 TO $2500)
- PATIENT SAFETY IS ENHANCED WITH GENETIC TESTING FOR MH AND OTHER DISORDERS.
- **WE HAVE ENTERED A NEW ERA IN ANESTHESIOLOGY**

ANÆSTHETIC DEATHS IN A FAMILY

SIR,—We have been asked to investigate a m[illegible]aged 21 who was recently admitted to this hospital with [illegible]mpound fractures of the tibia and fibula. He agreed to being given general anæsthesia provided ether was not used because several close relatives had died during or shortly after anæsthesia, and it was believed in the family that ether was responsible.

After premedication with pethidine 100 mg. and atropine 0·6 mg., he received thiopentone, nitrous oxide, oxygen, and halothane. Ten minutes after the operation began his systolic blood-pressure fell from 120 to 100 mm. Hg, and halothane was reduced. Ten minutes later the patient was pale and cyanosed with a dry skin; the systolic blood-pressure was 80 mm. Hg, and the pulse rose from an initial 100 to 160 per minute. Anæsthesia was stopped and the operation concluded within the next ten minutes. However, the patient remained deeply unconscious. His skin now felt very hot and sweaty. He was transfused with blood and packed with ice; half an hour later he began to open his eyes but seemed at first unable to move. Recovery ensued over 1½ hours during which time he sweated profusely and complained of feeling burning hot. His subsequent course has been uneventful.

Inquiry shows that of the 24 relatives of the propositus who have had general anæsthetics 10 have died. In only 1 case has the condition necessitating the operation been likely to cause death on its own accord. The propositus is the only one who has been affected and has survived. Of the relatives affected 3 were first cousins and 7 were uncles or aunts of the propositus. Study of the family tree suggests that the factor causing the reaction is inherited as a dominant gene. From the evidence available each reaction appears to have followed the same pattern as in this patient. There has been sudden hyperpyrexia either during or shortly after the operation, followed by convulsions and death. Postmortem has revealed no abnormality, except that in 2 cases the thymus was said to be enlarged.

Prior to the present case it was thought that the affected members in the family were sensitive to ether, but that explanation could not be invoked in the propositus, and the cause is not known.

We should be grateful to hear whether any of your readers know of a similar history or of a possible explanation for the sudden deaths in this family. It is believed that the family came originally from Wales.

Royal Melbourne Hospital, Victoria.

M. A. DENBOROUGH
R. R. H. LOVELL

1. Grants to Students. H.M. Stationery Office, 1960.
2. Kelsall, R. K. Applications for Admission to Universities. London, 1957.
3. E.g., Early Leaving. H.M. Stationery Office, 1954.

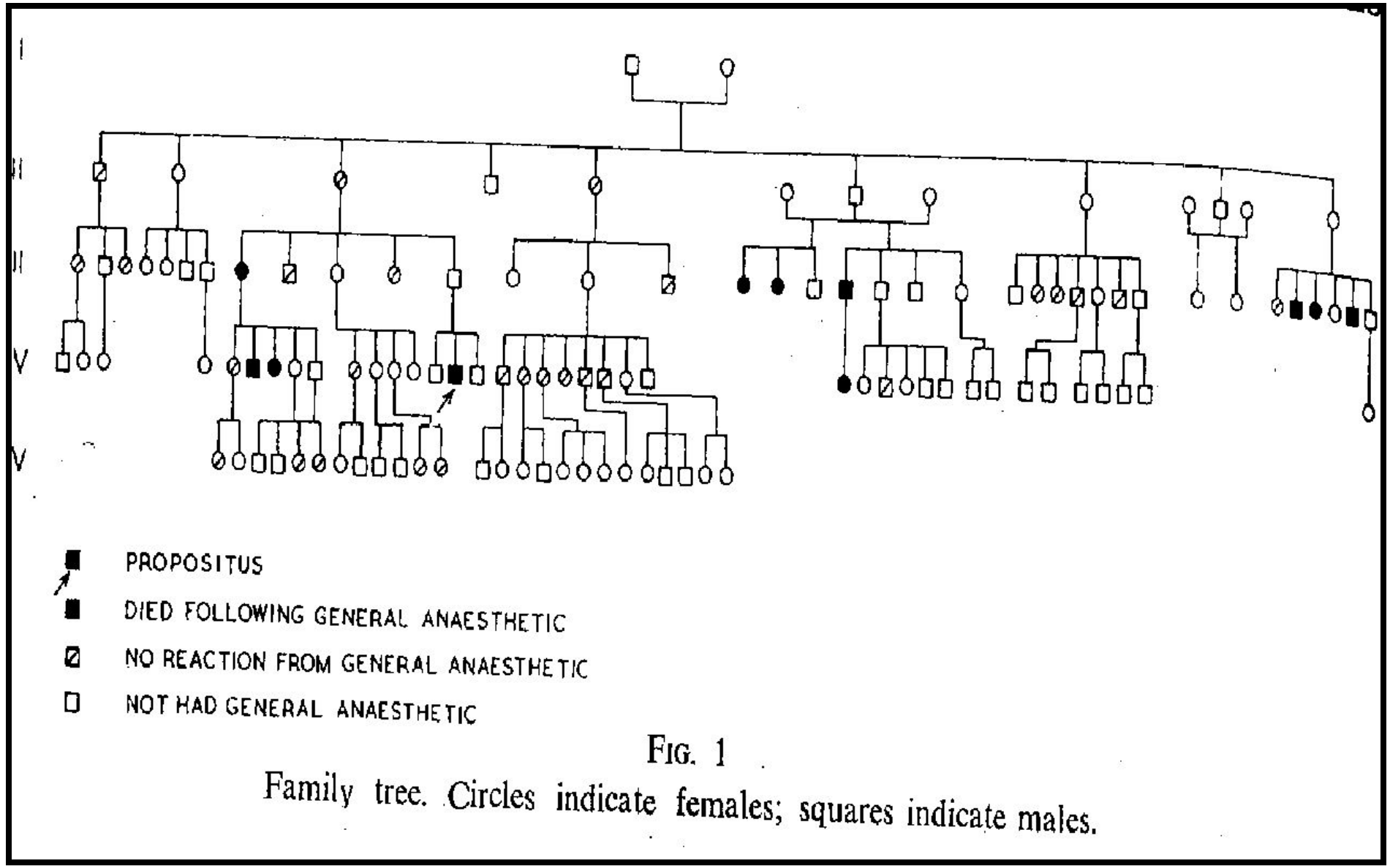
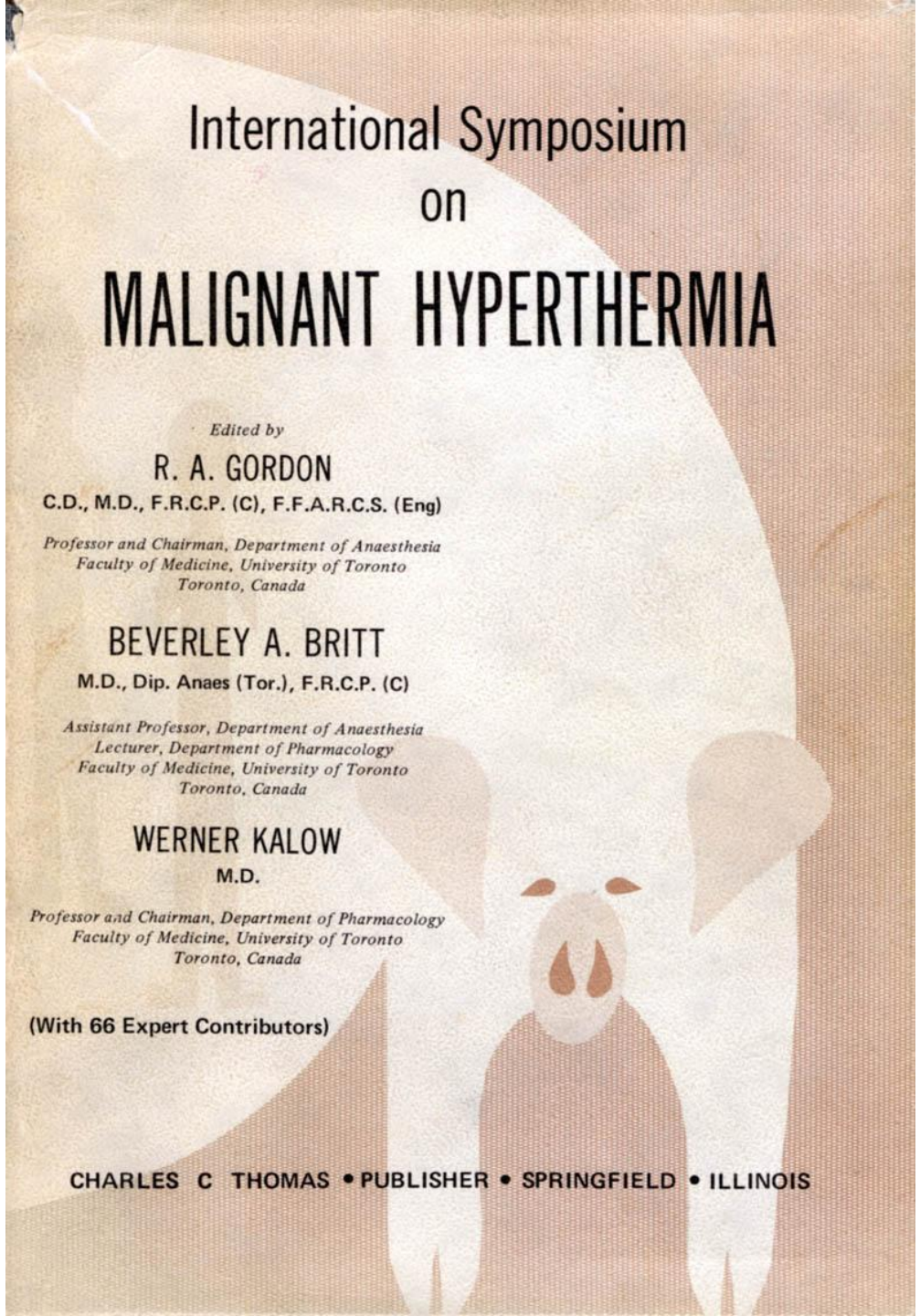
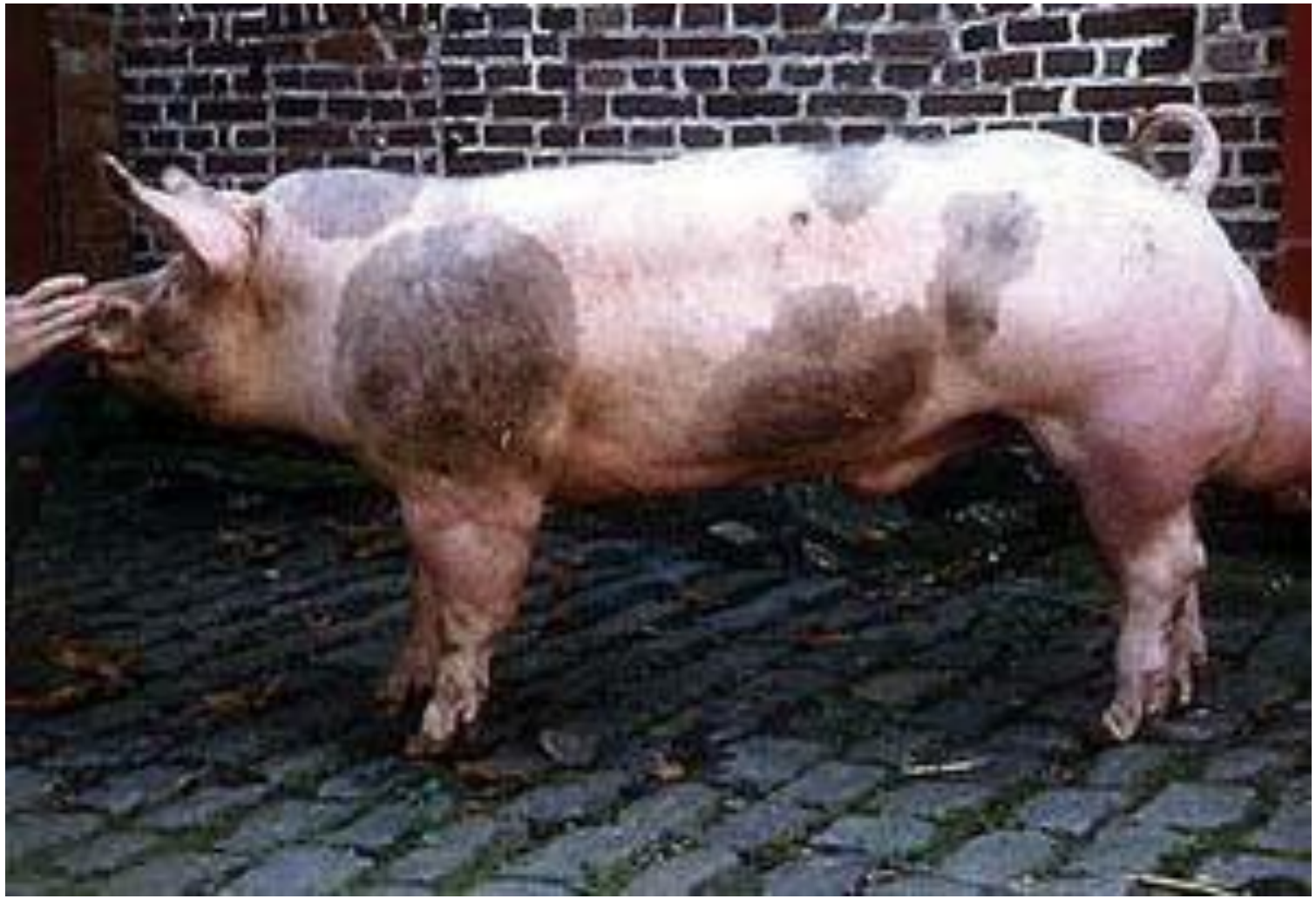


FIG. 1

Family tree. Circles indicate females; squares indicate males.



Univ of Toronto 1974



Definition

- Malignant hyperthermia is an autosomal dominant disorder of skeletal muscle triggered in susceptibles (human or animal) by inhalation anesthetic agents, and succinylcholine resulting in hypermetabolism, skeletal muscle damage, hyperthermia and death if untreated.
- *Heat and exercise alone may lead to MH and/or rhabdo in some susceptibles*.

- Mutations in the Ryanodine Receptor gene for skeletal muscle are found in a majority of MH susceptibles (RYR-1)

- Other genes that are causal include CACNA1S (DHPR), STAC-3

- MH is an international problem related to Anesthesia care.

- *Autosomal recessive* RYR 1 mutations are causal for a variety of chronic myopathies, such as Nemaline Myopathy, Central Core Disease

Incidence and Prevalence

- The prevalence of Pathogenic,Likely pathogenic mutations for MH is about 1 per 800 people!
- The incidence of clinical episodes is about 1 in 100,000 to 1 in 200,000 general anesthetics in adults
- 1 in 15,000 in children
- The mortality from MH is 5~10% in US, Canada, Europe
- Estimates of deaths from MH in the US are not accurate. Approximately 8-10deaths/yr