describes: "... edema of the lungs, with general asphyxia. Livid cyanosis with great dyspnea is the outstanding clinical feature... A yellow serous fluid fills the air passages in such quantities that it may drip from the mouth of the living patient when the stretcher is tilted head downwards. Death in this stage may occur at any time from the first to the fourth or fifth day. ... Secondary infection of the bronchial passages and lungs may develop, causing purulent bronchitis, bronchopneumonia, pleurisy, or even empyema and gangrene of the lung. These may be fatal in the second or third week."

The seven-page description includes accurate physical and gross pathological findings and appropriate treatment considering the medical technology of 1915. The role of secondary infection was recognized long before modern case series reported this complication. This report may represent one of the earliest detailed descriptions of ARDS.

Unfortunately, poison gas causing epidemic ARDS may not be a historic curiosity, as recent Third-World regional conflicts have seen the reemergence of poison gas as a weapon. Even in the nuclear age, we should not forget the lessons of the First World War on the dangers inherent from the proliferation of chemical weapons.

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Antiarrhythmic Effect of H-2 Antihistamines

To the Editor:

Histamine, since its isolation from ergot,1 has been recognized to possess arrhythmogenic activity. This property is considered to be mostly due to H1 receptor-mediated slowing of atrioventricular conduction and H2-mediated increase in sinus rate and ventricular automaticity.2,3

Cellular events, which parallel the above effects, include activation of adenylyl cyclase of cyclic adenosine monophosphate and the generation of an inward (Ca2+) current due to opening of slow channels.4

Clinical conditions where histamine's arrhythmogenicity has been recognized include secondary disorders of the heart such as anaphylaxis5 and drug reactions.6,7

The authors tried to determine whether ventricular arrhythmias associated with primary myocardial diseases could have been mediated by cardiac histamine release.

Myocardial mast cells were examined by light (toluidine blue stain) and electron microscopy in biopsy fragments from ten patients with complex ventricular arrhythmias (Lown 3-4B) who underwent ventricular endomyocardial biopsy (three to five biopsies per patient) for histologic evaluation.

Cardiac contractility was normal (LVEF >0.50) in four patients, moderately depressed (LVEF between 0.50 and 0.50) in four patients, and severely compromised (LVEF 0.20 and 0.25, respectively) in two. In every case, the valvular pattern, coronary network, plasma electrolytes (Na+, K+, Ca2+, Mg2+), and thyroid function test results were within normal limits. In this patient population, cardiac histamine (H) release, was also evaluated in simultaneous blood samples from the aorta (Ha) and coronary sinus (Hcs) taken at the beginning of cardiac catheterization (in order to avoid possible interference due to biopsy and angiography). Histamine level was then determined by fluoronefometric method using a Technicon-Autoanalyzer2 after blood samples were treated with perchloric acid.

Our study included evaluation of antiarrhythmic effect of H2-antihistamines, monitoring (24-h Holter) cardiac rhythm before and after 5 days of therapy with 1 g/day cimetidine.

Histologic results provided evidence of myocarditis in six patients (healing in four; healed in two) and of cardiomyopathic changes in four cases.

Myocardial mast cells were significantly increased (6±3/section) and partially degranulated at ultrastructural examination in patients with myocarditis, compared with cardiomyopathic patients (1±3/section) and normal control subjects (four patients undergoing surgery for atrial septal defect) (1±3/section).

As far as cardiac histamine is concerned, Hcs was found to be 10-30 percent higher (6±1.4 μg/ml) than Ha (6±1.2 μg/ml, confidence <0.1 μg/ml) in patients with myocarditis, while unchanged Hcs vs H values were observed in the cardiomyopathy group.

Analysis of cardiac rhythm revealed, following cimetidine treatment, reduction >80 percent of ventricularextrasystolic beats in four of six and >50 percent in two of six patients with myocarditis, and no response of ventricular extrasystoles associated with cardiomyopathy.

In conclusion, in patients with ventricular arrhythmias and histologic evidence of myocarditis our data document: 1) increased number and degranulation of myocardial mast cells; 2) rise of myocardial histamine release; and 3) susceptibility of ventricular arrhythmias to H2-antihistamines.

These results suggest that histamine might have a role in the pathogenesis of electrical instability associated with inflammatory disorders of the heart.

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Chlorinated Solvents, Welding and Pulmonary Edema

To the Editor:

Sjögren et al (Chest 1991;99:237) reported a case of toxic pulmonary edema probably caused by phosgene during tungsten inert gas welding of stainless steel in the presence of trichloroethylene. In a similar case involving methyl chloroform (MCF), we extensively investigated the phosgene theory but with a frustrating outcome, illustrating the inherent problems of retrospective exposure assessment.

A 62-year-old skilled welder who was a smoker was admitted to hospital on March 1, 1981 with fever (38.6°C) and severe respiratory distress. Initially, myocardial infarction or Legionella pneumonia was suspected, but these diagnoses were later discarded. Instead, toxic pulmonary edema with secondary fibrosis was suspected. The patient was treated in a respirator with positive end-expiratory pressure, but his condition remained unstable and he could not be disconnected from the respirator until the end of April. However, due to recurrent gastrointestinal bleeding (probably due to the massive steroid treatment in combination with metabolic stress) the patient died on May 20. The underlying cause of death based on a medico-legal autopsy was phosgene intoxication.

When this case was revealed to us after one week of hospital care, several attempts were made to find the cause. However, we were not able to interview the welder in person.

During three consecutive days ending February 27, the patient had been welding mild (carbon) steel items covered with a drawing oil containing 1.7 percent chlorine. A consumable electrode and a 4:1 mixture of argon/carbon dioxide metal inert gas was used. Lack of time forced him to use an MCF formula stabilized with dioxane for on-site degreasning between welding operations. The welding was performed in a corner of a voluminous (approx. 40,000 cu cm) workshop with fairly simple general and local ventilation. On the night between February 27 and 28 he started to feel "uneasy". At lunchtime on February 28 he was shivering and his body temperature was 40.5°C. According to his wife, he had recognized symptoms of "intoxication" (possibly alluding to metal fume fever). The situation progressed with a severe dyspnea and some instances of diarrhea; the next morning he was taken to the hospital.1

During a work site reconstruction one month after the incident, no phosgene could be detected using reagent tubes (Dräger; detection limit 0.05 ppm), not even at high MCF levels (maximum 740 ppm).1 In a separate experiment with the reagent tubes, phosgene could not be detected until the MCF concentration reached 1,000 ppm during welding.

According to Dahlberg et al, 100 ppm exposure to unstabilized MCF during the type of welding relevant to this case would yield approximately 1 ppm phosgene.4 Consequently, a second reconstruction of the incident, assisted by the National Board of Occupational Safety and Health, was undertaken one year later. No phosgene could be found by gas chromatography and electron capture detection even at a maximal MCF level of 250 ppm.5 Ozone or nitrous oxides were not detected either. Thus, we could not verify Dahlberg's findings, possibly due to insufficient sampling or analysis or other shortcomings.

Although no technical support for a toxic phosgene exposure could be found in this particular case, the overall evidence suggests that this nevertheless was an example of toxic pulmonary edema following welding in the presence of a chlorinated solvent. The combination should always be discouraged.

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How Long Do Patients with Cor Pulmonale Secondary to Pulmonary Fibrosis Survive?

To the Editor:

The mortality rate in patients with cor pulmonale secondary to chronic obstructive pulmonary disease (COPD) is well documented. The 6-months-1 year survival rate (despite intensive medical treatment) is generally very poor: approximately 30 to 35 percent.1

To our knowledge, there is very little information on the mortality rate of patients with cor pulmonale secondary to pulmonary fibrosis (PF) alone or in association with COPD. Pulmonary fibrosis is a common sequel of repeated and improperly treated lower respiratory bacterial, viral, protozoal, and mycobacterial infections during childhood and early adulthood, especially in developing

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