**Patient:** ID # T -3967, case # 5, Non-human primate- cynomolgus macaque, 4 month of age, female/intact, 1.1 kg. The patient was purchased for use in a biomedical research study. The patient would receive an intraportal islet transplant to study the effects of this surgical procedure along with immunosuppressive therapy to treat diabetes.

**Summary of patient's physical status:**

Physical examination results were within normal limits. The patient had received 165 mg of streptozotocin on 3/21 to induce diabetes. This drug depletes the islet cells in the pancreas and causes the animal to become hyperglycemic. Prior to surgical appointment, the patient had experienced hyperglycemic episodes. Results showed blood glucose levels from 203 mgidl to 350 mg/dl. She received regular insulin at designated doses to control her diabetes, but was generally not well regulated. Blood was drawn for a complete blood count, chemistry panel, and virology screening. All results were within normal limits with the exception of blood glucose (result 275 mgidl). Virology screening for herpes-B, cytomegalovirus, measles, simian retrovirus, and simian infectious virus were negative. Also, patient was tuberculin (TB) tested (results were negative). One week before surgery, the patient was placed on a short-term induction therapy consisting of the use of clinically approved anti-T lymphocyte depletion with anti-thymocyte globulin (Thymoblobulin- ATG) and anti-B cell antibody (Rituximab- Anti-CD20).

The patient had a severe case of gastroenteritis 1 month prior to surgical procedure. This was the patient's first surgical procedure. She had been sedated for transport, blood collection, and physical examinations multiple times with no complications. After evaluating physical exam results, blood work, and history, I categorized this patient as an ASA Physical Status III (severe systemic disease with functional limitations). The patient's diabetes had been poorly controlled and she suffered from episodes of hyperglycemia. Also, she was immunosupressed, which made her more susceptible to infection.

**Reason for anesthesia:**

Monkey was anesthetized for an intraportal islet transplant. On the day before surgery, the pancreas was harvested from a donor animal and the islet cells were isolated. During the transplant surgery, these islet cells will be injected into the liver of the recipient via the hepatic portal vein.

**Anticipated patient complications:**

1) Intra-operative and post-operative pain.

2) Hypothermia due to size, anesthetic drugs, shaving/prepping of surgical site, and cooler ambient temperature of the surgical suite.

3) Compromised airway due to position (surgeon wants diaphragmatic area hyper extended due to animal's size).

4) Hypo tension due to the use of anesthetic agents that can be cardio depressing, and can lead to vasodilatation and decreased cardiac output.

5) Hyperglycemia due to patient's diabetic status.

6) Hypoglycemia due to bolus islet injection.

7) Metabolic complications due to ul1fegulated diabetes (electrolyte imbalances, acidosis/alkalosis). 8) Infections due to immunosupression and diabetes.

**Anesthetic plan:**

My drug plan consisted of 10 mg/kg Ketamine 1M and 0.04 mg/kg Atropine sulfate 1M as sedation and a pre-medication. The Ketamine is a dissociative anesthetic drug that will provide significant sedation and moderate analgesia (according to manufacturer's package insert) to aid in removing monkey from cage, transporting, and placing peripheral IV catheters. Atropine was the anticholinergic I used to offset bradycardia, decrease salivary secretions, and reduce vagal tone. For induction, I used the benzodiazepam Midazolam at I mg/kg IV. This drug calms muscle rigidity and would aid in the transition to general anesthesia. As an analgesic, the opioid buprenorphine would be given pre-op at 0.01 mg/kg 1M. This would allow for decreases in the percentage of Isoflurane used during the surgical procedure, as well as provide pain relief as the monkey recovers. Finally, the monkey will be placed on a combination of Isoflurane and oxygen via an endotracheal tube to maintain general anesthesia. This volatile agent will provide a rapid onset to general anesthesia, uncomplicated adjustment during the case, and a rapid recovery.

The fluid therapy plan was Normosol-R (Norm-R) at a dose of5 ml/kgihr. I chose this rate because the monkey would also be receiving a total volume of 50 mls in the islet preparation, as well as 2 additional intraoperative infusions totaling 20 mls volume. Due to the animal's size, I thought this would be adequate.

Monitoring would consist of manual techniques to check depth, such as jaw tone, anal tone, palpebral reflex, eye position, toe pinch, and rigidity. Mucous membrane color and consistency and capillary refill time would be monitored. Pulse oximetry, HR, pulse quality, EKG, RR, ETCO2, rectal temperature, and indirect blood pressure would also be monitored. I wanted to maintain the heart rate between 100- 150 bpm, and a mean blood pressure> 60 mmHg. If the patient becomes hypotensive, I could decrease the Isoflurane percentage being administered, bolus fluids, or administer an adrenergic agent. If the patient becomes hypertensive, I could increase the percentage of lsoflurane or administer a vasodilator. I would like to maintain end-tidal CO2 (ETCO2) at about 40 mmHg. IfETCO2 is too low; I could decrease respiration or tidal volume. IfETCO2 is too high; I could increase respiration or tidal volume. If these adjustments are not adequate, I will monitor arterial blood gas parameters and check for any indications of acidosis or alkalosis. I would like to maintain the body temperature between 95- 98 degrees Fahrenheit. Monkey will be placed on a forced warm air blanket to aid in this expectation.

The patient would be taken off food from 5pm prior to the scheduled 8:30 AM surgery start time. Due to the surgical procedure being performed, I did not plan on administering insulin before or during the surgery. The islet transplant could rapidly decrease glucose values and if insulin was to be administered, severe hypoglycemia could result. If the islet transplant does cause a significant acute drop in glucose level « 100mg/dl), a 2.5% Glucose solution could be administered. The anesthetic regimen used was followed as part of a protocol, so there was no need to seek veterinary approval. I did, however, present my management plan in the event that complications should arise. The veterinarian agreed and approved of my plan.

**Anesthesia care and patient support:**

The patient was bright, alert, and responsive. She was sedated/pre-oped with 11 mg Ketamine 1M and 0.044 mg Atropine 1M, and then transported to the prep area. A blood sample was drawn for blood glucose and the result was 214 mg/dl. No insulin was given (as described in the anesthesia plan). The patient was then pre-medicated with 0.011 mg buprenorphine 1M. Two intravenous catheters were aseptically placed. A 24g was placed in the left cephalic vein and was to be used for 44mg Rituximab CRI over 2 hours (This immunosuppressive depletes the B-cells). A 22g catheter was placed in the left saphenous vein and was to be used for intra-operative fluids and 6 mg Thymoglobulin CRI over 2 hours (This immunosuppressive depletes the T-cells). The patient was induced with 1.1 mg Midazolam IV. The patient was then intubated with a 3.0 rom-cuffed endotracheal tube. The airway was sealed and the tube was secured in place. The lungs were ausculted for proper placement. Isoflurane was administered via a precision vaporizer at 2% with an oxygen flow rate of 1.5L/minute via a non-rebreathing system. SpO2 monitor was placed via a lingual probe with a resulting saturation of 100%. Heart rate was 150 bpm, respiratory rate was 30 bpm, and body temperature

was 99.4 degrees Fahrenheit. In the prep room, the patient was covered with blankets and placed beneath a heat lamp to maintain body temperature. Arterial pressure was measured with an occlusion cuff and a stethoscope with a result of 100/70 mmHg. EKG pads were placed on the left and right carpal areas, as well as the left and right tarsal areas. The patient was then shaved and prepped and shortly after, brought into the OR. Once in the OR, the patient was placed in dorsal recumbency on a forced warm air blanket. She was maintained on 2% Isoflurane with 2L/ minute of oxygen. Immediately, Rituximab, Thymoglobulin, and Norm-R infusions were started. The patient was connected 10 all monitoring equipment as described in the anesthesia plan. Indirect blood pressure was measured with an automatic occlusion cuff device (Dinamap). The patient had quickly become hypothermic, despite our efforts in the prep room. This is a common concern with young non-human primates. The patients body temperature decreased from 96.4 to 93 within 25 minutes. The temperature on the warm air blanket was increased and the surgeon irrigated the abdominal cavity with warm saline. The intravenous fluids were also warmed. 1.5 hours into surgery, oxygen saturation began to fall, resulting with SpO2 readings of70- 90%. The patient's mucous membranes remained pink and moist, capillary refill time was 1.5 seconds, pulses were WNL, endotracheal tube was not occluded or kinked. Arterial blood pressure began to decrease. This is also a concern in the YOWlg non-human primates. This is also a concern in the YOWlg non-human primates. The mean arterial pressure (MAP) was 49- 55 mmHg. Isoflurane was decreased to 1.5% and the fluid rate was not adjusted. 1nere was a concern that the Sp02 may have dropped due to the bolus of fluids administered during the islet transplant, so increasing the fluid rate was not acceptable. If decreasing the volatile agent was unsuccessful, an adrenergic agent would be considered. Two mg of furosemide (Lasix) was administered IV. I manually breathed for the patient (20- 25 bpm) to ensure adequate oxygenation and a tidal volume of 15mls. Thirty minutes post Lasix injection, Sp02 returned to 95- 100%, also body temperature increased to 97.3. The MAP increased to 60 mmHg. This was acceptable and the procedure was near completion. A blood glucose sample was taken after closure with a result of 109 mg/dl. Due to this result, no alteration in the amount of fluid administration was needed. All other parameters monitored remained WNL during the surgical procedure. Isoflurane was turned off and the patient remained on oxygen for 5 minutes.

**Post anesthesia recovery:**

The patient was extubated, analgesia was being provided by the preoperative buprenorphine administered. The patient was breathing well and continued to maintain an 02 saturation of 95- 100%. Due to the disposition Qf this patient and to maintain a safe environment for both patient and personnel, she was then returned to her cage. Her recovery was smooth and uneventful. No signs of pain or distress were noted. The patient would receive 0.0 1 mg/kg buprenorphine 1M 8 hours after initial dose, and would receive 0.0 1 mg/kg buprenorphine 1M **BID** for 2 days post-op then PRN depending on pain assessment. Blood glucose levels would be checked daily by the research staff and any abnormalities would be reported to the veterinary staff. The patient recovered well and the surgical procedure was a success. The patient remained comfortable and normoglycemic throughout the duration of the study.