Rationale for BCT Organ Donor Management Provincial Guidelines

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If you have any questions about the contents of these Provincial Guidelines please call BC Transplant Organ Donation & Hospital Development (ODHD) at 604-877-2240 or 1-800-663-6189.
INTRODUCTION

The purpose of this rationale is to provide currently accepted best practices for organ donor management in the Province of BC. They are based on expert consensus recommendations on multi-organ protective therapy to ensure optimal organ utilization.

The recommended treatments referred to throughout this document are adapted from the "Canadian Council for Donation and Transplantation. Medical Management to Optimize Donor Organ Potential: A Canadian Forum", 2004. Dosing recommendations do not apply to Pediatric Donors, defined as children < 60 kg, and under the age of 16. Please consult with a BC Children’s Hospital ICU Intensivist for questions regarding the medical management of Pediatric donors.

There are no predefined demographic factors or organ dysfunction thresholds that preclude the consent for donation and offering of organs for transplantation.

Resuscitation and re-evaluation can improve reversible organ dysfunction and can allow for the evaluation of organs that at first may seem unsuitable for transplant. This treatment / evaluation period can range from 12–24 hours and should be accompanied by frequent re-evaluation to demonstrate improvement in organ function toward defined targets. It is important to take the time necessary to optimize multi-organ function for the purposes of improving transplant outcomes.

Multi-organ donor management involves:

A. Organ Perfusion and Organ Oxygenation.
B. Organ Specific Evaluation.

The principle guidelines for organ perfusion and organ oxygenation include:

1. Cardiac function
2. Hemodynamic stability
3. Fluid balance and electrolytes
4. Adequate urine output
5. Adequate organ/tissue oxygenation
6. Temperature regulation
7. Coagulopathies
8. Glycemia and nutrition
9. Prevention of infection
10. Combined Hormonal Therapy
SECTION A. Organ Perfusion and Organ Oxygenation

1. Cardiac Function

Standard Monitoring and Targets:
- 3 Lead ECG- Heart rate ≥ 60 ≤ 120 bpm
- Under 16 years and < 60 kg see “BCT Organ Donor Management Recommended Guidelines – Pediatric” for age appropriate norms

EKG abnormalities may be seen in organ donors with intracranial injury. The effects of vasopressors or hypothermia are abnormalities of ST segments, including:
- elevation and depression (most common)
- atrial arrhythmias
- prolonged QT intervals
- intraventricular conduction delays
- Q waves (without enzyme changes) sometimes seen in intracranial hemorrhages

Sinus Tachycardia
Prolonged periods of tachycardia at rates >150 beats/minute are frequently seen when cerebral herniation is taking place. It is generally transient, requiring no treatment and does not compromise cardiovascular function.

Recommended Treatment Options:
- If the tachycardia persists, causing clinical compromise (hypotension) and it is felt to be of CNS origin (not due to hypovolemia, vasodilators, or vasopressors), give propranolol 0.5 mg IV push. Repeat in 5 minutes if necessary or give metoprolol 5 mg IV push over 1 minute, may repeat q2-5min until a total of 15mg.

Sinus Bradycardia
If the heart rate is > 50 beats/min and BP is > 100 mm Hg systolic, then the potential donor is able to maintain an adequate BP at a lower rate and there may be no need for therapeutic intervention.

Recommended treatment option if symptomatic bradycardia:
- Dopamine <10 mcg/kg/min (if heart is being considered for donation d/t concerns myocardial ATP depletion and downregulation of beta-receptors)
  - Mean arterial pressure > 70 mmHg
  - Systolic blood pressure ≥ 100 mmHg
  - Heart rate 60-120 beats per minute
  - Central venous pressure 6-10 mmHg

Atropine is never effective in treating sinus bradycardia in neurologically deceased donors due to loss of the vagus nerve function.
2. Hemodynamic Stability

Hyper/hypotension is frequently found in varying degrees in the neurologically deceased donor. The origin is multifactorial, some being the course of treatment of the patient prior to neurological death as well as the changes induced by neurological death itself.

Cerebral Hypertension

When cerebral herniation is occurring, the potential organ donor generally becomes profoundly hypertensive. It is not uncommon to see systolic blood pressures of > 200 mm Hg accompanied by tachycardias. Cerebral hypertension is due to ischemia of the vasomotor centre of the brain stem and the resultant powerful sympathetic discharge.

Key Considerations:

There is a need to distinguish acute intracranial pressure (ICP)-related autonomic storm hypertension that may occur during herniation but prior to Neurological Determination of Death (NDD), and hypertension due to other causes.

Hypertension in the setting of vasopressor use or inotropic support is an indication for decreasing support rather than initiating antihypertensives.

Recommended Treatment Options:

- If the hypertension is of short duration, no treatment is required. If, however, it is prolonged, intervention with a continuous infusion of nitroprusside (dosage: 0.5 – 8 µg/kg/min) is recommended.
- If arterial blood pressure (ABP) ≥ 160/90 then:
  a. Wean inotropes and vasopressors, and, if necessary
  b. Start preferred treatment
     ✓ nitroprusside 0.5–5.0 µg/kg/min, or
     ✓ esmolol 100–500 µg/kg bolus followed by 100–300 µg/kg/min
  c. alternatives
     ✓ nitroglycerin 30 mcg/min, range 30 – 300 mcg/min or
     ✓ labetolol 0.25mg/kg (20 mg) IV push over 2 minutes, may repeat q10mins 0.5mg/kg (40 mg)
The use of Nitroprusside with a HR<80 and Esmolol with a HR>80 is preferential as these agents are short acting. However, if Nitroprusside is not readily available, use of nitroglycerin can be considered starting at 30mcg/min, dose is increased by 5 to 10 mcg/minute to 20 to 40 mcg/minute every 3 to 5 minutes. Similarly, if Esmolol is not readily available, the use of Labetalol can be considered. With Labetalol, use initial dose of 2.5 mg to assess patient responsiveness. If effective, then consider 2.5 -10 mg IV prn.

**Hypotension**

Hypotension is the most commonly encountered clinical problem in the management of the potential multi-organ donor. It is due to hypovolemia secondary to:

- inadequate circulating intravascular volume, and/or
- increased vascular capacitance due to loss of vasomotor tone and the resultant peripheral vascular vasodilation

Hypotension may also be due to primary cardiac dysfunction

**Key considerations:**

If volume expansion alone is not sufficient to maintain an adequate blood pressure, then the use of inotropes may become necessary.

*Caution: Large doses can result in vasoconstriction and ultimately may compromise the perfusion of the organs being considered for transplant.*

**Recommended Treatment Options:**

- Fluid resuscitation to maintain normovolemia, central venous pressure (CVP) 6–10 mmHg
- Agents for Hemodynamic Support in order of preferred use:
  1. Vasopressin ≤ 2.4 units/hour (0.04 units/minute), if not effective try:
  2. Norepinephrine, epinephrine, phenylephrine, with no predetermined upper limit
3. **Fluid Balance and Electrolytes**

**Key Considerations:**
In potential lung or heart/lung donors, filling pressures should be kept at the lower end of the range of values.

**Recommended Treatment Options:**
IV solution depends on serum sodium concentration as follows:

<table>
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<th>SERUM SODIUM CONCENTRATION (MEQ/L)</th>
<th>IV SOLUTION TO BE USED</th>
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<tr>
<td>&gt;145</td>
<td>D5W</td>
</tr>
<tr>
<td>130-145</td>
<td>D5 / 0.45% Saline</td>
</tr>
<tr>
<td>&lt;130</td>
<td>NS</td>
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To run at previous hours output plus approximately 1 – 2 ml/kg/hr to allow for insensible losses.

Hypovolemia can be one of the most common problems associated with blood pressure control and poor urine output and can be due to:
- hemorrhage
- deliberate volume depletion during cerebral resuscitation
- increased intravascular space due to loss of sympathetic tone
- third spacing

**Avoidance of Hypovolemia:**
Each potential donor should be evaluated for the following:
- pre-existing deficits or excesses
- continuing losses or gains
- hemodynamic integrity.
Rationale for BCT Organ Donor Management Provincial Guidelines (ADULT)

Recommended Treatment Options:
Crystalloids for Vigorous Volume Expansion:
- Calculate intake and output for the past 48 hours to determine fluid deficit.
- Have at least two large bore peripheral IVs in the upper limbs, plus a CVP line in the right jugular.
- Increase maintenance IV fluids to 2 ml/kg/hr.
- Infuse Ringer's lactate or normal saline at 5 ml/kg over 30 min and repeat equivalent size boluses of crystalloid over equivalent time frame (30 minutes) to obtain a CVP of 6 – 10 mm Hg and a SBP of 100 mm Hg or greater (Do not use dextrose IV solution for vigorous rehydration, to avoid hyperglycemia and resultant osmotic diuresis).
- If unable to obtain the desired parameters following an infusion of 1 – 2 litres of crystalloid, administer colloids.
- Avoid femoral IV and femoral arterial lines if possible

Transfusion Thresholds

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<td>- A hemoglobin target of 90-100 g/L for unstable donors, lowest acceptable of 70 g/L</td>
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<tr>
<td>- CBC baseline values then q6h and prn</td>
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Key Considerations:
Blood drawing for donor serology and tissue typing should occur prior to transfusions to minimize the risk of false results related to hemodilution. No special transfusion precautions are required in organ donors. Crystalloids and colloids will dilute hemoglobin and may necessitate transfusion of blood.

Recommended Treatment Options:
Colloids for Volume Expansion
- Blood products, albumin, pentaspan
- If hemoglobin is <80 g/L and/or hematocrit is < 30, consult with ODHD regarding the administration of blood.
4. **Adequate Urine Output**

Drug intervention to promote diuresis is not generally required and can be harmful. If the urine output falls below 0.5 ml/kg/hr for two consecutive hours, a specific cause should be sought (i.e., blockage of urinary catheter, hypovolemia, low mean blood pressure) before drug therapy, using furosemide or mannitol, is considered.

**Diabetes Insipidus**

Diabetes insipidus (DI) is a true free water loss that causes depletion of total body water. Diabetes insipidus can be defined as: urine output > 4 ml/kg/hr, associated with rising serum Na > 145 mmol/L and rising serum osmolarity > 300 mosM and decreasing urine osmolarity < 200 mosM.

**Key Considerations:**

Prior to treatment of diabetes insipidus, rule out the possibility of osmotic diuresis secondary to hyperglycemia.

**Recommended Treatment Options:**

- IV vasopressin infusion ≤ 2.4 units/hour (preferred)
  - Prepare an infusion of aqueous vasopressin (Pitressin) by diluting 10 units in 250 ml D5W (0.04 unit/ml concentration)
  - Give 2 units aqueous vasopressin (Pitressin) as a bolus priming dose IV, begin the infusion at 25 ml per hour (1 unit/hr) via an infusion pump
  - Increase or decrease by 5-10 ml (0.2- 0.4 u/hr) per hour increments to titrate urine volume < 300ml/hr.
  - If necessary, the concentration of the infusion may be increased by 10 units per 250 ml increments to a maximum concentration of 50 units in 250 ml D5W

If required, intermittent 1-desamino-D-arginine vasopressin (DDAVP) 1–4 µg IV then 1–2 µg IV q6h.

The most commonly seen electrolyte imbalances during donor maintenance involve sodium and potassium.
Hypernatremia (Na>145)

When diagnosing, rule out:

- water depletion secondary to diabetes insipidus
- excessive sodium administration (NaHCO₃ or NaCl solutions)
- osmotic diuresis secondary to hyperglycemia or mannitol, resulting in excess free water loss
- volume replacement in the presence of diabetes insipidus using Ringer's lactate or normal saline.

Recommended Treatment Options:

- Correct hypovolemia.
- Administer sodium poor IV fluid.
- Correct hyperglycemia, if present.

Hyponatremia (Na<130)

When diagnosing, rule out:

- water overload (excessive H₂O intake relative to Na)
- sodium deficit (excessive gastrointestinal losses or diuretic therapy)
- if factitious in the presence of hyperglycemia greater than 25 mmol/L.

Recommended Treatment Options:

- Replace sodium. Concentration depends on blood volume. Isotonic saline can be used in hypovolemic donors.
- If hypervolemia exists, consider using hypertonic saline.
- Add other electrolytes, as needed.
- Correct hyperglycemia, if present.

Hyperkalemia (K >5.5) is seen frequently in volume depleted, oliguric donors. When diagnosing, rule out:

- metabolic acidosis
- excessive use of supplementary potassium
- secondary to hemolysis or crush injury.

Recommended Treatment Options:

- Correct acidosis, if present.
- Discontinue supplementary potassium.
- Promote diuresis with furosemide.
- Administer NaHCO₃ in IV fluids (IVF).
- Induce hyperventilation.
- Administer insulin IV direct/continuous infusion. Maintaining serum glucose 6-10mmol/L
- Administer calcium (emergent treatment to diminish irritability of the myocardium).
Hypokalemia (K<3.5)
When diagnosing, rule out:
- alkalosis
- high potassium loss due to excessive urine output
- abnormally high gastrointestinal (g.i.) losses.

Recommended Treatment Options:
- Monitor urine electrolytes for replacement.
- For severe deficits, give 20 – 40 mmol of KCL in 100cc over 1 hour until reach normal range

Key Considerations:
In addition to sodium and potassium control, calcium, phosphate, potassium and magnesium levels should be normalized.

5. Organ/Tissue Oxygenation

Standard Monitoring and Targets:
- Routine ABGs should be done every 4 – 6 hours to assess oxygenation, ventilation, and acid-base balance.
- pH should be maintained between 7.35 and 7.45.
- PaCO₂ should be maintained between 35 and 45 mm Hg.
- PaO₂ should be maintained > 90mm Hg
- O₂ saturation should be 95% or greater.
- Maintain lowest FiO₂ to keep PaO₂ as per above
- Hgb 80-100
- Peep of 10
- CXR

Oxygenation is essential to organ and tissue viability. Although the kidneys are more resistant, extra-renal organs are very susceptible to damage caused by hypoxia. Do not continue to hyperventilate a neurologically deceased donor, as it may compromise the hemodynamic status (especially in the hypovolemic individual). Ventilation requirements will decrease with brain death due to loss of muscle tone.
Oxygenation Problems
The following oxygenation problems may be seen in organ donors:

1. Adult Respiratory Distress Syndrome (ARDS)
2. Pulmonary Edema:
   - Atelectasis:
     - inadequate inspired tidal volume
     - immobility
     - mucous plug in bronchial tree

Neurogenic Pulmonary Edema:
This condition is a direct result of the process of brain death and the resulting powerful sympathetic discharge. It is characterized by:
- altered capillary permeability resulting in extravasation of fluid into the intra-alveolar space, and;
- increased sensitivity to circulating oxygen radicals.

The nature of this fluid shift is not dependent on cardiac filling pressures, and diuresis is not effective in correcting the problem.

Key Considerations:
The presence of neurogenic pulmonary edema does not necessarily contraindicate the retrieval of the lungs for transplant.

Recommended Treatment Options:
- If hemoglobin drops below 70g/L (due to hemorrhage, hemolysis, or dilution of blood by crystalloid/colloid infusion), speak with BCT ODHD regarding transfusion
- Tidal volumes of 6 to 8 ml/kg
- PEEP 10 cm H₂O up to 15 cm H₂O if cardiac function is not impaired use vasopressor agents rather than excess volume repletion to maintain BP at > 100 mm Hg.
- Recruitment maneuvers
- Maintain good pulmonary care with pulmonary toileting and turning prn
- Bronchoscopy and bronchoalveolar lavage
6. Temperature Regulation

Temperature trends seen frequently in organ donors include:

- Hyperthermia
- Frequently occurs just prior to brain stem herniation.
- Hypothermia

Due to destruction of the hypothalamus coupled with the loss of muscle tone (decreased heat production) and loss of vasoconstriction (failure of heat conservation). If uncorrected, hypothermia can result in decreased glomerular filtration rate and renal blood flow (secondary to decreased cardiac output), as well as hyperglycemia (partly due to inhibition of insulin release from the pancreas). Hypothermia can also result in refractory hemodynamic instability.

Recommended Treatment Options:

- warming blanket
- warmed IVF
- heated inspired airway gases
- radiant heat devices

7. Coagulopathies

Disseminated Intravascular Coagulation (DIC)

The syndrome of DIC is complicated. It consists of activation in the clotting cascade, resulting in widespread thrombosis of the microcirculation of the kidneys, lungs, heart, brain and skin etc. Ischemia and necrosis of the affected area follows. The excessive clotting leads to the consumption and depletion of the clotting factors and platelets, producing bleeding.

This syndrome does not occur as a primary disorder but always as a complication of an underlying problem. Small clots occlude the microcirculation and the larger clots embolize to the other components of the vascular system. This severely impairs gas exchange and the delivery of oxygen with subsequent ischemia, infarction and necrosis primarily in the renal, respiratory, circulatory and integumentary systems.
Defects in the reticuloendothelium system (RES) may potentate the problem even further. Normally the RES removes fibrin, procoagulants, and endotoxins and activated clotting factors from the vascular system.

The accelerated and extensive clotting characterized by the disorder initially results in excessive free thrombin. Free thrombin converts fibrinogen to fibrin, causes platelet aggregation and converts plasminogen to plasmin. The free thrombin triggers the fibrinogen-fibrin reaction, which in turn consumes large numbers of platelets and coagulation factors.

The free thrombin also activates the fibrinolysis system producing large amounts of Fibrin Degradation Products (FDP) that, in turn, inhibit the action of thrombin in hemostasis. FDPs, in combination with depleted clotting factors and platelets leads to uncontrolled bleeding. Microvascular thrombosis leads to ischemia of the organs.

Key Considerations:

DIC in a potential donor could be the result of one, or many triggering factors that stimulate the coagulation cascade:

- Trauma: causes massive, prolonged or widespread spillage of tissue thromboplastin into the blood.
- Hypoxia: damages vascular endothelium and exposes large areas of collagen which stimulates the intrinsic system and initiates clotting.
- Shock: causes extensive alterations or destruction of the vascular endothelium.
- Sepsis: endotoxins cause endothelium cell damage, exposing large areas of collagen, thereby stimulating the intrinsic system and initiating clotting.

Recommended Treatment Options:

- The main principle of therapy is to treat the underlying cause; cure of DIC will only occur once the underlying disorder is corrected. In the case of potential organ donors, the main principle is to use therapeutic interventions aimed at breaking the clotting – bleeding cycle in order to minimize damage to the organs.
8. Glycemia and Nutrition

Recommended Treatment options:
- Routine enteral feeding should be continued as tolerated and discontinue on call to the operating room.
- Parenteral nutrition should not be initiated; however, in circumstances where it has been initiated, it should be continued.
- Recommend glucose control with insulin infusions titrated to a blood glucose target 6-10 mmol/L.

Hyperglycemia (glucose >20)
When diagnosing, rule out if hyperglycemia is secondary to excessive infusion of dextrose containing IV fluids to maintain blood pressure or replace urine losses.

Recommended Treatment Options:
- Change IV fluids to normal saline or Ringer's lactate.
- Initiate and titrate insulin infusion to maintain serum glucose.

9. Prevention of Infection

Potential infections in organ donors are:
- respiratory tract infections (primarily bacterial in nature)
- skin (abrasions, lacerations, burns)
- genito-urinary infections (introduced by Foley catheter)
- generalized (bacteremia, septicemia)
Key Considerations:
- Organ donors are susceptible to nosocomial infections such as respirator-associated pneumonias, catheter-induced bladder colonizations, and septicemia resulting from intravenous access.
- Patients who are ventilator dependent and have an indwelling Foley catheter should be expected to develop a respiratory and a urinary tract infection within 48 – 72 hours.
- Local, limited infections which do not involve the organs to be recovered generally will not prevent organ donation.

Recommended Treatment Options:
- Culture blood, sputum, urine, and other suspected sites of infection, and treat suspected infections with appropriate antibiotics.
- Antibiotic therapy should be initiated in cases of proven or presumed infection. Duration of therapy depends on the virulence of the organism, and is determined in consultation with the transplant team and infectious disease services.
- Switch to appropriate antibiotic when sensitivities become available.

10. Combined Hormonal Therapy (discuss with BCT ODHD prior to initiation)

Key Considerations:
Indications
1. 2D echocardiographic ejection fraction ≤ 40%, or;
2. Hemodynamic instability (includes shock unresponsive to restoration of normovolemia and requiring vasoactive support [dopamine >10 μg/min or any vasopressor agent]);
3. Consideration should be given to its use in all donors.

Recommended Treatment Options:
Triple hormonal therapy that includes the following:
1. Tetra-iodothyronine (T₄) 20 μg IV bolus followed by 10 μg/hour IV infusion (or 100 μg IV bolus followed by 50 μg IV bolus q12h).
2. Vasopressin 1 unit IV bolus followed by 2.4 Units/hour IV infusion.
3. Methylprednisolone 15 mg/kg (≤ 1 gm) IV q24h.

Please see Section B. for Organ Specific Evaluations.
B. Organ Specific Evaluations

The specific requirements for donation of individual organs are shown below. **These are not meant to be rigid parameters, but merely guidelines.** For example, with the advancement of immunosuppressive therapy and transplant and recovery techniques, it is now possible to transplant organs from older donors. Also, in urgent situations, it may be necessary for transplant surgeons to accept organs that might otherwise be turned down. The final decision regarding the suitability of the specific organ donor lies with the transplant surgeons.

**HEART**

Evaluation Requirements:
- 12 Lead ECG
- 2D Echo
- Coronary Angio: males > 55 yrs, female > 60 yrs, male > 40 yrs or female >45 in presence of 2 risk factors, or any age if 3 or more risk factors, Hx of cocaine use
- Troponin
- CK
- ABG’s

Key Considerations:
- Patients suffering acute brainstem injury leading to brain death may display changes in heart rate and blood pressure due to CNS impairment and circulating blood volume deficits due to increased vascular capacity. Bradycardia, tachycardia, or hypertension that is secondary to acute brainstem compression does not contraindicate cardiac donation. Tachycardia and hypovolemic hypotension due to volume deficits are also not significant barriers to cardiac donation, as long as aggressive hydration has restored normal blood pressure.
- No evidence of significant cardiac disease or trauma.
- No significant abnormalities as shown by electrocardiogram and echocardiogram while the patient is on less than 10 μg/kg/min of dopamine.
- Coronary angiograms may be required for older donors.

Hearts, which are otherwise unsuitable for transplant, may be used for heart valve donation.

**LUNGS**

Evaluation Requirements:
- CXR
- CT (as requested)
- ABG
- 100% O₂ Challenge
- Sputum cultures/Gram stain
- Bronchoscopy and bronchoalveolar lavage (as requested)
Key Considerations:
- No evidence of significant lung disease or trauma.
- Smoking history reviewed on an individual basis.
- Significant abnormalities on chest X-ray will be reviewed by the transplant surgeon.
- $\text{PaO}_2 \geq 80\, \text{mm Hg}$ on $\text{FiO}_2 \leq 0.4$ or less with PEEP
- Recruitment maneuvers should be used in all donors.
- Bronchoscopic examination may be requested.

**LIVER**
Evaluation Requirements:
- PT/INR, PTT
- AST, ALT, Alk Phos,
- T&D Bili, GGT, LDH,
- TProtein, Albumin

Key Considerations:
- No history of liver disease or chronic alcohol abuse.
- No evidence of significant hepatic trauma.
- Acceptable values for AST (SGOT), ALT (SGPT), SGGT, alkaline phosphatase and bilirubin.
- Normal Prothrombin Time (PT) and Partial Thromboplastin Time (PTT).
- Liver biopsy: ultrasound guided percutaneous in the ICU prior to procurement in consultation with the liver team for weights > 100 kg or body mass index > 30 or HCVAB positive donor OR Hx of ETOH abuse

**KIDNEYS**
Standard Evaluation
- Urinalysis, creatinine/albumin ratio
- BUN, Creatinine

Key Considerations:
- No history of significant renal disease, trauma history of hypertension or diabetes.
- Normal urinalysis or minor abnormalities explained by acute events.
- Elevation of serum creatinine, if present, explained by pre-renal factors (i.e., dehydration).
- Adequate urine output.
**PANCREAS**

Standard Evaluation:
- Glucose
- Amylase or Lipase

**Key Considerations:**
- No history of chronic alcohol abuse.
- No history of diabetes mellitus in patient.

Pancreas may be transplanted as a whole or may be used for the transplantation of islet cells.
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