The choice of drugs to provide anaesthesia for patients with asthma has always posed a number of problems. This has been particularly so with regard to muscle relaxants as most of these drugs have been shown to liberate histamine and thereby provoke bronchospasm in susceptible individuals.

It has been claimed that pancuronium, an antidepolarizing muscle relaxant with a steroid structure and introduced into clinical practice in 1967, does not cause the release of histamine. For this reason it may be the relaxant of choice in the asthmatic patient (Nana, Cardan and Leitersdorfer, 1972).

It may not be entirely free from this activity, however, and the following case report is presented as a possible instance of histamine release in a susceptible patient following the administration of pancuronium.

CASE HISTORY

A female patient aged 42 years and weighing 55 kg was admitted in 1972 for investigation of a suspected subarachnoid haemorrhage. The past medical history was relevant in that following the birth of her first child 14 years previously, she developed bronchial asthma of a mild nature. This was treated intermittently with Amsec (aminophylline 130 mg, ephedrine 25 mg and amylobarbitone 25 mg) at a maximum dose of three capsules daily. No other treatment was required and there was no history of severe attacks. At no time did the patient need bronchodilator aerosols or steroid therapy. In 1966 she underwent a termination of pregnancy and sterilization by tubal ligation, and was unaware of any adverse reaction to the anaesthetic agents used at that time. Before the present admission the patient was taking diazepam 5−10 mg daily and quinalbarbitone 100 mg for night sedation.

The presenting complaint was severe headache without loss of consciousness and preoperative neurological examination revealed no abnormality. The cerebrospinal fluid was uniformly bloodstained. The respiratory and cardiovascular systems were normal apart from a blood pressure of 190/110 mm Hg. Haemoglobin level, chest radiograph and electrocardiogram were within normal limits.

Histamine release following pancuronium

A Case Report

R. W. Buckland and A. F. Avery

SUMMARY

A case report is presented in which an asthmatic patient appears to have developed bronchospasm after being given pancuronium. A review of the literature indicates that this agent is the least likely of muscle relaxants in clinical use to provoke such a response, and that no such case has hitherto been reported. It is suggested that caution should be exercised even when pancuronium is used in asthmatic patients, and that those susceptible to bronchospasm in association with this agent might be identified by preanaesthetic skin sensitivity testing.

Anaesthetic sequence.

Premedication was with atropine 0.6 mg intramuscularly 1 hour before anaesthesia. When the patient arrived in the Radiology Department for bilateral carotid angiography her blood pressure was 180 mm Hg systolic and her pulse rate 80 beats/min. Thiopentone 400 mg followed by suxamethonium chloride 75 mg were administered through a butterfly-type indwelling needle in the dorsum of the right hand. After inflation of the lungs with 100% oxygen the larynx was sprayed with 4 ml of 4% lignocaine solution and the trachea intubated with a 9.0 mm cuffed latex armoured tube lubricated with water-soluble jelly. No untoward reaction was noted at this stage. The tube was firmly strapped in position and manual ventilation of the lungs was continued; expansion of the chest was normal and air entry equal on both sides.

Resumption of spontaneous ventilation was not long delayed and the patient was allowed to breathe nitrous oxide and oxygen (70%/30%) through a Cape-Waine ventilator on a non-return circuit. The blood pressure at this stage was 180 mm Hg systolic. Phenoperidine 1.5 mg was given intravenously and spontaneous ventilation allowed to continue for 10 minutes at a rate of approximately 12 b.p.m. During this interval, plain skull radiographs were taken with the patient supine and with necessary positioning of the head. The blood pressure and pulse rate remained unchanged. Pancuronium 4 mg was then given intravenously and intermittent positive pressure respiration commenced with the Cape-Waine ventilator using a non-return circuit to give a tidal volume of 800 ml and a rate of 13 per minute, with nitrous oxide and oxygen (70%/30%). The peak inflation pressure was 20 cm H2O. The systolic blood pressure fell from 180 to 110 mm Hg over the next 3−4 minutes, the pulse rate rose to 90 beats/min, and the patient's face became flushed. The peak inflation pressure on the ventilator pressure gauge rose gradually from 20 to 40 cm H2O over the next 10 minutes. The apparatus was checked throughout, but no fault was found. Both sides of the chest were expanding equally, but manual ventilation was more difficult than during the initial apnoeic phase after suxamethonium. Gentle movement of the endotracheal tube produced no improvement. Auscultation of the chest revealed poor air entry on both sides with prolongation of the expiratory phase.
This case report describes a rise in inflation pressure in a mildly asthmatic patient following the intravenous administration of pancuronium. This pressure rise when controlled ventilation is employed during anaesthesia, may occur for several reasons. Faults in the apparatus include kinking and obstruction of the anaesthetic tubing, the catheter mount or the endotracheal tube. The tube itself may become blocked in a variety of ways: by mucus, by the terminal end impinging on the tracheal mucosa, which is unlikely with an armoured tube, or by the tube slipping into one main bronchus (Gilton, 1969; Heinonen, Takki and Tammiisto, 1969). Each of these possibilities was excluded by careful examination. The rapid reversal of the change in inflation pressure by aminophylline suggested that bronchospasm was responsible for that rise, as did the clinical examination.

Bronchospasm may be provoked in several ways in the anaesthetized patient (Colebatch and Halmagyi, 1962; Shnider and Papper, 1961; Simonsson, Jacobs and Nadel, 1967; Lee and Atkinson, 1964). This patient had been intubated for about 15 minutes before there was an increase in inflation pressure, and it seems improbable that the presence of an endotracheal tube would only then have induced bronchospasm. Foreign material such as regurgitated gastric contents may be aspirated and produce spasm, but in this case a cuffed endotracheal tube was in position, there were no other indications to suggest that aspiration might have occurred, and wheezing due to this cause is usually more prolonged and persistent (Mendelson, 1946). Drug-induced bronchospasm must always be considered, and in this patient all of the drugs used except pancuronium have been known to be causative factors (Goodman and Gilman, 1970). However, the results of skin testing (see table I) show that of the drugs used for the first anaesthetic only pancuronium produced a significant reaction. Unfortunately the real significance of skin tests is unknown; but these results taken with the time pattern of events after the administration of pancuronium suggest that it was the causative agent, inducing bronchospasm by the release of histamine.

The release of histamine by many of the muscle relaxants is well known. Curare and tubocurarine were the first widely used members of this group, and histamine liberation was soon noted both experimentally (Alam et al., 1939) and clinically (Comroe and Dripps, 1946; Westgate and Van Bergen, 1962; Whitacre and Fisher, 1945). The latter reports suggested that erythema, hypotension, bronchospasm, excess salivation and bronchial secretion were pro-

**DISCUSSION**

This case report describes a rise in inflation pressure in a mildly asthmatic patient following the intravenous...
duced by the liberated histamine. In a patient who already has airways obstruction due to pre-existing bronchial asthma, the additional bronchospasm produced by these agents may be critical, and there have been case reports, such as that of Salem, Kim and Eletr (1968), where this situation has arisen.

Amongst the other muscle relaxants, dimethyl-tubocurarine and suxamethonium cause histamine release to a significant degree; decamethonium and gallamine do so only when given in very high doses (Goodman and Gilman, 1970; Sniper, 1952). Alcuronium is practically devoid of such activity following ordinary doses (Lund and Stovner, 1962; Bush, 1965). However pancuronium has been shown to have no such activity, either experimentally in animals, even at the very high dose level of 10 mg/kg in guineapigs (Buckett et al., 1968) or clinically in man (Baird and Reid, 1967; Cruil, 1968; Sellick, 1968; Baird, 1968; McDowell and Clarke, 1969). This has been confirmed by 5 years of clinical experience and the manufacturers have not been informed of any side-effects attributable to histamine release (Farrell, C., 1972, personal communication).

The features of this case which suggest histamine release and its association with the use of pancuronium are the occurrence of facial erythema, a fall in blood pressure and bronchospasm which were specifically time-related to the intravenous injection of pancuronium, after a stable anaesthetic state had been achieved with other agents. The presence of a moderate skin weal following subcutaneous sensitivity testing with pancuronium is also suggestive. A marked skin weal also occurred after the subcutaneous administration of a test dose of tubocurarine, and this was presumably due to local histamine release. It is interesting to note that the prior injection of hydrocortisone in particular before the intravenous administration of this relaxant may have been a significant factor in preventing another episode of bronchospasm.

It is suggested that while pancuronium is still the relaxant of choice for use in the asthmatic patient, it would seem possible for untoward effects to occur even with this agent, and preanaesthetic sensitivity testing might indicate in which patients this is likely to occur.

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REFERENCES


**LIBERATION D'HISTAMINE APRES PANCURONIUM**

**SOMMAIRE**

Les auteurs présentent le cas d'un patient asthmatique, qui semblait avoir développé des bronchospasmes après avoir reçu du pancuronium. Une revue de la littérature indique que cet agent est parmi les relâchants musculaires en usage clinique, le moins probable à causer une pareille réaction, et qu'aucun cas de ce genre n'a été rapporté jusqu'à présent. La prudence est conseillée lors de l'emploi de pancuronium chez des patients asthmatiques et il est possible que ceux, qui sont susceptibles aux broncho-spasmes en association avec ce médicament, pourraient être identifiés par un test cutané de sensibilité avant l'anesthésie.

**ÜBER DIE HISTAMINFREISETZUNG NACH PANCURONIUM**

**ZUSAMMENFASSUNG**


**LIBERACION DE HISTAMINA A CONSECUENCIA DE PANCURONIUM**

**RESUMEN**

Se presenta el caso de un paciente asmático que parece haber desarrollado broncoespasmo después de administrarle pancuronium. Una revisión de la literatura sobre este agente indica, que éste es el más improbable de todos los relajantes musculares de uso clínico que pueda provocar esta reacción, y que no se conoce ningún caso hasta ahora. Se sugiere que se deberían tomar medidas de precaución en los pacientes asmáticos, incluso cuando se emplee pancuronium; aquéllos que sean susceptibles a los broncoespasmos, relacionados con este agente, pueden ser identificados por un test de sensibilidad de la piel realizado antes de la anestesia.