Suxamethonium and respiration

Investigation of a possible central action of suxamethonium chloride during clinical anæsthesia

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Respiratory depression may be produced either by interference with the relevant effector neuromuscular apparatus or by depression of the sensitivity of the respiratory 'centre'.

In the absence of central depression, impairment of the effector mechanism usually causes an increase in respiratory rate in compensation for the diminution of tidal volume, and brought about by the increasing pCO_2 and pH and the decreasing pO_2 of the blood. Absence of increase in respiratory rate in the presence of impairment of the neuromuscular mechanism suggests depression of the sensitivity of the respiratory 'centre'.

Clinically it is our experience, when using muscle relaxants, in doses insufficient to cause complete respiratory paralysis, that this increase in respiratory rate often occurs, if allowed to do so, but less frequently with suxamethonium chloride than with d-tubocurarine chloride, gallamine triethiodide or decamethonium iodide, such increase being almost invariable with the latter three drugs. This difference in response prompted us to investigate the possible depressant effect of suxamethonium chloride on the respiratory 'centre'.

In order to do this, it is necessary to free the patient from physiological consequences of muscular weakness and also to protect him from changes in environment.

The respiratory 'centre' aims at maintaining for itself a stable environment in respect of pCO_2, pO_2 and pH, and it does so by altering the rate and depth of respiration[1]. If a standard, adequate inflation of the lungs be substituted for each attempt at inspiration, then the patient is deprived of one of his adjustment mechanisms. The depth

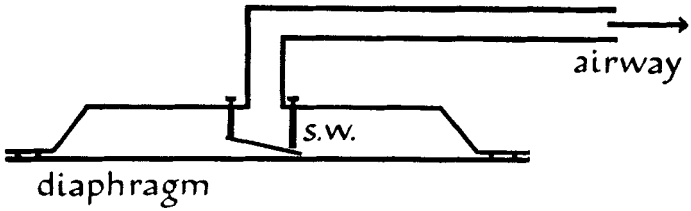

FIG. 1 Device for patient actuation of respirator

of respiration is then fixed, but his respiratory 'centre' is still free to respond to change in arterial pCO_2, pO_2 and pH, by altering the rate at which it initiates attempts ar respiration.

In such a system, the anæsthetised patient, freed from cortical and reflex disturbance of respiration, can maintain the arterial pCO_2, pO_2 and pH levels which best suit his respiratory 'centre'. The arterial pCO_2 will, of course, be reflected by the alveolar carbon dioxide tension and a sustained rise in the latter tension will indicate a diminished sensitivity of the respiratory 'centre' to its normal driving force.

METHOD

The apparatus consists of a machine for performing artificial respiration in a closed circuit, together with a device for instituting inflation of the lungs whenever the patient attempts to breathe.

The pressure to which the lungs can be inflated and the length of the respiratory pause may both be altered and a device is incorporated whereby an inspiratory effect by the patient sufficient to create a negative pressure of only −2mm Hg will 'trigger-off' the inspiratory phase of the machine, and inflation of the patient's lungs to a predetermined pressure will take place.

FIGURE 1 shews the principle whereby the patient may activate the respirator. An attempt at inspiration creating a negative pressure of 1.5mm Hg or more, moves the large loose diaphragm and closes the micro-switch S W.

The circuit controlled by this is in parallel with the main circuit which initiates inspiration and performs the same function, regardless of what part of the cycle the machine has reached at the time.

FIGURE 2 shews simultaneous pressure and flow tracings in the respirator during an attempted breath by the patient. The negative pressure alters to positive at P, when inspiration is initiated and a simultaneous inflow of air is shewn in the lower tracing.

Four samples, each of 2ml, of air are taken from the deep trachea during the end part of successive expirations, and the carbon dioxide

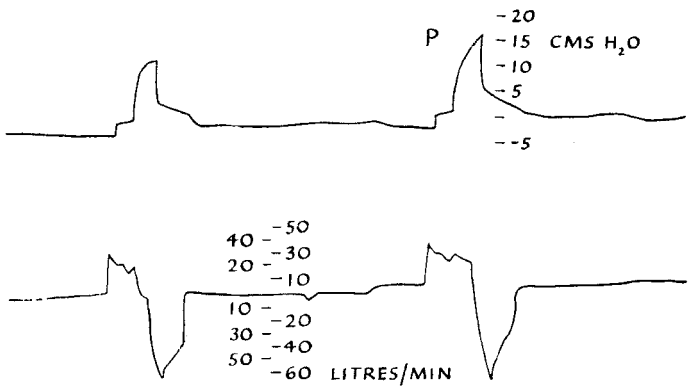

FIG. 2 Simultaneous pressure and flow tracing in respirator

concentration in this 8ml mixture is measured by bringing the sample into contact for one minute with an indicator solution lightly buffered with sodium bicarbonate, the change in colour being measured on a previously calibrated colorimeter[2]. The indicator is itself periodically tested against a gas of known carbon dioxide content and a correction graph obtained.

These samples from the deep trachea are unvaried during stable conditions and may reasonably be taken to reflect constantly the carbon dioxide concentrations in the alveolar air.

The anæsthetic procedure adopted for this investigation was as follows.

After light premedication, usually morphine gr 1/6th and atropine gr 1/100th, one hour before anæsthesia, sufficient sodium thiopentone was given, slowly in a 5% solution, just to send the patient to sleep. Nitrous oxide–oxygen and ether were then given by a Boyle's machine, until oral intubation with a size 10 cuffed tube could be atraumatically performed, the cords having first been sprayed with 1ml of 4% lignocaine hydrochloride solution. Anæsthesia was maintained in plane one of stage three, until successive end-expiratory air samples, containing equal carbon dioxide concentrations, had been obtained. The patient was then connected to the respirator, set to inflate his lungs twice or thrice a minute, with a nitrous oxide–oxygen–ether mixture from the same Boyle's machine. Under such circumstances, the patient's inspiratory efforts 'triggered-off' the machine, and equilibrum, reflected by the end-expiratory carbon dioxide readings, was soon established.

The effect upon these readings, of giving a known respiratory depressant, was then tried, in order to test the method. Pethidine, 25mg intravenously, was given to a series of ten patients and end-expiratory

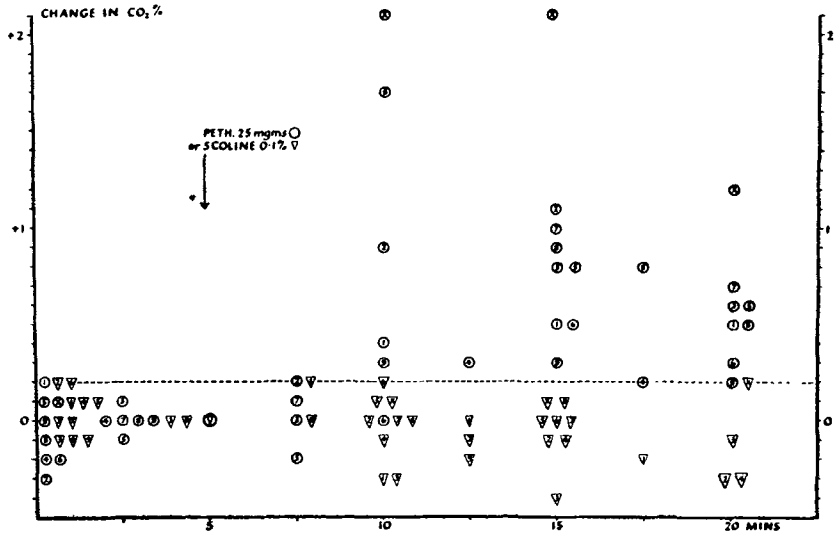

FIG. 3 Percentage change in end-expiratory CO_2 after giving pethidine or suxamethonium chloride. It is to be noted that no triangles (suxamethonium chloride cases) occur above the dotted line, and, after 10 minutes, no circles (pethidine cases) occur below it.

carbon dioxide samples taken for fifteen minutes thereafter. FIGURE 3 shews that an increase of carbon dioxide concentration occurred in each case, the minimum increase being 0.3%, and the maximum 2.1%.

On the same graph is shewn the effect of a 0.1% infusion of suxamethonium chloride upon ten other patients. There is no upward trend in the carbon dioxide readings, and we conclude that, in the dosage given, suxamethonium chloride had no depressant action on the central respiratory mechanism of these patients.

It is emphasised that these results were obtained in the circumstances described and with subparalysant doses of suxamethonium chloride. The possibility of central respiratory depression by this drug in other circumstances, or in larger doses, is not eliminated.

References

[1]GRAY, J. S. (1950). 'Pulmonary Ventilation and its Regulation'. Springfield, Illinois. Page 29.

[2]INKSTER, J. S. and REES, L. T. (1956). *Brit. J. Anæsth.*, *28*, 1. 37.