their care before they go home, and to reduce their need to return to the ED.

James B. Fink, RRT
Hines, Illinois

Division of Pulmonary and Critical Care Medicine, The Edward Hines, Jr. Hospital.

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An Analysis of Platypnea-Orthodeoxia Syndrome Including a “New” Therapeutic Approach

This issue of CHEST (see pages 1681 and 1682) contains two separate case reports, each describing a patient with a patent foramen ovale, and each patient manifesting platypnea (increased dyspnea in the erect position relieved by assuming a recumbent position) and orthodeoxia (accentuated hypoxemia in the erect position, improved by assuming a recumbent position). In each patient, closure of the foramen ovale led to a remission of platypnea-orthodeoxia.

The platypnea-orthodeoxia syndrome appears to be exceedingly rare. By 1994, it was estimated that only 17 cases of this syndrome involving interatrial right-to-left shunting had been described in the medical literature. The additional two cases reported in this issue of CHEST make a total of 19 cases. The rate of incidence of the syndrome not associated with intracardiac shunting is not known, but presumably is very low.

These reports provide an opportunity to review the medical history of the platypnea-orthodeoxia syndrome. In this review, our goal is threefold: (1) to provide a clinical and physiologic perspective; (2) to indicate the application of the disordered physiology to a more common, current problem, diffuse endocardial disease; and (3) to suggest a “new,” previously untried form of therapy.

HISTORY

The original description of patients with platypnea-orthodeoxia dates back to 1949 when Burchell et al described a patient with an atrial septal defect manifesting platypnea-orthodeoxia and subsequently described the reversal of both following closure of a patent foramen ovale. “Platypnea” and “orthodeoxia” were not used to describe the manifestations of this syndrome until they became commonly accepted in 1969 and 1976, respectively.

In 1956, two patients with upright dyspnea and oxygen desaturation were described. Each had the combination of an atrial septal defect and unilateral pneumonectomy. However, the term “platypnea” was not used. The upright desaturation was called “orthostatic cyanosis.” These workers speculated on the mechanism of the two phenomena, suggesting that the dyspnea was caused by the orthostatic cyanosis.

The term “platypnea” was introduced by our group in 1969. A patient with severe COPD was noted to develop severe dyspnea in the sitting position relieved by assuming a prone position. An autopsy documented severe obstructive lung disease. There was no interatrial communication. There was a significant fall in PaO₂ in the upright vs the prone position, but we did not connect the hypoxia with the platypnea. We also overlooked the prior case reports mentioned above. Medical history is not an exact discipline.

Seven years later we reported three patients with significant, accentuated arterial hypoxemia in the upright compared to the supine position. All three manifested platypnea. We coined the term “orthodeoxia” to describe the phenomenon. None of the three patients had significant intrinsic pulmonary disease. Two of the patients had chronic liver disease (lung spiders) and one had multiple congenital arte-
rioroventous communications in the lung. There were no atrial septal defects in any of the three patients.

A major contribution was published in 1984.6 Seven patients were described. All seven had interatrial communications. Four of the seven developed platypnea-orthopnea after pneumonectomy, two after pulmonary embolism. The seventh patient had no obvious lung disease, yet manifested platypnea and orthopnea. Surgical closure of the interatrial communication was carried out in five of the patients. Four improved dramatically, but the fifth died postoperatively of massive cerebral infarction. Two patients were managed without surgery.

It was noted that the syndrome could occur without overt pulmonary disease. A major observation was that right-to-left shunting occurred without a mechanism to explain the right-to-left shunt. Pulmonary hypertension usually was absent, and right-sided hemodynamics were normal. There was no obvious explanation for the right-to-left shunt.

Since 1984, a number of isolated reports have described the same findings: right-to-left shunting across interatrial communications despite normal right-sided intra-cardiac pressure.5 Various theories have been advanced to explain the mechanism.

**Clinical Features**

Table 1 outlines the etiologic background of the platypnea-orthodeoxia syndrome. It is not surprising that interatrial communications are the most common etiologic association. The population at risk is huge. Approximately 25% of the general population have a patent foramen ovale.7 Platypnea-orthodeoxia may theoretically occur with other sites of interatrial right-to-left shunting, but this occurrence has not been documented thus far.

There are no data which can be used to estimate the incidence of platypnea-orthodeoxia in patients with anatomic lung shunts or chronic pulmonary disease. It is not standard practice to evaluate the effects of position on the degree of dyspnea or to measure the PaO$_2$ in the sitting vs the upright position. Intuitively, one might speculate that the incidence is very low.

**Physiologic Features**

The precise mechanisms for both platypnea and orthodeoxia are unknown. In the several isolated case reports, speculation over mechanisms is often geared to whatever special features were found in the patient being reported.

This is particularly puzzling in patients with the syndrome related to interatrial communications. What is the mechanism for a right-to-left shunt in patients without pulmonary hypertension and normal hemodynamics? This puzzle has been restated as a question: “What causes water to flow uphill?”8 Most right-to-left shunting with normal hemodynamics is found in patients who do not have platypnea or orthodeoxia.

An explanation commonly offered is that unequal diastolic compliance has developed in the right heart as compared to the left heart. As a result, blood flows from a relatively stiff right atrium to a more compliant left atrium. In the normal adult, the right ventricle is more compliant than the left ventricle.9 This relationship can be altered by disease.

Whatever the merits of the theory applied to the rare syndrome of platypnea-orthodeoxia, it can be applied to a very common disorder, endocardial injury in general, and to the endocardial damage specifically produced by the Swan-Ganz catheter (SGC).

The excess mortality associated with the use of the SGC has been well documented.10,11 Less well known to clinicians is the fact that 50% or more of patients studied at postmortem following the use of the SGC have diffuse endocardial lesions.12,13 There are at least seven studies dating back to 1972 establishing the development of diffuse endocardial disease following the use of the SGC. These lesions almost certainly alter right-sided diastolic compliance and in turn have an unfavorable effect on both right-sided and left-sided hemodynamics. This sequence may well explain some of the excess mortality associated with the use of the catheter.

**A New Therapeutic Approach**

Given a patient with an interatrial communication and platypnea-orthodeoxia, the current approach is to consider surgical closure of the communication, say a patent foramen ovale. Indeed, investigation of the possibility of an interatrial communication is commonly justified by the availability of a surgical remedy, including new techniques using percutaneous catheters. The attractiveness of surgical closure is enhanced by the possibility of preventing paradox-

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**Table 1—Disorders Associated With the Platypnea-Orthodeoxia Syndrome**

<table>
<thead>
<tr>
<th>Category</th>
<th>Disorder</th>
</tr>
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<tbody>
<tr>
<td>1. Intracardiac shunts</td>
<td></td>
</tr>
<tr>
<td>Interatrial:</td>
<td></td>
</tr>
<tr>
<td>Without overt lung disease</td>
<td></td>
</tr>
<tr>
<td>With lung disease</td>
<td></td>
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<tr>
<td><em>pneumonectomy</em></td>
<td></td>
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<tr>
<td><em>obstructive lung disease</em></td>
<td></td>
</tr>
<tr>
<td><em>other</em></td>
<td></td>
</tr>
<tr>
<td>2. Anatomic pulmonary vascular shunts</td>
<td></td>
</tr>
<tr>
<td>Pulmonary artery-pulmonary vein communications</td>
<td></td>
</tr>
<tr>
<td>Pulmonary parenchymal shunts</td>
<td></td>
</tr>
<tr>
<td>Significant areas of low or zero Va/Qc ratio</td>
<td></td>
</tr>
</tbody>
</table>
rical emboli. As a result, aged patients with platypnea-orthodeoxia may be subjected to surgery.

In the past 15 years increasingly it has been recognized that (1) dyspnea associated with chronic pulmonary disease may be treated safely with opiates, and (2) that the dangers of addiction with this form of treatment is minimal.14 To our knowledge, opiates have never been used in the treatment of the platypnea-orthodeoxia syndrome.

Accentuation of hypoxemia with opiates, of course, could be managed with oxygen therapy. From the standpoint of safety, we cite the six patients in the literature whose PCO₂ values were published. Five had hypocapnia (increased alveolar ventilation) and one had a normal PCO₂. In the face of alveolar hyperventilation, opiate therapy should be particularly safe. The failure to use opiates resembles treatment of orthopnea, for which opiate therapy had not been used for many years.15 Opiates are now, of course, an important part of therapy.

In any case, a careful trial of opiate therapy would seem to be a reasonable approach, especially in older patients with platypnea-orthodeoxia. It is a reasonable guess that for most patients, even if they are candidates for surgical closure of an interatrial communication, opiate therapy would have a more favorable risk-benefit and cost-benefit ratio compared to surgery.

In summary, the apparently rare syndrome of platypnea-orthodeoxia has been reviewed. The historical steps in the description of the syndrome have been outlined, the various causes have been classified, the disordered physiology has been analyzed and used to call attention to a more common (and frequently iatrogenic) disease, diffuse endocardial injury, and the use of opiates to treat the syndrome has been suggested.

Eugene D. Robin, MD
Trinidad, California
Robert F. McCauley
Anaheim, California

Active Professor Emeritus (Dr. Robin), Stanford University School of Medicine, and Internist (Dr. McCauley), West Anaheim Medical Center.
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Reprint requests: Dr. Eugene D. Robin, PO Box 1185, Trinidad, CA 95570-1185

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The Antiphospholipid Antibody Syndrome
A Vascular Disease With Pulmonary Manifestations

It is rare that a new disease with respiratory manifestations arrives on the scene. The antiphospholipid antibody syndrome (APS) is a perplexing new entity that is approximately a decade old. APS is a hypercoagulable state characterized by the presence of autoantibodies to membrane phospholipids. Its major clinical features are vascular occlusion (e.g., stroke, myocardial infarction, peripheral gangrene, visceral infarct, deep vein thrombosis), fetal loss, and hematologic abnormalities that mimic vasculitis (e.g., thrombocytopenia, Coombs’s positive hemolytic anemia, livedo reticularis).1,2 Circulating immunoglobul-