SUXAMETHONIUM SPASM
A differential diagnostic conundrum

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SUMMARY
Spasm of muscle in association with suxamethonium is not uncommon. As an accepted early sign of malignant hyperpyrexia (MH), patients have been referred for MH screening who have shown only this abnormality. Case histories of 277 probands have been analysed and grouped according to final diagnosis, depending on results of muscle biopsy and in vitro screening. When muscle spasm is induced with suxamethonium, malignant hyperpyrexia must be considered a probable diagnosis.

Spasm of skeletal muscle is a well recognized complication of the administration of depolarizing neuromuscular blocking drugs. This may be recognized initially as a cause of difficulty in laryngoscopy before tracheal intubation when the spasm involves the masseter and other muscles of mastication. Although, in some instances the spasm is limited to these muscles, in other patients it can be observed more generally and may cause restrictive respiratory failure and even opisthotonos. The degree and distribution of muscle spasm following suxamethonium may relate to the total dose administered and the initial distribution of the drug; fasciculations of skeletal muscle are usually seen first in the upper torso and upper arms and then, subsequently, in the legs.

Increasingly, suxamethonium-induced muscle spasm has been recognized as a valuable early sign of malignant hyperpyrexia. There are, however, other causes, including the response seen in patients with one of the myotonic muscular dystrophies, in particular myotonic congenita (an association between malignant hyperpyrexia and myotonia congenita has been suggested previously (Saidman, Havard and Eger, 1964)).

Since 1971, 277 probands (or selected members of their families if the proband died) have been screened for malignant hyperpyrexia using in vitro halothane and in vitro caffeine challenge of muscle tissue taken from the vastus internus muscle. Of these, 100 (36%) had reacted to suxamethonium by some clinically recognized increase in muscle tone.

In this paper the results of an analysis of this group are presented in an attempt to clarify the significance of suxamethonium spasm so as to help the clinical anaesthetist determine the optimal management of patients with this complication.

PATIENTS AND METHODS

The diagnosis of malignant hyperpyrexia in the proband (or other family member if the proband had died) was confirmed retrospectively by demonstrating specific abnormalities in the biopsied muscle, and the 277 probands under review were classified into either susceptible to malignant hyperpyrexia (MHS) or unsusceptible to malignant hyperpyrexia (MHI). (In previous publications we have used MHN to indicate a normal member of a malignant hyperpyrexia family.)

Details of the anaesthetics given to the probands were obtained from the referring anaesthetists. This information was used to subdivide the subjects according to whether they developed any clinically recognizable muscle spasm in association with the administration of suxamethonium. This information was lacking for a few probands.

The probands developing suxamethonium spasm who were shown to be MHS were further subdivided as follows:

Suxamethonium spasm without any other abnormal sign.

Suxamethonium spasm with minimal and non-specific signs of MH such as arrhythmia, tachycardia, increase in body temperature of $>0.56^\circ$C (1°F).
Suxamethonium spasm with obvious signs of developing MH including increase of body temperature >0.56°C (1°F), respiratory and metabolic acidosis, hyperkalaemia, cyanosis, myoglobinuria.

Insufficient details available for meaningful analysis.

The probands developing suxamethonium spasm who were shown to be MHI were also subdivided according to whether a cause for the muscle abnormality, such as a myotonic muscle disease, could be identified.

RESULTS
Of the 277 probands, 147 (53%) were shown to have developed malignant hyperpyrexia and, consequently, were classified as MHS, and 130 (47%) to be MHI. The distribution of the probands in the various sub-groups is shown in figure 1.

Of the 64 suxamethonium reactors in the MHS group, 48 (75%) had other obvious collateral signs and could have been, or were, given a confident provisional diagnosis of MH. No signs specific to MH were observed in seven (11%) of these patients, and minimal signs in a further nine (14%).

Of the 36 suxamethonium reactors in the MHI group, in nine (25%) other diagnoses were given which could account for the abnormal reaction to suxamethonium. These diagnoses included myotonia congenita in three patients, myopathy with abnormal electromyogram (EMG) in three patients, thyrotoxic myositis in one patient, porphyria in one patient and proliferative glomerular nephritis in one patient. Of the remainder, 12 (33%) had no obvious cause and normal EMG. In 15 (42%) no cause had been determined, but EMG investigations had not been performed.

DISCUSSION
Spasm of skeletal muscle following the administration of suxamethonium has been accepted as a part of the acute malignant hyperpyrexia syndrome for many years (Britt and Kalow, 1970).

With an increasing knowledge of the early presentation of MH, anaesthetists are more aware of suxamethonium spasm as an important sign which should lead to a provisional diagnosis of MH followed by the appropriate monitoring and therapeutic action. The figures presented demonstrate that almost 5% of all MH probands presented with suxamethonium spasm as the only abnormal sign. Out of these seven patients, the procedure was aborted, because of the suxamethonium spasm, in two. One of these seven patients died as a result of restrictive respiratory failure induced by myotonia.

Suxamethonium-induced muscle spasm was evident in around 80% of the MHS patients receiving suxamethonium studied by Britt and Kalow (1970). In the present series the figure was 65% (64 of the 99 MHS probands who received suxamethonium) and although quantitatively different from Britt and
Kalow's findings, is qualitatively similar. It is difficult to understand why all MHS probands do not develop muscle spasm with suxamethonium, yet muscle spasm is only one of several signs which occur during an MH reaction. Occasionally the rate of development of MH is greatly retarded in pigs (Harrison, 1973), and frequently MHS probands have received similar anaesthetics on previous occasions without any evidence of MH abnormality (Halsall, Cain and Ellis, 1979). The presence or absence of muscle spasm and its variation in degree must reflect the variable expression of the disease from one individual to another, and from one time to another within the same individual.

Many details of the probands' anaesthetics are incomplete, as indicated clearly in the figure. There are many reasons for this. Some probands developed their reaction many years previously and the family had only recently been recognized as MHS. Sometimes details of the anaesthetic are recorded poorly, and some anaesthetists are unwilling to provide the details requested. It is possible that many of the anaesthetics recorded under the heading "no information" were not associated with suxamethonium spasm since it would have been difficult for the anaesthetist involved to forget the incident. It is also possible that suxamethonium was not used in many of these anaesthetics.

Comment should be made about the subdivision of the MHS patients who developed suxamethonium spasm. Clearly there is a grey area between those who developed obvious signs of MH and those who developed early signs which were insufficient for a provisional diagnosis of MH to be made. We are aware that the subdivision between these two groups is arbitrary and the dividing line could justifiably be set differently. The subdivision does indicate, however, that most patients with suxamethonium spasm who were shown to be MHS did have other major signs of MH following the suxamethonium-induced abnormality, thus underlining the importance of suxamethonium spasm as an early sign.

One of the fascinations of the present study was to recognize the sizeable group of probands who developed suxamethonium spasm but who were not shown to be MHS. Where patients were shown to be myotonic, etc., the suxamethonium spasm could be explained satisfactorily. However 12 patients had no abnormality on EMG or on microscopy. Critics of the screening procedure would claim, perhaps, that these patients represented screening test failures.

Yet all patients were subjected to the same rigorous screening procedures involving estimations of serum CPK concentration and, latterly, measurements of muscle biochemistry, which are abnormal in MHS muscle (Ellis et al., 1982). We believe that this group is worthy of further evaluation. It may be they have inherited a part of the syndrome, as suggested by Wingard (1977), who believes in a complex relationship between muscle disease and MH. It is possible also that these patients suffer from a hitherto undescribed disease.

In conclusion, it must be stressed that suxamethonium spasm is abnormal. A second dose of suxamethonium cannot be justified nor should continuation of the anaesthetic with MH trigger drugs be contemplated. Whenever muscle spasm develops with suxamethonium a cause should be sought and until it is found the patient should be assumed to be potentially at risk from MH.

REFERENCES

LE SPASME AU SUXAMETHONIUM
L'énigme diagnostique

RESUME
L'apparition d'un spasme musculaire lors d'une injection de suxamethonium n'est pas exceptionnelle. Dans la mesure où ce signe est reconnu comme un signe précoce d'hyperthermie
maligne (HM), des patients qui n’avaient présenté que lui, ont néanmoins été soumis au dépistage du risque d’HM. Les dossiers de 277 sujets ont été analysés et regroupés selon le diagnostic final, d’après les résultats de la biopsie musculaire et de l’étude in vitro. Lorsqu’un spasme musculaire est induit par le suxamethonium, il faut considérer l’hyperthermie maligne comme un diagnostic probable.

SUXAMETHONIUM-SPASMUS
Ein differentialdiagnostisches Rätsel

ZUSAMMENFASSUNG

ESPASMO DEL SUXAMETONIO
Un acertijo diagnosticº diferencial

SUMARIO
El espasmo del músculo en asociación con el suxametonio es bastante común. En cuanto es una primera señal aceptada de hiperpirexia maligna (MH), se refirieron a los pacientes con mirar a detectar una MH cuando demostraron padecer de dicha anormalidad. La historia clínica de 277 casos probables fue analizada y se agrupó a dichos casos según el diagnóstico final dependiendo de los resultados de la biopsia del músculo y del examen radioscópico in vitro. Cuando el suxametonio induce el espasmo del músculo, es menester considerar como diagnóstico probable a una hiperpirexia maligna.