

## Review

# *Cardiopulmonary Bypass and the Pregnant Patient: A Review*

John Josephs, MS, CCP and Roger Hindman, BS, CCP

St. Vincent's Medical Center, Jacksonville, Florida

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### ABSTRACT

Increasing maternal age within the general population in conjunction with cardiac disease during pregnancy, increases the probability that perfusionists will be called upon to provide extracorporeal support to the gravid patient.

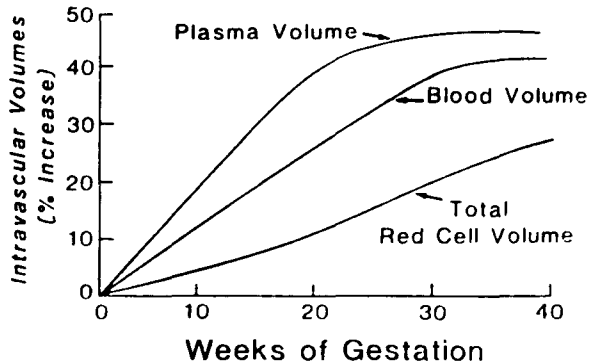
Reviewing the available literature regarding cardiopulmonary bypass (CPB) during pregnancy produces some satisfying, isolated single-case reports. However, in the majority of reports, fetal compromise resulted from maternal cardio-surgical intervention.

Given the occurrence of CPB during pregnancy with resultant fetal loss, a need has been identified to provide perfusionists with a guide to patient management. Toward this effort, insights into normal physiologic and hemodynamic changes of pregnancy and their relationship to technical management of perfusion is presented. Concise information is provided regarding fetal responses to CPB and fetal distress. Situations most associated with intrauterine fetal loss and premature labor are identified. Constant monitoring of fetal heart rate is emphasized and optimal pharmacological management to achieve desired maternal effect while minimizing fetal response is also presented.

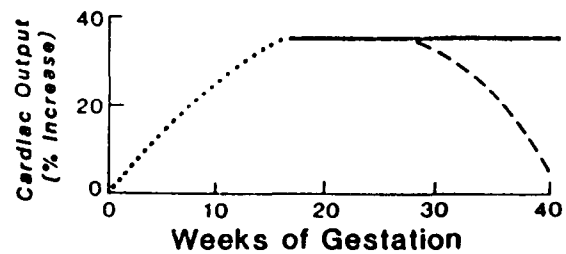
Address correspondence to:  
John Josephs, MS, CCP  
Staff Perfusionist  
Department of Cardiovascular Surgery  
St. Vincent's Medical Center  
1800 Barrs Street  
Jacksonville, Florida 32204

**Figure 1**

Schematic representation of the % increase in the intravascular volumes that occur during pregnancy. Source: Burrow GN and Ferris TF. *Medical Complications During Pregnancy*. WB Saunders Co. 1998; pg. 181.

**Figure 2**

Cardiac output increases by 40% above non-pregnant levels, reaching its maximum by the 20th week of pregnancy. The dashed line indicates the susceptibility of cardiac output to a decrement of venous return, most noticeable in the supine position and becoming more pronounced as pregnancy advances. Source: Burrow GN and Ferris TF. *Medical Complications During Pregnancy*. WB Saunders Co. 1998; pg. 181.



## INTRODUCTION

Pregnant patients requiring cardiopulmonary bypass (CPB) may not be candidates for referral to cardiac centers where experience in this select patient group is prevalent. Due to this sporadic and unpredictable occurrence, experience with this challenging clinical condition is limited. Those clinicians with experience may have no more than one or two occurrences over the course of an extended career. Such isolated incidents result in a lack of information, understanding and management regarding such cases. Advanced maternal age within the population has increased the probability that such cases will also increase. The following manuscript will address key clinical management issues related to physiologic, hemodynamic, pharmacologic and perfusion considerations for this select patient group.

## PERSPECTIVE

CPB during pregnancy presents substantial challenges and should be avoided whenever possible. However, there remains a 1 - 4% occurrence of clinical cardiac disease during pregnancy with rheumatic valve disease accountable for 60% of cardiac pathology. (1) Heart disease remains the principal non-obstetric cause of maternal mortality ranging from 0.4% in patients in New York Heart Association (NYHA) Class I and II to 6.8% in Class III and IV. (2,3) When cardiac disease must be treated with surgical intervention, it should be undertaken prior to maximal maternal hemodynamic load and before cardiac decompensation occurs. Multiple authors have suggested surgical intervention as early in the second trimester as possible following the conclusion

of first trimester organogenesis. (1,4-7) Staging of such surgical intervention following these gestational events lessens the probability of spontaneous disruption of pregnancy in the first trimester as well as induction of premature labor with later intervention. (8,9)

## PHYSIOLOGY & HEMODYNAMICS

Successful execution of CPB during pregnancy requires acute awareness of the normal physiological and hemodynamic changes associated with pregnancy.

**BLOOD VOLUME (BV)** - Beginning from the eighth week of gestation, maternal BV expands in a linear progression to 35% - 50% (Figure 1) above pre-pregnant levels by the 36th week. (3,8,10-14) This linear relationship of BV expansion permits a reasonable guideline for BV calculation with the 36th week gestational BV ranging from 90-100 ml/kg compared to 60-70 ml/kg for the pre-pregnant level. (14) Generally by the 32nd week of gestation, erythrocyte volume is increased by 20% - 30% above normal with plasma volume (PV) increased by at least 50%. (Figure 1) This disproportionate increase in PV accounts for the misleading relative anemia reported during normal pregnancy. In some instances, even larger increases in the volume of red blood cells (RBC) and PV of 50% and 100% respectively, have been reported. (11) In addition, hormonal factors, particularly an increased secretion of aldosterone by the adrenal cortex, markedly elevate total body sodium and contribute to a further increase in BV. (3)

**CARDIAC OUTPUT (CO)** - During pregnancy, CO progressively increases from the beginning and plateaus around the

20th week. (Figure 2) Peak CO of 35% - 45% above non-pregnant resting output occurs at about the 20th week. Such increases are common and result from an increase in heart rate (HR) of 10 - 12 beats per minute and an increase in stroke volume. These two changes appear as a direct response to the physiological confusion induced by a perceived relative anemia and alterations in the systemic vascular resistance. Toward term, the enlarged uterus and fetal movement may disrupt venous return by compression of the inferior vena cava resulting in a reduction of CO. Caval compression is most pronounced in the supine position and least notable in the left lateral decubitus position. (3,8,10,11,12)

**OXYGEN CONSUMPTION (VO<sub>2</sub>)** - Changes in CO are potentiated further by an increased oxygen demand with VO<sub>2</sub> gradually increasing 15% - 18% by the end of the 12th week. (3,8,11,13) Values for arterial blood pCO<sub>2</sub> decrease by approximately 10 mmHg below normal with a coincidental decrease in bicarbonate, contributing to the maintenance of a normal pH value. (8,10-12)

**VASCULAR RESISTANCE (VR)** - Uterine blood vessels in pregnancy function as an arteriovenous shunt in which blood flow is directly controlled by hormones secreted by the placental-uterine vascular plexus. Dilation of uterine blood vessels early in pregnancy results in a decreased VR. This decreased resistance, however, is frequently well compensated by an increased CO with only a mild decrease or no change in blood pressure (BP). In brief, while both preload and ventricular end diastolic volume (VEDV) are increased, ventricular end diastolic pressure (VEDP) and central venous pressure (CVP) remain unchanged attesting to enhanced cardiac compliance and a decreased VR. (3,11,12)

**PERIPHERAL EDEMA** - As noted, significant elevation in sodium levels contributes to increases in BV. Elevated sodium levels also contribute to increases in extracellular fluid, which when compounded by caval compression of the gravid uterus, results in peripheral edema. (11)

**UTERINE BLOOD FLOW** - The prepregnant uterine blood flow is normally around 50 ml/min and accelerates to term values of 500 to 1000 ml/min. This flow accounts for 20% of CO and can be adversely affected by maternal and fetal positioning as well as pharmacological intervention. (11)

**HYPERCOAGULABLE STATE** - Increases in clotting factors, particularly Factors VII, VIII, X, and XIII, contribute to a hypercoagulable state during pregnancy. In addition, a slight increase in platelet and a decrease in plasminogen activator levels result in a decrease in fibrinolysis, further contributing to the hypercoagulable state. (11) These factors, while beneficial for the control of hemorrhaging in the normal postpartum course, are not beneficial when extracorporeal intervention becomes necessary.

## PERFUSION CONSIDERATIONS

**FETAL HEART RATE MONITORING** - Monitoring the fetal heart rate (HR) is essential during CPB in the pregnant patient. Fetal HR monitoring provides the surgical team immedi-

ate information related to the physiological status of the fetus. If not present within the surgical suite, mechanisms should be in place to secure an abdominal doppler unit and qualified personnel from the labor and delivery unit to assist in proper placement and operation of the doppler. Fetal movement prior to or during CPB may result in dampening or disruption of the fetal HR signal. Considerations should, therefore, be given to bilateral placement of abdominal probes. Such placement will allow alterations from one probe to the other to compensate for fetal movement.

Low blood flow rates during CPB result in diminished blood delivery to the fetus and may be associated with fetal distress. Fetal bradycardia may develop as a direct result. (12) The normal fetal HR is between 120 and 160 bpm. All available reports have shown a direct relationship between fetal bradycardia and blood flow during CPB regardless of maternal acid-base status. With restoration of normal blood flow, the stressed fetal HR returns to baseline or may over-compensate with transient tachycardia relative to the degree and duration of stress. (1,2,9) During periods of increased distress, the fetus will compensate by autoregulating available blood flow to the brain, heart, and adrenal glands and decrease VO<sub>2</sub> by 50%. Such autoregulation will continue with progressive fetal bradycardia until restoration of adequate blood flow or fetal compromise occurs. (10) Insufficient fetal blood flow and hypoxia may result from insufficient uterine blood flow, insufficient umbilical blood flow, or a decrease in maternal arterial oxygen content. After ten minutes of oxygen deprivation fetal survival is unlikely, with lesser periods of hypoxemia associated with increased incidence of cerebral palsy or other profound neurological sequelae. (10)

Fetal bradycardia may be favorably influenced by adjustment of CPB flow rates and should be the first modification undertaken in response to early fetal distress. Further measures noted to reduce fetal distress have been shown to include: modification of the maternal position to eliminate umbilical cord compression, correction of maternal hemorrhaging quickly with fresh whole blood and minimizing or eliminating the use of vasopressors, increase maternal oxygen saturations during fetal hypoxia, correction of maternal acid-base deficits with sodium bicarbonate, and close monitoring and maintenance of maternal glucose levels with glucose infusions to replenish fetal glycogen stores lost during fetal hypoxia. (10)

**PRIMING VOLUME** - Since the pregnant patient presents with a greatly expanded BV, a reduced pump prime is advised. Consideration should also be given to the capacity of the selected pump circuit to accommodate anticipated volume. During CPB, the perfusionist should anticipate a decrease in predicted hemoglobin levels due to the disproportionate increase in plasma volume. The hematocrits for CPB in the pregnant patient should be maintained between 20% - 25%. (12, 15)

**PERFUSION FLOW RATES** - The pregnant patient's resting CO is increased by as much as 45% with co-existing decreased VR, therefore, a higher flow rate will be required to achieve adequate tissue perfusion and mean pressure. Pump flow rates should be calculated utilizing a cardiac index (CI) of 2.6 -

3.0 L/min/m<sup>2</sup> with flows adjusted up or down in response to the fetal heart rate. (12) A second method to estimate pump flow is to use a CI of 2.4 L/min/m<sup>2</sup> and use pre-pregnant measurements to determine body surface area (BSA) and add 30% - 50% to the calculated flow. (11) Regardless of the methodology selected to determine flow, a direct correlation should be noted between blood flow and fetal HR. The significance of fetal blood flow becomes more apparent when considering that the fetus normally exists in a relative hypoxic state. Through placental autoregulation, umbilical blood flow remains constant at approximately 11 ml per 100 gm. of fetal weight per minute from the 12th to the 28th week of gestation. Fetal arterial oxygen saturation varies between 52% and 65%. In spite of these low saturations, O<sub>2</sub> supply is adequate when adequate blood flow is maintained. (5) However, these values indicate how quickly oxygen debt and threatening distress occur with diminished blood flow and intensify the need for early correction of flow deficit.

**TEMPERATURE MANAGEMENT** - Multiple authors have reported fetal compromise through cardiac arrhythmias or fibrillation in association with exposure to moderate and deep hypothermia. Despite a contrary report regarding temperature management (16), most authors conclude that fetal rewarming results in decreased fetal HR, and induces uterine contractions and may precipitate premature labor. (1,8,9,11,12) Unless long aortic cross clamp times are anticipated, surgery should be carried out under normothermic to mild hypothermic conditions. During CPB, maternal core temperature should start near normothermic levels and be allowed to drift slowly to 34°C. Maternal blood temperature should not be permitted to fall below 30°C.

**SCAVENGING OF CARDIOPLEGIC SOLUTION** - Regardless of the cardioplegic mixtures selected to accomplish maternal electro-mechanical cardiac standstill, clinicians must be conscious that potassium ions easily traverse the placental barrier, and may induce depression of the fetal heart activity or cardiac arrest. Therefore, administration of high-dose potassium cardioplegia may necessitate bi-caval venous cannulation followed by opening of the right atrium and scavenging of cardioplegia from the coronary sinus. An ultrafiltrator or cell-washer may be used to avoid fetal hyperkalemia. Following initial high potassium cardioplegic induction, subsequent redosing of cardioplegia should be with lower non-potassium containing cold blood or crystalloid solutions. Additional potassium containing cardioplegia should be employed only when ineffective cessation of electro-mechanical maternal cardiac activity is apparent.

**ANTICOAGULATION MANAGEMENT** - Due to the elevated BV in pregnancy and a disproportionate PV increase, pregnant patients frequently present with an increased antithrombin III titer, and require substantially higher than usual heparin doses. (5) In addition, since heparin does not cross the placental barrier due to its large molecular weight (MW=20,000), the fetus is not in jeopardy of intra-abdominal or intracranial bleeding seen with the heparinization of neonates. (5,17) However, maternal heparinization is reported to carry increased risks

of uterine hemorrhage and placental disruption. (8,12,18) Therefore, strict heparin monitoring is required to avoid both sub-therapeutic heparinization or excessive anticoagulation. Essentially adequate heparinization per normal institutional protocols should be confirmed prior to initiation of CPB with more frequent coagulation testing performed throughout the CPB period.

**CANNULATION** - Unless critical emergency situations predominate, cannulation of the femoral artery and vein should be avoided due to the possibility that fetal and uterine position may obstruct the vena cava and cause reduced venous return. Additionally, femoral cannulation with non-physiologic retrograde arterial blood flow may result in hypoperfusion of uterine blood vessels, even in the presence of increased pump flows.

**POSITIONING** - To optimize venous return to the caval cannula, the patient should be placed in mild, left lateral decubitus position. By elevating the right hip 15 degrees, the uterus is rotated away from the inferior vena cava with an enhanced venous return. Some authors have reported an increase in placental perfusion through decompression of the posterior vasculature in this position. (5,12) The supine position should always be avoided due to aortocaval compression. (11) (Figure 2)

**SELECTION OF MEDICATIONS** (Appendix) - The pregnant patient has certain special responses to cardiovascular drugs. The four major concerns are: 1: the effect on the uteroplacental blood flow; 2: the effect on uterine muscle tone and labor; 3: the direct and indirect fetal effects; and 4: undesirable maternal and fetal side effects. (19)

Arteriolar regulation of blood flow to the uterine vasculature is controlled by alpha receptors, therefore, alpha agonists should be strictly avoided to pharmacologically treat hypotension during CPB with pregnant patients. Epinephrine is the vasopressor of choice because at low doses it has a primary beta stimulatory effect. Sympathomimetic agents that are primary alpha (norepinephrine and phenylephrine) decrease uteroplacental blood flow and should not be used. Hydralazine is the drug of choice for a hypertensive crisis during CPB because in low doses it will decrease BP in the mother while increasing renal and uterine blood flow. The use of sodium nitroprusside is contraindicated in pregnant patients because of the risk of cyanide toxicity to both mother and fetus, and the chance that blood flow is shifted away from the uterus. Utilization of any vasodilating agent requires careful titration and appreciation that a reduction in uterine blood flow accompanies any decrease in maternal peripheral VR. (11) Consideration should be given to the effect of any medication on uteroplacental blood flow and teratogenic possibilities. Consultation with the patient's gynecologist, perinatologist, and/or neonatologist is advised when possible. Drugs should be given to the pregnant patient only when the benefits justify the risk to the mother and the fetus.

## CONCLUSION

A search of the literature reveals only sparse reports of successful management of extracorporeal circulation in the gravid

patient. Most frequently, cardio-surgical intervention in such patients results in either fetal and/or maternal compromise. We have identified those areas most representative of fetal demise

and have provided hemodynamic, physiologic and pharmacological information essential to the management of this challenging clinical condition.

**APPENDIX**

**CARDIOVASCULAR DRUGS FOR THE PREGNANT PATIENT**

In order to allow optimal pharmacological intervention while providing maximal maternal fetal benefit, the perfusionist should become familiar with the pharmacokinetics and pharmacodynamics of the following agents: (11,20,21).

**1. Diuretics:**

- Furosemide -
  - 1) used for edema and hypertension.
  - 2) crosses the placenta and may decrease placental perfusion.
  - 3) may prevent normal plasma volume expansion.

- Thiazide -
  - 1) may increase risk of congenital defects as a result of placental transfer.
  - 2) induces electrolyte imbalance (hypoglycemia, hyponatremia, hypokalemia, and thrombocytopenia).
  - 3) secondary fetal bradycardia.

**2. Inotropic Agents:**

- Digoxin -
  - 1) crosses the placenta without causing fetal harm.
  - 2) considered drug of choice for persistent fetal tachycardia

- Dopamine -
  - 1) no known adverse effects.
  - 2) increases uterine blood flow and may stimulate uterine contractions.

- Norepinephrine -
  - 1) may cause constriction of uterine blood vessels and reduce blood flow.
  - 2) may stimulate uterine contraction.
  - 3) primarily alpha.

- Phenylephrine -
  - 1) same as norepinephrine.
- Epinephrine -
  - 1) crosses the placenta and may cause fetal tachycardia.
  - 2) human teratogenicity has not been shown.
  - 3) at low doses it has a beta effect.
  - 4) vasopressor of choice.

**3. Vasodilators:**

- Hydralazine -
  - 1) crosses the placenta.
  - 2) in low doses will decrease BP in mother while increasing renal and uterine blood flow.
  - 3) no association seen with congenital defects.
  - 4) drug of choice for hypertensive crisis.

- Sodium Nitroprusside
  - 1) contraindicated in pregnant patients because of the risk of cyanide

- 2) may shift blood flow away from the uterus.
  - 3) crosses the placenta

- Nitroglycerin -
  - 1) use of nitroglycerin sublingually for angina without fetal harm has been shown.

**4. Antiarrhythmic Agents:**

- Quinidine -
  - 1) not related to congenital defects.
  - 2) crosses the placenta and related to fetal thrombocytopenia.
  - 3) used with digoxin to treat fetal supraventricular tachycardia.
  - 4) second drug of choice after digoxin for the treatment of persistent fetal tachycardia.

- Atropine -
  - 1) rapidly crosses the placenta.
  - 2) no evidence found for an association with fetal malformations.
  - 3) no significant changes were noted in fetal heart rate.
  - 4) no effect on uterine activity.

**5. Beta-Blocking Agents:**

- Propranolol -
  - 1) readily crosses the placenta.
  - 2) intrauterine growth retardation may be related to drug.
  - 3) fetal bradycardia and fetal toxicity found to suggest a relationship to malformations.
  - 4) lowers umbilical and uterine blood flow.

- Atenolol -
  - 1) crosses the placenta with no fetal malformations noted.
  - 2) a decrease in fetal heart rate may be observed.

**6. Calcium-Channel Blockers:**

- Verapamil -
  - 1) placenta passage was demonstrated with no relationship to congenital defects.
  - 2) may reduce uterine blood flow with fetal hypoxia a potential risk.

Nifedipine -	1) no adverse effects in fetus observed.	Erythromycin -	tal defects noted. 1) crosses the placenta but no relationship with congenital defects have been determined.
<b>7. Antibiotics:</b>		Ampicillin -	1) rapidly crosses the placenta. 2) does not exert a toxic effect on the developing fetus. 3) teratogenic effects unlikely.
Cefazolin -	1) cephalosporin antibiotic. 2) readily crosses the placenta. 3) adverse effects have not been observed. 4) antibiotic of choice.	<b>8. Hemostatic Agents:</b>	
Tetracycline -	1) use with extreme caution. 2) crosses placenta with associated adverse effects on fetal teeth and bones. 3) maternal liver toxicity and congeni-	Aprotinin -	1) no relationship to congenital defects noted. 2) crosses the placenta and decreases fibrinolytic activity.

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