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CRITICAL CARE ALERT™

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Ketoconazole Practice Guideline Reduces ARDS Incidence

ABSTRACT & COMMENTARY

The purpose of this study was twofold: first, to increase the use of ketoconazole (KZ) prophylaxis and second, to identify the effect of KZ prophylaxis on the development of acute respiratory distress syndrome (ARDS). Historically, the use of KZ prophylaxis was not common (7.5%) in the test hospital. A multidisciplinary team developed a protocol to identify high-risk patients, detail treatment, and list contraindications to KZ prophylaxis. In addition to developing and publicizing the guideline, Sinuff and colleagues discussed the guideline frequently with house officers and nurses, circulated a summary of the studies used to support the use of KZ prophylaxis, displayed the actual KZ prophylaxis performance data, confronted physicians failing to follow the guideline, and presented the ARDS incidence data. Another ICU in the same hospital system served as a contemporaneous control.

Patients at risk were given 200 mg KZ by tube or mouth two hours following feeding once a day for 21 days or until they were discharged from the ICU. Pregnancy, age less than 16, congestive heart failure, esophageal surgery, cirrhosis, liver enzymes elevated beyond two times the normal values, established ARDS at ICU admission, or strict nothing-by-mouth status resulted in disqualification from the study. Forty consecutive high-risk patients were entered into the study, 20 in each hospital. There were no differences at entry, and most patients had severe sepsis or pneumonia. The mortality was 55% in the guideline hospital and 50% in the control. No patients with exclusion criteria were placed on KZ; two patients receiving cisapride were started on KZ, but after intervention it was stopped. Twelve of 20 patients in the test hospital (60%) were placed on KZ, while only one of 20 (5%) was started on KZ in the control hospital ($P < 0.0001$). ARDS, as defined by a shunt greater than 15% or an oxygenation ratio of less than 150 in a patient requiring ventilatory support for at least 48 hours, absence of heart failure, and bilateral infiltrates on chest radiograph, occurred in only one of the 20 patients at the test hospital and in seven (35%) of the patients at the control hospital. (Sinuff T, et al. *J Crit Care* 1999;14:1-11.)

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INSIDE

COMMENT BY CHARLES G. DURBIN, Jr., MD, FCCM

This study shows how difficult it is to change physician behavior. Using a consensus model and including all involved disciplines, a practice guideline was created with the intent that all eligible patients would receive KZ prophylaxis. The guideline was circulated, advertised, discussed, and displayed. Sinuff et al devoted substantial time and effort to educating and re-educating caregivers on the benefits of this practice change. The staff was provided continuous feedback about performance, and interventions were carried out when discrepancies were seen. Despite these efforts, only 60% of eligible patients received the appropriate care regimen.

What we don't know from this study is the time course of change in practice. Others have noted that changes in caregiver behavior increase with time if the wanted behavior is continually reinforced. It is also easy to demonstrate that without continued reinforcement, behavior reverts quickly to the status quo. The important message is that if one wants to produce a lasting change in behavior with an educational intervention, such as with a practice guideline, simply issuing the guideline is only the beginning. Continued education through feedback and direct intervention is necessary to achieve the desired change.

The effectiveness of KZ in preventing ARDS is demonstrated in this study. The impressive reduction from 35% to 5% of patients developing ARDS is remarkable. The lack of effect on mortality is surprising and concerning, however. As with any study, control group selection and bias is a concern. That the control group was treated at a different hospital by different clinicians may indicate that different treatment strategies were used. Since Sinuff et al made the determination of the diagnosis of ARDS in both groups, the difference in ARDS incidence is probably real. A large NIH study addressing the role of KZ prophylaxis and treatment in ARDS is in progress and should shed light on this problem. ❖

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A New Treatment for Ethylene Glycol Poisoning

ABSTRACT & COMMENTARY

Synopsis: *Fomepizole, a new inhibitor of alcohol dehydrogenase, can prevent renal injury in patients with ethylene glycol poisoning if administered soon after ingestion.*

Source: Brent J, et al. *N Engl J Med* 1999;340: 832-838.

Ethylene glycol poisoning can be one of the more devastating ingestion-related problems encountered in critical care. This article reports a clinical evaluation of fomepizole, a new inhibitor of alcohol dehydrogenase, in patients with acute ethylene glycol poisoning.

Intravenous fomepizole was administered to 19 patients with ethylene glycol poisoning in this multicenter case series. The patients had severe poisoning, with plasma ethylene glycol concentrations of at least 20 mg/dL, and 15 had metabolic acidosis (mean initial serum bicarbonate, 12.9 mmol/L). Fomepizole was given as a loading dose of 15 mg/kg body weight, followed by 10 mg/kg every 12 hours for 48 hours, after which the dose was increased to 15 mg/kg every 12 hours because of increased metabolism of the drug. Hemodialysis was used if arterial pH fell below 7.10, if arterial pH or serum bicarbonate fell beyond threshold levels despite intravenous bicarbonate invusion, if the initial plasma ethylene glycol concentration exceeded 50 mg/dL, or if the serum creatinine increased by 1 mg/dL or more.

Acid-base status tended to normalize within hours of initiation of treatment with fomepizole. One patient with severe acidosis died. Renal function worsened in nine of the 19 patients during therapy. In these nine patients, serum creatinine concentrations were markedly elevated, as were concentrations of plasma glycolate. If serum creatinine was normal at the start of fomepizole therapy, renal dysfunction did not subsequently develop. Renal injury was independent of the initial ethylene glycol concentration, but correlated with plasma glycolate levels. Plasma glycolate and urinary oxalate excretion, both measures of ethylene glycol metabolites, fell in all the patients once therapy with fomepizole was initiated. Fomepizole was well tolerated by the patients, with no adverse effects definitely resulting from its administration; episodes of bradycardia in one patient, seizures in two patients, and headaches in two patients were classified as possibly related to the drug.

COMMENT BY DAVID J. PIERSON, MD, FACP, FCCP

This study's results suggest that fomepizole is a safe and effective antidote in the treatment of ethylene glycol poisoning, one of the most serious ingestions encountered in the ICU. This drug may represent a genuine advance over the time-honored standard therapy of intravenous ethanol. Potential advantages include more predictable metabolism and fewer adverse effects, including avoidance of changes in the patient's mental status. This paper reports the collected yet still anecdotal experience of Brent and colleagues. A prospective controlled trial comparing fomepizole with traditional ethanol therapy would better justify the widespread adoption of this new agent as standard care. ❖

Mechanical Ventilation of Children After Marrow Transplantation: Not Just Small Adults?

ABSTRACT & COMMENTARY

Synopsis: *A Canadian group reports that the outcome of mechanically ventilated children after bone marrow transplantation is superior to that reported in adults.*

Source: Rossi R, et al. *Crit Care Med* 1999;27: 1181-1186.

Uniformly, the survival rates for patients requiring mechanical ventilation after blood and marrow transplantation have been dismal. Discharge from the ICU averages less then 20% and long-term survival is in the single digits. Rubenfeld and Crawford (*Ann Intern Med* 1996;125:625-633) reported specific postintubation complications that were associated with no survivors in a large cohort of patients. In the present study, Rossi and colleagues at the Hospital for Sick Children in Toronto reviewed the records of 355 consecutive bone marrow transplants in children (median age, 6.5 years). Mechanical ventilation was used in 39 children on 41 occasions. Overall, 17 of 39 patents were discharged from the PICU and 18 of 41 episodes of ventilation were successful. Six-month survival was 36%.

Patient characteristics such as malignant disease, transplant type, time after transplant, and organ dysfunction at admission to the PICU were not associated with outcome. Factors statistically associated with poor outcome were physiological score (PRISM), four or more organ failures, deterioration of lung function, and severe liver or renal dysfunction. However, there were survivors among many of these high-risk groups. On the basis of these results, Rossi et al believe that initiation of aggressive critical care treatment is warranted in pediatric marrow transplant recipients.

COMMENT BY STEPHEN W. CRAWFORD, MD

Rossi et al are to be commended on the high rate of success with mechanical ventilation after marrow transplantation. I wish I knew why they were so successful and whether their experience can be generalized to other centers.

There are several possible explanations for these results. One is that the children may not have been "that sick." The PRISM scores were relatively low on average, although multiple organ failures and low PiO_2/FiO_2 ratios were seen. I believe that many physicians are more likely to intubate and ventilate a sick child than a similarly ill adult. It is possible that ventilated children may be "less ill" than the average ventilated adult.

Regardless of the reason for the outstanding results reported by Rossi et al, they are vastly different from those reported by Rubenfeld and myself. Our report included adults and children. We did not see a survival rate anywhere near that reported by Rossi et al. Unfortunately, the two reports cannot be directly compared. The criteria for organ failure used by Rossi et al were different from those we used. It would be important to know whether any of the survivors in the Rossi study met the criteria we noted as associated with 100% mortality. Did any patients survive severe respiratory failure with associated sepsis and/or combined renal and hepatic failure?

From my perspective, the benchmark has been set for assessing mortality with mechanical ventilation

after marrow transplantation. It is of relatively little value to state survival rates for specific patient groups without assessing whether the patients survived complications otherwise reported as 100% fatal.

I wholeheartedly concur with Rossi et al that aggressive intervention is warranted until one determines that the patient will not survive. The report by Rubenfeld and myself supports that same conclusion. Unfortunately, this study by Rossi et al does not help us determine when a child will not survive after marrow transplant once on the ventilator. That is when the dilemma begins. ❖

Hyperbaric Oxygen for CO Poisoning?

ABSTRACT & COMMENTARY

Synopsis: *In a large randomized, controlled trial of patients referred for hyperbaric oxygen treatment following acute carbon monoxide poisoning, those who received hyperbaric treatments did no better by any measure, and had worse outcomes by several measures, than those who received sham treatments with normobaric oxygen.*

Source: Scheinkestel CD, et al. *Med J Aust* 1999;170: 203-210.

Hyperbaric oxygen (hbo) treatment is widely used in carbon monoxide (CO) poisoning, both to accelerate the displacement of CO from hemoglobin and to prevent neurologic or neuropsychiatric sequelae. In this randomized, controlled trial conducted in Melbourne, Australia, patients referred to a multiplace hyperbaric oxygen (HBO) facility because of acute CO poisoning were randomized to receive either HBO or sham treatments in the chamber with normobaric oxygen. All other aspects of therapy were the same in the two groups. One-hundred-minute HBO treatments were administered daily for three days, with all patients receiving supplemental oxygen between treatments. Those with persistent neurologic or neuropsychologic abnormalities at the end of the three-treatment series received an additional three treatments. Patients were stratified by circumstances of poisoning (suicidal or accidental) and by need for intubation and mechanical ventilation. Scheinkestel and associates administered seven different neuropsychological tests to all patients in assessment of both short-term (at conclusion of series of treatments) and delayed (after 1 month) outcomes.

During the 28-month study period, 191 patients (mean age 36 years, 82% men) were enrolled in the study. Patients with cutaneous burns, children, and pregnant women were excluded. Although patients with all grades of poisoning were included, 73% were classified as having severe poisoning and 26% were initially mechanically ventilated. The two patient groups were well matched by all the criteria examined by Scheinkestel et al.

Overall mortality was 3%. Persistent neurologic sequelae were judged to be present in 71% of the patients at hospital discharge and in 62% at one-month follow-up. More patients in the HBO group received additional treatments (28% vs 15%; P = 0.01). HBO patients had worse outcomes in the learning test at completion of treatment and a greater number of abnormal test results at completion of treatment than did the normobaric oxygen group. No outcome measure was worse in the normobaric oxygen group. Scheinkestel et al conclude that, under the circumstances of this trial in which both groups received high doses of oxygen, HBO offered no benefit and may even have worsened the outcome.

COMMENT BY DAVID J. PIERSON, MD, FACP, FCCP

The neuropsychiatric syndrome seen in some patients after CO poisoning has been difficult to study objectively and remains a source of controversy. Although both arms of the treatment regimen used in this Australian study likely differ from the way many patients are managed in this country, Scheinkestel et al are to be commended for the care and objectivity they brought to bear on the problem.

Although HBO is available in most larger U.S. cities, most patients with CO poisoning are treated by physicians who do not have direct access to HBO therapy, particularly in the emergency situation. This study provides reassurance to such physicians that outcomes from a rigorous treatment regimen using normobaric oxygen should be as good as those that include HBO. However, the results should not be extrapolated to an assumption that a shorter, less intensive supplemental oxygen exposure would yield clinical results as good as those observed in this study. ❖

Special Feature

The Acute Chest Syndrome of Sickle Cell Anemia

By Mark T. Gladwin, MD

A 24-year-old african-american man immigrated to the United States from Ghana 15 months before presentation. His past medical history was sig-

nificant for a diagnosis of sickle cell anemia, complicated by frequent painful crises (vaso-occlusive crisis) and priapism, as well as a distant history of malaria. One week before this admission, he presented with severe leg and lower back pain and his hematocrit was found to have dropped from 21% to 16%. He was transfused to a hematocrit of 25% and discharged home on acetaminophen and oxycodone. He subsequently developed recurrent lower back, leg, and abdominal pain, along with wheezing, dyspnea, cough, and fever. On this admission his hematocrit was 18% and his temperature was 38.7°C. Oxygen saturation by pulse oximetry was 85% while breathing room air, and his chest radiograph revealed bibasilar opacities with small effusions. His oxygen requirement increased and he was endotracheally intubated. His white blood cell count was 12,000 per mm^3 and his hematocrit was 16%. The patient received a red blood cell transfusion, antibiotics, and hydration. On pressure-controlled ventilation with an FIO_2 of 1.0 and positive end-expiratory pressure (PEEP) of 15 cm H_2O, his PaO_2 was 65 mmHg. The chest radiograph demonstrated diffuse bilateral parenchymal opacities. He became progressively more confused. All cultures were negative. After 36 hours of mechanical ventilation, the arterial saturation dropped to 50%, and cardiopulmonary arrest followed. At postmortem examination, the lung weight was twice normal, and microscopic examination revealed small 2-3 mm occlusive thrombi composed of sickled red cells, fibrin, fat, and infarcted bone marrow. All organs contained sickled red cells and there was extensive avascular necrosis of the right femoral head.

Sickle Cell Anemia and the Acute Chest Syndrome

This case illustrates severe manifestations of the acute chest syndrome of sickle cell anemia. An intensivist's exposure to sickle cell disease is often limited to this type of presentation. The sudden severe desaturation prior to the patient's demise likely represented massive diffuse bone marrow fat embolization from infarcted vertebrae, femurs, and, in this case, the femoral head.

Sickle cell anemia is the most common genetic disease affecting African-Americans, with 0.15% of African-American children homozygous for the sickle cell gene and 8% having the sickle cell trait (heterozygous condition). This autosomal recessive disorder is characterized by a single amino acid substitution (glutamic acid to valine) in each of the beta subunits of hemoglobin. Upon deoxygenation, hemoglobin S undergoes conformational changes that expose a hydrophobic region surrounding the valine moiety in the beta subunit. Polymerization with other hemoglobin tetramers occurs, with the formation of long polymer chains that ultimately distort the erythrocyte membrane.[1] The rigid polymer-containing erythrocytes occlude the microvasculature, resulting in acute and chronic ischemic injury to the lungs, kidneys, liver, spleen, skeleton, skin, and central nervous system. Sickle cell disease is characterized by periods of stability, punctuated by episodes of severe pain involving the back, chest, abdomen, and joints. This syndrome is referred to as the acute painful crisis or vaso-occlusive crisis (VOC).

Pulmonary disease, manifested as the acute chest syndrome (ACS), is a common complication of sickle cell anemia. Half of individuals with sickle cell anemia develop this syndrome at least once. It is the second most common cause of hospitalization, and it accounts for 25% of premature deaths.[2] ACS occurs more commonly in sickle cell individuals with higher steady-state leukocyte counts, higher hemoglobin concentrations, and lower hemoglobin F levels.[3] ACS can be thought of as a specific form of acute lung injury that can progress to the acute respiratory distress syndrome (ARDS). This injury is caused by multiple insults superimposed upon the genetically based pathophysiology of sickle cell disease. These multiple insults include vascular obstruction due to sickling and adherence of erythrocytes in the pulmonary microvasculature, with infarction of the pulmonary parenchyma, bone marrow fatty embolization from infarcted bone, and, to a lesser extent, macrovascular pulmonary embolism and infection.[4] The figure illustrates the pathogenesis of ACS schematically.

Patients with ACS present with fever (80%), cough (74%), chest pain (57%), dyspnea (28%), productive cough (24%), hypoxema (mean PaO_2 of 71 mmHg), leukocytosis, and infiltrates on chest radiographs. The illness often progresses to multilobar pulmonary disease indistinguishable from ARDS in other settings.[5] There are some differences between adults and children with ACS. Fifty percent of adults experience a vaso-occlusive crisis prior to developing ACS, while only 11% of children have an antecedent crisis. Adults present with lower lobe disease and more frequently develop multilobe involvement (36% vs 24% of children) and pleural effusion (21% vs 3%) and receive more frequent transfusions (39% vs 22%), are hospitalized longer (9 vs 5.4 days), and suffer a higher mortality (4.3% vs 1.1%).[4,5] Compared to adults, children are more frequently bacteremic with *Streptococcus pneumoniae*.

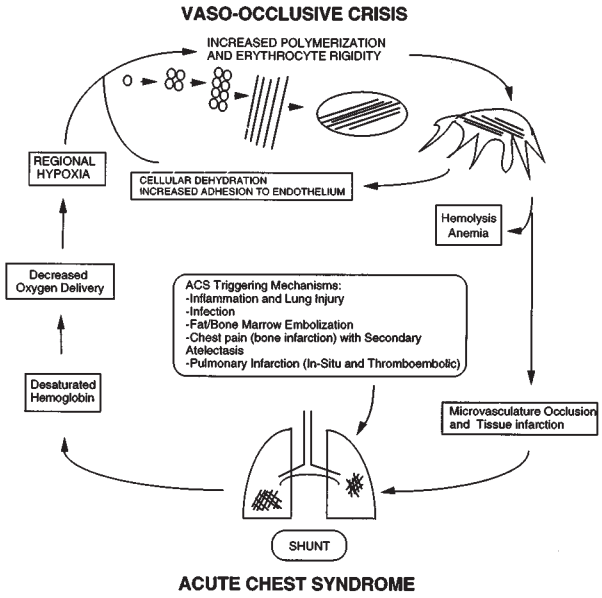
Treatment of the Acute Chest Syndrome

At this time, preventive and treatment options for ACS are based on a number of standard therapies, such as cautious hydration, oxygen therapy, pain control, antibiotics, simple and exchange transfusion, and incentive spirometry (*see Table 1*). While there are no hard data that hydration, oxygen therapy, and narcotic analgesia prevent or treat ACS, experience suggests that these interventions are helpful. Pain control should be sufficient to offer relief of suffering and prevent splinting during breathing, while avoiding excessive sedation that could lead to hypoventilation. Incentive spirometry (10 maximum inspirations every two hours while awake) has been demonstrated to reduce pulmonary infiltrates or atelectasis in patients admitted to the hospital with a VOC and should be considered standard of care.[6]

Although infection occurs in less than 20% of cases of ACS, empiric antibiotic coverage is indicated and should include coverage for *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*. Cultures should include nasal washings for viral pathogens (influenza, respiratory syncytial virus, adenovirus, parainfluenza virus, cytomegalovirus, and parvovirus). Up to 70% of patients with sickle cell anemia have evidence of reactive airways disease on pulmonary function testing, and this fact should be considered when managing these patients on the ventilator. Efforts to detect auto-PEEP and prevent dynamic hyperinflation and its sequellae (e.g., hypotension, barotrauma, and increased work of breathing) are indicated.

Figure

The "Vicious Cycle" of Vaso-Occlusive Crisis and Acute Chest Syndrome



Vaso-occlusive crisis can precipitate acute chest syndrome, leading to shunt physiology and desaturation of hemoglobin. The desaturated hemoglobin, in turn, leads to further hemoglobin S polymerization, sickling of erythrocytes, and further lung injury.

Table 1

Therapy of the Acute Chest Syndrome of Sickle Cell Anemia

Judicious Hydration

- 1-1.5 times daily requirement; fluid restriction may be indicated in patients with severe ACS and capillary leak

Oxygen

- Indicated to maintain adequate oxygenation; does not offer benefit for vaso-occlusive crisis in the absence of hypoxemia

Pain Management

Mild pain

- Codeine, acetaminophen, ibuprofen

Moderate to severe pain

- Medication can be administered on a fixed time schedule with interval analgesics to obtain adequate pain control
- Morphine is drug of choice; meperidine use has been associated with an increased incidence of seizures and should be avoided in patients with renal insufficiency or neurologic disease; hydromorphone and fentenyl are acceptable
- Ketorolac
- Consider patient-controlled analgesia

1. Loading dose 0.05 mg morphine/kg
2. Basal infusion 2-4 mg/h
3. Bolus q 15 min with 1-2 mg/dose

Prevention of Atelectasis

- Incentive spirometry: 10 maximum inspirations every two hours while awake

Empiric Antibiotics

- Include macrolide or quinolone for coverage of atypical pathogens *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*
- Cultures should include nasal washings for viral pathogens (influenza, respiratory syncytial virus, adenovirus, parainfluenza virus, cytomegalovirus, and parvovirus)

Diagnosis and Treatment of Reactive Airways Disease

- Consider occult auto-PEEP and its complications

Consider Exchange Transfusion or Simple Transfusion

- See Table 2

Inhaled Nitric Oxide

- May prove efficacious but cannot be recommended at this time

Blood transfusion and exchange transfusion are likely to significantly affect the course of ACS by replacing hemoglobin S with hemoglobin-A-containing erythrocytes and correcting anemia. Virtually all patients presenting with ACS are anemic (mean hemo-

globin is 7.8 g/dL, range 2.7-10.9 g/dL), and more than half continue to hemolyze, with mean reported hemoglobin decreases of 1.6 g/dL during their acute illness.[7] Reports of several case series suggest that transfusion rapidly improves oxygenation and the clinical course of ACS.[8-10] Emre and colleagues[8] measured arterial PaO_2 following transfusion in 27 patients with ACS. The mean pretransfusion oxygen tension was 65 ± 15 mmHg and 12-24 hours after transfusion increased to 86 ± 19 mmHg.

Although there are no data to establish an appropriate transfusion threshold, it has been recommended that transfusion be considered in patients with pulmonary infiltrates (especially multilobar), rapidly progressive disease, signs of respiratory distress, a PaO_2 less than 60 mmHg in an adult breathing supplemental oxygen (70% for children), or a drop of more than 25% from baseline in a patient with known hypoxemia.[11] I believe that these recommendations are conservative and that exchange transfusion should be initiated earlier, at first sign of pulmonary infiltrate, dyspnea, or any significant drop in PaO_2 from baseline. This view is based on the idea that pulmonary infiltrates, especially when caused by bone marrow fat embolization, are a late complication of significant bone marrow infarction and therefore early transfusion may abrogate this process. It would be reasonable to initiate exchange transfusion in any sickle cell anemia patient sufficiently ill to warrant ICU admission.

The goal of simple transfusion is to increase the hematocrit to 30%, although the hemoglobin level should not exceed 10-12 g/dL in order to avoid hyperviscosity; the percentage of hemoglobin S should be maintained less than 30% (*see Table 2*). Exchange transfusion is performed if there is concern about volume overload, if the initial hematocrit is greater than 25-30%, or if a rapid reduction in hemoglobin S is required. This can be accomplished by removing 500 mL of whole blood by phlebotomy from one arm while transfusing one unit of whole blood into the other. Alternatively, 500 mL of blood is removed followed by infusion of 500 mL of normal saline. Then, a second 500 mL of blood is removed, followed by transfusion of two units of packed red cells. This process is usually repeated until the goals are met. Automated apheresis devices can be used for exchange transfusion as well. A typical adult will require six to eight units of blood for apheresis exchange.

Table 2

Exchange Transfusion in Sickle Cell Disease

Conventional Indications*

- Patients with pulmonary infiltrates (especially multilobar)
- Rapidly progressive disease
- Signs of respiratory distress
- A PaO_2 less than 60 mmHg in an adult breathing supplemental oxygen (70% for children) or a drop of more than 25% from baseline in a patient with known hypoxemia
- Patient requiring ICU admission

Goals

- Increase the hematocrit to 30% (hemoglobin should not exceed 10-12 g/dL to avoid hyperviscosity)
- Maintaining the percentage of hemoglobin S to less than 30%

Methods of Exchange Transfusion

- Exchange transfusion is performed if there is concern about volume overload, the initial hematocrit is greater than 25-30%, or a significant rapid reduction in hemoglobin S is required (which is usually the case)
- Remove 500 cc of whole blood by phlebotomy from one arm while transfusing one unit of whole blood into the other.
- Alternatively, remove 500 cc of blood then infuse 500 cc of normal saline. Then remove a second 500 cc of blood and transfuse two units of packed red cells. Repeat until the goals are met.
- Automated apheresis devices can also be used. A typical adult will require 6-8 units of blood for apheresis exchange.

*Note: I believe that exchange transfusion should be initiated earlier, at first sign of pulmonary infiltrate, dyspnea, or any significant drop in PaO_2 from baseline.

Inhaled Nitric Oxide and the Acute Chest Syndrome

While inhaled nitric oxide (NO) has recently been considered as a possible therapy for ACS, there are virtually no data on the effects of inhaled NO on the clinical course of ACS. Atz and Wessel[11] described the effects of inhaled NO on the clinical course of two mechanically ventilated pediatric patients with ACS. Following 15 minutes of 80 ppm inhaled NO, the two patients' PaO_2 values increased from 69 mmHg and 107 mm Hg to 176 mmHg and 185 mmHg, respectively. This was accompanied by decreases in right ventricular systolic and pulmonary artery pressures. While there was a clear initial improvement in oxygenation and a decrease in pulmonary artery pressures, it is not known whether the sustained improvement that followed was the result of the NO therapy or of the aggressive hydration, exchange transfusions, and oxygen therapy that both patients received.

Recent clinical studies of inhaled NO in patients with ARDS demonstrate an increase in PaO_2/FiO_2 ratio as compared to controls that only last for one to two days, with no effect on the duration of mechanical ventilation or mortality. However, in sickle cell indiv-

duals, even transient improvements in ventilation-perfusion matching would potentially improve hemoglobin saturation and reduce erythrocyte sickling, both in the pulmonary vasculature and in distal organs. The ACS of sickle cell anemia may represent a unique pulmonary disorder in which brief improvements in oxygenation may have profound effects on outcome. However, at this time the use of inhaled NO remains experimental and cannot be recommended until clinical trials provide supporting data. ❖

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CME Questions

1. **In the study of fomepizole in the treatment of ethylene glycol poisoning:**
   a. renal injury correlated with initial plasma ethylene glycol level.
   b. there was no correlation between renal damage and plasma glycolate level.
   c. mortality was 32%.
   d. adverse effects limited the use of fomepizole.
   e. None of the above

2. **The introduction of a clinical practice guideline:**
   a. results in immediate change in practice.
   b. increases the legal liability to caregivers.
   c. should be reserved for professional societies.
   d. may have little effect without continuous education.
   e. is best accomplished by making a change in the hospital bylaws.

3. **Increased mortality with mechanical ventilation after bone marrow transplantation is *not* associated with:**
   a. autologous vs. allogeneic transplantation.
   b. hepatic failure.
   c. renal failure.
   d. worsening respiratory status.
   e. Any of the above

4. **In comparison with those treated with only normobaric oxygen, patients with carbon monoxide poisoning who received a series of hyperbaric oxygen treatments:**
   a. had 12% higher survival.
   b. had 24% higher survival
   c. had no difference in survival but 12% less neuropsychiatric sequelae.
   d. had no difference in survival but 24% less neuropsychiatric sequelae.
   e. None of the above

5. **Exchange transfusion should be initiated in a patient with sickle cell anemia for all of the following indications *except*:**
   a. patients with multilobar pulmonary infiltrates.
   b. rapidly progressive disease or signs of respiratory distress.
   c. a PaO_2 less than 60 mmHg in an adult breathing supplemental oxygen.
   d. uncomplicated pregnancy.

In Future Issues:

An Automatic Monitor of Patient Distress for the ICU?