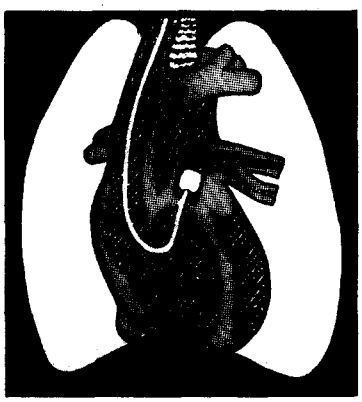

CASE CONFERENCE

Alan Jay Schwartz, MD, MSEd
William Lell, MD
Editors

CASE 2-1988

*Case Presentation**

A 51-year-old white man suffered an inferior wall myocardial infarction in 1981. He was treated at another hospital and subsequently underwent coronary artery bypass grafting (CABG) to four vessels. After this surgery he continued to have infrequent chest pain controlled with sublingual nitroglycerin.

In July 1986, the patient developed severe substernal chest pain unrelieved by nitroglycerin. He was seen in an emergency room at another hospital and was transferred to this hospital for emergent intervention. One year prior to this admission the patient had undergone repeat cardiac catheterization which reportedly revealed that one of his grafts had become occluded. An electrocardiogram done in the referring emergency room revealed an acute inferior wall myocardial infarction. Upon admission to this hospital he underwent repeat cardiac catheterization which revealed complete occlusion of the graft to his right coronary artery. Successful percutaneous transluminal graft angioplasty was performed and 100,000 units of intracoronary streptokinase were given. His hospital course was complicated by dysrhythmias and congestive heart failure, each of which was successfully treated. He was discharged on captopril, diltiazem, isosorbide dinitrate, and a metaproterenol inhaler.

The patient was readmitted in January 1987, for a repeat heart catheterization and coronary angiography. This revealed stenosis of the distal right coronary artery graft, occlusion of the left anterior descending and circumflex grafts, a left ventricular end-diastolic pressure of 29 mmHg, and an ejection fraction of approximately 40%. He was referred for repeat CABG.

The patient was readmitted for a second CABG 1 week later. In addition to his documented coronary artery disease, he carried the diagnoses of chronic obstructive pulmonary disease and hypothyroidism. The patient was kept NPO after midnight and given lorazepam, 3 mg, and morphine sulfate, 12 mg, intramuscularly (IM), at 6:00 AM. He was brought to the operating room, where two 14-gauge peripheral intravenous catheters, a left radial arterial catheter, and an Oximetric pulmonary artery catheter were inserted. During this period he was given 6 mg of midazolam intravenously. Anesthetic induction and endotracheal intubation were accomplished without incident using fentanyl, 50 μg/kg, with pancuronium and metubine used for muscle relaxation. Arterial blood gases following induction on an F_IO_2 of 1.0 revealed: PaO_2 290 mmHg, $PaCO_2$ 33 mmHg, and pH 7.40. Peak inspiratory pressure was 30 cmH_2O, pulmonary artery pressures were 25/9 mmHg, cardiac output 6.2 L/min, pulse rate was 75 beats/min, and systemic blood pressure was 110/70 mmHg.

The CABG procedure was uneventful until massive bleeding occurred during the repeat sternotomy. The patient was immediately heparinized and an activated coagulation time was measured at 600 seconds. Femoral vein-femoral artery partial bypass was rapidly instituted while

*Lawrence O. Larson, MD, FACS

Lawrence O. Larson, MD, FACS, Jeffrey V. Kyff, DO, Department of Anesthesiology; Joseph C. Fantone, III, MD, Department of Pathology; and G. Michael Deeb, MD, Section of Thoracic Surgery, University of Michigan, Ann Arbor.

Address reprint requests to Dr Lawrence O. Larson, Department of Anesthesiology, University of Michigan, Ann Arbor, MI 48109.

0888-6296/88/0202-0019$03.00/0

multiple transfusions were given. Once partial bypass was instituted, the cardiopulmonary bypass (CPB) pump was used as the vehicle for further transfusion. A total of 31 units of packed red blood cells was administered during the procedure. A total of six hours of total and partial bypass was required for repair of a tear in the right ventricle and completion of the CABG. During all but 90 minutes of this time the patient was normothermic. Difficulty was encountered during the initial attempts to terminate CPB. An intra-aortic balloon assist device was inserted and separation from CPB was achieved, although systolic blood pressure never exceeded 90 mmHg. Multiple cardiac outputs ranged from 2 to 4 L/min. Arterial blood gases on an F_IO_2 of 1.0 following separation from CPB revealed a PaO_2 of 41 mmHg, $PaCO_2$ 42 mmHg, and pH 7.21. Additional therapy included PEEP at 10 cmH_2O and infusions of dopamine at 5 μg/kg/min and norepinephrine/phentolamine (2:4) at 20 drops/min. The position of the endotracheal tube was checked and the tube suctioned free of a small amount of secretions. Peak inspiratory pressures were 40 to 45 cmH_2O after separation from CPB with a tidal volume of 1200 mL. Arterial blood gases following the institution of the above therapeutic measures revealed: PaO_2 64 mmHg, $PaCO_2$ 34 mmHg, pH 7.36 and a base excess -8.2 mEq/L. The patient was transferred to the thoracic intensive care unit (ICU) where the norepinephrine/phentolamine infusion was discontinued and an epinephrine infusion was begun. His course continued inexorably downhill and he died approximately 12 hours postoperatively. He maintained PaO_2s of 75 to 85 mmHg and $PaCo_2$s of 44 to 50 mmHg on an F_IO_2 of 1.0 with 10 cmH_2O PEEP in the ICU.

DISCUSSION

Diagnosis and Treatment of Diffuse Alveolar Damage†

There is ample evidence that this patient developed the adult respiratory distress syndrome (ARDS). The patient had relatively normal cardiac filling pressures and severe hypoxemia. An important question is whether the hypoxemia was secondary to an inadequate cardiac output. Cardiac output is one of the major determinants of oxygenation. With cardiac outputs of 2 to 4 L/min and a cardiac index of approximately 2 L/min/m^2, this may have contributed to the hypoxemia. The base excess remained approximately -8.2 mEq/L despite the intra-aortic balloon pump and inotropic support following surgery. The acidosis may have been contributed to by blood products, which the patient had in abundance. The prime reason for the lactic acidosis in this patient, however, was inadequate perfusion postoperatively.

The term "diffuse alveolar damage" (DAD) is being used more and more in the literature. Fetal hyaline membrane disease and ARDS are related in many respects. In the fetal form of this condition there is usually uniform atelectasis which may be secondary to lack of parenchymal development or lack of surfactant. In the adult form of DAD patchy atelectasis as well as areas of microatelectasis surrounded by essentially normal alveoli are seen. Both processes involve formation of a hyaline membrane. There are two phases in the adult syndrome. The initial exudative phase lasts one to six days and involves necrosis of the alveolar type-one cells without damage to the basement membrane. This leads to increased permeability and proteinacious exudates. These cause the formation of the hyaline membrane and, along with accumulation of cellular debris, result in atelectasis. The changes result in almost total loss of the type-one alveolar cells. The second, or reparative, phase usually lasts about 2 weeks and may result in proliferation of type-two cells as well as fibrosis with honeycombing and chronic interstitial pneumonia, or, more commonly, nearly total resolution if the patient survives.

There are many etiologies of ARDS or DAD (Table 1). This patient was in shock postoperatively. The low-flow state, multiple transfusions, and CPB are ample etiologic factors in the development of DAD. When an extensive list of etiologies exists for a disease, it usually means that it is not well understood. This seems true in terms of burn patients with inhalation injuries, as only a minority develop a clear syndrome of DAD. Some data from the MGM Grand Hotel fire are of interest. There were 600 patients evaluated for smoke inhalation. Of those, 318

†Jeffrey V. Kyff, DO

Table 1. ARDS-Associated Etiologies

Shock	Pancreatitis
Trauma	Multiple/massive transfusions
Fat embolism	DIC
CNS pathology	Direct pulmonary damage (inhalation)
Burns	Drug overdose/reaction
Aspiration	Leukemia
Asphyxiation	Cardiopulmonary bypass
Pulmonary infection	Poisoning
Sepsis	Radiation
Reexpansion of collapsed lung	Chemotherapy
	DKA
Liver failure	
Hypotension	

Abbreviations: CNS, central nervous system; DIC, disseminated intravascular coagulation; DKA, diabetic ketoacidosis.

were admitted with inhalation injuries, but not one patient developed DAD.[1] It was expected that this group with direct pulmonary damage would develop DAD.

To understand DAD and the various mechanisms of pulmonary edema, it is necessary to understand the Starling equation:

$$\text{Net filtration} = Kf[(Pmv - Ppmv) - \text{Sigma}(mv - pmv)]$$

Kf = capillary filtration coefficient
Pmv = microvascular hydrostatic pressure
Ppmv = perimicrovascular hydrostatic pressure
Sigma = protein osmotic reflection coefficient
mv = plasma oncotic pressure
pmv = perivascular oncotic pressure

The Starling equation describes fluid dynamics along a capillary bed. The protein osmotic reflection coefficient governs what happens with DAD. This coefficient expresses the relative permeability of the membrane to protein. As this number approaches zero, permeability increases. In patients for whom this figure approaches one, membranes are impermeable to protein. Further consideration of the plasma and perivascular oncotic pressures suggests that there are two types of pulmonary edema. The first would be secondary to increased hydrostatic pressure, ie, increased cardiac filling pressures. This, expressed as increased pulmonary capillary wedge pressure (PCWP), is generally cardiogenic in nature, delayed in onset, and characterized by low protein content in the edema fluid. The second type is due to changes in capillary permeability and is usually rapid in onset with essentially normal wedge pressures and a high protein content in the edema fluid. Pink frothy sputum is not common in DAD, although it is occasionally seen.

The pathophysiology of DAD and the mechanisms opposing its development are multifaceted. Usually the hydrostatic pressure increases the filtration across capillaries leading to a decrease in the interstitial oncotic pressure secondary to the dilution of protein in the interstitial space. This leads to an increase in the gradient between the plasma oncotic pressure and the perivascular oncotic pressure. Increasing lymph flow then works as a protective feature as long as the osmotic reflection coefficient (sigma) remains one and the barrier remains intact. Lymph flow can pick up any additional fluid by increasing to a phenomenal rate. This is the primary compensatory mechanism limiting pulmonary edema. Once the osmotic reflection coefficient approximates zero there is essentially no barrier between the intravascular and interstitial spaces. The lymphatics become overwhelmed and interstitial edema develops. Hydrostatic pressure then becomes much less important because there is essentially no barrier to fluid flow. Whether the wedge pressure is 3 mmHg or 10 mmHg is not terribly important. Probably the PCWP should not be markedly elevated, but there is apparently little benefit to lowering the PCWP to zero. Certainly there are hemodynamic reasons to maintain a higher filling pressure.

Changes in extravascular lung water in patients with DAD have been studied.[2] Whether the fluid utilized was lactated Ringers, saline, albumin, or hetastarch does not seem to make a great deal of difference in terms of the extravascular lung water.[2] Additionally, Shoemaker et al described varied hemodynamic and oxygen transport values in response to fluid therapy in the setting of DAD.[3]

Signs and symptoms of DAD include hypoxemia usually unresponsive to peak airway pressure, decreased pulmonary static compliance, and decreased functional residual capacity. The ARDS seen with high altitude pulmonary edema is an exception, being responsive to the administration of oxygen. Generally, patients with DAD will be tachypneic with elevated pulmonary hydrostatic pressures, normal-to-low PCWP, and pulmonary edema, with or without

x-ray evidence.[2] There is some debate as to whether or not x-ray findings are essential to the diagnosis of DAD. One of the key signs seen is a decrease in pulmonary compliance (defined as the change in volume divided by the change in airway pressure) usually to less than 50.

Mortality runs 50% to 60% in patients with mild degrees of DAD. When death occurs it usually occurs within 2 weeks of onset, most often due to the underlying disease process, not hypoxemia or inability to ventilate the patient.[4] Gram negative sepsis carries a mortality of 85% when it is associated with DAD. The management of DAD patients is directed toward the etiology. Hemodynamic monitoring must be used aggressively. Supportive care includes mechanical ventilation (with PEEP), nutritional support, and hemodynamic manipulation. Once the underlying cause is corrected, it is primarily a matter of supporting the patient through the exudative phase to the resolution phase. Deciding whether or not any given cardiac output is adequate is most helpful and can be accomplished effectively by recording all of the measured hemodynamic variables and calculating a number of derived values, including the cardiac index, stroke index, vascular resistances, and left and right ventricular stroke work indices. This patient's cardiac output was 2 to 4 L/min and that probably was not adequate in light of the arterial and mixed venous gases, the arterial and mixed venous O_2 content, the A-VDO_2, and the oxygen extraction. A decision about whether or not a given cardiac output is adequate is possible and therapy may be adjusted accordingly. Other important values are the alveolar O_2, A-a gradient, a-ADO_2, pulmonary shunt, oxygen consumption, and pulmonary compliance.

Ventilation with PEEP is important in the supportive care. The "best PEEP curve" can be used in the management of these patients. Generally patients are intubated and mechanically ventilated with added PEEP. The PEEP increases the functional residual capacity and decreases the pulmonary shunt by converting areas of atelectasis and complete shunt to areas of alveolar ventilation and partial shunt. A patient's progress can be followed by looking at the pulmonary compliance, shunt, and PaO_2. Nelson et al titrated PEEP in non-ARDS patients with early, moderate arterial hypoxemia.[5] They compared titrating PEEP by plotting the PEEP curve looking for a shunt of less than 20% to simply titrating PEEP to a given arterial oxygen saturation and a given PaO_2. No difference was noted in the two methods. In attempting to wean patients off PEEP they found it to be more economical to simply titrate to a given arterial saturation rather than to maintain the shunt at less than 20%. Whether this applies to ARDS patients or not needs to be confirmed.

The arterial-alveolar ratio is the ratio between the arterial O_2 and alveolar O_2 tensions with a normal value expressed as 0.8. The advantages of this value are that it allows comparison of different patients on different F_IO_2s and ventilator settings, as well as allowing comparison of the same patient on different days on different levels of F_IO_2 and PEEP. Following the a-ADO_2 in conjunction with the clinical picture and hemodynamic variables can be helpful in the management of this type of patient. Pervis et al used this ratio, and found the best clinical correlation when a patient had a ratio of 0.55 or less, defined as moderate-to-severe respiratory failure.[6]

Compliance is a parameter followed in the operating room or ICU which is easy to calculate: the tidal volume divided by the peak inspiratory pressure minus the PEEP equals the effective static compliance. Compliance decreases very early when patients begin to accumulate extravascular lung water or pulmonary edema.

The continuous measurement of SVO_2 may be very helpful, but is very expensive. Oximetric pulmonary arterial catheters cost $175.00 in comparison to a plain pulmonary arterial catheter costing $45.00. More and more studies are reporting the advantages of following SVO_2 as a method of monitoring oxygenation. This is problematic, however, as many factors affect SVO_2, including the cardiac output, arterial saturation, hemoglobin, and metabolic rate. Oxygen consumption is not a constant number. A patient does not stay at a given oxygen consumption throughout a 24-hour period in a critical care unit or operating room. Oxygen consumption tends to be extremely variable and nearly impossible to predict. If SVO_2 is monitored in these patients this variability must be kept in mind and the SVO_2 value should not be used alone to diagnose or treat patients.

COMMENTARY

Basic Pathologic Processes in Diffuse Alveolar Damage‡

There are multiple etiologies and clinical settings in which ARDS may occur.[7,8] Two of the most important targets of toxic insult to the lung are pulmonary capillary endothelial cells and type 1 alveolar epithelial cells. Depending upon the nature of the toxic insult, injury of one cell type may be of greater importance in the pathogenesis of the disease process. Pulmonary endothelial cell injury may lead to a breakdown in the intravascular-interstitial barrier resulting in increased vascular permeability and lung lymph flow. Injury to the alveolar type 1 epithelial cell results in a breakdown of the intra-alveolar and interstitial barriers with resultant alveolar edema. Depending upon the extent of injury to either of these cells, a predominance of interstitial edema or a mixture of interstitial and intra-alveolar edema is seen. In this patient, a combination of injury to both cell types probably existed. Once this pathologic process is initiated it may evolve over several days with the development of the histologic hallmark of diffuse alveolar damage: the presence of hyaline membranes along alveolar walls. These membranes consist primarily of cellular debris mixed with various amounts of fibrin. This injury frequently will progress over a 1-to-2 week period with the onset of a chronic interstitial inflammatory response, progressive interstitial fibrosis, and varying degrees of intra-alveolar fibrosis. This is the framework of the pathologic progression of ARDS as it applies to this case.

Many experimental models have been developed to investigate the pathogenic mechanisms that are functioning in this disease process. As expected in a disease process with multiple etiologies, there are multiple pathogenic mechanisms. One approach that has been taken is based on what has been referred to as the complement or complement-neutrophil hypothesis.[9-11] This hypothesis was proposed initially by Craddock et al to explain respiratory insufficiency associated with hemodialysis.[9] In these patients, significant complement activation was observed upon exposure of plasma to dialysis membranes and increased levels of circulating anaphylatoxins. In particular, the anaphylatoxin C5a, a low molecular weight polypeptide, is an important activator of circulating polymorphonuclear leukocytes (PMNs) and is the primary chemoattractant derived from plasma. The generation of C5a leads to PMN activation which is manifest as increased adherence to endothelial cells, cell aggregation, and the release of a variety of toxic agents, including reactive oxygen species, lysosomal enzymes, and several biologically-active lipid mediators. These phlogistic compounds have potentially potent effects both on endothelial cells and vascular smooth muscle cells. The two primary lipid mediators from PMNs are leukotriene B_4 (LTB_4), derived from arachidonic acid metabolism, and platelet activating factor (PAF). In ARDS, the early onset of interstitial edema is frequently associated with the presence of leukocyte aggregates in pulmonary capillaries. Similar pathogenic mechanisms have been proposed to explain CPB-induced lung injury (Fig 1).

Several experimental models of ARDS have been developed over the years. These include models in rabbits, rats, dogs, and sheep.[11] In each case, the models focus on defining the effects of systemic activation of complement on pulmonary function. Within a few minutes following systemic activation of the complement system the alveolar capillaries appear dilated and contain aggregates of PMNs mixed with platelets and red blood cells. This is frequently associated with injury to endothelial cells and exposure of denuded vascular basement membrane. In addition, there is interstitial edema indicative of breakdown in the intravascular-interstitial barrier. Depending on the experimental model and extent of injury, the breakdown of vascular basement membrane and aggregates of fibrin indicative of activation of the coagulation system are observed. This is the primary morphologic correlation developed in experimental model systems to explain the early phases of lung injury in ARDS.

A variety of therapeutic interventions in addition to the modulation of PMN function have been developed recently. These include the systemic administration of anti-oxidants in an attempt to remove the reactive oxygen species that may be generated by activated leuko-

‡Joseph C. Fantone, III, MD

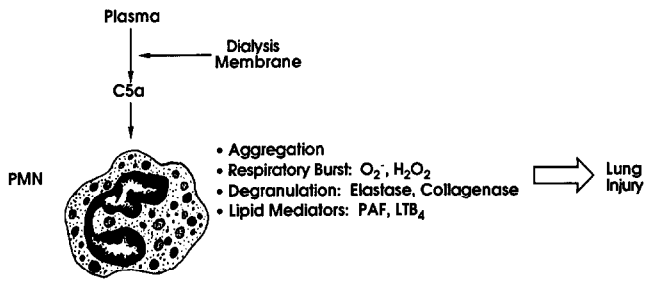

Fig 1. Pathogenic mechanisms of cardiopulmonary bypass-induced lung injury.

cytes.[12,13] Depending on the experimental model, varying success in inhibiting lung injury has been observed with the administration of these antioxidants. It is important to note that although a number of models have been proposed and evaluated for ARDS, none of them is fully satisfactory. None of the experimental models progresses with significant hyaline membrane formation and fibrosis as is frequently observed in patients. This may reflect the complexity of the pathologic process and the multiple factors that are functioning. In addition, there are at least four reports in the literature describing the development of ARDS in patients who were deficient in circulating PMNs and who nevertheless developed ARDS. These observations support the contention that ARDS is a multifactorial disease process. In the future, it will be important to examine the impact of a variety of mediators which may be generated in both the vascular and extravascular compartment of the lung as the result of toxic insult to circulating monocytes, as well as endothelial cells, alveolar epithelial cells, and pulmonary alveolar macrophages. Studies focused on defining the role of the monocyte as a potentially important cellular mediator of ARDS have increased. This is based on the multifunctional properties of this cell including its ability to secrete interleukin-1, tumor necrosis factor, and a variety of other inflammatory mediators that modulate the functions of multiple cell types both in the vascular compartment and interstitial tissues. In addition, significant attention is currently focused on the endothelial cell as a dynamic partner in the inflammatory response rather than a passive bystander. This is based on recent studies that have shown that inflammatory mediators such as interleukin-1 can directly activate these cells to express specific receptors on their surface and alter their biologic functions, including prostacyclin production. Thus, it appears that complex interactions are potentially occurring between circulating inflammatory cells and vascular and parenchymal cells during the evolution of ARDS. It is hoped that further understanding of the complex interactions between inflammatory cells and mediators with vascular and pulmonary parenchymal cells may provide insight into the pathologic mechanisms functioning in ARDS, and provide the basis for the development of more effective therapeutic intervention.

In certain experimental models pretreatment with various substances has shown promise. Pretreatment with corticosteroids has provided a protective effect in some models. In clinical studies, however, responses to steroid therapy in ARDS patients are quite variable and of questionable efficacy.

In experimental studies, Morganroth has shown a protective effect of lodoxamide, a xanthine oxidase inhibitor, after ischemic reperfusion injury in isolated perfused rat lungs.[14] A similar protective effect of allopurinol and oxypurinol has been observed in ischemic reperfusion injury of other tissues including heart and intestine.[15] The use of allopurinol, oxypurinol, and lodoxamide is based on their action as xanthine oxidase inhibitors and is presumed to primarily affect endothelial cells. These inhibitors block the conversion of hypoxanthine and xanthine to uric acid and the generation of superoxide anion and hydrogen peroxide (Fig 2). Recent studies indicate, however, that allopurinol and oxypurinol may also function as scavengers of the hydroxyl radical (°OH) and hypochlorous acid (HOCl). Therefore, the interpretation of experimental studies with these agents in the absence of direct measurements of purine metabolite formation must be carefully considered.

Evidence suggests that lung injury expands during reperfusion after the initial ischemic

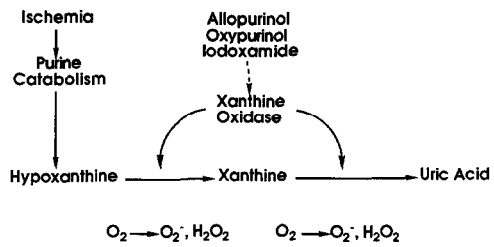

Fig 2. Mechanism by which xanthine oxidase inhibitors prevent superoxide anion production.

insult. Attenuation of the injury by xanthine oxidase inhibitors such as allopurinol is dependent upon treatment of the tissue prior to ischemia. If administration of the xanthine oxidase inhibitor is delayed until reperfusion, a marked decrease in the beneficial effect of the drug is observed. This requirement for pretreatment may reflect the need for the drug to be taken up by endothelial cells, or, regarding allopurinol, to be metabolized to a more active metabolite (oxypurinol).

Treatment of Intraoperative Right Ventricular Injury§

One of the major risks of a repeat sternotomy is massive bleeding secondary to right ventricular damage. In this case, as in most cases in which there is damage to the heart, the damage did not occur at the time of sternotomy. Rather, the damage occurred during retraction of the sternum. The appropriate treatment of this entity is the immediate institution of femoral-femoral bypass. In this instance, the heart was adherent to the undersurface of the chest wall. The chest wall was retracted up rather vigorously from the left side and a portion of the anterior wall of the right ventricle was retracted with the chest wall, causing severe hemorrhage. The wound was packed and femoral-femoral bypass was instituted immediately. The patient did not become hypotensive at the time and maintained systolic pressures of greater than 100 mmHg. Femoral-femoral bypass was instituted at normothermia allowing dissection to gain access to the anterior right ventricular wall to facilitate repair of the damage. The real danger in this situation lies in attempts to immediately dissect the anterior right ventricular wall off the undersurface of the sternum in an attempt to repair the damage. This would increase the size of the defect and the amount of bleeding; the patient would probably die. Partial bypass can be instituted by using arterial access via the femoral artery and partial venous drainage via the femoral vein. Total bypass cannot be sustained because adequate venous drainage cannot be achieved using one cannula through the femoral vein. However, the venous return for bypass can be increased by placing the pump suckers through the hole in the anterior wall of the right ventricle. This maneuver will give the necessary venous return. Once bypass is begun, the right ventricle will collapse, facilitating its dissection from the undersurface of the chest wall. Once the ventricle is freed from the chest wall the defect in the right ventricle can be repaired. When right ventricular repair was completed in this case, attempts were made to wean the patient from CPB. However, each time the heart was retracted for dissection of the coronary arteries, the patient's pressure dropped precipitously. Because significant adhesions from previous surgery necessitated the retraction of the heart, the patient was maintained on partial bypass.

The dissection was long (approximately three hours) and the patient was maintained on CPB at normothermia. The expected consequences of CPB at normothermia are a drop in systemic vascular resistance with vasodilation and the development of edema. The patient could not be cooled until access was gained to the left ventricle for decompression. Revascularization was performed without difficulty. During the process of weaning from cardiopulmonary bypass, there was good myocardial function. However, the patient could not be adequately oxygenated. Endotracheal suctioning produced pink, frothy material, and the chest x-ray showed bilateral interstitial pulmonary edema.

There are three theoretical reasons for this patient's pulmonary compromise. The first is CPB itself. There is much written in the literature today about activation of complement C3A and C5A which causes sequestration of white cells, release of histamine, and formation of pulmonary edema. Complement activation occurs by the alternate pathway as a result of blood contact with materials such as silicone. An interesting study was performed comparing CPB with

§G. Michael Deeb, MD

membrane oxygenators and bubble oxygenators with and without steroids.[16] There was evidence of significant sequestration of white blood cells and a marked increase in C3A with bubble oxygenators. There was no sequestration of white cells or activation of C3A with the membrane oxygenator, which was the type used in the case under discussion. With this method of oxygenation, the addition of steroids at the time of CPB decreased white cell sequestration. Steroids were not given in this case, and this may have allowed massive white cell sequestration. The second reason for a pulmonary capillary leak in this patient could have been multiple blood transfusions. Multiple blood transfusions can cause activation of complement and sequestration of white cells with the build-up of granulocytes in the lungs, release of histamine, and superoxide formation. A third reason for the formation of pulmonary edema in this case could have been the complement activation seen in trauma patients with shock. However, this patient was never hypotensive. The reason for this patient's pulmonary damage was probably twofold. It is unlikely that CPB elicits the activation of complement and sequestration of white cells; rather, massive transfusion was the culprit in this instance. Synergistic with this complement activation was the long period of time during which the patient had to be supported on partial bypass at normothermia, causing a drop in systemic vascular resistance, vasodilation, and a marked increase in blood flow to the lungs leading to complement activation and pulmonary edema.

This patient not only had pulmonary edema, but he also had total body edema. The myocardium functioned adequately, and the pulmonary artery and filling pressures were not high. The volume given to him went almost immediately into his soft tissues. His hematocrit rose above 30% in the early postoperative period and was kept above 30% thereafter. In the ICU, the problem was decreasing oxygenation, with subsequent deterioration of cardiac output and progressive acidosis. Because of hemodynamic instability, hemofiltration was not performed in this patient. The initial plan was to correct his coagulation factors and place him on ECMO eight to 10 hours postoperatively. The patient's family, however, did not want to proceed with this therapeutic modality. Diuresis did not seem to be indicated despite the patient's pulmonary edema. His filling pressures were not high and he was edematous. He was being given volume to try and maintain filling pressures and to increase his cardiac output. All fluid given, however, leaked into his soft tissue. It is appropriate to recognize that he had a total body capillary leak.

REFERENCES

1. Hudson LD: Cause of the adult respiratory distress syndrome: Clinical recognition. Clin Chest Med 3:195-212, 1982

2. Raheja R, Puri VK: Sequential changes in extravascular lung water in ARDS. Am Rev Respir Dis A138:, 1985

3. Shoemaker WC, Thompson WL, Holbrook PZ: Circulatory pathophysiology of ARDS and its fluid management, in Shoemaker WC (ed): Critical Care. Philadelphia, W.B. Saunders, pp 310-318

4. Pepe PE: The clinical entity of adult respiratory distress syndrome, in Critical Care Clinics, vol 2, no 3. Philadelphia, W.B. Saunders, July 1986, P387, pp 377-403

5. Nelson LD, Civetta JM, Hudson-Civetta J: Titrating positive end-expiratory pressure therapy in patients with early, moderate arterial hypoxemia. Crit Care Med 15:14-19, 1987

6. Pervis LV, Boix JH, Salom JV, et al: Clinical use of the arterial/alveolar oxygen tension ratio. Crit Care Med 11:888-891, 1983

7. Fowler AA, Hamman RF, Good JT, et al: Adult respiratory distress syndrome: Risk with common predispositions. Ann Intern Med 98:593-597, 1983

8. Rinaldo JE, Rogers RM: Adult respiratory distress syndrome. N Engl J Med 306:900-906, 1982

9. Craddock PR, Fehr J, Brigham KL, et al: Complement and leukocyte-mediated pulmonary dysfunction in hemodialysis. N Engl J Med 296:769-774, 1977

10. Rinaldo JE: Mediation of ARDS by leukocytes. Clinical evidence and implications for therapy. Chest 89:590-593, 1986

11. Brigham KL, Meyrick B: Interactions of Granulocytes with the Lungs. Circ Res 54:623-635,

12. Fantone JC, Ward PA: Polymorphonuclear leukocyte-mediated cell and tissue injury: Oxygen metabolites and their relations to human disease. Hum Pathol 16:973-978, 1985

13. Fantone JC, Feltner DE, Brieland JK, et al: Phagocytic cell-derived inflammatory mediators and lung disease. Chest 91:428-435, 1987

14. Morganroth M: Personal communication

15. McCord JE: Oxygen-derived free radicals in post-ischemic tissue injury. Mech Dis 312:159-163, 1985

16. Hardesty RL, Deeb GM, Griffith BP, et al: Clinical experience with the travenol TMOR membrane oxygenator for profound hypothermia. Arch Surg 115:1355-1358, 1980