INTRODUCTION

MALIGNANT HYPERTHERMIA

Hyperthermia in anaesthesia is not a new phenomenon but typically arise from the inability of a febrile patient, premedicated with atropine and anaesthetized with diethyl-ether, to lose heat in a hot humid environment. A new syndrome has been described called malignant hyperthermia or hyperpyrexia is an acute, life-threatening syndrome characterized by tachycardia, fever, muscle rigidity, and other signs of a hypermetabolic state **(Benca and Rockoff, 1988).**

However there is a great deal of variation in the presentation of this syndrome: it may have a fulminant or gradual onset; there may be no fever. It is usually initiated by exposure to general anaesthesia in a patient whose susceptibility has not been previously recognized. Since the initial description of this condition numerous cases and "clinical and laboratory" studies have been reported **(Benca and Rockoff, 1988).**

In this essay we will review what is known about this syndrome and emphasize those aspects of greatest importance to practicing anaesthesiologists.

The first description of malignant hyperthermia was from **Australia in (1960)** in a young man who required surgery to repair a fractured tibia. The patient was concerned about having general aneathesia because ten of his relatives had

died after receiving ether. He received general aneathesia with halothane and experienced a nonfatal malignant hyperthermia episode. Even though hyperthermia during general anaesthesia had been reported previously, this was the first suggestion that hyperthermia could be an inherited disease and provided an explanation far earlier reports of families in which there were multiple anaesthesia-related deaths **(Denborough and Lovell, 1960)**. Subsequently,similar cases occurring in Toronto and identified abnormal responses of skeletal muscle to halothane and caffeine in susceptible patients.Pigs developed very high temperatures and became rigid when exposed to stressful conditions **(Benca and Rockoff, 1988)**. Malignant hyperthermia in pigs exposed to halothane and succinylcholime, that were from the stress-susceptible breeds. Acute episodes of malignant hyperthermia in susceptible pigs could be aborted with dantrolene. Since then dantrolene has been used successfully to treat malignant hyperthermia in humans and has resulted in a great decrease in mortality from this syndrome **(Britt, 1984)**.

Malignant hyperthermia has been described in all racial groups. Male and female children are affected equally until puberty, after which Malignant hyperthermia appears more commonly in males. The incidence, however, varies with age. The reason for this is not clear but may be a result of the use of different anesthetic agents and techniques in patients of different ages. In children, malignant hyperthermia has been reported to occur in one in 7.000 to 14.000 anaesthetics

whereas in adults the incidence is from one in 50.000 to one in 200.000. Malignant hyperthermia occurs most commonly in patients from 3 to 30 years old, being unusual in children under 3 years of age or in the geriatric population **(Beverley and Britt, 1985).**

Malignant hyperthermia is rare in adults over the age of 50 years and in infants under the age of 2 years. The reasons for these differences are not entirely clear but appear to be related to muscle bulk, strength and activity **(Britt, 1976).**

Between 1978 and 1984, the fulminant form of malignant hyperthermia occurred in one in 25.000 anaesthetic procedures When both potent inhalation agents and succinylcholine were used, the incidence rise to one in 62.000 procedures.Possible malignant hyperthermia reaction (not fulminant) occurred in one in 16.000 anaesthetic procedures with an incidence of one in 4.200 when both a potent inhalation agent and succinylcholine were used **(Ording, 1985).** Masseter spasm occurred in one in 12.000 anaesthetic procedures when succinylcholine was used.A starting incidence of masseter spasm has been reported of one in 100 anaesthetic procedures among all patients receiving general anaesthesia at a children's hospital who received halothane followed by intravenous succinylcholine **(Schwartz et al., 1984).**

Though no cases progressed to the full-blown syndrome of fulminant malignant hyperthermia, some patients developed other clinical abnormalities including arrhysthmias and massive elevations in muscle enzymes. The frequency of masseter spasm with this anaesthetic technique has also been confirmed at another children's hospital, and this suggests that certain anaesthetic agents or their combinations, may be important factors in precipitating malignant hyperthermia. Although masseter spasm may actually represent an abnormality distinct from malignant hyperthermia, some fulminant episodes begin with masseter spasm, and therefore this sign cannot be taken lightly.

The incidence of patients susceptible to malignant hyperthermia is likely higher than the incidence of actual episodes.More than half of all patients who develop malignant hyperthermia have had one or more uneventful experiences with general anaesthetics before the malignant hyperthermia episode **(Ellis, 1981)**.

Most malignant hyperthermia-susceptible individuals appear normal, without obvious musculoskeletal disease. There do appear to be some diseases,however, that pose an increased risk of malignant hyperthermia susceptibility **(Groner,1983)**. Duchenne type muscular dystrophy stands out among all of them. Another strong association has been with children having surgery for strabismus **(Ellis, 1981)**.

Mortalities were very high among the initial reported cases of malignant hyperthermia. Now, with prompt diagnosis and therapy, mortality has been reduced to less than 10%. Significant morbidity can still occur, however, especially among those patients resuscitated after a sudden cardiac arrest in the setting of an malignant hyperthermia reaction. Recognition of susceptible patients-avoidance of anaesthetic triggering agents, and prompt recognition and treatment have been crucial in preventing catastrophes from this syndrome **(Benca and Rockoff, 1988).**

An investigation of an even larger family of 20 members who had acute malignant hyperthermia reactions suggested autosomal dominant inheritance. There are an affected father passed the trait on to his son,and this excluded sex linkage.

In some families malignant hyperthermia susceptibility may depend on two or more genes. Thus, in some patients, malignant hyperthermia has been observed in the families of both parents, each displayed the various stigmata of malignant hyperthermic myopathy **(Kalow et al., 1976).** With regard to malignant hyperthermia reactions and muscle defects, the off spring of susceptible pigs exhibit a mean severity equal to that of their parents and have more than three phenotypes **(Beverley and Britt, 1985).**

Pedigrees of human and porcine families affected by malignant hyperthermia demonstrate autosomal dominant autosomal recessive, multifactorial and sporadic inheritance

patterns **(Ellis, 1981)**. Relatives of malignant hyperthermia-susceptible individuals are at greater risk for developing malignant hyperthermia themselves,with first-degree relatives having a higher risk than more distant relatives and the most clinicians assume an autosomal dominant inheritance pattern, and this appears to be most common **(Benca and Rockoff, 1988)**.

The racial distribution of malignant hyperthermia is worldwide. In the majority of cases reported the patients were caucasian. However the disorder also occurs in oriental populations (Chinese, Filipino,Ceylanese and Japanese). It is rare but unknown among other racial group including Blacks, however, nearly all afflicted Blacks studied have exhibited some phenotype characteristics suggesting partial caucasian ancestry **(Beverley and Britt, 1985)**.

Some environmental factor is usually necessary for the development of an acute malignant hyperthermia crisis. In susceptible humans,this is most often a drug, these "triggering" drugs are almost entirely confined to anaesthetic practice.

Malignant hyperthermic crises can also be precipitated outside the operating room by high environmental temperatures, mild infections, extreme emotional excitement, muscle injury,or exercise.Muscle exercise on a hot day is especially likely to induce an malignant hyperthermia reaction in an emotionally tense individual **(Britt, 1976)**.