Communications

generation of the pulmonary edema in this patient. Indeed, endorphins are released in stress situations and they can adversely affect physiologic systems, such as respiration and circulation.¹ In the human fetus at term, plasma levels of beta-endorphins and beta-LPH are inversely correlated with arterial pH and Po₂, suggesting that hypoxia and secondary acidosis may be important stimuli controlling the release of these peptides.² Recently, Bar-Or et al³ reported a dramatic clinical improvement after naloxone therapy in a patient with high-altitude pulmonary edema. The finding of a high plasma beta-endorphin concentration in this patient suggested that endorphins may play a role in this disorder. Development of pulmonary edema in animals by selective cerebral perfusion with the hypoxic blood as observed by Moos et al⁴ might be explained in part by endorphinergic mechanisms. Interestingly, endogenous opioids might also play a role in the pathogenesis of apnea.⁵

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To the Editor:

The suggestion that endogenous opiates might play a major role in the pathogenesis of non-cardiac pulmonary edema occurring as a result of obstructive sleep apnea is an intriguing one. If severe hypoxemia is associated with the release of endogenous opiates, as suggested by Chernick et al,¹ Dr. Smitz's hypothesis is certainly quite reasonable. It is well known that overdoses of exogenous opiates may result in noncardiac pulmonary edema in some patients. Noncardiac pulmonary edema appears to be quite uncommon in patients with sleep apnea, and if the mechanism by which endogenous and exogenous opiates produce pulmonary edema is similar, one would almost have to postulate endogenous opiate "poisoning" in those patients who develop it. Since alternative mechanisms for the development of pulmonary edema in such patients seem quite plausible, it may be that multiple factors are involved. We agree with Dr. Smitz, however, that the role of endogenous opiates in the development of pulmonary edema in the patient we described was indeed, in the pathogenesis of sleep apnea syndrome, deserves careful investigation.

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Occupational Asthma and Rhinitis Caused by Urea Formaldehyde?

To the Editor:

I am writing to comment on an article by D. W. Cockcroft et al (Chest 1982; 82:49). I offer the following comments.

The conclusion that the authors documented, i.e., the occurrence of occupational asthma caused by (CUF), is not compatible with the data presented. However, they did document that CUF particle board dust caused asthma in both of their patients. The difference between these two conclusions is crucial! CUF particle board contains a number of known as well as industrially secret chemicals, each of which may be a cause of occupational asthma. Since the exact chemical/allergy exposure of the work environment of the patients in this study was never precisely defined, since each of the potential triggers was not evaluated to determine their relationship to the initiation of asthma, and especially since urea formaldehyde per se was never evaluated in this study, it is difficult to understand how the authors could possibly conclude the urea formaldehyde was the cause of asthma in either patient.

Occupational asthma has extensive health, social, economic, political, legal, ethical, and moral dimensions. Physicians engaged in the assessment of patients with occupational asthma have an obligation to define precisely the initiating and triggering stimuli following the tenets of the scientific method. Included in this obligation is the responsibility to refrain from publishing conclusions which are not in fact supported by data lest one invite misconception, misuse and abuse of findings.

Peter B. Boggs, M.D., F.C.C.P.
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To the Editor:

We are pleased to have the opportunity to reply to the important points raised in Dr. Boggs' letter. There appears to be confusion in interpretation, particularly concerning the terms "urea formaldehyde" and "urea formaldehyde resin." Asthma was provoked by particle board sawdust allegedly containing only wood particles, a low concentration (<1 percent) of an inert paraffin-like wax, and 6 percent urea formaldehyde resin bonding agent. Absence of asthma following exposure to the natural sawdust suggests the urea formaldehyde resin was responsible. The title of our paper, the discussion, and the conclusion ("it is likely that some component of the urea formaldehyde resin system was responsible . . . . . this could not be proved"), were carefully worded to embrace this hypothesis.

The precise composition of the various urea formaldehyde resin systems remains an industrial secret. We have been told that the bonding agent used in this particle board consists of seven components: urea, formaldehyde, an inorganic ammonium (NH₄+) salt which is the major acid catalyst, two other "common" organic salts, a "trace" of low molecular weight amine, and water as a solvent. The asthma in our carpenters may have been due to an individual component, a reaction product, or a breakdown product of this polymer resin system. For example, the reaction of formaldehyde with ammonia produces hexamethylene tetramine,² which is a documented cause of occupational asthma.³ Many other reaction products and breakdown products may be involved. As was clearly stated, the exact chemical(s) responsible for the asthma could not be identified.

The simple resin system used as a particle board bonding agent uses different reactants than the more complex urea formaldehyde foam insulation resin.¹ Consequently, the findings in our carpenters may not be applied to those exposed to urea formaldehyde foam.

In conclusion, we believe the urea formaldehyde resin system used to bond this particular particle board was responsible for asthma in our two carpenters. We emphasize again that any
component(s) of the “urea formaldehyde resin system,” rather than “urea formaldehyde” per se, might be implicated in the pathogenesis.

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Death from ARDS and Cardiovascular Collapse following Lidocaine Administration

To the Editor:

We read with interest the selected report of ARDS following administration of lidocaine by Howard and associates (Chest 1982; 81:644-45). A similar experience occurred at our institution and merits description.

A 19-year-old woman had fiberoptic bronchoscopy performed to evaluate new, bilateral interstitial infiltrates. A diagnosis of histiocytosis X was made three years earlier when a pathologic, long-bone fracture was noted. She had received cyclophosphamide and methotrexate in the past for this condition. At the time of bronchoscopy, she was receiving no chronic medications. The patient was pre-medicated with 1 mg of hydromorphone and 0.5 mg of atropine intramuscularly. Less than 30 ml of 1% lidocaine solution was employed for topical anesthesia. Bronchoalveolar lavage of the right middle lobe and four transbronchial biopsies of the right middle and lower lobe were performed without incident. The patient tolerated the procedure well, and post bronchoscopy, the chest film was unchanged.

Approximately 20 minutes after returning to her room, the patient was noted to develop hypotension and tachycardia and she became obtunded. An intravenous line was placed and saline solution and nalozone were administered without clear improvement. A respiratory arrest was observed, and she was promptly intubated. The vocal cords were widely patent and placement of an endotracheal tube yielded large amount of foamy pulmonary edema. She was placed on 100% oxygen with 5 cm PEEP and transferred to the Respiratory Intensive Care Unit. Corticosteroids, antihistamines and a vasopressor were started.

Arterial blood gases on 100% oxygen with 5 cm PEEP revealed a PaO2 of 58 mm Hg. A chest roentgenogram demonstrated extensive bilateral alveolar infiltrates; the frothy pulmonary edema fluid continued to be suctioned out of the endotracheal tube. Hypotension and refractory bradycardia occurred. The patient subsequently died five hours after bronchoscopy. Autopsy revealed pathology consistent with the adult respiratory distress syndrome and changes consistent with histiocytosis.

We feel our patient developed an anaphylactic, or delayed anaphylactoid, reaction to lidocaine with cardiovascular collapse and the adult respiratory distress syndrome. Although this case was similar to that of Howard and associates, the pulmonary deterioration in our patient was refractory to all forms of therapy. Since lidocaine is so frequently used in bronchoscopic procedures, this reaction should be looked for and an extensive history for lidocaine allergy should be sought before it is administered.

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Endobronchial Mucormycosis

To the Editor:

The recent case report of Schwartz and co-workers (Chest 1981; 81:653-54) of a young diabetic presenting with isolated tracheal mucormycosis and acute upper airway obstruction is noteworthy. Particularly gratifying is the successful combination of amphotericin B therapy with surgical resection, followed by primary reanastomosis. We have encountered three similar patients in our institution who presented with acute obstruction of major bronchi due to endobronchial mucormycosis. The patients are similar to those reported by Schwartz et al in that the disease was well-localized to major bronchi without distal invasion and combination therapy may have been appropriate.

Two adult patients with underlying diabetes mellitus presented with radiographic signs of central obstructing lesions. Bronchoscopy in both revealed granulation tissue and grey-white mucoid material blocking main-stem bronchi, with characteristic hypophase present on brushings. Both patients died of sudden massive hemoptysis while receiving amphotericin B, one after refusing pneumonectomy. The third patient, a five-month old child with recurrent urinary tract infection, presented with rapidly developing hyperinflation of the left lung due to a broncho-stenotic lesion in the left main-stem bronchus. Mucor was found in the pneumonectomy specimen. The child was treated with amphotericin B and has done well for three years. Examination of the pathologic specimens from these three cases revealed isolated mucormycosis in the central bronchi, locally invading through the wall into adjacent pulmonary arteries and lymph nodes. Mucor was identified only in the local sites.

A small number of additional patients with prominent disease in lobar or main-stem bronchi were identified in the literature.1-4 These cases, plus Schwartz's, may represent a specific type of pulmonary mucormycosis. The clinical features of this group include underlying diabetes mellitus or chronic renal failure, symptoms and signs suggesting an obstructing lesion in the major airway, serious local complications attributable to this lesion (distal atelectasis, fistulae into the adjoining arteries), with confinement of the pathology to one well-localized area. The illness can be insidious and the diagnosis is made at bronchoscopy. The treatment appears to be combined surgical resection plus amphotericin B.

In contrast, three patients with mucormycosis and acute leukemia presented with a fulminating disease diffusely involving multiple lobes, but difficult to diagnose because the sputum was negative, as was the bronchoscopy. Indeed, open lung biopsy or transbronchial biopsy was needed to establish diagnosis. These patients died, and postmortem examination revealed widespread angioctic disease.

Although the possibility that endotracheal/endobronchial mucormycosis is a distinct clinical entity in the spectrum of lower respiratory fungal disease is still conjectural, we do want to alert physicians encountering lesions in the central airways of diabetics to consider mucor. Furthermore, consideration must be given to the possibility of early resection along with therapy with amphotericin B in those patients with mucor in the central airways.

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