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# Functional Assessment of the Pharynx at Rest and during Swallowing in Partially Paralyzed Humans

## Simultaneous Videomanometry and Mechanomyography of Awake Human Volunteers

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**Background:** Functional characteristics of the pharynx and upper esophagus, including aspiration episodes, were investigated in 14 awake volunteers during various levels of partial neuromuscular block. Pharyngeal function was evaluated using videoradiography and computerized pharyngeal manometry during contrast bolus swallowing.

**Methods:** Measurements of pharyngeal constrictor muscle function (contraction amplitude, duration, and slope), upper

esophageal sphincter muscle resting tone, muscle coordination, bolus transit time, and aspiration under fluoroscopic control (laryngeal or tracheal penetration) were made before (control measurements) and during a vecuronium-induced partial neuromuscular paralysis, at fixed intervals of mechanical adductor pollicis muscle train-of-four (TOF) fade; that is, at TOF ratios of 0.60, 0.70, 0.80, and after recovery to a TOF ratio > 0.90.

**Results:** Six volunteers aspirated (laryngeal penetration) at a TOF ratio < 0.90. None of them aspirated at a TOF ratio > 0.90 or during control recording. Pharyngeal constrictor muscle function was not affected at any level of paralysis. The upper esophageal sphincter resting tone was significantly reduced at TOF ratios of 0.60, 0.70, and 0.80 ( $P < 0.05$ ). This was associated with reduced muscle coordination and shortened bolus transit time at a TOF ratio of 0.60.

**Conclusions:** Vecuronium-induced partial paralysis cause pharyngeal dysfunction and increased risk for aspiration at mechanical adductor pollicis TOF ratios < 0.90. Pharyngeal function is not normalized until an adductor pollicis TOF ratio of > 0.90 is reached. The upper esophageal sphincter muscle is more sensitive to vecuronium than is the pharyngeal constrictor muscle. (Key words: Monitoring: neuromuscular function; pharynx; manometry; train-of-four. Neuromuscular relaxants: vecuronium. Postoperative period: neuromuscular recovery, postanesthesia care unit.)

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RETURN to normal function of the pharynx and upper airway is essential for airway control in postoperative patients and in patients cared for in the intensive care unit after tracheal extubation or removal of a tracheostomy. In retrospective surveys, impaired ventilation and oxygenation or failed maintenance of the airway, due to residual effects of anesthetic agents or surgery, are the most frequent cause of complications and death in the postoperative period after general anesthesia and sedation.<sup>1,2</sup> In one half of patients admitted to an intensive care unit because of postoperative ventilatory failure, Cooper *et*



*al.*<sup>2</sup> identified residual neuromuscular block as the major reason for ventilatory failure. From studies of nonanesthetized persons we also know that subparalyzing priming doses of atracurium and vecuronium interfere with the electromyogram of pharyngeal muscles and may cause dysphagia and oral discomfort.<sup>3,4</sup> In partially paralyzed persons, impaired protection of the airway was demonstrated despite adequate recovery of respiratory muscles after subparalyzing doses of d-tubocurarine.<sup>5</sup> On the other hand, as supported by studies by Ali *et al.*,<sup>6</sup> a mechanical adductor pollicis train-of-four (TOF) ratio of 0.70 has for many years been regarded as being associated with adequately recovered muscle function, to allow safe extubation and spontaneous ventilation in the postoperative period.

Although routine neuromuscular monitoring during surgery and intensive care mainly are based on mechanical adductor pollicis responses after TOF ulnar nerve stimulation, we have only partial knowledge about the relation between recovery of adductor pollicis TOF responses and return of pharyngeal function and protection of the upper airway. Furthermore, we do not know what mechanisms are involved in pharyngeal dysfunction and aspiration in partially paralyzed persons. Extensive examination of the motility pattern of the pharynx and upper esophagus, including evaluation of airway protection and aspiration after barium contrast swallow, can be assessed using a videoradiographic recording under simultaneous solid-state manometry of the pharynx and upper esophagus; that is, after simultaneous videomanometry.<sup>7-10</sup> Functional assessment of the pharynx, upper esophagus, and of the integrity of the upper airway has thus been made in various populations of humans with pharyngeal dysfunction, such as those with dysphagia with or without aspiration. We did this study to evaluate pharyngeal function and airway protection at various degrees of residual adductor pollicis neuromuscular block in awake humans.

## Materials and Methods

The study protocol was approved by the local ethics committee for human research of Karolinska Hospital and Institute, Stockholm, Sweden. All volunteers gave their informed oral consent before being enrolled.

Fourteen healthy volunteers (7 men, 7 women) between the ages of 22 and 44 yr entered the study after 4 h of fasting. They denied neuromuscular, liver, or renal disease and were not taking any medication. None of them had undergone surgery of the pharynx, esophagus, or the upper airway and all denied gastroesophageal reflux disease or dysphagia.

After arrival in the laboratory, an intravenous cannula was placed in a cubital vein in the volunteers' arms that were not going to be used for neuromuscular monitoring, and a continuous infusion of normal saline was given at a rate of  $1-2 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ . ECG, peripheral arterial oxygen saturation, and systemic blood pressure (sphygmomanometry) were all monitored. Apart from the neuromuscular blocking agent, none of the volunteers received additional sedatives or other drugs.

### *Videomanometry of the Pharynx and Esophagus*

With the volunteer in an upright position, a catheter with four solid-state pressure transducers (Konigsberg Instruments, Pasadena, CA) separated 2 cm apart was inserted through one nostril and forwarded so as to place the distal tip in the cervical esophagus. The volunteers were then placed in a right lateral position on a servo-controlled radiography table, with the head of the table elevated 15 degrees from the horizontal axis. Under fluoroscopic control, correct catheter placement was then achieved by placing the most distal sensor within the upper esophageal sphincter muscle (UES) while the tip of the catheter was in the proximal part of the cervical esophagus. In this position, the most proximal sensor was at the level of the tongue base while the two intermediate sensors were positioned at the level of the pharyngeal constrictor muscle. The position of the transducer probe was confirmed and subsequently recorded using videoradiography. Intermittent fluoroscopy was thereafter used to ensure that the catheter position was maintained unchanged throughout the experimental procedure. The lower pharyngeal constrictor sensor and the UES sensor were recording circumferentially, and the two most proximal sensors recorded pressure in a 180 degree angel. The manometric tracings from the four sensors during normal pharyngeal function is presented in figure 1A (normal swallowing) and during partial paralysis in figure 1B (at a TOF ratio of 0.60).

The compliance of each sensor system was low (7



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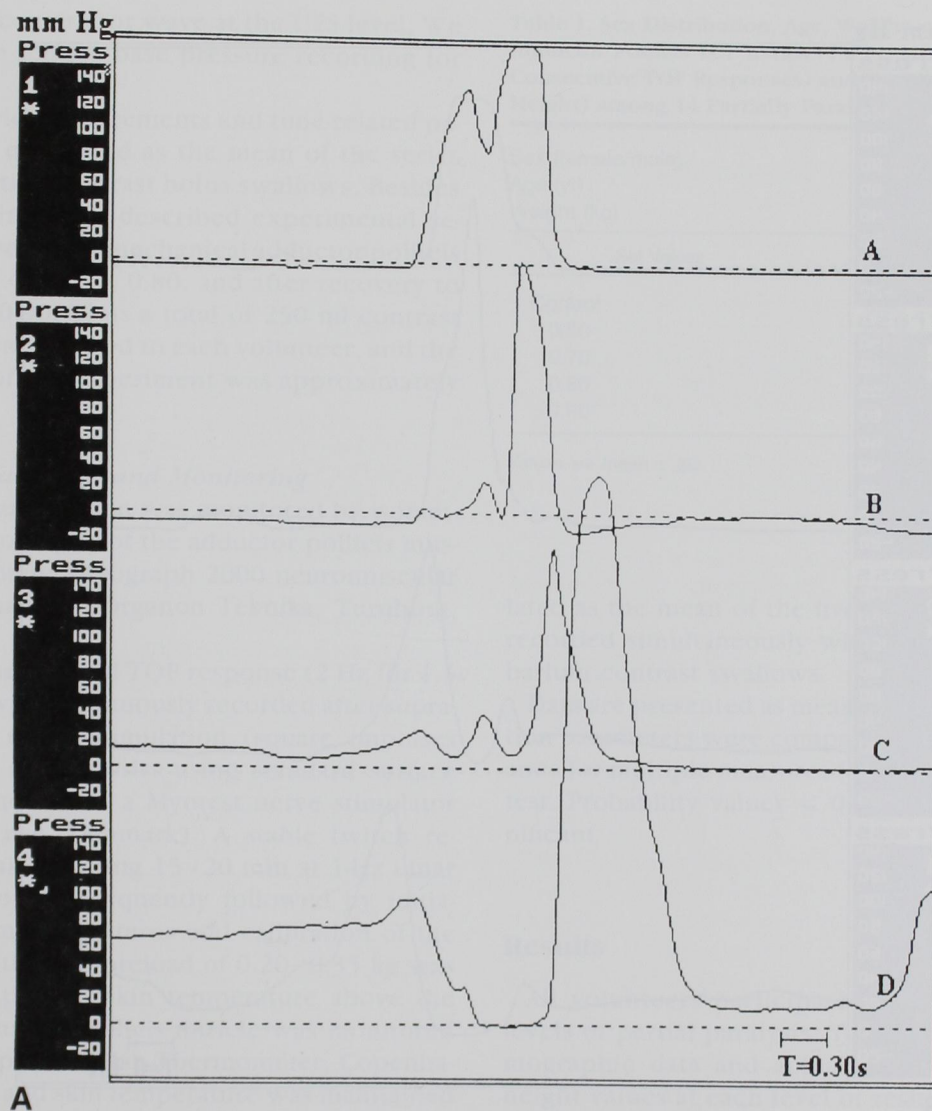
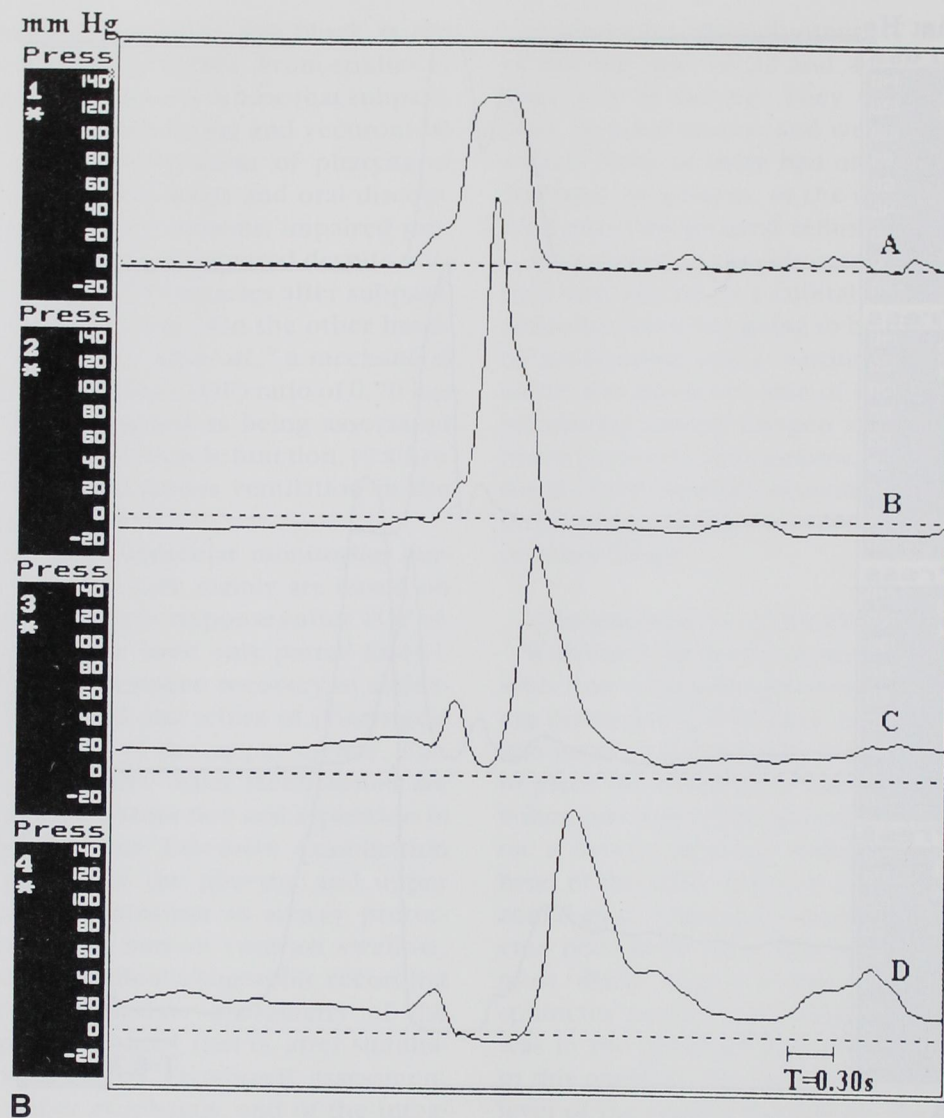


Fig. 1. (A) Manometric tracing from the four solid-state sensors representing normal pharyngeal activity during swallowing of bolus contrast medium. The tracing shows pressure changes during contraction at the upper margin of the tongue base (tracing A), the medial and inferior portion of the pharyngeal constrictor muscle (tracings B and C), and resting tone followed by complete relaxation and peristaltic contraction of the upper esophageal sphincter muscle (tracing D). (B) Manometric tracing from the four solid-state sensors (for description, see fig. 1) in a partially paralyzed awake volunteer at an adductor pollicis train-of-four ratio of 0.60. Please note the marked reduction in resting tone of the upper esophageal sphincter muscle (tracing D).

$\times 10^{-6} \text{ mm}^3/\text{mmHg}$ ), and the sampling frequency was 64 Hz. All four pressure sensors were pressure and temperature calibrated at the actual barometric pressures before each experiment. The pressure signal was digitized (Polygraph Synectics, Stockholm, Sweden) and stored on the hard disk of a computer. The videoradiographic image was mixed with the manom-

etry recording on a color video screen for on-line visual monitoring of the experiment and subsequently was recorded on a VHS video tape.

Volunteers rested in a lateral position with the catheter in place for 15–20 min before the start of recordings. Subsequent control recordings were made in the absence of neuromuscular drugs. The



volunteers were given series of five 10-ml iodine contrast boluses separated by approximately 10 s and were ordered to swallow on command (240 mgI/ml Omnipaque; Nycomed A/S, Oslo, Norway). At each of the five swallows, the following manometry and radiography parameters were measured and recorded under simultaneous videoradiography: (1) In the presence or absence of misdirected swallowing (an aspiration episode); that is, if the bolus penetrated into the laryngeal vestibule (laryngeal penetration) or the trachea (tracheal penetration) at one or several of the five swallows. (2) At the pharyngeal constrictor muscle pressure curve; that is, contrac-

tion peak amplitude (measured in millimeters of mercury), slope of contraction ( $\text{mmHg} \times \text{s}^{-1}$ , and duration (in seconds). (3) The UES resting tone (measured in millimeters of mercury); that is, resting pressure before five swallows. From the real-time pressure recording, the following time-related parameters were recorded: (4) Coordination between UES relaxation and pharyngeal constrictor activity; that is, the time (measured in seconds) from the start of UES relaxation until the start of pharyngeal constrictor contraction; (5) bolus transit time (measured in seconds); that is, the time interval between when the bolus head passed the faucial isthmus until



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passage of the constrictor wave at the UES level. We did not use the tongue base pressure recording for analysis.

All manometric measurements and time-related parameters were calculated as the mean of the series of five consecutive contrast bolus swallows. Besides control recordings, the described experimental sequence was repeated at mechanical adductor pollicis TOF ratios of 0.60, 0.70, 0.80, and after recovery to a TOF ratio  $> 0.90$ . Thus a total of 250 ml contrast medium was administered to each volunteer, and the total duration of the experiment was approximately 90 min.

### Neuromuscular Block and Monitoring

Neuromuscular function was monitored by isometric mechanomyography of the adductor pollicis muscle using a Biometer Myograph 2000 neuromuscular transmission analyzer (Organon Teknika, Turnhout, Belgium).

The evoked mechanical TOF response (2 Hz for 1.5 s every 11.5 s) was continuously recorded after supra-maximal ulnar nerve stimulation (square impulses lasting 0.3 ms) at the wrist using standard surface electrodes connected to a Myotest nerve stimulator (Biometer, Odense, Denmark). A stable twitch response was awaited during 15–20 min at 1-Hz ulnar nerve stimulation, subsequently followed by initiation of TOF stimulus patterns and calibration of the recorder. A continuous preload of 0.20–0.35 kg was applied to the thumb. Skin temperature above the contracting adductor pollicis muscle was monitored using a surface probe (Ellab Thermometer, Copenhagen, Denmark), and skin temperature was maintained above 32°C using a warming blanket.<sup>11</sup>

Vecuronium (5 mg Norcuron [Organon] dissolved in 50 ml normal saline; *i.e.*, 0.1 mg/ml) was administered as a continuous intravenous infusion using a motor syringe (Terumo, Tokyo, Japan). The infusion was given for 20–35 min before a neuromuscular block was established and then adjusted to obtain TOF ratios of 0.60, 0.70, and 0.80, at which time the infusion was stopped and spontaneous recovery to a TOF ratio  $> 0.90$  was anticipated.

The infusion rate was kept constant for 5–10 min before the experiment was started and the vecuronium dose requirement at steady-state neuromuscular block was  $23 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ . The TOF values at control and each level of neuromuscular block were calcu-

**Table 1. Sex Distribution, Age, Weight, and Mechanical Adductor Pollicis TOF Ratios (T4/T1, Mean of Five Consecutive TOF Responses) and T1 (% of Control T1 Height) among 14 Partially Paralyzed Subjects**

Sex (female/male)	7/7	
Age (yr)	$30.1 \pm 6.5$	
Weight (kg)	$69.7 \pm 12.6$	
Set Values	TOF Ratio	T1 (%)
Control	$0.96 \pm 0.02$	—
0.60	$0.58 \pm 0.04$	$90.0 \pm 5.05$
0.70	$0.70 \pm 0.02$	$92.0 \pm 5.45$
0.80	$0.81 \pm 0.01$	$94.9 \pm 4.75$
$>0.90$	$0.94 \pm 0.02$	$98.6 \pm 5.36$

Values are mean  $\pm$  SD.

lated as the mean of the five consecutive TOF ratios recorded simultaneously with the five simultaneous barium contrast swallows.

Data are presented as means  $\pm$  SD. Pharyngeal function parameters were compared using analysis of variance for multiple measures followed by Fisher's exact test. Probability values  $< 0.05$  were considered significant.

### Results

All volunteers participated in the protocol at all levels of partial paralysis. Table 1 presents their demographic data and actual TOF ratios and twitch height values at each level of residual paralysis. The duration of vecuronium infusion until a TOF ratio of 0.60 was reached was  $23.3 \pm 4.9$  min (table 1).

Volunteers showed misdirected swallowing with episodes of aspiration at TOF ratios of 0.60 ( $n = 4$ ), 0.70 ( $n = 3$ ), and 0.80 ( $n = 1$ ). All episodes showed penetration of the bolus contrast immediately above or to the level of the vocal cords (*i.e.*, laryngeal penetration). In none of the cases did aspiration occur below the vocal cords (tracheal penetration), and none of the volunteers with aspiration coughed or had respiratory discomfort. Aspiration episodes were not detected in any volunteer at a TOF ratio  $>0.90$  or at any swallow during the control recordings (*i.e.*, during a total of 70 control swallowing sequences). All volunteers had closure of the glottis,



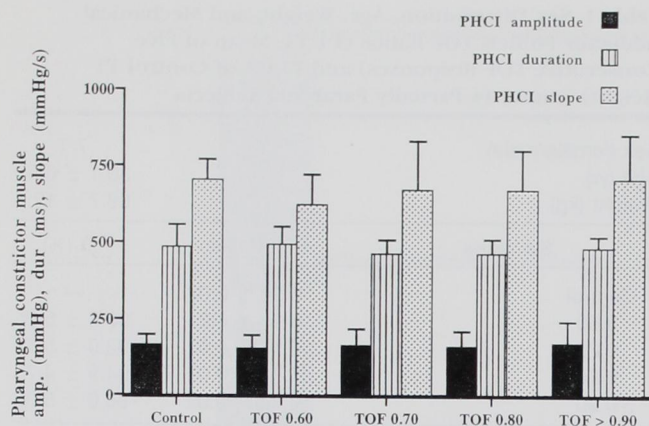


Fig. 2. Pharyngeal constrictor muscle function (PHCI) during partial paralysis in 14 awake volunteers. Contraction amplitude (mmHg), duration (ms), and slope (mmHg/s) at vecuronium-induced train-of-four ratios of 0.60, 0.70, 0.80, and after recovery to >0.90. Data presented as mean  $\pm$  SD. There was no significant change in any functional parameter (not significant, analysis of variance).

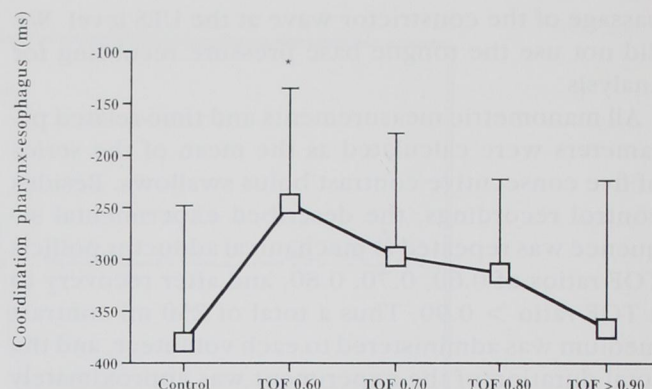


Fig. 4. Coordination (ms) between esophageal sphincter relaxation and pharyngeal constrictor contraction during partial paralysis in 14 awake volunteers. Data presented as mean  $\pm$  SD. \* $P$  < 0.05 (analysis of variance followed by Fischer's exact test).

as revealed by the change in radiodensity at the level of the vocal folds on the videogram.

The pharyngeal constrictor muscle contraction curve was unchanged during partial paralysis (fig. 2), and there were only minor variations in contraction amplitude, contraction slope, and duration of contraction. In contrast, there was a marked reduction in the UES resting tone at TOF ratios of 0.60, 0.70, and 0.80 (fig. 3). After recovery to an adductor pol-

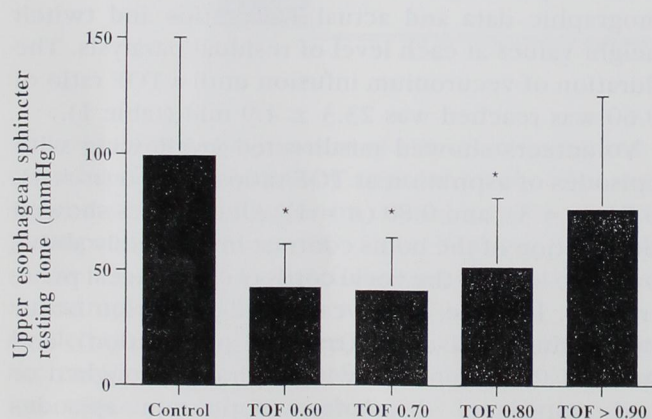


Fig. 3. Upper esophageal sphincter muscle resting tone (mmHg) during partial paralysis in 14 awake volunteers. Mean  $\pm$  SD at vecuronium-induced train-of-four ratios of 0.60, 0.70, 0.80, and after recovery to > 0.90. \* $P$  < 0.05 (analysis of variance followed by Fischer's exact test).

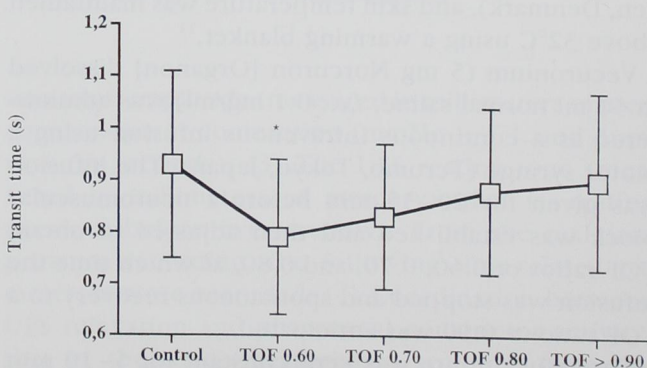


Fig. 5. Bolus transit time (s) during partial paralysis in 14 awake volunteers. Data presented as mean  $\pm$  SD at vecuronium-induced train-of-four ratios of 0.60, 0.70, 0.80, and after recovery to > 0.90. \* $P$  < 0.05 (analysis of variance followed by Fischer's exact test).



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ratios of 0.60 and 0.70. However, at a TOF ratio  $>0.90$ , none of them reported swallowing discomfort or residual diplopia.

## Discussion

The main finding of this study was that mechanical TOF ratios of the adductor pollicis muscle of less than 0.90 are associated with pharyngeal dysfunction and reduced resting tone in the upper esophageal sphincter muscle of awake volunteers. This resulted in impaired airway protection, with laryngeal penetrations occurring at TOF ratios of 0.80 or less.

### *Assessment of Impaired Pharyngeal Function*

The protocol focused on five pharyngeal variables and included fluoroscopic detection of laryngeal or tracheal penetration of swallowed bolus contrast medium. We assessed contraction characteristics of the pharyngeal constrictor muscle as an indicator of the initial pharyngeal stage of swallowing, by measuring pressure curves generated at the level of the inferior pharyngeal constrictor muscle. We also recorded the relaxation pattern and resting tone of the UES, responsible for opening the esophageal segment and protection against passive gastroesophageal reflux, regurgitation, and initiating peristaltic activity in the cervical esophagus. We subsequently calculated pharyngeal coordination and transit times, which represent the pharyngeal and esophageal muscle coordination and transport time for the bolus within the pharynx. Finally, an evaluation of the videoradiographic recording was made to evaluate closure of the glottis and to determine whether laryngeal or tracheal penetration occurred, and if so, to what level in the airway the penetrating contrast bolus was aspirated. These variables cover essential aspects of pharyngeal function, as previously described in various patient populations.<sup>8-10,12-14</sup> Despite the experimental procedure and the presence of a catheter probe in the pharynx and upper esophagus, aspiration did not occur in any of the volunteers during control recording or at the end of the experiment. Confirming the findings of previous investigators,<sup>8-10,12-14</sup> we thus regard the method appropriate to discriminate between normal and abnormal pharyngeal function.

### *Pharyngeal and Esophageal Muscle Activity*

We could not record any significant effect on the pharyngeal constrictor muscle activity; that is, the contraction amplitude, slope, and duration was nearly unchanged at all levels of partial paralysis. Interestingly, the pharyngeal constrictor muscle showed a very different sensitivity to the neuromuscular blocking agent than the upper esophageal sphincter. Although both muscles are classically striated skeletal muscles, this difference might be explained by the individual pattern of activity. The pharyngeal constrictor muscle is contracting only at each swallow while the upper esophageal sphincter has a continuous resting tension of approximately 90 mmHg.<sup>8-10</sup> During swallowing, the UES abruptly relax and the resting tension rapidly decreases to almost zero, before activation of the pharyngeal constrictor muscle, thus allowing safe passage of bolus into the esophageal segment. A contraction phase follows this event before the UES return to its resting tone (see fig 1A). The discrepancy in pattern of activity between the two closely located muscles may partly explain the different response to partial neuromuscular paralysis. The continuously contracting upper esophageal sphincter muscle was more sensitive to neuromuscular block than the intermittently active pharyngeal constrictor muscle. We also found a discoordination within the pharynx with impaired function of the UES and shortened bolus transit times. In some persons ( $n = 9$ ), the bolus penetrated partially into the larynx and passed down to the level of the vocal cords at mechanical adductor pollicis TOF responses below 0.90. None of the volunteers aspirated bolus contrast *below* the vocal cords as shown with fluoroscopy control. More important, these events occurred in awake, nonsedated volunteers without residual effects of other anesthetic agents or sedatives. Thus, in patients after anesthesia with a residual adductor pollicis TOF ratio  $< 0.90$ , the risk of aspiration may be even higher and must still be described.

Furthermore, the markedly reduced resting tone in the UES may constitute a significant risk for passive regurgitation of gastric contents present in the esophagus. However, the relation between misdirected swallowing, reduction in UES resting tone, and the shortened bolus transit time within the pharynx is unclear. The changes in manometric re-



cording may indicate a more profound impairment of pharyngeal function.

#### *Adductor Pollicis Muscle Function versus Pharyngeal Muscle Function*

To our knowledge, no studies have been performed in which pharyngeal function and simultaneous mechanical adductor pollicis TOF responses were assessed, including recording of esophageal sphincter function under videoradiographic supervision of aspiration events. This is a comprehensive approach and enabled us quantitatively to study the whole swallowing sequence and pharyngeal function in relation to a gradual recovery of the adductor pollicis muscle. As shown in figures 3–5, we found a close association between the adductor pollicis recovery and functional recovery of the esophageal sphincter muscle and coordination parameters. We could not, however, demonstrate impaired pharyngeal constrictor muscle activity. Our findings after vecuronium are somewhat different than those reported in a previous study after pancuronium.<sup>4</sup> After bolus dosing, the authors found that the pharyngeal peak contraction pressures were decreased, however, using a different method lacking fluoroscopic catheter supervision or other method to maintain the catheter position within the pharynx or esophagus. Those authors<sup>4</sup> also found that the swallowing response to water injected into the pharynx was unaltered during pancuronium-induced partial paralysis, indicating intact neuronal control. In our study, with a carefully controlled catheter position, none of our volunteers showed altered pharyngeal constrictor muscle function (amplitude, slope, or duration) while the UES function was markedly reduced and associated with pharyngeal dysfunction, and these data thus were unequivocal in this matter. There may be, however, a different drug sensitivity of pharyngeal muscles between vecuronium and pancuronium.

Other studies of pharyngeal function during partial paralysis have focused on electromyographic recordings of oropharyngeal muscles.<sup>3</sup> In humans, a decreased electromyogram activity was recorded in suprahyoid muscles shortly after intravenous administration of bolus doses of atracurium and vecuronium, but functional parameters of the pharynx were not studied.<sup>3</sup>

#### *Critique of Simultaneous Videomanometry*

The radiologic evaluation revealed aspiration, bolus transport patterns, and movements of anatomic structures within the pharynx. In addition, manometry as used in this study, measures quantitative pressure phenomena within the pharynx and the gullet, which reflects mechanical aspects of the muscle function. However, from the functional parameters we analyzed, it is still not clear whether the central control of the swallowing pattern is impaired and if initiation of the swallowing process is also disturbed by the residual neuromuscular block. Further, effects on the integration of respiration during swallowing remain to be assessed. Thus the results encourage further studies of pharyngeal function in association with the residual effect of anesthetic agents.

We conclude that vecuronium-induced partial paralysis causes pharyngeal dysfunction and increased risk for aspiration at mechanical adductor pollicis TOF ratios < 0.90. In humans allowed to recover spontaneously, pharyngeal function is not normalized until an adductor pollicis TOF ratio > 0.90 is reached. The upper esophageal sphincter function is more sensitive to vecuronium than the pharyngeal constrictor muscle function.

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