Suxamethonium chloride in hot climates

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We have found that suxamethonium chloride administered in adequate dosage fails to produce the duration of apnœa one is accustomed to in more temperate climates. This has also been observed by others working under similar conditions of heat and humidity,[1] [2].

A relatively normal response was obtained when a fresh refrigerated batch of scoline was supplied by the makers. We therefore decided to compare the duration of apnœa produced by the fresh refrigerated suxamethonium, with that obtained when using our old stock. The unrefrigerated suxamethonium had been stored for about four months at temperatures between 24 and 35 degrees centigrade, (75–95 degrees Fahrenheit). This unrefrigerated drug was also chemically analysed.

MATERIAL AND METHOD

All patients who received the drug were African.

It is a feature of the surgical practice in this hospital that emergencies form a large proportion of the operations performed. Such patients are in poor physical condition, and therefore unsuitable for research purposes. A consecutive series of cases was thus impossible. These observations were therefore confined to healthy patients of both sexes, between the ages of sixteen and fifty years on whom elective surgery was performed. All were premedicated with papaverine 10mg (gr 1/6) and scopolamine 0.2mg (gr 1/300) one hour preoperatively.

The following groups consisted of 100 cases each:

A 0.3gm 5% thiopentone, 100mg refrigerated suxamethonium
B 0.3gm 5% thiopentone, 100mg un-refrigerated suxamethonium.

The time was taken with a stop watch from the completion of suxamethonium injection until the first signs of diaphragmatic movement, this being a readily observable end point. Cases in which there was no period of apnœa but only respiratory depression were recorded as zero.

The lungs were inflated with oxygen before intubation, which was attempted in all cases. The larynx and upper trachea were sprayed with 4% lignocaine, using the Macintosh spray. The appropriate size tube was lubricated with 5% lignocaine ointment. Patient was ventilated with a 50% mixture of oxygen–nitrous oxide using the closed circuit with the absorber cut out of the circuit.

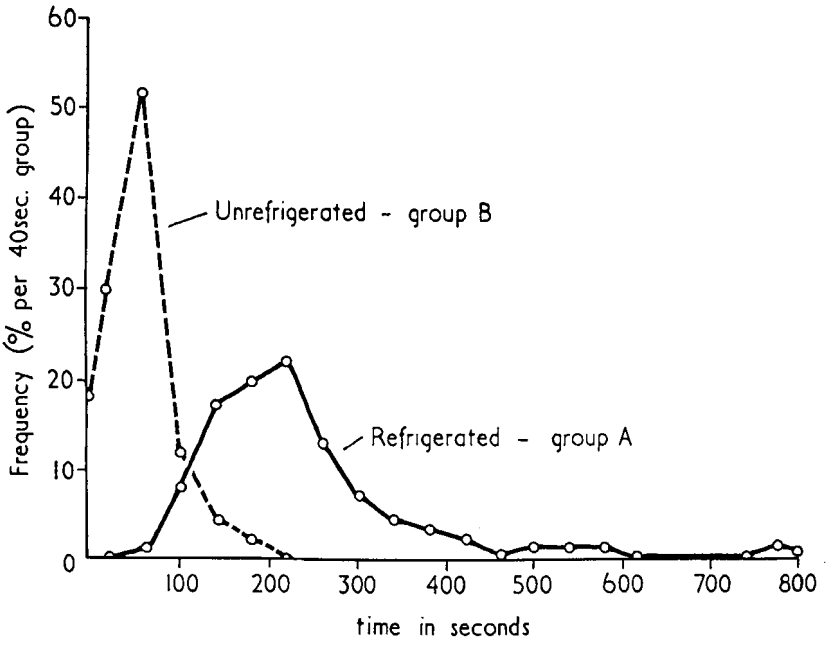
Table 1

Results

	GROUP A	GROUP B
Average apnœic period	229 seconds	57.5 seconds
Standard error of mean	10.7 seconds	3.5 seconds
Confidence limits	195–265	45–70

All cases in group A were intubated, sixteen cases in group B could not be intubated because of insufficient relaxation.

Muscular fibrillary twitchings of varying intensity were noted in practically all cases of group A, however this was a rare occurrence in group B, and when it was observed it was comparatively mild.



Graph showing relationship of apnœic period produced by refrigerated and un-refrigerated suxamethonium chloride

Chemical assay on the un-refrigerated drug produced the following results:

Table 2

pH.	1.5 (normal 3.5)
Succinic acid content	0.0028gm = 0.024gm suxamethonium per 2ml ampoule = 24.6% hydrolysis (method of Earles *et al*[3]).
Suxamethonium chloride	61mg per ampoule, that is 39% hydrolysis[4].

DISCUSSION

Many factors may influence the duration of apnœa such as: premedication; dosage of thiopentone[5] and suxamethonium; hyperventilation during apnœic period; alkaline hydrolysis rate[6]; blood pseudo-cholinesterase levels [7 8]; reflex breath holding[9] and surgical stimuli.

There are other circumstances in which the apnœic period is altered such as poor kidney function and dehydration[10], hypocalcæmia[11 12], advanced liver disease or malnutrition[6 13], and low serum potassium. Procaine by competing for serum cholinesterase[14] and exposure to certain insecticides[15] may also modify the action of suxamethonium.

Factors likely to decrease the duration of apnœa are: small dosage, high plasma pseudo-cholinesterase levels and drug deterioration.

Premedication and drug dosage were constant in all cases. Hyperventilation would tend to prolong apnœa but hypoventilation with carbon di-oxide build up would not speed up hydrolysis of suxamethonium. All patients were ventilated at approximately twelve respirations per minute; the inflation pressure being kept as constant as possible with the hand alone to guide one.

Alkaline hydrolysis may have played a part in shortening the duration of apnœa; but had this been so it would have effected both series of cases. The blood pH was not estimated in either series.

Blood pseudo-cholinesterase levels may be normal in prolonged apnœa,[7]; and its titre does not alone explain the difference in intensity and duration of neuro-muscular block[6]. Although the synthetic preparation cholase can shorten the duration of apnœa,[7] the marked difference in the two groups A and B suggests drug deterioration, rather than an abnormally high pseudo-cholinesterase titre in the local population. Serum cholinesterase estimations have not been performed.

The results of chemical assay show hydrolysis, but the degree depends on the method used. If the succinic acid content alone is estimated, no allowance is made for the drug hydrolysed to the monocholine. As the first stage of hydrolysis, (succinyldicholine to monocholine chloride) is faster than the second, (monocholine

chloride to succinic acid and choline), there will be a greater amount of suxamethonium present in the monocholine phase than in the succinic acid and choline phase. This is the case until there is more than 60% hydrolysis[17]. Therefore succinic acid estimation does not give a true picture of the extent of deterioration. Estimation of the suxamethonium remaining gives a more accurate picture, and this showed 39% hydrolysis.

Other references to scoline deterioration when exposed to heat, apart from in the tropics, have appeared[4 17 18]. It has also been shown that the rate of hydrolysis increases with rise in temperature[19]. Other investigators[3] have observed suxamethonium deteriorates chemically as well as biologically not only when stored at 37 degrees centigrade, but also with age when kept at room temperature. They state that after sixteen weeks storage at room temperature there was 6% hydrolysis, and at 37 degrees centigrade for the same period 22% hydrolysis.

No loss of potency was found after forty-six weeks storage at 0 degrees centigrade[3], and the makers claim full maintenance of potency for two years if the drug is kept below 4 degrees centigrade[20].

CONCLUSIONS

The duration of apnœa in the two groups is significantly different; the un-refrigerated drug has lost considerable potency from a clinical point of view. (TABLE 1). The fact that it has undergone hydrolysis is supported by chemical analysis. (TABLE 2).

In hot climates scoline must be stored below 4 degrees centigrade, as recommended by the manufacturers. Alternatively, when short acting muscular relaxants are required, suxamethonium and suxamethonium bromide can be prepared from the powder[21], this method has also given us satisfactory results.

SUMMARY

An investigation into the clinical response to refrigerated and un-refrigerated suxamethonium chloride has been carried out and described.

A chemical examination of the un-refrigerated drug has been made, and the results quoted.

Methods of overcoming suxamethonium deterioration are quoted from the literature, and these are endorsed by our own experience.

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References

[1]KEATING, V. J. (1956). *Anæsthesia, 11*, 169.
[2]RAJAGOPALAN, V., LOMAZ, J., and LEWIS, GWENDA M. (1956). *Anæsthesia, 11*, 352.
[3]EARLES, M. P., *et al* (1954). *J. Pharm., Lond., 4*, 773.
[4]Estimation of Succinylcholine Chloride, (1953). *J. Amer. Med. Ass., 153*, 726.
[5]WALKER, O. (1954). *Lancet, 1*, 103.
[6]FOLDES, F. F., SWENDELOW, M., LIPSCHITZ, E., VAN HESS, G. R., and SHANOR, S. P. (1956). *Anæsthesiology, 17*, 559.
[7]EVANS, F. T., GRAY, P. W. S., LEHMAN, H., and SILK, E. (1953). *Brit. Med. J., 1*, 136.
[8]CALVERT, J., LEHMAN, H., SILK, E., and SLACK, W. K. (1954). *Lancet, 2*, 354.
[9]FOLDES, F. F., MCNALL, P. G., BIRCH, J. H. (1954). *Brit. Med. J., 1*, 967.
[10]FOLDES, F. F. (1955). Proceedings of World Congress of Anæsthesiologists, Schevenigen, p. 310.
[11]IRWIN, R. L., WELLS, J. B., and WHITEHEAD, R. W. (1956). *Anæsthesiology, 17*, 759.
[12]MAYRHOFER, O. K. (1952). *Anæsthesia, 7*, 250.
[13]MCCANCE, R. A. (1950). *Proc. R. Soc. Med., 43*, 272.
[14]FOLDES, F. F., *et al.* (1953). *Science*, 383.
[15]BARNES, J. M. and DORIS, D. R. (1951). *Brit. Med. J., 11*, 816.
[16]REID, E. H. (1954). *J. Pharm., Lond., 4*, 778.
[17]DAVIS, J. I. (1956). Canadian Anæsthetists Society Journal, *3*, 11.
[18]*Brit. J., Pharmacol.* (1954). *9*, 429.
[19]TAMMELIN, L. E. (1953). *Acta Chem. Scand., 7*, 185.
[20]Personal Communication.
[21]BULLOUGH, J. (1957). *Anæsthesia, 12*, 114.