cases of anomalous origin of the right pulmonary artery from
the ascending aorta, either bilateral medial hypertrophy in
the presence of pulmonary pressure of 35 mm Hg, or in one
case (pulmonary pressures not measured), medial hypertro-
phy in the left lung and medial atrophy in the right lung were
described. In our patient, venous changes consistent with
pulmonary veno-occlusive disease were present in both
lungs (Fig 1 and 2). The number of affected veins was not as
great as sometimes seen, but in this case, the right lung was
already nonfunctioning as documented by perfusion scan
and displayed extensive interstitial pneumonitis and fibrosis.
This inflammation is possibly basic to the development of
pulmonary veno-occlusive disease in this case and was also
clinically confirmed. The thrombotic lesions occasionally
seen in many pulmonary arteries of the right lung were
probably embolic from the accessory vessel. The PVOD is a
rare and usually fatal condition in which there is gradual
obliteration of the pulmonary veins and venules. In the
absence of clinical characteristics, the diagnosis has to be
confirmed by lung biopsies. Symptoms of pulmonary hyper-
tension, roentgenographic appearance of pulmonary edema
without venous markings of the upper lobes, Kerley-B lines,
and patchy infiltrates, as well as unilateral absence of radio-
nuclides in perfusion scanning, are vague clinical clues. 

This case is outstanding because of the coincidence of
UARPA and PVOD, the latter offering an explanation for the
rare condition of late onset of PH in UARPA. Pulmonary
arterial changes were more pronounced in the right lung
which must be due to the extraordinary blood supply in this
disorder. Increased vascular sensitivity to infectious agents,
as well as to environmental and physical changes in either
vascular bed, may potentially lead to rapid increase of
pulmonary pressure, as it has been shown in patients with
UARPA at high altitudes. This special susceptibility of
pulmonary vessels might also have been a trigger for the
onset of PVOD.

This first finding of PVOD in a case of UARPA provides an
explanation for the extraordinary observation of adult-onset
PH in a so far asymptomatic patient.

ACKNOWLEDGMENT: We are very much indebted to Prof C.A.
Wagenvoort (Amsterdam) for establishing the diagnosis by reviewing
the histologic specim of both lungs.

REFERENCES
1 Wagenvoort CA, Neufeld HN, Birge RF, Caffrey JA, Edwards JE.
Origin of right pulmonary artery from ascending aorta.
Circulation 1961; 23:84-90
2 Pool PE, Vogel JHK, Blount SG. Congenital unilateral absence
of a pulmonary artery: the importance of flow in pulmonary
hypertension. Am J Cardiol 1962; 10:706-32
3 DuShane JW, Weidmann WH, Ongley PA, Swan HJC, Kirklin
Heart J 1960; 59:782-88
4 Heath D, Edwards JE. The pathology of hypertensive pulmo-
mary vascular disease: a description of six cases of structural
changes in the pulmonary arteries with special reference to
congenital cardiac septal defects. Circulation 1958; 18:533-47
5 Wagenvoort CA. Grading of pulmonary vascular lesions: a
6 Fraser RG, Pare JAP. Absence (proximal interruption) of the right
or left pulmonary artery. In: Diagnosis of diseases of the chest,
7 Wagenvoort CA. Pulmonary veno-occlusive disease: entity or
syndrome? Chest 1976; 69:82-86
Arch Dis Child 1967; 42:322-27
9 Wagenvoort CA, Wagenvoort N. The pathology of pulmonary
veno-occlusive disease. Virchows Arch A Path Anat Histol
1974; 364:69-79
Thorax 1971; 26:663-75
veno-occlusive disease. Am J Cardiol 1973; 31:78-83
12 Pawewski M, Reif R, Manor H, Starinsky B, Katzir D. Pulmonary
veno-occlusive disease in a unilateral hypertransradiant lung.
Thorax 1981; 36:397-99
13 Grover RF, Vogel JHK, Averill KH, Blount SG. Pulmonary
hypertension: individual and species variability relative to
14 Hackett PH, Creagh CE, Grover RF, Honigman B, Houston CS,
Reeves JT, et al. High altitude pulmonary edema in persons
302:1070-73

Amyotrophic Lateral Sclerosis
Presenting with Sleep Hypopnea Syndrome

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Yves M. Tibierge, M.D.;† Louis J. Arbus, M.D.;† and
Paul J. Leophonte, M.D.*

Described is a 67-year-old man whose initial symptoms
evoked an obesity-hyperventilation syndrome. Polysom-
ography showed hypopneas associated with O₂ desatura-
tion episodes, and no apnea; maximal changes were noted
during REM sleep. A few months later, in spite of marked
weight loss, acute alveolar hypoventilation occurred and
necessitated mechanical ventilatory support. Tracheostomy
was performed. The patient appeared to be dependent on
nocturnal ventilatory assistance. Diaphragmatic paralysis
was noted in addition to clinical and electrodiagnostic
 evidence of amyotrophic lateral sclerosis. While the patient
was not ventilated, a nocturnal recording of SaO₂ again
revealed desaturation episodes partly corrected by O₂ 2 L/
min administered through the tracheostomy tube. With
volume-controlled ventilation, desaturations completely
disappeared, although no oxygen enrichment of the air
was provided. We speculate that sleep disorders with hypopneas
and O₂ desaturation episodes were the initial symptoms of
amyotrophic lateral sclerosis. This leads us to suggest that
nonspecific respiratory muscle fatigue frequently seen in
COPD might be included in the hypothetic causes of
nocturnal hypoxemia.

Patients with amyotrophic lateral sclerosis (ALS) are
known to have respiratory complications, but they usu-
ally occur late in the course of the disease. A few cases of ALS

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have been reported in which the original symptom was exertional dyspnea or acute respiratory failure. We have observed one case of ALS in which sleep-induced respiratory disorders may have been the initial symptoms.

**CASE REPORT**

On June 6, 1985, a 68-year-old white man was referred to the hospital for evaluation of suspected obesity-hyperventilation syndrome. He complained for six months of disturbed nocturnal sleep, morning headaches and daytime hypersomnolence. For one year he experienced gradually increasing dyspnea on exertion. He was a ten pack-years cigarette smoker and had no history of chronic bronchitis. The only pertinent physical finding was obesity (92 kg; 1.69 m); his weight had not changed for five years. No neurologic abnormality was noted. At rest, arterial oxygen tension ($PaO_2$) was 65 mm Hg; carbon dioxide tension ($PaCO_2$): 38 mm Hg; pH: 7.40; oxygen saturation ($SaO_2$): 93 percent. Pulmonary function test results included the following values: total lung capacity: 4.8 L (80 percent pred); vital capacity: 3.1 L (75 percent pred); forced expiratory volume in one second: 2.2 L (76 percent pred); FEV1/VC: 71 percent; residual volume: 1.7 L (95 percent pred). Findings on chest x-ray films, electrocardiogram and routine laboratory tests were normal. Minimal exertion (30 watts, 2 min) elicited a marked fall in $PaO_2$: 46 mm Hg and a rise in $PaCO_2$: 43 mm Hg.

Two night sleep studies were conducted using routine electroencephalographic, electrocardiographic and electrooculographic lead placement with standard interpretation of sleep stages. Also monitored were electrocardiogram, chest wall and abdomen motions by strain gauges, airflow at the nose and mouth by thermistors and $SaO_2$ by a Biox II ear oximeter. A hypoxemic episode was defined as a fall in $SaO_2$ of at least 10 percent from the preceding stable $SaO_2$ asleep. Hypopnea was defined as a decrease, but not complete cessation of airflow at the nose and mouth causing thermistor recording deflection of less than one-third baseline levels for at least 10 s, with a simultaneous decrease in $O_2$ saturation. Results are shown in Table 1.

The initial polysomnography was performed while the patient was breathing room air; sleep architecture was abnormal with frequent arousals, reduced amount of REM sleep, and absence of NREM sleep stages 3 and 4. The breathing pattern was irregular during most of the night, with very frequent spells of hypopnea of the central type. No apnea was recorded. Associated with these hypopneas were transient falls in $SaO_2$, maximal changes in breathing pattern and $SaO_2$ were noted during REM sleep. On the second night, the patient breathed oxygen at a flow of 2 L/min, through a nasal cannula: sleep architecture normalized and desaturation peaks disappeared while his breathing pattern remained abnormal. The patient was discharged with a prescription of reducing weight by diet, and nasal oxygen therapy (2 L/min 15 h/day).

On September 30, 1985, he was readmitted for evaluation of acute respiratory distress with a $PaO_2$ level of 45 mm Hg, $PaCO_2$ of 95 mm Hg, and a pH of 7.53. No clinical sign of bronchial obstruction was noted. Chest x-ray films showed only an elevation of the left diaphragm. Fiberbronchoscopic findings were normal. An endotracheal tube was placed. The patient was initially treated with a volume-controlled ventilator (CPAP). A tracheostomy was performed five days after admission. During the following weeks, the patient's condition improved and permitted weaning from diurnal mechanical ventilatory support. At this time, arterial blood gas levels returned to nearly normal. We noted also that a weight loss up to 30 kg had occurred within four months. Physical examination showed generalized muscle atrophy with normal sensation, left Babinski's sign, prominent diffuse fasciculations, and paradoxical breathing.

Electrodiagnostic studies revealed severe axonal and demyelinating neuropathy involving legs, arms and face. The cell counts, glucose, and protein levels of the cerebrospinal fluid were normal as well as cervical rachis x-ray films and CT scan of the brain. With these findings, diagnosis of ALS was made.

There was no clinical sign of bulbar or intercostal muscular paralysis. Diaphragmatic impairment was suspected at this time. Fluoroscopic examination of the chest showed a paradoxical movement of the right diaphragm, and no movement of the left. Electrocardiography of the diaphragm revealed very poor activity with neurogenic abnormalities on the right. No activity was recorded on the left.

Ear nocturnal $SaO_2$ was monitored during three consecutive nights (Table 1). While the patient was breathing room air, severe nocturnal desaturations were again noted, partly corrected by administration of $O_2$ 2 L/min through the tracheostomy tube. With mechanical ventilatory support but no oxygen enrichment of the air, desaturation completely disappeared. Two attempts at weaning the patient from nocturnal ventilatory assistance were unsuccessful since at each attempts his condition progressively deteriorated over the ensuing days, with increasing dyspnea, clinical evidence of respiratory muscle fatigue and severe respiratory acidosis. Therefore, nocturnal ventilatory support through the tracheostomy tube was continued. The patient is still alive (August, 1987).

**DISCUSSION**

Since it is now recognized that hypopnea may affect blood gas levels and hemodynamics, and elicit clinical features similar to that of the sleep apnea syndrome, our initial diagnosis in this patient of sleep hypopnea syndrome in an obese man, according to the definition recently proposed by Gould and colleagues was based on simultaneous occurrence of two clinical features (snoring, somnolence, disturbed sleep, cardiac failure or polycythemia) associated with more

<table>
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<th>Table 1—Polysomnographic Tracing</th>
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<td><strong>A</strong></td>
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<tr>
<td>Wakefulness</td>
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<tr>
<td>Time (min) spent in each sleep stage</td>
</tr>
<tr>
<td>NREM</td>
</tr>
<tr>
<td>30</td>
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<tr>
<td>191</td>
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<td>6</td>
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<td>0</td>
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<tr>
<td>Total sleep time</td>
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<tr>
<td>Hypopnea index*</td>
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<td>REM sleep index*</td>
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<td>Sleep time with $SaO_2 &lt;80$% (%)</td>
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<td>Lowest oximeter reading (%)</td>
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A: 11/6/85: breathing room air.
B: 12/6/85: with $O_2$ 2 L/min.
*With Stanford terminology: the hypopnea index corresponds to the total number of abnormal respiratory events during sleep, divided by total sleep time in minutes, then multiplied by 60; the REM sleep index gives the number of abnormal respiratory events per hour of REM sleep.

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<th>Table 2—Ear Oxygen Saturation Measured While Patient Had Tracheostomy Tube in Place</th>
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<tr>
<td><strong>Breathing Room</strong></td>
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<td><strong>Air</strong></td>
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<td>Sleep time with $SaO_2 &lt;80$% (%)</td>
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<td>Lowest oximeter reading (%)</td>
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than 15 hypopnea episodes per hour of sleep. However, acute alveolar hypoventilation occurred in spite of a weight loss of up to 30 kg. Initially, the cause of the respiratory failure was obscure, but diaphragmatic paralysis was subsequently demonstrated and further neurologic evaluation supported the diagnosis of ALS.

Alveolar hypoventilation is a serious complication of advanced neuromuscular disease, and is consistently observed in ALS. Conversely, acute respiratory failure with diaphragmatic paralysis and dependence on mechanical ventilation already has been described in the literature as an initial presentation of ALS. The predominance of lesions in the anterior columns of the ventral horn, from C2 to C5, corresponding to the phrenic nuclei, explained the diaphragmatic paralysis and the prominent respiratory symptoms. We believe that the respiratory failure was related to diaphragmatic involvement of ALS.

The respiratory sleep disorders noted on first admission were initially related to the patient's obesity. Nevertheless, their aggravation in spite of his weight loss negated this possibility. Further evolution of ALS made us hypothesize that sleep-disordered breathing was already due to a neuromuscular cause. It is currently known that central or obstructive apnea, related to decreased respiratory center output or failure of upper airway muscle activity, may occur in a variety of neuromuscular diseases such as poliomyelitis or myotonic dystrophy. Furthermore, similar nonapneic arterial oxygen desaturations in REM sleep have been well described in limb girdle muscular atrophy and adult-onset spinal muscular atrophy, also in association with bilateral diaphragmatic paralysis. We suggest that in our patient, diaphragmatic impairment was already present on first admission, and was involved in the sleep respiratory disorders and abnormal lung function. Chest x-ray film findings were normal, but may be misleading if bilateral diaphragmatic paralysis is not complete. The patient's obesity may have aggravated the sleep disorders, but also may have masked the cardinal clinical feature of bilateral diaphragmatic paralysis (paradoxical movement of the abdominal wall) as well as beginning peripheral signs of ALS. In addition, we cannot exclude the influence of the weight loss in the rapid respiratory deterioration.

The reason why patients with paralysis or severe weakness of both halves of the diaphragm are at risk during sleep (and particularly during REM sleep) is not well defined. The diaphragm receives the major part of the central respiratory drive, which is known to be decreased during sleep. Thorpy et al recently suggested that inhibition of intercostal and accessory muscle activity (a physiologic feature of REM sleep) leaves a mechanically inefficient or weak diaphragm that alone may be ineffective in sustaining tidal volume and alveolar ventilation.

Since it has been shown that in neuromuscular disease, a diaphragmatic weakness, sometimes difficult to diagnose, can induce nonapneic oxygen desaturation episodes, particularly during REM sleep, it would seem to have a parallel in other clinical situations, such as chronic lung disease. Similar sleep disorders are often reported in patients with chronic obstructive pulmonary disease (COPD). Their pathogenesis is not well known; however, a variety of mechanisms have been suggested, such as increased oxygen uptake, overall hypoventilation, changes in the distribution of ventilation-perfusion ratios or diminution of mucociliary clearance. The role of the diaphragm has not been studied extensively, although abnormal mechanisms and fatigue of the diaphragm are known to be important features of disabling COPD. We suggest that our case gives support to the working hypothesis which proposes that the fatigue of the diaphragm is included in possible mechanisms of nocturnal hypoxemia in COPD. This fatigue, sometimes not clinically evident, might be intensified during REM sleep in COPD, and transient hypoxemia might be related to these episodes of maximal muscular impairment.

**References**

9. Meyrignac C, Poirier J, Degos JD. Amyotrophic lateral sclerosis presenting with respiratory insufficiency as the primary complaint. Eur Neurol 1985; 24:115-20
Pneumoconiosis in an Elderly Dentist*

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Numerous dusts found commonly in the dental laboratory have been suggested as potential pulmonary hazards. We recently noted a case of severe interstitial pulmonary fibrosis with intraalveolar deposition of unique foreign body inclusions in an elderly dentist. The composition of these particles was shown to be consistent with that of alginate impression powder. This is in contrast to previously reported pneumoconioses in dental workers, which are usually induced by metallic alloys or silicates. Further studies are needed to identify the causes and prevalence of pneumoconiosis in the dental lab.

Various dusts commonly found in the dental laboratory have been implicated as potential etiologic agents of pneumoconiosis. We recently noted a unique case of pneumoconiosis which appeared to be produced by alginate impression powder.

CASE REPORT

A 79-year-old retired dentist with a history of interstitial lung disease of unknown etiology presented to the hospital with fever, cough with purulent sputum, and dyspnea of three days' duration. He was an ex-smoker. Past medical history also included pernicious anemia, chronic atrial fibrillation, and stable angina pectoris. He had retired from the solo practice of general dentistry approximately 15 years previously. His practice included frequent production of impressions of edentulous arches using alginate impression material, and infrequent casting of gold for crowns and occasional finishing of partial dentures (chromium-cobalt alloy).

On physical examination, the patient appeared acutely dyspneic.

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Figure 1. Scanning electronmicrograph reveals intra-alveolar deposition of “mulberry-shaped” foreign body inclusions.

Oral temperature was 40.0°C, pulse was irregularly irregular at 96 beats per minute, respiration were 32 per minute, and BP, 90/60 mm Hg. The lungs disclosed low-pitched wheezes throughout all fields with inspiratory crackles in the right base. Clubbing was not present, and the remainder of the examination was normal.

Arterial blood gas obtained on 2 L of O2 per nasal cannula revealed pH of 7.49, PCO2, 30 mm Hg; PO2, 53 mm Hg; and a calculated O2 saturation of 90 percent. Chest roentgenogram disclosed an infiltrative process in the right lung superimposed on a severe diffuse interstitial pattern. Sputum revealed Gram-positive diplococci.

Despite aggressive supportive care, including antibiotics, bronchodilators and chest physiotherapy, respiratory failure supervened, and the patient died.

At necropsy, lung consolidation with pulmonary edema was superimposed on severe diffuse interstitial fibrosis with honeycombing. Pulmonary vascular changes consistent with severe pulmonary hypertension were present. Light microscopy disclosed moderate numbers of birefringent particles within fibrotic areas and within alveolar macrophages. Scanning electron micrographs revealed numerous “mulberry-shaped” intra-alveolar foreign body inclusions measuring approximately 4 μ in diameter (Fig 1). Dispersion analysis revealed these particles to be composed primarily of calcium.