IATROGENIC METHEMOGLOBINEMIA FROM BENZOCAINE SPRAY IN TRAUMA

To the Editor:—Acquired methemoglobinemia is frequently reported in the literature, but rarely in association with trauma in which new-onset cyanosis might present a more confounding picture, particularly in association with traumatic injuries to the cardiopulmonary system. An understanding of the physiology and causes of methemoglobinemia will hasten its diagnosis, enable timely treatment, and thus potentially prevent needless morbidity.

A 64-year-old man presented to our trauma center after a fall of 16 feet from a roof. He suffered a head injury, open mandible fracture, and an open fracture dislocation of the left elbow. On arrival, the patient was felt to require endotracheal intubation.

During preoxygenation with 100% oxygen, peripheral saturations were 98% by finger probe. Wanting to avoid airway collapse with paralytic agents, we elected to pursue an awake oral intubation using etomidate and topical anesthetics. Benzocaine spray was thus applied to the posterior pharynx. Shortly after administration of the benzocaine pulse oximetry (SpO_2) decreased to 80% and cyanosis was visible on the lips and tongue. The cyanosis did not respond to further oxygenation, and chest auscultation remained normal. Concerned with progressive airway obstruction, we completed the oral intubation with some anxiety, but without difficulty. Despite oxygenation through a endotracheal tube with 100% oxygen, pulse oximetry remained near 80%.

An arterial blood gas was collected and revealed the following: pH 7.40, PaO_2 237 mm Hg, $PaCO_2$ 43 mm Hg, calculated SaO_2 77.0%, methemoglobin 21.0%. Hemoglobin level was 8.1 g/dL. The methemoglobinemia was recognized as the result of benzocaine and treated with methylene blue.

Methemoglobin (MHb) describes the oxidized form of the iron moiety (Fe3+) within the hemoglobin molecule. MHb is formed in the presence of an oxidizing substrate and is useless for delivering oxygen to the tissues at the cellular level. MHb is continuously formed and then reduced to the ferrous (Fe2+) hemoglobin in the body. Under normal physiology, MHb exists in concentrations of less than 1%. The cytochrome-b5-MHb reductase system is responsible for the vast majority of MHb reduction.

MHb is formed in excess through the ingestion of exogenous toxins, systemic acidosis, dietary intake of oxidizing substances, and genetic causes.[1-3]. Exposure to exogenous oxidizing toxins is the most commonly encountered cause. Some of these agents directly oxidize hemoglobin to the ferric state, whereas others act indirectly creating oxygen-free radicals that subsequently oxidize hemoglobin. There is wide variability in individual susceptibility to toxin-induced MHb, that is, not every person exposed to oxidizing agents will develop significant methemoglobinemia. Common causative medications include dapsone, phenazopyridine, nitrates, nitrites, naphthalene, and the anesthetics benzocaine, bupivacaine, and lidocaine.[1,2]

Clinical cyanosis resulting from MHb becomes apparent at a level of 1.5 g/dL. In a healthy individual, this usually corresponds to an MHb of 15% of total hemoglobin. MHb levels between 20% and 30% will often cause headache, tachycardia, and anxiety, whereas levels above 30% will frequently cause alterations in consciousness. MHb levels of greater than 70% are typically fatal. The clinical effect of methemoglobinemia can be magnified by the concurrent presence of anemia, like in our patient. As noted by Wright et al., a patient with a hemoglobin of 15 g/dL and a MHb level of 20% has a functional hemoglobin level of 12 g/dL, whereas a patient with a hemoglobin of 8 g/dL and 20% MHb has a functional hemoglobin level of only 6.4 g/dL.[1]

Because of limitations inherent to the devices, and the absorption wavelengths of the various hemoglobin forms, oximeters cannot measure the percentage of MHb in the blood and could provide inaccurate SpO_2 values when MHb is present.[4] A low pulse oximetry value, however, in the presence of cyanosis that does not respond to oxygen therapy, should suggest the presence of dysfunctional hemoglobin—most commonly MHb.[1] Arterial blood gas analysis using co-oximetry with spectroscopy will be diagnostic of MHb. The qualitative presence of methemoglobinemia can also be confirmed by simple bedside tests using potassium cyanide or oxygen.[1]

Intravenous methylene blue remains the standard treatment for symptomatic MHb. Methylene blue is metabolized to leukomethylene blue, which serves as a reducing agent for MHb. Because glucose-6-phosphate dehydrogenase (G6PD) is required to convert the oxidizing methylene blue to its reducing metabolite, persons with G6PD deficiency are at risk for complications of methylene blue therapy, including hemolysis and paradoxically increased MHb levels.[1,2] The administration of methylene blue will further interfere with accurate SpO_2 readings. Therefore, SpO_2 should be ignored following methylene blue administration.[4]

As EPs acquire increasing facility with advanced airway techniques, methemoglobinemia resulting from topical anesthetics could become more common. The rapid onset of cyanosis in a traumatically injured patient with an airway or breathing abnormality during an intubation procedure will present a more confusing clinical picture compared with more controlled settings. Familiarization with the causes and treatment of MHb will certainly help in these instances.

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STRESS REACTIONS AND ISCHEMIC CVAs AFTER THE SEPTEMBER 11, 2001 TERRORIST ATTACKS

To the Editor:—After the tragic events of September 11 in New York, many stress reactions have been reported. In particular, a study conducted by the University of California reported that after terrorist attacks, the 44% of adults who were not present at those events developed substantial symptoms of stress.[1] Furthermore, severe psychologic trauma and related stress can alter mental and physical healthness,[2,3] and the recent Caerphilly Study showed that psychologic distress has been associated with fatal ischemic strokes.[4]

We evaluate, from our register of acute cerebrovascular accidents, whether this circumstance led to an increase in ischemic cerebrovascular events.

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TABLE 1. Distribution of Data for Every Year

	1998	1999	2000	2001
No. of patients	37	33	29	36
Percent per year	6.7	8.9	7.7	9.5
Male (%)	18 (48.6)	17 (51.5)	14 (48.3)	12 (33.3)
Female (%)	19 (51.4)	16 (48.5)	15 (51.7)	24 (66.7)
Mean age (± SD)*	73 ± 10	79 ± 11	72 ± 14	79 ± 10
Median age*	75	77	75	81
Mean age/year (± SD)	76 ± 12	76 ± 12	75 ± 12	74 ± 14
Median age/year	78	78	77	77

Abbreviation: SD, standard deviation.
*Data in considered period (September 11-October 7).

Since 1998 at Fatebenefratelli Hospital, in Milan, Italy, we have registered every patient arriving at the ED because of an acute cerebrovascular event. Between 1998 and December 31, 2001, we registered 1528 patients with an ischemic stroke. From this register we tabulate every case of ischemic stroke in the period between September 11 and October 7 (the day of the first U.S. attack on Afghanistan). We compare the relevant data during the interval September 11 and October 7 since 1998. We also calculate the number of registered patients born before 1940 as subjects who have already been through a war experience. Data are analyzed by the Student *t* test and chi-squared test. A *P* value lower than .05 is considered significant.

In the considered period (September 11-October 7), the percentage of the registered cases was higher in 2001 than in other years (Table 1). There were more females with an acute cerebrovascular accident and mean and median age were higher in 2001. In the 2001 cohort, there was a higher percentage of subjects born before 1940 in the considered period than the annual percentage for 2001. This difference was higher in 2001 than in the other years (Table 2). Only in 2001, the median age of the considered period was higher than median age of cases registered in the year. None of the data were statistically significant.

The relationship between stressful life events and onset of disease is well documented.[2,3,5] The brain mediates and integrates all the cognitive activities, the emotional experiences, and finally the behaviours.[6] Devries et al. demonstrated that stressful experience significantly compromises an endogenous molecular mechanism of neuroprotection in an injured brain.[2] In this way, stress could play a role as cofactor in increasing the stroke risk. Our data show that in the period between September 11 and October 7, the percentage of stroke was higher than during the same period in other years. As a result of the chronobiologic rhythm, the onset of ischemic stroke is more common in September, in fact, an increase in ischemic events in the autumnal months has been already reported,[7] but the percentage of events in September 2001 was higher than in other years in any case. In addition, mean age in the considered period was higher and there were more patients born before 1940.

We believe that those who have already experienced a war could be more susceptible to events that recall these experiences.

Our data represent a relatively limited number of a local register and thus do not constitute an epidemiologic study. However, they could suggest that even in our reality, which seems far from New York, such a dramatic event can provoke psychologic stress that can contribute to the precipitation of a cerebrovascular event.

TABLE 2. Percentage of Subjects Born Before 1940

	1998	1999	2000	2001
Annual percentage	92.1	90.7	90.6	85.4
Period * percentage	89.2	90.9	86.2	91.7
Δ percentage (period *— year)	−2.9	+0.2	−4.4	+6.3

*Period = September 11–October 7.

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SUBARACHNOID HEMORRHAGE PRESENTING AS CHEST PAIN

To the Editor:—Patients presenting with chest pain continue to be a difficult challenge to the emergency doctors.[1] Cardiovascular causes must be ruled out first because the history cannot distinguish between coronary artery disease and other causes of chest pain. The percentage of patients who present at the ED with acute chest pain and are admitted to the hospital is growing,[2] and costs increase as well. At the same time, discharging patients with myocardial infarction because of a missed diagnosis can have dire consequences.[3] However, chest pain sometimes could be a dilemma between different life-threatening cardiovascular diseases,[4] be a common symptom of noncardiac diseases,[5] or masquerade unfrequent neurologic diseases.[6]

We describe a patient with spinal subarachnoid hematoma whose clinical presentation with sudden acute chest pain without any neurologic sign at onset prompted the initial diagnostic suspicion of an acute vascular emergency.

A 74-year-old man presented to the ED with the sudden, abrupt onset of acute pain, described as very severe and tearing, associated with diaphoresis, paleness, and hypotension. The pain was felt in the center of the chest and radiated to the back. In his medical history, there was only mild hypertension. On admission, the electrocardiogram excluded acute myocardial ischemia, the blood chemistry panel did not show elevations of cardiac enzymes, whereas a chest radiograph revealed a significant aortic root dilatation. An aortic dissection was therefore suspected, but a computed tomography scan with contrast excluded this diagnosis.

Physical and neurologic examinations resulted in normal findings. The pain propagated distally down within a few hours. The day after, he experienced paresthesias with a sock distribution in the left lower limb. Neurologic examination revealed only a Babinski sign on the left. Panspinal magnetic resonance image (MRI) showed the presence

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