Section of Anæsthetics

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Registrar's Prize Essay

Residual Post-operative Paralysis

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For several hours after anæsthesia in which a non-depolarizing muscle relaxant has been used, many patients show ptosis and nystagmus which suggest a minor degree of paralysis. Particularly striking is the associated finding of a divergent position of the eyes and the extent of this divergence can be used as a very sensitive measure of the effects of small amounts of muscle relaxant. The results are presented here of the application of such measurements in the investigation of the incidence and nature of residual paralysis in the post-operative period.

Methods

The position of rest of the eyes is in divergence, and in normal binocular vision it is the tone of the medial recti which adducts the eyes to maintain single vision. The degree of tone of the medial recti may be assessed in the conscious patient by the Maddox wing (Lyle & Wybar 1967), in which the relative position of the eyes is directly measured in prism dioptres. A small dose of muscle relaxant causes a wide divergence of the eyes (exophoria) and in the Maddox wing used here the horizontal scale was extended from 22 to 28 dioptres (Fig 1). A similar, though smaller, divergence results from the administration of sufficient anæsthetic agent to make the patient sleepy without loss of consciousness; for instance, such effect can be produced by 25–50 mg of thiopentone. It appears that a generalized reduction of muscle tone resulting from a dose of muscle relaxant or anæsthetic agent causes ocular divergence because in the normal eye any weakness of the extraocular muscles has a proportionately greater effect on the medial recti. The Maddox wing can measure relative vertical and rotatory movements of the eyes, but these are less common and only the horizontal scale is shown in the modified Maddox wing (Fig 1).

During the study all patients anæsthetized by me for gynæcological surgery were included, with the exception of 2 patients who had unilateral vision and 4 patients with language difficulty. A total of 91 patients were investigated, 52 having minor procedures lasting about 20 minutes and 39 having major surgery lasting about one hour. The minor cases were used as controls for the major cases to provide some comparison of the effects on the Maddox wing readings of general anæsthesia alone and general anæsthesia with a muscle relaxant. The two groups of patients were

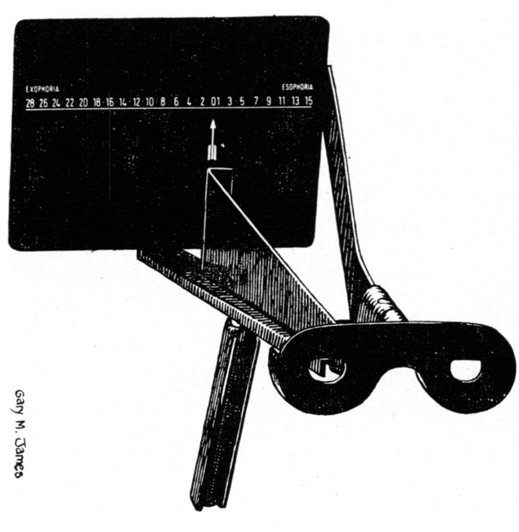

Fig 1 *The modified Maddox wing. Exophoria, divergence of eyes. Esophoria, convergence of eyes. Scale in prism dioptres*

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Table 1
Ages of patients in the study

	Minor surgery		*Major surgery*	
Age (years)	*No. of patients*	*Percentage of total*	*No. of patients*	*Percentage of total*
15–24	7	13	3	8
25–34	15	29	12	31
35–44	15	29	12	31
45–54	10	19	6	15
55–64	3	6	3	8
65–74	2	4	3	8
Total	52	100	39	101

similar in age (Table 1) and many of the minor cases would later be on the list for major surgery.

Measurements were made with the Maddox wing at the following times: (1) When the patients were first admitted. (2) After premedication (except in day cases who received no premedication). (3) Within the first four hours after operation. (4) Five to twelve hours after operation. (5) On the consecutive two days in the major cases.

Patients who used spectacles were made to wear them whenever their eyes were tested. Concurrently with the Maddox wing tests, changes in the near point of accommodation for each eye were measured with the Royal Air Force gauge (Neely 1956). Accommodation and convergence are linked in a reflex so that changes in accommodation can affect the Maddox wing readings. Such changes in accommodation as occurred were not considered sufficient materially to affect the Maddox wing readings. This conclusion is supported by Drucker *et al.* (1951), who found that muscle relaxants had very little effect on the near point of accommodation. The study required the storage, retrieval and correlation of much information and a comprehensive multiple-choice questionnaire was designed in such a form that the details for each patient could be transferred to punch cards and processed by a computer.

Details of Anæsthesia

Patients were premedicated, one hour before operation, with pethidine 1·2 mg/kg and atropine 0·009 mg/kg by intramuscular injection. However, 31 of the 52 minor cases were admitted only for the day and therefore were given no premedication apart from intravenous injection of atropine 0·009 mg/kg at the time of induction of anæsthesia. General anæsthesia in all patients was induced with intravenous thiopentone 3·1–4·7 mg/kg. In the minor cases anæsthesia was continued with nitrous oxide, oxygen and halothane 1·5–2·0%. In the major cases the trachea was intubated after intravenous injection of suxamethonium 0·8 mg/kg and anæsthesia maintained with nitrous oxide, oxygen and halothane 0·5%; muscle relaxation was continued with intravenous injection of gallamine 1·9 mg/kg. Patients were mechanically ventilated at 8–10 litres/min as measured with a Wright meter. At the end of operation gallamine was reversed by intravenous injection of neostigmine 0·04 mg/kg three minutes after atropine 0·02 mg/kg.

Results

There was no significant difference between the Maddox wing readings in patients undergoing major or minor surgery when they were first admitted to hospital. One hour after premedication there was no significant change in the readings. In the first four hours after operation readings were obtained in 50 of the 52 minor cases and 32 of the 39 major cases: 2 of the minor cases were unable to co-operate and 7 major cases were drowsy following post-operative pethidine or were unable to co-operate. These readings showed that on the whole there was greater divergence of the eyes in the major than in the minor cases and this difference is highly significant ($P<0·001$, Fig 2). There was still a significant difference between the two groups in the 5–12 hour period. In 5 major cases an appreciable degree of exophoria persisted over the next two days.

In several of the patients from both groups the early post-operative recovery was studied more closely and readings were taken at frequent intervals from the time of first awakening. In a typical example of recovery from anæsthesia for minor surgery (Fig 3) the patient was able to give a reading five minutes after discontinuation of anæsthesia and further readings showed a rapid recovery within a few minutes. Following anæsthesia for major surgery patients awakened within five minutes of the administration of neostigmine and were able to give readings within a further minute or two provided that they were not prevented from co-operating by pain. The recovery of a patient following major surgery is shown in Fig 4. The initial recovery was similar to that in the minor case (Fig 3); however, within 30 minutes of injection of the neostigmine the eyes began to diverge again. This suggests that the effects of the neostigmine were wearing off and paralysis was recurring, although this was otherwise not clinically obvious. About 50 minutes after the original dose, a further half dose of neostigmine was given and the divergence of the eyes rapidly became less within three minutes. The onset of neostigmine activity is normally within 2–4 minutes (Foldes 1960) and it is likely that the initial dose of neostigmine produced a rapid effect which was not apparent because it coincided with the period of recovery from anæsthesia. It is to be noted that the eyes began to diverge again within about 30 minutes of the second dose of neostigmine. This patient showed a slow recovery

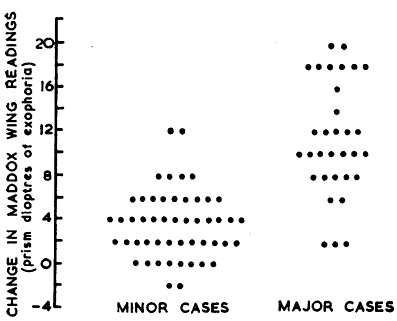

Fig 2 *Scatter diagram which shows the change in the Maddox wing readings in the first four hours post-operatively in the minor and major cases. The two groups are significantly different* ($t=7{\cdot}4286$, $P<0{\cdot}001$)

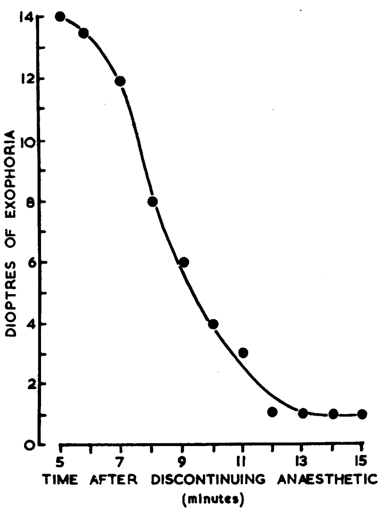

Fig 3 *Recovery of a woman aged 30 years following anæsthesia for minor surgery. Before operation the Maddox wing reading was zero*

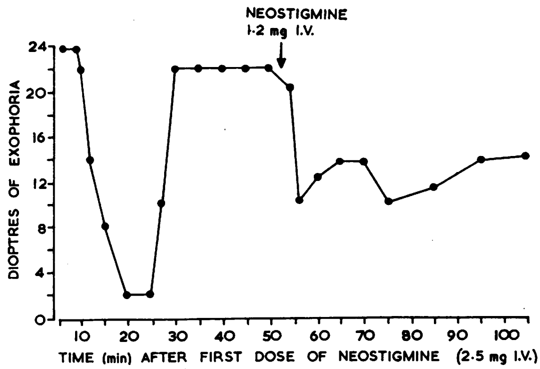

Fig 4 *Maddox wing readings following the administration of neostigmine to reverse gallamine, after operation for sterilization in a woman aged 33 years, weight 62 kg. Before operation the Maddox wing reading was zero*

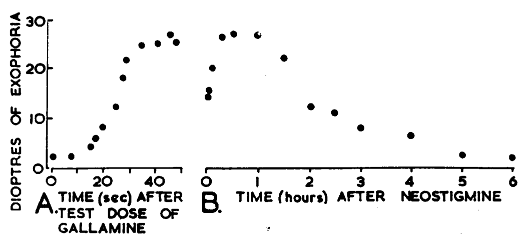

Fig 5A, *development of exophoria after a test-dose of intravenous gallamine (10 mg) in a woman aged 31 years, weight 60 kg. Return to normal in five minutes.* B, *Maddox wing readings after reversal of gallamine with neostigmine in the same patient after operation for sterilization*

over the next seven hours from the last reading shown in Fig 4.

The high sensitivity of the test is shown by the response of a patient to an intravenous injection of gallamine 10 mg before the induction of anæsthesia (Fig 5A); indeed such is the degree of sensitivity that the test has become 'saturated'. The Maddox wing reading became normal within five minutes and the patient suffered no discomfort apart from very slight blurring of vision interpreted as drowsiness. (In other subjects it was found that 5 mg of gallamine gave satisfactory readings without saturation of the test, the effect lasting about two minutes.) In the post-operative study of this patient (Fig 5B) the first part of the recovery following neostigmine has been missed, but it may be seen that the obvious effect has worn off in about 20 minutes. The slow recovery which occurred over several hours post-operatively explains the clinical impression of prolonged activity of muscle relaxant which led to this investigation. As would perhaps be expected with the very sensitive Maddox wing test, in only a proportion (about 30%) of cases did the chosen dose of neostigmine produce precise reversal of the relaxant to demonstrate the neostigmine activity seen in Figs 4 and 5.

A further study has shown that the findings described above in relation to gallamine also apply to patients given tubocurarine 0·4 mg/kg. Those patients given either of these relaxants in the absence of halothane during maintenance showed similar persistence of post-operative paralysis and it is unlikely, therefore, that such delayed recovery was due to the potentiation of relaxant by this agent. Indeed the dosage of muscle relaxant was kept to a minimum by the use of halothane.

It is emphasized that the demonstration of a small degree of residual paralysis with the Maddox wing did not mean that the patients were clinically unsafe. However, there did seem to be an association between restlessness and residual paralysis post-operatively; for instance, one of the patients in the study, a woman aged 34 years, became very restless about two hours after operation for sterilization, during which she had been anæsthetized by the routine already described for major cases. Assessment with the Maddox wing showed wide divergence of the eyes, confirming residual paralysis, and she was given neostigmine 1·25 mg three minutes after atropine 0·6 mg by intravenous injection: the Maddox wing reading quickly became normal and she promptly relaxed and soon fell asleep. At the bedside was a dose of pethidine which was about to be given before the arrival of the anæsthetist on the ward. It is possible that the respiratory depression caused by a potent analgesic drug could cause deterioration in the condition of a partially paralysed patient.

In another study several patients for minor surgery were anæsthetized using the routine described for minor cases, but with the addition of suxamethonium 0·8 mg/kg prior to intubation of the trachea. Maddox wing readings showed no evidence of residual post-operative paralysis, which is an important consideration when suxamethonium is given to day cases requiring intubation.

Discussion

The re-establishment of the signs of neuromuscular block, after its apparent reversal by neostigmine, is a recognized complication of the use of relaxants in general anæsthesia (Foldes 1960). The mechanisms which have been offered for the persistence of residual relaxant activity post-operatively have been discussed by Jenkins (1961) and he emphasizes that any theory must explain apparently normal reversal for a period of time followed by recurrence of paralysis. An explanation is offered by the results here which show that neostigmine has a relatively short duration of maximum activity and this finding is supported by an *in vitro* study of the inhibition of cholinesterase by neostigmine (Kitz 1964). It may be that neostigmine causes sudden accumulation of acetylcholine which displaces relaxant from the neuromuscular end-plates and the displaced relaxant can then be excreted together with that in the plasma. When the neostigmine begins to wear off, the end-plates will re-equilibrate with the plasma level of the relaxant and, if this is significant, the patient will recurarize. Initial work with the Maddox wing suggests that this may be a useful tool in the evaluation of methods of prolonging the period of anti-cholinesterase activity; for example, by supplementing the initial neostigmine with an extra dose intramuscularly or with the longer-acting pyridostigmine.

It would be an advantage to avoid excessive dosage of muscle relaxant during anæsthesia and therefore minimize the amount present in the body post-operatively: in this respect a weak concentration of halothane could be useful to potentiate the relaxant and reduce its requirement. It is known that gallamine (Mushin *et al.* 1949) and probably tubocurarine (Cohen *et al.* 1967) are largely excreted in the urine and so care should be taken to avoid such conditions as dehydration and hypotension, which can decrease urinary output. Perhaps insufficient attention is paid to water requirements on the day of operation and, certainly, the urine output should be carefully observed in the post-operative period.

A further practical point which arises from this study is that, if the hospital routine is to keep patients in the recovery area for only 30 minutes, then recurarization, should it occur, will begin after return to the ward. The diagnosis may well be missed by the nursing staff in the ward because partial paralysis causes restlessness, which can be mistaken for pain. The administration of a potent analgesic with its attendant respiratory depression may be hazardous in these circumstances.

Conclusion

Residual paralysis in the post-operative period, following the routine clinical use of non-depolarizing muscle relaxants, has been assessed by measuring the balance of the extraocular muscles with a Maddox wing. This method has revealed that neostigmine has a relatively short duration of action and a degree of recurarization can occur when the effect of neostigmine is waning. It is possible to judge the sensitivity of a patient to a very small test-dose of relaxant before anæsthesia and initial work suggests that the Maddox wing may provide a useful method of measuring the rate of decay of drugs used in the reversal of muscle relaxants.

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