Pathogenesis of upper airway occlusion during sleep

J. E. REMMERS, W. J. deGROOT, E. K. SAUERLAND, AND A. M. ANCH
Departments of Medicine, Physiology, and Anatomy, University of Texas Medical Branch, Galveston, Texas 77550

REMMERS, J. E., W. J. DEGROOT, E. K. SAUERLAND, AND A. M. ANCH. Pathogenesis of upper airway occlusion during sleep. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 44(6): 931-938, 1978. - Ten patients with daytime somnolence and obesity were found to have periodic airway occlusion (AO) during nocturnal sleep. The cyclical ventilatory pattern consisted of a series of regular inspiratory efforts against an occluded airway (occlusive phase) alternating with a period of regular breathing (ventilatory phase). Significant periods of central respiratory apnea were observed only in one case. The effects of pharyngeal intubation and pharyngeal pressure recordings showed that the locus of airway closure lay in the oropharynx. The genioglossal electromyogram (EMG) consistently revealed periodicity: low level activity at the onset of occlusion and prominent discharge at the instant of pharyngeal opening. In one case, this activity was closely related to pharyngeal patency, whereas in other cases there was considerable overlap between EMG values recorded during occluded and ventilatory phases. In these cases, the relationship of genioglossal discharge to pharyngeal pressure correlated with the presence or absence of pharyngeal occlusion. We speculate that genioglossal force acts to open the oropharynx and that negative pharyngeal pressure promotes pharyngeal closure. The results are consistent with the idea that, once the pharynx has collapsed, relative recruitment of genioglossal and inspiratory muscle activity is such that the latter influence outstrips the former, so that pharyngeal transmural pressure increases more than genioglossal force. Pharyngeal opening occurs coincident with arousal and preferential activation of the genioglossus muscle of the tongue.

METHODS

Background information. Preliminary results with nasopharyngeal intubation indicated that the pharynx, not the larynx, was the site of occlusion (see RESULTS). Therefore, the motor activation of the genioglossus was investigated electromyographically. This muscle spans a large portion of the anterior wall of the oropharynx (1) (Fig. 1), and relapse of the tongue can occlude the oropharynx in anesthetized man (20). Sauerland and Mitchell (22) have described rhythmic, inspiratory activation of the genioglossus in normal humans in the upright posture. They also noted that in the supine posture the muscle displays a tonic expiratory component as well. These findings suggest that genioglossal activity may control the aperture of the oropharynx. In the sleeping human, Sauerland and Harper (21) have shown that rhythmic genioglossal activation continues during synchronized sleep, as shown in Fig. 1, but declines to low levels during desynchronized sleep.

Patients. Seventeen studies were performed on 10 patients. The only criterion for patient selection was that the individual must display periodic AO during sleep as indicated by rhythmic inspiratory efforts in the absence of no inspiratory airflow (see below). All patients were obese and complained of daytime somnolence. Their age, height, weight, and pulmonary function data are listed in Table 1. Most showed reduced lung volumes and the alveolar-arterial PO2 difference (measured while seated) was increased in eight. These changes are consistent with obesity. Supine awake and sleeping blood gas and pH values are given. Waking hypocapnia (arterial PCO2 > 44 Torr) was documented in six patients.

Recording techniques. Bioelectrical and mechanical signals were recorded on an eight-channel rectilinear polygraph producing full-scale response with frequencies up to 60 Hz (Gould, Brush 200). All recordings were made during the night, and the period of study lasted from 4 to 6 h. The following variables were recorded in all patients: electroencephalograms (EEG), eye movements, genioglossal electromyograms (GGEMG), esophageal pressure (Pes), inspiratory flow and volume, and rib cage and abdominal circumference changes. EEG recorded from the central and occipital positions (C3/A2; O3/OzPz) and monopolar eye movements were recorded bilaterally. Bipolar GGEMG was recorded from fine wire electrodes implanted using a peroral approach as described by Sauerland and Mitchell (22).
TABLE 1. Age, height, weight, and pulmonary function data of patients

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<th>% Predicted, liters</th>
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<td>M</td>
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TLC, total lung capacity; VC, vital capacity; FRC, functional residual capacity; FEV₁, forced expiratory volume at 1 s; Vd/Vt, dead space-to-tidal volume ratio; (A-a)Po₂, alveolar-to-arterial oxygen pressure difference; Pco₂ and Po₂, partial pressure of carbon dioxide and oxygen, respectively, in the blood.

during inspiration and tonic discharge persists during expiration.

FIG. 1. Drawing of a sagittal section of upper airways showing position of pressure transducer above vocal cords (VC) and location of genioglossal EMG electrodes. Arrow indicates possible point of oropharyngeal occlusion. Recording illustrates normal pattern of activity of GGEMG during sleep. AvEMG: averaged GGEMG; ΔLV: lung volume excursion with tidal breathing; Pes: esophageal pressure. A genioglossal burst accompanies each inspiration (dashed line gives onset of inspiration) and tonic discharge persists during expiration.

potentials were amplified using a suitable AC preamplifier (Grass P15), rectified, and averaged continuously to yield a signal related to intensity of muscle discharge (3). Esophageal pressure was measured with a transducer catheter (Milar, 2 mm OD) passed transnasally and positioned in the midesophagus. Rib cage and abdominal circumference changes were monitored with mercury-in-rubber gauges. In some experiments these signals were adjusted to yield comparable volume gains by use of isovolume maneuvers, and unless chest wall distortion was severe, a summation of the two provided a semiquantitative estimate of volume excursion. However, to document unequivocally the existence and pattern of periodic AO, inspired volume was derived by integrating an inspiratory flow signal. The mouth and nose were intermittently covered with a low dead space mask connected to inspiratory and expiratory valves. A sensitive, symmetrical pressure transducer was connected to Fleisch pneumotachograph placed in the inspiratory line. An indwelling catheter was placed in the radial artery in all patients. Samples were withdrawn at 1- to 2-h intervals during the study and analyzed for pH, Pco₂, and Po₂ with standard blood gas electrodes.

Supraglottic, pharyngeal pressure (Pph) was recorded in five patients (nos. 2, 3, 4, 6, and 10) using a transducer catheter passed transnasally. The catheter was positioned radiographically at the level of the tip of the epiglottis as shown in Fig. 1. As with the esophageal pressure catheter, this catheter was taped securely to
the nose and face, and its location was confirmed on several occasions during the study by the recording of atmospheric pressure during Valsalva and Mueller maneuvers. Both transducers were calibrated by immersion in 37°C water before and after the study and showed negligible drift. Pharyngeal resistance, the ratio of instantaneous supraglottic pressure to inspiratory flow, was calculated at 100-ms intervals throughout the period of inspiratory flow in selected breaths. These values were averaged over the entire inspiration to produce average inspiratory pharyngeal resistance for a breath. The nasopharynx was intubated in four patients (nos. 1, 2, 8, and 9) after periodic AO had been documented. A soft rubber tube (7 mm OD) was passed through the nose and into the oropharynx, and the recordings described above were repeated after the patient resumed sleeping.

RESULTS

All patients displayed periodic AO and, with two exceptions (patients 3 and 6), this was the only pattern observed throughout the period of study. Patient 6 showed periods of nonocclusive apnea as well, and patient 3 intermittently breathed regularly. All patients were observed to breathe orally during sleep, the mouth remaining open during periods of airway occlusion.

A typical record obtained during periodic AO is shown in Fig. 2. The cycle usually lasted 30–40 s: the patient breathed regularly for 10–15 s (ventilatory phase) and displayed airway occlusion for 20–30 s (occlusive phase). This pattern of periodic AO continued throughout the night. During the occlusive phase, active contractions of expiratory muscles produced slight, audible flow (5). During the latter half of the occluded phase, peak inspiratory values of Pes increased progressively, usually reaching values of 30–60 cmH\(_2\)O. As shown in Fig. 2 and in an expanded illustration in Fig. 3, EEG evidence of arousal (alpha activity) generally appeared in EEG traces coincident with, or as much as 1 s before, termination of occluded phase. The arousal pattern persisted throughout most of the ventilatory phase, and termination of the ventilatory phase generally coincided with EEG manifestation of sleep, as described by Gustafson, Tassinari, and Duron (5).

Evidence of pharyngeal occlusion. In all four patients tested, nasopharyngeal intubation eliminated periodic AO and resulted in regular breathing during sleep. Experimental occlusion of this airway reestablished complete airway obstruction. In all five patients in whom supraglottic pressure was recorded, P\(_{\text{ph}}\) and Pes showed similar respiratory fluctuations during the occluded phase. Intra-breath comparisons of these two pressures were performed by plotting P\(_{\text{ph}}\) against Pes (values measured at 100-ms intervals) for a series of representative occluded efforts. In all five patients, values for esophageal and supraglottic pressure closely approximated the line of identity during inspiratory efforts, demonstrating a patent glottis and lower airways (Fig. 4). Since the mouth was open during the occluded inspiratory effort, the total pressure drop occurred between the supraglottic space and the oral airway. Accordingly, we conclude that the occlusion occurs in the oropharynx approximately at the level of genioglossus (Fig. 1, arrow). During the expiratory phase of the occluded effort the two pressures diverge somewhat, Pes becoming more positive than P\(_{\text{ph}}\). This incomplete transmission of pressure during the expiratory phase was commonly observed but unexplained by our data.

The typical sequence of events during the transition from occluded to ventilatory phases is shown in Fig. 3. During each occluded inspiratory effort, Pes and P\(_{\text{ph}}\) are identical until the last occluded effort. One-half second after the onset of this effort, inspiratory flow appeared and, simultaneously, P\(_{\text{ph}}\) suddenly departed from Pes. This abrupt divergence of P\(_{\text{ph}}\) from Pes indicates that unocclusion is a discrete event whereby a pharyngeal airway is suddenly reestablished (5).

Cyclical genioglossal activity. GGEMG fluctuated systematically in relation to the apneic-ventilatory cycle. This behavior can be seen in Fig. 2 for two occlusive cycles, and Fig. 5 displays mean inspiratory values for averaged GGEMG throughout the occluded and unoccluded phases for seven sequential cycles in one patient.

**FIG. 2.** Typical record obtained during periodic AO showing three occluded periods (AO), electroencephalogram (EEG), genioglossal discharge (EMG) and its instantaneous average (AvEMG), inspiratory tidal volume (VT), and esophageal (Pes) and pharyngeal (P\(_{\text{ph}}\)) pressures. Close up of indicated section shown in Fig. 3 (patient 10).
Averaged Genioglossal EMG

Inspiratory Tidal Volume

Intra-esophageal Pressure

Pharyngeal (Supraglottic) Pressure

Time in sec.

FIG. 3. Expanded portion of the record shown in Fig. 2 showing EEG evidence of arousal (alpha activity) just prior to termination of occlusive phase and loss of this activity coincident with onset of AO. Note that abrupt deviation of Pph from Pes (left vertical dashed line) occurs coincident with the first appearance of inspiratory flow and with large genioglossal activity.

FIG. 4. Correspondence between supraglottic and esophageal pressures during occluded inspiratory efforts is shown. Simultaneous values for each pressure were obtained at 100-ms intervals for a period that included four respiratory efforts during the occluded phase (patient 10). Dashed line is identity line.

In one case (patient 4), where the duration of occlusion was brief and fluctuations in Pes were minimal, a strong association between the state of the pharyngeal airway and genioglossal activity was evident, as illustrated in Fig. 6. During the ventilatory phase a graded reduction in EMG was associated with a progressive rise in pharyngeal resistance and ultimately obstruction (Fig. 6, lower panel, sequence A-D). Abrupt release of obstruction occurred coincident with a discrete, large burst in the genioglossus, and EEG evidence of arousal was commonly observed (Fig. 6, top panel and segment C, lower panel). In this patient alone, genioglossal activity recorded during the occlusive phase was consistently lower than that observed during the ventilatory phase. By contrast, in all other cases, there was considerable overlap in the value of GGEMG in the two phases as indicated above.
Pharyngeal occlusion as a function of GGEMG and Pph. The possible contributory role of pharyngeal pressure was evaluated by plotting genioglossal activity against supraglottic pressure. Representative results for one patient (no. 2) are shown in Fig. 7 where peak values of GGEMG and Pph are plotted for all inspiratory efforts in a series of cycles. Points for breaths early in the ventilatory phase lie to the extreme right, and those for subsequent breaths scatter horizontally to the left owing to a decrease in GGEMG (lower arrow). The first efforts against the occluded airway are associated with an upward and leftward movement and, thereafter, progressively stronger inspiratory efforts against an occluded airway produce an upward linear scatter of points (solid line). Release of occlusion is associated with a rightward displacement of points (upper arrow). A dashed line segregates occluded from unoccluded points on this and subsequent plots. Note that the EMG range, 4-8 mV, includes both occluded and unoccluded efforts, demonstrating that peak GGEMG is not a unique correlate of pharyngeal patency or occlusion. However, the upward displacement of occluded efforts on this plot suggests that a combination of Pph and GGEMG (i.e., their ratio) will consistently predict whether the oropharynx is occluded or patent.

DISCUSSION

The results justify the conclusion that periodic AO during sleep arises from oropharyngeal occlusion; during occluded inspiratory efforts the entire alveolar-to-atmospheric pressure drop occurs in the oropharynx. That the larynx and lower airways are not primary factors in the genesis of periodic AO is demonstrated by the return to a regular respiratory rhythm with naso-pharyngeal intubation. The present results substantiate the original findings reported by Gastaut, Tassinari, and Duron (5) in a remarkable and landmark paper that first documented periodic AO. The views advanced by these investigators are in complete agreement with the present findings. They postulated that occlusion resulted from a "backward movement of the tongue." This view was based on the characteristics of the occlusion (i.e., its inspiratory nature and the abruptness of release), the importance of body position, the beneficial effects of pharyngeal intubation, and the relative hypotonia of the floor of the mouth during onset of the occluded phase. Walsh et al. (28) confirmed the last two findings and demonstrated radiographically the occlusive movement of the tongue. Further radiographic documentation of this process has been supplied by others (8, 23, 25).

Despite these suggestions that relapse of the tongue is important in producing periodic AO, the importance of genioglossal activity in determining pharyngeal resistance or in preventing oropharyngeal occlusion is uncertain. Rhythmic inspiratory activity and tonic expiratory component in supine humans (22) invites such speculation, but no direct evidence is available. That genioglossal motoneurons receive an automatic, respiratory motor drive is evidenced by the persistence of the
awake activity pattern during synchronized sleep (21). In fact, the behavior of the genioglossus during sleep resembles that of the laryngeal abductors (16, 17) and inspiratory intercostals (15, 27); the respiratory activity of these muscles persists, although somewhat reduced, during synchronized sleep but decreases greatly during desynchronized sleep. By contrast, the diaphragm discharge remains unaltered during both stages of sleep (18, 27).

Our results fail to demonstrate a unique relationship between the presence or absence of occlusion and genioglossal activity in most cases. However, in all studies, occlusion was released coincident with the highest level of GGEMG recorded throughout the cycle. This finding suggests that contraction of the genioglossus participates in reestablishing an oropharyngeal lumen. Our failure to find a unique relationship between GGEMG and the presence or absence of occlusion is attributable to one or more of the following possibilities: 1) GGEMG may poorly indicate genioglossal force (GGF); 2) GGF may not be important in determining the oropharyngeal aperture; or 3) other factors may participate in determining oropharyngeal patency. We have no evidence relative to the first possibility; during the occlusive phase the tongue is probably contracting isometrically and, therefore, force-velocity and force-length relationships should not influence the mechanical action of the muscle. Moreover, GGEMG recorded during the terminal portion of the occluded phase usually exceeded that recorded during the terminal portion of the ventilatory phase (Figs. 5 and 7). A lack of correlation between GGEMG and GGF can be expected to result in comparable values of GGEMG during the two phases, but will not explain the observed disparity in discharge during the two phases.

As mentioned above, the available evidence, albeit indirect, does not favor the second possibility. The third possibility is supported by our observation that peak Pph and peak GGEMG, together, sufficed to predict the state of the pharyngeal airway, whereas neither variable alone uniquely correlated with airway occlusion or patency (Fig. 7). Two characteristics of the occlusion, its restriction to inspiration and its abrupt release, suggest to us that intrapharyngeal pressure plays a role. We propose that subatmospheric pressure in the supraglottic space exerts a retracting action on the passive tongue so that the tongue behaves like a check valve or a Starling resistor. Furthermore we propose that contraction of the genioglossus counteracts this effect of subatmospheric supraglottic pressure. In other words, we hypothesize that the oropharynx occludes whenever the constricting action of transpharyngeal pressure exceeds the dilating action of GGF.

The intrabreath dynamics of Pph in relation to GGEMG during various inspiratory efforts, shown in Figs. 8 and 9, suggests their possible combined role in initiating, maintaining, and releasing pharyngeal occlusion.

**Onset of pharyngeal occlusion.** Instantaneous values of Pph and GGEMG are plotted in Fig. 8 for the first nine inspiratory efforts of a typical cycle, beginning with the first unoccluded breath. Typically, GGEMG leads Pph, resulting in a counterclockwise loop. For the first five inspirations (right panel, mean pharyngeal resistance (PR) = 49 cmH₂O/l per s) the loop is relatively wide and lies to the right of the line segregating occluded and unoccluded efforts. For the last two inspirations of the ventilatory phase (nos. 6 and 7, middle panel) the loops become more narrow and more vertical (mean PR = 84 cmH₂O/l per s) and approach the segregating line. This observation indicates that as genioglossal activity wanes during the ventilatory phase, Pph and PR rise, possibly due to a decrease in the dilatory action of the genioglossus. The loops for the first two occluded inspiratory efforts (nos. 8 and 9, left panel) project more vertically and cross the segregating line of segregation.
REFERENCES