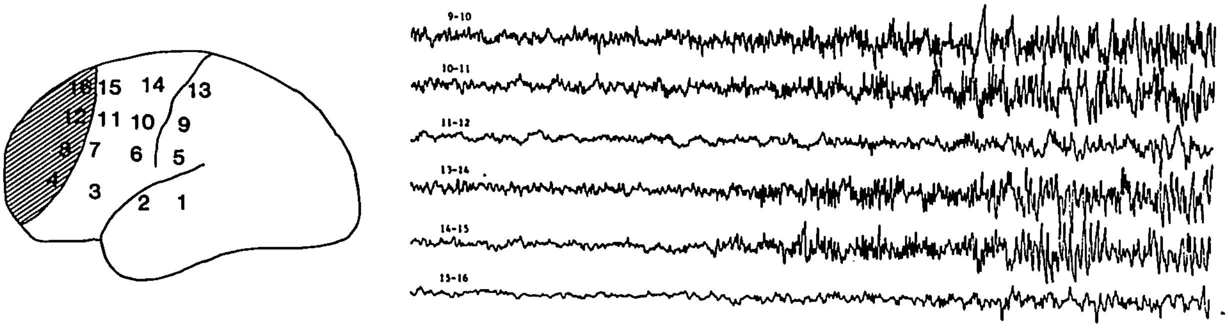

FIG. 3. Postexcision recording following partial left frontal lobectomy. Etomidate administered 20 s prior, again producing an increase in fast activity, but no clear epileptogenic activity. Calibration is the same as in Figure 1.

makes it a potentially useful drug to deliberately enhance epileptogenic activity in patients undergoing electrocorticography as part of cortical resection of epileptogenic tissue for the treatment of refractory epilepsy and would be an acceptable alternative to methohexital, especially in those patients allergic to barbiturates.

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Precurarization Inhibits Maximal Ventilatory Effort

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Pretreatment with 3–5 mg *d*-tubocurarine (*d*TC) prevents succinylcholine- (SCh) induced muscle fasciculation.[1–3] This has been shown to attenuate the increased intragastric[4] and intraocular[5] pressures that usually accompany fasciculation and to reduce the incidence of post-SCh myalgia.[6] Most patients today are given SCh before tracheal intubation, and many of these are pretreated with a nondepolarizing drug such as *d*TC. In the interval between injection of *d*TC and the induction agent, an occasional patient becomes dyspneic and, very rarely, one develops apnea and must be ventilated.[7] In these circumstances, dyspnea may be due to respiratory muscle weakness, airway obstruction, or apprehension. Previous studies of low-dose *d*TC effect on muscle power of awake subjects employed doses of 0.1 mg/kg or greater.[8,9] The usual dose of *d*TC used clinically to pretreat adults is 3 mg,[10] which is 0.043 mg/kg for a 70-kg patient. We chose a comparable dose, 0.05 mg/kg, to study *d*TC effect on negative inspiratory pressure (NIP) and respiratory flow-volume loops of premedicated

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patients. A somewhat similar study in volunteers given 0.014 mg/kg pancuronium was reported in 1980.[11]

Methods

NIP measurements were made in 62 adult patients requiring surgical anesthesia, in a project approved by the Human Subjects Review Committee of NYU Medical Center. Patients were unselected for site or type of surgery, were of ASA physical status 1 or 2, and were premedicated according to preferences of the anesthesiologists scheduled to provide their care. Ten were not premedicated, eight were given oral diazepam preoperatively, two received only hydroxyzine, and the remainder received an opiate alone (8) or in combination with hydroxyzine (27) or pentobarbital (7). The patients' ages were from 19 to 62, with a mean of 33.4 years.

Preanesthetic preparations were made in a routine manner; then NIP was measured with a respiratory force meter (Boehringer) calibrated to register from 0 to 60 cmH_2O, positive or negative. Multiple measurements were made until reproducible values were obtained. They were then given intravenous *d*TC, 0.05 mg/kg, without their knowledge, and NIP was measured 1, 2, and 3 min later. At each interval, patients were asked: "Are you comfortable?"; "Does your breathing feel normal to you?"; "Does your eyesight seem normal?" Anesthesia and operation then proceeded as usual without further investigative intervention. A second study subsequently was performed with healthy patients at Mercy Hospital, Urbana, Illinois, with approval of their institutional review board. Starting from their residual volumes, these patients inspired and expired maximally during spirometric flow-volume loop recordings (Hewlett-Packard Pulmonary Function System®). After stable baseline measurements were reproduced, 0.05 mg/kg *d*TC was given and the spirometry was repeated 1, 2, and 3 min later. These patients were not asked about symptoms. Anesthesia and operation then proceeded according to routine. The ratio of mid-expiratory to mid-inspiratory flow rates (MEF_{50}/MIF_{50}) were calculated from the airflow tracings.[12] Statistical analyses of data were by two-way analysis of variance and Bonferroni *t* test.[13] A *P* value less than 0.01 was considered significant.

Results

Mean NIP values decreased after *d*TC, as shown in table 1. Analysis of individual changes showed that, at all three post-*d*TC intervals, these changes were highly significant statistically. However, not all patients had diminutions in NIP, as shown in table 2. Approximately one-third of the patients showed either no change or an increase, *i.e.*, a greater negative pressure generated, at these times. Of the 62 patients, 40 reported visual disturbances (usually diplopia), four had dyspnea at 2 and 3 min after *d*TC, and one had mild fasciculations after SCh. Two of these four were given no premedicants; the others had only hydroxyzine. Their NIP data are shown in table 3. All four of these patients also had diplopia, and none fasciculated after SCh.

Flow volume loops from the 15 patients in the second study showed an increased MEF_{50}/MIF_{50} in 12, no change in 2, and a very slight decrease for 1. For the total group, the mean control ratio was 0.90 ± 0.32 (SD) and the ratio 2 or 3 min after *d*TC was 1.42 ± 0.65 ($P < 0.01$). Some tracings were technically unsatisfactory, requiring the selection of the better of the 2- or 3-min post-*d*TC records. A representative tracing is reproduced in figure 1, which shows a control expiratory to inspiratory ratio greater than usual, an insignificant reduction of vital capacity (VC) after *d*TC, and a distinct flattening of the inspiratory limb of the loop after *d*TC, causing the MEF_{50}/MIF_{50} to increase from 1.41 to 2.32. This was the only case in which VC decreased after *d*TC.

TABLE 1. Negative Inspiratory Pressure of 62 Patients

Time	Mean	SE	*P*
Before curare	54.6	2.6	—
After curare, 0.05 mg/kg			
1 min	48.8	2.8	NS
2 min	41.7	3.1	<0.001
3 min	43.4	3.3	<0.001

Discussion

Our patients were studied under clinical conditions to assess the incidence of problems from "precurarization." The effect of *d*TC undoubtedly would have been greater if the interval between this drug's injection and induction of anesthesia were allowed to be longer than 3 min. We chose not to do this, because our experience suggests that most clinicans wait no longer than 3 min. The study was deliberately designed to reflect the reality of routine practice. Because our patients were premedi-

TABLE 2. Numbers of Patients with NIP Changes

Change	Time, Postcurare, 0.05 mg/kg		
	1 min	2 min	3 min
Decrease	43	43	44
None	7	3	4
Increase	12	16	14
Total patients	62	62	62

TABLE 3. NIP Values of Dyspneic Patients (NIP, cmH_2O)

Patient	Baseline	1 min	2 min	3 min
1	30	18*	20*	20*
2	80	75	60*	60*
3	22	26	23	16*
4	32	32	24*	22*

* Dyspneic.

cated, and were not required to generate NIP beginning from their point of residual volume, their baseline values were, in general, lower than those obtained in studies of unmedicated healthy volunteers. Some patients showed an *increase* in NIP after *d*TC, probably because repeated measurements aroused them from previously somnolent states.

The change from a mean NIP of 54.6 to 41.7 cmH_2O 2 min after *d*TC is significant statistically but probably not of clinical consequence. The later value, 41.7 cmH_2O, is still far from the normal limit of 20 to 25 cmH_2O suggested by Bendixen *et al.* as necessary for adequate ventilation.[14] This suggestion of safety is strengthened by our finding that some patients' NIP changed from 50 to 20 cmH_2O after *d*TC, with no accompanying dyspnea.

Why, then, did four patients report dyspnea? Their changes were no greater than those measured in many other patients without this symptom. None had any evidence, either preoperatively or postoperatively, of cardiopulmonary problems. Their premedication was either minimal or nonexistent, so this was not contributory. It is likely that individual patients have different

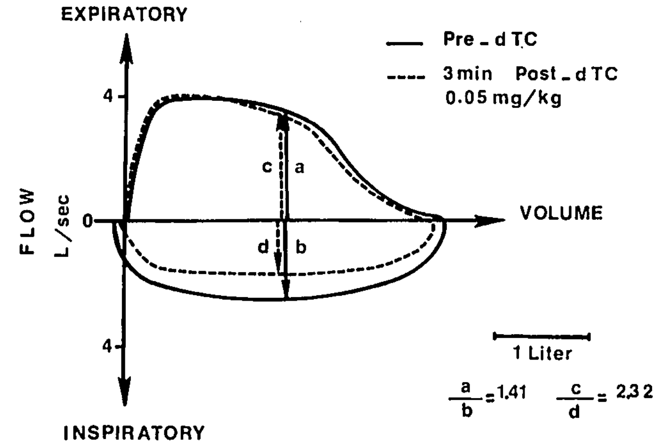

FIG. 1. Flow volume loops of patient before and after receiving *d*TC, 0.05 mg/kg. Arrows *a* and *b* indicate mid-VC airflows during expiration and inspiration, respectively, in the control condition (*solid line*). Arrows *c* and *d* indicate the corresponding flows after *d*TC (*broken line*). A marked reduction in mid-VC inspiratory airflow is evident.

sensitivities to the sensation of breathing impairment, just as there are large differences in pain threshold. We suspected that the site of this sensation would be the larynx rather than the thorax. If the striated muscle causing vocal cord abduction during inspiration were relaxed somewhat by a low dose of *d*TC, a slightly smaller laryngeal inlet would result in changes in laryngeal inspiratory airflow that could be experienced as shortness of breath.

The flow volume loops confirmed our suspicion of a laryngeal effect of *d*TC, 0.05 mg/kg. The only reasonable explanation for the flattened, reduced inspiratory airflow loops in 12 of 15 patients is that vocal cord abduction was impaired by the *d*TC. Although VC was unaffected, and patient safety presumably was not compromised by *d*TC pretreatment, a laryngeal effect of relaxants should not be considered unimportant. The occasional patient may perceive this change and suffer significant anxiety from it, just before hypnosis is induced, if he or she is ignored by the anesthetist.

Rao and Jacobs reported that 4 of 15 healthy volunteers suffered significant pulmonary dysfunction and dyspnea after 0.014 mg/kg pancuronium.[11] It is difficult to compare their data with ours, because they studied volunteers over a longer time period than 3 min, but easy to agree with their conclusion, "ventilation should be monitored in all patients following pretreatment."

Those patients for whom such pretreatment is chosen should be monitored closely and reassured that visual difficulties they may experience are harmless and temporary. Their ventilation also should be observed closely to watch for the rare occurrence of the "mild myasthenic state,"[15] while reassuring them that they are breathing normally even if they feel they are not. Once a nondepolarizing relaxant has been given, it is imprudent to direct one's attention to anything or anyone other than the patient until hypnosis and a protected airway have been established.

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