Low Bispectral Index Values in Awake Volunteers Receiving a Combination of Propofol and Midazolam

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THE Bispectral Index (BIS) is increasingly used to monitor the level of (un)consciousness during surgical anesthesia and conscious sedation.1 Generally, an intraoperative BIS of 40–60 is considered sufficient to maintain adequate hypnosis for surgery.2,3 Recently, a new version of the BIS® monitor has been introduced: the BIS-XP® (Aspect Medical Systems, Newton, MA). The BIS-XP® is said to exhibit improved resistance to artifacts from electrocautery devices and to detect and filter interference from electromyographic activity and other conditions commonly encountered during monitored anesthesia care sedation that may cause artifacts.#

We report three cases in which volunteers receiving combinations of propofol and midazolam as part of a pharmacokinetic–dynamic interaction study remained responsive to verbal command, although the BIS-XP® values were at, or just above, 40. A Web enhancement is provided with an MPEG1 digital video file displaying the responsiveness of one of the volunteers in relation to the BIS-XP® values.

Case Reports

With the approval of the Leiden University Medical Center ethics committee and informed consent from the subjects, a study on the pharmacokinetic–dynamic interaction between propofol and midazolam at varying concentration combinations was performed. For each subject, the electroencephalogram was recorded continuously using the BIS® Quatro sensor (Aspect Medical Systems), placed as prescribed on the left side of the skull and connected to the BIS-XP®. For all subjects, the impedance was low (on the order of 2–4 kΩ), and the signal quality index was high (0–100; well above 50) at the times of sedation assessments. The processed electroencephalogram variables were stored on a disk for offline analysis. In addition, the electrocardiogram, transcutaneous arterial oxygen saturation, end-tidal carbon dioxide concentration, respiratory rate, and arterial blood pressure were monitored continuously throughout the study.

The volunteers breathed spontaneously through a mask with an inspiratory oxygen fraction of 40%. All three volunteers maintained adequate spontaneous respiration and were hemodynamically stable throughout the study. After a 10-min baseline recording period, a target-controlled infusion of propofol was started using the Diprifusor® (AstraZeneca, Macclesfield, United Kingdom) with maintenance of a constant target propofol concentration for 455 min. Fifteen minutes after the start of the target-controlled infusion of propofol, midazolam was given as a rapid infusion for 1 min, followed by a slower continuous infusion for 59 min. At regular intervals, when blood samples were taken from the arterial line for analysis of blood midazolam and propofol concentrations, the level of sedation was assessed by verbal command and/or mild prodding.

Case 1

The first subject was a 27-yr-old man who weighed 85 kg and was 185 cm tall. The target propofol concentration for this subject was 0.6 μg/ml, and the initial and secondary midazolam infusion rates were 0.05 mg · kg⁻¹ · min⁻¹ and 0.05 mg · kg⁻¹ · h⁻¹, respectively (total midazolam dose in 60 min, 8.5 mg). For the awake volunteer, the BIS exceeded 95 in the absence of any medication. Then, with the target propofol concentration of 0.6 μg/ml, the BIS was maintained at 97 after blood–effect site equilibration (fig. 1). Thereafter, during the first 40 min after the start of the midazolam administration, the BIS decreased to ∼60 during unstimulated periods and increased to 98 after verbal stimulation. Forty minutes after the start of the midazolam infusion, the BIS gradually decreased further to 40 at the end of the midazolam infusion. Unexpectedly, throughout the study period the volunteer remained responsive to verbal commands and/or mild prodding at the shoulder to a degree equivalent to an Observer’s Assessment of Alertness/Sedation score between 2 and 4, even at BIS levels of 40–45.

Case 2

The second subject was a 25-yr-old man who weighed 100 kg and was 195 cm tall. The target propofol concentration for this subject was also 0.6 μg/ml, and the initial and secondary midazolam infusion rates were 0.05 mg · kg⁻¹ · min⁻¹ and 0.05 mg · kg⁻¹ · h⁻¹, respectively (total midazolam dose in 60 min, 10 mg). For the awake volunteer, the BIS exceeded 95 in the absence of any medication. Then, with propofol at a target concentration of 0.6 μg/ml, the BIS was maintained at 97 after blood–effect site equilibration (fig. 2). Thereafter, within 5 min after the start of the midazolam administration, the BIS decreased to 67 and gradually decreased further to as low as 40 at the end of, and just after termination of, the midazolam infusion. Again, throughout the study period the volunteer remained responsive to verbal commands and/or mild prodding at the shoulder to a degree equivalent to an...
midazolam infusion. For the awake volunteer, the average BIS was 96 in the absence of any medication. With a target-controlled infusion of propofol of 1 \( \mu \text{g}/\text{ml} \), the BIS decreased to mean level of 92 after blood–effect site equilibration (fig. 3). Then, within 3 min after the start of midazolam administration, the BIS decreased to values as low as 44. During midazolam administration, the BIS varied between 40 and 60. Again, throughout the study period the volunteer remained sensitive to verbal commands and/or mild prodding to a degree equivalent to an Observer’s Assessment of Alertness/Sedation score between 2 and 4, even with BIS levels of 40–45. The videotape, displayed as a Web enhancement, furthermore provides data on the responsiveness of this volunteer at low BIS levels. Additional information regarding this case is available on the ANESTHESIOLOGY Web site at http://www.anesthesiology.org.

**Discussion**

We describe three cases in which the BIS-XP\textsuperscript{®} provided BIS values of 40–50 for volunteers who were responsive to verbal commands while receiving a combination of propofol and midazolam. In our hospital, we tend to administer propofol infusion regimens during propofol–opioid anesthesia on the basis of the BIS level. Based on the current literature, we advise our residents to maintain the BIS level between 40 and 60 intraoperatively.\textsuperscript{2} Most of our patients receive midazolam for premedication. The observations described herein therefore raise various questions that are relevant to our daily clinical practice.

Two issues must be considered when interpreting our observations in relation to data from the current literature. First, most data in the literature were determined using earlier versions of the BIS\textsuperscript{®} monitor.\textsuperscript{4} Second, few data exist from careful evaluation of the effect of combinations of agents on the BIS.

Regarding the first issue, it may well be that the BIS-XP\textsuperscript{®} provides lower BIS values than previous versions at sim-
Transitory Hypnotic Levels in Similar Subjects. As stated earlier, the BIS-XP® is claimed to be less sensitive to artifacts of the electromyographic activity than earlier versions of the BIS® monitor. Previously, it was reported that electromyographic activity falsely elevates the BIS.® Introducing a version that is less sensitive to this may thus result in lower BIS levels in the absence of full muscle relaxation (as occurs in most patients).

Regarding the second issue, we note that the electroencephalographic activation induced by both propofol and midazolam has been difficult to interpret and model in the past.® It may well be that the particular combination of propofol and midazolam at these low concentrations is not part of the BIS-behavioral database on which the BIS calculation is based. As a result, the electroencephalographic pattern induced by this combination may well be misinterpreted by the BIS® monitor as an electroencephalographic pattern associated with a patient experiencing a surgical hypnotic sedation level instead of actually being responsive to verbal commands. However, to our knowledge, no controlled studies have been done to examine hypnotic drug interactions and their effect on BIS, especially not using the BIS-XP®.

In conclusion, we report on the responsiveness of three volunteers with BIS-XP® values of 40–50 while receiving a combination of propofol and midazolam. The case reports draw attention to the relationship between the BIS and the responsiveness of patients as derived by the BIS-XP® in the presence of a combination of two hypnotic agents. The BIS user should be aware that the BIS is a measure of drug effect, not an independent measure of brain function. Consequently, the clinical anesthesiologist has no guarantee that a particular BIS will relate to the desired effect when a particular drug, or combination of drugs, is not part of the data file used to train the algorithm of the BIS calculation. As such, the case reports stress the need for further investigation of both the BIS-XP® itself and the effect of combinations of hypnotic agents on the BIS-XP®. Furthermore, the case reports stress the need for careful interpretation by the anesthesiologist of the BIS-XP® values in the clinical setting as long as the scientific basis for the clinical application of the BIS-XP® is not yet completely clear.

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Transient Cardiovascular Toxicity with Unintentional Intravascular Injection of 3% 2-Chloroprocaine in a 2-month-old Infant

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The caudal approach to epidural anesthesia is a safe and effective analgesic technique for neonates and infants. However, amide local anesthetics may cause serious cardiovascular complications such as arrhythmias and life-threatening depression of myocardial contractility.1–3 We describe transient cardiovascular toxicity in a 2-month-old infant after unintentional intravascular injection of 3% 2-chloroprocaine through an epidural catheter. To our knowledge, this is the first report of cardiovascular toxicity after accidental intravenous injection of an ester local anesthetic.

Case Report

A 4-kg 2-month-old girl with biliary atresia presented for a liver biopsy and Kasai procedure. Continuous epidural analgesia via the caudal approach was planned to supplement intraoperative anesthesia and provide postoperative pain relief. After induction of general anesthesia and tracheal intubation, an 18-gauge angiocatheter inserted into the epidural space via the sacrococcygeal ligament was used to facilitate insertion of an epidural catheter equipped with a stylette (Portex, Keene, NH) to a presumed T7 level. Aspiration of the catheter was performed and failed to produce cerebrospinal fluid or blood. Test
dosing was not performed. Four milliliters of 3% 2-chloroprocaine without epinephrine was administered over ~ 30 s. Immediately thereafter, the patient developed a wide complex bradycardia without evidence of atrial activity at a heart rate of 30 beats/min. While preparations were being made to begin chest compressions and administer atropine, the event terminated spontaneously. The duration of the event was ~ 30 s. Oxyhemoglobin desaturation and loss of the capnogram did not occur, but hypotension cannot be excluded because the noninvasive blood pressure cuff did not cycle. However, the first blood pressure reading determined immediately after the event was 70/36 mmHg. Because the event appeared to be self-limiting, a decision was made to proceed with the surgical procedure. The catheter was left in place for the duration of the surgery but was not used. Aspiration of the catheter was again negative. Fentanyl was given intravenously for intraoperative analgesia. After the surgical procedure, fluoroscopy with concomitant injection of 0.5 ml metrizamide (Omnipaque 180; Amersham Health, Princeton, NJ) through the epidural catheter revealed an apparent venogram of the epidural vessels (fig. 1). Aspiration of the catheter at this time was positive for blood, and the catheter was then removed. Postoperatively, the infant was well without evidence of neurologic or cardiovascular sequelae.

**Discussion**

In anesthetized children with epidural anesthesia, unintentional intravascular administration of the local anesthetic occurs in less than 1% of cases. All previously reported cases of this occurrence described the cardiac effects of intravenously administered amide local anesthetics that contained epinephrine. These effects primarily include tachyarrhythmias and cardiovascular collapse. These findings differ from those of the current case, in which a wide complex bradycardia was observed with chloroprocaine. It is unknown whether there are inherent differences in the type of cardiac toxicity between amide and ester local anesthetics, or if the absence of epinephrine resulted in a different type of observed arrhythmia.

To our knowledge, the current case represents the first report of cardiac toxicity secondary to accidental intravenous injection of 2-chloroprocaine during regional anesthesia. The minimal toxicity associated with intravenous administration of chloroprocaine is presumed to be secondary to its rapid metabolism by nonspecific plasma cholinesterases, with a resulting half-life ranging from only 1–4.5 min. Despite the absence of reported complications, the package insert for chloroprocaine describes “hypotension, bradycardia, ventricular arrhythmias, and possibly cardiac arrest . . . with unintended intravascular injection.” Mild cardiac effects (e.g., tachycardia and junctional rhythm) have been described in the setting of intravenous regional anesthesia in adults.

To detect intravascular administration of local anesthesia, test dosing has been used and advocated for adults, but this strategy is not routinely advocated for the pediatric population. Desparmet et al. observed an approximate 30% incidence of false-negative results of test dosing for children using epinephrine (0.5 μg/kg) during halothane anesthesia. Pretreatment with atropine improved the sensitivity of test dosing for this population to 94%, but false-negative results still occurred when the heart rate criterion of greater than 20 beats/min was used. In a prospective survey in 1991 by Veyckemans et al., none of the 1,100 single-dose caudal blocks were tested before injection. However, recent studies of children anesthetized with isoflurane and sevoflurane indicated an increased sensitivity with epinephrine test dosing. Using an increase in heart rate of greater than 10 beats/min, Tanaka et al. demonstrated 100% sensitivity for sevoflurane- and nitrous oxide-anesthetized children with and without atropine pretreatment. If the positive test dose criterion was increased to greater than 20 beats/min, there was 53% and 67% sensitivity with and without atropine pretreatment, respectively. If test dosing had been performed for our patient, intravenous administration of local anesthetic may have been detected. On the other hand, if we had administered the initial dose of chloroprocaine (1 ml/kg) more slowly, we may not have observed any adverse effects other than block failure. Nevertheless, given the potential benefit and the lack of harm involved with test dosing, this should have been performed for our patient and should be routine during use of all pediatric regional anesthetics.

The use of the epidural catheter equipped with a
stylet is controversial. These catheters have been advocated to facilitate epidural placement, especially from the caudal approach. It is possible that the increased rigidity of the catheter may have played a role in the unintentional intravascular placement in our patient.

In summary, we report a case of cardiovascular toxicity secondary to unintentional intravascular administration of 2-chloroprocaine during epidural anesthesia. Although this case seems to highlight the safety of 2-chloroprocaine, it also serves to remind us of its potential hazards. Test dosing is recommended to rule out most intravascular placements of epidural catheters, and initial administration of the local anesthetic should be performed slowly and incrementally.

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Anesthesia Management of Orthotopic Liver Transplantation in a Patient with Mustard Repair of Transposition of Great Arteries and Superior Vena Caval Obstruction

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AS an increasing number of patients with surgically repaired congenital heart disease survive into adulthood, more of these patients may require complex, lifesaving surgical procedures. We report our experience with providing anesthesia for liver transplantation in a patient with surgically corrected D-transposition of the great arteries.

Case Report

Our patient was born with D-transposition of the great arteries and underwent Mustard repair in infancy. Transfusion resulted in hepatitis B and subsequently progressive liver failure. By 29 yr of age, he was experiencing fatigue, encephalopathy, and refractory ascites and was referred to our center for liver transplantation. Aggressive diuretic therapy was limited by hyponatremia. His exercise tolerance was limited by fatigue after the climbing of one flight of stairs. Evaluation for possible liver transplantation included a cardiology consultation. Radionuclide angiography demonstrated normal biventricular function with a systemic ejection fraction of 51%. An echocardiogram was reported to show normal biventricular size and mild tricuspid regurgitation. The atrial baffle could not be clearly visualized. Cardiac catheterization was not recommended. After discussion of risks and alternatives, the patient was listed for transplantation (Child-Pugh score B). He returned to our medical center when an appropriate matching liver became available.

The patient had an allergy to iodinated contrast. Medications included lactulose, spironolactone, furosemide, carbamazepine, and levofloxacin. His weight was 66.7 kg, brachial blood pressure was 100/45 mmHg, and pulse was 80 beats per min. A grade 3/6 systolic murmur was noted over the left chest, and rhonchi were noted in both lung bases. Radial pulses were full. Femoral sites were scarred, and femoral pulses were not palpable. Serum sodium was 122 mEq/l, potassium 5.2 mEq/l, and hematocrit 26%.

General anesthesia was induced with fentanyl, midazolam, and thiopental. Tracheal intubation was facilitated by rocuronium. Anesthesia was maintained with lorazepam, fentanyl, and low concentrations of isoflurane in oxygen/air. Vascular access included bilateral radial arterial catheters (Radial Artery Catheterization Set, REF product No. RA-04020, Arrow International, Reading, PA) and venous cannulas (MAC two-lumen venous access kit, product No. AK-11142 9 fr; Arrow International) in the right internal jugular and right subclavian veins. Attempts at placement of a pulmonary artery catheter were unsuccessful, but a single-lumen infusion catheter, REF product No. SC14701, Arrow International) was advanced via the internal jugular vein and displayed a waveform with a, v, and c waves consistent with central venous pressure. Transesophageal echocardiography (TEE) demonstrated right and left atrial enlargement with an interatrial baffle, moderate mitral and tricuspid regurgitation, and biventricular systolic function (fig. 1). The right ventricle was hypertrophied. Saline contrast echocardiography confirmed the transit of systemic venous blood from the caval system to the left atrium, ventricle, and, ultimately, the pulmonary artery via the atrial baffle (fig. 2).

Removal of the native liver required 6 h and was performed by use of the piggyback technique. Oxygen saturation remained between 98% and 100% throughout the operation, with PaCO2 between 86 and

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Tris(hydroxymethyl)aminomethane (Abbott Laboratories, Abbott Park, IL) and sodium bicarbonate to prevent rapid changes in serum sodium and osmolarity. Furosemide and insulin were given to reduce serum potassium in anticipation of graft reperfusion. Serum potassium declined from 5.2 mEq/l to 3.8 mEq/l immediately before reperfusion. Thirty seconds after reperfusion, it increased to 5.3 mEq/l. Reperfusion of the donor liver was accompanied by a brief episode of sinus bradycardia that responded to a small bolus of epinephrine. Hepatic arterial and duct-to-duct biliary reconstruction proceeded uneventfully. Four units of erythrocytes, 2 units of plasma, and 6 units of platelets were infused, resulting in a final hematocrit of 51%. Blood component therapy\(^2\) was guided by serial thromboelastography (Hemoscope Corporation, Skokie, IL). At the end of surgery, the TEE probe was removed. Norepinephrine was discontinued in the early postoperative period, and the trachea was extubated on the second postoperative day. Lack of TEE made assessment of the adequacy of ventricular filling difficult in the intensive care unit. A pulmonary artery catheter was placed under fluoroscopic guidance \(\text{via}\) the right femoral vein. Mean pressure in the superior vena cava was 28 mmHg; the atrial pressure was 25 mmHg at end expiration and 0–5 mmHg on inspiration. Pulmonary artery systolic pressure was 45–50 mmHg. Computer tomography was obtained to evaluate the biliary system. This demonstrated that the superior vena cava was interrupted. Collateral flow through the ayzygous system carried blood to the atrial baffle and anatomic left ventricle. The patient subsequently returned to the operating room for a revision of the biliary anastomosis and was eventually discharged to home in stable condition.

**Discussion**

This patient with complex congenital heart disease developed cirrhosis secondary to transfusion-related viral hepatitis. Liver transplantation is a potentially lifesaving operation for patients with end-stage liver disease, but it is a complex procedure, made more so by residual cardiovascular abnormalities.

In patients with transposition of the great arteries, the right ventricle supplies blood to the aorta. The left ventricle supplies blood to the pulmonary artery. The systemic and pulmonary circuits coexist in parallel rather than intersecting pathways. Survival after delivery depends on intracardiac mixing of blood through atrial or ventricular septal defects or a patent ductus arteriosus. A variety of surgical techniques have been developed for the correction of this condition, all of which cross the pulmonary and systemic circulation at the level of the atria, the ventricles, or the great arteries themselves. The Mustard and Senning operations\(^3\) are atrial repairs. The Rastelli procedure\(^4\) is a ventricular repair using a ventricular septal defect and a valve conduit from the right ventricle to the aorta. The arterial switch procedure reimplants the aorta and pulmonary artery. Atrial repairs such as the Mustard operation retain the right ventricle as the systemic ventricle. With the Mustard operation,\(^5\) the atrial septum is excised, creating a common atrium. An atrial baffle is created with pericardium. The baffle isolates blood returning from the venae cavae and redirects it through the atrium and into the left ventricle. Oxygenated blood returning from the pulmonary veins passes into the atrium on the other side of the baffle. The oxygenated blood then passes through the tricuspid valve into the right ventricle and from there into the aorta. The systemic circulation remains dependent on the right

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**Fig. 1.** Transesophageal echocardiographic image showing a portion of the atrial baffle. LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

**Fig. 2.** Transesophageal echocardiographic image showing spontaneous saline contrast in atrium and left ventricle (with illustrated chamber outline superimposed). LV = left ventricle; RA = right atrium; RV = right ventricle.
ventricle. Survival into adulthood is common after a successful repair, but patients continue to be at risk for premature death, heart failure, and dysrythmias. Conduction defects and attenuated augmentation of cardiac output with exercise because of flow restriction through the atrial baffle are not uncommon in these patients. We are unaware of any previous reports of liver transplantation in patients with this condition.

Common problems encountered during liver transplantation include massive blood loss, vasodilatation, progressive acidosis, and coagulopathy. Because our patient’s femoral pulses were not palpable, a radial artery catheter was placed for blood pressure monitoring; a second radial arterial catheter was placed to permit frequent arterial sampling. Venous access for rapid infusion was established, but fluid management was complicated by the limitations of monitoring. It was anticipated that measurement of central venous pressure would reflect preload. The anesthesia team anticipated that navigating a pulmonary artery catheter through the atrial baffle would be difficult, although not necessarily impossible; pacemaker placement via this route has been performed in other patients. Attempts at placement of a pulmonary artery catheter through the jugular and subclavian canulae failed. Fluoroscopy was not used but would not have resulted in successful placement. Obstruction at the level of the superior vena cava, a recognized complication of the Mustard operation, was present but was not adequately appreciated preoperatively in our patient. The report of his cardiac catheterization, which had been performed 20 yr previously, was not available at the time of the operation. Subsequent computed tomography clarified the residual anatomy and confirmed that the superior vena cava was interrupted. Preoperative placement of a pulmonary artery catheter through the inferior vena cava was not attempted because liver transplantation requires surgical manipulation of both the hepatic vein and the inferior vena cava. A catheter in this location would have been at risk for surgical entrapment during the operation. A pulmonary artery catheter placed from the femoral route postoperatively demonstrated that the mean superior vena cava pressure exceeded atrial pressure.

Obstruction of the superior vena cava complicated the anesthetic management, not only by preventing the intraoperative use of a pulmonary artery catheter but also by making the central venous pressure unreliable, and it limited the options for venous return during removal of the native liver. In the absence of reliable conventional monitors of preload, observation of right and left ventricular filling by TEE was especially helpful. Examination by TEE before attempts at pulmonary artery catheter placement might have been useful in this case. Other commercially available methods to measure cardiac output, such as bioimpedance and Doppler interrogation of the aorta from the esophagus, may also be considered.

During liver transplantation, venovenous bypass is sometimes used to decompress the splanchic and systemic venous systems during native liver removal and graft insertion. Drainage cannulae are placed in the portal vein and inferior vena cava, and a pump returns blood to the superior vena cava through a cannula in an axillary or jugular vein. This preserves venous return during complete clamping of the inferior vena cava. Alternatively, the piggyback technique permits continuous flow through the inferior vena cava, which is only partially clamped. Venovenous bypass can be cumbersome, requires additional cannulations, and is associated with complications such as air embolism and injury to the brachial plexus and vessels. Had it been used in our patient, venous return might have exceeded the capacity of the axillary collaterals that, in our patient, carried blood from the superior vena cava to the atrium. Fortuitously, blood loss was relatively small. Both the subclavian and jugular venous lines led to the superior vena cava and dilated axillary collaterals. Rapid replacement of lost blood may have been limited by the capacity of this system.

We administered methylene blue, norepinephrine, and vasopressin to help maintain systemic vascular resistance and contractility. Methylene blue may reduce hypotension and inotropic requirements during liver transplantation. These agents, used in combination, maintained systemic arterial blood pressure without significant tachycardia during periods of relative hypovolemia.

Candidacy for noncardiac organ transplantation need not be denied to well-compensated patients who have undergone repair of congenital heart defects. Careful preoperative evaluation is especially important in these patients. TEE can be extremely helpful intraoperatively.

References
WE report an oxygen supply tank failure at our institution that occurred during the morning of a busy operating room schedule when medical center oxygen use was maximal.

Case Report

The bulk oxygen supply at our facility consists of three cryogenic oxygen storage tanks: a primary tank, A; a secondary tank, B; and a reserve tank, C (fig. 1). Tanks A and B are physically situated next to each other. The reserve tank (C) is located approximately 1 block (approximately 305 m) away and normally serves as the primary oxygen source for our hospital's second large inpatient bed facility. Valves, piping, and regulators between the primary tank and primary reserve were installed in compliance with the National Fire Protection Association's guidelines and commonly accepted installation practices.1,2 The tank failure and resulting major liquid oxygen spill were caused by the separation of a brazed joint between the stainless steel primary tank A and a brass pipe fitting. The resulting sudden release of approximately 8,000 gallons of liquid oxygen from tank A precluded the initial use of the adjacent secondary tank B. Tank B was inaccessible because of massive ice and vapor cloud formation, which initially made it impossible to determine whether the tank was stable and functional (fig. 2). As the pressure in the primary tank rapidly decreased, an automatic switch-over valve opened tank B to provide oxygen to our medical center. With uncertainty regarding the integrity of the reserve system (because of inability to immediately assess the secondary tank), an adjacent valve was immediately closed to isolate both tanks until the damage could be assessed.

Our hospital engineers reacted almost immediately, closing the valves to isolate both the primary supply within 1 h. At the same time, valves were opened to bring the reserve tank C online as the alternate supply source. Fire and police officials were notified of the situation, and personnel in critical areas (intensive care units, operating rooms, and chiefs-of-staff) also were simultaneously notified. Reserve oxygen E-cylinders were collected and distributed to critical areas within the medical center. Our bulk oxygen supplier was notified, and a supply tanker was dispatched to provide additional liquid oxygen. Fortunately, we never experienced total loss of pipeline supply pressure. However, in the operating rooms, the pipeline pressure was noted to be decreased from 55 to 48 psi gauge. This decreased pressure was thought to be most likely a result of relatively high friction losses as the oxygen was routed through regulators near the distant reserve tank C to the main hospital and operating room facility. Forty-five minutes after the failure, the secondary tank B was determined to be functional and was put back into service. The valves to the reserve tank C were then closed.

The failure of our primary oxygen supply tank could have caused complete oxygen pipeline system failure if the secondary tank had been damaged concurrently. The redundancy in our system with the remote reserve tank provided a continuous supply during the event. Very soon after the failure occurred, the low liquid oxygen volume alarms were activated at the engineering control center. Because of the design of our alarm system, however, these alarms alone would not have given enough advance warning to prevent loss of pipeline pressure. The inability of our alarm system to provide timely warning in this situation was due to the rapid rate at which the liquid oxygen was lost. These alarms were set to communicate when the level fell below a preset threshold value and were not designed to give engineers ongoing, quantitative information on the level of liquid oxygen within the tank. Typical alarm systems do not provide this quantitative information.2,3 Furthermore, if the main and reserve tanks had not been situated in a location that was readily visible, then engineers might have believed that the low oxygen level alarm was simply a result of normal use. The rapid response time to this system failure at our facility was at least partially because of easy visibility of the tanks and the quick reaction of our engineers, who were at the bulk oxygen storage facility at the time of the failure.

The failure of the liquid oxygen pipeline that caused this event was determined to be due to both electrolysis of the stainless steel-to-brass joint and thermal expansion damage. The primary tank A and piping were 12 yr old at the time of the event. After the event, the joint was replaced with a stainless steel-to-stainless steel welded joint. The repaired primary tank was subsequently tested and put back in service as the primary supply within 10 h.

Discussion

Our review of the literature uncovered instances of bulk oxygen system failures secondary to events such as pipeline crossover, filling with the wrong gas, faulty installation, modification of the pin index or diameter index safety systems, contamination, and other factors.4,5 We were unable to find a similar reported case of oxygen supply failure secondary to a scenario such as described above.

Cataclysmic bulk liquid oxygen supply failure is problematic not only for anesthesiologists but also for the entire medical center. At the time of this failure, oxygen use in our medical center was at peak. All 30 operating rooms (24 noncardiac, 6 cardiac) were in use. Several patients were in the postanesthesia care unit, and nine separate intensive care units were filled to capacity. The emergency department was busy, and many patients were receiving oxygen by facemask or nasal cannula in their hospital rooms throughout the medical center. Complete loss of oxygen supply could have been disastrous.
In the operating room suite, several actions were taken as soon as a problem was identified. First, all anesthesia care providers were informed about the possibility of a bulk oxygen system failure. Additional E-cylinders were delivered to all anesthetizing locations. Low-flow anesthesia techniques were used where possible. Attempts were made to keep oxygen flowmeter flow below 1,000 ml/min. Mechanical ventilation was discontinued, and manual bag ventilation was instituted. Finally, all elective procedures were postponed until the problem was isolated.

When using gas-driven anesthesia ventilators such as the Datex-Ohmeda models 7800, 7810, 7100, or 7900 (Madison, WI), the drive gas used to compress the bellows is normally 100% oxygen, and the drive gas volume consumed equals the minute ventilation.6,7 Thus, in adult patients with a minute ventilation of 8–10 l, an equal quantity of drive gas can be conserved per minute by discontinuing mechanical ventilation and switching to manual ventilation. Interestingly, some newer ventilators may be switched between using either oxygen or air as their drive gas, and doing so would also conserve oxygen supplies. When one compares oxygen consumption in a low-flowmeter setting with manual ventilation and an intermediate-flowmeter setting with mechanical ventilation, the difference is dramatic. With fresh gas flow of 500 ml/min in conjunction with manual ventilation, a total of 500 ml/min oxygen is consumed. In contrast, when an intermediate-oxygen flowmeter setting of 2 l/min is used in conjunction with mechanical ventilation, providing 10 l/min of minute ventilation, the total oxygen utilization is 12,000 ml/min. In this scenario, manual ventilation with low oxygen flow would consume only 4.2% of the amount of oxygen that would be used during mechanical ventilation with intermediate flow. For anesthesia workstations that use a push drive (piston type) ventilator rather than a gas-driven one (e.g., Narkomed 6000, North American Dräger, Telford, PA), oxygen use would be comparable to the manual ventilation scenario described above.

The failure of the oxygen supply system at our facility was caused by multiple factors. As is the case in many institutions, the main and reserve bulk oxygen storage tanks of our medical center are owned by the bulk oxygen supplier. The plumbing to the tanks and the rest of the oxygen supply system is owned and maintained by our medical center. This connection between the vendor-owned tank and the hospital-owned pipeline was the point of failure in our system. Maintenance and upkeep of all components should be coordinated and documented between all parties involved.2

The problem resulting from the close proximity of the primary and secondary tanks would have been much more difficult to manage if we did not have a reserve tank. In our case, if there had been either a spatial or physical barrier between the primary and secondary tanks, engineers could have more easily and quickly assessed the status of the secondary tank. As it was, the liquid oxygen spill produced massive ice and vapor on and around the secondary tank, precluding inspection of its integrity. Usually, hospitals have only two liquid oxygen sources. If these two are somehow isolated from each other, a problem such as the one we encountered could be avoided. Separation of the primary tank and reserve tanks could be achieved simply by construction of a noncombustible barrier between the tanks and creation of a sloping surface away from the tanks and barrier wall for runoff. In addition, consideration should be given to providing enough room for runoff of the amount of liquid oxygen stored in the tanks.

Continuous measurement of the quantity of oxygen in the cryogenic tanks may provide an earlier warning of a massive system failure. This alarm monitor should commu-
nicate not only when the volume falls below a threshold level but also when the rate of volume loss is excessive.

Conclusion

We were fortunate that during this event, our cryogenic oxygen system failure was noted very soon after it occurred and that it was limited to only one tank. No adverse patient outcome or even significant delay in the elective surgery schedule resulted. Predetermined oxygen system failure protocols were immediately implemented. Careful planning and thoughtful consideration to the design of the bulk oxygen supply system most likely prevented a catastrophic failure of the oxygen supply system at our institution. Tying together bulk oxygen systems in large facilities that use more than one such system adds redundancy to the system that can allow continued use even when a major system failure has occurred.

To summarize, based on this case and review of the literature, we have several specific observations regarding possible bulk liquid oxygen supply system failure. (1) The events outlined in this case reinforce the importance of having a thoroughly prepared hospital-wide disaster plan available. It is critical to be able to identify key individuals in a timely manner to deal with the various responsibilities required to avoid making an already bad situation worse. (2) Anesthesia care providers who serve in leadership roles in the operating room are responsible for the safety of all patients within the surgical facility. As such, they should have a comprehensive understanding of their own hospital’s oxygen delivery system and associated disaster plans. Anesthesia care providers should know the locations of all major bulk oxygen supply components such as the tanks and associated shutoff valves. (3) Anesthesiology leaders must be involved in any new construction or remodeling planning. (4) Medical center leadership might consider separating the location of primary and secondary oxygen supply tanks or building a barrier between them to isolate one from the other in the event of a tank failure. (4) The National Fire Protection Association’s Standard for Bulk Oxygen Systems at Consumer Sites (NFPA-50) addresses both “Location of Bulk Oxygen Systems” (2.1-

Fig. 2. Extent of the liquid oxygen leak. The main oxygen storage tank A (right) and the primary reserve tank B (left) are shown. Eight thousand gallons of liquid oxygen escaped from tank A, making it temporarily impossible for the engineers to assess either the primary or secondary reserve tank. At the time of the leak, medical center oxygen use was at a maximum, with approximately 30 operating rooms in use. At the time of this photograph, the temperature was 56°F and the relative humidity was 100%.

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2.1.5) and “Distances Between Bulk Oxygen Systems and Exposures” (2.2–2.2.14). However, it does not specifically address the placement of an isolation barrier between bulk storage tanks, which could have been helpful in our case. Furthermore, in addition to primary and secondary tanks, large medical centers with high oxygen use should consider having an additional reserve tank in the event that the primary and secondary tanks are simultaneously unusable, as in our case. (6) Finally, if catastrophic bulk oxygen supply failure does occur, oxygen consumption conservation techniques as described above should be instituted. Adequate oxygen cylinder supplies must be on-site, and a disaster plan that includes obtaining an additional supply of cylinders must be readily available in the event that the bulk oxygen supply system cannot be rapidly restored.

References