

## QUANTITATIVE EVALUATION OF THE BRONCHOCONSTRICTOR ACTION OF CURARE IN THE ANESTHETIZED PATIENT: A PRELIMINARY REPORT \*

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Received for publication November 14, 1951

THE bronchoconstrictor action of curare has been recorded and studied in the spinal dog (1) and in the decerebrate guinea pig (2). However, although it has been observed in the anesthetized patient (3, 4) and produced in the human volunteer (2), the bronchoconstrictor action of curare in man has been neither recorded nor thoroughly studied.

The present study was initiated in an attempt to record and evaluate quantitatively the bronchoconstrictor action of curare in the anesthetized patient under ordinary clinical conditions. A small group of patients has been studied to date, and, although the limited data thus far obtained are not suitable for statistical analysis, typical kymographic tracings which have been recorded are of interest.

### METHOD

The present study was conducted according to the basic principles of a method previously described (5) for recording the effect of various agents upon the caliber of the human bronchial tree. The employment of this method depends upon an apparatus which will maintain automatic controlled respiration (6, 7) at a constant rate and force in the anesthetized patient and record changes in the tidal volume under these conditions. The apparatus originally designed to accomplish this (fig. 1) was simplified and refined for the present study (fig. 2) without changing the basic principles of operation.

All subjects were surgical patients for whom endotracheal anesthesia with a completely closed system was selected. Various combinations of preoperative medication and anesthetic agents were employed to facilitate endotracheal intubation and controlled respiration, but curare was not administered until after the patient had been intubated and automatic controlled respiration at a constant rate and force had been instituted. As soon as automatic controlled respiration was estab-

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lished, anesthesia was kept at as constant a level as possible while a control kymographic tracing of the tidal volume was recorded. Then, without interrupting the tracing and before the surgical incision was made, d-tubocurarine chloride, 15 to 24 mg. (100 to 160 units), was administered by rapid (2) intravenous injection.

Under the conditions of these experiments, any changes in the tidal volume, as recorded and measured on the kymographic tracing, reflected changes in the *effective* bronchial caliber (5), that is, the over-all resistance to inflation of the lungs by automatic controlled respiration at a constant rate and force.

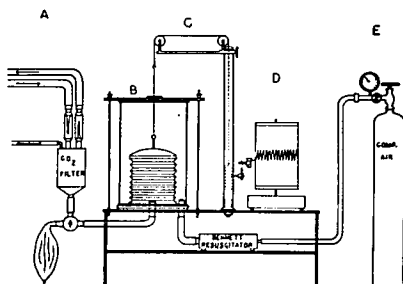


FIG. 1. Diagrammatic illustration of apparatus: A. Closed circle system leading to and from patient showing inlet for anesthetic mixture, CO<sub>2</sub> absorption unit, three-way stopcock, and anesthesia breathing bag. B. Cylindrical glass-walled compression chamber containing bellows breathing bag. C. Counterweight system with capillary ink writer. D. Kymograph. E. Compressed air tank connected to and driving Bennett resuscitator.

FIG. 1. Diagrammatic sketch of the original apparatus designed for recording the effect of various agents upon the caliber of the human bronchial tree (5).

## RESULTS

In 9 anesthetized patients the influence of curare upon the effective bronchial caliber was manifested in three general types of response.

(1) An increase in the effective bronchial caliber, as shown by an increased tidal volume, occurred in 3 patients (fig. 3). This type of response is attributed to a decreased resistance to inflation of the lungs produced by the relaxant effect of curare upon the thoracic and abdominal muscles and the diaphragm in the absence of concomitant bronchoconstriction.

(2) Little or no change in the effective bronchial caliber, as reflected in the tidal volume, occurred in 5 patients (fig. 4). It is possible that in these cases the decreased resistance to inflation of the lungs usually produced by the relaxant effect of curare upon the thoracic and abdominal muscles and the diaphragm was nullified by a mild bronchoconstrictor response.

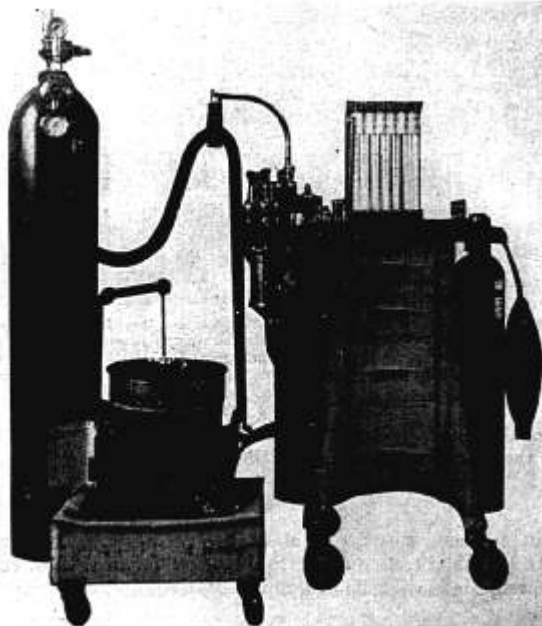


FIG. 2. The simplified and refined apparatus employed for recording the bronchoconstrictor action of curare in this study. The large tank of compressed oxygen delivers intermittent positive pressure at a constant rate and force to the compression chamber (constructed from a McKesson Metabolor, Model 175)<sup>†</sup> by virtue of a pneumatic balance resuscitator (8) which acts as a cycling device. The intermittent positive pressure is exerted upon a calibrated bellows breathing bag (enclosed within the compression chamber) to produce automatic controlled respiration at a constant rate and force through the closed circle absorption system of the anesthesia machine. Excursions of the calibrated bellows breathing bag are recorded directly upon a telechron kymograph by a capillary ink writer incorporated in the counterweight system.

(3) A decrease in the effective bronchial caliber, as manifested by a diminished tidal volume immediately following the intravenous administration of d-tubocurarine chloride, 21 mg. (140 units), occurred in one patient (fig. 5). This type of response is attributed to bronchoconstriction of a magnitude sufficient to increase the resistance to infla-

<sup>†</sup> The technical assistance of Mr. Thomas Rankin, of Thomas A. Edison, Inc., in the construction of this part of the apparatus is gratefully acknowledged.

<sup>‡</sup> Manufactured by the Mine Safety Appliance Company, Pittsburgh, Pennsylvania, as the M. S. A. Pneophore.

L. P., 59 yrs., w. f. 10/10/50  
 Subtotal Gastrectomy  
 Sod. Amytal, Morphine, Scopolamine  
 Pentothal I.V., Cyclopropane  
 Endotracheal Cyclopropane-Oxygen

d-TUBOCURARINE TIDAL VOL: 520 to 640  
 140 u. I.V. B. P.: 110/80 to 80/60



FIG. 3. Kymographic record showing the type of response characterized by an increase in the effective bronchial caliber following the intravenous administration of d-tubocurarine chloride, 21 mg. (140 units). The tidal volume increased from 520 cc. to 640 cc. while the blood pressure fell from 110/80 mm. to 80/60 mm. of mercury (each small square represents 80 cc. of tidal air vertically and six seconds of time horizontally).

tion of the lungs in spite of the accompanying relaxant effect of curare upon the thoracic and abdominal muscles and the diaphragm.

#### COMMENT

The evidence thus far obtained suggests that the response of the human bronchial tree to the intravenous administration of curare during anesthesia is variable and unpredictable. So far, a frank broncho-

I. S., 37 yrs. w. f. 9/23/50  
 Thoraco-lumbar Sympathectomy  
 Nembutal, Demerol, Scopolamine  
 Pentothal I.V., Pontocaine Spray  
 Endotracheal Oxygen

d-TUBOCURARINE TIDAL VOL: No change  
 140 u. I.V. B. P.: 200/140 to 140/100

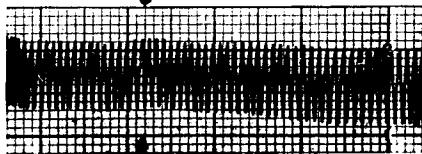


FIG. 4. Kymographic record showing the type of response characterized by little or no change in the effective bronchial caliber following the intravenous administration of d-tubocurarine chloride, 21 mg. (140 units). The tidal volume remained constant at 640 cc. while the blood pressure fell from 200/140 mm. to 140/100 mm. of mercury (each small square represents 80 cc. of tidal air vertically and six seconds of time horizontally).

constrictor response has been recorded only once. Because of the apparently infrequent occurrence of detectable bronchoconstriction following the intravenous administration of curare in anesthetized patients, it has been impossible as yet to attempt a thorough study of its mechanism in human beings. However, it is likely that when broncho-spasm caused by curare does occur in the anesthetized patient its mechanism is on a histamine-liberating basis since there is evidence that curare produces histaminic reactions in human beings (9, 10) as well as in animals (1, 2, 11, 12).

That curare produces detectable bronchoconstriction apparently much less regularly in anesthetized patients than in laboratory animals

W. F., 60 yrs. w. m. 9/22/50  
 Radical Mastectomy  
 Nembutal, Demerol, Atropine  
 Pentothal I. V., Cyclopropane,  
 Endotracheal Oxygen

d-TUBOCURARINE TIDAL VOL: 560-400  
 140 u. I.V. B. P: 124/70 to 94/50

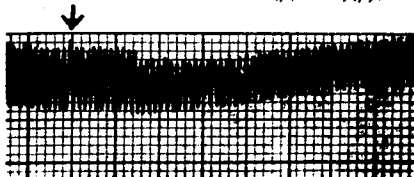


FIG. 5. Kymographic record showing the type of response characterized by a decrease in the effective bronchial caliber following the intravenous administration of d-tubocurarine chloride, 21 mg. (140 units). The tidal volume decreased from 560 cc. to 400 cc. while the blood pressure fell from 124/70 mm. to 94/50 mm. of mercury (each small square represents 80 cc. of tidal air vertically and six seconds of time horizontally).

(1, 2) is fortunate, but the reason for this difference remains to be explained. It is possible that the explanation is simply one of species difference. On the other hand, it is also possible that the explanation is one of differences in experimental methods, that is, in the spinal animal, which is completely flaccid to begin with, the muscle relaxant effect of curare cannot mask a bronchoconstrictor response as it may in the anesthetized patient. Still other possibilities which might be further explored are suggested by reports relating to the depressant effects of certain anesthetic agents and methods upon the liberation and action of histamine (14-19).

§ Miller (13) stated: "The lungs of the guinea pig contain, proportionally, a large amount of smooth muscle than those of any other animal I have studied. It is the presence of this large amount of muscle in the bronchial tree and in the pleura that makes the lung of the guinea pig so difficult to distend."

## SUMMARY

An apparent bronchoconstrictor response to the intravenous administration of d-tubocurarine chloride in the anesthetized patient has been recorded. Variations in this response have been described.

Detectable bronchoconstriction following the intravenous administration of d-tubocurarine chloride apparently occurs much less regularly in the anesthetized patient than in the laboratory animal. Possible explanations for this are suggested.

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