monitored electrocardiographic lead showed complete heart block, 4.8 seconds of asystole terminating in a junctional escape rhythm (Fig 1). The patient spontaneously recovered within 30 seconds, prior to the administration of any drugs. Subsequent ECGs were entirely within normal limits, and cardiac enzyme levels remained normal. On a subsequent exercise ECG, the patient reached 100 percent of his maximal age-predicted heart rate without symptoms or electrocardiographic changes.

**DISCUSSION**

Hypotension with bradycardia after sublingual nitroglycerin has been well documented. This response, which can be ablated by pretreatment with atropine, is probably due to enhanced vagal tone. The latter may be a result of decreased blood flow in higher cortical centers, or of deformation of afferent vagal fibers in the myocardium after nitroglycerin-induced changes in venous capacitance. Another (less likely) explanation is nitroglycerin-induced reduction in regional blood flow to the sinus node.

High-grade block at the atrioventricular node after sublingual nitroglycerin is quite rare. Our review of the literature reveals only one other case of complete atrioventricular nodal block after sublingual nitroglycerin. In that case, a 68-year-old woman with hypertension and documented prior episodes of vasovagal syncope was given 1.3 mg of nitroglycerin sublingually. Complete heart block with a junctional escape rhythm occurred 16 minutes later.

The mechanism of high-grade atrioventricular nodal block in our case may be atrioventricular nodal hypersensitivity to enhanced vagal tone. Strasberg et al have reported two cases of unprovoked paroxysmal atrioventricular nodal block in otherwise healthy individuals. Atrioventricular nodal hyperresponsiveness was the postulated mechanism. An interaction with lidocaine must also be considered. Rare complications of therapy with lidocaine include asystole and complete heart block; however, these complications have generally been observed either at high serum concentrations or in patients with underlying defects in conduction. Lidocaine alone, which was continued for several hours after the bradyarrhythmic episode, did not induce any abnormalities of conduction in this patient.

Our case demonstrates that complete atrioventricular nodal block may occur after sublingual nitroglycerin in an apparently healthy individual in the absence of ischemia.

**REFERENCES**


**Ventilatory Dysfunction Resulting From Bilateral Anterolateral High Cervical Cordotomy**

**Dual Beneficial Effect of Aminophylline**

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Because of metastatic pain resistant to medical treatment after left pneumonectomy for squamous cell carcinoma, a 46-year-old patient underwent a bilateral cervical cordotomy at the C1-C2 anterolateral level, in two phases. The second intervention was followed by severe ventilatory problems requiring mechanical ventilation, and at a later stage, the implantation of a phrenic pacemaker on the right side. Analysis of the ventilatory pattern during spontaneous breathing and during phrenic pacing and measurement of

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the transdiaphragmatic pressure during phrenic nerve stimulation revealed the existence of a beneficial effect of aminophylline on both the regulation of ventilation and diaphragmatic contractility.

Major ventilatory troubles are well recognized complications following bilateral anterolateral high cervical cordotomies. Alterations in both the control of ventilation and the function of inspiratory muscles have been advocated to explain these disturbances. We would like to report an observation illustrating the potential usefulness of aminophylline to treat this complication on the basis of its probable impact on both the control of ventilation and diaphragmatic contractility.

**Case Report**

In August 1979, a left pneumonectomy was performed in a 46-year-old man for squamous cell carcinoma. Dissemination of metastases to rib cage, mediastinum, and pericardium was already noted in October 1980. Because of severe pain resistant to all forms of medical treatment, a right anterolateral cordotomy at the C1-C2 level was performed in June 1981. The relief was only of short duration so that a left cordotomy at the same level was performed three weeks later. Two days after the second operation, the patient had a respiratory arrest and was intubated and mechanically ventilated.

Weaning from the ventilator could not be achieved and, 11 days after the second operation, a phrenic pacemaker was implanted on the right side (Model S 202, Monopolar Electrode, Avery Labs). Alternance of phrenic stimulation and of spontaneous breathing allowed extubation and weaning from the respirator, but development of several episodes of severe alveolar hypoventilation led to the use of more prolonged periods of phrenic stimulation. Despite a progressive increase of stimulation intensity, the neuromuscular response decreased and mechanical ventilation was required. Failure of this form of treatment prompted us to test the effect of aminophylline ten days after pacemaker implantation.

**Material and Methods**

Oxygen saturation was continuously measured by an ear oximeter (Hewlett Packard 47201 A). Changes in abdominal (AB) and rib cage (RC) circumferences were assessed, as well as tidal volume, with a respiratory inductive plethysmograph (Respiracor, Ambulatory Monitoring). Exsophageal and gastric pressures were obtained by placing two latex balloons in the lower third of the esophagus and in the stomach, and by connecting them to pressure transducers (Hewlett Packard 287 B); the use of a differential transducer gave the transdiaphragmatic pressure (Pdi).

For blood gas measurements, an indwelling radial catheter was inserted and the samples analyzed with an automatic blood gas analyzer (Radiometer ABL 2). Plasma theophylline levels were monitored.

**Protocol and Results**

**Phase 1 (31.07.1981)**

Spontaneous ventilation and ventilation under phrenic stimulation were recorded under control conditions and during aminophylline infusion (loading dose: 6 mg/kg body weight over 20 minutes, maintenance dose 1.2 mg/kg/hour) resulting in a theophylline plasma level of 18 mg/L when the physiologic measurements were made. The patient breathed through a Venturi mask with a FIO₂ of 0.24 for the control period and during the phrenic stimulations (duration, 20 minutes; respiratory rate of 20 per minute; inspiratory time, 1.3 seconds; stimulation frequency, 24 Hz with an intensity of 3.3 mA). Arterial blood gas values were taken at the extreme end of the stimulation period. During stimulated and spontaneous inspiration, the thorax moved inward and the abdomen outward. A prolonged period of stimulation (20 minutes) was followed by an apneic episode (Fig 1); administration of aminophylline prevented the occurrence of these apneic episodes, despite the fact that, immediately after pacing, PaCO₂ was lower with aminophylline (PaCO₂ 35 mm Hg; pH 7.56) than under control conditions (PaCO₂ 50 mm Hg; pH 7.48). Aminophylline also influenced the pattern of breathing during spontaneous ventilation as shown in Figure 2.

**Phase 2 (2.08.1981)**

Measurements of Pdi were recorded during phrenic stimulation (respiratory rate, 22 per minute, inspiratory time, 1.3 seconds; stimulation frequencies, 18, 24 and 36 Hz; intensity, 3.3 mA); for each frequency, a sequence of stimulations lasted one minute, followed by a 15 minute pause; control run duration was therefore 33 minutes, and after an aminophylline load was infused in 20 minutes, the same sequence of stimulations as in control was undertaken. The patient, breathing room air, was in the supine position, head and chest elevated at 45°. The circumference of the abdomen and the rib cage, as well as the transpulmonary pressure, were monitored and found to be constant, so that we can be reasonably sure that FRC did not change during the experiment. Aminophylline infusion resulted in a highly significant (p<0.001) increase in Pdi at the three stimulation frequencies tested (Table 1).

![Figure 1](http://journal.publications.chestnet.org/pdaccess.ashx?url=/data/journals/chest/21369/ on 03/31/2017)
DISCUSSION

Two types of respiratory disturbance can result from high cervical bilateral anterolateral cordotomy: a) alteration in the control of breathing and respiratory muscle dysfunction. Episodes of apnea following inhalation of 100 percent O₂ or diminished CO₂ response have already been described.1-4 Our patient also presented a picture characteristic of alveolar hypoventilation as well as a periodic pattern of breathing of the Cheyne-Stokes type.5 Moreover, prolonged stimulation of the phrenic nerve was followed by apneic episodes. All these abnormalities disappeared during the infusion of aminophylline at dosages associated with a full bronchodilator effect,15 even though after pacing, PaCO₂ was lower and pH higher during aminophylline administration than under control conditions. This combination of changes suggests that aminophylline was stimulating the ventilation: whether this action was mediated by the O₂ sensitive chemoreceptors or due to a direct nonspecific stimulating effect on the central nervous system is difficult to decide. It seems to us that the first hypothesis is the most likely one since Cheyne-Stokes breathing is generally considered to be essentially O₂ dependent and since aminophylline is known to restore a normal breathing pattern in patients presenting Cheyne-Stokes respiration associated with heart failure or neurologic disorders.16

The other target of aminophylline appears to be the diaphragm. Respiratory muscle dysfunction with decreased VC, MBC, and maximal inspiratory static pressure has already been reported in patients with bilateral anterolateral high cordotomy.12,14 This was probably also the case for our patient when breathing spontaneously, as suggested by the findings compatible with an alveolar hypventilation syndrome. We also hypothesize that muscle fatigue was likely to develop for the following reasons: because many of the bulbospinal efferent fibers for the phrenic nerve may have been disrupted by the bilateral cordotomy, effective contraction may have involved only part of the diaphragm; in such a case, during spontaneous respiration only a portion of the diaphragm had to sustain the totality of the inspiratory work; moreover, because of the inward movement of the thorax during inspiration, there was an increase in the work of breathing. This situation is similar in many respects to that present in quadriplegic patients who, when breathing through an inspiratory resistance, quickly develop inspiratory muscle fatigue.20-23 On the other hand, improvement in skeletal muscle contractility resulting from aminophylline administration as well known in vitro24 and evidence for the existence of this effect on diaphragmatic contractility in normal subjects has recently been presented.25 The same results were obtained in our patient.

In summary, this observation suggests that aminophylline may have a dual effect on both the regulation of ventilation and diaphragmatic contractility in cordotomized subjects; the administration of this drug had a clear-cut beneficial effect on the outcome of this patient. It blocked the development of a downhill course (respiratory muscle fatigue to phrenic stimulation by the pacemaker at increasing intensities to phrenic nerve stimulation inefficiency to intubation and mechanical ventilation), and allowed the patient to be weaned from the respirator and to breathe spontaneously without alveolar hypoventilation. Aminophylline may be the drug of choice during the critical days following high cervical bilateral anterolateral cordotomy.

REFERENCES


Table 1—Effects of Aminophylline on Transdiaphragmatic Pressure (Pdi) During Phrenic Nerve Pacing at Different Stimulation Frequencies*

<table>
<thead>
<tr>
<th>Pdi (cm H₂O)</th>
<th>Stimulation Frequency (Hz)</th>
<th>18</th>
<th>26</th>
<th>38</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td>5.3</td>
<td>6.7</td>
<td>8.2</td>
</tr>
<tr>
<td>+ aminophylline</td>
<td></td>
<td>8.7</td>
<td>10.6</td>
<td>13.2</td>
</tr>
</tbody>
</table>

*Values represent the mean ± SD of ten consecutive measurements. The difference between control conditions and aminophylline was statistically significant (p<0.001; t-test) at all the frequencies tested.
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