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DONOR MANAGEMENT ISSUES

BY DAVID J. POWNER, MD

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Management of variations in blood pressure during care of organ donors

The organ procurement coordinator commonly must correct and maintain the arterial blood pressure during donor care. This article reviews considerations in the accurate measurement of the blood pressure, causes of hypertension and hypotension, and desirable standards to use in order to provide adequate organ perfusion. Recommendations are presented for treatment of hypotension in a titrated response of intravenous fluids, inotropic support, and vasopressor infusion to maintain the mean arterial pressure above 65 mm Hg. Collaborative interaction between the coordinator and physician consultant remains important throughout management of blood pressure changes during donor care. (*Progress in Transplantation*. 2000;10:25-32)

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Notice to CE enrollees:

A closed-book, multiple-choice examination following this article tests your ability to accomplish the following objectives:

1. Discuss how to calculate mean arterial pressure.
2. Discuss the treatment of hypotension.
3. Discuss the treatment of hypertension.

Of the many challenges presented to the organ procurement coordinator (OPC) during donor care, the most common (and one of the most difficult) is the diagnosis and treatment of variations in the blood pressure, especially hypotension. These blood pressure changes are usually related to the primary or associated conditions that caused brain death, such as multiple trauma with head injury. However, preexisting illness, such as coronary artery disease with a recurrent ischemic syndrome, may, in addition, complicate ongoing care. Poor perfusion of donor organs from any cause is the most important risk factor in rendering those organs unacceptable for transplantation. Therefore, the OPC must rapidly evaluate several possible causes of hypotension while implementing effective treatment as the highest clinical priority.

Blood Pressure Assessment

Blood pressure is defined by the systolic, diastolic, and mean arterial pressures. It is generally agreed that the mean arterial pressure (MAP) is the most important to organ perfusion and should be maintained between 60 and 70 mm Hg. MAP is automatically calculated by the bedside monitor when an arterial catheter is in place or by a noninvasive automatic blood pressure machine. When neither the monitor nor the machine is available, MAP can be calculated from the systolic and diastolic pressures as one third of the difference between the systolic and diastolic pressures, added to the diastolic pressure. Another recently recommended formula[1] is diastolic pressure + 1/3(systolic – diastolic pressure) + 5. Noninvasive automatic blood pressure monitors are in use in most intensive care units. The correlation between their measurements and traditional auscultatory methods with a blood pressure cuff is well within acceptable clinical limits, particularly when MAP is followed. However, variations between the techniques occur, especially when hypotension is present due to vasodilation.[2] The pressure displayed by such machines using the oscillometric method of measurement was higher than recorded via arterial catheters and routine auscultation. Placement of an arterial catheter is, therefore, recommended when the systolic pressure is consistently less than 100 mm Hg or the MAP is less than 60 mm Hg. Arterial catheters also

facilitate acquisition of blood samples when frequent laboratory testing is needed.

The best location for placement of an arterial catheter may depend upon the anticipated number of organs to be recovered, the sequence of organ removal, and the surgical team's preference. An upper extremity (radial, brachial, or axillary) or a lower extremity (femoral) location may be preferred. Although arterial cannulation is usually not performed by OPCs, they should be familiar with the sites used and possible short-term complications.[2] The accuracy of the pressure measurement obtained via an arterial catheter is dependent upon a variety of technical details, such as proper transducer leveling and zeroing, system calibration, type and length of connecting tubing, and absence of air bubbles in the tubing circuit.[3] These matters are usually the responsibility of the bedside nurse but must also be appreciated by the OPC.

Although both high and low blood pressure extremes may be harmful to donor organs, hypertension is rare following brain death. It is, however, very common during the evolution of brain death and will be discussed further below. More often, the OPC will find the donor to be hypotensive and will need to rapidly evaluate possible causes and begin effective therapy. Treatment of hypotension is the first and highest priority throughout donor care.

Causes of Hypotension

In general, hypotension may result from one of 4 types of shock: hypovolemic, cardiogenic, obstructive, or distributive. Obstructive causes of shock in the donor are very unusual but might include cardiac tamponade, tension pneumothorax, or pulmonary embolus. Those etiologies of obstructive shock would probably have been recognized and managed as part of the patient's initial evaluation and stabilization.

Hypovolemic Shock

Hypovolemic shock should be considered as a cause of hypotension in situations where significant blood or fluid loss has occurred and/or may be continuing. Examples include hemorrhage following trauma and polyuria due to diabetes insipidus, residual effects of diuretic drugs, or osmotic diuresis secondary to hyperglycemia. Hypovolemia may be *absolute* that is, a true reduction of intravascular volume below normal, or *relative*, that is, the vascular space is abnormally dilated such that the normal blood volume is inadequate to provide sufficient blood pressure. Evaluation of both types of hypovolemia may require measurement of the pressure produced by the intravascular volume within a large intrathoracic vein, that is, the central venous pressure (CVP). The vessel usually chosen for insertion and CVP measurement is the subclavian, internal jugular, or, rarely, the external jugular vein.[4] This access allows the CVP to be measured as it is affected by the intrathoracic pressure variations induced by mechanical ventilation. However, venous pressure measured via a femoral vein catheter has also recently been shown to accurately reflect the CVP during mechanical ventilation in intensive care unit patients.[5]

In older donors, when chronic lung or atherosclerotic coronary artery disease may be present, and in all donors in whom primary cardiac injury or secondary cardiac ischemia may have occurred, the CVP may overestimate the intravascular volume reaching the left ventricle. Because the left ventricular end-diastolic volume, also called the left ventricular preload, is an important determinant of cardiac output, its measurement would be useful. Unfortunately, it cannot be directly measured as a volume but is estimated by the left ventricular end-diastolic pressure, which, itself, is approximated by the pulmonary artery occluded, or "wedge," pressure (PAOP). This evaluation requires the insertion of a pulmonary artery balloon flotation catheter by a physician. The methods of insertion and possible complications are reviewed elsewhere.[6] Because of the potential for injury to the endocardium and internal structures of the heart even with short-term use,[7] placement of a pulmonary artery catheter should be part of the accepted organ procurement organization (OPO) protocol, especially if the heart is to be transplanted. In general, a PAOP of 12 to 15 mm Hg is associated with adequate left ventricular preload unless the donor heart has diastolic dysfunction, as discussed later.

Replacement intravascular fluids during absolute or relative hypovolemia may be crystalloids (standard sodium chloride, Ringer's lactate, or other electrolytic solutions), colloids (5% albumin), or blood products. Some experimentation suggests that starch-based colloid solutions such as hetastarch may have adverse effects on donor kidneys.[8] The final choice of resuscitation fluid depends on what fluid is or has been lost. If blood loss continues to cause anemia, packed red blood cells should be given; if blood loss is complicated by a coagulation defect, fresh frozen plasma and/or cryoprecipitate should be given; if diabetes insipidus is present or other sources of bloodless fluid loss, a crystalloid solution is preferred.

Distributive Shock

Distributive shock is generally associated with dilation of the vascular space, as may occur in advanced inflammation or infection, after spinal cord injury and possibly following brain death. This vasodilation produces a "relative" hypovolemic effect, with low CVP or PAOP, tachycardia, and

increased cardiac output. If hypotension persists after resuscitation with 2 or 3 liters of crystalloid, the OPC should discuss with a physician consultant the use of a vasopressor medication such as norepinephrine or phenylephrine. Given as a continuous infusion, these agents induce vasoconstriction so as to restore MAP.

Cardiogenic Shock

Failure of cardiac contractility may occur in older donors as a manifestation of longstanding congestive heart failure or secondary to acute coronary ischemia related to the primary process causing brain death. Blunt or penetrating trauma to the heart may also cause reduced cardiac output at any age. However, the apparent injury to the donor heart that occurs during the evolution of brain death is more common.

Extensive experimental[9-11] and human[12] data strongly suggest that two important cardiovascular events occur during the final stages of brain death, especially when the intracranial illness or injury progresses rapidly.[13] First, it is generally accepted that patients with significant brain injury of many types release a large amount of catecholamines (epinephrine, norepinephrine, and dopamine), which circulate freely throughout the body.[14] In addition, during the final process of brain herniation a large neuronal discharge may occur from the sympathetic nervous system that produces intense coronary artery vasospasm. This vascular constriction may lead to myocardial ischemia,[15] abnormal function of cardiac β-adrenergic receptors,[16] and production of a myocardial inhibitory protein,[17] all resulting in reduced cardiac contractility. This process often begins with significant hypertension, followed (in from minutes to perhaps an hour) by dramatic hypotension. Secondly, as brain death is completed and the spinal cord is physiologically "disconnected" from higher brain centers, a neurogenic event may occur similar to that observed in primary spinal cord injury. This loss of sympathetic innervation to the vascular system may produce vasodilation and a form of distributive shock (relative hypovolemia).

In addition to these primary changes within the heart, some research[11] has suggested that secondary effects on the myocardium occur because of reduced amounts of circulating thyroid hormone. This hypothesis remains controversial, as similarly injured patients who do not proceed to brain death but have similar changes in circulating thyroid hormones do not develop heart failure.[18]

Medications

Another cause of hypotension that should be considered is the residual effect of medications administered during earlier patient care. These may include diuretics and mannitol, which may produce hypovolemia, or treatment of elevated intracranial pressure with barbiturates, which may reduce cardiac contractility and/or cause vasodilation. Treatment with anticonvulsants rarely causes hypotension, but these medications can be discontinued after brain death.

Treatment Recommendations

The following suggestions presume that the arterial blood pressure is being accurately measured by either standard auscultation, an automatic oscillatory or auscultative blood pressure monitor, or via a properly positioned arterial catheter. It is also assumed that the OPC can request assistance from a physician or other colleague for placement of arterial, central venous, or pulmonary artery catheters and that this procedure(s) will be accomplished quickly. The recommended algorithm for treating blood pressure variations is presented in the Figure and is discussed below:

Hypertension (MAP > 90 mm Hg)

1. If present, titrate any inotropic or vasopressor infusions downward to maintain the MAP at 60 to 70 mm Hg.

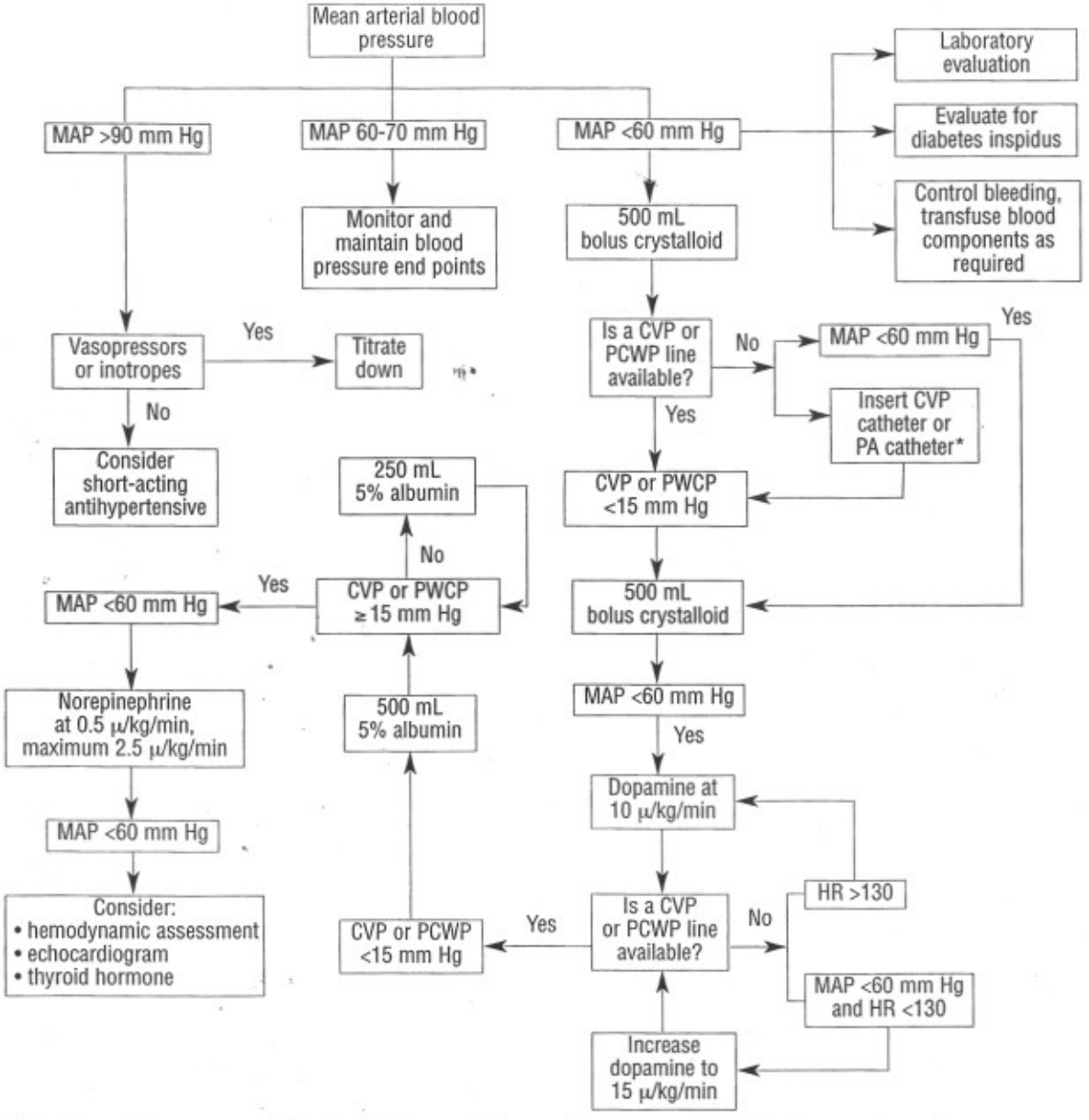
2. Review the medical record for a prior history of hypertension, prior medications, and the blood pressure pattern since admission. Abrupt withdrawal of some antihypertensive medications may lead to "rebound" hypertension.

3. Discuss short-term antihypertensive medications with a physician consultant. A quick-acting agent, such as nitroprusside or esmolol, is preferred.

4. Although the OPC usually does not provide care before brain-death certification, advice may be requested about the moderate-to-severe hypertension which occurs in about 50% of patients during the final stages of brain herniation. This is a difficult situation because the duration of the hypertension is unpredictable and may be quite short. No data exist to prove that harm occurs to donor organs during this period, but it is reasonable to assume that the heart is under considerable stress when attempting to overcome the increased outflow resistance during hypertension. Treatment, if given, should again be with an extremely short-acting medication such as nitroprusside or possibly esmolol, although the possible later hypotensive effects of even this short-acting β-blocker may be of concern. The duration of action of all other commonly available antihypertensive agents is likely to be too long and produce an undesirable effect as the anticipated posthypertensive hypotension evolves. Common practice has been to observe this hypertensive episode without treatment.

Hypotension (MAP <60 mm Hg)

1. Administer 500 mL Ringer's lactate or isotonic sodium chloride solution intravenously as quickly as possible via a central venous catheter, if present.



CVP indicates central venous pressure; HR, heart rate; MAP, mean arterial pressure; PA, pulmonary artery; PCWP, pulmonary capillary wedge pressure
* PA catheter if donor is more than 50 years old or has heart disease.

Blood pressure algorithm

To maximize the infusion rate, use a compression "pressure" bag around the bag of fluid. The treatment goal is to infuse the 500 mL in less than 20 minutes.

2. During those 20 minutes:

a. Confer with the nurse regarding current medications and stop any that may contribute to low blood pressure.

b. Assess urine output. If it is less than 250 mL/hour, measure the glucose concentration in the urine (glycosuria) and a urine specific gravity. Although not discussed here, polyuria can rapidly produce hypovolemia and hypotension. When polyuria is caused by diabetes insipidus, the excessive loss of "free water" via the urine will cause hypernatremia. A large amount of free water in the urine will cause the urine specific gravity to be low, <1.005. In this situation, consider replacing urine output milliliter per milliliter each hour intravenously with a dextrose-free crystalloid, such as quarter-strength isotonic sodium chloride solution. In addition, intravenous desmopressin acetate should be considered to replace the deficient antidiuretic hor-

mone. Aqueous vasopressin is often administered as an infusion or as repeated boluses to replace antidiuretic hormone. However, some authors[19] caution that peripheral arterial vasoconstriction, which may harm donor organs, is greater with vasopressin than with desmopressin. Dextrose is excluded from the infusion fluid because when large volumes are needed, hyperglycemia may occur and cause an osmotic diuresis as glucose is "spilled" into the urine. Therefore, information about blood and urine glucose concentrations is important. If the blood glucose is >250 mg/dL and/or the urine glucose is > 250 mg/dL (2+), dextrose should be removed from any intravenous fluids and treatment with insulin may be considered.

c. Ensure that any external site of bleeding is controlled. Depending upon local OPO policy and practice, administer blood if the hemoglobin and hematocrit are low (<9 gm/dL and <30%, or as defined by OPO policy). If ongoing or recent bleeding is or has been present, evaluate coagulation tests (prothrombin and partial thromboplastin times) and platelet count. Correct these parameters if abnormal. Blood and/or coagulation factors (fresh frozen plasma, liquid plasma, cryoprecipitate, or platelets) should be infused rapidly.

d. Obtain laboratory measurements important for cardiac function and assessment of intravascular volume. These include ionized calcium, magnesium, phosphorous, potassium, arterial blood gas analysis, hemoglobin/hematocrit, serum glucose, chloride and bicarbonate, and the serum urea nitrogen–to–creatinine ratio (if >10:1, this may suggest intravascular dehydration). Plan to correct electrolyte concentrations below normal limits and assess the acid-base status with the physician consultant.

3. Determine whether CVP or PAOP is known. If either is <15 mm Hg after the initial 500 mL infusion, repeat the infusion. One study[20] reports a worsening of oxygenation after crystalloid infusion to CVP >10 mm Hg. If no CVP or PAOP is available but the MAP remains <60 mm Hg, repeat the infusion and proceed to secure central venous access. We recommend placing a central venous "introducer" in either an internal jugular or subclavian vein. This catheter allows CVP measurement and provides direct access for a pulmonary artery catheter if needed later. If the donor is more than 50 years old and/or has a history of heart disease or prior cardiac surgery, request placement of a pulmonary artery catheter if the MAP remains <60 mm Hg after the second infusion of fluid.

4. If the MAP is <60 mm Hg after the second infusion and while a central venous or pulmonary artery catheter is being placed, begin a dopamine infusion at 10 µg/kg/min. Observe the heart rate carefully, as dopamine often causes tachycardia.

The above steps should be accomplished within 30 to 45 minutes of the time the OPC begins care or if hypotension occurs at any time. *Don't waste time.*

5. If the CVP or PAOP is <15 mm Hg, give 500 mL 5% albumin over 20 minutes. If catheter placement is delayed or in progress on dopamine, the MAP remains <60 mm Hg, and the heart rate is <130 beats per minute (bpm), increase dopamine to 15 µg/kg/min. If the heart rate is >130 bpm, maintain dopamine at 10 µg/kg/min and proceed as below.

6. Maintain CVP or PAOP >15 mm Hg with repeated infusions of 250 mL of albumin every 20 minutes. If no CVP or PAOP can be obtained and the MAP is <60 mm Hg, continue these albumin infusions.

7. If MAP remains <60 mm Hg 15 minutes after increasing the dopamine to 15 µg/kg/min, or if the heart rate is >130 bpm and CVP or PAOP is >15 mm Hg or albumin infusions are being given, begin a norepinephrine infusion at 0.5 µg/kg/min. Advance the norepinephrine infusion by .5 µg/kg/min each 10 or 15 minutes until the MAP is >60 mm Hg or an infusion rate of 2.5 µg/kg/min is reached. Only the smallest amount of dopamine or norepinephrine needed to maintain the MAP should be used, as both may produce vasoconstriction in donor organs, thereby reducing needed blood flow.

8. If the MAP remains <60 mm Hg on maximum doses of dopamine and norephinephrine, discuss with the physican consultant other diagnostic (eg, hemodynamic profile measurement,[21] echocardiogram[22]) or therapeutic (eg, thyroid hormone or vasopressin administration) options. As noted earlier, circulating forms of thyroid hormone are decreased in many forms of medical illness, trauma, and surgical stress.[18] Thyroid hormone may increase myocardial contractility independent of β-receptor stimulation,[23] possibly by sensitization of calcium-dependent cardiac contractile proteins.[24] It has been strongly suggested by some that triiodothryronine be administered to the hypotensive donor,[25] although other authors disagree.[18,26,27] The use of thyroid hormone during donor care, therefore, should be a protocol-based decision made by the OPO. Similarly, intravenous vasopressin has been advocated to improve or stabilize MAP,[25,28,29] but this therapy is not widely used and should also be addressed as an OPO protocol.

As the amount of hemodynamic support is increased in support of the blood pressure, efforts should simultaneously increase to expedite the other processes necessary to more quickly move the donor to the operating room for organ removal. Complete loss of organs and a reduction in the quality of transplanted organs may both result from persistent hypotension.

Summary

The most important priority challenging the OPC

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CE

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Management of variations in blood pressure during care of organ donors

Objectives
1. Discuss how to calculate mean arterial pressure.
2. Discuss the treatment of hypotension.
3. Discuss the treatment of hypertension.

Mark your answers clearly in the appropriate box. There is only one correct answer. You may photocopy this form.

1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
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❑b	❑b	❑b	❑b	❑b	❑b	❑b	❑b	❑b	❑b
❑c	❑c	❑c	❑c	❑c	❑c	❑c	❑c	❑c	❑c
❑d	❑d	❑d	❑d	❑d	❑d	❑d	❑d	❑d	❑d

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during donor care is to maintain optimal nutrient blood flow to donor organs. Failure to do so risks loss of organs and/or removal of organs that may perform less well in the recipient. Hypotension is a common sign that organ perfusion is at risk. The necessarily rapid response by the OPC should ensure that blood pressure is being correctly measured, discover the probable cause(s) of hypotension, provide proper vascular access for monitoring or therapy, and implement an appropriately titrated treatment plan. The guidelines provided in this article are recommended to achieve those objectives.

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CE Test Questions

Management of variations in blood pressure during care of organ donors

1. Which of the following donors could benefit from an arterial catheter?
   a. A 20-year-old with a mean arterial pressure of 80 mm Hg over the last 8 hours
   b. A 40-year-old with systolic blood pressure of 80 mm Hg for the last 6 hours
   c. An 18-year-old with a mean arterial pressure of 70 mm Hg
   d. A 60-year-old with systolic blood pressure of 160

2. Mean arterial pressure can be calculated by the following formula:
   a. 1/3 (systolic – diastolic) + diastolic
   b. 1/3 diastolic + (systolic – diastolic)
   c. 1/3 systolic + (systolic – diastolic)
   d. 1/3 systolic + diastolic + 5

3. Which of the following treatments would be recommended for relative hypovolemia?
   a. Inotropes, blood replacement
   b. Crystalloids, nitrates
   c. Crystalloids, vasopressors
   d. Fresh frozen plasma, colloids

4. What are symptoms of brain herniation?
   a. Hypotension then hypertension
   b. Normal blood pressure, hypotension
   c. Hypertension, normal blood pressure
   d. Hypertension, hypotension

5. For a hypertensive donor, what treatment is recommended?
   a. Elevate head of bed, administer inotropes
   b. Modified Trendelenburg position, administer nitrates
   c. Vasodilator, decrease vasopressor
   d. Increase vasopressors, crystalloids

6. For a hypotensive donor with a mean arterial pressure of 40 mm Hg, what is the first treatment of choice?
   a. Vasopressors
   b. Vasopressin
   c. Implement central venous pressure readings
   d. Bolus with lactated Ringer's solution

7. What is the treatment for diabetes insipidus?
   a. Desmopressin, replace each mL urine with 1 mL quarter strength isotonic sodium chloride solution
   b. Vasopressin, replace each mL urine with 1 mL 5% dextrose in water
   c. Measure urine specific gravity, bolus with 5% dextrose in water
   d. Measure serum osmolality, administer colloids

8. Which of the following hypotensive donors would benefit from insertion of a pulmonary artery catheter?
   a. 20-year-old trauma victim
   b. 40-year-old donor with intracranial bleeding
   c. 60-year-old donor with coronary artery disease
   d. 48-year-old donor with chronic obstructive pulmonary disease

9. After a 500-mL bolus of Ringer's lactate solutions, the donor's central venous pressure is 8 mm Hg and the mean arterial pressure remains less than 60 mm Hg. What should be done next?
   a. Insert a pulmonary artery catheter.
   b. Measure hemoglobin and hematocrit.
   c. Begin vasopressin.
   d. Repeat bolus.

10. After boluses of Ringer's lactate solutions, the donor remains hypotensive and tachycardic at 110 beats per minute. What therapy should be initiated?
    a. Norepinephrine drip and colloids
    b. Blood transfusion and dopamine
    c. Dopamine and 5% albumin
    d. Repeat bolus and start a neosynephrine drip

Abnormalities in fluids, electrolytes, and metabolism of organ donors

Abnormal serum concentrations of electrolytes, hormones, and glucose are common throughout donor care. The organ procurement coordinator must properly interpret and plan treatment for these changes to prevent intracellular dysfunction in donor organs. This article describes abnormalities in magnesium, phosphorous, calcium, sodium, potassium, and glucose levels; polyuria; and thyroid and pituitary changes. Their potential consequences are discussed, and recommendations for treatment options are presented. (*Progress in Transplantation*. 2000;10:88-96)

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Notice to CE enrollees:
A closed-book, multiple-choice examination following this article tests your ability to accomplish the following objectives:

1. Describe clinical implications of fluid and electrolyte imbalances in organ donors.
2. Discuss the physiological effects of hormonal and glucose abnormalities in organ donors.
3. Identify nursing interventions that address abnormal fluid, electrolyte, and metabolic processes.

Abnormalities in fluids, electrolytes, and metabolic homeostasis are commonly encountered during donor care (Table 1).[1-7] These changes may result from treatment given during earlier patient care, from the neurological process leading to hospital admission, or from the effects of brain death. For example, plasma free-water is often reduced to produce a hypernatremic hyperosmolar condition during treatment of intracranial hypertension after head trauma; hyponatremia due to the syndrome of inappropriate antidiuretic hormone secretion or "cerebral salt-wasting" may follow subarachnoid hemorrhage; and donors may develop central diabetes insipidus, leading to a severe free-water deficit and hypernatremia after brain death.

However, as Table 1 illustrates, these abnormalities are not universal among donors, which shows that the organ procurement coordinator (OPC) must screen

Table 1 Incidence of metabolic abnormalities among donors

Condition	Incidence, %
Hypernatremia	59[1]
Hyponatremia	38[1]
Hyperkalemia	39[1]
Hypokalemia	91[1]
Hypophosphatemia	66[2]
Polyuria	66[1]
Diabetes insipidus	9-87[1,3-7]
Low growth hormone	0, 3[5,8]
Low adrenocorticotropic hormone	0, 16[5,6]
Low thyroid stimulating hormone	0, 48, 23[5-7]
Low follicle stimulating hormone	5[5]
Low lutenizing hormone	5[5]
Low serum cortisol	23[5]
Low triiodothyronine	62, 81[6,7]
Low thyroxine	9, 29[6,7]

each donor and often titrate subsequent treatment using serial laboratory measurements. The clinical effect of individual abnormalities may be readily apparent (eg, hypotension and arrhythmias due to hypocalcemia, etc) or silent. Indeed, many changes in electrolytes, hormones, and fluid balance alter intracellular biochemical processes that may not be demonstrable clinically. Therefore, the recommendations presented here assume that therapy(ies) should be directed toward maintaining these physiological indicators within normal laboratory limits.

Solutes and Solvents

The human body is structured within a water-based medium, the solvent. The total body water (TBW) is divided into the intracellular (IC) (60% of TBW) and extracellular (EC) (40% of TBW) spaces. EC spaces are further subdivided into the intravascular (plasma) (8% TBW), interstitial (around the cells but outside capillaries) (28% TBW), and transcellular (4% TBW) areas.[8] Electrolytes, glucose, hormones, and other substances are dissolved throughout the TBW as solutes. They are distributed unevenly among the various compartments of the TBW because of a variety of cellular membrane permeability differences, active ionic pumps, molecular size considerations, osmolar gradients, and electrochemical or hormonal factors. Electrolyte concentrations, in particular, are often very different depending on the fluid compartment being analyzed. Sodium, chloride, and bicarbonate are largely detained in the EC spaces, while potassium, magnesium, calcium and phosphorous are predominantly IC ions. Although it may be possible to calculate the total quantity of these substances present in the body, clinical decisions are generally based on concentrations found in plasma or serum. However, because of the different distribution of ions within the TBW spaces, sampling from the plasma compartment of the EC spaces does not necessarily provide sufficient information about total body reserves of all these substances. For example, because 98% of total body sodium is evenly distributed throughout the EC spaces, a plasma sample provides a satisfactory estimate of sodium stores. However, because < 1% of total body potassium is within the EC spaces, estimating total body potassium deficits based on serum potassium concentration is imprecise at best. This sampling variable directly influences how treatment is implemented for abnormalities in fluids and electrolytes.

Because most clinical decisions are based on the concentration of a specific solute of interest within the water-based plasma solvent, a concentration abnormality may represent a change in either the amount of the solute itself or the quantity of solvent in which it is dissolved. Therefore, additions to or losses from either or both of the solute and solvent amounts must be considered by the OPC. For example, hypernatremia after brain death may be due to a slight increase in total body sodium because of administration of isotonic sodium chloride solution during earlier therapy, a loss of free water because of diabetes insipidus, or a combination. In general, when abnormalities in both the solvent and solute might be present, the apparent predominant deficit in solute or solvent needed to return the electrolyte value to the normal range is treated. For example, the free-water deficit is calculated in response to hypernatremia, while the sodium deficit is calculated in hyponatremia. Hospital laboratories establish normal concentration values that may vary slightly between hospitals, depending on testing methods. Analysis and treatment of abnormal results should be guided by the normal laboratory values in the facility where the donor care is provided. Information from the medical record, laboratory, and bedside personnel should also be considered to determine if solute or solvent changes occurred. The frequency of laboratory testing for electrolytes or other substances is highly variable, depending on the individual donor's physiologic status. In general, the distribution of any administered electrolyte or glucose throughout its respective TBW compartment can be considered complete 30 minutes after its infusion, so repeated testing will reflect the treatment given. Routine monitoring of electrolytes each 2 to 4 hours is usually sufficient for the stable donor.

Osmolality influences the movement of free water between TBW spaces. As a difference (gradient) in the osmolality between TBW spaces develops, water generally moves into the space containing the higher osmolality to achieve osmolar equilibrium. Plasma osmolality reflects the number of molecular particles restricted in their distribution within the plasma space[8] and is measured in units of milliosmoles (mOsm) per liter of plasma water (mOsm/L) (normal range: 280-290 mOsm/L).[9] Plasma osmolality can be closely estimated from the equation[10]

$$mOsm = 2(Na) + (SUN \div 2.8) + (glucose \div 18)$$

where SUN is serum urea nitrogen. This equation emphasizes the importance of serum sodium and its corresponding anions (Cl and HCO_3) in determining osmolality. Hyperglycemia also significantly contributes to the creation of an increase in plasma osmolality and the potential for a gradient favoring movement of water into the plasma space. SUN is also important in contributing to plasma osmolality, but because urea freely diffuses into other fluid compartments, SUN contributes less to the development of osmolar gradients.

A high plasma osmolality (hyperosmolality) indicates a larger amount of plasma molecular particles

relative to the water solvent present. This condition produces an "attractive" force for water from adjacent fluid compartments to move into the space having a higher osmolality. Thus, osmolar differences (gradients) between TBW compartments cannot normally exist for very long, as free water moves quickly into compartments of hyperosmolality to equalize the osmolality. Creation of a hyperosmolar gradient between the plasma and brain tissue using mannitol, isotonic sodium chloride solution, and diuretics is often attempted during treatment of increased intracranial pressure to reduce cerebral edema. The residual plasma hyperosmolality will usually persist after brain death and during donor care. This hyperosmolality may maintain or promote the movement of free water from the IC to the EC spaces throughout the body, including from cells within donor organs. If IC water is substantially reduced, alteration of IC enzymatic or other functions may occur and limit organ survival. Similarly, plasma hypo-osmolality may lead to excessive IC free water, which can also alter important structures and/or functions within donor organs. It is appropriate, therefore, to restore normal plasma osmolality through manipulation of the plasma free water.

High urine output (polyuria) occurs commonly during donor care and affects both solute and solvent amounts. Uncontrolled or uncompensated polyuria will rapidly produce profound hypovolemia and hypotension and will place donor organs at high risk for injury. Factors which may contribute to polyuria include hypothermia, residual mannitol or diuretic effect, hyperglycemia, and a "physiological" diuresis whereby accumulated excess fluids are excreted. The 2 most common causes are hyperglycemia and diabetes insipidus.

Although some experimental animal data show low insulin levels after brain death[11] that might contribute to high serum glucose concentrations, this finding has not been confirmed in humans.[12] Hyperglycemia usually results from infused glucose and/or "relative" insulin resistance due to elevated circulating "stress" hormones such as cortisol, glucagon, and catecholamines. When the serum glucose exceeds about 200 mg/dL, excretion of glucose occurs (spills) into the urine (glycosuria) and can be quantified by laboratory measurement or estimated by a bedside "dipstick" method. Glycosuria above 250 mg/dL (2+ dipstick) may contribute to polyuria as an "osmotic diuretic." The resulting diuretic effect will increase electrolyte loss via the urine but will cause an even greater loss of free water.

Central diabetes insipidus occurs because of decreased or absent antidiuretic hormone following loss of hypothalamic or pituitary gland interaction after brain death. Circulating vasopressin (antidiuretic hormone) normally controls the absorption of free water from the urine. The absence of vasopressin, therefore, allows very large quantities of urinary water to be excreted and may rapidly produce intravascular hypovolemia and hypotension. Because the urine contains some electrolytes, both solute and solvent changes occur. However, because of the greater loss of water, a resultant concentration of serum electrolytes occurs. This is especially noted as hypernatremia because of the dual effect of increasing sodium absorption by the kidney as the donor becomes hypovolemic and experiences excessive free water loss. In addition to hypotension, severe hyperosmolality and its consequences, including reduced donor organ viability, may result as diabetes insipidus continues.

Electrolytes

The physiological function of electrolytic ions in general depends on their absolute concentration within the IC or EC spaces where each is distributed. In addition, the relative concentration of some ions (eg, sodium, potassium, calcium) across the cell membrane is also important. Electrolytic ions have various roles in cellular physiology: they are catalysts to facilitate many IC biochemical reactions, they are direct participants in energy-generating processes, they maintain the transmembrane resting potential on all cells, they create and propagate transcellular action potentials, they create the coupling of the bioelectrical stimulation and mechanical muscle contraction in the heart, etc. Maintaining optimal electrolytic concentrations is, therefore, an important goal in caring for all donor tissues.

Table 2 lists representative normal values and potential consequences of abnormal electrolyte concentrations of donors. Note that other effects expected in patients, such as neurological, muscular, gastrointestinal, or respiratory changes, which do not apply after brain death, have been omitted.

Metabolic Considerations

Significant changes in other metabolic parameters also may be caused by the primary injury or illness or as a consequence of brain death:

Glucose. as previously discussed, several factors may contribute to hyperglycemia. The consequences of hyperglycemia result largely from the hyperosmolality produced and the resulting effects on IC free water and polyuria.

Hormones. The important control of the hypothalamus over the pituitary gland's production of several hormones is usually lost after brain death, although considerable variation is present, as shown in Table 1.[5] Loss of some of these hormones from the anterior portion of the pituitary gland (eg, follicle stimulating hormone, lutenizing hormone) is of no clinical importance during donor care. Reduced amounts of corticotropin and the resultant decrease in circulating corticosteroids remain controversial. Plasma cortisol has been reported

Table 2 Abnormalities in electrolytes of donors

Electrolyte, reference range*	Abnormality	Comment/consequences†
Phosphorus[13] .89–1.44 mmol/L (2.5–4.5 mg/dL)		Predominantly an IC ion; 15% of total body phosphorus in EC spaces; laboratory measurement is of phosphate.
	Hyperphosphatemia	Rare in donors. Usually suggests advanced or chronic renal failure, but may occur with severe muscle or red blood cell breakdown and acidosis; may contribute to hypocalcemia and its effects, but otherwise has few consequences.
	Hypophosphatemia	Common. Results from loss of phosphorus from kidneys (diuretics, osmotic diuresis, acetazolamide) or gastrointestinal tract, respiratory alkalemia, or during dextrose or insulin administration; may cause decreased cardiac contractility, red blood cell and muscle breakdown (rhabdomyolysis), low platelets, reduced white blood cell function.
Magnesium[13] .75–.95 mmol/L (1.5–1.9 mEq/L)		Predominantly an IC ion; 1% of total body magnesium in EC spaces.
	Hypermagnesemia	Rare in donors. Usually from kidney failure; may cause hypotension, electrocardiogram changes, and bradycardia.
	Hypomagnesemia	Common. Ionized magnesium testing is becoming available and may show low levels in children even if total magnesium is normal.[14] Causes: magnesium loss from kidneys after diuresis, loss from gastrointestinal tract. Hypocalcemia and hypokalemia often present; may worsen glucose intolerance and hyperglycemia; may cause dangerous dysrhythmia, electrocardiogram changes; may increase likelihood of toxic effects from digitalis.
Calcium[15,16] ionized 1.0–1.4 mmol/L (4.0–5.6 mg/dL) total 2.12–2.62 mmol/L (8.5–10.5 mg/dL)		98% total body calcium is in bone; present in serum bound to protein or other anions and as the ionized calcium which is the biologically active form; when available, only measure ionized calcium.
	Hypercalcemia	Rare. Usually from preexisting parathyroid gland disorder, kidney failure, malignancy, or use of thiazide diuretics; may increase polyuria or increase potential for toxic effects from digitalis.
	Hypocalcemia	Common. Causes: chronic kidney failure, parathyroid disease, rhabdomyolysis, and sepsis. Alkalemia increases caldium-protein binding and lowers ionized calcium; occurs with hypomagnesemia; may produce dangerous dysrhythmia, decreased cardiac contractility, and hypotension.
Potassium[17,18] 3.5-5.0 mmol/L (3.5–5.0 mEq/L)		IC ion; < 1% total body potassium in EC spaces; movement from EC to IC spaces promoted by insulin, catecholamines, alkalemia, and β-2 receptor adrenergic medications.
	Hyperkalemia	Unusual. Causes: the reverse of above factors (especially acidosis) moving potassium into cells, preexisting kidney failure, adrenal failure (rare), red blood cell lysis or massive transfusion (rare).
	Hypokalemia	Common. Possible causes noted above (especially alkalosis), diuretics, polyuria from any cause, concomitant hypomagnesemia; may produce arrhythmia, increase potential for toxic effects from digitalis.
Sodium[9] 138–142 mmol/L (136–146 mEq/L)		The major EC spaces cation, nearly balanced by EC spaces chloride and bicarbonate; responsible for most of EC spaces' osmolality. Controversial harmful effect of donor hypernatremia upon recipient liver function and survival.[19]
	Hypernatremia	Common. Causes: prior dehydration and sodium administration, free-water loss from diuretics or partial or complete diabetes insipidus. Produces EC spaces hyperosmolality.
	Hyponatremia	Uncommon. Causes: kidney salt-wasting or the syndrome of inappropriate antidiuretic hormone secretion, factitial hyponatremia, thiazide diuretics, hypovolemia, preexisting congestive heart failure, cirrhosis. Produces hypo-osmolality.

EC indicates extracellular; IC, intracellular.

* Conventional units are given in parentheses.

† Limited to those present after brain death. Other neurological, gastrointestinal, or respiratory consequences which might occur prior to brain death are omitted.

as low after brain death in animals,[11] but not in humans.[6,12,13] The posterior portion of the pituitary gland produces vasopressin and, as previously discussed, the loss of vasopressin leads to diabetes insipidus.

Two other proposed hormonal changes not directly under pituitary or central nervous system control include reduced production of insulin, noted in animals[11] but not found in humans,[12,20] as previously discussed, and alteration in the conversion and availability of thyroid hormone. The tissue conversion of thyroxine to triiodothyronine is altered in a large variety of medical, traumatic, and surgical conditions. This change does not produce recognizable clinical consequences and is termed the "sick euthyroid syndrome" or the "euthyroid sick syndrome." It is characterized by low triiodothyronine, low or normal thyroxine, normal thyroid stimulating hormone, and increased reverse-triiodothyronine blood levels. Such changes have been well documented in humans after brain death[6,7,11,12] but do not differ from changes in similarly injured, but not brain dead, patients.[12] Administration of thyroid hormone has been advocated by some authors[11] as part of routine donor care or during treatment of hypotension, although other authors disagree.[6,7,12] Excessive intravenous (IV) thyroid hormone may produce arrhythmias, hyperthermia, hypotension, and increased cellular oxygen demands.

Cytokines and acute-phase reactive proteins have also been evaluated in donors after brain death, and some of these postinflammatory proteins are elevated.[21] Although the cytokine most elevated, interleukin-6, may cause some biochemical or hemodynamic changes, no direct manipulation of its production or action is proposed.[21]

Recommendations for Donor Care

Assessment

• Review the medical record to determine the most recent administration of mannitol or diuretics, type and amount of current IV fluids, and urine output.

• If not measured within the last 2 hours, obtain measurements for serum sodium, potassium, chloride, bicarbonate, magnesium, ionized calcium, phosphorous, glucose, and serum osmolality, plus urine specific gravity (if urine output > 200 mL/h).

Interventions

• Hyperphosphatemia, hypermagnesemia, and an elevated ionized calcium level (but < 2.0 mmol/L) do not require specific therapy other than to discontinue further administration of the ionized calcium. An ionized calcium level > 2.0 mmol/L should be discussed with a physician consultant.

• Hyperkalemia (> 3 mmol/L [6 mEq/L]) may require treatment if associated with arrhythmias and should be discussed with a physician consultant. Therapy is usually directed toward translocation of potassium from the EC spaces into the IC spaces by IV administration of sodium bicarbonate (1 prepackaged syringe, 44-50 mEq), insulin (10-15 units of regular insulin) and dextrose (1 prepackaged syringe of 50% dextrose). Calcium (1 ampule of 10% calcium gluconate given slowly) may be necessary to directly counter arrhythmia production in the heart.

• Because phosphorus, magnesium, calcium, and potassium are primarily IC ions and thus poorly sampled in serum testing, actual total body or EC space deficits for these ions cannot be reliably calculated when the serum concentrations are low. Therefore, replacement amounts should be ordered and serum levels rechecked each 2 to 4 hours. Most hospitals have policies regarding the amount and rapidity of IV electrolyte infusion. Those policies should be followed. In all cases, electrolyte replacement should be IV. Suggested replacement options include

Phosphorous: 30 mmol potassium phosphate IV over 2 to 3 hours, or 30 mmol sodium phosphate IV over 2 to 3 hours (preferred if serum potassium > 4.0 mmol/L).

Magnesium: 2 to 4 g magnesium sulfate IV over 2 to 3 hours. Severe dysrhythmias associated with low magnesium may, in emergency, be treated with 1 to 2 g magnesium over 1 to 2 minutes.[22]

Calcium: one 10-mL ampule 10% calcium gluconate via slow IV bolus over 10 minutes (emergency administration may be as quickly as over 4 minutes[15]); one 10-mL ampule 10% calcium chloride via slow IV bolus over 15 minutes.

Potassium: 20 to 40 mmol potassium chloride via a central venous catheter over 1 hour.

• Hypernatremia should initially be treated by replacing current IV fluid with a more dilute (hypotonic, greater free water) option, such as 0.5N or 0.25N sodium chloride solution. Dextrose is often omitted because of current or potential concern about causing hyperglycemia. Attention should also be given to the calculated serum osmolality (see earlier) versus the measured osmolality from the laboratory. If the measured osmolality is > 10 mOsm/L higher than the calculated osmolality, another osmotically active substance (usually mannitol) is present that will likely be excreted or metabolized quickly, thus resolving the osmolar difference.[10] However, if the serum sodium level is > 160 mmol/L, additional free water as a rapid infusion should be considered and discussed with the physician consultant. This may be particularly useful if the donor is hypotensive. The water deficit is approximated from the formula below:

Donor's current Na(y) = 140(.6 × donor's usual weight in kg)

Solve for y, then subtract y from (.6 × donor's usual weight in kg)

The resulting value, in kilograms, equals the liters of free water needed. Replace half this amount with 0.25N sodium chloride solution as quickly as possible. Pure water must never be given intravenously. For example, if your 80-kg donor has a serum sodium concentration of 164 mmol/L,

$164(y) = 140(.6 \times 80)$

$y = 40.9$ kg or L

$48 - 41 = 7$ L water deficit

Infuse about 3.5 L of 0.25N sodium chloride solution over 2 to 3 hours (or more rapidly if the donor is hypotensive), then reassess the serum sodium. If hypernatremia is accompanied by polyuria, consider treatment with desmopressin, as discussed below.

• Treatment of hyponatremia is usually not necessary unless the serum sodium is < 125 mmol/L. The measured sodium concentration must first be considered relative to the simultaneous serum osmolality and glucose measurements. Factitial or "pseudo-" hyponatremia represents dilution of the sodium within the serum by high concentrations of lipid, abnormal protein, or glucose. When the serum glucose is > 16.7 mmol/L (300 mg/dL) and the serum osmolality is normal or high, a "corrected" serum sodium should be calculated.[10]

Corrected Na = reported Na + [1.6 × each 5.6 mmol/L (100 mg/dL) glucose above 500 mmol/L (100 mg/dL)]

For example: Laboratory results include Na 120 mmol/L; osm 275 mOsm/L; glucose 33.3 mmol/L (600 mg/dL). The "corrected" serum sodium would be $120 + (1.6 \times 5) = 128$ mmol/L, and no sodium infusion is needed. However, if sodium replacement is needed, begin isotonic sodium chloride solution and discuss with a physician consultant. A more concentrated sodium chloride solution (3%) is available. Either solution may then be considered to replace half the sodium deficit, as calculated from the formula below:

mmol Na deficit = (140 – donor Na) × (.6 × usual donor weight in kg)

• Hyperglycemia (> 13.9 mmol/L [250 mg/dL]) should initially be treated by removal of dextrose from IV fluids. Discontinue any enteral feedings or corticosteroid medication. If the donor is receiving parenteral nutrition ("hyperalimentation") containing > 10% dextrose, replace it with a 5% dextrose infusion. This continuing dextrose is needed to avoid hypoglycemia due to high circulating insulin after the parenteral nutrition is stopped. If the glucose remains > 13.9 mmol/L (250 mg/dL) after 2 hours, discuss possible insulin therapy with a physician consultant. Hypoglycemia (< 4.2 mmol/L [75 mg/dL]) is only rarely encountered but should be treated with a 5% or 10% dextrose infusion.

• Polyuria should be quantified by hourly urine output measurements. If mannitol or other diuretics have been given recently, their effect may last for several hours. Replace intravascular fluid volume as needed to maintain blood pressure. Assess glycosuria, as discussed earlier, and discontinue glucose infusions if glycosuria is present. Urine specific gravity estimates urinary dilution and hence the relative amount of free water being excreted. The specific gravity of pure water is 1.000. If the donor's urinary specific gravity is low (< 1.005), it can be assumed that a significant amount of free water is being excreted. If the serum sodium is also high, diabetes insipidus is likely. Begin replacement of urine each hour with 0.25N sodium chloride solution (no dextrose) and consider IV administration of 1 to 2 µg desmopressin every 2 hours if urine output exceeds 300 mL/h. The use of desmopressin is controversial, as some data suggest it may reduce kidney function after kidney transplantation,[23] but other authors disagree.[4,24] Aqueous vasopressin may be given instead as an IV bolus (5-10 units[9]), followed by an infusion titrated to maintain urine output between 200 and 300 mL/h. Concern about the greater vasoconstrictive properties of vasopressin and potential ischemic injury to donor organs compared to desmopressin has been expressed.[4,24] If urine specific gravity is > 1.005 and the serum sodium concentration is < 150 mmol/L, physiologic diuresis may be occurring. Repeat the measurement of serum sodium every 2 hours, and replace fluids only to maintain the arterial blood pressure.

• Routine hormone replacement is not recommended.[6,7,12] Thyroid hormone supplementation as treatment for hypotension that remains unresponsive to inotropic (dopamine, dobutamine) and vasopressor (norepinephrine or phenylephrine) treatment remains controversial but is used by some organ procurement organizations. The suggested[11] hourly IV dose would be 2 to 3 mg triiodothyronine as titrated to the blood pressure, with 100 mg cortisol and 10 to 20 units of insulin.

Summary

The OPC must integrate multiple priorities during donor care. Fluids given to support blood pressure will obviously alter acid-base, electrolyte, and free water solute or solvent concentrations. Similarly, fluids and electrolytes lost during polyuria will influence intravascular volume, blood pressure, and cardiac output. Therefore, no single process during donor care can be completely separated from the greater goal of maintaining an optimal milieu in which donor organs may be supported before removal. These recommendations form only a part of that complex process and significant challenge.

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Abnormalities in fluids, electrolytes, and metabolism of organ donors

Objectives

1. Describe clinical implications of fluid and electrolyte imbalances in organ donors..
2. Describe the physiological effects of hormonal and glucose abnormalities in organ donors.
1. Identify nursing interventions that address abnormal fluid, electrolyte, and metabolic processes.

Mark your answers clearly in the appropriate box. There is only one correct answer. You may photocopy this form.

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❑c	❑c	❑c	❑c	❑c	❑c	❑c	❑c	❑c	❑c	❑c	❑c
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CE Test Questions

Abnormalities in fluids, electrolytes, and metabolism of organ donors

1. Which of the following constitutes total body water?
   a. Intracellular 75%, intravascular 12%, interstitial 10%
   b. Intracellular 60%, intravascular 8%, interstitial 28%
   c. Intracellular 50%, intravascular 20%, interstitial 23%
   d. Intracellular 40%, intravascular 38%, interstitial 26%

2. Which of the following is evenly distributed throughout the extracellular spaces?
   a. Sodium
   b. Calcium
   c. Potassium
   d. Phosphorus

3. Which of the following results in increased plasma osmolality?
   a. Decreased serum chloride
   b. Decreased serum urea nitrogen
   c. Infusion of mannitol
   d. Decreased serum glucose

4. Which of the following serum glucose levels will lead to glycosuria?
   a. 4.7 mmol/L (85 mg/dL)
   b. 7.8 mmol/L (140 mg/dL)
   c. 9.2 mmol/L (165 mg/dL)
   d. 12.5 mmol/L (225 mg/dL)

5. What normally controls the absorption of free water from the urine?
   a. Aldosterone
   b. Urine sodium
   c. Urine glucose
   d. Vasopressin

6. What is the possible effect of diabetes insipidis on donor organs?
   a. Hypertension, leading to poor perfusion
   b. Hypotension and reduced organ viability
   c. Hyperkalemia, leading to dangerous cardiac arrhythmias
   d. No known effect on donor organs

7. Hypophosphatemia has been associated with which of the following problems?
   a. Decreased cardiac contractility
   b. Increased white blood cell production
   c. Glucose intolerance
   d. Increased likelihood of toxic effects from digitalis

8. What is one of the most common causes of hypokalemia in organ donors?
   a. Use of diuretics
   b. Metabolic acidosis
   c. Hypermagnesemia
   d. Decreased urine output

9. Excessive intravenous thyroid hormone has been associated with which of the following?
   a. Hypothermia
   b. Hypertension
   c. Cardiac arrhythmias
   d. Decreased cellular use of oxygen

10. According to the authors, which of the following is a recommended treatment for hyperkalemia in organ donors?
    a. Dialysis
    b. Administration of free water
    c. Administration of insulin and glucose
    d. Administration of mannitol and sodium

11. What is the recommended initial treatment for a 65-kg donor with a serum sodium level of 169 mmol/L?
    a. Infuse 1.5 L hypotonic sodium chloride solution over 2 to 3 hours
    b. Infuse 2.5 L hypotonic sodium chloride solution over 2 to 3 hours
    c. Infuse 3.5 L hypotonic sodium chloride solution over 2 to 3 hours
    d. Infuse 5.0 L hypotonic sodium chloride solution over 2 to 3 hours

12. Which of the following are indicators of diabetes insipidis in potential donors?
    a. Urine specific gravity 1.003, serum sodium 156 mmol/L, polyuria
    b. Urine specific gravity 1.004, serum sodium 135 mmol/L, polyuria
    c. Urine specific gravity 1.010, serum sodium 145 mmol/L, polyuria
    d. Urine specific gravity 1.013, serum sodium 160 mmol/L, polyuria

Maintaining acid-base balance in organ donors

An abnormal blood pH may cause the loss of donor organs through harmful physiological consequences. The organ procurement coordinator must correctly analyze the acid-base abnormality and treat its cause while normalizing the blood pH. We recommend that treatment of acidemia or alkalemia be first directed toward changing parameters on the mechanical ventilator, using the $Paco_2$ to modify blood pH. Thereafter, hydrochloric acid or sodium bicarbonate may be administered to correct the calculated metabolic acid-base deficit. The types of acidosis or alkalosis, dead space effect during mechanical ventilation, base excess, base deficit, and the appropriate evaluation of blood lactate are also discussed as related to the correction of the acid-base status throughout donor care. (*Progress in Transplantation.* 2000;10:98-105)

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Notice to CE enrollees:
A closed-book, multiple-choice examination following this article tests your ability to accomplish the following objectives:

1. Describe the physiological consequences of acid-base abnormalities that are relevant to donor care.
2. Discuss causes of acid-base imbalance common in donors.
3. Identify approaches to treatment of acid-base imbalance that are pertinent to donor care.

Maintaining acid-base balance within the blood and throughout body tissues is an important objective in caring for organ donors. Imbalances in the acid-base status may cause serious effects in cellular function and render the donor organs unsuitable for transplantation. The organ procurement coordinator (OPC), therefore, is frequently required to analyze acid-base derangements and to change or implement treatment to assure that optimal balance is maintained.

-Osis Versus -Emia

The terms *acidosis* and *alkalosis* most correctly refer to conditions of excess acid or alkali within the body's tissue environment. It is often assumed that the acidotic or alkalotic state is uniformly present in all tissues. This is usually not true, as individual tissues or organs may show wide variations in the ways they compensate for an acid-base change initiated elsewhere in the body. Similarly, in some circumstances an individual organ may sustain a local change within that organ, but not throughout the body. For example, head injury may limit adequate circulation to the brain and produce acidosis in the brain without affecting other organs. Therefore, the suffix *-osis* refers to a regional or generalized process that is tissue based.

Acidemia and alkalemia refer to abnormalities in the acid-base status of the blood. The final condition of the blood reflects the acid-base status of the tissues, respiratory function through release of volatile carbon dioxide from the lungs, and the interaction of serum electrolytes and proteins. An acid-base imbalance in the blood is usually reflected by a change in the blood pH. To avoid the influence of regional tissue factors in which a venous blood sample might be obtained, the pH of a sample of arterial blood is used. The arterial pH is normally 7.36 to 7.44 and is measured by a pH electrode in a blood gas analyzer. The pH is a logarithmic calculation of the concentration of hydrogen ions within the arterial blood sample. An arterial pH below normal limits indicates acidemia; alkalemia is present when the pH is above normal.

Altered blood or tissue acid-base balance is always a symptom of the underlying metabolic or respiratory condition(s) that led to the change. However, the resultant change in the acid-base status alone can cause its own symptoms. Therefore, the OPC must not only treat the acidemia or alkalemia directly, but identify and correct its cause(s).

Effects of Acid-Base Imbalance

Those physiological consequences of acid-base abnormalities that are relevant to donor care are listed below. Neurological and respiratory effects that commonly occur in other patients do not apply after brain death.

Alkalemia may produce[1]:

- coronary artery constriction (heart failure or arrhythmias)
- reduced serum ionized calcium (arrhythmias and decreased cardiac contractility)
- decreased serum potassium (arrhythmias, increased ammonia production, and polyuria)
- increased production of lactic and keto acids
- increased binding of oxygen and hemoglobin (possibly reduced oxygen availability to tissues, although this effect is usually offset by regional vasodilation in the tissues)
- reduced serum magnesium and phosphates (arrhythmias)

Acidemia may cause[2]:

- reduced cardiac contractility (especially below pH 7.2), resulting in lower cardiac output
- cardiac arrhythmias
- increased pulmonary artery constriction
- increased blood volume
- reduced blood flow to kidney and liver
- decreased cardiovascular response to endogenous and exogenous catecholamines
- insulin resistance (hyperglycemia that can cause or worsen polyuria)
- elevated serum potassium (arrhythmias)
- decreased glycolytic flux and oxygen consumption by inhibition of phosphofructokinase (decreased cellular energy metabolism)

Analysis of Acid-Base Imbalance

Respiratory Causes

Because the donor has lost the ability to breathe spontaneously, acid-base changes due to hyper- or hypoventilation (ie, respiratory alkalemia or acidemia, repectively) will result from inappropriate settings on the mechanical ventilator. For example, respiratory alkalemia is commonly used to reduce cerebral blood flow or volume during treatment of head injury. If alkalemia is present after certification of brain death, the OPC should be prepared to make the corrective adjustments in ventilatory tidal volume (V_T) or the frequency (rate) (f) so as to increase the $Paco_2$ and restore the pH to normal.

Dissolved CO_2 in the blood, usually measured from an arterial blood specimen as its partial pressure ($Paco_2$), causes acidemia through its interaction with plasma water:

$$CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-$$

The hydrogen ion created by the above reaction lowers the blood pH. Conversely, during hyperventilation, lower amounts of CO_2 (low $Paco_2$) are present, which reduces hydrogen ion availability, thus increasing the pH. In general, the OPC can assume that hyperventilation is present if the $Paco_2$ is less than 35 mm Hg. Hypoventilation should be assumed if the $Paco_2$ is greater than 45 mm Hg.

Case Study. A 58-year-old donor with known coronary artery disease had been treated for increased intracranial pressure prior to brain death. His arterial blood gas analysis shows pH 7.57, $Paco_2$ 24 mm Hg, Pao_2 142 mm Hg, HCO_3^- 20 mmol/L, base excess 0. Rule of thumb: for each acute decrease in the $Paco_2$ by 10 mm Hg, the pH can be expected to increase by 0.08 to 0.1 pH units. Therefore, this donor's arterial blood gas values are consistent with a primary respiratory alkalemia. Frequent premature ventricular contractions are noted on his cardiac monitor. Because the premature ventricular contractions are possibly related to his alkalemia, his hyperventilation should be corrected by adjusting the ventilator, as discussed below.

Carbon dioxide elimination during controlled, volume-limited mechanical ventilation throughout donor care is determined by the variables which define minute alveolar ventilation ($\dot{V}_A$):

$$\dot{V}_A = (V_T - \dot{V}_{DS})f$$

where V_T is tidal volume, f is rate, and $\dot{V}_{DS}$ is dead space ventilation. The term *dead space* applies to areas of the lung where blood perfusion is relatively lower than alveolar gas exchange (ventilation). The effect of this type of ventilation-perfusion abnormality is that less blood that is carrying carbon dioxide passes through pulmonary capillaries from which the carbon dioxide can diffuse into the alveolar gas. Therefore, more carbon dioxide remains in the blood, is circulated through the lung, and returns to the heart and arterial circulation. The result of a high dead space effect, therefore, is carbon dioxide retention and elevation of the $Paco_2$. The retained carbon dioxide also forms hydrogen ions (acid) through its interaction with plasma water, as noted above, resulting in respiratory acidemia.

The OPC can recognize that a high dead space effect is present by comparing the $Paco_2$ as measured from arterial blood gas and the minute ventilation ($\dot{V}_E$)

($V_T \times f$) delivered by the mechanical ventilator. If the delivered minute ventilation is greater than 9 L/min and the $Paco_2$ is higher than 35 mm Hg, some increased $\dot{V}_{DS}$ should be assumed.

Three types of dead space are present during mechanical ventilation:

- Anatomic dead space: non–gas exchanging areas within the trachea and major bronchi. No therapy is available to reduce this type of dead space.
- Mechanical dead space: the segment of ventilator tubing between the endotracheal or tracheostomy tube and the Y-connector of the ventilator tubing circuit. The Y-connector separates the inspiratory from the expiratory portions of the circuit. During the exhalation cycle of the ventilator, the dead space tubing segment fills with CO_2-rich gas emptied from the alveoli. At the start of the next inhalation from the ventilator, the CO_2-rich dead space gas is returned to the distal airways. The reinjected alveolar CO_2 lowers the CO_2 gradient between the pulmonary capillary blood and the alveolar gas, which is the driving force for CO_2 diffusion. The effect of mechanical dead space, therefore, is to decrease the diffusion of CO_2 from the blood, promoting CO_2 retention in the donor circulation and elevation of the $Paco_2$. The length of this tubing segment and, hence, the amount of mechanical dead space is usually small. However, the respiratory care practitioner can often reduce the tubing length further as one way to reduce the $Paco_2$.
- Physiological dead space: the largest component of abnormally high $\dot{V}_{DS}$ and may result from a variety of inflammatory, traumatic, or other abnormalities in the lung or cardiovascular system. One subcategory of physiological dead space occurs when high airway pressure during mechanical ventilation impairs blood flow through the lung or when inadequate pulmonary blood flow occurs because of systemic hypovolemia or impaired cardiac output. This subcategory should be suspected if the $Paco_2$ is elevated and the peak airway pressure is above 40 cm H_2O or the donor's systolic blood pressure is less than 100 mm Hg or requires inotropic or vasopressor support. To reverse this form of physiological dead space, the overall goals are to improve cardiac output and/or increase intravascular volume and/or reduce the peak and mean airway pressures. Discussion between the OPC and medical consultant will be helpful in planning and implementing such complex therapy.

Case Study. An 18-year-old donor has received a lethal head injury and severe chest trauma in an accident. Patient data: V_T 800 mL; f 16; $\dot{V}_E$ 12.8 L/min; heart rate 147 bpm; blood pressure 100/56 mm Hg; peak airway pressure 48 cm H_2O; arterial blood gas values: pH 7.20, $Paco_2$ 60 mm Hg, Pao_2 137 mm Hg, HCO_3^- 26 mmol/L. The donor's acidemia with hypoventilation (elevated $Paco_2$) must be caused by increased $\dot{V}_{DS}$ (note high $\dot{V}_E$—normal is about 8 L/min). Her chest injury has caused poor lung compliance, resulting in high airway pressure. She has tachycardia and low blood pressure, perhaps related to low intravascular volume. Rule of thumb: for each acute increase of 10 mm Hg in the $Paco_2$, expect the pH to fall by 0.08 to 0.1 and the bicarbonate to increase by 1 mmol/L. Although the donor's arterial blood gas is consistent with a primary respiratory acidemia, her $Paco_2$ may not respond to ventilator changes until the blood flow (perfusion) to her lungs is improved, thus reducing her physiological dead space. Therefore, the OPC must investigate the cause of her hypotension as ventilator adjustments are made to lower the $Paco_2$.

Metabolic Causes

Changes in organ, tissue, and cellular function may lead to acidemia or alkalemia in patients before and after brain death. In general, the OPC can use the concentration of bicarbonate measured as part of the electrolytes or calculated when arterial blood gases are analyzed to evaluate the presence and/or severity of a metabolic component to the acid-base imbalance. Bicarbonate values above 28 mmol/L indicate metabolic alkalosis; measurements below 20 mmol/L indicate metabolic acidosis.

Another indicator of the metabolic acid-base status of the plasma space is the base excess or base deficit reported as part of the arterial blood gas analysis. The base excess and deficit are the calculated amounts of strong acid or base which should be added to the blood to return the pH to normal, when adjusted for a normal $Paco_2$. The base excess and deficit are normally zero. Each is presented as a number preceded by either a plus or minus sign. The magnitude of the number indicates the severity of the metabolic acid-base abnormality; that is, a large number means a greater imbalance, as more acid or base is needed to correct the pH. The interpretation of the sign differs for the base excess or deficit. A plus sign preceding the base excess indicates an excess of base in metabolic alkalosis, whereas a minus sign before the base excess will be seen in metabolic acidosis. The reverse is used for base deficit: a plus sign before the base deficit indicates a deficit of base or metabolic acidosis; a minus sign before the base deficit represents metabolic alkalosis. The base excess or deficit is, therefore, helpful in estimating the severity and nature of a metabolic acid-base abnormality, which may contribute to an altered blood pH.

Metabolic alkalosis is occasionally encountered during donor care if intravascular dehydration or hypovolemia has occurred, for example after diuretics or mannitol are given as treatment of high intracranial pressure. Metabolic alkalosis may also be caused, worsened, or prolonged by the loss of large amounts of

gastric acid via nasogastric suction, high doses of corticosteroid medication, or decreased serum potassium.

More commonly, the OPC is called upon to diagnose and treat metabolic acidosis. Although many causes of metabolic acidosis are described during patient care, 2 are most common in donors. The first is associated with administration of intravenous isotonic sodium chloride solution,[3,4] commonly administered during shock resuscitation. It is also frequently given during treatment of neurosurgical illnesses or injury when hypernatremia is desired. In this type of metabolic acidosis, the serum bicarbonate will be low as expected, but the serum chloride will be high (reference range, 98-107 mmol/L) due to the increased amounts of chloride in isotonic sodium chloride solution. Isotonic sodium chloride solution contains 154 mmol chloride per liter, much higher than the level normally present in the blood. The difference between the sum of $Na^+ + K^+$ and the sum of $Cl^- + HCO_3^-$, ie, the anion gap (AG), will be normal (8-12 mmol or mEq/L, or less):

$$AG = (Na^+ + K^+) - (Cl^- + HCO_3^-)$$

Other causes of hyperchloremic, normal anion gap metabolic acidosis that may be encountered during donor care include early kidney failure, parenteral nutrition, prolonged hyperventilation, and after use of acetazolamide, in some neurosurgical situations.

The other major category of metabolic acidosis in donors is inadequately treated shock. Shock is physiologically defined as the failure of oxygen delivery to meet the oxygen demands of donor tissues, including potentially transplantable organs. A full review of the 4 major categories of shock (ie, hypovolemic, cardiogenic, distributive, and obstructive) is beyond the scope of this discussion, but is covered elsewhere.[5] In this category of acidosis, the serum bicarbonate is low, base excess is negative, and the chloride is not increased. Therefore, the anion gap is increased. Other causes of an increased anion gap acidosis are uncommon in donor care but include established kidney failure. Ingestion of a variety of drugs or substances, diabetic ketoacidosis, and hyperosmolar nonketotic states produce this form of acidosis in patients who are not donors, but these causes should have been corrected or excluded before brain death testing.

Serum lactate may be elevated in some conditions associated with hypotension, low tissue perfusion, and increased anion gap acidosis. High lactate (reference range, 0.3-0.8 mmol/L for arterial blood; 0.5-2.2 mmol/L for venous blood) has been used as another possible indicator of the severity of shock and tissue hypoxia, although this opinion remains controversial.[6-8] Hyperlactemia, however, also occurs secondary to increased aerobic metabolism, after lung injury, in the presence of high circulating catecholamines, following cytokine induction, and during respiratory alkalosis.[6,9,10] In these conditions, hyperlactemia is not associated with other signs of failed tissue metabolism or acidosis.

Case Study. A 25-year-old donor has been hypotensive since his injury and brain death. His arterial blood gas values: pH 7.29, $Paco_2$ 25 mm Hg, Pao_2 94 mm Hg, HCO_3^- 12 mmol/L, base excess –13. Serum lactate is 6.3 mmol/L. Metabolic acidosis is diagnosed by the low bicarbonate and elevated negative base excess, contributing to his acidemia. The $Paco_2$ has been lowered during prior adjustments of the ventilator, but this amount of acidemia may still impair organ function. While the cause of the donor's hypotension should continue to be diagnosed and treated, additional changes in the ventilator settings are warranted. Further respiratory hyperventilation should be considered only a temporizing measure while the donor's metabolic acidosis is being addressed and steps are being taken to expedite his transfer to the operating room for organ removal.

A confusing situation may arise when the patient has both severe hypoalbuminemia (serum albumin < 25 g/L) and an increased blood lactate concentration.[11] In this circumstance, the anion gap may appear to be normal (8-12 mmol/L or mEq/L) despite lactic acidosis. This paradox occurs because the normal anion gap is produced by the negative charges on albumin and, to a small degree, phosphate. Thus, a patient with a very low serum albumin (eg, 10 g/L) would have a very low baseline anion gap (eg, 2.5 mmol/L or mEq/L). The normal range for the anion gap (8-12 mmol/L or mEq/L) should not be used when profound hypoalbuminemia is present. A patient-specific normal range for the anion gap can be estimated from the patient's albumin and phosphate concentrations:

AG range: 0.2(albumin g/L) + 0.16(phosphate mmol/L) ± 2

or

2(albumin g/dL) + 0.5(phosphate mg/dL) ± 2

As previously noted, other causes of metabolic acidosis or alkalosis are possible secondary to conditions present before or following the illness or injury that led to the patient's brain death. Therefore, all possible causes for metabolic abnormalities should be thoroughly discussed by the OPC and the physician consultant.

Approach to Treatment

As with other aspects of donor care, the acid-base status of the blood may change over time so that repeated evaluations may be necessary. The primary diagnostic tool and process will be analysis of sequential arterial blood gas specimens and titration of interventions so as to normalize the blood pH. Electrolyte

evaluation is also useful when considering the serum chloride, bicarbonate, and anion gap. It should be customary, therefore, for the OPC to request blood gas analysis and measurement of electrolytes as an early part of donor evaluation.

Emphasis should be placed on maintaining the blood pH within the normal range of 7.35 to 7.45. If organs will be removed within a short period, pH adjustments can often be made easily by changing the minute ventilation delivered by the mechanical ventilator, which will alter the $Paco_2$. The $Paco_2$ can be manipulated over a significant range because the donor is not breathing spontaneously. In the absence of a significant dead space effect, the $Paco_2$ will respond quickly to changes in minute ventilation, ie, ventilator tidal volume and/or rate. In general, 20 to 30 minutes between the ventilator change and a follow-up arterial blood gas measurement will be sufficient to reflect the change in $Paco_2$ and pH.

Manipulation of the pH by changing the $Paco_2$ is also safe because the direct physiological effects of carbon dioxide, independent of its influence on the pH, are minimal within the ranges recommended here. The primary effects of a low $Paco_2$ are upon cerebral blood flow in areas of injured brain. This effect, of course, is no longer relevant after brain death. Intentional hypoventilation so as to allow the $Paco_2$ to rise and correct alkalemia may, however, contribute to intracellular acidosis. This is because the carbon dioxide dissolved in the blood as reflected by the $Paco_2$ can easily diffuse into cells where it may contribute to intracellular acidosis. This effect is considered minimal at the $Paco_2$ levels suggested here. Therefore, in the unique situation of donor care, ventilation can be manipulated extensively to facilitate the primary goal of maintaining a normal pH.

When the initial blood gas analysis shows the pH to be outside the normal range, the OPC should first adjust the frequency set on the mechanical ventilator while maintaining the tidal volume at 10 mL/kg of donor body weight per breath. The rate should be increased to raise minute ventilation, lower the $Paco_2$, and elevate the pH. A slower rate will achieve the reverse effect. It is not possible to predict precisely how much of a change in the ventilator rate will produce the desired change in $Paco_2$ and pH. Therefore, the OPC should initially change the rate by 2 to 4 breaths per minute and then assess the effect on the pH with another blood gas analysis after 20 or 30 minutes. Additional changes may then be indicated, using the same strategy. It is recommended that the rate not be reduced below 6 or increased above 24 breaths per minute. Similarly, it is recommended that the $Paco_2$ not be lowered below 16 mm Hg or raised higher than 60 mm Hg.

When the above respiratory interventions are not adequate to return the pH to normal, other actions may be needed to correct significant metabolic alkalosis or acidosis. These actions should be discussed with a physician consultant before being initiated.

Metabolic alkalosis is uncommon in donors. Most often it is due to a low intravascular fluid volume ("contraction alkalosis") and is easily corrected by additional intravenous fluids supported by "extra" chloride as present in isotonic sodium chloride solution. It is very rare to encounter metabolic alkalosis of such severity that the administration of hydrochloric acid (HCl) would be necessary to correct the pH. Its administration, however, would be preferable to the use of acetazolamide, which acts within the kidney to increase bicarbonate excretion and chloride retention. This medication should not be used prior to kidney removal and implantation. The amount of HCl needed to treat severe metabolic alkalosis is estimated from the calculated simultaneous deficit of chloride:

$$\text{mEq acid needed} = (103 - \text{donor } Cl^-) \times .5(\text{donor weight in kg})$$

Most hospital pharmacies supply a 0.1N or 0.2N HCl solution that provides 0.1 or 0.2 mEq of hydrogen ion (acid) per milliliter of solution, respectively. Because the final blood pH is determined by the hydrogen ion given and by the final charge balance of electrolytes, buffers, and CO_2, only half of the calculated acid deficit should be administered via a central venous catheter at a maximum rate of 0.2 mEq/kg per hour. Thereafter, the donor's acid-base status should be reevaluated by another arterial blood gas analysis.

More commonly, $NaHCO_3$ administration may be needed to correct the pH during metabolic acidosis of either a normal or increased anion gap type. The apparent bicarbonate deficit is similarly calculated from the equation:

$$\text{mEq } HCO_3^- \text{ needed} = (24 - \text{donor } HCO_3^-) \times .4(\text{donor weight in kg})$$

Bicarbonate is most often administered from commercially available premixed syringes of sodium bicarbonate which contain either 44 mEq or 50 mEq each. Once again, the above calculation is only an estimate, so half the calculated bicarbonate deficit is administered as a slow intravenous bolus or mixed in another intravenous solution such as 500 mL of 5% dextrose in water to be delivered over 1 hour. Prior efforts to increase the pH by hyperventilation will have lowered the donor's bicarbonate, thus affecting the above calculation, so that care must be used not to administer too much bicarbonate. The donor's acid-base status must be reassessed with another arterial blood gas analysis after bicarbonate therapy.

It is important to remember that the causes of metabolic alkalosis or acidosis should be sought and

treated. Therefore, in metabolic alkalosis, ensure that diuretics previously ordered are discontinued and full replacement of serum potassium and other electrolytes is planned. Concurrent treatment for metabolic acidosis might include changing intravenous fluids from isotonic sodim chloride solution, ensuring that all external sites of blood loss are controlled, maintaining an optimal hemoglobin level, providing sufficient intravascular volume as titrated by the central venous or pulmonary artery occluded pressures, or administering inotropic or vasopressor drugs to support the arterial blood pressure.

Finally, there is controversy about the appropriate goals for acid-base correction even after the underlying conditions have been addressed. During acidemia, most authors favor increasing the pH to above 7.20, since profound inhibition of intracellular phosphofructokinase leading to decreased cellular energy production occurs below that pH. We agree with that position but favor achieving a pH closer to normal.

Summary

Abnormal acid-base balance occurs commonly during donor care and can jeopardize the quality and survival of organs awaiting removal. Procurement coordinators, therefore, must identify and correct the cause(s) of acid-base imbalance while treating the abnormal blood pH. Classification of the type of acidosis or alkalosis by using laboratory measurements is helpful in planning treatment. We recommend that the mechanical ventilator be used to manipulate the $PaCO_2$ as the first intervention to normalize the pH. Thereafter, in collaboration with physician consultants, the coordinator may need to proceed with acid or bicarbonate administration.

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Maintaining acid-base balance in organ donors

Objectives

1. Describe the physiological consequences of acid-base abnormalities that are relevant to donor care.
2. Discuss causes of acid-base imbalance common in donors.
3. Identify approaches to treatment of acid-base imbalance that are pertinent to donor care.

Mark your answers clearly in the appropriate box. There is only one correct answer. You may photocopy this form.

1. ❑a	2. ❑a	3. ❑a	4. ❑a	5. ❑a	6. ❑a	7. ❑a	8. ❑a	9. ❑a	10. ❑a	11. ❑a	12. ❑a
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❑d	❑d	❑d	❑d	❑d	❑d	❑d	❑d	❑d	❑d	❑d	❑d

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CE Test Questions

Maintaining acid-base balance in organ donors

1. In organ donors, the acid-base imbalance of acidemia may cause all of the following except which condition?
   a. Reduced cardiac contractility
   b. Increased production of lactic and keto acids
   c. Cardiac arrhythmias
   d. Insulin resistance

2. Adjustments in pH can often be made easily in organ donors by changing which of the following mechanical ventilation settings?
   a. Minute volume
   b. Physiological dead space
   c. Pa_{O_2} concentration
   d. Positive end-expiratory pressure

3. When an intubated donor is receiving mechanical ventilation, dead space which results from the segment of ventilator tubing between the endotracheal tube and the ventilator connecting tubing is referred to by which of the following terms?
   a. Anatomic dead space
   b. Physiological dead space
   c. Mechanical dead space
   d. Control ventilation dead space

4. A positive base excess is seen in which of the following acid-base imbalances?
   a. Metabolic acidosis
   b. Metabolic alkalosis
   c. Respiratory acidosis
   d. Respiratory alkalosis

5. A positive base deficit is seen in which of the following acid-base imbalances?
   a. Metabolic acidosis
   b. Metabolic alkalosis
   c. Respiratory acidosis
   d. Respiratory alkalosis

6. The administration of intravenous isotonic sodium chloride solution is a common cause of which of the following acid-base imbalances in organ donors?
   a. Metabolic acidosis
   b. Metabolic alkalosis
   c. Respiratory acidosis
   d. Respiratory alkalosis

7. Which of the following outlines the correct equation for determining the anion gap?
   a. $(Na^+ + K^+) - (Cl^- + HCO_3^-)$
   b. $(Na^+ + K^+) + (Cl^- - CO_2)$
   c. $(Na^+ - K^+) - (Cl^- + HCO_3^-)$
   d. $(Na^+ - K^+) + (Cl^- - CO_2)$

8. Inadequate treatment of shock in donors is a common cause of which of the following acid-base imbalances?
   a. Metabolic acidosis
   b. Metabolic alkalosis
   c. Respiratory acidosis
   d. Respiratory alkalosis

9. Which of the following conditions accurately reflects what will occur with an increase in minute ventilation ($V_T \times f$)?
   a. Decrease in Pa_{O_2}
   b. Increase in Pa_{CO_2}
   c. Decrease in pH
   d. Increase in pH

10. Which of the following conditions is *not* seen with hypoventilation in donor care?
    a. Blood pH is increased.
    b. Higher amounts of CO_2 are present.
    c. Hydrogen ion availability is increased.
    d. Pa_{CO_2} is often greater than 45 mm Hg.

11. Concurrent treatment for metabolic alkalosis in organ donors involves all of the following except which intervention?
    a. Changing intravenous fluids to isotonic sodium chloride solution
    b. Administering HCl
    c. Administering diuretics to control arterial blood pressure
    d. Providing sufficient intravenous volume

12. Which of these statements about metabolic alkalosis in organ donors is incorrect?
    a. Metabolic alkalosis is a common acid-base imbalance in donors.
    b. Metabolic alkalosis is most often caused by low intravascular volume.
    c. Metabolic alkalosis is corrected by administration of HCl.
    d. Metabolic alkalosis is often caused by contraction alkalosis.

Regulation of coagulation abnormalities and temperature in organ donors

The 3 most common reasons for abnormal coagulation of blood in organ donors result from prior medications, consumption or dilution of coagulation factors and platelets during massive transfusion, and disseminated intravascular coagulation. Evaluation and treatment of these conditions are reviewed, and recommendations are provided for ordering appropriate laboratory tests and blood bank products. (*Progress in Transplantation*. 2000;10:146-153)

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Notice to CE enrollees:
A closed-book, multiple-choice examination following this article tests your ability to accomplish the following objectives:

1. Describe the physiology of blood clotting.
2. Identify the expected outcome from the delivery of 1 unit or 1 pack of blood products.
3. Describe 3 nursing interventions to care for an organ donor at risk for coagulopathies.

Abnormal blood coagulation (coagulopathy) causes hemorrhage that requires blood transfusion in about 60% of organ donors.[1] Although transplanted organs from donors who demonstrate a significant coagulopathy from disseminated intravascular coagulation (DIC) may function normally,[2-4] hypovolemic shock, anemia, and reduced oxygen delivery to donor organs may secondarily jeopardize organ function prior to removal. The organ procurement coordinator (OPC) should, therefore, be familiar with clinical assessment and therapy methods for the most common causes of disordered blood coagulation in organ donors.

Overview

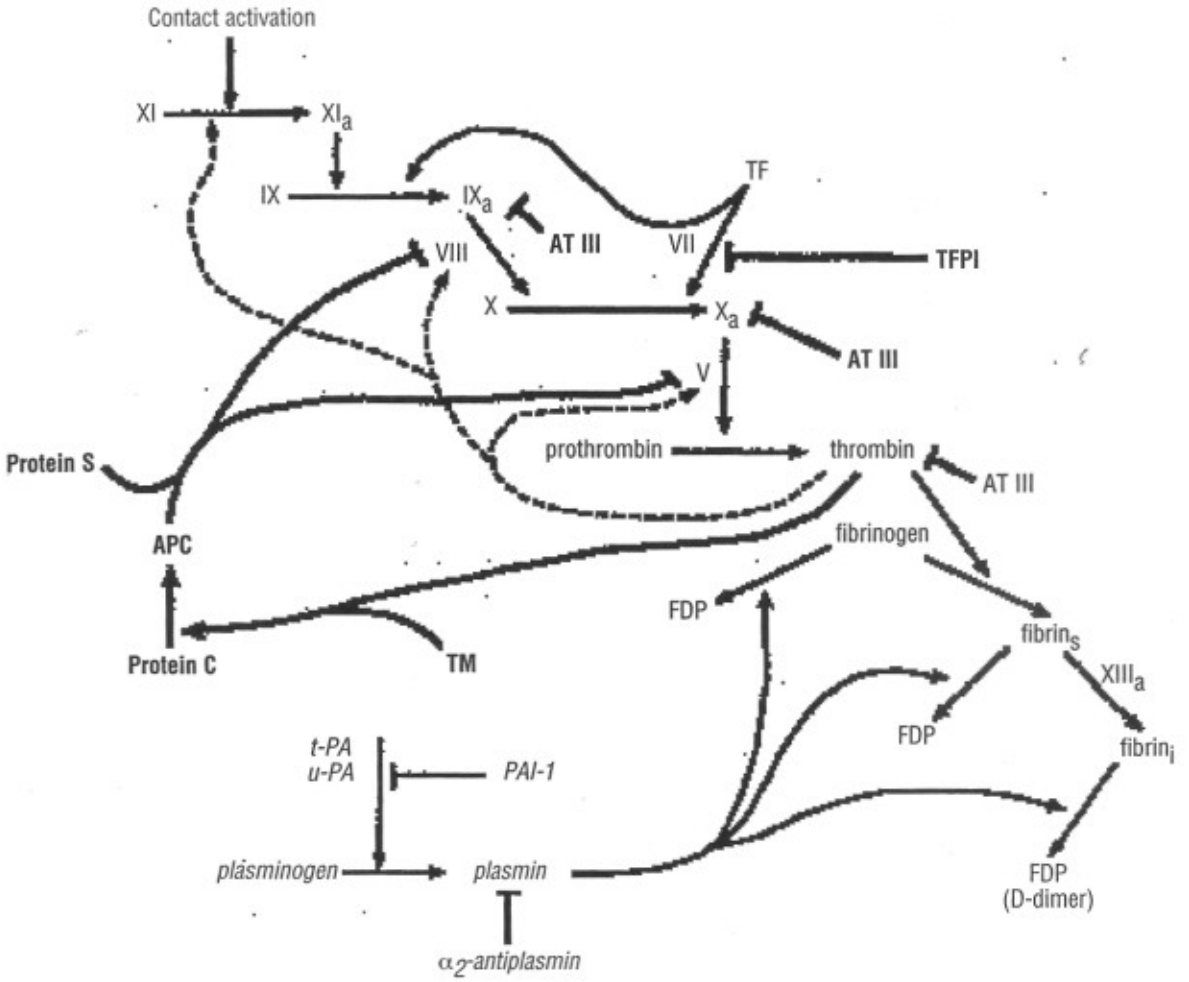
The complex process of normal coagulation is illustrated in the Figure. Also shown is the normal plasmin pathway for clot dissolution (lysis). These 2 plasma protein systems coexist within the vascular compartment and are necessary to balance ongoing normal clot formation and resolution throughout the body.

Clot formation follows sequential activation of serum and/or tissue proteins (coagulation factors), blood elements (ie, platelets) and electrolytes or other substances needed to accomplish hemostasis (arrest of bleeding). In the Figure, some coagulation factors are traditionally known by their Roman numeral designation as shown and do not have other specific names. The interaction of platelets often precedes activation of coagulation factors; this interaction is included in the notation of "contact activation" on the figure. Abnormalities of specific coagulation factors may be caused by congenital errors of production or metabolism, but such abnormalities are rarely encountered in organ donors. Similarly, unusual causes of a low platelet count (thrombocytopenia) or dysfunction of platelets (thrombocythemia) may occur which are not discussed here.

The 3 most common causes of coagulopathy in donors:

- anticoagulants such as warfarin, or agents that alter the function of platelets, such as aspirin, dypyridamole, ticlopidine, and nonsteroidal anti-inflammatory drugs, which may have been used by the donor
- consumption of coagulation factors or platelets after severe injury, compounded by further intravascular dilution during large-volume resuscitation
- DIC syndrome

Therapeutic changes in coagulation induced by



APC indicates activated protein C pathway; AT III, antithrombin III; FDP, fibrin degradation products; fibrin-I, insoluble fibrin; fibrin-s, soluble fibrin; PAI-1, plasminogen activator inhibitor-1; TF, tissue factor from injured (disrupted) tissue; TFPI, tissue factor pathway inhibitor; TM, thrombomodulin; t-PA, tissue-plasminogen activator; u-PA, urokinase-plasminogen activator.

Elements within the opposing blood coagulation and clot lysis processes (clot lysis processes shown in *italics*). Some coagulation factors are listed by their Roman numeral designations. Normal anticoagulation proteins, shown in **bold**, function to block activation of the indicated coagulation factors. The dotted line shows a feedback loop that enhances further clot formation when activated.

Reprinted with permission from Carey and Rodgers.[5]

warfarin are often prescribed for prior cardiovascular or neurological conditions. Warfarin acts by causing decreased production of some vitamin K–dependent coagulation factors. It is uncommon for bleeding to occur de novo during controlled anticoagulation, although patients who have received anticoagulants may bleed excessively after injury. Further, errors in dosing or interactions with other medications or substances may produce "overanticoagulation" and lead to spontaneous bleeding, including intracerebral hemorrhages resulting in brain death. Like warfarin, aspirin and similar compounds are prescribed in treating a variety of cardiac and neurological diseases. The effect of such compounds is to decrease platelet adhesion or aggregation within the clotting process. In general, this "antiplatelet" effect does not induce spontaneous hemorrhage because of the other components of the coagulation system. However, if hemorrhage occurs, the result of this type of platelet dysfunction may contribute significantly to bleeding.

The rapid consumption of coagulation factors during very active bleeding, such as after multiple trauma, is often compounded by the rapid infusion of resuscitation fluids which do not contain coagulation factors, such as crystalloid fluids, 5% albumin, or packed red blood cells. Such a combination of injury and treatment may dramatically decrease the intravascular concentration of remaining coagulation factors

or platelets and produce a so-called "consumption," "dilutional," or "wash-out" coagulopathy.[6]

Commonly, DIC in the donor results from excessive release of tissue-based substances which promote microvasular clotting. These clots cause activation of the plasminogen (defibrinogen or fibrinolytic) system normally intended to dissolve clots.[7] Although DIC is generally initiated by excessive clot formation, hemorrhage is usually the predominant clinical manifestation. Injury to donor organs may occur because of early thrombosis leading to poor organ perfusion[8] or, secondarily, from anemia, hypotension, and the resultant decreased oxygen delivery caused by the hemorrhage.

Assessment and Intervention

Table 1 summarizes laboratory tests frequently used to assess parts of the coagulation process. Measurements of individual factors are rarely performed on donors. Many hospital laboratories group these and similar tests into coagulation "panels" or "screens" for convenience in ordering. Some tests will need to be repeated during treatment as coagulation factors or platelets are replaced or further losses occur. The frequency of testing will depend on the severity of the ongoing hemorrhage, the speed at which replacement therapy is available from the blood bank, and the infusion rate of the replacement products. In general, repeating laboratory tests 30 to 60 minutes after administration of blood products will adequately measure the effects of the treatment given. Table 2 lists products available from most hospital blood banks to replace deficient parts of the coagulation system, recommended dosages, and advisory comments.

Prior Medications

If bleeding is caused or complicated by warfarin, aspirin, dypyridamole, ticlopidine, or nonsteroidal anti-inflammatory drugs, the obvious first step is to assure that the medications have been stopped. When disordered coagulation is caused by warfarin, the prothrombin time (PT) is prolonged, while the partial thromboplastin time (PTT), platelet count, and bleeding time are normal. Administration of fresh frozen plasma in the dose recommended in Table 2 is usually sufficient to reverse the drug effect. Whereas treatment with Vitamin K is a common method to restore production of coagulation factors, it does not work quickly enough (8-12 hours[8]) to be helpful during active bleeding or for organ removal. A prolonged bleeding time occurs when platelet dysfunction is caused by aspirin. This potential contribution to hemorrhage can be circumvented by giving fresh platelets even if the donor's platelet count is normal. The transfused platelets are able to adhere within the bleeding area and initiate platelet aggregation, which even aspirin-affected platelets can accomplish. Therefore, a 5-unit platelet "pack" is usually given. Rarely, the OPC may care for a uremic donor who is being considered for removal of other organs. Uremia also causes platelet dysfunction, which is best treated by dialysis but can be improved by giving cryoprecipitate (up to 10 units each 12 hours) and/or intravenous desmopressin acetate (0.3 µg/kg each 6-12 hours)[8] during short-term care of donors.

The above diagnoses and treatment are usually completed during the initial patient care, prior to brain death. However, the OPC should be aware of these causes of hemorrhage and be prepared to manage residual medication effects if the effects are not reversed by earlier therapy.

Dilutional Coagulopathy

A dilutional coagulopathy is also manifested by prolonged PT and PTT, thrombocytopenia, and low fibrinogen. The function of remaining platelets is normal, and the bleeding time will be normal if the platelet count is above 100×10^9/L. The ongoing consequences of injuries and vigorous resuscitation continue to promote consumption and dilution. There are no specific tests to confirm the diagnosis of a dilutional coagulopathy. The absence of progressive fibrinolysis (Table 1) may be helpful to rule out DIC but does not usually alter treatment. In clinical practice, separating dilutional coagulopathy from DIC precipitated by severe trauma can be difficult, as the 2 often occur concurrently. Treatment is again directed toward replacement of factors and platelets[6] as guided by sequential laboratory testing. Because ongoing hemorrhage, consumption of coagulation elements, and fluid resuscitation promote this coagulopathy, operative intervention to correct the cause of bleeding is appropriate in support of organ donation even after brain death.

Disseminated Intravascular Coagulation

DIC[7-9] occurs in 25% to 30% of donors[1] because of a variety of injuries or conditions which appear to have in common the occurrence of thrombin and clot formation followed by imbalance between the normal clotting and clot lysis (fibrinolysis) processes. This abnormal imbalance often begins with disruption of normal blood vessels, exposing tissue to the coagulation elements within the blood. Powerful proteins (cytokines) may be simultaneously released from the injured or exposed tissue and promote activation of the coagulation process.[10] Extensive clotting in small blood vessels may then follow and activate the counterbalancing plasma protein system designed to promote clot lysis, ie, the plasminogen system, as shown in the Figure. The balance between clotting and lysis is a normal part of the hematologic system. However, during the above pathological circumstances, the balance becomes disrupted, usually favoring clot breakdown. The large amount of circulating plasmin

Table 1 Tests of blood coagulation[6]

Test	Normal parameters*	Comments
Bleeding time, minutes	3-10	A standardized puncture wound is made on the forearm (Ivey method) or earlobe (Duke method) and the time necessary for clot formation is measured. Platelet function is tested. Platelet count must be $>100 \times 10^9$/L for the bleeding time to be reliable.
D-dimer	No D-dimer fragments present	A test to detect fibrin breakdown by plasmin
Fibrinogen, µmol/L (mg/dL)	4.4-10.3 (200-400)	Low values reflect consumption or breakdown of fibrinogen, but not specific for any etiology. Treat with cryoprecipitate if level <2.9 µmol/L (<100 mg/dL).
Fibrin split products or fibrin degradation products	Negative result at 1:4 dilution	Positive test result after the serum has been diluted more than 1 part plasma to 4 parts diluent (1:4) indicates lysis of both fibrin and fibrinogen by plasmin or fibrinolytic system.
Platelet count, $\times 10^9$/L	140-400	Direct count usually by machine; reduced in dilutional coagulopathy, DIC, or from many other causes (ie, not specific to etiology).
Partial thromboplastin time, seconds	30-45	Measures time for clot formation using standardized test reagents and techniques; test of coagulation factors not evaluated by prothrombin time
Activated partial thromboplastin time, seconds	23-26	
Prothrombin time, seconds	10-12.2	Measures time for clot formation using standardized laboratory reagents and methods and evaluates prothrombin; fibrinogen; and factors V, VII, and X amounts and function. The International Normal Ratio is a reference standard used during warfarin treatment and is not otherwise an independent test of coagulation.

D-dimer indicates dimerized plasmin fragment D; DIC, disseminated intravascular coagulation.
* Normal values may vary at different hospitals depending on test methodology.

destroys both fibrinogen and fibrin. Hence, laboratory evidence of a decreased level of fibrinogen is present. Likewise, during clot lysis, positive fibrin degradation product (FDP) and dimerized plasmin fragment D (D-dimer) tests serve as laboratory markers of the lytic process. FDPs are also important because they decrease platelet function and prevent formation of new clots by inhibiting formation of new fibrin polymers. Injury to red blood cells may also occur within small blood vessels, producing varied fragmentation forms such as "helmet" or "burr" cells seen on microscopic examination of the blood smear. Although during DIC some laboratory evidence (thrombocytopenia) of the clot-formation phase of the syndrome may be found, most clinical concerns relate to persistent hemorrhage caused by secondary fibrinolysis.

DIC may be specifically diagnosed using a variety of laboratory measures.[7] However, many of the more elaborate tests are not routinely available. The D-dimer and FDP assays are more commonly performed. "DIC panels" usually include PT, PTT, platelets, fibrinogen, and FDP or D-dimer analyses. In the presence of DIC, the PT and PTT are prolonged, the platelet count and fibrinogen levels are low, and the results of FDP and D-dimer tests are reported as positive.

Treatment of DIC begins with correction of its cause. During the care of a donor, this may be impractical if severe trauma has been the cause of brain death and continuing hemorrhage. Other causes of DIC, such as sepsis, cancer, or vasculitis, usually preclude the patient's being accepted as a donor. Obstetrical causes of DIC are commonly treated by delivery of the baby and rarely lead to brain death in the mother. Therefore, trauma is the most likely cause of DIC to be encountered by the OPC. Although accelerated clot formation may be responsible for initiating DIC, the use of anticoagulants, such as heparin, remains controversial[7] and appears to be helpful in more chronic conditions producing DIC that do not apply to donors. Therefore, heparin therapy is not advised for organ

donors. Therapy in DIC is most commonly directed toward replacement of coagulation factors and platelets. In addition, correction of 2 other factors, temperature and ionized calcium levels, which influence coagulation, must be considered.

Common Pathway for Assessment and Intervention

Although the causes of a coagulopathy in the donor may be divided as discussed above, its assessment and treatment during the relatively short time a donor is cared for usually follows a common pathway of laboratory testing and replacement of blood products. If the OPC is concerned about the donor's ongoing bleeding during the initial evaluation, he or she should order fibrinogen, ionized calcium, PT, and PTT tests and a platelet count, and note the body temperature. If the fibrinogen and calcium levels and the platelet count are low, these should be corrected first[5] while maintaining intravascular volume and blood pressure to assure organ perfusion. Fibrinogen levels <2.9 µmol/L (100 mg/dL)[3] should be treated with 6 units of cryoprecipitate. Ionized calcium below the laboratory normal value may be increased with 1 ampule of 10% calcium gluconate or 10% calcium chloride given intravenously over 15 to 30 minutes. Platelets are given in the amounts shown in Table 2 to maintain the platelet count above 50×10^9/L. If bleeding continues thereafter and the PT and PTT are prolonged, fresh frozen plasma should be administered.

The end point of treatment is cessation of bleeding even though some laboratory measurements may remain abnormal. Thus, sequential clinical and laboratory assessments are used to titrate replacements by using doses of each component as listed in Table 2. Other agents to treat DIC have been evaluated but remain experimental or unproven and are not recommended for use in caring for donors:

- antithrombin III, a normal plasma protein that limits thrombin-mediated coagulation. It is decreased after injury, which could further increase clot formation. Replacement would limit excessive clotting and secondary stimulation of fibrinolysis. Clinical trials have not shown definite value.
- antifibrinolytic agents, which stop plasmin-induced clot lysis. However, their use may result in significant rebound clotting and can potentially place donor organs at risk of ischemia.

Alterations in Temperature

Changes in donor body temperature occur commonly and may have significant consequences for donor organs. Fever in the donor may be caused by external pyrogens acting within an inflammatory or

Table 2 Blood component therapy*

Product	Volume	Dose	Comments†
Packed red blood cells	1 unit, 250 mL	Based on Hct and Hgb measurements	Obtained from a single blood donor. General guideline: 1 unit PRBC should raise Hct by 0.03; ABO and other cross-matching necessary
Fresh frozen plasma	1 unit, 200 mL	15 mL/kg. Convert to units and order as the number of FFP units desired	Obtained from a single blood donor. Provides all coagulation factors; must be ABO group compatible; requires approximately 45 minutes to thaw
Cryoprecipitate	1 unit, 15-20 mL	Usually 2-6 units	Obtained from a single blood donor per unit, but units pooled because of low volume, hence higher risk of transmission of infectious agents. Primarily used to replace fibrinogen; each unit contains approximately 250 mg fibrinogen and will raise plasma fibrinogen 0.1 to 0.3 µmol/L
Platelets	1 pack, 50 mL	1 pack per 10 kg donor body weight	Each pack obtained from a single blood donor, but usually multiple packs given. "Special" use of single blood donor and apheresis or HLA-matched platelets rarely given to organ donors. General expectation is that 1 pack should raise platelet count by approximately 10×10^9/L.

ABO indicates the ABO blood group system; Hct, hematocrit; Hgb, hemoglobin; HLA, human leukocyte antigen.

* All blood products carry a small risk of transmission of infectious diseases.

† Estimates of the effectiveness of transfusions assume no ongoing bleeding.

infectious process or by some preservation of hypothalamic mechanisms of temperature regulation. Fever in general elevates cellular metabolic rate, increases oxygen needs, and may indicate infection. However, after brain death, hypothalamic control of body temperature is usually lost, and hypothermia occurs as the body tissues cool to room temperature. Infusion of room-temperature intravenous fluids or cold blood products further contributes to the fall in body temperature of the donor.

Data[11,12] show that below 34°C (93.2°F), enzymatic processes associated with normal coagulation and platelet function are significantly reduced. In some patients, changes may occur between 34°C and 37°C. Conversely, fewer patients whose temperature is in this range may experience hypercoagulation. In general, however, maintaining the donor's body temperature above 34°C is a reasonable goal to assure that hypothermia is not contributing to ongoing hemorrhage.

Hypothermia may also contribute to other physiological changes that may place donor organs at risk. These include arterial vasoconstriction; cold-induced diuresis; cardiac arryhythmias; increased oxygen binding to hemoglobin, which might reduce oxygen availability to all cells; increased blood viscosity; pancreatic dysfunction; and decreased cardiac contractility.[13,14] These changes in donor physiology induced by hypothermia may contribute to hypovolemia, reduced regional or systemic blood flow, or hypotension.

Hypothermia should be prevented by warming the gas delivered by the mechanical ventilator and using blankets. More "active" measures, such as using heated forced air or water "warming" blankets, are commonly required when the donor's body temperature has already fallen. Rarely would more aggressive measures be needed, such as heated intravenous fluids, lavage of various body cavities (stomach, colon, thorax, or abdomen) with heated fluid, or use of extracorporeal circuits to warm the blood through hemodialysis or full cardiopulmonary bypass. Such interventions should be discussed with a physician consultant or be part of the organ procurement organization's treatment protocols. While complications related to hypothermia will vary among donors depending on other physiological factors such as age, prior cardiovascular disease, and other medications, the previously stated goal of maintaining the donor's body temperature above 34°C is desirable.

Summary

The common treatment pathway for altered blood coagulation in organ donors is sequential administration of coagulation factors and platelets as titrated by laboratory testing. Occasionally a directed intervention toward a primary cause of external blood loss or DIC may be appropriate, and the primary cause should be identified. Correction and maintenance of normal body temperature and ionized calcium level are also important in treatment. The consequence of not attempting to treat coagulopathies will be loss of donor organs.

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Regulation of coagulation abnormalities and temperature in organ donors

Objectives
1. Describe the physiology of blood clotting.
2. Identify the expected outcome from the delivery of 1 unit or 1 pack of blood products.
3. Describe 3 nursing interventions to care for an organ donor at risk for coagulopathies.

Mark your answers clearly in the appropriate box. There is only one correct answer. You may photocopy this form.

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Objective 3 was met	❑	❑	❑
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CE Test Questions

Regulation of coagulation abnormalities and temperature in organ donors

1. Coagulopathy results in hemorrhage requiring blood transfusion in what percentage of organ donors?
   a. 70%
   b. 50%
   c. 40%
   d. 60%

2. What is the normal parameter for bleeding time?
   a. 2 to 5 minutes
   b. 3 to 10 minutes
   c. 4 to 8 minutes
   d. 6 to 14 minutes

3. Which of the following is 1 of the 3 most common reasons for coagulopathy in organ donors?
   a. Anticoagulants
   b. Chronic kidney failure
   c. Past use of antineoplastic agents
   d. Refusal of blood products

4. Which of the following acts by causing decreased production of vitamin K–dependent coagulation factors?
   a. Ticlopidine
   b. Aspirin
   c. Warfarin
   d. Dipyridamole

5. Which of the following tests of blood coagulation detects fibrin breakdown by plasmin?
   a. D-dimer
   b. Platelet count
   c. Partial thromboplastin time
   d. Prothrombin time

6. Typically, how much should 1 unit of packed red blood cells raise the hematocrit?
   a. 0.03
   b. 0.01
   c. 0.10
   d. 0.05

7. Typically, how much should 1 pack of platelets raise the platelet count?
   a. Approximately 15×10^9/L
   b. Approximately 1.0×10^9/L
   c. Approximately 1.5×10^9/L
   d. Approximately 10×10^9/L

8. How is platelet dysfunction resulting from uremia often treated?
   a. By administration of desmopressin
   b. By administration of platelets
   c. By administration of warfarin
   d. By administration of fresh frozen plasma

9. Disseminated intravascular coagulation occurs in what percentage of organ donors?
   a. 30% to 35%
   b. 15% to 20%
   c. 20% to 25%
   d. 25% to 30%

10. Enzymatic processes required for normal coagulation and platelet function have been shown to be significantly reduced at which temperatures?
    a. 35°C
    b. 34°C
    c. 37°C
    d. 36°C

Recommendations for mechanical ventilation during donor care

The organ procurement coordinator usually directs adjustments to the mechanical ventilator during donor care. It is often difficult to achieve optimal oxygen uptake and carbon dioxide removal while avoiding barotrauma or undesirable effects on the cardiac output. Interrelationships among a variety of ventilator parameters must be understood in order to achieve the desired goal of providing the best organs possible. These recommendations review the key ventilator parameters of tidal volume; positive end-expiratory pressure; auto–positive end-expiratory pressure; fraction of inspired oxygen; and flowrate and frequency and their interactions in controlling peak, plateau, and mean and end-expiratory airway pressures. (*Progress in Transplantation*. 10:33-40)

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Notice to CE enrollees:

A closed-book, multiple-choice examination following this article tests your ability to accomplish the following objectives:

1. Define various mechanical ventilation terms.
2. Analyze the interrelationships between the various ventilator parameters that will achieve maximal oxygenation.
3. Discuss the method of ventilation most commonly used in donor management.

Inappropriate or inadequate mechanical ventilation during donor care may cause significant harm to the donor and loss of donor organs. Injury to the donor results primarily from reduced cardiac output or direct expansion injury (barotrauma or volutrauma) to the lung(s) caused by excessive airway pressure or overdistension of lung tissue. Secondarily, mechanical ventilation may contribute to acid-base abnormalities or changes in the core body temperature, which may also affect donor organ function. The following recommendations focus on the issue of providing the benefits of optimal oxygenation and ventilation during mechanical ventilation while minimizing the potentially harmful effects of excessive airway pressure.

Following brain death and the loss of spontaneous breathing, controlled mechanical ventilation (CMV) is always the method of ventilation during donor care. CMV may be administered through a volume-limited (lung inflation stops after delivery of a preset tidal volume) or pressure-limited (pressure-controlled) (lung inflation stops when a preset airway pressure is reached) method of gas delivery. This review will discuss only volume-limited CMV, the more common technique. If pressure control ventilation is being used or is required, the physician initially involved with the case should continue to provide input.

Although CMV simplifies some aspects of ventilatory care, intrathoracic and airway pressures are directly dependent upon the ventilator parameters selected. Therefore, the organ procurement coordinator (OPC) must be familiar with the interrelationships of the possible settings on the ventilator. The advice and recommendations of the respiratory care practitioners (RCP) or physicians present in the hospital and available to the OPC may often be needed, and the effects of ventilatory changes should be monitored by arterial blood gas measurements. However, the OPC should be familiar with the ventilation parameters discussed in

these recommendations and be able to identify and avoid potentially harmful settings or parameters. A brief glossary of terms used in this article is provided in Table 1.

Airway Pressure and Tidal Volume Goals

Although many aspects of lung injury during mechanical ventilation remain controversial,[1-3] and a specific peak or mean airway pressure or tidal volume at which lung injury or reduced cardiac output will occur cannot be predicted in any donor, the following guidelines are recommended:

- peak airway pressure: less than 45 cm H_2O
- plateau airway pressure: less than 35 cm H_2O
- tidal volume: 8 to 12 mL/kg of ideal or usual body weight unless diffuse lung injury is already present, then 6 to 8 mL/kg[4]

Lung injury resulting from overexpansion of lung tissue by high pressure or volume may be influenced by other variables. These include shear forces produced against the tissue surface by the flow rate of inspired gas, lung friability or fragility caused by any inflammatory or infectious process, the presence of interstitial edema, the duration of lung inflation, and the pressure gradient between the airway and intravascular space.[5]

Expansion injury to the lung parenchyma releases gas from the airway lumen into the adjoining interstitial space to produce interstitial emphysema. This "extra-alveolar" gas may then spread along tissue planes of the lung, mediastinum, and abdomen to produce pneumomediastinum, pneumothorax, pneumopericardium, pneumoperitoneum, pneumoretroperitoneum, subcutaneous emphysema, and lung cysts. Although most of these manifestations of barotrauma do not harm the donor, tension pneumothorax, tension pneumomediastinum, tension pneumopericardium, and tension lung cysts have been reported and may cause impairment in cardiovascular function and/or gas exchange in the lung.[6]

Increased airway pressure causes an elevation in total intrathoracic pressure which may reduce cardiac output. This reduction usually happens because venous blood return to the heart is reduced by the increased thoracic pressure. Other contributing factors may include increased resistance to the flow of blood from

Table 1 Glossary

Alveolar ventilation (V_A): The volume of gas per minute that participates in gas exchange. It is the primary determinant of the partial pressure of CO_2 in the arterial blood as minute alveolar ventilation: $V_A = (V_T - V_{DS}) \times f$, where V_T = tidal volume, f = respiratory frequency, and V_{DS} = dead space ventilation. Normal alveolar ventilation is 5 to 6 L/min, assuming normal anatomic and physiologic dead space.

Auto-PEEP: Positive airway pressure at the end of expiration that is not preset on the ventilator. Auto-PEEP results from dynamic airway closure in small airways, producing air trapping. It may occur as a manifestation of obstructive airway disease or bronchospasm when the expiratory time (T_E) is too short to allow full exhalation of airway gas. Normal auto-PEEP is 0.

Compliance: A measure of the distensibility of the lung and/or chest wall. It is expressed as a change in volume per unit change in distending pressure (mL/cm H_2O). Normal compliance varies with sex, age, and other variables but is generally 100 to 200 mL/cm H_2O.

Cycle time (duty cycle): The time allowed for one cycle of the mechanical ventilator (inspiration and exhalation). Cycle time comprises inspiratory time (T_I) and T_E.

Dead space ventilation: The volume of gas (V) or proportion of the V_T delivered to the donor in inspiration that does not participate in gas exchange. This volume or proportion usually represents areas of the lung receiving more gas ventilation than blood perfusion. Usually given as a ratio of dead space–to–tidal volume as calculated by special testing. Normal dead space ventilation is <.4 (40%).

Inspiratory pause (plateau, hold): A delay in the initiation of exhalation, set on the ventilator. This delay is set for the time (usually from 0.2 to 2.0 seconds) the V_T is held in the lung before exhalation starts.

Mean airway pressure: Average airway pressure in 1 minute, as calculated by the mechanical ventilator.

Peak airway pressure: Maximum airway pressure created during the mechanical ventilator's inspiratory cycle.

Positive end-expiratory pressure (PEEP): Positive airway pressure applied by the ventilator at the termination of exhalation. PEEP is set as part of the ventilator parameters but may be augmented when auto-PEEP occurs.

Resistance: A measure of the impedance to gas flow into or from the lung, expressed as the change in airway pressure caused by incremental changes in gas flow. See text for discussion.

the right ventricle into the pulmonary artery, which reduces blood flow to the left atrium/ventricle; displacement of the interventricular septum of the heart toward the left ventricle, which reduces the left ventricular filling volume; and external compression of the heart sufficient to lower coronary artery blood flow.[5,7]

Airway pressure during lung inflation by the mechanical ventilator is primarily a reflection of pulmonary compliance (distensibility) and resistance to gas flow within the lung. These physiological parameters are determined by the anatomy of the lung tissue and the connecting airways. Pulmonary compliance is reduced and the lungs become somewhat stiff in many conditions encountered during donor care, including pulmonary contusion, pneumonia, acute respiratory distress syndrome, pulmonary edema, hemothorax, and aspiration pneumonia. When lung compliance decreases, airway pressure increases in response to the tidal volume breath delivered during CMV. Naturally, appropriate treatment for any of the above causes of decreased compliance should be continued throughout donor care.

Airway resistance may increase because of mucous plugging, bronchospasm, obstruction, or kinking of the endotracheal tube or if obstructive or emphysematous changes occur throughout the smaller airways. Airway pressure also rises when airway resistance increases. Therefore, careful attention to suctioning for excess mucus and treatment with bronchodilators may also be indicated during donor care.

The numeric difference between peak and plateau airway pressures is often used to determine whether high airway resistance or decreased compliance is the predominant cause of elevated airway pressure. Plateau pressure is usually measured by introducing a brief inspiratory "pause" or "hold" (usually 0.4 seconds) at the end of the inspiratory phase of the ventilator cycle. This pause allows the inspiratory flow of gas to stop and the inspired gas volume to be distributed more evenly throughout the airways. The airway pressure recorded at the end of this inspiratory pause generally falls below the peak airway pressure (AWP). This "plateau," the pressure during the pause, reflects lung compliance more accurately; peak AWP is more influenced by airway resistance. A numeric difference of more than 10 cm H_2O between peak and plateau pressures suggests that a substantial amount of the high peak AWP is due to increased airway resistance. When the pressure difference is less than 10 cm H_2O, decreased lung compliance is probably the cause of the high airway pressure. This information should be obtained whenever peak AWP exceeds 40 cm H_2O; it can be useful in directing ongoing therapy. When the peak-plateau difference is high (above 10 cm H_2O), vigorous treatment with bronchodilators, use of agents to thin excessive mucus, and frequent suctioning may be helpful.

Ventilation and Oxygenation Determinants

The primary determinants of oxygenation during mechanical ventilation are the fraction of inspired oxygen (FIO_2) and the mean AWP.[8] Oxygenation will generally improve if either of these factors is increased. Although the concept of "oxygen toxicity" to the lung and the FIO_2 at which it may occur remain controversial, it is generally agreed that an FIO_2 of about 0.4 (40%) is not harmful. A higher FIO_2 needed to preserve an adequate arterial partial pressure of oxygen (PaO_2) often predicts a condition unfavorable for lung transplantation, although criteria vary greatly among transplantation centers. A high FIO_2 or PaO_2 does not harm other donor organs. The FIO_2 may be varied from .21 (21%) (room air) to 1.0 (100%). Because increasing the FIO_2 reduces intra-alveolar nitrogen and may produce "resorption atelectasis," leading to a slight increase in ventilation-perfusion mismatching in the lung and hypoxemia, the lowest FIO_2 required to assure a PaO_2 between 70 and 100 mm Hg should be selected.[9]

The PaO_2 determines the percentage of the circulating hemoglobin which is carrying its maximum amount of oxygen (ie, is saturated). The arterial saturation of oxygen (SaO_2) is reported as that numeric percentage and should be maintained well above 90%: that is, 90% of the hemoglobin in the red blood cells is carrying its maximum amount of oxygen. The pulse oximeter is an instrument that closely estimates the SaO_2 and is commonly used in the intensive care unit for monitoring patients and donors. The numeric value provided by the oximeter is called the SpO_2. In order to assure an adequate PaO_2 (and SaO_2), the SpO_2 should be maintained above 92% in donors with light skin pigmentation and above 94% in donors with dark pigmentation.[10]

The alveolar ventilation during 1 minute is the primary determinant of the lung's elimination of carbon dioxide (CO_2) and hence the remaining partial pressure of CO_2 in the arterial blood ($PaCO_2$). The determinants of alveolar ventilation are tidal volume (V_T), respiratory frequency or rate (f) as breaths per minute (bpm), and the amount of dead space ventilation (V_{DS}). The $PaCO_2$ will generally fall as minute alveolar ventilation is increased when V_T or f is elevated or V_{DS} is decreased. During donor care, the $PaCO_2$ is often adjusted to ensure a normal blood pH. Although profound physiological changes may occur when the pH is abnormal, there is considerable latitude in adjusting the $PaCO_2$. Changes in the $PaCO_2$ alone have few primary effects important in the donor. A low $PaCO_2$ will elevate the pH (alkalemia), but the decrease in $PaCO_2$ itself has no other significant physiological effects. Increased $PaCO_2$ will lower the pH (acidemia) and at high levels may cause increased pulmonary artery constriction, a potentially

harmful effect. However, the effects on airway pressure of making changes in VT and f are of great importance, as discussed below.

Interrelationships of Ventilator Parameters

During CMV several parameters ordered by the OPC or set by the RCP interact to determine final airway pressures during the inspiratory and expiratory cycles of the ventilator. The OPC will usually specify VT, f, FIO_2, and the preset positive end-expiratory pressure (PEEP). The RCP will set several alarms and establish the flow rate in liters of gas delivered per minute (L/min) which determines the speed of gas entry into the lung from the ventilator during inspiration. Once the VT has been set, the flow rate also determines the time taken for the prescribed VT to enter the lung, that is, the inspiratory time (TI). As the flow rate is increased (made higher or faster) for a set VT, the VT is delivered more quickly and the TI is shortened.

The ventilation cycle time (duty cycle) is the time, in seconds, available for an entire ventilation cycle (inhalation and exhalation) to occur. The cycle time is determined by the respiratory frequency (f) and calculated by dividing f into 60 seconds, for example, an f of 6 produces a cycle time of 10 seconds, indicating that a new inhalation from the ventilator will begin each 10 seconds. Each ventilator cycle is composed of the TI and the amount of time for exhalation (TE). Both TI and TE occur within and fill the cycle time. TI is actively determined by the VT and flow rate, that is, a higher VT prolongs TI when flow rate is constant, and for a fixed VT, a slower flow rate will lengthen TI. TE is passively determined as the time remaining ("left over") in the cycle time after TI is complete. For example, if f = 10, the cycle time is 6 seconds; if the VT and flow rate are set so that lung inflation (TI) consumes 2 seconds, then TE is 4 seconds. However, if VT is increased or flow rate is slowed as f remains constant, TI will lengthen and may take (for example) 3 seconds, leaving 3 seconds for exhalation to occur during TE. Therefore, TE is the passive component of the cycle time. This fact becomes very important in the discussion of auto-PEEP that follows.

The inspiratory-to-expiratory (I:E) ratio relates the relative proportion of time spent during inhalation to that spent during exhalation, that is, TI:TE. In the first example, above, when TI was 2 seconds and TE 4 seconds, the I:E ratio was 1:2. The second example, where TI = 3 and TE = 3, has an I:E ratio of 1:1. The I:E ratio is always adjusted and stated in relation to a TI of 1, and it is presented as a ratio, not a fraction. Thus, in the first example above, the I:E is stated as 1:2, not 2:4 or 0.5. The I:E ratio in individuals with normal lungs during spontaneous breathing is about 1:2.

Because the OPC requests adjustments in ventilator settings, the effect of those changes on airway pressure during both inhalation and exhalation must be understood. Of special note is the airway pressure change during exhalation caused by auto-PEEP. Auto-PEEP occurs because of lung diseases (eg, emphysema) or conditions (eg, bronchospasm) which delay gas egress from the lung during exhalation. Individuals with such diseases or conditions often spontaneously slow their breathing rate to assure a longer exhalation time, reflected as an I:E ratio of 1:>2. These same diseases or conditions and the need for a longer TE may also be present in donors. If the full VT has not been exhaled before the next inspiratory cycle begins, the "trapped" gas remaining in the lung will create an unintended end expiratory pressure, called auto-PEEP, intrinsic PEEP, or inadvertent PEEP. During donor care with CMV, the most common causes of auto-PEEP are bronchospasm or ventilator changes that shorten TE to less than the time needed for full exhalation. AutoPEEP plus the PEEP ordered (preset PEEP) together define the total PEEP. AutoPEEP may be directly measurable on some ventilators or may be estimated on others. The RCP should assist with determing PEEP. The effect of the preset and auto-PEEP is to increase the functional residual capacity of the lungs at the end of exhalation. The subsequent inhalation is thereby initiated from a larger lung volume and the delivered VT creates higher peak and mean airway pressures than if no PEEP were present. The potentially harmful effects of total PEEP, and its components, are those previously described for high airway pressure, that is, reduced cardiac output and expansion injury.

Changes in airway pressure that occur and reflect the interrelationships of several ventilator parameters during CMV are shown in Table 2. Often a prescribed ventilator change will have both desirable and undesirable effects. The practical application of making changes in parameters to improve oxygenation or ventilation while attempting to avoid the harmful effects of elevated airway pressure is illustrated in the case examples which follow. This balance between the benefits of proper ventilator management through optimal oxygenation and ventilation and the risks of donor injury must be achieved by the OPC.

Case Examples

Case A

J.W. is an 18-year-old, 70-kg donor who sustained severe bilateral lung contusions and a lethal closed-head injury during a motor vehicle crash.

- Ventilator parameters: VT, 850 mL (12 mL/kg); PEEP, 12.5 cm H_2O; FIO_2, .8 (80%); f, 12 bpm; flow rate, 100 L/min.
- Patient data: peak AWP, 48 cm H_2O; plateau AWP, 40 cm H_2O; mean AWP, 22 cm H_2O; auto-PEEP, 0. Arterial blood gas analysis: pH, 7.51; PaO_2,

Table 2 Interrelationships of parameters during mechanical ventilation

Parameter increase*	Effect**
V_T	↑ Peak AWP ↑ Mean AWP ↑ T_I ↓ T_E (beware of auto-PEEP)
Set PEEP	↑ Peak AWP ↑ Mean AWP No effect on T_I or T_E
Flow rate	↑ Peak AWP ↓ Mean AWP ↓ T_I ↑ T_E
frequency (or rate)	No change in AWP unless auto-PEEP occurs No change in T_I ↓ T_E (beware of auto-PEEP)
Pause time	↑ T_I ↓ T_E (beware of auto-PEEP) ↑ Mean AWP No change in peak AWP unless auto-PEEP occurs

AWP indicates airway pressure; PEEP, positive end-expiratory pressure; T_I, inspiratory time; T_E, expiratory time; V_T, tidal volume; ↑, increased; ↓, decreased.

* A decrease in these parameters will have the opposite effect from that shown here.

** Effect on mean AWP may be variable, but increased flow rate shortens T_I, causing the lung to be gas filled for less time during 1 minute; hence mean AWP usually falls.

59 mm Hg; $Paco_2$, 28 mm Hg; HCO_3, 22 mEq/L; Sao_2, 90%. Chest radiograph shows bilateral infiltrates throughout all lung fields consistent with severe contusions or acute respiratory distress syndrome. Vital signs: blood pressure, 100/68; heart rate 120 beats/min; temperature, normal. Central venous pressure (CVP), 4 mm Hg.

- Analysis: severe hypoxemia relative to FIO_2; high peak AWP; relatively low blood pressure, tachycardia, and low CVP that may be caused by high airway pressures; ventilation is satisfactory.
- Goal: reduce peak and plateau airway pressures while improving oxygenation
- Actions and concerns:
  1. Limited therapy is available to treat the primary injury of contused lung tissue. However, bronchodilators are frequently administered as supportive treatment.
  2. Oxygenation can be improved by increasing the FIO_2 or mean AWP. The FIO_2 here should be increased immediately to 0.9 or 1.0 as the initial intervention. As the lungs from this donor are likely to be unacceptable for transplantation, the FIO_2 change will not cause further lung damage during short-term donor care.
  3. Frequently, the OPC must attempt to increase mean AWP while lowering or maintaining peak AWP. The peak-plateau airway pressure difference here is 8, suggesting poor compliance as the probable major cause of the high peak AWP, a finding consistent with the chest radiograph. Options:
     a. Decrease V_T to 6 to 8 mL/kg. Assess effect on $Paco_2$ (will likely increase). The effect of this change will be to decrease the peak AWP, but also the mean AWP, a less desirable effect because lower mean AWP will generally lower the Pao_2.
     b. Decrease flow rate. This will increase mean AWP while decreasing peak AWP, both desirable. However, this change will also lengthen T_I and thus shorten T_E. Therefore, beware of auto-PEEP.
     c. Add an inspiratory pause. This change will increase mean AWP but not change peak AWP (unless auto-PEEP occurs). It will also lengthen T_I and shorten T_E, so beware of auto-PEEP.
     d. Decrease set PEEP. This will decrease both the peak AWP and the mean AWP, a less desirable option when improved oxygenation is the goal.
     e. A change in frequency will not significantly change oxygenation.

Therefore, a combination of changes that included a decrease in V_T and flow rate and the addition of a short inspiratory pause would be reasonable first changes. Thereafter, arterial blood gases should be measured again to direct further adjustments.

Case B

L.F. is a 52-year-old, 80-kg donor with known chronic lung disease who has sustained a lethal intracerebral hemorrhage.

- Ventilator parameters: V_T, 750 mL (9 mL/kg); PEEP, 8 cm H_2O; FIO_2, 0.5 (50%); f, 14 bpm; flow rate, 65 L/min
- Patient data: peak AWP, 47cm H_2O; plateau airway pressure, 34 cm H_2O; mean AWP, 19 cm H_2O; auto-PEEP, 10 cm H_2O. ABG analysis: pH ,7.21; Pao_2, 82 mm Hg; $Paco_2$, 62 mm Hg; HCO_3, 26 mEq/L. Donor assessment reveals bilateral wheezing over all lung areas and a large amount of tenacious sputum.
- Analysis: significant respiratory acidemia; high peak AWP and auto-PEEP; wide difference between peak AWP and plateau airway pressure suggests high airway resistance due to bronchospasm; accumulated

sputum may be a significant cause of the high peak AWP; adequate oxygenation.

- Goal: improve alveolar ventilation while reducing airway resistance, peak AWP, and auto-PEEP
- Actions and concerns:
  1. Ensure bronchodilator therapy is being given at maximum dosage and frequency.
  2. Continue suctioning as needed.
  3. Increase minute alveolar ventilation by evaluation and possible reduction of dead space ventilation (not further discussed here), increase V_T, or increase frequency.
     a. An elevation in V_T will probably also raise peak (undesirable) and mean (unnecessary) airway pressures unless the interventions listed in 1 and 2 above are highly effective. As V_T increases, T_I will also increase, if flow rate is constant. This effect shortens T_E and may worsen auto-PEEP, assuming the bronchospasm and expiratory airway obstruction are not relieved.
     b. Increasing the frequency while maintaining V_T and keeping flow rate constant will shorten T_E. This is because T_I, as determined by V_T and flow rate, remains the same, but the cycle time shortens. The time "left over" for exhalation, the T_E, is therefore reduced. The I:E ratio will also change as a consequence of the shorter T_E. A shorter T_E may increase the auto-PEEP, thus potentially elevating total PEEP, peak AWP, and mean AWP.
     c. Decreasing V_T and increasing flow rate in an attempt to increase T_E (and thus reduce auto-PEEP) may have the undesirable effect of lower minute ventilation (from the lower V_T), causing higher $PaCO_2$ or increased peak AWP (from faster flow rate), although this latter effect may be offset by the lower V_T.

Once again, a balanced combination of treating the primary causes of the delayed exhalation and gradual augmentation of the V_T or frequency should be initiated. A slight adjustment upward in flow rate may also be helpful. The auto-PEEP and peak-to-plateau pressure difference should be monitored to measure the effectiveness of the pulmonary treatments and ventilator changes. Subsequent changes in ventilatory parameters should be titrated using arterial blood gas measurements.

Other ventilatory techniques, such as pressure control, high frequency (jet or oscillatory), prone positioning, permissive hypercapnea, tracheal insufflation, and/or fluorocarbon-assisted breathing during donor care are generally not needed or applicable. However, if attempts to balance the various parameters as described above are not successful, some of these methods should be discussed with a physician consultant.

Summary

Significant injury to donor organs may occur quickly if inappropriate ventilatory parameters are ordered by organ procurement coordinators. Tidal volume, flow rate, ventilatory times, and PEEP are interrelated and, if used incorrectly, may cause harmful effects such as increased airway pressure upon lung tissue and/or reduced cardiovascular function. Organ procurement coordinators therefore have an important opportunity to benefit organ donation through careful attention to the details of mechanical ventilation.

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CE Test Questions

Recommendations for mechanical ventilation during donor care

1. After brain death is determined, what mode of ventilation is recommended?
   a. Intermittent mechanical ventilation
   b. Controlled mechanical ventilation
   c. Assist-control ventilation
   d. Pressure control

2. What harmful conditions can result when a donor is maintained on improper mechanical ventilation?
   a. Pneumonia and tachycardia
   b. Decreased cardiac output and barotrauma
   c. Hypertension and pneumothorax
   d. Respiratory distress syndrome and hyperthermia

3. Which of the following parameters is acceptable for donor ventilator management?
   a. Tidal volume 8 mL/kg, peak airway pressure 40 cm H_2O, plateau pressure 35 cm H_2O
   b. Tidal volume 10 mL/kg, peak airway pressure 45 cm H_2O, plateau pressure 40 cm H_2O
   c. Tidal volume 15 mL/kg, peak airway pressure 20 cm H_2O, plateau pressure 30 cm H_2O
   d. Tidal volume 10 mL/kg, peak airway pressure 25 cm H_2O, plateau pressure 30 cm H_2O

4. What is airway pressure a reflection of?
   a. Pulmonary blood flow
   b. Pulmonary oxygenation
   c. Pulmonary dead space
   d. Pulmonary resistance

5. What does a difference of 20 cm H_2O between peak and plateau pressure indicate?
   a. Increased airway resistance
   b. Increased compliance
   c. Decreased compliance
   d. Decreased airway resistance

6. For a peak-to-plateau difference of 30 cm H_2O, what therapy is recommended?
   a. Positive end-expiratory pressure, pressure control ventilation, bronchodilators
   b. Inverse inspiratory-to-expiratory ratio, antitussives, bronchoscopy
   c. Suctioning, bronchodilators, agents to thin mucus
   d. Suctioning, bronchodilators, pressure support ventilation

7. What is the primary determinant of the elimination of CO_2?
   a. pH
   b. Dead space ventilation
   c. Alveolar ventilation
   d. Respiratory rate

8. Auto-PEEP (positive end-expiratory pressure) would most commonly occur in which of the following donors?
   a. A 45-year-old with bronchospastic airway disease
   b. A 20-year-old with chest trauma
   c. A 60-year-old with an inspiratory-to-expiratory ratio of 1:2
   d. A 35-year-old with a positive end-expiratory pressure of 5 cm H_2O and a mean pulmonary artery pressure of 10 mm Hg

9. Which of the following parameters are important in the formation of auto-PEEP?
   a. Alveolar ventilation
   b. Dead space ventilation
   c. Fraction of inspired oxygen
   d. Expiratory time

10. Which of the following parameters is defined as a volume of gas that does not participate in gas exchange?
    a. Alveolar ventilation
    b. Dead space ventilation
    c. Positive end-expiratory pressure
    d. Compliance

Using pressure-limited mechanical ventilation in caring for organ donors

Pressure-limited (controlled) ventilation is commonly employed to provide mechanical ventilation in the intensive care unit when lung compliance is poor or when airway resistance is irreversibly high. Modification of the inspiratory-expiratory ratio to include inspiratory-expiratory ratio reversal and permissive hypercapnia can also be used when lung disease or injury is severe. Because other donor organs often can be saved for transplantation even when the lungs have been badly damaged, the organ procurement coordinator should adopt pressure-limited ventilation as well as inspiratory-expiratory ratio reversal and permissive hypercapnia as potentially helpful methods while providing mechanical ventilation to selected donors. (*Progress in Transplantation.* 2001;11:174-181)

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Notice to CE enrollees:
A closed-book, multiple-choice examination following this article tests your ability to accomplish the following objectives:

1. Discuss indications and goals of pressure-limited mechanical ventilation.
2. Identify differences in the components of pressure-limited mechanical ventilation including tidal volume, ventilator rate, and flow rate.
3. Describe the clinical recommendations for the use of controlled volume-limited mechanical ventilation.

In a review of controlled volume-limited mechanical ventilation (CVLMV), variables that interact to influence peak, plateau, and mean airway pressures; arterial oxygenation; carbon dioxide elimination; positive end-expiratory pressure (PEEP); and auto-PEEP were discussed.[1] The potentially harmful effects[2,3] of high airway pressures (barotrauma), excessive distending alveolar volumes (volutrauma), shear forces acting upon lung units during opening and closing (atelectrauma), release of harmful cytokines (biotrauma), or reduced cardiac output are outcomes that the organ procurement coordinator (OPC) must avoid when caring for donors who are receiving mechanical ventilation.

Another method, pressure-limited mechanical ventilation (CPLMV), may also be selected by the OPC and will be discussed in this article. Pressure-limited mechanical ventilation is controlled because the donor is apneic, that is, ventilatory support is available only at the frequency determined by the operator. Collaboration with the respiratory care practitioner and bedside nurse are, as usual, critical to ensuring proper implementation and monitoring of the respiratory care plan. Table 1 contains a glossary of terms used throughout this article.

Indications and Goals

CPLMV is most commonly used when the lung compliance (distensibility) is low (ie, the lungs are stiff) or the airway resistance to gas flow is high and cannot be reversed. These pulmonary changes may occur with trauma, aspiration, acute respiratory distress syndrome, or pneumonia of any cause and may lead to high airway and intrathoracic pressures. Such changes are unrelated to the process of brain death; therefore, the OPC will most often find CPLMV already in use at the time the OPC assumes responsibility for care of the donor. The purpose of CPLMV is to limit (control) high peak airway, plateau, and transpulmonary pressures as well as alveolar overdistention[3,4] to prevent a decrease in cardiac

output or the potentially harmful effects of barotrauma, for example, lung rupture, alveolar epithelial injury, and pulmonary capillary damage.[4]

Many variables and goals discussed in earlier manuscripts about CVLMV,[1] acid-base balance,[5] and hemodynamic function[6] also apply during CPLMV:

- Keep peak airway pressure <35 to 40 cm H_2O.
- Maintain minute alveolar ventilation to promote carbon dioxide removal and a normal arterial pH.
- Provide satisfactory oxygenation (oxygen saturation >92%).
- Ensure adequate intravascular volume and cardiac output.
- Avoid or recognize auto-PEEP.

Components

Inspiratory Pressure Setting

During CPLMV, the delivery of gas from the mechanical ventilator during the inspiratory phase is stopped, and exhalation begins when the airway pressure in the ventilator circuit equals the inspiratory pressure setting ordered. The pressure is then held until the set inspiratory time or inspiratory-expiratory (I:E) ratio set on the ventilator is completed. The inspiratory pressure setting is usually determined by subtracting the set PEEP amount from the maximum allowable (desirable) peak airway pressure (usually 35-40 cm H_2O). For example, if a donor is requiring 15 cm H_2O PEEP to support oxygenation, an initial pressure limit of 25 cm H_2O [40 cm H_2O (maximum allowable peak pressure) - 15 cm H_2O PEEP] should be ordered. Inspiratory gas will then be delivered to the airway beginning from the pressure in the airway at the start of inhalation (ie, PEEP) and ending when the pressure setting pressure is reached. Gas flow into the airway then ceases and the pressure is held for the duration of the inspiratory time as determined by the I:E ratio ordered.

The peak airway pressure applied to the lung at the end of inspiration and shown on the mechanical ventilator pressure gauge is the sum of the PEEP plus the pressure setting (40 cm H_2O in the example above). Because the PEEP is present at the end of exhalation, the inspiratory tidal volume (VT) increases airway pressure above PEEP until the additional inspiratory pressure setting level is reached.

Tidal Volume

Unlike volume-limited ventilation, VT is not set in the pressure-limited mode. VT is secondarily determined through the balance between the pressure setting and the current lung or chest wall stiffness and airway resistance. As the inspiratory phase of ventilation is initiated from the ventilator, gas flows into the lung until the proximal airway pressure equals the set inspiratory pressure. This pressure is held until the inspiratory time is completed, then exhalation is initiated. The amount of gas that has entered the lung during the increase of inspiratory pressure (the inspiratory phase of ventilation) is the VT.

Therefore, VT is a dependent variable during CPLMV and may fluctuate if the pressure setting is altered or if lung compliance or airway resistance changes. To increase VT and partial pressure of carbon dioxide removal, the pressure setting could be increased, but this change will also elevate the end-inspiratory peak pressure, which may be an undesirable effect. In addition, if increased airway resistance or decreased lung or thoracic compliance occurs, the pressure setting will be reached, but with a decreased flow rate to prevent "overpressurization" of the airway. Because the inspiratory time is preset, the result is a decreased delivered VT. Conversely, if the lungs improve and resistance decreases or compliance increases, the VT increases as the flow rate required to reach the set inspiratory pressure within the set inspiratory time increases.[7] Such variations in VT may be large enough to modify the arterial partial pressure of carbon dioxide ($PaCO_2$), and hence blood pH. Therefore, after the calculated pressure setting has been implemented, the OPC should observe the exhaled VT delivered by the ventilator. This exhaled VT, not the peak airway pressure, should be monitored by the OPC and bedside nurse while the donor is receiving CPLMV.

Ventilator Rate

The primary determinants of carbon dioxide elimination and the resultant $PaCO_2$ are shown in the equation for alveolar minute ventilation: alveolar minute ventilation = (VT - volume of dead space [VDS]) x ventilator rate. VDS, reviewed more completely in another study,[6] is dependent on parts of the ventilator tubing circuit and increased by low intravascular volume, low cardiac output, or reduced blood flow to the lung for any reason. Often, however, no specific cause for increased VDS can be found other than the lung disease that is present. If VDS does fall with improvement of the lung condition or after therapy, alveolar ventilation increases, the $PaCO_2$ falls, and the pH rises. The reverse occurs if VDS increases.

Because VDS is usually not measured, minute ventilation (VE) (VE = VT x ventilator rate) is used to determine the ventilator rate during CPLMV. The desired VE is that being utilized when an acceptable $PaCO_2$ has been documented in a recent arterial blood gas (ABG) value test. Often, this VE and ABG value are known during some other mode of ventilation, before CPLMV is begun. When CPLMV is initiated, the pressure setting selected, and the VT measured, the

initial ventilator rate is calculated by dividing the observed VT into the desired minute ventilation.

For example, a donor's ABG value shows a normal $PaCO_2$ level during CVLMV when a VT of 800 mL is being delivered 12 times a minute (VE = 800 x 12 = 9600 mL/min). However, these ventilator parameters produce a high airway pressure, and CPLMV is initiated. The pressure setting chosen yields a 600-mL VT during each inspiration from the ventilator. To equal the prior VE, and hopefully achieve the same alveolar ventilation and normal $PaCO_2$, a CPLMV rate of 16 (9600 ÷ 600 = 16) should be ordered, and a subsequent ABG value measurement should be obtained to verify the $PaCO_2$. If the $PaCO_2$ is lower than desired, the rate can be reduced. If the $PaCO_2$ is too high, the rate may be increased (see PEEP and Auto-PEEP below) or the $PaCO_2$ may be accepted (see Permissive Hypercapnia below).

Fraction of Inspired Oxygen

The fraction (or percentage) of inspired oxygen (FIO_2) delivered by the ventilator is adjustable from 0.21 (21%) to 1.00 (100%) in CPLMV as in other modes of ventilation.

Mean Airway Pressure

During CPLMV, mean airway pressure and FIO_2 remain the determinants of oxygen movement from the alveolus to the red blood cells. Prolongation of the inspiratory time by direct changes in the I:E ratio is the primary method to increase mean airway pressure (treat hypoxemia) in donors receiving CPLMV. Although the mean airway pressure is also increased by raising the inspiratory pressure setting and the set PEEP, these changes are less desirable because they may also increase the peak airway pressure or reduce VT, respectively.

Flow Rate

The flow rate is perhaps the most significant difference between volume- and pressure-limited ventilation. During CPLMV, the flow rate and gas delivery waveform are not set by the clinician, as they are during volume-limited ventilation. Gas flow into the lung during CPLMV is determined by the set inspiratory pressure, the I:E ratio, or length of the inspiratory time, and the flow algorithm of the ventilator installed by the manufacturer.[7,8] As the inspiratory phase begins, flow is initially high, reflecting the pressure gradient between the smaller lung units and the proximal airway. The flow rate then decelerates because this pressure gradient falls as airway pressure rises.[8] The inspiratory gas flow pattern is, therefore, decelerating or a so-called "ramp" configuration. Gas flow, however, occurs rapidly and quickly increases airway pressure to the pressure setting limit.

Variability in flow rate does occur when patients who spontaneously breathe receive mechanical ventilation with a pressure-limited mode. However, when apnea occurs, as in donors, a fixed flow rate configuration is in place.

Inspiratory Pause

No inspiratory pause option is available during CPLMV. Therefore, no separate plateau pressure measurement is available. Typically, the inspiratory pressure setting becomes equivalent to the plateau pressure.

PEEP and Auto-PEEP

PEEP can be added to the ventilator parameters during CPLMV, as in other modes of ventilation. Similarly, the preset PEEP may be augmented by auto-PEEP (inadvertent or intrinsic PEEP) if the donor's pulmonary condition (eg, chronic obstructive pulmonary disease) prolongs the time needed for the full VT to be exhaled. If the time needed for exhalation is longer than the exhalation time provided by the ventilator, air-trapping (air stacking) may occur and auto-PEEP is created. Expiratory time will decrease if the ventilator rate is increased and all other parameters remain constant, making auto-PEEP more likely. In donors receiving CPLMV, however, changes in the I:E ratio are more likely to cause the expiratory time to shorten and predispose the susceptible donor to auto-PEEP. Techniques used to detect auto-PEEP vary with different ventilators. The respiratory care practitioner should be consulted to assist.

If auto-PEEP occurs in donors receiving CPLMV, lung inflation begins from a higher total end-exhalation pressure (preset PEEP + auto-PEEP) and inspiratory flow is decreased so that the set pressure is reached within the specified inspiratory time. This combination results in a decreased delivered VT. Therefore, one clue to the occurrence of auto-PEEP is a decrease in the delivered VT.

Inspiratory-Expiratory Ratio

Cycle time, inspiratory time, and expiratory time, which are defined in Table 1, interact during CPLMV as during the volume-limited mode.[1] The I:E ratio reflects the relative proportion of time spent in inhalation (inspiratory time) to that spent in exhalation (expiratory time). During normal spontaneous breathing, most people have an I:E ratio of about 1:2, spending about twice as long in the exhalation phase of ventilation as in inhalation. Individuals with chronic obstructive pulmonary disease often spontaneously prolong the expiratory phase of their breathing to allow complete exhalation of the VT, and their I:E ratio may become 1:>2.

During CPLMV, the I:E ratio may be directly manipulated on most ventilators to improve oxygenation. This ordered change in the I:E ventilator setting

Table 1 Glossary

Alveolar minute ventilation (V_A) – The primary determinant of carbon dioxide elimination. Measured and calculated by the formula: $V_A = (V_T - V_{DS}) \times$ frequency. Normal V_A is 5-6 L/min, assuming normal anatomic and physiologic dead space.

Auto–positive end-expiratory pressure (auto-PEEP) – Positive airway pressure at the end of exhalation that is not preset on the ventilator or intended. Also called intrinsic or inadvertent PEEP. Normal auto-PEEP = 0.

Compliance – A measure of the distensibility of the lung and/or chest wall, expressed as the change in lung volume produced by a given change in distending airway pressure. Normal compliance changes with variables such as age and sex, but is about 100-200 mL/cm H_2O.

Cycle time – The time allowed for 1 complete inspiration and exhalation cycle of the mechanical ventilator; includes the inspiratory and expiratory times.

Volume of dead space (V_{DS}) – The volume of gas delivered during inspiration that does not participate in gas exchange, representing lung units receiving more ventilation than blood perfusion. Usually given as a ratio of dead space volume to tidal volume (V_{DS}/V_T) (normal = <.4) as measured in special testing.

Flow rate – The speed with which the inspired tidal volume is delivered to the airway from the ventilator; adjustable on the ventilator as liters per minute.

Inspiratory-expiratory (I:E) ratio – The relative proportion of time spent during inhalation to that spent during exhalation.

Inspiratory pause – A time delay in the initiation of exhalation set on the ventilator, usually from 0.2-2.5 seconds, during which the inhaled tidal volume is held in the lungs.

Mean airway pressure – Average airway pressure over 1 minute as calculated by the mechanical ventilator.

Minute ventilation (V_E) – Amount (liters) of gas delivered by the ventilator in 1 minute; $V_E = V_T \times$ ventilator rate.

Peak airway pressure – Maximum airway pressure created during the ventilator's inspiratory cycle.

Plateau airway pressure – Airway pressure at the end of an inspiratory pause time; measures airway pressure after airflow has stopped.

Positive end-expiratory pressure (PEEP) – Positive airway pressure applied by the ventilator at the termination of exhalation (set PEEP); is set as a ventilator parameter, but may be augmented by auto-PEEP.

Resistance – A measure of the impedance to gas flow into or from the lungs, expressed as the change in airway pressure caused by incremental changes in gas flow.

Oxygen saturation – Percentage of hemoglobin saturated by oxygen.

prolongs inspiratory time, thus increasing the mean airway pressure. Such orders to change the I:E ratio reflect the relative prolongation of inspiratory time over expiratory time. For example, the I:E ratio may be ordered as 1:2 → 1:1.8 → 1:1.2 → 1:1, indicating that the relative inspiratory and expiratory times have moved from the normal 1:2 to a longer inspiratory time relative to expiratory time. When the I:E ratio is changed to make the inspiratory time longer than the expiratory time, the I:E ratio is "reversed"; for example, 1.1:1→ 1.2:1→ 2:1.

If the ventilator rate, and thus the cycle time, remains constant during I:E ratio changes that reverse or prolong the inspiratory time—the concomitant shortening of the expiratory time increases the possibility of auto-PEEP. Similarly, as the inspiratory time is prolonged, the gas flow during inhalation is active longer and a greater V_T may be delivered, even though the pressure setting remains constant. This increase in V_T may occur because gas distribution throughout the lung may improve during the longer inflation time or other alveoli may be opened,[9] causing the airway pressure to rise more slowly toward the pressure setting. Therefore, the exhaled V_T from the donor should also be carefully monitored as the I:E ratio is varied.

During prolongation of the inspiratory time into reversal of the I:E ratio, the mean airway pressure rises as positive airway pressure is present in the chest for a greater part of each minute. This prolonged positive intrathoracic pressure has the potential to limit return of venous blood to the heart and reduce cardiac output[10] as another consequence of I:E ratio change.

It is possible to "reverse" the I:E ratio in the volume-limited controlled mode by adjusting combinations of V_T, flow rate, and an inspiratory pause. Therefore, either CPLMV or CVLMV can accomplish the goal of raising mean airway pressure, without ele-

Table 2 Comparison of controlled volume- and pressure-limited mechanical ventilation

Goal	CVLMV	CPLMV
Treat hypoxemia	1. Increase F_{IO_2} 2. Increase mean AWP without increasing plateau AWP* • Decrease flow rate† • Inspiratory pause† 3. Increase PEEP‡	1. Increase F_{IO_2} 2. Increase inspiratory time by change in I:E ratio† 3. Increase PEEP§
Increase ventilation (decrease P_{aCO_2})	1. Increase ventilator rate† 2. Increase V_T (will increase peak AWP and inspiratory time†) 3. Minimize V_{DS}, by ensuring intravascular volume and cardiac output are optimal	1. Increase ventilator rate† 2. Increase pressure limit (will increase V_T and peak AWP) 3. Same 4. Increase inspiratory time (may increase V_T)

*Assumes peak and plateau AWPs are already elevated and of concern.
†Will change inspiratory and expiratory times. Beware of auto-PEEP.
‡May increase peak and plateau AWPs.
§Will reduce V_T.[11]
AWP indicates airway pressure; CPLMV, controlled pressure-limited mechanical ventilation; CVLMV, controlled volume-limited mechanical ventilation; F_{IO_2}, fraction of inspired oxygen; I:E ratio, inspiratory-expiratory ratio; P_{aCO_2}, arterial partial pressure of carbon dioxide; PEEP, positive end-expiratory pressure; V_{DS}, volume of dead space; V_T, tidal volume.

vating peak airway pressure, by altering or reversing the I:E ratio. In Table 2, these 2 methods are compared.

Permissive Hypercapnia

When lung compliance is extremely low or airway resistance is irreversibly high, it may be difficult to provide adequate ventilation and carbon dioxide removal at "safe" airway pressures with either CVLMV or CPLMV. Therefore, a low V_T (5-6 mL/kg body weight) may be accepted and the P_{aCO_2} permitted to rise, that is, permissive hypercapnia. Although permissive hypercapnia can be implemented in either volume- or pressure-limited ventilation, it is more commonly associated with CPLMV because this mode is more often used when airway pressure becomes excessive.

Under most circumstances the elevated P_{aCO_2} causes respiratory acidemia, which may lead to the potentially harmful effects of the following[5,12,13]:

- decreased myocardial contractility,
- systemic vascular dilatation,
- dysrhythmias,
- decreased cellular energy metabolism,
- insulin resistance, and
- decreased P_{aCO_2}.

Possible changes related to acidemia become most significant when pH falls below approximately 7.2. Therefore, some authors advocate administration of metabolic buffering agents such as sodium bicarbonate[14] or tromethamine[12] to raise the pH above 7.2.

Clinical Recommendations

As clinical experience is gained, the OPC may become comfortable with both volume- and pressure-limited modes of ventilation. However, the OPC may have greater exposure to one than the other and may prefer to use that technique in caring for organ donors. The literature does not clearly establish one mode to be superior to the other.[6,15] Both modes permit low-pressure ventilation and reversal of the I:E ratio for treatment of extreme hypoxemia and permissive hypercapnia if needed to maintain low airway pressures and volumes. The rate of barotrauma has been shown to be the same[15,16] or similar[4] when CVLMV and CPLMV have been compared in patients at similar airway pressures. In our clinical experience, we have observed numerous cases in which switching from CVLMV to CPLMV has preserved V_T at a lower peak airway pressure. No studies compare CVLMV and CPLMV in donors. The OPC should be free to utilize the method with which he or she is more comfortable.

The relative safety of larger V_T and higher pressure versus lower V_T and lower pressure ventilator strategies remains controversial,[14,17,18] especially when mortality is not an issue. However, it is currently considered accepted practice to use either volume- or pressure-limited modes to maintain airway, alveolar, and transpulmonary pressures below the levels previously listed.[19] In our clinical experience, however, we have found that reduced airway pressure techniques simply do not work

in some patients when lung compliance is severely reduced, such as in advanced acute respiratory distress syndrome. This failure is usually manifested by continuing or progressive severe hypoxemia despite an FIO_2 approaching 1.0 and either a mean airway pressure above 30 cm H_2O (CVLMV) or I:E reversal to about 3:1 (CPLMV).[13] In such extreme and uncommon situations, it may be necessary to return to higher VT and/or PEEP and, therefore, to higher peak airway pressures.[20,21] Older methods of mechanical ventilation have stressed the importance of reaching a "critical opening pressure or volume" with the inspired volume to force less compliant lung units open, a process termed "recruitment." Unfortunately, such high volumes and pressures may overdistend less diseased lung units, raising concern about barotrauma. However, rarely, this may be the only alternative that reverses severe hypoxemia and if barotrauma occurs, its consequences (eg, pneumothorax) may require treatment. Similarly, such high pressures may reduce cardiac output and require extra intravenous fluid and/or inotropic support. When such extreme measures appear needed, considerable discussion between the OPC, respiratory care practitioner, and physician is mandatory.

Summary

CPLMV is a mode of mechanical ventilation available in caring for donors. VT is the parameter that potentially becomes limited or variable during CPLMV, as airway pressure is protected. Permissive hypercapnia and I:E ratio changes and reversal are adjuncts to both volume- and pressure-limited modes of ventilation to further permit low volumes and airway pressures and to improve oxygenation, respectively. The OPC may encounter or employ CPLMV and these other techniques in caring for donors and should be familiar with them and their potential harmful effects on donor organs.

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Using pressure-limited mechanical ventilation in caring for organ donors

Objectives

1. Discuss indications and goals of pressure-limited mechanical ventilation
2. Identify differences in the components of pressure-limited mechanical ventilation including tidal volume, ventilator rate, and flow rate
3. Describe the clinical recommendations for the use of controlled volume-limited mechanical ventilation

Mark your answers clearly in the appropriate box. There is only one correct answer. You may photocopy this form.

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❑b	❑b	❑b	❑b	❑b	❑b	❑b	❑b	❑b	❑b	❑b	❑b	❑b
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CE Test Questions

Using pressure-limited mechanical ventilation in caring for organ donors

1. Controlled pressure-limited mechanical ventilation (CPLMV) is commonly used when lung compliance demonstrates which of the following parameters?
   a. High and cannot be reversed
   b. High and can be reversed
   c. Low
   d. Equal to plateau pressure

2. During CPLMV, what is the goal of peak airway pressure?
   a. >40 cm H_20
   b. <50 cm H_20
   c. <35 to 40 cm H_20
   d. <20 cm cm H_20

3. Which one of the following conditions can be caused by high airway pressures?
   a. Volutrauma
   b. Barotrauma
   c. Atelectrauma
   d. Biotrauma

4. Which one of the following conditions can be caused by excessive distending alveolar volumes?
   a. Volutrauma
   b. Barotrauma
   c. Atelectrauma
   d. Biotrauma

5. Shear forces acting upon lung units during opening and closing can cause which condition?
   a. Volutrauma
   b. Barotrauma
   c. Atelectrauma
   d. Biotrauma

6. Which one of the following parameters is not set in the pressure-limited mode of ventilation?
   a. Ventilator rate
   b. Tidal volume
   c. Inspiratory pressure
   d. Mean airway pressure

7. Gas flow into the lung during CPLMV is determined by which parameter?
   a. Set inspiratory pressure
   b. Mean airway pressure
   c. Inspiratory-expiratory ratio
   d. Ventilator rate

8. Which one of the following parameters is not available during CPLMV?
   a. Positive end-expiratory pressure (PEEP)
   b. Inspiratory pressure
   c. Inspiratory pause
   d. Inspiratory-expiratory ratio

9. If the time needed for exhalation is longer than the exhalation time provided by the ventilator, what condition may occur?
   a. Prolonged inspiratory time
   b. Shortening of expiratory time
   c. Auto-PEEP
   d. Increased airway pressure

10. Changes related to acidemia become most significant when the pH falls below what level?
    a. 7.35
    b. 7.30
    c. 7.25
    d. 7.20

11. Which one of the following terms is used to describe the average airway pressure over 1 minute as calculated by the mechanical ventilator?
    a. Peak airway pressure
    b. Mean airway pressure
    c. Plateau airway pressure
    d. Inspiratory pressure

12. What is the maximum airway pressure created during the ventilator's inspiratory cycle?
    a. Peak airway pressure
    b. Mean airway pressure
    c. Plateau airway pressure
    d. Inspiratory pressure

13. In comparison to controlled volume-limited mechanical ventilation, what is done in CPLMV to meet the goal of increasing ventilation?
    a. Increase tidal volume
    b. Increase pressure limit
    c. Minimize dead space volume
    d. Increase ventilator rate

Challenges in donor care

This article is provided as a self-study feature on care of organ donors. Questions and possible responses are provided. Review all the responses for each question.

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Each donor presents a unique set of diagnostic and therapeutic challenges. Single laboratory or hemodynamic abnormalities such as hypernatremia and hypotension will be encountered repetitively by the organ procurement coordinator (OPC) in many donors. However, combinations and degrees of severity of the many possible physiological changes in each donor always require the following:

- an individualized assessment,
- development of a problem list, and
- a titrated resolution for each problem.

In this series of self-study articles, these and future challenges in donor care are developed to follow those 3 steps within the format of a patient scenario. An interactive process will be attempted through a series of questions. It is recognized that this method of instruction is artificial and falls short of the discussions you will have with physicians and nurses at the donor's bedside. Although presented as questions that have correct and incorrect answers, you are encouraged to review all of the possible responses as review information will be contained within each. It is also recognized that many interventions can and should occur almost simultaneously, but questions about priorities will be asked so as to reinforce the relative importance of several disorders. Likewise, as donor care continues, problems evolve, become resolved, or appear so that the fluidity of care and changing priorities should be appreciated. Finally, in such exercises there is always room for discussion about "the right answer" and the nuances or opinions about care to be provided. I reluctantly offer my opinions and experiences in choosing the areas of emphasis and correct responses. They are based on the recent series of articles published in *Progress in Transplantation*.[1-5] I regret that we cannot directly discuss these care issues, as should occur between colleagues.

The scenarios to follow do not address criteria used to determine if organs are acceptable for transplantation. We will focus on donor care issues only. Proceed through the series of questions based upon the patient situation presented. Although some answer choices are incorrect for the question asked, each has information that may be useful to you.

Patient Case

M.L., a 46-year-old man, was riding an off-road motorcycle and struck a tree. Despite aggressive treatment of his closed head injury, the diagnosis of brain death was confirmed according to hospital policy 2 days after he was brought to the hospital. The family agreed to organ donation. As the on-call OPC, you have been belatedly called with the request that you assume care.

Donor Assessment

Initial donor evaluation includes data important in assessing suitability of organs for transplantation (not discussed here) and in continuing donor care. A detailed review of the medical record is mandatory to identify all significant prior medical and surgical history, allergies, medications before and during this

hospitalization, and any notations from the admitting review of systems. A careful analysis of the donor's medical and surgical course since admission and discussion with nurses and other care providers will contribute important information about specific and current care issues. Although laboratory testing of blood or other specimens may be expensive and requires consumption of important resources, it is a critical component of the OPC's initial evaluation and subsequent care planning. Symptoms caused by many electrolyte abnormalities, acid-base imbalance, altered serum glucose concentrations, and coagulation disorders are nonspecific or difficult to detect. Therefore, a broad initial laboratory database is justified and the following should be obtained: arterial blood gas levels, electrolyte levels (sodium, potassium, chloride, and bicarbonate), magnesium and phosphorous concentrations, ionized calcium concentration, albumin concentration, complete blood cell count (including platelets), serum urea nitrogen (SUN) level, creatinine concentration, prothrombin time, and partial thromboplastin time (Tables 1 and 2). Other specialized tests such as measurement of levels of urine electrolytes, fibrinogen, and lactate may be needed as indicated by these initial laboratory data.

M.L. had a history of adult onset diabetes about 5 years before the accident and had been taking a "pill" to control his blood sugar. In addition, he had angina 2 years before the accident and underwent cardiac catherization and angioplasty at that time. M.L.'s current nurse relates that over the past 3 hours M.L.'s blood pressure has fallen and his urine output has been increasing.

Table 1 Patient data

Body weight, 70 kg
Temperature, 32.9°C (91.2°F)
Blood pressure, 92/42 mm Hg
Central venous pressure, 4 mm Hg
Mean blood pressure, 58 mm Hg
Heart rate, 142 beats per minute (sinus rhythm)
Spo_2 (Sao_2), 92%
Urine output, 500-700 mL/h

Ventilator settings
- Tidal volume, 750 mL
- Rate, 10 breaths per minute
- Minute ventilation, 7.5 L/min
- PEEP, 5 cm H_2O
- Peak airway pressure, 28 cm H_2O
- Fraction of inspired oxygen, 0.40

Laboratory data
- Sodium, 158 mmol/L
- Potassium, 3.1 mmol/L
- Chloride, 132 mmol/L
- Bicarbonate, 14 mmol/L
- Urine sodium, 5 mmol/L
- Arterial blood gas values:
  - pH, 7.20
  - $Paco_2$, 37 mm Hg
  - Pao_2, 72 mm Hg
  - Bicarbonate, 13 mmol/L
  - Base excess, -12
- Albumin, 22 g/L
- SUN, 8.6 mmol/L (24 mg/dL)
- Creatinine, 79.6 µmol/L (0.9 mg/dL)
- Phosphorus, 0.45 mmol/L (1.4 mg/dL)
- Glucose, 16.5 mmol/L (297 mg/dL)
- Urine specific gravity, 1.003
- PT, PTT, and platelets, within normal limits
- Hematocrit, 0.34
- Magnesium, 0.50 mmol/L (1.2 mg/dL)

$Paco_2$ indicates arterial partial pressure of carbon dioxide; Pao_2, arterial partial pressure of oxygen; PEEP, positive end-expiratory pressure; PT, prothrombin time; PTT, partial thromboplastin time; Sao_2, arterial oxygen saturation; Spo_2, oxygen saturation as measured by pulse oximetry; SUN, serum urea nitrogen.

List of Problems

Having established a database, the donor care plan evolves on the basis of findings from the patient's history, medical record, laboratory studies, or discussions with other care providers. At this point, the list of problems for M.L. would include the following:

- Evaluation of suitability of donor organs for transplantation (not discussed here)
- History of coronary artery disease and diabetes mellitus
- Multiple electrolyte abnormalities
- Hypothermia
- Hypotension
- Hypoalbuminemia
- Sinus tachycardia
- Hyperglycemia
- Acidemia

Table 2 Normal laboratory values

Sodium, 136-145 mmol/L
Potassium, 3.5-5.1 mmol/L
Chloride, 98-107 mmol/L
Bicarbonate, 22-29 mmol/L
Urine sodium, 20-40 mmol/L
Arterial blood gas values:
- pH, 7.38-7.46
- $Paco_2$, 32-46 mm Hg
- Pao_2, 74-108 mm Hg
- Bicarbonate, 24-32 mmol/L
- Base excess, 0

Albumin, 35-50 g/L (3.4-5.0 g/dL)
Serum urea nitrogen, 2.9-8.2 mmol/L (7-18 mg/dL)
Creatinine, 53-106 µmol/L (0.6-1.3 mg/dL)
Phosphorus, 0.74-1.52 mmol/L (2.5-4.7 mg/dL)
Glucose, 3.9-6.1 mmol/L (70-100 mg/dL)
Urine specific gravity, 1.010
Hematocrit, 0.37-0.48
Magnesium, 0.6-0.95 mmol/L (1.8-2.4 mg/dL)

- Polyuria
- Continuing family support

Although it is possible, and usual, to initiate several corrective measures simultaneously, it is important to establish treatment priorities for nursing and respiratory care personnel. Follow-up assessments in each of these problem areas will also be required as donor care proceeds. Detection of new problems may also require repeated surveillance testing.

Question 1

Which one of the problems listed below is of greatest concern to you at this time?

a. Electrolyte abnormalities (Review response 6)
b. Acid-base status (Review response 9)
c. Vital signs (Review response 7)
d. Body temperature (Review response 1)

Question 2

M.L.'s high urine output may cause hypovolemia and hypotension, potentially injuring donor organs. In what ways can you compensate for or correct his polyuria? (First, review response 6, then select the best answer below.)

a. Replace the urine output each hour with an equal volume of isotonic sodium chloride solution. (Review response 2)

b. Administer 5% dextrose in water to correct the calculated water deficit. (Review response 12)

c. Use vasopressin nasal spray each hour until the urine volume decreases. (Review response 5)

d. None of the above (Review response 10)

Question 3

Within 2 hours you have slowed the polyuria and partially corrected the acidemia and electrolyte changes. However, despite a 2.5-L hypotonic crystalloid infusion, the mean arterial pressure (MAP) is still less than your goal of 65 mm Hg. The central venous pressure (CVP) is 8 mm Hg; MAP, 58 mm Hg; heart rate, 120 beats per minute; and urine output, 150 to 200 mL/h. You had to increase the fraction of inspired oxygen (FIO_2) to 0.60 to sustain the oxygen saturation as measured by pulse oximetry greater than 92%. Because of several emergency surgeries no operating room is likely to be available for another 4 hours. You plan to continue correction of the electrolyte abnormalities and to balance fluid intake and urine output but are concerned about the persistent tachycardia and increasing oxygen requirement. Your next step should be which one of the following?

a. Continue observation and fluid titration—no new treatment. (Review response 3)

b. Administer a rapid intravenous (IV) infusion of 5% albumin. (Review response 8)

c. Request placement of a pulmonary artery catheter. (Review response 11)

d. Begin dopamine at 10 mg/kg per minute. (Review response 4)

Response 1

Body temperature

At this body temperature, coagulation abnormalities may occur and oxygen delivery to donor organs may be impaired due to vasoconstriction, altered cardiac contractility, or arryhythmias and a shift of oxygen-hemoglobin association that "tightens" the binding of oxygen and hemoglobin. Clearly these are important physiologic consequences that must be considered, but this is *not* the highest treatment priority.

Admittedly, a lower body temperature may lower metabolic tissue demands within donor organs thereby, perhaps, making them more tolerant of other physiological stress. However, hypothermia, at any level has not been shown to be beneficial to transplanted organs. Therefore, although limited, available data suggest that donor body temperature should be maintained above 34°C (93.2°F).

As one of the "simultaneous" interventions you initiate, the respiratory gas delivered by the mechanical ventilator should be heated. The respiratory care practitioner will initiate and monitor this adjustment at your request. In addition, "active" body rewarming techniques, such as forced air or water "warming blankets," will be effective in raising the body temperature.

Return to question 1 and select another response.

Response 2

Replace the urine output each hour with an equal volume of isotonic sodium chloride solution.

The likely causes of polyuria, as discussed in response 6, all produce a greater loss of free water than sodium. Therefore, the plasma space is dehydrated (ie, less water) as well as having less total volume. Isotonic sodium chloride solution (0.9% sodium chloride) contains 154 mmol/L of sodium and chloride in each liter. Thus, both chloride and sodium are higher in the IV solution than normally in the plasma. Because this donor already has high sodium and chloride levels in the plasma, the therapeutic goal is to reduce both by using a hypotonic solution containing lower amounts of both and more free water.

Although it is common to replace the urine output milliliter per milliliter with a hypotonic crystalloid solution, it is often difficult for nursing staff to administer the high volumes produced during diabetes

insipidus. Therefore, simply replacing volume may not be enough! Because of the patient's low intravascular volume (review response 7), you would necessarily need to "catch up" before you can hope to "keep up" with the high urine output. Urgent fluid resuscitation, therefore, should be a part of your intention to titrate urine volume against replacement fluid. It is important to replace fluid losses with a hypotonic solution. Replacement of urine output with isotonic sodium chloride solution is, therefore, an *incorrect* response.

Return to question 2 and make another choice.

Response 3

Continue observation and fluid titration—no new treatment.

This conservatively *correct* answer is acceptable as long as no further decline in cardiorespiratory function occurs. Therefore, it is important to establish and monitor critical parameters such as (1) decreasing oxygen saturation as measured by pulse oximetry, which may reflect fluid accumulation in the lung that could adversely affect oxygen diffusion; (2) increasing heart rate, which may indicate compensation for worsening cardiac contractility; and (3) further decline in MAP or increase in CVP, which may suggest further heart failure.

Urine output is an unreliable indicator of cardiac output when diabetes insipidus is present. Free water diuresis will continue until severe hypovolemia is present and well beyond when treatment should have been started.

Return to question 3 for other options.

Response 4

Begin dopamine at 10 mg/kg per minute.

Dopamine is an effective positive inotropic agent intended to improve cardiac contractility. It may also have a positive chronotropic effect and increase the sinus tachycardia, which, in general, would be an undesirable effect.

Even though you have administered a reasonable volume challenge, the low MAP and CVP but high heart rate could indicate either inadequate intravascular volume (preload) or poor cardiac contractility. In addition, a high systemic vascular resistance (afterload) might be present given his history of coronary artery disease. Therefore, of the 4 determinants of cardiac output (heart rate, preload, afterload, and contractility), only heart rate is known at this time. The CVP may not reflect the pulmonary artery occlusion (PA_O) wedge pressure, the better measure of left ventricular preload in patients with existing heart disease or failure.

Therefore, this is an *undesirable* option and may risk further tachycardia. If you wish to try dopamine, begin at a lower infusion rate, perhaps 3 to 5 mg/kg per minute, and observe its effect. Dobutamine would be another option if a positive inotropic agent is desired.

Return to question 3 and consider another option.

Response 5

Use vasopressin nasal spray each hour until the urine volume decreases.

Vasopressin, antidiuretic hormone (ADH), is available in several forms. Nasal spray is often used after surgical removal of the pituitary gland when chronic replacement therapy is needed. Vasopressin may also be given as an oil or aqueous preparation. Aqueous vasopressin is more applicable during donor care and may be given intravenously as an infusion or a bolus, repeated as necessary. Both may be titrated to control urine output during polyuria because of diabetes insipidus. Because vasopressin may also have a vasoconstrictive effect, some concern exists that, at higher doses, it may decrease blood flow to donor organs.

Desmopressin (DDAVP) is considered the drug of choice for the replacement of ADH when diabetes insipidus occurs in donors. It is given intravenously in titrated bolus doses, usually beginning at 1 µg. Its effect begins quickly so that if polyuria persists over the hour following drug administration, the dose may be repeated. Desmopressin has a variable duration of action, usually a few hours. Once polyuria resumes, another dose can be given. A dose that is too large will cause a low urine output, also an unfavorable result, so be careful! Therefore, although IV aqueous vasopressin is possibly a correct answer, this method of ADH administration during donor care *is not correct.*

Return to question 2 and select another response.

Response 6

Electrolyte abnormalities

Although the laboratory data document significant changes in several electrolyte levels and glucose metabolism, these will *not* be your primary concern. The electrolyte abnormalities shown here likely result from the donor's polyuria and prior therapy. These abnormalities indicate free water loss in excess of salt loss resulting in hypernatremia and reductions in levels of several other important ions.

Reasons for the polyuria may include:

• *Hyperglycemia.* Blood glucose levels greater than about 10.0 mmol/L (180 mg/dL) allow passage of glucose into the urine, which may cause an osmotic diuresis wherein more water than salt is lost.

• *Prior use of diuretics and mannitol.* Mannitol is often used during management of intracranial hypertension but also produces an osmotic diuresis, free water loss, and an increased sodium level. Similarly, most currently used diuretics (eg, furosemide) also cause more free water loss than salt excretion (naturesis).

• *Diabetes insipidus (partial or complete).* ADH (vasopressin) production is usually reduced or lost after brain death. ADH normally increases water reabsorption in the kidney. A reduction in ADH, therefore, is associated with a loss of water (free water) from the body via the kidneys, hence polyuria and dehydration of the plasma, resulting in hypernatremia.

• *Physiological diuresis.* Prior excessive fluid administration may cause a normal physiologic diuresis to return fluid balance to normal. However, although leading to polyuria, this response would not cause hypernatremia to this level. Therefore, a physiological diuresis is not a likely cause of this donor's polyuria.

Hypernatremia may have a significant impact upon organ function. Sodium predominantly remains in the extracellular fluid compartment. However, it effectively increases serum osmolarity and may cause water to leave the intracellular space and enter the extracellular compartment. This intracellular "dehydrating" effect may be injurious to donor organs.

The serum potassium concentration is low. This value is important relative to the blood pH, as potassium will leave the cell and enter the plasma when the blood is acidemic. As the acidemic state is corrected the potassium may move back into the cell and worsening hypokemia may result. Therefore, urgent replacement of potassium should be planned as you begin additional fluid resuscitation. The amount and infusion rate of potassium is usually governed by hospital policy. Therefore, administer potassium at the maximum allowable amount and recheck serum concentrations frequently.

Both phosphorus and magnesium concentrations are low and should be replaced. Low levels of these ions can produce arrhythmias and intracellular changes within donor organs. Most hospitals also have guidelines for phosphorus and magnesium replacement.

The SUN-to-creatinine ratio is elevated (normal = about 10), which often indicates some degree of intravascular hypovolemia. Other causes include some other source from which additional urea is being added to the serum, such as a hematoma from which blood is being reabsorbed.

Hyperglycemia may contribute to the polyuria as noted above and should be corrected. Remove dextrose from IV fluids and reassess the serum glucose level. Although the glucose level at which hyperglycemia should be treated is controversial, I prefer to maintain the blood glucose level less than 11.1 mmol/L (200 mg/dL). Insulin will likely be necessary because of the patient's history of diabetes mellitus. Dosing should be discussed with your medical consultant.

Return to question 1 and choose another response.

Response 7

Vital signs

Correct! Based on the vital signs—low MAP (goal >65 mm Hg), tachycardia (goal <100 beats per minute), low CVP (goal 8-12 mm Hg)—and laboratory data, the donor is in shock! Of the potential types of shock (hypovolemic, distributive, cardiogenic, or obstructive) the most likely cause is hypovolemia. Such a conclusion is supported by the SUN-creatinine ratio, serum sodium concentration, vital sign changes, and prolonged uncorrected or uncompensated polyuria. The donor's prior cardiac history, however, is important and cardiogenic causes must also be considered (see response 11).

Rapid infusion of fluid is suggested by these data. Because the serum glucose level is already elevated, a fluid that does not contain dextrose should be chosen. The selection of fluid is also limited by the high levels of serum sodium and chloride. Additional isotonic sodium chloride solution (154 mmol/L of both sodium and chloride per liter) may contribute further to the metabolic acidemia already present. Ringer's lactate solution or even hypotonic solutions such as 0.45% sodium chloride solution would be preferred. Because of the high serum sodium and hence osmolality already present, the hypotonic solution will likely stay within the vascular compartment and provide volume expansion.

Blood is presently not indicated as the hematocrit level is 0.34. As other fluid is given, however, the hematocrit level may fall as the red blood cells become more diluted within the vascular space. Periodic hematocrit measurements would, therefore, be indicated.

Although you have chosen the correct response, please review the other possible choices for this question for additional information.

Proceed to question 2 and continue your donor care.

Response 8

Administer a rapid IV infusion of 5% albumin.

This response may also be considered *correct* if the low CVP accurately reflects preload (venous return). The CVP, however, may not be a good measure of the left ventricular preload (see response 11) in donors with intrinsic heart disease.

The choice of a colloid solution, such as 5% albumin, would be considered appropriate by some authors because of the low serum albumin, although the selection of a colloid versus crystalloid solution for rapid infusion remains controversial. Those advocating colloid suggest that the larger molecular size of albumin, starch solutions (eg, Hespan) or dextran would reduce movement of the liquid across capillaries into the interstitial fluid spaces. For example, less interstitial fluid in the lung may improve oxygen diffusion and allow adequate arterial oxygenation at a lower FIO_2. The opposing opinion suggests that depending on the presence and severity of a "capillary leak" in the pulmonary or other capillaries, the colloid molecules may also traverse the capillary and enter the interstitial space. Because the presence and amount of capillary leakage cannot easily be measured, these differing opinions continue to be discussed and investigated. Some authors believe starch solutions should not be used during donor care. Therefore, this response would be acceptable with caution based on the prior history of coronary artery disease in this donor and because of the rising FIO_2 requirement noted by the nurse.

Return to question 3 and consider other options

Response 9

Acid-base status

The pH of 7.20 represents a significant acidemia that may reduce myocardial contractility and hence cardiac output. However, this is *not* the primary concern demanding your first intervention.

Both respiratory and metabolic components to the acidemia are present. The initial correction should be to increase either the ventilator rate (recommended maximum of 24 breaths per minute) or tidal volume (recommended maximum of 10 mL/kg), and hence the minute ventilation, to lower the arterial partial pressure of carbon dioxide ($PaCO_2$) and raise the pH. Using sequential arterial blood gas measurements, the $PaCO_2$ may be titrated down to 16 mm Hg to achieve a pH above 7.35, as long as the peak airway pressure remains below 45 cm H_2O. If adjustment of the ventilator does not increase the pH to 7.30 to 7.35, treatment with bicarbonate may be considered as discussed with your medical consultant. Administration of sodium bicarbonate, however, may increase the hypernatremia and hyperosmolar conditions already present.

Note that the anion gap (sodium – [chloride + bicarbonate]) is normal at 12, indicating that a normal anion gap acidosis is present likely because of the hyperchloremia caused by prior administration of isotonic sodium chloride solution. Recall also that as you improve the pH toward normal, potassium will move into the cell, thus potentially worsening the hypokalemia (see response 6).

Return to question 1 and select another option.

Response 10

None of the above

Correct! None of these responses is correct. Please review each response to refresh your memory about why it is not correct.

Polyuria is a potentially highly dangerous occurrence as it may produce significant hypovolemia, leading to hypotension and damage to the organs awaiting transplantation. The volume of urine produced by the donor may be surprisingly large, exceeding several hundred milliliters per hour. Rapid control of the urine output, through use of an IV ADH preparation, and replacement of the intravascular volume lost, usually with hypotonic fluid, remain critical interventions.

Proceed to question 3.

Response 11

Request placement of a pulmonary artery catheter.

Although this may appear to be an extreme intervention, I believe it is the *most correct* response. More information is needed to guide your choice of the next intervention because:

- this donor's preexisting heart disease makes the CVP a less reliable indicator of left ventricular preload,
- the increasing FIO_2 requirement may indicate accumulating interstitial fluid in the lung,
- of the delay in obtaining operating room time,
- the low MAP and high heart rate may suggest either a low or high left ventricular filling pressure (preload), and
- cardiac contractility cannot otherwise be estimated.

Following ischemic injury to the heart, the left ventricle may develop either or both changes in systolic contraction or diastolic relaxation. The former can be estimated either by calculation of the left ventricular stroke work index (LVSWI):

$LVSWI = 0.0136\ (MAP\text{-}PA_o) \times$ stroke volume index

LVSWI calculation requires a pulmonary artery catheter or evaluation of the left ventricular ejection fraction using an echocardiogram or right ventricular ejection fraction catheter. Reduced left ventricular systolic function may respond to administration of a positive inotropic agent such as dobutamine or dopamine.

Diastolic dysfunction is more difficult to document at the bedside and may only be suggested by the echocardiogram. This abnormality in relaxation of the ventricle during diastole reduces left ventricular volume during diastole. The left ventricular "stiffness" also has the effect of falsely elevating the PA_o so that a smaller preload volume is "overrepresented" by a

higher PA_O (wedge) pressure reading. In this situation more intravascular volume may be helpful despite the heart appearing "full" as indicated by a normal PA_O.

Therefore, placement of pulmonary artery catheter would allow assessment of the PA_O and calculation of the LVSWI. The CVP does not always reflect the PA_O in patients with ischemic heart disease. Therefore, if the PA_O is also found to be low (<8 mm Hg), fluid administration is still needed. If the PA_O is generous (>18 mm Hg) and the cardiac output and LVSWI are low, cautious use of an inotropic agent is indicated. Subsequent monitoring of these parameters will also assist treatment over the next 4 or more hours before the operating room is available.

Review other options in question 3.

Response 12

Administer 5% dextrose in water to correct the calculated water deficit.

The amount of free water needed to "dilute" the high sodium back to normal is calculated from the free water deficit:

Current sodium x D = 140 (0.6 x body weight in kilograms). (D is the unknown effective volume of distribution of the current serum sodium.) Solve for D (in this donor, it is 37 kg [or liters]). Subtract D from the product of 0.6 x current weight in kilogram. In this donor, 42-37 = 5 kg (L) is the water deficit.

One half of the calculated deficit may be replaced quickly and the serum sodium levels measured again.

Pure water cannot be given intravenously and must be combined with dextrose or some amount of salt. The volume of water needed to replace even one half of a calculated deficit can be quite large and when given as a dextrose solution may produce or worsen hyperglycemia. Response 6 reviews the potentially harmful consequences of hyperglycemia. Therefore, this is an *incorrect* choice for this question.

Administration of a hypotonic saline solution, such as quarter or half isotonic sodium chloride solution without dextrose would provide free water although also adding some salt to the plasma compartment. The advantage of one of these solutions is that dextrose is not needed and hyperglycemia can be avoided. The calculated free water deficit may serve as a rough guideline for hypotonic salt solution administration, but measurements of sodium concentration should be repeated frequently.

Return to question 2 and make another selection.

Thank you for completing this review of some challenges in donor care. I look forward to discussing others with you in future issues of *Progress in Transplantation.*

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Interactive Grand Rounds

Challenges in donor care: part 2

This article is provided as a self-study feature on care of organ donors. Questions and possible responses are provided. Review all the responses for each question.

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As introduced in the first Challenges in Donor Care article (December 2001),[1] combinations and degrees of severity of the many possible physiological changes in each donor requires the following:

- a repetitive individualized assessment of the donor's physiological status derived from physical examination, laboratory testing, chart review, bedside discussions, and measurement of hemodynamic parameters;
- development of a list of problems; and
- titrated treatment of each problem including periodic reassessments.

This case-based discussion and interactive process will attempt to simulate the clinical environment encountered by organ procurement coordinators (OPCs) through a series of questions. I regret that this method falls short of the discussions you will and should have with physicians, nurses, and other care providers at the donor's bedside.

Many interventions can and should occur almost simultaneously, but questions about priorities and sequences of actions will be asked to reinforce their relative importance. Likewise, as donor care continues, problems evolve, resolve, or appear. This fluidity of care and changing priorities should also be appreciated.

Finally, in such exercises, there is always room for discussion about the "right" answer and the nuances of care to be provided. I reluctantly offer my opinions and experiences in choosing the areas of emphasis and correct responses. They are based on a series of articles published in *Progress in Transplantation*.[2-6] I regret that we cannot directly discuss these care issues at the bedside.

The case example that follows does not address criteria used to determine if organs are acceptable for transplantation. We will focus only on donor care issues. Proceed through the series of questions and fully answer each one. When several alternative responses are offered, review each answer, because all contain useful information.

Patient Case

M.W., a 24-year-old male pedestrian, was struck by a car. Three days later, his sustained injuries—a severe pelvic fracture, chest trauma, and blunt head injury—culminated in brain death certification. His chest injuries necessitated placement of bilateral thoracostomy (chest) tubes. The settings on the mechanical ventilator were progressively changed as M.W.'s hypoxemia and hypercarbia worsened.

Donor Assessment

A detailed review of the medical record is mandatory to identify significant prior medical and surgical histories, allergies, medications before and during this hospitalization, and any notations from the admitting review of systems. A careful analysis of the donor's hospital course since admission and discussion with nursing and other care providers will provide information about specific and current care issues. Although laboratory testing of blood or other specimens may be expensive and consumes important resources, a broad initial laboratory database is a critical component in the OPC's initial evaluation and problem list. Therefore, the following values should be obtained: arterial

blood gas (ABG), electrolyte levels, magnesium and phosphorous concentrations, ionized calcium concentration, albumin concentration, complete blood cell count (including platelets), serum urea nitrogen level, creatinine concentration, prothrombin time, and partial thromboplastin time (Table).

M.W. had no significant medical or surgical history, allergies, medications, or findings from review of systems. His family history was also unremarkable. At the time of his admission, a large left hemothorax was present, but was evacuated by the left thoracostomy tube. A pneumothorax within the right hemithorax, also present at admission, was reduced in size, but a persistent "bubbling" from the chest tube continued.

List of Problems

The subsequent care plan evolves from findings and data including the donor's history, course in the hospital, medical record review, physical assessment, laboratory data, discussions with other care providers. At this point, the list of problems for M.W. would include the following:

- Hypoxemia—absolute and relative to the fraction of inspired oxygen (F_{IO_2})
- Hypercarbia—absolute and relative to the minute ventilation
- Chest trauma with a persistent gas leak via a bronchopleural fistula
- Acidemia with elevated P_{aCO_2} but normal base excess
- Elevated peak and plateau airway pressures

Although it is possible, and usual, to initiate several corrective measures simultaneously, it is important to establish treatment priorities for nursing and respiratory care personnel. Follow-up assessments in each of these problem areas will also be required as donor care proceeds.

Patient data
Body weight, 65 kg
Temperature, 37°C (98.6°F)
Blood pressure, 110/60 mm Hg
Central venous pressure, 12 mm Hg
Mean blood pressure,[4] 82 mm Hg
Heart rate, 94 beats per minute (sinus rhythm)
Spo_2 (Sao_2), 88%
Urine output, 40-70 mL/h
Ventilator settings
Mode, volume controlled
Tidal volume, 800 mL
Rate, 12 breaths per minute
Minute ventilation, 9.6 L/min
PEEP, 5 cm H_2O
Flow rate, 90 L/min
Fraction of inspired oxygen, 0.75
Peak airway pressure, 48 cm H_2O
Plateau airway pressure, 42 cm H_2O
Mean airway pressure, 20 cm H_2O
Auto-PEEP, 0 cm H_2O
Exhaled tidal volume, 700 mL
Laboratory data
Sodium, 142 mmol/L (142 mEq/L)
Potassium, 4.3 mmol/L (4.3 mEq/L)
Chloride, 103 mmol/L (103 mEq/L)
Bicarbonate, 27 mmol/L (27 mEq/L)
Arterial blood gas values:
pH, 7.20
$Paco_2$, 60 mm Hg
Pao_2, 56 mm Hg
Bicarbonate, 26 mmol/L (26 mEq/L)
Base excess, -1
Renal and liver function tests, magnesium, ionized calcium, phosphorous, glucose, platelet count, complete blood cell count, and coagulation studies are normal.

PEEP indicates positive end-expiratory pressure; Sao_2, arterial oxygen saturation; Spo_2, oxygen saturation as measured by pulse oximetry.

Question 1

Select from the choices below the problem you will address with the greatest urgency:

a. Acidemia
b. Elevated peak and plateau airway pressures
c. Hypoxemia
d. Gas leak via the bronchopleural fistula

Question 2

The changes in ventilator settings prompted by question 1 resulted in the following ABG values: pH 7.31, P_{aCO_2} 50 mm Hg, P_{aO_2} 69 mm Hg, bicarbonate 25 mEq/L, base excess 0. At this time, ventilator settings and observations included volume-controlled mode, set tidal volume (V_T) 800 mL, respirations 12/minute, minute ventilation 9.6 L/min, positive end-expiratory pressure (PEEP) 5 cm H_2O, F_{IO_2} 0.95, inspiratory hold 0.5 seconds, flow rate 90 L/min, peak airway pressure 48 cm H_2O, plateau airway pressure 42 cm H_2O, mean airway pressure 28 cm H_2O, auto-PEEP 0 cm H_2O, exhaled V_T 600 mL, and oxygen saturation as measured by pulse oximetry 92%.

You are concerned about the high peak and plateau airway pressures and wish to lower them. From the list of options below, select all that might be effective in lowering peak and plateau airway pressures. Identify what harmful consequence(s) might possibly occur from each option.

a. Decrease V_T
b. Decrease inspiratory hold
c. Decrease flow rate
d. Increase ventilator rate

Question 3

The changes you completed in question 2 have not decreased the airway pressures sufficiently; therefore, you wish to initiate the pressure-controlled (limited) mode of ventilation. At this point, ventilator parameters and ABG values are volume-controlled mode, set VT 500 mL, respirations 22/minute, minute ventilation 11.0 L/min, PEEP 5 cm H_2O, FIO_2 0.95, inspiratory hold 0.5 seconds, flow rate 45 L/min, peak airway pressure 42 cm H_2O, plateau airway pressure 40 cm H_2O, mean airway pressure 28 cm H_2O, auto-PEEP 0 cm H_2O, exhaled VT 480 mL, inspiratory:expiratory (I:E) ratio 1.4:1.0. ABG values are pH 7.28, $PaCO_2$ 56 mm Hg, PaO_2 68 mm Hg, bicarbonate 26 mEq/L, base excess 0.

As you and the respiratory care practitioner collaborate about initiating pressure-controlled ventilation, indicate from the list below the sequence in which you will request the ventilator changes be made:

a. Inspiratory hold
b. Pressure-limit setting
c. Ventilator rate
d. VT
e. I:E ratio or percent inspiratory time
f. Flow rate

Question 4

The initial ABG values on pressure-controlled mechanical ventilation are pH 7.22, $PaCO_2$ 60 mm Hg, PaO_2 62 mm Hg, bicarbonate 26 mEq/L, base excess -2. What ventilator parameters will you change to improve oxygenation and ventilation?

Summary

Congratulations! You have completed this case scenario and some difficult problems in ventilator management commonly encountered during donor care. Please refer to the publications listed in the reference list for further information.

Response 1a

Acidemia

Although the pH of 7.2 is a serious abnormality[5] that may reduce cardiac contractility, current hemodynamic variables for M.W. are acceptable. Of the 4 choices available, this is not of highest priority; however, this problem must also be corrected.

The ABG values indicate that the acidemia is of respiratory origin, with a normal base excess and an appropriate change in the pH corresponding to an acute change in the $PaCO_2$ (pH changes 0.1 pH unit for each 10 mm Hg change in $PaCO_2$).[5] Therefore, correction of the pH will require an increase in minute alveolar ventilation ($\dot{V}A$) to facilitate carbon dioxide removal. It is important to recall that intravenous sodium bicarbonate should not be given because it will be metabolized to volatile carbon dioxide that ordinarily would be removed via the lungs. However, at present, carbon dioxide is not adequately removed. Therefore, further production of carbon dioxide could worsen the acidemia until $\dot{V}A$ and/or lung function can be improved. In addition, excessive dissolved carbon dioxide may diffuse into tissue cells to create an intracellular acidosis. $\dot{V}A$ is determined by the following equation[5]:

$\dot{V}A = (VT - \text{dead space}) \times \text{ventilator rate}$

In this case, VT should not be increased because the plateau airway pressure is already too high (>35 cm H_2O). Therefore, increasing the ventilator rate (ie, frequency) should be the initial step to increase $\dot{V}A$ and to decrease $PaCO_2$. Note that the auto-PEEP is now zero.

By increasing the frequency without changing the VT or inspiratory flow rate, the time for a complete inhalation-exhalation cycle (the so-called cycle time) is shortened.[2] During controlled ventilation, the cycle time is defined by the ventilator rate divided into 60 seconds. Here, the cycle time is 60 seconds/12 = 5 seconds.

The cycle time includes the inspiratory time (Ti) and expiratory time (Te). Ti is determined "actively" by various parameters (ie, VT, flow rate, inspiratory pause), whereas Te is "passive," that is, what is "left over" within the cycle time. The shorter cycle time created by increasing the ventilator rate (without changing other Ti parameters) causes the passive expiratory time to shorten. If the donor has a medical history of lung disease such as chronic obstructive pulmonary disease or asthma that causes "air trapping," the shortened Te may not allow sufficient time for full lung exhalation to occur and may worsen air trapping that might cause auto-PEEP. Therefore, in collaboration with the respiratory care practitioner, carefully reassess the auto-PEEP measurement on the ventilator after increasing the ventilator rate by 2 to 4 breaths/minute. A subsequent ABG measurement is indicated to assess improvement in the pH and $PaCO_2$. Further rate increases may be indicated (recommend to maximum of 24 breaths/minute[5]) to raise the pH above 7.30, as titrated by serial ABG measurements.

Physiological dead space[5] represents an increase in the number of lung units wherein ventilation is relatively better than capillary perfusion. Increased dead space is likely to be present in M.W.'s lung because the $PaCO_2$ is elevated in the presence of a $\dot{V}A$ (9.6 L/min) that is already higher than is usually required (about 7.5 L/min) to maintain a normal $PaCO_2$. In general practice, measurement of the dead space-to-VT ratio by the respiratory care practitioner is not pursued if the change in ventilator rate is effective in lowering the $PaCO_2$. However, blood pressure, heart rate, and other hemodynamic variables should be carefully

monitored. Reduced cardiac output and high airway pressures may worsen physiologic dead space.

Return to the answers for question 1 and select another option.

Response 1b

Elevated peak and plateau airway pressures

Two potentially harmful effects of high airway pressure may be barotrauma, lung rupture secondary to airway pressure and its related effects, and reduced venous return to the heart, causing systemic hypotension and possibly lower delivery of oxygen and other nutrients to donor organs. Although the exact airway pressure at which these consequences may occur cannot be predicted for an individual donor, the plateau airway pressure should remain below 35 cm H_2O.[2] The present airway pressures in this case represent an urgent situation, but are not your first priority.

Note that the difference between the peak and plateau airway pressures is less than 10 cm H_2O. Therefore, the cause of both elevations is likely an intrinsic change in lung compliance (ie, increased stiffness), as may occur in acute respiratory distress syndrome after trauma.[2] This problem will soon be discussed further as M.W.'s care continues.

Return to the answers for question 1 and select another choice.

Response 1c

Hypoxemia

Correct! Hypoxemia and hypotension place organs at high risk for cellular injury before removal. The donor's PaO_2 shows a significant decrease in the partial pressure of oxygen within his blood. This secondarily reduces the amount of oxygen carried on the hemoglobin molecule within the red cell and, potentially, the oxygen delivered to the donor organs. In general, if the hemoglobin concentration is normal in the blood, a PaO_2 above 70 mm Hg should be maintained to ensure an oxyhemoglobin saturation well above 90%

The 2 primary determinants of the PaO_2 are the FIO_2 and the mean airway pressure.[2] In M.W., the FIO_2 is already high at 0.75 but should be further increased by the OPC as an initial response to the documented low PaO_2.

During volume-controlled ventilation, mean airway pressure may be increased, without increasing the peak or plateau pressures, by adding an inspiratory pause (usually ordered as seconds). Start with 0.5 seconds and assess the effect on the pulse oximetry estimate (oxygen saturation as measured by pulse oximetry) of the blood oxyhemoglobin saturation. Changes in other ventilator parameters (increasing VT, PEEP, and flow rate) will also increase the mean airway pressure.[2] However, these 3 changes also elevate the peak airway pressure, already too high in M.W., and may further predispose the donor lung to barotrauma.

Proceed to question 2 or review the other responses to this question.

Response 1d

Gas leak via the bronchopleural fistula

Not the correct response to this question, but an import consideration!

A significant part of the inspired VT delivered by the ventilator may be lost because of a defect in the lung parenchyma. Gas flows from the airspace through the pleural space and into the chest drainage unit via the chest (thoracostomy) tube.[7] Loss of this volume may contribute to or produce both hypoxemia and hypercarbia (increasing $PaCO_2$). The amount of gas leak can be measured through chest drainage units, but is most often closely estimated by subtracting the exhaled VT measured by the ventilator from the known inspiratory set VT. In this case, the delivered VT during the inspiratory phase of the mechanical ventilation is 800 mL and the measured exhaled VT is 700 mL. Therefore, approximately 100 mL (13%) of each inspiratory VT is lost via the chest tube. Some gas exchange may occur in the lung before the inspiratory gas reaches the lung defect, all 100 mL might therefore not be truly "wasted." Although the carbon dioxide and oxygen levels in the gas moving through the chest tube can be measured, this is rarely done.

Occasionally, it is possible to decrease the gas leak by either increasing or removing the vacuum (suction) applied to the chest tube drainage unit. Both options can be safely tried and the effect can be evaluated by noting any decrease in the "bubbling" through the water seal compartment of the drainage unit and an increase in the exhaled VT. In addition, decreasing the peak airway pressure (as discussed in question 2) will lower the positive pressure gradient between the airway and chest drainage system and may reduce gas flow through the bronchopleural fistula.

Return to the options for question 1 and select another choice.

Responses to Question 2

High airway pressure occurs because of an unfavorable balance between the action of the ventilator and abnormally high airway resistance and/or low lung compliance (less distensible lungs).[2] Naturally, the first intervention in lowering high airway pressure would be to assess if any factors causing the increased airway resistance (eg, bronchospasm, kinked tubing, excessive amounts or viscosity of secretions) or low compliance (eg, pulmonary edema)[2] could be reversed. Thereafter,

attention should be directed toward manipulation of the ventilator settings.

During volume-controlled mechanical ventilation, high peak and plateau airway pressures might be lowered if the VT, flow rate, PEEP, or auto-PEEP are decreased. Therefore, the correct responses to question 2 are (a) decreasing VT and (c) decreasing the flow rate. Interestingly, in this case, if the lung defect enlarged so that more inspiratory gas escaped via the chest tube, the peak and plateau pressures would also fall. Such a large leak would likely prove disastrous for the processes of ventilation and oxygenation.

Response 2a

Decrease VT

As explained in response 1a, VT is a critical component of $\dot{V}_A$ ($\dot{V}_A$ = (VT - dead space) × rate) and hence carbon dioxide exchange. By reducing the VT (and high pressures), the $PaCO_2$ would again likely rise and the pH fall. On the other hand, a cause of high physiological dead space may be high airway pressure.[5] When high airway pressure impairs venous return (preload) enough to reduce cardiac output or directly compresses perialveolar blood vessels, less blood perfuses some pulmonary capillaries (relative to the gas ventilation supplied), creating or increasing dead space. When this type of ventilation-perfusion mismatch occurs, less carbon dioxide is exchanged across the alveolocapillary membrane and more carbon dioxide remains within the circulation. By reducing the high airway pressure, therefore, it may be possible to improve venous return, pulmonary perfusion, and carbon dioxide loss even though the $\dot{V}_A$ (VT × rate) falls. An increase in dead space effect is more commonly suspected if the donor's blood pressure is marginal or other evidence of hemodynamic compromise (eg, increasing heart rate, decreasing central venous pressure) is present. Because M.W.'s vital signs were stable, an increase in dead space effect due to the high airway pressure would not likely be the cause of the high $PaCO_2$. Therefore, the most common consequence of decreasing VT will be an increase in $PaCO_2$.

Response 2b

Decrease inspiratory hold

The inspiratory hold (pause) merely prolongs the plateau airway pressure through a longer inspiratory time.[2] It does not otherwise contribute to increasing the peak airway pressure unless auto-PEEP occurs because of prolongation of the inspiratory time (see response 1a). Therefore, the potentially dangerous consequence of the inspiratory hold is auto-PEEP in susceptible donors. M.W. does not appear susceptible because auto-PEEP has been zero and his medical history was negative for prior lung diseases.

Response 2c

Decrease flow rate

A decrease in flow rate decreases high airway pressures but also prolongs Ti and shortens Te. As discussed above, this change in the I:E ratio (Ti:Te) places the susceptible donor at a higher risk of developing auto-PEEP.

Response 2d

Increase ventilator rate

As a primary effect, the ventilator rate will not alter airway pressure as long as the other variables of VT, flow rate, and PEEP/auto-PEEP remain constant. But how might a change in the rate alter one of those variables? As the rate is increased, the cycle time decreases. For example, at the ventilator rate of 12 breaths/minute, the cycle time is 5 seconds. If the rate is increased to 16 breaths/minute, the cycle time falls to 3.75 seconds, but the Ti remains the same unless the VT or flow rate also are changed. The shortened cycle time, but constant Ti, demands that the Te becomes shorter, again exposing the susceptible patient to auto-PEEP, which will elevate the airway pressure further.

Proceed to question 3.

Response to Question 3

As discussed in an earlier publication,[6] the pressure-controlled mode of mechanical ventilation is employed as a "protective" technique to avoid 2 consequences of high airway pressure, lung injury (barotrauma) and decreased venous return and cardiac output. As always, assistance from the respiratory care practitioner is essential. The following is a commonly used method to implement pressure-controlled ventilation.

Preparation

Obtain ABG values during volume-controlled ventilation, and particularly observe the $PaCO_2$ produced during the minute ventilation (VT × rate) from the ventilator. The initial goal will be to duplicate that minute ventilation during pressure-controlled ventilation, anticipating the same $PaCO_2$ and pH. The ABG values shown in the question should be considered current. Also record all volume-controlled pulmonary and ventilator data shown in the question for use as a reference as you initiate pressure-controlled ventilation.

Step 1

Order the acceptable pressure-limit setting. This is the airway pressure during which the ventilator delivers the inspiratory gas and from which the ventilator's inspiratory phase is terminated and exhalation begins. The usual pressure limit is generally 30 to 35 cm H_2O. Some ventilators display this value inclusive of the set PEEP, whereas others require that you

subtract the set PEEP and enter the pressure-limit setting independent of PEEP.

The set PEEP is carried over unchanged from the volume-controlled mode. The F_{IO_2} is usually initiated at 1.0 to minimize any risk of hypoxemia during the transition to pressure-controlled ventilation. The same ventilator rate is ordered, but may be subsequently adjusted, as discussed below. Therefore, the first ventilation orders are for the pressure-limit setting, ventilator rate, PEEP, and F_{IO_2}.

For M.W., orders are pressure limit 30 cm H_2O, respirations 22 breaths/minute, PEEP 5 cm H_2O, and F_{IO_2} 1.0. Some hospital protocols also ask for inclusion of an inspiratory time or I:E ratio as part of the initial orders. If requested, use the I:E ratio present when the ABG value was obtained during the volume-controlled mode.

Step 2

Adjust the ventilator rate. As pressure control is initiated, note the VT displayed by the ventilator as gas is delivered to the pressure-limit setting. This volume reflects the balance between the pressure-limit setting and the lung's resistance and compliance. Divide the displayed VT into the desired minute ventilation you observed earlier during volume-controlled ventilation when ABG values were obtained. This quotient is the new pressure-controlled ventilator rate you should order. For M.W., you have ordered a pressure-limit setting of 30 cm H_2O and note that the exhaled VT at that pressure-limit setting is 400 mL for each of the 22 breaths delivered by the ventilator. As recorded in question 3, your goal minute ventilation is 11 L/min. Therefore, about 28 breaths/minute (11 000/400) is your new adjusted rate setting. At this rate, the cycle time will be short (60 seconds/28 = 2.2 seconds), so watch for auto-PEEP!

Step 3

Order ABG analysis to assess ventilation via the $PaCO_2$ and oxygenation from the PaO_2.

Proceed to question 4.

Response to Question 4

To improve oxygenation during pressure-controlled ventilation[6] do the following:

Increase the F_{IO_2}

This is an acceptable response for most donor care situations. However, if an extensive delay of more than several hours is anticipated before transfer to the operating room, a high F_{IO_2} may cause slightly more pulmonary atelectasis. This occurs because as more oxygen is added to the inspired gas, the percentage of inhaled nitrogen decreases. Similarly, as more oxygen and less nitrogen are used during ventilation, nitrogen is progressively "washed out" of the lung's distal airways. Because nitrogen is not absorbed from the lung, it functions to "splint" airways open. As it is "washed out" during ventilation with high oxygen levels, some airways may become atelectatic, thereby worsening overall oxygen exchange. This process and possible outcome is one reason that the lowest F_{IO_2} that provides an adequate PaO_2 (>70 mm Hg) is always preferred.[2]

Increase the mean airway pressure by prolonging the inspiratory time

Depending upon the ventilator's manufacturer, this may be accomplished by increasing the percentage inspiratory time (percentage of the cycle time) or by changing the I:E ratio (Ti:Te) to extend the Ti. Ultimately, as the Ti becomes longer, one may "reverse" the I:E ratio from the normal pattern of Te-longer-than-Ti to Ti-longer-than-Te. Consequently, as the Te is shortened by prolongation of the Ti, the susceptible donor may develop auto-PEEP (see below).

Increase the set PEEP

This action will also produce the beneficial effect of raising the mean airway pressure. However, modern ventilators differ in their response to this change and you should consult the respiratory care practitioner about the particular ventilator being used. With some ventilators in the pressure-control mode, inspiratory gas is delivered during lung inflation from the end-expiratory pressure level to the inspiratory pressure limit. If the end-expiratory pressure level is raised by adding PEEP, less VT is delivered during each ventilator cycle because the inspiratory pressure limit is reached more quickly. This same consequence of a reduction in VT also results if auto-PEEP occurs. Other ventilators compensate for an increase in the PEEP setting by automatically raising the pressure limit to ensure that the VT remains relatively constant. The potentially adverse consequence of this compensation is, of course, an increase in the peak airway pressure. Therefore, if the set PEEP is increased during pressure-limited ventilation, careful monitoring of the VT and/or airway pressures is mandatory.

To improve ventilation during pressure-controlled ventilation:

1. Increase the ventilator rate. This is the most direct way to increase alveolar minute ventilation and, therefore, reduce the $PaCO_2$. Unfortunately, 2 conditions apply. First, the physiological dead space cannot be so high as to offset any direct benefit (see response to question 2). Secondly, as reviewed earlier (response to question 1a), when only the rate is

increased, the Te may shorten enough so that the susceptible patient induces auto-PEEP. This might be particularly a concern in pressure-controlled ventilation when the I:E ratio has been "reversed," thus also shortening the Te. If auto-PEEP occurs during pressure-controlled ventilation, the consequence may be reduced VT actually delivered to the lung, exactly the opposite effect upon minute ventilation you are attempting to accomplish.

2. Increase the pressure limit. This action serves to increase the delivered VT, but, of course, at the expense of increasing the airway pressure exerted against the lung tissue and possibly raising the risk of barotrauma or hemodynamic compromise.

3. Minimize the amount of physiological dead space present[2] (see response to question 2).

4. In some ventilators, the flow algorithm creates a slight increase in VT when the inspiratory time is increased. This, method, however, would not be considered the first intervention to attempt to increase minute ventilation.

Return to the question section.

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