Transient Lower Esophageal Sphincter Relaxations and Esophageal Body Muscular Contractile Response in Normal Humans

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Background & Aims: Gastroesophageal reflux frequently occurs during spontaneous transient lower esophageal sphincter relaxations (TLESRs). The aim of this study was to determine the motor activity in the body of the esophagus during TLESRs in 10 healthy subjects. Methods: Esophageal contractions were recorded 13, 8, and 3 cm above a sleeve that measured LES pressure. A balloon was inflated 8 cm above the sleeve to induce an esophageal tonic contraction (artificial high-pressure zone). Results: No relaxation of the artificial high-pressure zone was detected at the onset or during spontaneous TLESRs before gastroesophageal reflux. Esophageal acidification provoked no changes or increased the pressure in the artificial high-pressure zone by 47.9% ± 12%. When gastroesophageal reflux abruptly distended the esophagus (common cavity), a relaxation of the artificial high-pressure zone of 51.1% ± 6.6% was observed in 78% of the instances. Deglutitive or secondary contractions during spontaneous TLESRs traveled down the esophagus in 96.5% of the instances. Conclusions: Stimuli that induced spontaneous TLESRs did not by themselves inhibit muscle contractility in the body of the esophagus. Acidification without distention of the lower esophagus frequently increased esophageal tonic contractility. Arou In the body of the esophagus during spontaneous TLESRs did not by themselves inhibit muscle contractility in the body of the esophagus. Acidification without distention of the lower esophagus frequently increased esophageal tonic contractility. Arou

Complete lower esophageal sphincter relaxation (LESR) is a normal response to swallowing. However, a significant number of episodes of gastroesophageal reflux occur in both normal subjects and patients with reflux esophagitis during spontaneous transient lower esophageal sphincter relaxations (TLESRs) whose onset does not directly follow a swallow. Spontaneous TLESRs are generally believed to be normal physiological events because they are frequently observed in healthy subjects and are involved in the mechanism of belching. The cause of spontaneous TLESRs is still unclear. Some investigators suggest that they are triggered by a subthreshold pharyngeal stimulus, whereas others suggest that gastric distention is the major triggering factor. Whatever the initial stimulus, spontaneous TLESRs are induced by inhibitory neural discharges that can be eliminated by blocking the vagal nerve.

Little information is available about the motor function in the body of the esophagus during spontaneous TLESRs. It is unclear whether the vagal inhibitory discharges that provoke spontaneous TLESRs also result in inhibition of the contractility of the smooth muscle in the body of the esophagus. In patients with reflux disease, the progression of deglutitive contractions in the lower esophagus is often interrupted during the occurrence of spontaneous TLESRs associated with acid gastroesophageal reflux. This phenomenon has been interpreted as the result of concomitant neural inhibition of muscle contractility in the body of the esophagus during spontaneous TLESRs. However, it is unknown whether such a simultaneous inhibition, if present, is triggered by the same stimulus that induces the spontaneous TLESRs or is related to the presence of refluxed acid or air in the esophageal lumen. To our knowledge, the muscle activity in the body of the esophagus during spontaneous TLESRs that are not accompanied by gastroesophageal reflux has not been described.

We recently developed a method that is able to measure inhibition of muscle contractility in the body of the esophagus in humans. We have shown that normal primary peristaltic contractions in the smooth muscle part of the esophageal body are preceded by a short period

Abbreviations used in this paper: HPZ, high-pressure zone; LERS, lower esophageal sphincter relaxation; TLESR, transient lower esophageal sphincter relaxation.

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of complete muscle inhibition that starts almost simultane-ously with the onset of LESR and lasts progressively longer in progressively more distal esophageal seg-ments. This inhibition is incomplete or absent with abnormal contractions (very rapidly propagated or simulta-neous pressure waves).

The aim of the present study was to determine whether spontaneous TLESRs are accompanied by inhibition of the contractility of the smooth muscle in the body of the esophagus and, if so, to analyze the role of reflux-induced esophageal acidification or distention in the induction of this inhibition.

Materials and Methods
Subjects
Simultaneous esophageal motility and pH studies were performed in 10 healthy volunteers (7 men and 3 women; mean age, 24.3 years; age range, 18–30 years). None of the subjects had esophageal symptoms or were taking any medication. The studies were conducted after an overnight fast of at least 10 hours. The participants gave written informed consent to participate in the study.

Esophageal Catheter Assembly and Recording Technique
A special catheter assembly was designed. A standard motility catheter with a 6-cm Dent sleeve (Arndorfer Medical Specialties Inc., Milwaukee, WI) was used to monitor pressures in four esophageal sites, the lower esophageal sphincter (LES), and gastric fundus simultaneously. A pH glass electrode with combined reference electrode (Ingold 440-M3; Urdorf, Switzerland) was attached to the catheter 3 cm above the upper end of the sleeve. A flaccid latex balloon with a separate polyvi-nyl tube was attached to the catheter assembly so that the middle of the balloon was located opposite the side opening at 8 cm above the upper end of the sleeve. To eliminate any displacement between the manometric catheter and the bal-loon, they were fixed tightly together (Figure 1). Via the sepa-rate catheter and a three-way stopcock, air was inflated into the balloon at 1-mL increments using a calibrated syringe.

The catheter assembly was swallowed and positioned so that the sleeve monitored the LES pressure. In this position, the motor activity of the esophageal body was monitored by pressure measurements obtained through side holes at the proximal margin of the sleeve and 3, 8, and 13 cm proximal to the sleeve. The assembly was perfused using a low-compliance pneumohydraulic perfusion system (Arndorfer Medical Special-ties Inc.) at a flow rate of 0.4 mL/min and connected to external pressure transducers (Siemens Elema 746; Siemens, Iselin, NJ). Swallowing was monitored with a separate water-filled, non-perfused catheter in the hypopharynx above the upper esophageal sphincter. The pH electrode was calibrated in buffers of pH 1 and 7 before and after each study. Signals from the

Induction of an Artificial High-Pressure Zone in the Body of the Esophagus
After placement of the catheter assembly, the balloon (opposite the recording port located 8 cm proximally to the sleeve) was inflated with 3–5 mL of air, which was sufficient to induce a local sustained increase in esophageal pressure of 15–20 mm Hg (measured by the side hole on the opposite catheter wall from the balloon) but insufficient to induce contractions above or below the balloon or to hamper the passage of the swallow-induced contractions into the distal esophagus. In this way, an artificial high-pressure zone (HPZ) was created in the esophageal body, and esophageal muscle inhibition could be visualized as a relaxation of this HPZ. The strength of inhibition was expressed as a percentage, and 100% inhibition was defined as a decrease in pressure to the baseline before balloon inflation. The onset of the inhibition was the point where the downstroke of the relaxation left the high-pressure baseline, and the end was the point where the upstroke crossed that baseline. The catheter and its dynamics have been described in detail in a previous article.
Experimental Measurements

Once the pressure in the artificial HPZ was stabilized around 15–20 mm Hg, 10 wet swallows (3 mL water) were recorded. The subjects then remained semirecumbent (reclining at an angle between 30° and 45°) for 1 hour to provide a baseline recording while the balloon was inflated and the artificial HPZ was maintained. Then the balloon was deflated, and the subjects ate a standard 700-kcal meal consisting of 200 mL of milk, cooked vegetables, mashed potatoes, and soft meat. After the meal, they resumed the semirecumbent position and the artificial HPZ was restored by inflating the balloon. Manometric and pH recordings were then continued for another 2 hours.

In 3 subjects, the complete study protocol was repeated with the same recording catheter but without inflation of the esophageal balloon (i.e., no artificial HPZ in the esophageal body). This part of the study was performed to assess the effect of intraesophageal balloon inflation and the presence of an artificial HPZ on the frequency, duration, and characteristics of spontaneous TLESRs.

Analysis of Manometric and pH Recordings

LESRs. The baseline LES pressure was measured from the sleeve tracing 3–5 seconds before every swallow-induced LESR or spontaneous TLESR at end expiration and compared with the intragastric pressure. The duration of the LESRs was measured as the time between the point at which the LES pressure decreased and the start of the upstroke of the LES pressure that ended the sphincter relaxation. A swallow-induced LESR was defined as a relaxation that started in a time window from 2 seconds before to 4 seconds after the swallow. A spontaneous TLESR was defined as a decrease in LES pressure to <2 mm Hg, with a relaxation rate of >1 mm Hg/s while no swallows or other motor events in the esophageal body were taking place from 4 seconds before to 2 seconds after the onset of LESR.

Esophageal distention and esophageal acidification. During a spontaneous TLESR, esophageal distention caused by reflux of gastric contents was identified by the presence of an abrupt sustained increase in intraesophageal pressure. This phenomenon has been called the common cavity effect. Esophageal distention events were defined as those common cavity episodes that provoked an abrupt and sustained increase of 5–10 mm Hg of esophageal body pressure so that the intraesophageal pressure transiently equaled the gastric pressure. Esophageal acidification during spontaneous TLESRs was defined as a decrease of esophageal pH to ≤4 for 4 or more seconds. To better distinguish the effect of esophageal acidification from that of distention, we separately analyzed acidification episodes without distention and episodes of distention either accompanied or not accompanied by acidification. Therefore, uneventful spontaneous TLESRs were defined as spontaneous TLESRs not associated with gastroesophageal reflux of acid or esophageal distention. Eventful spontaneous TLESRs were associated with reflux of gastric contents and were divided into three types: spontaneous TLESRs with esophageal acidification, spontaneous TLESRs with esophageal distention, and spontaneous TLESRs with esophageal distention plus acidification.

Pressure changes in the artificial HPZ during swallow-induced and spontaneous TLESRs. Pressure changes in the artificial HPZ were studied during the 10 wet swallows and during spontaneous TLESRs (Figure 2). These events were considered for analysis when they occurred during a period of stable pressure of about 15–20 mm Hg in the artificial HPZ. Pressure changes in the artificial HPZ were evaluated at the onset of the TLESR (both at the time of complete (100%) sphincter relaxation). Pressure changes in the artificial HPZ during eventful spontaneous TLESRs were analyzed before (a) and after (b) the occurrence of the event. Sw, swallow.

Motor responses in the body of the esophagus during spontaneous TLESRs. The motor responses that occurred in the esophageal body during spontaneous TLESRs were classified in function of their relation to swallowing, their peristaltic or nonperistaltic nature, and their presence in all or part of the esophageal recording sites. We identified complete primary, secondary, and simultaneous contractions (deglutitive or spontaneous) and incomplete sequences (contractions starting in the upper esophagus but not progressing in the lower esopha-
Table 1. Effect of Intraesophageal Balloon Inflation on Frequency and Characteristics of Spontaneous TLESRs in 3 Healthy Subjects

<table>
<thead>
<tr>
<th></th>
<th>Without balloon inflation</th>
<th>With balloon inflation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous TLESRs/hour</td>
<td>3.6 ± 0.5</td>
<td>3.7 ± 0.9</td>
</tr>
<tr>
<td>Duration of spontaneous</td>
<td>22.6 ± 1.5</td>
<td>20.9 ± 1.6</td>
</tr>
<tr>
<td>TLESRs (seconds)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% of spontaneous TLESRs</td>
<td>44.9 ± 11</td>
<td>51.2 ± 7.9</td>
</tr>
<tr>
<td>with esophageal acidification</td>
<td></td>
<td></td>
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</table>

Results

LESRs

In 10 subjects, swallow-induced LESR characteristics were measured after 90 swallows. The LESRs started 1.6 ± 0.5 seconds after swallowing and lasted 10.1 ± 0.7 seconds. A total of 123 spontaneous TLESRs were recorded. The mean frequency of spontaneous TLESRs per hour was 4.0 ± 0.7 in the fasting period and 4.15 ± 0.6 in the postprandial period.

The percentage of spontaneous TLESRs followed by acid reflux (with or without distention) was 35.3% ± 8.6%. In the 3 subjects who were studied with and without balloon inflation, spontaneous TLESRs occurred with the same frequency and had the same duration in the two experimental study conditions (3.7 ± 0.9 vs. 3.6 ± 0.5 spontaneous TLESRs per hour and 20.9 ± 1.6 vs. 22.6 ± 1.5 seconds, respectively). The percentage of spontaneous TLESRs that were followed by acid reflux was also similar with the intraesophageal balloon inflated (51.2% ± 7.9%) compared with control conditions (44.9% ± 11%) (Table 1). Spontaneous TLESRs without balloon inflation were not taken into consideration for further description of the results.

Ninety-one of the 123 spontaneous TLESRs occurred during a period of stable pressure of about 15–20 mm Hg in the artificial HPZ (mean, 9.3/subject; range, 5–18). Because only these 91 spontaneous TLESRs met the criteria for analysis, data on the behavior of the artificial HPZ during spontaneous TLESRs were calculated from these 91 events. Forty-two of these spontaneous TLESRs were found to be uneventful. Forty-nine spontaneous TLESRs were eventful: 23 were accompanied by esophageal acidification, 18 by esophageal distention, and 8 by both distention and acidification.

The duration of spontaneous TLESRs was 21.6 ± 0.6 seconds (range, 8.4–36 seconds), which was significantly longer than that of swallow-induced LESRs (10.1 ± 0.7 seconds; range, 7.8–15.2 seconds; P < 0.05). Spontaneous TLESRs with esophageal acidification tended to last longer than the other types (Figure 3), but the difference was not statistically significant.

Pressure Changes in the Esophageal Body Artificial HPZ After Swallowing

Primary peristaltic contractions after wet swallows were preceded by a relaxation of the artificial HPZ. The relaxation started 0.4 ± 0.2 seconds after swallowing and lasted 5.0 ± 0.3 seconds until the arrival of the peristaltic contraction. When a swallow-induced LESR had reached 50% relaxation, the inhibition in the artificial HPZ was already 77.0% ± 6.3%. At maximal LESR, there was always a nearly complete inhibition in the artificial HPZ (91.6% ± 3.3%).

Pressure Changes in the Esophageal Body Artificial HPZ During Spontaneous TLESRs

The pressure events in the artificial HPZ during uneventful spontaneous TLESRs or during the period that preceded the reflux in case of eventful spontaneous TLESRs differed considerably from those observed after...
swallowing. Examples of uneventful spontaneous TLESRs are shown in Figure 4. At the onset of spontaneous TLESRs, no simultaneous inhibition of the artificial HPZ was observed; when 50% of completeness of the spontaneous TLESR was reached, the relaxation of the artificial HPZ was negligible, i.e., 1.7% ± 1.1%. At the moment the spontaneous TLESR was complete, the relaxation of the artificial HPZ was only 4.2% ± 1.6%.

During the complete duration of uneventful spontaneous TLESRs (before the occurrence of any spontaneous swallow) or during the period of eventful spontaneous TLESRs that preceded the occurrence of the event (present in 33 instances), no or only small changes in pressure were observed in the artificial HPZ. During the uneventful spontaneous TLESRs (n = 42), no changes in pressure were observed in the artificial HPZ in 18 instances, a slight increase in pressure (21% ± 5.1%) was found in 13 instances, and a decrease in pressure of 18.8% ± 3.6% occurred in 11 instances. During the first part of eventful spontaneous TLESRs before the occurrence of the event (n = 33), no changes in pressure were observed in 12 instances, an increase in pressure of 30.5% ± 6% occurred in 9 occasions, and a decrease of 15.6% ± 4% occurred in 12 instances.
The pressure pattern in the artificial HPZ during the period after the event in case of eventful spontaneous TLESRs was markedly different. Twenty-three eventful spontaneous TLESRs with esophageal acidification could be analyzed. The decrease in pH detected 5 cm above the LES occurred 9.9 ± 1.0 seconds after the start of the spontaneous TLESRs. As already noted, there were no significant changes in the artificial HPZ during the period between the onset of the spontaneous TLESR and the detection of acid gastroesophageal reflux. Once the decrease in pH was detected, a slow but moderate increase in pressure in the artificial HPZ (47.9% ± 12%) was observed in 13 of 23 instances (Figure 5A). There were no changes in the artificial HPZ in 6 instances, and an incomplete inhibition of the artificial HPZ (45.1% ± 12%) was observed only in 4 instances (Table 2). Eighteen eventful spontaneous TLESRs with esophageal distention were observed (Table 2). The distention occurred 4.1 ± 0.7 seconds after the start of the spontaneous TLESRs. Simultaneously with the abrupt increase in basal pressure (common cavity) in the lower esophageal body, a rapid but
Table 2. Changes in Pressure in the Esophageal Body Artificial HPZ After Reflux Events During Eventful Spontaneous TLESRs

<table>
<thead>
<tr>
<th></th>
<th>No. of instances in which artificial HPZ showed</th>
<th>Increase in pressure</th>
<th>No changes in pressure</th>
<th>Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous TLESRs with acidification (without distention)</td>
<td>n = 23 (100%)</td>
<td>13 (56.5%)</td>
<td>6 (26.1%)</td>
<td>4 (17.4%)</td>
</tr>
<tr>
<td>Spontaneous TLESRs with distention (without acidification)</td>
<td>n = 18 (100%)</td>
<td>2 (11.1%)</td>
<td>2 (11.1%)</td>
<td>14 (77.8%)</td>
</tr>
</tbody>
</table>

partial decrease of pressure in the artificial HPZ (51.1% ± 6.6%) was observed in 14 of the 18 occasions (Figure 5). In only 8 instances, esophageal distension was accompanied by acidification. The early rapid decrease in pressure in the artificial HPZ was followed by a slow increase in pressure (related to the acid reflux).

Motor Events in the Esophageal Body During Spontaneous TLESRs

No swallows and no esophageal contractions were observed in 8 spontaneous TLESRs. These 8 TLESRs were all uneventful and ended spontaneously after 17.8 ± 2.3 seconds. In all other spontaneous TLESRs (n = 83), either swallow-induced or spontaneous esophageal contractions occurred after some time; in most instances, they ended the spontaneous TLESR (Table 3). Primary peristalsis occurred and ended uneventful spontaneous TLESRs in 23 cases; the swallows occurred 12.1 ± 1.1 seconds after the start of the spontaneous TLESR (Figure 4B). During spontaneous TLESRs with esophageal acidification, primary peristalsis was observed in 15 cases, swallows occurred 15.1 ± 1 seconds after the start of the spontaneous TLESR, and simultaneous contractions (deglutitive or nondeglutitive) were observed in 8 cases. During spontaneous TLESRs with esophageal distention, a secondary peristaltic contraction was observed in 10 cases (10.2 ± 1 seconds after the start of the TLESR) (Figure 5B) and primary peristalsis was observed in 3 cases. Five of 8 spontaneous TLESRs with distention and acidification (62.5%) were ended by primary peristaltic contractions.

In only 3.6% of the 83 spontaneous TLESRs that were accompanied by swallow-induced or spontaneous motor activity in the esophageal body, the contractions that started in the upper esophagus died out and were not observed in the lower smooth muscle portion of the esophagus (5 cm above the LES).

Primary and secondary peristaltic contractions were always preceded by an almost complete relaxation of the artificial HPZ (83.3% ± 4.7% and 99% ± 0.7%, respectively; Figures 4B and 5B). However, simultaneous contractions, either deglutitive or nondeglutitive, were not preceded by a relaxation of the artificial HPZ (5.8% ± 4%) (Figure 5A).

Discussion

Spontaneous TLESRs are an important mechanism of gastroesophageal reflux of acid and air.1–4 It has been suggested that the inhibition of the LES responsible for spontaneous TLESRs also affects the smooth muscle portion of the tubular esophagus, thus facilitating the flow of acid into the esophageal lumen.13 We studied the motor function in the body of the esophagus during spontaneous TLESRs using a recently developed method that measures both contractile and inhibitory events in the smooth muscle portion of the tubular esophagus.14 Our results showed that spontaneous TLESRs in healthy subjects were not associated with inhibition of tonic or phasic contractions in the distal part of the esophageal body. In contrast, acid reflux without abrupt esophageal distention was accompanied by a small increase in muscle contractility. Abrupt esophageal distention by refluxed gastric contents provoked partial inhibition of muscle contractility in the lower esophagus.

Spontaneous TLESRs differ from swallow-induced LESRs; they are not accompanied by pharyngeal contraction and subsequent esophageal peristalsis, usually last longer, and are frequently followed by gastroesophageal reflux.1–4

The precise stimulus and the mechanism underlying spontaneous TLESRs are still controversial, but several

Table 3. Motor Events Observed in the Esophageal Body During Spontaneous TLESRs

<table>
<thead>
<tr>
<th></th>
<th>Primary peristalsis (%)</th>
<th>Secondary peristalsis (%)</th>
<th>Simultaneous contractions (%)</th>
<th>Incomplete sequences (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uneventful spontaneous TLESRs (n = 34)</td>
<td>23 (67.6)</td>
<td>2 (5.8)</td>
<td>7 (20.5)</td>
<td>2 (5.8)</td>
</tr>
<tr>
<td>Spontaneous TLESRs with acidification (n = 23)</td>
<td>15 (65.2)</td>
<td>0</td>
<td>8 (34.7)</td>
<td>0</td>
</tr>
<tr>
<td>Spontaneous TLESRs with distention (n = 18)</td>
<td>3 (16.6)</td>
<td>10 (55.5)</td>
<td>4 (22.2)</td>
<td>1 (5.5)</td>
</tr>
<tr>
<td>Spontaneous TLESRs with distention + acidification (n = 8)</td>
<td>5 (62.5)</td>
<td>2 (25)</td>
<td>1 (12.5)</td>
<td>0</td>
</tr>
</tbody>
</table>
hypotheses have been proposed. Spontaneous TLESRs could be caused by a vagovagal reflex initiated by gastric distention. Afferent signals from stimulation of mechanoreceptors in the gastric wall are carried by the vagus nerve to the nucleus solitarius in the brain stem, from where they stimulate the dorsal motor nucleus of the vagus and vagal motor efferents.10,21 Another hypothesis assumes a long train subthreshold vagal stimulus elicited by incomplete pharyngeal stimulation (incomplete swallow).8,9 Spontaneous TLESRs could also be caused by a reflex LESR in response to stretching of the gastric wall via direct intramural neural connections.22 The suppression of spontaneous TLESRs by cervical vagotomy suggests that direct intramural neural connections between the stomach and the LES are unlikely to play an important role in spontaneous TLESRs.6,12

It has been suggested that the intrinsic inhibitory nerves may well represent a final common pathway for LESR induced by several stimuli, i.e., swallowing, bolus-induced secondary peristalsis, electrical vagal stimulation, or intraluminal balloon distention.23 In patients with achalasia, in whom swallow-induced LESRs are absent or incomplete, gastric distention is unable to provoke spontaneous TLESRs. Because only a partial or patchy extrinsic vagal damage has been found in these patients, dysfunction of the intrinsic inhibitory nerves is more likely to be responsible for the virtual absence of LESRs.23

Using currently accepted criteria,16 we identified a total of 123 spontaneous TLESRs. We found a mean frequency of 4 spontaneous TLESRs per hour and found the frequency to be similar for the fasting and for the postprandial states. In the literature, the rate of spontaneous TLESRs is reported between 2 and 6 per hour,4,7,21,24,25 depending on the criteria for identification and the experimental setting. In most studies, the rate of spontaneous TLESRs is higher in the postprandial period than during fasting. Our relatively high rate of spontaneous TLESRs during fasting is probably caused by the semirecumbent position of the subject24 and by the positioning of the catheter via the mouth. The thickness of the catheter assembly used for the induction of the artificial HPZ precluded nasopharyngeal intubation.

We have recently developed a technique that allows visualization and measurement of the inhibition of muscle contractility in the body of the human esophagus. We showed that deglutition induces in normal subjects an inhibition of the smooth muscle segment of the esophageal body that starts slightly earlier than the LESR, spreads very rapidly over the entire distal esophageal body, but lasts progressively longer in progressively more distal segments.14 In another study, we found that this inhibition is incomplete or absent in patients with primary esophageal motility disorders, which may be responsible for the nonperistaltic nature of the contractions.15 We used the same technique to examine the motor behavior (muscular inhibition vs. excitation) of the distal esophagus during spontaneous TLESRs.

There are at least two mechanisms that could explain our observation that spontaneous TLESRs per se were not accompanied by inhibition of muscle contractility in the body of the esophagus. The stimuli responsible for the induction of spontaneous TLESRs may induce afferent signals that stimulate the motor nucleus of the vagus to trigger the same type of inhibitory discharge as that induced by swallowing and that is carried down by the same set of vagal efferent fibers. In the case of spontaneous TLESRs, the efferent discharge may not be strong enough to induce inhibition in the esophageal body but could be sufficient to induce a spontaneous LESR as a result of higher sensitivity of the sphincter. Arguing against this hypothesis is the completeness and long duration of spontaneous TLESRs, which does not support the idea of a reduced inhibitory discharge. An alternative mechanism is that the inhibitory discharge that induces spontaneous TLESRs affects only the LES, travels through a different set of efferent vagal fibers, and is triggered by afferent information different from that involved in swallowing. If so, the esophageal body smooth muscle will not necessarily be inhibited during a spontaneous TLESR and will be able to develop primary or secondary peristaltic contractions, if it is required to do so. This hypothesis is more in agreement with our observations.

Dent et al.13 observed that, during spontaneous TLESRs accompanied by acid gastroesophageal reflux, swallows did not trigger a complete peristaltic sequence and that the progression of most of the postdeglutitive contractions was interrupted in the lower esophagus. They suggested that this observation could be caused by neural inhibition of the smooth muscle contractility in the esophageal body during spontaneous TLESRs. Our studies do not confirm these findings. When a swallow or a secondary contraction occurred during a spontaneous TLESR, the ensuing contraction traveled down the entire esophageal body in 96.5% of the cases for uneventful as well as for eventful spontaneous TLESRs. The reason for the discrepancy between these observations is unclear. If it is because we studied normal subjects, whereas the observations of Dent et al. were made in symptomatic patients (most of them with gastroesophageal reflux disease), the different findings in normal subjects and patients may be important for the understanding of the mechanism of pathological reflux.
Eventful spontaneous TLESRs were accompanied by changes in muscle contractility in the body of the esophagus. These changes seemed to be related to the entrance of refluxed air or acid in the esophageal lumen with the subsequent distention and/or acidification and not to the spontaneous TLESR itself. In instances of abrupt distention, rapid relaxation of the artificial HPZ was consistently observed; however, in instances of acid gastroesophageal reflux without abrupt distention, the presence of acid in the lower part of the esophagus frequently triggered an increase in pressure in the artificial HPZ. This increased contractility in the body of the esophagus may help prevent acid from moving upwards. The pressure changes of the artificial HPZ observed in our study mimic those in the upper esophageal sphincter during spontaneous TLESRs followed by belching. As described for the upper esophageal sphincter, sensory information on the rapidity and extent of distention of the lower esophagus may determine whether the artificial HPZ (in the body of the esophagus) undergoes relaxation or not. The abrupt distention of the lower esophagus, indicated by the occurrence of a common cavity phenomenon, may induce partial inhibition in the esophageal body sufficient to favor venting of gastric air and belching. In contrast, slow and localized distention by acid gastroesophageal reflux may not induce inhibition but may trigger a mechanism to prevent the rise of the acid bolus.

When primary or secondary peristaltic contractions occurred during spontaneous TLESRs, not only did they end the TLESRs but the underlying inhibitory and excitatory sequence that determines their peristaltic performance was similar to what we have observed previously: if the contraction was preceded by a short but complete inhibition of the artificial HPZ, the contraction progressed in a peristaltic fashion; if the inhibition was incomplete or absent, the progression was disturbed, eventually resulting in simultaneous contractions.

In conclusion, our studies of healthy subjects showed that stimuli that induce a spontaneous TLESR do not by themselves provoke inhibition of muscle contractility in the body of the esophagus. When spontaneous TLESRs were followed by acid gastroesophageal reflux without esophageal distention, the smooth muscle of the body of the esophagus tended to increase its contractility. When spontaneous TLESRs were followed by abrupt esophageal distention, a partial inhibition of muscle contractility in the body of the esophagus ensued, which probably favors the increase of gastric refluxed material into the esophagus and venting.

Further studies on the inhibition of muscle activity in the body of the esophagus are needed in patients with reflux disease to better understand the contribution of esophageal body contractility in the pathophysiology of this disorder.

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