

# A Multicenter Investigation into the Occurrence of High-Pressure Excursions

Gerard J. Myers, CCP;\* Patrick R. Weighell, CPC;\* Brian J. McCloskey, CCP;†  
Alison M. Holt, CCP;† Scott McTeer, CPC;‡ Sandy L. Maxwell, CPC‡

\*QEII Health Sciences Center, Halifax, Nova Scotia; †Foothills Hospital, Calgary, Alberta; ‡University Hospital, Edmonton, Alberta, Canada

**Abstract:** The occurrence of sudden increases in premembrane pressures and membrane pressure differentials has drawn considerable attention and debate in the perfusion community. Several terms have been applied to this phenomenon, but the term that best describes this event is “high-pressure excursion” (HPE). The exact causes of HPE are still uncertain, but nonetheless widely speculated. However, their increased appearance seems to be very closely related to the removal/absence of human serum albumin from priming solutions. To investigate the reasons why HPE occur in some cardiopulmonary bypass cases, we present our findings in a multicenter, retrospective analysis of 2696 cardiopulmonary bypass cases. Of the 31 cases of HPE that were documented from the analysis, 60 preoperative and peri-

operative variables were gathered from the participating tertiary care centers. Our findings indicate that these pressure excursions had an occurrence of 1.14% in the three centers involved with this analysis. The largest occurrence of HPE tended to be in male (87.1%) coronary artery disease patients (96.8%) during the presence of the IV anesthetic Diprivan (74.2%). In conclusions, HPE are not perfusate related because it occurred in the presence of three perfusate combinations. They also do not seem to be oxygenator related or exclusive to hypothermic temperatures or heat exchangers. **Keywords:** pressure excursion, oxygenator, thrombosis, platelets, premembrane, coronary artery bypass graft (CABG), resistance, Diprivan, von Willebrand. *JECT.* 2003;35:127-132

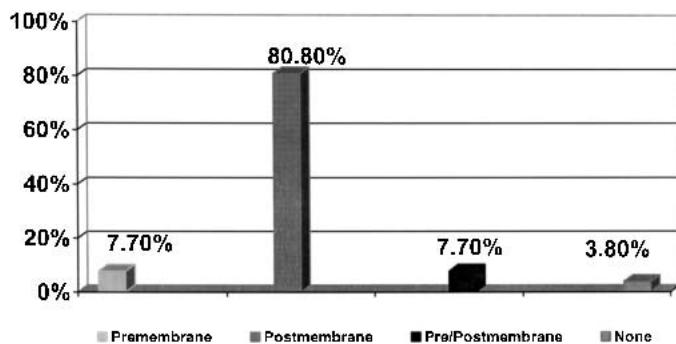
The potential for oxygenator failure has always been the perfusionist’s worst nightmare. In every procedure, there are always those inherent risks that something may go wrong. In 1980, Stoney, Alford, Burrus, et al. (1) reviewed the many problems associated with extracorporeal procedures, including oxygenator failures and change outs, making some recommendations to address the state of the art perfusion practice at that time. In 1992, Henderson, MacDonald, Mayer, et al. (2) presented what may have been the first published report on extreme platelet drops during the use of two types of hollow fiber (Bard 5700, Medtronic Maxima) and one type of flat plate (Cobe CML 30) oxygenators. Unfortunately, pressure differentials were not reported, but their retrospective look at 183 cases found that 9.3% (17/183) of them had platelet drops greater than 80%, after 10 min on cardiopulmonary bypass (CPB).

It was not until 1995 when a paper by Blomback, Kronlund, Aberg, et al. (3) appeared, when perfusionists truly began to understanding that it may not be the oxy-

genator that was failing, but the platelet protection afforded by our priming fluids and extracorporeal circuitry. Blomback’s landmark paper was followed in 1996 by another, Bearss, Ericson, Parks, et al. (4), which addressed the perfusion community on the topic of agglutination and cryoprecipitation. The phenomenon began to generate such terms as cryofibrinogenation, oxygenator thrombosis, pressure excursions, abnormal high-pressure gradient, and oxygenator vasoconstriction. However, the term that most aptly applies is “high-pressure excursion” (HPE), simply because the vast majority of these high pressure journeys start at one point and then return to its baseline later.

HPE has been found to occur more frequently in the absence of albumin and the presence of uncoated extracorporeal circuitry (5-7). In modern, low-prime, high-performance membranes, it is very difficult to detect the presence of HPE without the measurement of both premembrane and postmembrane pressures (8-10). A 1998 survey of 52 North American cardiac centers (Figure 1) revealed that 80.8% of these centers measured postmembrane pressures only (8). At present, this suddenly occurring, often transient phenomenon has become one of the most interesting problems facing extracorporeal circulation today. The literature shows it occurs in all types of

Address correspondence to: Gerard J. Myers RRT,CCP, Coordinator, Cardiovascular Perfusion Services Cardiac OR, NHI Campus QEII Health Sciences Center, P.O. Box 9000, Halifax, Nova Scotia, Canada. B3K 6A3. E-mail: edit@ns.sympatico.ca  
Received March 25, 2002; accepted March 26, 2003.



**Figure 1.** Pressure measurements on CPB in 52 North American cardiac centers. Premembrane = premembrane pressures; Postmembrane = postmembrane pressures.

oxygenators, with all types of primes, and probably in all centers (7,8,11). In other words, it does occur . . . but why, and in what patient population?

The purpose of this article was an attempt to identify and isolate any of the predominant factors associated with the occurrence of HPE, and perhaps eliminate those suspected factors that are not causative in nature.

## METHODS

In March of 2000, a retrospective look was made into the occurrence of HPE, during 2696 routine CPB cases at three Canadian tertiary care centers. The centers selected to participate in this retrospective analysis were chosen for three reasons: (1) they all used the same uncoated bypass circuitry and Monolyth® oxygenator; (2) they all measured pre- and postmembrane pressures; and (3) with the exception of perfusates, all centers used similar practice (no albumin in the prime, roller pumps, most patients not actively cooled).

### Inclusion Criteria

1. Based on our previous work done with the Monolyth® (7,12), we established a normal *in vivo* pressure differential (inlet–outlet) of approximately 20 mmHg/L of blood flow. Inclusion was considered in those cases where pressure differentials exceeded 125% of expected.
2. Abnormal pressures differentials that occurred within the first 30 min of bypass.
3. Platelet counts (if measured) that decreased more than 55% at the start of bypass.

### Exclusion Criteria

1. re-operations
2. homologous blood products in prime (including albumin)
3. active cooling of the patient at the start of CPB

Those found to have recorded incidents of HPE and fit into the inclusion criteria had their charts reviewed under eight categories. In all, there were originally 81 different variables proposed, but because of the nature of retrospective data analysis, 21 of them were unobtainable from all three centers.

1. operation–type of surgical procedure
2. equipment used–oxygenators, filters
3. perfusates/perfusate medications added before bypass–crystalloid, crystalloid/Pentaspan® (Bayer, Inc. West Haven, CT) crystalloid/autologous blood, heparin type, heparin dose, Amicar® (Epsilon aminocaproic acid (Wyeth-Ayerst, Markham, ON, Canada), Cyklokapron® (Tranexamic acid (Pharmacia & Upjohn, Toronto, ON, Canada), Trasylo® (Aprotinin, Bayer)
4. preoperative variables–age, weight, gender, blood type, cancer, lupus, congestive heart failure, diabetes, pregnancy, other hypercoagulable states, platelets, WBC, proteins, hemoglobin, hematocrit, PTT, INR
5. preoperative medications–heparin, aspirin, beta blockers, calcium channel blockers, ACE inhibitors, streptokinase, urokinase
6. prebypass variables–ACT type, ACT control, ACT prebypass, patient temperature, perfusate temperature
7. prebypass anesthesia–heparin loading dose (units and units/Kg), Amicar®, Cyklokapron®, Trasylo®, Diprivan®, (propofol, Zeneca Pharma, Oakville, ON, Canada)
8. on bypass variables–ACT, Amicar®, Cyklokapron®, Trasylo®, Diprivan®, platelets, patient temperature, arterial blood temperature, premembrane pressure, postmembrane pressure, pressure differential, time for HPE to occur, fibrin glue used, Gelfoam®, (Upjohn, USA) used, sodium nitropruside (SNP) used, resolution time

## RESULTS

Patient demographics for non-HPE cases were only obtainable from two participating centers (total of 1765) and are reported in Table 1. Out of 2696 bypass cases in this

**Table 1.** All patient demographics.

	Halifax N = 1460	Calgary N = 305	Edmonton N = 931	HPE N = 31
Age (yrs)	64.4 ± 12.4	66 ± 11.3	**	61.9 ± 13.6
Weight (kg)	81.2 ± 17.1	80 ± 15.2	**	84.2 ± 15.1
Gender (%)				
Males	71.8	69	**	87.1
Females	28.2	31		12.9

Results reported as ± standard deviation of the mean.

\*\*Unavailable.

HPE = high pressure excursion; Halifax, QEII Hospital; Calgary, Foot-hills Hospital, Edmonton, University of Alberta Hospital.

retrospective investigation, there was a total of 35 patients who possibly fell into the category of HPE. Unfortunately, we were unable to obtain sufficient data on four of these patients; therefore, the variable used in this analysis was on 31 patients. Patient demographics of the 31 HPE cases are also represented in Table 1. The mean age of these patients was  $61.9 \pm 13.6$  years, and the mean weight was  $84.2 \pm 15.1$  kg. In addition, 12.9% (4/31) of the cases were female, and the other 87.1% (27/31) were male. The recognition of HPE occurring took place between 1 and 30 min after going on bypass, with a mean time of  $7.9 \pm 7.2$  min. The mean premembrane pressure was  $468.9 \pm 78.6$  mmHg (range 350–600 mmHg). The mean postmembrane pressure was  $142.2 \pm 36.9$  mmHg (range 91–178 mmHg), and the mean pressure differential was  $336.6 \pm 75.8$  mmHg (range 250–460 mmHg).

High transmembrane pressures tended to resolve themselves without treatment (SNP, etc.) between 4 and 60 min, with a mean time of  $27.5 \pm 14$  min. In those cases (10 in total) where SNP was used in an attempt to passivate the platelets during the occurrence of HPE, the time to resolution was between 15 and 42 min, with a mean of  $24.8 \pm 10$  min.

A breakdown of surgical procedures in both the HPE group and the non-HPE patients can be found in Table 2. As with patient demographics mentioned in Table 1, surgical data from the non-HPE patients was unavailable with the Edmonton group and was, therefore, not included in Table 2. Coronary artery bypass graft (CABG) procedures made up 87.1% of the HPE cases and 71% of the non-HPE cases. Furthermore, 96.8% of the HPE cases had coronary artery disease (CAD), while 80.6% of the non-HPE cases had CAD as well.

Despite attempting to collect data with a single oxygenator, one center had used some Affinity® oxygenators (Medtronic, Inc., Parker, CO) and had two incidents of HPE that fell into the investigations protocol. Therefore, 93.5% (29/31) of the HPE cases involved the Monolyth®, and 6.5% (2/31) of the cases involved the Affinity® oxygenators. The Pall EC Plus® arterial filter (Pall Corpora-

tion, Ann Arbor, MI) was used in 38.7% (12/31) HPE cases, the Dideco D734® arterial filter (Dideco, Mirandola, Italy) was used in 38.7% (12/31) cases, and the Affinity® arterial filter (Medtronic, Inc., Parker, CO) was used in 22.6% (7/31) cases.

In only one case was the arterial blood and patient temperature both at  $28 \pm 0.1^\circ\text{C}$  during the time of the HPE incident. As shown in Figure 2, the mean arterial blood temperature at the time of the HPE incident was  $34.7 \pm 2.1^\circ\text{C}$ . (range  $32.0\text{--}37.0^\circ\text{C}$ ), and the mean patient temperature at the time of the HPE incident was  $35.1 \pm 1.8^\circ\text{C}$ . (range  $34.0\text{--}37.0^\circ\text{C}$ ).

Looking at perfusates, 51.6% (16/31) of the cases used either Plasmalyte A® (Baxter, Deerfield, IL) or Normosol R® (Abbott Laboratories, Montreal, PQ, Canada) as their perfusates for bypass, 25.8% (8/31) used a combination of crystalloid and 50 mL of autologous blood, as described by Myers, Legare, Sullivan, et al. (7), and 19.4% (6/31) used a combination of crystalloid and 500 mL of Pentaspan® (Bayer). A mean of  $8419 \pm 3,394$  units (range 3000–20,000 units) of porcine heparin (Hepalean®, Organon Teknika, Toronto, ON, Canada) was added to the perfusate prior to bypass, and the mean loading dose of heparin administered by anesthesia before bypass was  $361.1 \pm 81.5$  units/kg (263–666 units/kg). Table 3 details the activated coagulation times (ACT) as measured by the Medtronic Hemotec ACT III® machine (Medtronic) in all cases.

Prebypass hematology showed the mean WBC of  $7.7 \pm 4.6^{10^9/L}$  (range  $3.2\text{--}28.4^{10^9/L}$ ). Hemoglobin had a mean of  $137.4 \pm 12.4$  g/L, with a range of 104–164 g/L, and hematocrit was  $0.41 \pm 0.04$ , with a range of 0.33–0.45. The PTT was slightly elevated at a mean of  $46.3 \pm 23.6$  sec (range 23–111 sec) and the mean INR at  $1.1 \pm 0.23$  (range 0.9–1.9). Prebypass platelet count had a range of  $145.0 \times 1000/mm^3$ – $548.0 \times 1000/mm^3$  (mean  $258.7 \pm 107.9 \times 1000/mm^3$ ).

There was no fibrin glue, Gelfoam® or other procoagulants used during any of the cases. None of the patients presented preoperatively with Lupus, 16% (5/31) had a

**Table 2.** Procedures and diseases.

	Halifax N = 1460	Calgary N = 305	Edmonton N = 931	HPE (N = 31)
Valves	13.4%	18.4%	**	3.2%
Valves + CABG	9.7%	9.5%	**	9.7%
CABG	74.0%	67.9%	**	87.1%
Other	2.8%	4.3%	**	0
CAD	83.8%	77.4%	**	96.8%

Results reported as  $\pm$  standard deviation of the mean.

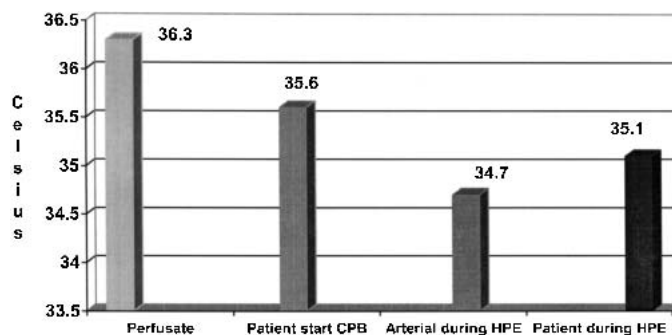
\*\*Not available.

Valves = aortic or mitral valve surgery.

Valves + CABG = valve surgery plus coronary artery bypass grafts.

CAD = coronary artery disease.

Sec = seconds.



**Figure 2.** Temperatures during HPE cases. Perfusate = priming fluids; Patient start CPB = nasopharyngeal temperature at start of CPB; Arterial during HPE = arterial blood temperature during HPE; Patient during HPE = nasopharyngeal temperature during HPE.

**Table 3.** Activated coagulation times in HPE cases.

Loading dose heparin	361.1 ± 81.5 units/kg
Control ACT	147.3 ± 56.2 sec
Prebypass ACT	559.1 ± 156.6 sec
On bypass ACT	744 ± 134.5 sec

Results reported as ± standard deviation of the mean.

previous malignancy, 22.5% (7/31) had diabetes, and 32.3% (10/31) had presented with congestive heart failure.

As seen in Table 4, Amicar® was used in 38.7% (12/31) of the cases before going on bypass, Trasylol® in 12.9% (4/31) of the cases before bypass, Cyklokapron® in 35.5% (11/31) of the cases before bypass, and Diprovan® was given in 74.2% (23/31) of the HPE patients prebypass.

Looking at preoperative medications, none of the HPE patients had received streptokinase or urokinase before coming to the operating room. As expected, with the majority of them being CAD patients, 32.3% (10/31) were on calcium channel blockers, 45.2% (14/31) were on ACE inhibitors, and 87.1% (27/31) were on beta-blockers. Finally, only 38.7% (12/31) of the cases had been on heparin before bypass, and 48.4% (15/31) had been on aspirin several days before coming to the operating room.

## DISCUSSION

Even in today's state of the art understanding of extracorporeal circulation, HPE continues to be the leading cause of oxygenator dysfunction (6,10). The reported incidence of HPE with heparin-coated oxygenators has been as low as 0.03%, or 1 in every 3036 cases (6) and as high as 0.4%, or 1 in every 256 cases (10). In the case of uncoated oxygenators, the percentage of HPE events was as low as 0.6%, or 1 in every 163 cases (3) and as high as 4.3%, or 1 in every 23 cases (6). The latter findings indicate that coated bypass systems can dramatically reduce the incidence of HPE, but they cannot completely eliminate them. Our multicenter investigation into HPE using uncoated oxygenators and extracorporeal circuitry, found the overall incidence of HPE to be 1.3% at our centers, or 1 in every 87 cases. The latter seems to be well within the previously reported incidence for this event. A breakdown

**Table 4.** Drugs used during HPE cases ( $N = 31$ ).

	Perfusate	Prebypass	On-bypass
Amicar (EACA)	6.5%	38.7%	25.8%
Trasylol			
Aprotinin	9.7%	12.9%	9.7%
Cyklokapron			
Tranexamic acid	0.0	35.5%	22.6%
Diprovan			
Propofol	0.0	74.2%	48.4%

of the overall and individual incidence of HPE in the three centers is shown in Table 5.

The early detection of HPE is as simple as measuring pre- and postmembrane pressures, which are essentially used as diagnostic tools for oxygenator problems. In a survey of four oxygenator manufacturers that covered a span of 4 years (1994–1998), a total of 61 oxygenators had been returned to the manufacturers with the report of failed to oxygenate (8). All of these oxygenators had been used during CPB, and all of them had been changed out because of failure to oxygenate the patient. After thorough laboratory investigation by the manufacturer, they all seemed fully functional and fell within the manufacturers specifications. As shown in Figure 3, 92.9% (57/61) of the centers returning the oxygenator to the manufacturer, had measured postmembrane pressures only, and only 7.1% (4/61) had measured both pre- and postmembrane pressures (8). Most of our European colleagues have been using the practice of measuring pre and post membrane pressures for years, which is perhaps why most of the pertinent literature regarding the detection of HPE has come from Europe (3,6,10,13,14).

As shown in Table 2, our retrospective analysis of 2689 cases found 96.8% of the 31 HPE incidents presented with CAD, as did 89.4% of the HPE cases reported by Wahba, Philipp, Behr, et al. (10), in their retrospective look at 1959 patients. Those patients with CAD present two areas of interest in the presence of HPE. The first is the fact that one of the clinical findings in this disease state is an increased level of lipids in the circulation of most CAD patients, and the other is that they have an increased amount of von Willebrand factor (VWF) (15,16). Both of these biological substances can create a layered effect on biomaterial surfaces (17,18). VWF not only acts as a mediator between platelet adhesions on thrombogenic surfaces, but it also acts as a carrier for the procoagulant, factor VIII (18).

Age was suspected as another indicator, but the mean age of those patients in the HPE group was  $61.9 \pm 13.6$  years (range 36–85 years), while those reported by Wahba, Philipp, Behr, et al. was  $67.0 \pm 9$  years. The average age of all CPB cases where HPE did not occur was  $65.2 \pm 11.9$  years. However, some authors indicated that this phenomenon may not occur in small patients (19), the range of the 31 HPE patients was 54–108 kg, with a mean of  $84.2 \pm 15.1$  kg. The mean weight of those non-HPE patients was  $80.6 \pm 16.2$  kg.

**Table 5.** Incidence of HPE.

	QEII (1460)	Foothills (305)	University (931)	Overall (2696)
HPE cases	16	7	12	35
Ratio	1:91	1:45	1:78	1:87
Incidence	1.2%	2.3%	1.3%	1.3%

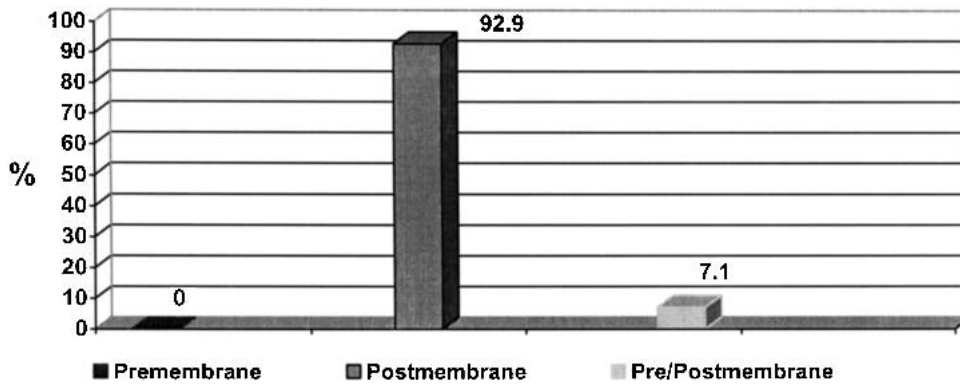


Figure 3. Measured pressure on 61 failed oxygenators.

Nothing was notable in arterial filters, heparin dosing, postheparin ACTs, preoperative medications, prebypass hemoglobins/hematocrits, and white blood cell counts. Other reports have indicated that blood type may play a role in the development HPE (9,20), but our results (Table 6) indicate there were no dominant blood groups, with O positive making up only 51.6% (16/31) of the HPE cases.

This phenomenon had initially been associated with cryofibrinogens and their subsequent fibrin gel networks during hypothermic CPB (3,4). In some cases where hypothermia is associated with the activation of a pressure event, this may be a distinct possibility. However, only one patient in this investigation was actively cooled to 28°C, and the others were allowed to drift to a mean of 35.6 ± 0.7°C (Figure 2). This does not seem to indicate cold-induced incidents, such as that reported by Bearss, Ericson, Parks, et al. (4).

In some of the cases examined, a blood sample had been drawn during the occurrence of HPE. Because platelets are known to deposit on the membranes surface area during HPE, the platelet counts measured were found to have decreased by as much as 62 and 98%. These were similar to decreases in circulating platelet counts found by Wendel, Philipp, Weber, et al. (6). The latter may explain why, after an oxygenator is changed out, the replacement oxygenator works so much better, with 98% of the patients' platelets being discarded with the first oxygenator.

In 10 cases out of the 31, a sodium nitroprusside (SNP) bolus of 100–200 mcg was placed directly into the oxygenator reservoir at the time the event was occurring, which

was followed by a drip of 1–5 mcg/kg/min. With this treatment process, the mean time to resolution of the HPE was 24.8 ± 10 min (range 15–42 min); not much different than the resolution times found with untreated cases. The use of nitric oxide in the form of SNP was first described in animals by De Somer, Foubert, Schacht, et al. (13), as a means of passivating platelets during times of HPE. So, why did it not work rapidly in all 10 cases treated here? We do not know, but perhaps it is attributable to the timing of the SNP administration. That is, if the platelets are not treated with SNP as they are being attracted to a foreign surface, it may become more difficult to have those platelets respond to passivation during their adhesion stage.

Clear-cut answers to the problem with HPE remain to be found. Investigation into a phenomenon that is sporadic, unpredictable, and often goes undetected because of (lack of) pressure measurements is difficult to predict. One factor that may have been overlooked in the possible links to HPE during CPB is the use of lipid-based drugs before and during CPB. Diprivan® is a lipid-based drug that is described in its product monograph as an oil (soybean and glycerol) in a water emulsion (21). Is this significant to extracorporeal surfaces in hyperlipidemic CAD patients? In a study that investigated the effects of Diprivan on gas transfer, Nader-Djalal, Khadra, Spaulding, et al. (22) looked at extracorporeal oxygenation with an FiO<sub>2</sub> of 100%, in 10 patients undergoing CPB during Diprivan® infusion. They concluded that there was no interference with oxygen transfer as long as the Diprivan® emulsion was not injected directly into the oxygenator. One thing that does seem clear is the incidence of HPE seems to have dramatically increased since albumin was removed for priming fluids for CPB (5,6,7,8). Altmayer, Buch, Buch, et al. (23) found that a 4% solution of albumin was able to bind up to 88.7% of the circulating anesthetic Diprivan®. In fact, the more Diprivan® was present, the more it was bound by albumin. Mazoit and Samii (24) found that Diprivan® readily bound to ultrafiltration and dialysis membranes. They also indicate that Diprivan® is readily bound by erythrocytes and human serum albumin,

Table 6. Blood type of patients with HPE (N = 31).

Blood type	# Cases	Percentage
O Pos	16	51.6
A Pos	10	32.3
B Pos	4	13.0
A Neg	1	3.2

O pos = O positive.

A pos = A positive.

B pos = B positive.

A neg = A negative.

so much so that hypoalbuminaemia will increase the unbound Diprivan® free fraction in circulating blood.

Over the years, the use of this injectable anesthetic has been widely used in cardiac operations (22). None of the HPE patients in this investigation had Diprivan® in their perfusates (Table 3); however, 74% of them had received it as part of their anesthetic induction before going on bypass. In a report by Hammaren, Rosenberg, Hynynen, et al. (25), they found that Diprivan® was also sequestered in extracorporeal circuitry, regardless of whether the setup was heparin-coated or uncoated. Diprivan® sequestration on extracorporeal circuitry has also been reported by other authors (26,27).

From the results of our investigation and that of Wahba, Philipp, Behr, et al. (10), the causative and noncausative factors involved with HPE become a little clearer. For example, we know that HPE is not perfusate related because it has occurred in the presence of all perfusates, possibly even albumin, as indicated in our previous survey (8). HPE does not seem to be device related either, given that several reports demonstrate that it occurs in all types of membrane oxygenators. Our findings indicate that HPE is also not exclusively triggered by hypothermic temperatures or blood contact with cold heat exchangers. The literature also makes it clear the HPE can be reduced, but not eliminated, by the use of coated oxygenators.

The eventual outcome of these incidents can be directly influenced by the response of the operator. Keeping a cool head, warming the patient, observation of saturations, controlling blood flow, increasing FiO<sub>2</sub>, supporting systemic pressures, and the use of platelet passivating agents carry a better chance of successful outcomes than cooling the patient, panic, and change out of the offending oxygenator.

Whatever the reasoning behind HPE, previously published literature has demonstrated that albumin and coated oxygenators dramatically reduce the incidence of this phenomenon. Future areas of investigation should be directed toward several coagulation factors (especially von Willebrand), male patients undergoing CPB with coronary artery disease, and the use of lipid-based drugs used in cardiac surgery.

## REFERENCES

1. Stoney WS, Alford WC, Burrus GR, et al. Air embolism and other accidents using pump oxygenators. *Ann Thorac Surg.* 1980;29:336-40.
2. Henderson, M., MacDonald, J., Mayer, R. et al: Platelet count reduction during cardiopulmonary bypass: a membrane comparison study. *Proceed Can Soc Clin Perfusion.* 1992;10:25-9.
3. Blomback M, Kronlund P, Aberg B, et al. Pathologic fibrin formation and cold induced clotting of membrane oxygenators during cardiopulmonary bypass. *J Cardiothorac Vasc Anesth.* 1995;9:34-43.
4. Bearss, MG, Ericson, D, Parks, PJ et al: The puzzling case of the cryoprecipitates. *AmSECT Today.* 1996;6:21-5.
5. Palanzo DA, Zarro DL, Manley NJ, et al. Effects of Carmeda Bioactive surface coating of the oxygenator on circulating platelet count drop during cardiopulmonary bypass. *Perfusion.* 2001;16:279-83.
6. Wendel HP, Philipp A, Weber N, et al. Oxygenator Thrombosis: worst case after development of an abnormal pressure gradient - incidence and pathway. *Perfusion.* 2001;16:271-8.
7. Myers, GJ, Legare, JF, Sullivan, JA et al: The use of autologous blood as part of the perfusate for cardiopulmonary bypass: A priming technique *Perfusion.* 2002;17:211-6.
8. Myers GJ. An update on perfusate composition. *Proceed Mechanisms of Perfusion XIII 1998.*
9. Schaadt J. Oxygenator Thrombosis: an international phenomenon. *Perfusion.* 1999;14:425-35.
10. Wahba A, Philipp BS, Behr R, et al. Heparin coated equipment reduces the risk of oxygenator failure. *Ann Thorac Surg.* 1998;65:1310-2.
11. Miller, MJ, Aniuk, L, McAdoo, S: The Multifactorial Aspects of Biocompatibility *Proceed Can Soc Clin Perf.* 1998
12. Myers GJ, Johnstone RJ, Swyer WJ, et al. Evaluation of Phosphorylcholine (Mimesys) coated Monolyth oxygenators during cardiopulmonary bypass in adults. *J Extra Corp Tech.* 2003;35:6-12.
13. De Somer F, Foubert L, Schacht E, et al. Nitric oxide donors attenuate increase in pressure drop across membrane oxygenators. *Perfusion.* 1999;14:331-6.
14. Wendel HP, Ziemer G. Coating techniques to improve the biocompatibility of artificial devices used for extracorporeal. *Eur J Cardiothorac Surg.* 1999;16:342-50.
15. He S, Cao H, Magnusson CG, et al. Are increased levels of von Willebrand factor in chronic coronary heart disease caused by decrease in von Willebrand cleaving protease activity? A study by an immunoassay with antibody against intact bond 842Tyr-843 Met of the von Willebrand factor protein. *Thromb Res.* 2001;103:241-8.
16. Di Bitondo R, Cameron CL, Daly ME, et al. The 1185 A/G and 1051 G/A dimorphisms in the von Willebrand factor gene promoter and risk of myocardial infarction. *Br J Haematol.* 2001;115:701-6.
17. Bromberg M, Nygren H. Von Willebrand factor, a key protein in the exposure of CD62P on platelets. *Biomaterials.* 2001;22:2403-9.
18. Ruggeri ZM, Zimmerman TS. Von Willebrand factor and von Willebrand disease. *Blood.* 1987;70:895-904.
19. Aniuk, L, Miller, M, McAdoo, S et al: The phenomenon of pressure excursion ("Oxygenator Vasoconstriction"). *Proceed Am Acad Cardiovasc Perf.* 1999;20.
20. Luckras H, Boolauky D, Mohangee A. Cryofibrinogination: did it really happen? *Perfusion.* 2001;16:83-6.
21. Diprivan 1%: Product Monograph Zeneca Pharma, Inc. Mississauga, Ontario 1996.
22. Nader-Djalal N, Khadra WZ, Spaulding W, et al. Does Propofol alter the gas exchange in membrane oxygenators? *Ann Thorac Surg.* 1998;66:298-9.
23. Altmayer P, Buch U, Buch HP. Propofol binding to human blood proteins *Arzneimittelforschung.* 1995;45:1053-6.
24. Mazoit JX, Samii K. Binding of Propofol to blood components: implications for pharmacokinetics and for pharmacodynamics. *Br J Pharmacol.* 1999;47:35-42.
25. Hammaren E, Rosenberg PH, Hynynen M. Coating of extracorporeal circuit with heparin does not prevent sequestration of Propofol in vitro. *Br J Anesth.* 1999;82:38-40.
26. Hynynen M, Hammaren E, Rosenberg PH. Propofol sequestration within the extracorporeal circuit. *Can J Anesth.* 1994;41:583-8.
27. Su HB, Tseng CC, Jenn CT, et al. Changes in Propofol levels in isolated cardiopulmonary bypass circuit. *Acta Anaesthesiol Sin.* 1996;34:17-20.