PROSTAGLANDIN E₂, PROSTACYCLIN, AND THROMBOXANE CHANGES DURING NONPULSATILE CARDIOPULMONARY BYPASS IN HUMANS

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Reprinted from THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY, St. Louis

Vol. 91, No. 6, pp. 858-866, June, 1986
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(Printed in the U.S.A.)
Prostaglandin E$_2$, prostacyclin, and thromboxane changes during nonpulsatile cardiopulmonary bypass in humans

To study the effect of lung bypass on the production of prostaglandin E$_2$, prostacyclin, and thromboxane A$_2$, we measured simultaneously arterial and venous plasma concentrations of prostaglandin E$_2$, 6-keto-prostaglandin F$_1\alpha$, (stable metabolite of prostacyclin), and thromboxane B$_2$ (stable metabolite of thromboxane A$_2$) before, during, and after cardiopulmonary bypass. Seventeen patients (age range 46 to 69 years) undergoing aorta-coronary bypass grafts were investigated. The prostaglandin E$_2$ production rose sharply immediately after the onset of bypass (baseline: 9.7 ± 2.9 pg/ml to 85 ± 16.6 pg/ml in venous and 87 ± 12 pg/ml in arterial plasma, p < 0.03) and rapidly decreased after pulmonary reperfusion (53 ± 6.4 and 57 ± 20 pg/ml, respectively, in venous and arterial plasma at the end of bypass). The increase in prostaglandin E$_2$ was influenced by the heart-lung machine itself (as demonstrated by a closed "bypass" circuit) and by lung bypass. Pulmonary metabolism of prostaglandin E$_2$ was maintained after bypass. The prostacyclin production rose significantly at the beginning of bypass (154 ± 26 pg/ml venous prebypass level to 361 ± 94 pg/ml after aortic clamping, p < 0.03). Prostacyclin decreased progressively during rewarming of the patient, pulmonary reperfusion, and discontinuation of bypass. When prostacyclin decreased, thromboxane B$_2$ production rose significantly and reached peak arterial levels when the lungs were reperfused (112 ± 33 pg/ml prebypass levels to 402 ± 101 pg/ml, p < 0.01). Except for prostaglandin E$_2$, there were no significant differences between arterial and venous plasma levels of these substances. The same prostanoids were also measured in five patients undergoing major orthopedic operations, and no significant changes in prostanoids were observed. Our data demonstrate significant production of prostaglandin E$_2$ in the systemic circulation during cardiopulmonary bypass in humans. They further indicate that lung bypass disturbs the plasma prostaglandin/thromboxane balance.

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Prostaglandins are implicated in the pathophysiology of pulmonary dysfunction.$^{1,2}$ The lung rapidly converts (few seconds) prostaglandin H$_2$ into prostaglandin E$_2$

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Received for publication June 12, 1985.
Accepted for publication July 19, 1985.
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and prostaglandin F$_{2\alpha}$, as shown by Nugteren and Hazelhof.$^3$ Thromboxane synthetase was also identified in the pulmonary parenchyma.$^4$ Prostacyclin and thromboxane have been considered the main metabolites of arachidonic acid in the lung,$^6,7$ however, in a recent review,$^7$ the predominant prostaglandins that formed in the bronchial tree and in the pulmonary vasculature seemed to be prostaglandin E$_2$ and prostacyclin. In addition to synthesis and release of prostaglandins, the lung is a major organ in the metabolism of prostaglandins of the E and F types, which are nearly completely inactivated during a single passage through the pulmonary circulation.$^8,10$ Moreover, prostaglandins exert potent physiologic effects.$^{11,12}$ The important role of the
lungs as a major metabolic site for synthesis, release, and degradation of prostaglandins may be altered during lung bypass. Recent reports published the results of prostaglandin measurements during cardiopulmonary bypass (CPB), but great discrepancies appeared in these different works. For example, Davies and associates described a significant rise in plasma levels of thromboxane A₂ in the early phase of bypass, followed by a progressive return to prebypass values. On the other hand, Ylikorkala, Saarelma, and Viinikka showed a rise in prostacyclin and thromboxane A₂ levels with a sustained prevalence of prostacyclin in nonpulsatile bypass. Watkins and co-workers described a predominance of prostacyclin at the onset of nonpulsatile CPB, followed by an inversion of the prostanooid balance (prevalence of thromboxane A₂) at the end of CPB (rewarming period). Therefore, to study the effects of racoroporeal circulation on the production of prostaglandins, and to clarify the discrepancies found in the literature, we measured plasma concentrations of prostaglandin E₂, prostacyclin, and thromboxane A₂ in 17 patients before, during, and after CPB. A control group of five patients undergoing major operations without CPB (total hip replacement) was also investigated.

Patients and methods

Patients with heart disease. Seventeen patients scheduled for elective aorta-coronary artery bypass grafting with standard nonpulsatile cardiopulmonary perfusion were selected for study. Their ages ranged from 46 to 69 years (mean 62 years). None of the patients had received drugs known to interfere with the synthesis of prostaglandins for 15 days preceding the operation. Informed consent was obtained from all patients and the protocol was approved by the ethical committee of the hospital. Each patient was anesthetized with intravenous injection of morphine sulfate (1.5 mg/kg of body weight) and diazepam (0.4 mg/kg), and muscular relaxation was obtained at pancuronium bromide (0.2 mg/kg). Ventilation with 50% nitrous oxide was controlled by a Servo 900 ventilator, maintaining normocapnia. The condition of each patient was monitored by surface electrocardiogram, systemic arterial blood pressure (radial artery), central venous pressure (internal jugular vein), pulmonary arterial and capillary pressures, and cardiac output (thermodilution Swan-Ganz catheter). Heparin (3 mg/kg) was given before cannulas were inserted for CPB.

A disposable membrane oxygenator (CML Cobe) with polyvinyl chloride tubing and a roller pump were used. The extracorporeal circuit prime consisted of a mixture of Hartmann's solution (800 ml), 5% dextrose in water (800 ml), sodium bicarbonate (100 mEq) and heparin (50 mg); 20% human albumin solution (250 ml) and 20% mannitol solution (100 ml) were used, and the hematocrit value was maintained at 25% ± 1% during bypass. Hypothermic (28°C esophageal) nonpulsatile CPB (2.4 L/min/m² of body surface area) was established via a cannula in the ascending aorta and a double-lumen cannula for venous return. More than 90% of pulmonary perfusion was so eliminated. Nevertheless, a small amount of lung perfusion persisted and was returned to the heart-lung machine via the left ventricular aspiration. The repair was performed during a single period of aortic occlusion with cold (4°C) cardioplegic solution (St. Thomas' Hospital) being injected into the coronary arteries. This solution partially perfused the lungs and was collected outside the extracorporeal circuit. CPB lasted from 58 to 215 minutes (mean 132 minutes). Blood samples were taken at the following times (mean minutes):

- 0 minutes—Before operation: patient premedicated, after placement of intravenous catheter, but before induction of anesthesia
- 60 minutes—Anesthesia: after induction of anesthesia, patient hemodynamically stable, but before start of operation
- 95 minutes—Operation: after sternotomy but before CPB
- 130 minutes—Bypass: beginning of CPB, at 1 minute of full flow
- 165 minutes—Bypass: during cross-clamping of aorta
- 205 minutes—Bypass: during rewarming of patient
- 225 minutes—Bypass: under CPB, heart having recovered its own mechanical activity, lungs are reperfused
- 260 minutes—After bypass: end of CPB, cannulas removed
- 275 minutes—After bypass: 15 minutes after end of CPB
- 325 minutes—Operation completed: before patient is transferred to intensive care unit

Day 1: first postoperative morning

At each of these times, arterial and venous blood samples were obtained simultaneously for measurement of prostacyclin and thromboxane metabolites, 6-keto-prostaglandin F₁α and thromboxane B₂, respectively. The same procedure was applied for prostaglandin E₂ measurements, but only in the last seven patients.

Heart-lung machine itself. In vivo, during CPB, we compared plasma concentrations of prostaglandin E₂, 6-keto-prostaglandin F₁α, and thromboxane B₂ in the blood leaving the extracorporeal circuit (arterial line) with those levels entering the circuit (venous line). In vitro, the same prostanooids were also measured in fresh
Fig. 1. Mean prostaglandin E₂ concentrations in arterial and venous plasma samples before, during, and after cardiopulmonary bypass (CPB), in seven patients having coronary bypass. There is a significant increase during bypass, when lung perfusion ceases (arrow). Star indicates a significant change from the preceding measured mean value (p < 0.05). Circled star indicates a significant difference between arterial and venous values (p < 0.005).

Table I. Summary of data comparing simultaneous inflow versus outflow plasma concentrations of prostaglandin E₂ at the heart-lung machine during CPB

<table>
<thead>
<tr>
<th>Heart-lung machine</th>
<th>Prostaglandin E₂ plasma levels (pg/ml)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>One minute</td>
</tr>
<tr>
<td>Inflow</td>
<td>76 ± 14</td>
</tr>
<tr>
<td>Significance</td>
<td>NS</td>
</tr>
<tr>
<td>Outflow</td>
<td>130 ± 26</td>
</tr>
</tbody>
</table>

Legend: NS, Not significantly different.
*Mean ± standard error.

human blood running through the heart-lung machine in a closed “circuit” without the patient. Fresh blood (1.5 L) from three donors, who abstained from aspirin and were given heparin, served as a control for biochemical modifications during closed “bypass.” An incorporated cardiomyocyte filter, a CML Cobe membrane oxygenator, and polyvinyl chloride tubing were primed with our standard priming solution, identical to in vivo conditions. During closed “bypass,” hematocrit value decreased to 25% and blood temperature to 28°C. Blood samples were taken simultaneously above and below the membrane oxygenator during 2 hours of closed “bypass.”

Patients having orthopedic operations. A control group of five patients undergoing total hip replacement was also studied. Men between 50 and 75 years of age volunteered for this study after receiving detailed information about its course and purpose. None of the patients had used drugs known to interfere with the synthesis of prostaglandins for 15 days before the operation. Anesthesia with endotracheal intubation and balanced administration of thiopental sodium, fentanyl, and pancuronium bromide was standardized in all patients. Blood samples were drawn from the superior vena cava catheter at the following fixed intervals (mean minutes):

0 minutes—Before operation: on arrival in the operating room, before anesthesia
40 minutes—Anesthesia: soon after induction of anesthesia
65 minutes—Operation: after surgical incision
80 minutes
110 minutes
155 minutes—Cement: placement of hip cement
160 minutes
165 minutes
235 minutes—Awake: after operation, patient awake and breathing spontaneously

Blood sampling. Arterial blood samples were gently drawn through a 20 gauge indwelling radial artery catheter into sterile disposable syringes. Venous blood samples were also gently collected from an internal
jugular vein catheter (16 gauge). The blood samples were immediately centrifuged with heparin (148 USP units/10 ml whole blood) and indomethacin (10⁻⁷mol) at 5,000 rpm for 2 minutes. Care was taken to avoid platelet and leukocyte contamination during plasma pipetting. Immediately after centrifugation, samples were frozen (−30 °C) until radioimmunoassay (RIA).

Prostanoids. Plasma thromboxane B₂ and 6-keto-prostaglandin F₁α, the stable metabolites of thromboxane A₂ and prostacyclin, respectively, were measured in 100 μl of plasma, without extraction, by RIA.¹⁷ Antisera, ³H-labeled thromboxane B₂ and ⁴H-labeled 6-keto-prostaglandin F₁α, precipitating material, and the RIA control were purchased from New England Nuclear. RIA was verified by plasma samples containing known values of 6-keto-prostaglandin F₁α and thromboxane B₂. When the error on these overloaded samples was greater than 10%, all measurements were discarded. The lower limits of sensitivity of our RIA measurements were 30 pg/ml for both thromboxane B₂ and 6-keto-prostaglandin F₁α. We avoided extraction of the samples, because this procedure introduces considerable artifacts, falsely elevating the results.¹⁸ When thromboxane B₂ or 6-keto-prostaglandin F₁α values were lower than 30 pg/ml, the term unmeasurable was employed.

The cross-reactivity of thromboxane B₂-antisemur with prostaglandin E₂ was 0.2% and was lower than 0.2% with 6-keto-prostaglandin F₁α and prostaglandin F₂α. The cross-reactivity of 6-keto-prostaglandin F₁α antisemur was 2.7% with prostaglandin F₂α. 2% with prostaglandin E₂, and lower than 0.2% for thromboxane B₂. In previous work we¹⁹,²⁰ have established "normal" values for thromboxane B₂ and 6-keto-prostaglandin F₁α in both healthy, unstresssed volunteers and in patients leaving the operating room after noncardiac interventions. These "normal" values for thromboxane B₂ and for 6-keto-prostaglandin F₁α ranged from unmeasurable to 120 pg/ml.

Prostaglandin E₂ was also measured by RIA on 100 μl plasma samples, without extraction. The immunologic material (³²P-labeled prostaglandin E₂, unlabeled prostaglandin E₂, and antiserum) was purchased from New England Nuclear. The cross-reactivity of antiserum was insignificant, except for prostaglandin E₂ (3.7%). The lower limit of sensitivity was 1 pg/ml. The mean normal value measured on 20 volunteers was 10.0 ± 3.0 pg/ml.

Statistics. Mean and standard deviation were calculated for each variable. Mean values corresponding to different time points were compared by a paired Student’s t test, whereas arterial and venous plasma levels were compared by classical analysis of variance; p values < 0.05 were considered statistically significant. Plotting of curves and calculations were performed on an Apple II computer and a Servogor Plotter 281.

Results

Prostaglandin E₂. Prostaglandin E₂ was measured in seven of our patients having coronary bypass. Changes in venous and arterial plasma concentrations of prostaglandin E₂ before, during, and after CPB are shown in
Fig. 3. Alteration in mean prostacyclin (6-keto-prostaglandin \( \text{F}_2\text{b} \)) concentrations expressed as percent of preoperative values in 17 patients having cardiac operations. Peak values were obtained at 165 minutes (aortic clamping). Star indicates a significant change from the preceding measured mean value (p < 0.05).

Fig. 1. Plasma concentrations are expressed in picograms per milliliter. Mean control levels were 9.7 ± 2.9 pg/ml (mean ± standard error). These levels increased slowly but significantly (26 ± 4.2 pg/ml) in venous plasma after induction of anesthesia and sternotomy. Immediately after lung bypass, at 1 minute of full flow, prostaglandin \( \text{E}_2 \) levels in arterial and venous plasma rose significantly to 87 ± 12 pg/ml and 85 ± 16.6 pg/ml, respectively. Highest levels were observed during aortic clamping (100 ± 14 pg/ml). When lungs were reperfused, plasma levels decreased to a significant extent by the end of CPB after cannula removal (53 ± 6.4 pg/ml). Fifteen minutes after the end of bypass until the end of the operation, venous plasma levels averaged 44 ± 4 pg/ml, but arterial levels were significantly lower: 20.4 ± 4.5 pg/ml. Venous plasma levels were significantly higher than arterial levels 15 minutes after the end of bypass (p < 0.005), at the end of the operation (p < 0.004), and on the first postoperative morning (p < 0.05). On the first postoperative morning, mean prostaglandin \( \text{E}_2 \) levels were 35 ± 4.5 pg/ml in venous plasma and 19.3 ± 3.03 pg/ml in arterial plasma. Plasma levels of prostaglandin \( \text{E}_2 \) were always higher at outflow versus inflow of the heart-lung machine itself, but the results were not statistically significant (Table I).

In a closed heart-lung machine circuit (no patient), we found a significant increase in prostaglandin \( \text{E}_2 \) from 60 to 148 pg/ml above and 126 pg/ml below the membrane oxygenator soon after 1 minute on "bypass." During 2 hours of "bypass," mean prostaglandin \( \text{E}_2 \) concentrations were 136 ± 15 ng/ml above and 134 ± 18 ng/ml below the membrane.

As shown in Fig. 2, during orthopedic operations, no significant changes in venous plasma levels were observed during the total surgical procedure. Mean control plasma levels were 34 ± 4.1 pg/ml in the five patients. The highest mean plasma levels were 55 ± 6.06 pg/ml, 10 minutes after placement of the cement.

Prostacyclin. Plasma concentration changes in prostacyclin, measured as plasma 6-keto-prostaglandin \( \text{F}_2\text{b} \), are shown in Fig. 3 (concentrations are expressed in percent, compared to 100% preoperative control values). The preoperative concentration of 6-keto-prostaglandin \( \text{F}_2\text{b} \) was 238 ± 44.9 pg/ml. After induction of anesthesia, this mean concentration decreased to 136 ± 19.4 pg/ml. At the beginning of CPB, plasma levels of 6-keto-prostaglandin \( \text{F}_2\text{b} \) increased significantly (p < 0.03) and reached highest plasma activity when the aorta was clamped (p < 0.03): 361 ± 94 pg/ml in venous plasma and 398 ± 90 pg/ml in arterial plasma. Plasma concentrations decreased slowly at the end of CPB and returned to control values when the operation was terminated. There were no significant changes between arterial and venous plasma levels and no
Fig. 4. Thromboxane concentration expressed as percent of preoperative values in 17 patients having cardiac operations. Note the arterial peak level at 225 minutes (lung reperfusion) and the venous peak level at 260 minutes (end of bypass). Star indicates a significant change from the preceding measured mean value (p < 0.05).

Differences in plasma concentrations entering or leaving the heart-lung machine. Furthermore, prostacyclin concentration was unmeasurable after 2 hours of closed-circuit “bypass.”

During orthopedic operations, no significant changes were observed.

Thromboxane. In Fig. 4, thromboxane concentrations, reflected by thromboxane B₂ measurements, are shown in arterial and venous plasma, expressed as percent of control values (166 ± 49.5 pg/ml in 17 patients). Thromboxane B₂ rose significantly (p < 0.03) during rewarming of the patient. Peak concentrations were observed in arterial plasma during pulmonary perfusion: 402 ± 101 pg/ml. Venous plasma levels of thromboxane B₂ were maximal at the end of CPB (415 ± 109 pg/ml). Thromboxane B₂ decreased slowly and reached 73 ± 17.2 and 71.5 ± 12.3 pg/ml in venous and arterial plasma, respectively, by the morning of the first postoperative day. No significant changes were noted between arterial and venous plasma levels at inflow versus outflow of the heart-lung machine itself during CPB.

The closed circuit “bypass” (with fresh blood) induced no thromboxane A₂ production, and plasma concentration of thromboxane B₂ remained unmeasurable during 2 hours of “bypass.”

During hip replacement, no statistically significant changes of thromboxane B₂ concentrations were observed.

Discussion

Prostaglandin E₂. Under normal conditions, the lung rapidly converts prostaglandin H₂ into prostaglandin E₂.³ This prostaneid is inactivated during its passage across the pulmonary vascular bed, the half-time of prostaglandin E₂ normally being less than 1 minute.⁴

At the beginning of CPB, plasma concentrations of prostaglandin E₂ increased tenfold. A possible explanation (supported by the observation in closed circuit “bypass”) might be liberation of prostaglandin E₂ by the white cells trapped and injured in the heart-lung machine. Furthermore, bypassing the pulmonary vascular bed increases the half-time of prostaglandin E₂, resulting in a sharp rise in its plasma concentration at the beginning of CPB. Nonpulsatile flow and hypothermia may possibly influence peripheral production of this prostaglandin. Immediately after lung reperfusion (still during extracorporeal circulation), prostaglandin E₂ plasma concentrations decreased significantly. This is probably related to pulmonary inactivation of this prostanoïd.

Fifteen minutes after the end of bypass and when the operation was completed, arterial plasma levels of prostaglandin E₂ were significantly lower than venous plasma levels. This difference pleads in favor of an effective pulmonary prostaglandin catabolism along with an increased peripheral prostaglandin E₂ synthesis or liberation.

Our results demonstrate an important increase of
prostaglandin E₂ during CPB in humans. This increase cannot be explained by surgery per se, because no significant changes in prostaglandin E₂ plasma levels were observed during total hip replacement.

Prostacyclin. Prostacyclin is synthesized and released primarily by pulmonary vascular endothelium.21,22 Prostacyclin is not metabolized in the lungs. It is nonenzymatically metabolized by hydrolysis into the more stable 6-keto-prostaglandin F₁α.23 Measurement of the hydrolysis product, 6-keto-prostaglandin F₁α, is commonly used as an index of prostacyclin production. This method of chemical quantification is conservative, because intracellular prostacyclin can be enzymatically converted to both 13, 14-dihydro-6-15-diketo-prostaglandin F₁α and 6-keto-prostaglandin F₁α.24

We demonstrated that circulating 6-keto-prostaglandin F₁α was significantly elevated at the beginning of CPB. It is surprising to find an increased level of prostacyclin when lung perfusion is reduced to about 10% (passive perfusion and bronchial vessels). This increase occurred immediately after cannulation of the large vessels, and the peak level of 6-keto-prostaglandin F₁α was observed after placement of the aortic clamp. This prostanoid increase is probably related to a liberation of prostacyclin from injured vessel walls and manipulation of the heart and great vessels.

During CPB 6-keto-prostaglandin F₁α decreases. This could be partially explained by a decreased metabolism of prostacyclin because of hypothermia.25 Despite the common belief that lungs are the major source of prostacyclin, complete lung reperfusion did not increase plasma levels of prostacyclin. Three hypotheses may explain this observation:

1. Hypothermia during bypass could inhibit pulmonary prostaglandin metabolism.

2. Under such nonphysiologic conditions, and with the presence of heparin, prostacyclin may be removed by the endothelial cells of the lung. In fact, the endothelial cell coat is a heparin-like coat26 that may be modified by the action of heparin combined with hypothermia and ischemia, enhancing the permeability of the cell membrane to prostacyclin.

3. Cold cardioplegic solution infused partially in the lung during bypass may influence prostacyclin synthesis and release from lungs.

Thromboxane. Plasma thromboxane B₂ may originate from platelets or be produced in other tissues, such as lung, spleen, and white cells. Generation of thromboxane B₂ during collection of samples is minimized by gentle withdrawal of blood and immediate transfer into indomethacin-containing anticoagulant solution.18

Lung thromboxane A₂ synthesis occurs in vivo, and normally thromboxane A₂ is catabolized (inactivated) during its passage across the pulmonary vascular bed.8

Complement activation observed during CPB may directly stimulate thromboxane A₂ synthesis or may cause pulmonary sequestration of neutrophils followed by release of thromboxane A₂.27,28 Furthermore, platelet damage may occur in the extracorporeal circuit. There is an actual loss of platelets that are retained in the extracorporeal circuit,29 sequestered in the liver and spleen, or in the lung.30 Thus, it seems surprising that lung bypass did not immediately increase thromboxane A₂ concentration. The heart-lung machine itself probably does not play a direct role in thromboxane A₂ production during CPB. This theory is confirmed by the observation that no statistical differences were observed in blood concentration of thromboxane B₂ entering or leaving the machine. Furthermore, fresh human blood recirculated in circuits containing a membrane oxygenator showed no thromboxane A₂ production, contrasting with the results of Addonizio and associates,31 who showed thromboxane B₂ release in a closed "bypass" circuit.

Our finding that the thromboxane B₂ concentration rises at the end of CPB (when lungs are completely reperfused) is probably a consequence of thromboxane A₂ release from sequestered pulmonary platelets and pulmonary microemboli. The elevation of thromboxane level at rewarming and pulmonary reperfusion (measured in our cardiac patient group) is consistent with the data of Watkins and associates.32 However, our thromboxane B₂ values were about twofold less than those of the nonpulsatile group reported by Watkins and colleagues and may reflect differences, either in patient population or in the estimation techniques.

Prostacyclin/thromboxane A₂ balance. Thromboxane may be associated with a significant alteration of cardiovascular and platelet function, and it is considered to exert biochemical effects opposite to those of prostacyclin.33 It is not possible to accurately measure the true potency of thromboxane A₂ because no direct chemical determinations are possible owing to its short half-life.24 Although not quantitative, the ratio of prostacyclin/thromboxane A₂ (reflected by 6-keto-prostaglandin F₁α and thromboxane B₂) may be a useful index of the net physiologic effects of these eicosanoids.

At the beginning of CPB, in the presence of platelet dysfunction, high levels of thromboxane were expected but not obtained. The mechanism of this is unclear but may be due to feedback inhibition of thromboxane A₂ synthesis by high prostacyclin concentrations. Our results contrast with those of Ylikorkala,11 Davies,13 and
their associates, who showed thromboxane B, increase in early bypass. Ylikorkala, Saarela, and Vihnikki
temperatures increased prostacyclin production at the onset
of CPB and during bypass, a possible explanation for
this persistently high prostacyclin level during bypass
could also be due to the use of furosemide before
starting bypass. In fact, furosemide strongly increases
prostacyclin synthesis in rabbits.31

Conclusions

In conclusion, our investigation tends to confirm the
metabolic role of the lung in prostaglandin balance in
man. CPB induces a profound prostaglandin imbalance.
Prostaglandin E1 is released by the heart-lung machine and
clarified by the lung, as suggested by a major
increase in its concentration during pulmonary bypass
and its decrease when lungs are subsequently completely
perfused. Prostacyclin is increased after heart cannulation
and aortic clamping during lung bypass but
surprisingly, is not influenced by lung reperfusion.
Thromboxane is released from pulmonary circulation after
total lung reperfusion from sequestered pulmonary plaques and microemboli.

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The Journal of Thoracic and Cardiovascular Surgery

866 Faymonville et al.