Control of Breathing in a Subset of Patients With Systemic Lupus Erythematous*

Giorgio Scano, MD, FCCP; Patrizio Coti, MD; Roberto Duranti, MD; Gianni Misuri, MD; Lorenzo Emmini, MD; and Elisabetta Rosi, MD

Background: Inspiratory muscle weakness and abnormalities in breathing pattern and in respiratory drive have been reported in patients with multisystem disorders. In patients with systemic lupus erythematous (SLE), data on respiratory muscle strength and control of breathing are scarce.

Methods: We studied a subset of nine female patients with SLE with no major findings of cardiovascular, renal, or neurologic involvement, and with a normal routine chest radiograph. An age- and sex-matched normal group was also studied as a control. We evaluated lung volumes, diffusing lung properties (TLco, TLC/VA), maximal inspiratory (MIP) and expiratory (MEP) pressures, end-tidal carbon dioxide tension (Pco2), and breathing pattern: ventilation (Ve), tidal volume (Vt), inspiratory time (Ti), and respiratory frequency (Rf). Neural respiratory drive, assessed in terms of mean inspiratory flow (Vt/Ti), mouth occlusion pressure (P0.1), and surface electromyographic activity of the diaphragm (Edi) and intercostal (Eps) muscles was also evaluated.

Results: As a whole, patients exhibited mild decrease in MIP; vital capacity was slightly reduced in two patients and TLC/VA was moderately reduced in three. During a hypercapnic rebreathing test, AVt/ΔPco2 was lower, ΔP0.1/ΔPco2 was normal, while AEdi/ΔPco2 and Aeps/ΔPco2 were higher in patients compared with normal control subjects. AVt/ΔPco2 significantly related to MIP. At 60 mm Hg of Pco2 patients maintained the rapid and shallow pattern of breathing (RSB) exhibited during room-air breathing; lower Vt, shorter Ti, and greater Rf, with Ve, Vt/Ti, and Edi being greater compared with the normal control subjects.

Conclusions: These data seem to indicate that in this SLE subset, mild decrease in respiratory muscle strength may accompany an increased respiratory drive, and contribute to a qualitatively abnormal ventilatory response (RSB) to carbon dioxide stimulation.

(CHEST 1995; 108:759-66)

Edi=EMG from diaphragm; EMG=electromyogram; Eps=EMG from intercostal parasternal muscles; MEP=maximal expiratory pressure; MIP=maximal inspiratory pressure; P0.1=mouth occlusion pressure 0.1s after beginning of inspiration; Rf=respiratory frequency; SLE=systemic lupus erythematous; Ti=inspiratory time; Vt=tidal volume

Key words: control of breathing; respiratory drive; respiratory muscle strength; SLE, control of breathing

Patients with multisystem disorders may exhibit pulmonary involvement, respiratory muscle dysfunction, and abnormalities in the control of breathing. A variety of pulmonary lesions, including pleurisy, pulmonary hemorrhage, fibrosing alveolitis, and shrinking lung syndrome (small lung fields and elevated diaphragm) may complicate systemic lupus erythematous (SLE). In patients with SLE, the shrinking lung syndrome has been ascribed to diaphragm malfunction or weakness while in SLE without radiologic findings of chest involvement, respiratory muscle weakness has been reported in very few circumstances.

Studies that have evaluated the control of breathing are extremely scarce in SLE. In patients with decreased respiratory muscle force, Jacobelli et al showed that light exercise resulted in increased ventilation, mostly sustained by increase in respiratory frequency (Rf), with modest changes in tidal volume (Vt). Incomplete respiratory muscle activation during maximal voluntary efforts and a shallow pattern of breathing during maximal voluntary ventilation have recently been reported in SLE with shrinking lung syndrome. The pattern of breathing characterized by increase in Rf and decrease in Vt is in common with a number of respiratory disorders in which such a pattern may eventually result in arterial blood gas abnormalities. The latter have occasionally been reported in either spontaneously breathing or exercising patients with SLE with severe lung impairment; however, data dealing with the pattern of breathing were not men-

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Supported by grants from the Ministero dell'Universita' e della Ricerca Scientifica e Tecnologica of Italy.

Manuscript received September 6, 1994; revision accepted March 20, 1995.

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mentioned in these studies.

In patients with SLE without major cardiovascular, renal, and neurologic involvement and with a normal routine chest radiograph, it would be worthwhile evaluating the respiratory muscle strength and the control of breathing considering that in other multi-system disorders, inspiratory muscle weakness, abnormalities in breathing pattern, and in respiratory drive appear to be interrelated.3

METHODS

Subjects

We selected nine female patients (range, 21 to 56 years) with SLE, as defined by the American Rheumatism Association diagnostic criteria,11 seen at the University Department of Clinical Immunology. Criteria for inclusion in the study were absence of the following: (1) major cardiovascular involvement as assessed in terms of ECG and echocardiography; (2) renal involvement, as assessed in terms of echography of the kidney, and creatinine clearance ≥40 mL/min; (3) central nervous system involvement, assessed by cranial CT scan; (4) peripheral nervous system involvement assessed by motor and nerve conduction studies of the tibialis anterior, deltoid, sural, and sciatic nerves; and (5) findings of parenchymal lung involvement on routine chest radiograph (ILO scoring system). Informed consent was obtained from each subject. The anthropometric and clinical data of the patients are provided in Table 1. All patients fulfilled at least 4 or more of 14 diagnostic criteria for SLE. Antinuclear antibody, extractive nuclear antigen, antinative DNA (anti-nDNA), and complement fractions (C3, C4) were measured. The serum levels of creatine phosphokinase and lactate dehydrogenase were also determined in each patient. None of the patients showed any clinical manifestations of mixed connective tissue disease; the only patient with negative antinuclear antibodies fulfilled six criteria for SLE and she was extractive nuclear antigen positive (SSA/RO). Active disease was assessed in patients 6 and 9 on the basis of at least three of four of the following criteria: low levels of C3 (<66 mg/dL) and C4 (<10 mg/dL), high erythrocyte sedimentation rate and blood lymphocyte count <1.5×10^9/mm^3. Eight patients were dyspneic, their dyspnea being graded 1 (walking up a slight hill) according to a Modified Medical Research Council Dyspnea Scale.12 All patients were nonsmokers and no one fulfilled the diagnostic criteria of asthma or chronic bronchitis or emphysema as suggested by the American Thoracic Society.13 Patients had being given corticosteroids for 1 to 15 years. Clinical data of patients are reported in Table 1. A group of eight normal women (aged 20 to 52) whose height ranged 1.50 to 1.65 m were studied as a control.

Measurements

Routine spirometry and carbon monoxide transfer factor (TLco) and transfer coefficient (TLco/Va) (single breath method; P.K. Morgan Ltd) were measured in a seated position as previously described.14 The normal values for lung volumes are those proposed by the European Community for Coal and Steel.15 Maximal static inspiratory (MIP) and expiratory (MEP) pressures were measured using a differential pressure transducer (Statham SC 1001; Hato Rey, Puerto Rico). The subject comfortably seated, wearing a noseclip, performed maximal respiratory efforts either at functional residual capacity (FRC) for MIP or at total lung capacity (TLC) for MEP against an obstructed mouthpiece with a small leak (internal diameter, 0.6 mm) to minimize oral pressure artifacts. Measurement of MIP at FRC does not include the contribution of the static recoil pressure of the respiratory system, and reflects the pressure exerted by contraction of the inspiratory muscles. The maneuvers were repeated until three measurements sustained for at least 1 s and with less than 5% variability were recorded. The highest value obtained was utilized for analysis.

After baseline routine testing, while subjects breathed room air, ventilatory pattern, mouth occlusion pressure, and electromyography (EMG) of the respiratory muscles were evaluated. The subjects, wearing a noseclip, were put in a comfortable supine position breathing through a mouthpiece on a circuit where the inspiratory line was separated from the expiratory one by a one-way valve (Hans-Rudolph; Kansas City, Mo). Airflow was measured with a Fleisch type 3 pneumotachograph and the flow signal was integrated into volume. From the spirogram, we derived breath-by-breath time and volume components of the respiratory cycle: inspiratory time (Ti), expiratory time (Te), total time of the respiratory cycle (Ttot), and every mean inspiratory flow (Vt/Ti), duty cycle (Vt/Tot), respiratory frequency (Rf=1/Ttot×60) and instantaneous ventilation (Ve=Vt×Rf) were also calculated. Mouth pressure during Vt maneuvers was measured using a pressure transducer (Statham P23ID). Mouth occlusion pressure 0.1 s after the beginning of inspiration (P0.1) was recorded as previously described.31617 Expired CO2 (Pco2) was sampled continuously at the mouth by an infrared CO2 meter. The values for dead space and resistance of the system up to a flow of 4 L/s were 178 mL and 0.92 cm H2O/L/s, respectively.
The EMG of the respiratory muscles was recorded as previously described.3,16,18 The EMG of the chest wall muscles was recorded from the second intercostal muscles (Eps), and EMG of the diaphragm (Edi) was recorded from the lower anterolateral rib cage via large surface electrodes as described by Gross and co-workers.19 Muscle action potentials (“raw”) were differentially amplified, filtered between 100 and 1,000 Hz to remove as much electrocardiogram as possible, without significantly filtering EMG, and were displayed on a single-beam storage oscilloscope (Tektronix 5115; Tektronix Inc; Beaverton, Ore.). The EMG activity was full-wave rectified and “integrated” over time (time constant, 100 ms) using a third-order, low-pass filter to provide a measurement of change in average electrical activity as a function of time, referred to as “moving time average.”20 This method of analysis allows the description of the time course of diaphragmatic inspiratory activity. Inspiratory activity was quantified both as peak activity (Edi and Eps) and as rate of rise of activity (Edi/Ti) and Eps/Ti). The former was directly measured in arbitrary units (millimeters of amplitude) and the latter was obtained by dividing the peak by the relevant inspiratory time (Ti).

Because of the variability of the impedance between diaphragm and electrodes, absolute values are not comparable in different subjects. To overcome this problem and to obtain a reference value, EMG activity was measured while the subject inspired to total lung capacity (TLC). This maneuver was repeated at least three times, and in each subject the intensity of the recorded diaphragmatic EMG was closely reproducible (<5% variability). The mean level of this EMG activity was taken as a reference; all successive measurements recorded at Vi have been expressed as a percentage of this reference value obtained at TLC.19 The TLC maneuver was repeated at the end of the CO2 rebreathing test.

The output of the CO2 meter, the flow signal, the integrated flow signal, the mouth pressure, and the moving time average were recorded continuously on a multichannel chart recorder. After a 10-min adaptation period, baseline evaluation began.

Successively, subjects underwent a CO2 rebreathing test following the procedure recommended by Read.21 A gas mixture (7% CO2, 93% O2) was inhaled for 3 to 5 min from a 5- to 8-L bag, the largest bag being reserved for normal subjects. In each subject, the rebreathing test was repeated twice on the same day. The resistance of the circuit used during the CO2 rebreathing test was such that mouth pressure during unoccluded breathing was always <2 cm H2O greater than or less than atmospheric pressure. During CO2 inhalation, when the open-loop condition was achieved, occlusions were randomly performed every 10 to 20 s.

Ventilatory parameters and EMGs were calculated from the data averaged from three breaths preceding each occlusion. As EMG activity of an inspiratory muscle may include cardiac muscle activity, as proposed by Gross et al.,20 we checked cardiac artifacts to gate electrocardiograms manually when necessary, so that it was not contributing to the progressive increase of EMG.

For each rebreathing run, changes in Vi, timing and volume components of breathing pattern, P0.1, and EMG were plotted against corresponding P<sub>co2</sub> values of 3,16 and subjected to least square linear regression analysis. We made sure that in no case the response exhibited on one study was 20% greater or lower than the response obtained on each of the other studies. For each subject, the mean slope for the two runs was calculated. Data were averaged for patients and normal subjects. In two patients (cases 6 and 8), no satisfying records of Eps were obtained during CO2 rebreathing; therefore, relevant data were not considered.

**Protocol**

Treatment with medication had been withdrawn from all patients at least 12 h prior to the study. Baseline functional evaluation and MIP and MEP were carried out on the same day. The following day, ventilatory pattern and EMG activity were evaluated. Since the influence of fatigue must be avoided as much as possible while performing maneuvers, evaluation required between 1 to 2 h, thus allowing patients to rest between hypercapnic runs.

**Data Analysis**

Data are presented as the mean ± SD. Regression analysis was carried out by least square method. An overview of the different variables suggested that the data were not to be regarded as normal. Indeed a check of distributions revealed a significant positive skew for most variables. Therefore, nonparametric statistical procedures were used to test group differences: the Mann-Whitney U test for unpaired samples.22

**Results**

Baseline pulmonary function data, lung diffusing properties, and maximal inspiratory and expiratory pressures of the patients are summarized in Table 2. No patients were considered to be undernourished, their average body weight expressed as percentage of ideal weight23 being 92 ± 6. Most patients exhibited normal spirometric values. In two cases (cases 4 and 5), a mild reduction in VC, and in three (cases 3, 6, and

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### Table 2—Baseline Function Data of Nine Patients With SLE

<table>
<thead>
<tr>
<th>Patients</th>
<th>Age, yr</th>
<th>Height, m</th>
<th>VC, % pred</th>
<th>FRC, % pred</th>
<th>TLC, % pred</th>
<th>FEV&lt;sub&gt;1&lt;/sub&gt;, %</th>
<th>FEV&lt;sub&gt;1&lt;/sub&gt;/VC, %</th>
<th>MIP, cm H&lt;sub&gt;2&lt;/sub&gt;O</th>
<th>MEP, cm H&lt;sub&gt;2&lt;/sub&gt;O</th>
<th>TLCO, mmol/min/l</th>
<th>TLCO/VA, mmol/min/l</th>
<th>PaO&lt;sub&gt;2&lt;/sub&gt;, mm Hg</th>
<th>PaCO&lt;sub&gt;2&lt;/sub&gt;, mm Hg</th>
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<td>12.2</td>
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<td>16.1</td>
<td>3.90</td>
<td>2.15</td>
<td>5.84</td>
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</table>

*VC=vital capacity; FRC=functional residual capacity; TLC=total lung capacity; FEV<sub>1</sub>=forced expiratory volume in 1 s; MIP=maximal inspiratory pressure; MEP=maximal expiratory pressure; TLCO=transfer factor and transfer coefficient for carbon monoxide; PaO<sub>2</sub>=arterial partial pressure of oxygen; PaCO<sub>2</sub>=arterial partial pressure of carbon dioxide.
7) a moderate reduction in TLC/VA, were found. In
the normal control group VC was 105% pv±10 SD, FRC was 105% predicted; 9 SD, FEV₁ was 99% pv±8 SD, and FEV₁/VC was 80%±7 SD. Values of MIP and MEP were compared with those of three- and height-matched normal control groups: group A, 20 to 30 years (11 subjects), group B, 30 to 40 years (9 subjects), and group C, 40 to 60 years (9 subjects). In these groups, values of MIP were as follows: group A, 97.5 (17.8), range 70 to 126 cm H₂O; group B, 99.1 (16.6), range 75 to 116 cm H₂O; and group C, 83.2 (15.8), range 69 to 117 cm H₂O. Values of MEP were as follows: group A, 131.5 (16), range 110 to 157 cm H₂O; group B, 111 (32), range 123 to 150 cm H₂O; and group C, 110 (21), range 109 to 141 cm H₂O. In six patients (cases 2 through 4, 6, 8, and 9) MIP, and in three cases (cases 4, 6, and 8) MEP were significantly lower (<mean-1.65 SD) than values of the age-matched normal control group.

No significant relationship was found between MIP and either the duration of the disease or the estimate of the total dose of steroid administered (daily dose per duration of administration).

While breathing room air (Table 3), patients exhibited smaller Vt (p = 0.015), Ti (p = 0.029), and greater Rf (p = 0.038), and similar VE and Vt/Ti and mouth occlusion pressure (P0.1), compared with the normal control group. Table 3 also shows average fractional EMG activity expressed in terms of both peak activity and rate of rise of inspiratory activity. The Edi/Ti and Eps/Ti were slightly higher in patients (p = 0.014 and p = 0.048, respectively).

In the patients as a whole, hypercapnic rebreathing (Table 4) resulted in lower ΔVt/ΔPCO₂ (p = 0.006), normal ΔP0.1/ΔPCO₂, and higher Δ(Edi/Ti)/ΔPCO₂ (p = 0.0024) and Δ(Eps/Ti)/ΔPCO₂ (p = 0.038). MIP, but not VC or TLC/VA, was related to ΔVt/ΔPCO₂ (r = 0.83; p = 0.0053) (Fig 1).

At 60 mm Hg of PCO₂ (Table 5 and Fig 2), patients maintained a rapid and shallow pattern of breathing: lower Vt (p = 0.038) and Ti (p = 0.011), with greater Rf (p = 0.0006), VE (p = 0.038), Vt/Ti (p = 0.048), and Edi/Ti (p = 0.008), compared with the normal control subjects. The greater VE and Vt/Ti reflected the greater intercept of the ΔVt/ΔPCO₂ and Δ(Vt/Ti)/ΔPCO₂ relationships.

**DISCUSSION**

**Muscle Strength**

In this selected group, most patients with SLE exhibited a mild decrease in respiratory muscle strength; mild reduction in VC and a moderate decrease in lung diffusion were found in a few patients.

Decrease in diffusing lung properties indicates some degree of parenchymal lung involvement, a finding in line with previous reports in which TLC and TLC/VA were slightly or markedly affected without a clear-cut radiographic finding of lung involvement. The present data are also somewhat consistent with those of a previous study by Jacobelli et al showing normal lung volumes and marked decrease in MIP in 50% of patients with SLE with normal chest radiographs. The decrease in MIP and MEP we noted is less than that observed in patients with SLE with radiographic and functional findings of lung involvement. The de-
crease in respiratory muscle force could depend on a number of factors. Mouth pressures generated during static maximal inspiratory (MIP) or expiratory (MEP) efforts are voluntary maneuvers, and factors such as individual motivation and experience with tests of respiratory muscle performance could explain, at least in part, the difference in mouth pressure between patients and the normal control groups. However, none of the normal subjects included in the control group had ever undergone tests of respiratory muscle function and were unaware of the purpose of the study. Thus, the observed decrease in MIP and MEP may actually reflect inspiratory muscle weakness, i.e., their failure to generate force.

Several factors are thought to be involved in respiratory muscle weakness: malnutrition, polymyopathy, steroid therapy, myasthenia-like conditions, and peripheral neuropathy are the most likely.

Malnutrition: It has been shown that poor nutrition impairs respiratory muscle function.\(^{26}\) Since nutrition as assessed by body weight (relative to their own ideal) in our patients was good, this factor is not likely to play a major role in the reduced inspiratory muscle strength.

Diffuse Myopathy and Steroids: Polymyositis is a possible reason for decrease in both MIP and MEP.\(^{27}\) Myopathic processes are known to occur in SLE,\(^{9,28,29}\) but relevant data to the respiratory muscles argue against this.\(^{7,25}\) In the present study, creatine phosphokinase and lactate dehydrogenase did not provide evidence of myositis. Nevertheless, one has to keep in mind that corticosteroids have been reported to improve myositis and muscle weakness associated with SLE.\(^{9,29}\) If this applies to our patients, steroid treatment might have minimized the clinical manifestations of myositis. However, the existence of long-term steroid myopathy should also be considered\(^{30-32}\) even if, unlike previous results in multisystem disorders,\(^{3}\) correlation between either the duration of administration or the approximate estimation of the total doses of steroid administered (daily doses per duration of administration) on the one hand, and the degree of respiratory muscle weakness on the other, was not observed in the present study. We must point out, however, that we studied outpatients in whom the effects of repetitive bursts of steroids, which may be more harmful, were not investigated.

Myasthenia-like Conditions: These may coincide with SLE.\(^{25}\) Although no clinical reasons were there for us to suspect the latter, such a syndrome could not drastically be excluded as no edrophonium chloride (Tensilon) test was performed.

Peripheral Neuropathy: Peripheral neuropathy may be responsible for reduction in muscle strength in SLE,\(^{25}\) a possibility that has not, however, been confirmed in other studies.\(^{25}\) In the present study, clinical and limb muscle electrophysiologic evaluation served to exclude it. Severe phrenic nerve neuropathy is also unlikely. In fact, normal phrenic nerve latency,\(^{6,25}\) and normal contractility of the diaphragm, assessed in terms of transdiaphragmatic pressure (Pdi) during electrical stimulation of phrenic nerves (twitch Pdi),\(^{6}\) have recently been reported in SLE. The mild decrease in MIP and the normal or even increased ventilation (VE) is consistent with the lack of severe phrenic nerve neuropathy.

The present data cannot contribute to define the exact reasons for the decrease in respiratory muscle force. On the one hand, proof is lacking to show that respiratory muscle weakness is the result of the simple myopathy of SLE in the patients of this study. On the other hand, while previous data show that long-term steroid myopathy may severely affect striated muscles (Iib fibre atrophy) including respiratory muscle structure and function,\(^{30-32}\) some observations are against the possibility that steroid myopathy is the sole explanation for respiratory muscle weakness: (1) the clinical presentation of this condition has been reported to occur prior to the initiation of corticosteroid therapy,\(^{25}\) and (2) improvement in respiratory muscle strength has been noted with high-dose steroid therapy\(^{9,29}\) in SLE.

Breathing Pattern

Wearing a mouthpiece may alter breathing pattern by increasing Vt and shortening Rf. However, as both groups wore a mouthpiece, we believe that the mouthpiece is not likely to have influenced our results substantially.

In patients the respiratory "central" output was modulated via shorter Ti into a tachypneic pattern of
breathing and smaller Vt. This more rapid and shallower breathing is similar to that observed in patients with other pulmonary disorders: chronic obstructive lung disease, multisytem disorder with normal chest radiograph, and several neuromuscular disorders. In neuromuscular disorders, nonvagal afferent information from either weak respiratory muscles or stiffened rib cage and/or vagal afferent information from the lung have been thought to act on the central inspiratory controller to terminate inspiration. Restriction in chest wall expansion, which has been suspected in shrinking lung syndrome of SLE, could modify the activity of rib cage muscle mechanoreceptors. An early pulmonary interstitial involvement, which has been reported in multisystem disorders, may increase pulmonary vagal afferent information.

The contribution of all these factors to the shortened T1, smaller Vt, and higher Rf response to carbon dioxide stimulation was not specifically investigated in the present study. However, the relationship of change in Vt per unit change in Pco2 (ΔVt/ΔPco2) with MIP (Fig 1) seems consistent with the hypothesis that respiratory muscle weakness is involved in the observed responses.

Table 4—Slopes of Vt, Vt, Vt/Ti, P0.1, and EMG vs Pco2, During CO2 Rebreathing in the Two Groups of Subjects*

<table>
<thead>
<tr>
<th></th>
<th>Edi</th>
<th>Eps</th>
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<tbody>
<tr>
<td>ΔVt/ΔPco2</td>
<td>ΔVt/ΔPco2</td>
<td>ΔVt/ΔPco2</td>
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<tr>
<td>mm Hg</td>
<td>mm Hg</td>
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<td>1.26</td>
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<td>1.05</td>
<td>0.005</td>
</tr>
<tr>
<td>9</td>
<td>1.47</td>
<td>0.034</td>
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<tr>
<td>Mean (patients)</td>
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<td>Mean (normals)</td>
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<td>p</td>
<td>NS</td>
<td>0.006</td>
</tr>
</tbody>
</table>

*For definition of abbreviations, see Table 3. Peak EMG activity (Edi and Eps) measured at Vt is expressed as percentage of the activity recorded at TLC during room-air breathing.

Table 5—Breathing Pattern and EMG in the Two Groups of Subjects at Pco2 of 60 mm Hg*

<table>
<thead>
<tr>
<th></th>
<th>Edi/Ti, % TLC/s</th>
<th>Edi/Ti, % TLC/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vt, L/min</td>
<td>Vt, L</td>
<td>Ti, s</td>
</tr>
<tr>
<td>Patients</td>
<td>26.37</td>
<td>1.24</td>
</tr>
<tr>
<td>Normals</td>
<td>(6.7)</td>
<td>(0.27)</td>
</tr>
<tr>
<td>P</td>
<td>0.038</td>
<td>0.038</td>
</tr>
</tbody>
</table>

*For definition of abbreviations, see Table 3. Values are mean±SD.
On the other hand, although we cannot exclude an early interstitial involvement in some of our patients, the observation that $\Delta V_t/\Delta P_{CO_2}$ was not related to either vital capacity or diffusing lung properties makes it unlikely that lung disease was primarily concerned in the ventilatory response.

**Respiratory Drive**

Electromyography of the respiratory muscles along with P0.1 and mean inspiratory flow ($V_t/T_i$) were used in assessing respiratory drive. We have criticized the use of either surface or esophageal EMG recording to assess respiratory drive in humans.3,16,40,41 Nevertheless, many data in normal and in disease states3,16,18,20,40-42 support the contention that the slope of the moving time average ($Edi/T_i$) is a reliable measure of respiratory center activity.

A finding in this study was the greater fractional EMG activity of the respiratory muscles during both spontaneous breathing and hypercapnic rebreathing in many patients. The fractional EMG activity of a muscle indicates the amount of its activation per breath relative to its total available activity. We have previously noted3,16,41 higher fractional EMG activity in patients with a number of respiratory diseases in which the inspiratory drive is expected to increase. Under the conditions of the present study, fractional neural activation of the respiratory muscles ($Edi/T_i$, $Eps/T_i$), for any spontaneous breath, was comparatively greater in patients than in the normal control group. In many respiratory disorders, the respiratory drive has commonly been assessed in terms of both $V_t/T_i$ and P0.1.10 However, in patients with respiratory muscle weakness, either $V_t/T_i$35,37 or P0.135,36 can underestimate the effective respiratory drive. Therefore, the observation in patients that a greater fractional EMG was associated with supernormal $V_t$ and $V_t/T_i$ (Table 5 and Fig 2) is likely to reflect an increased respiratory drive. To this regard it has been hypothesized that in patients with muscular diseases the neural drive could be increased in response to respiratory muscle weakness.43 Respiratory muscle receptors able to transmit sensory information related to muscle tension (tendon organs) can modify the respiratory drive44 and could be involved in this compensatory reflex. One can also argue, however, that although $V_t/T_i$, P0.1, and the level of EMG activation were thought to represent a normal or even high "central" respiratory activity, $V_t$ remained low during both spontaneous breathing and hypercapnic rebreathing. In this sense, the respiratory drive might be considered to be inadequate.

In conclusion, the present investigation indicates in a subset of patients with SLE a mild inspiratory muscle weakness that may accompany an increased respiratory drive and contribute to a qualitatively abnormal ventilatory response to carbon dioxide stimulation (rapid and shallower breathing). Studies specifically directed to the respiratory muscles will be required before it can be concluded that a myopathy is the cause of respiratory muscle weakness.

**ACKNOWLEDGMENTS** We are in debt to Drs. A. Spinelli, I. Iandelli, M. Bramati, and M. Gorini for giving valuable advice.

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