Efficacy of Particulate Removal by a Pre-bypass Filter With Different Oxygenation Systems

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INTRODUCTION

Pre-bypass filtration has recently become feasible during and after priming of cardiopulmonary bypass systems. Previous investigations have pointed to the need for filtering particulates in the crystalloid prime solution and the residua in extracorporeal circuit components.[1] Widespread use of pre-bypass filtration has been limited due to the lack of commercially available disposable filters designed to remove particles ≥ 5 microns. Approximately one year ago, a disposable pre-bypass filter was introduced by the William Harvey Corporation.* This filter was designed to remove solid particles ≥ 5 microns from the extracorporeal circuit prior to the initiation of bypass. These studies were designed to determine the need for pre-bypass filtration, the particle sizes entrapped and the problems associated with the Harvey H-600 pre-bypass filter. (Fig. I)

METHOD

A series of control pre-bypass H-600 filters were carefully opened and the filter media examined by light microscopy for cleanliness to rule out intrinsic particulate contamination. The control series included the following: (1) clinical filters as received (N = 6); (2) six filters flushed with two liters of 5% Dextrose in normal saline (D5 NaCl); (3) six filters incorporated in the extracorporeal tubing circuit without an oxygenator through which two liters of D5 NaCl were recirculated at a flow rate of 3 liters/minute for 5 minutes; and (4) six filters rinsed with one liter of twice filtered (5 μM) distilled water.

Five commercially available oxygenators were examined for particulate contamination: the Bentley** BOS-10 (N = 6); Cobe*** II (N = 7); Harvey H-1000 (N = 4); Shiley**** S-100 (N = 7); and the Sci-Med.***** 3.5 M^2 membrane oxygenator (N

* William Harvey Corporation, Santa Ana, CA.
** Bentley Laboratories
*** Cobe Laboratories
**** Shiley Laboratories
***** Sci-Med.

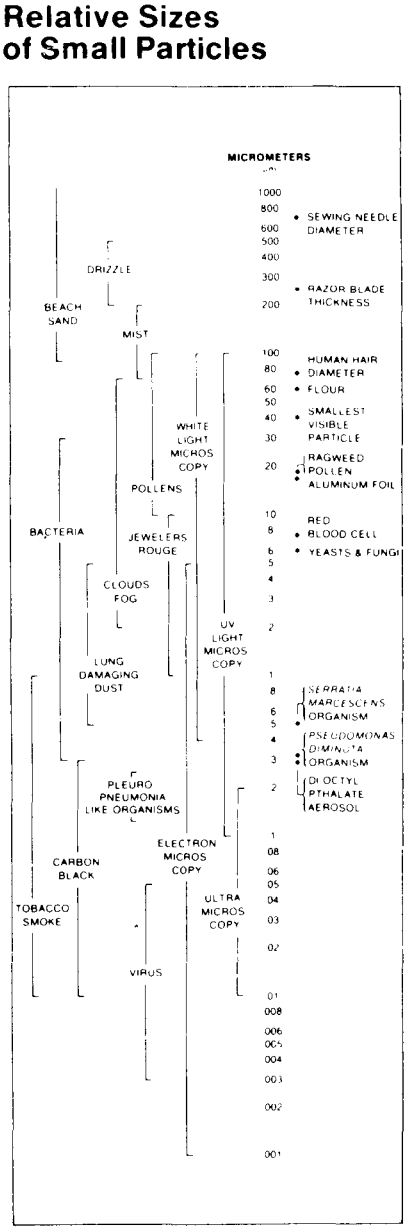

Figure 1. The Relative Sizes of Small Particles. (Reproduced from the Gelman Instrument Co. Product Pamphlet.)

= 5). The Harvey H-600 pre-bypass filter was attached to the venous line near the venous inlet port of each oxygenator. Only the oxygenator and tubing circuit were included in the recirculation pathway. Two liters of D5 NaCl were added directly to the oxygenator and recirculated through the extracorporeal circuit and pre-bypass filter at 3 liters/minute for 5 minutes. The pump was stopped after 5 minutes of recirculation. Clamps were placed just proximal and distal to the filter to avoid losing captured particles. The filter was

TABLE I
Characteristics of Harvey H-600 and Delta Medical PB-005

	Harvey H-600	Delta Medical PB-005
Filter Media	Gelman Acropor*	Gelman Acropor
Pore Size	5 microns	5 microns
Filter Depth	125 microns	125 microns
Priming Volume	125 milliliters	135 milliliters
Air Purge Port	No	Yes
Available Connection-ports	$\frac{3}{8}'' \times \frac{1}{2}''$; $\frac{1}{2}'' \times \frac{1}{2}''$;	$\frac{3}{8}'' \times \frac{1}{2}''$
Filter Surface area	72 cm.^{2}	36 cm.^{2}

* Acropor is an acrylic copolymer using a nylon cloth sandwiched between the filter media for strength. The filter media is 125 microns thick at all points. (Fig. 11)

removed from the circuit and flushed with one liter of filtered distilled water to rinse out electrolyte crystals which may be falsely construed as particles under light or scanning electron microscopy. A 0.2 micron filter was attached to the inlet port of the pre-bypass filter to prevent airborne contamination. A mild ($\leq$20 mm Hg) vacuum was applied to the outlet port of the filter to remove excess fluid. The filter was then aerated at 38°C for 24 hours. Preparation of the pre-bypass filters for microscopic inspection included careful removal of the outer casing and then cutting away the filter material from the support frame with the use of a battery operated cautery. The cautery effectively heat-sealed the cut edge of the filter to avoid self-contamination. One-fourth of the filter was inspected under light microscopy at 35X and 100X magnification to examine the integrity of the filter material, and to determine the number and sizes of microparticles trapped by the filter. A custom designed reticle* displaying a 10 and 100 micron grid, was used for particle sizing. Only those particles visible on the surface of the filter were counted. The variability of the filter pore sizes visible on the surface of the media (1–10 microns) limited the particles counted to those greater than 10 μM. Particles trapped under the surface of the filter material were not easily visible under light microscopy. The total counts were multiplied by 4 to estimate the total number of particles per filter. Those segments of filter examined under light microscopy containing interesting information were cut away, prepared; and examined with the scanning electron microscope.

An additional study was conducted to compare two commercially available pre-bypass filters; the Harvey H-600 and the Delta Medical PB-005,* the characteristics of which are shown in Table I. Pressure measurements across both filters at selected flow were made with calibrated transducers and a recorder. Maximal, mean and pressure differences were measured as a function of flow rate.

Sixteen H-600 pre-bypass filters were used to determine the number of microparticles captured at various time intervals of recirculation. A filter was placed in the extracorporeal circuit for 5 minutes of recirculation (3L/min) and removed. Another filter was placed in the circuit for an additional 10 minutes and then removed. This technique was repeated with additional 15 and 30 minute intervals. This series of filters was used to determine the number of particles released and captured from the extracorporeal circuit over selected intervals of recirculation.

* Roger K. Sherman Company, Los Altos, California 94022.
* Delta Medical Products, Costa Mesa, CA 92626.

TABLE II
The Number of Particle Counts Per Filter for Each Oxygenator Group

Oxygenator (n)	$\bar{x}$	S_x	$S_{\bar{x}}$	Particle Size Range
BOS-10 (6)	2550	1216	497	10–25 microns
Cobe II (7)	965	140	53	20–45 microns
Harvey (4) H-1000	830	420	209	20–45 microns
Shiley (7) S-100	1830	715	270	10–25 microns
Sci-Med membrane (5) $\bar{x}$ <100 counts/filter				
$\bar{x}$ = mean number of particles counted per filter				
S_X = the standard deviation				
$S_{\bar{x}}$ = the standard error				
(n) = the number of oxygenators tested per group				

Comparisons by the unpaired student t test showed that the Sci-Med, the Cobe II and Harvey H-1000 had statistically significantly less particles ($p < 0.05$) than the other two oxygenators tested.

RESULTS

The pre-bypass filters used in all the control conditions were found to have less than 100 particles ≥10 microns per filter. The priming fluids and the extracorporeal circuit tubing did not contribute a statistically significant number of particles. Therefore, the pre-bypass filters, fluids and tubing did not affect the results of the oxygenator studies.

The results of the number of particles released by the five different oxygenator groups are listed in Table II. The BOS-10 had the highest average number of particle counts ($\bar{x}$ = 2550/filter). The Shiley S-100 oxygenator group followed with $\bar{x}$ = 1830 counts/filter; the Cobe II had $\bar{x}$ = 965 counts/filter; the Harvey H-1000 released $\bar{x}$ = 830 particles/filter; and the Sci-Med membrane oxygenator group had less than 100 particle

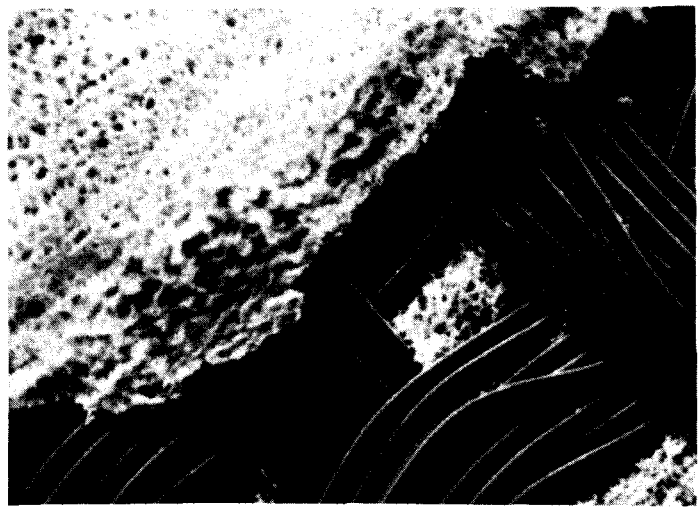

Figure 2. A 117X magnification of the Harvey H-600 pre-bypass filter media exhibiting the fibrous filter material and nylon cross-weave inner support.

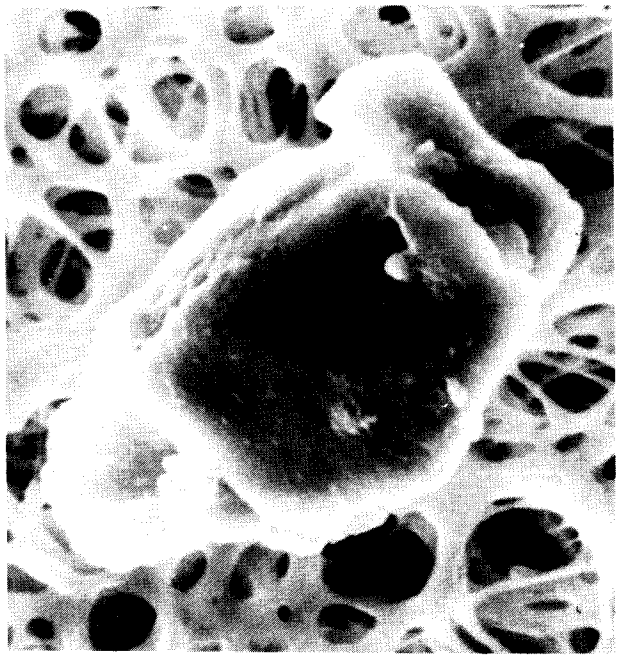

Figure 3. A 48 × 30 micron particle captured from a Cobe II oxygenation system. (Photomicrograph 1100×)

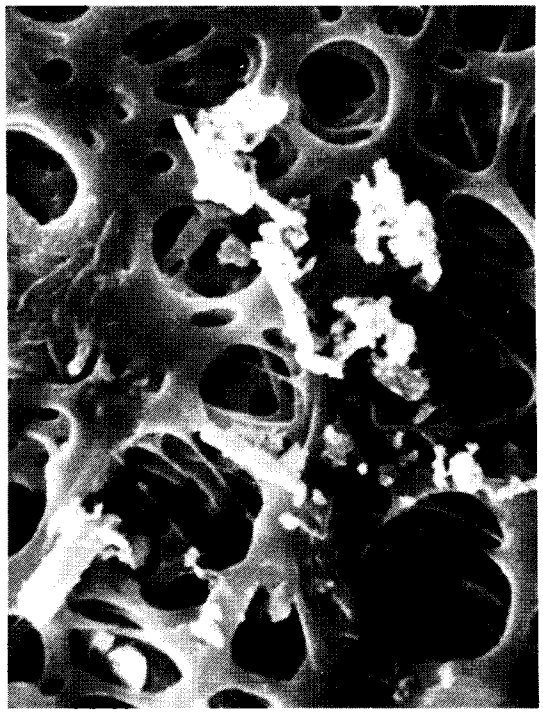

Figure 4. A group of 40 micron particles captured from a Shiley S-100 oxygenation system. (Photomicrograph 1100×)

TABLE III
Pressure Measurement Comparison of Two Pre-Bypass Filters

Fluid Flow Rate in L/Min	Peak Inlet/Peak Outlet Pressures in mm Hg	Mean Inlet Pressure	Peak Pressure Difference Across Filter in mm Hg
	Harvey H-600		
2	75/37	0	38
3	105/15	0	90
4	180/37	15	143
5	220/50	37	170
6	285/100	60	185
	Delta Medical PB-005		
2	75/25	0	50
3	110/20	0	90
4	180/40	12	140
5	225/50	30	175
6	300/90	55	210

counts per filter. The first two oxygenators had statistically more particles ($p \leq 0.05$) than the other three oxygenators tested. The size range of particles was found to vary between oxygenator groups. While the BOS-10 and Shiley S-100 oxygenator groups released particles ranging from 10–25 microns, the Cobe II and Harvey oxygenator groups released particles ranging from 20–45 microns. (Figs. III & IV)

Study of the pressure differences across the Delta Medical PB-005 and Harvey H-600 pre-bypass showed that the pressures measured at all flow rates tested were equivalent (Table III). The two-fold difference in the filter surface areas of the Harvey H-600 and Delta Medical PB-005 pre-bypass filters did not appear to generate any significant difference in the resultant pressure measurements. The pressures measured were well within the maximum limits set for the filter material (>500 mm Hg) and the sealed edges of the filter to the support structure (400 mm Hg).

The results for the efficacy of the pre-bypass filters are shown in Table IV. All particles were removed after one hour period of recirculation, 65% were captured in the first 5 minutes, 85% were captured after 15 minutes and 95% were captured after 30 minutes of recirculation.

The microscopic inspection of the filter media integrity demonstrated variability of the new filters. A particular lot of new H-600 pre-bypass filters appeared to contain particles of different sizes encased in the filter material as well as a large number of cavities, none of which appeared to be a direct channel through the filter material. The encased particles, initially thought to be contaminants, were found to be cabisol, a non-soluble high grade polysilicate used as a bridging support for the fibrous filter material. This constituted approximately 5% of the filter volume. The filter lots exhibiting either

TABLE IV
Filter Efficiency as a Percent of All Particles Removed at Selected Intervals of Time (N=4)

5 Minutes	15 Minutes	30 Minutes	60 Minutes
65%	85%	95%	100%

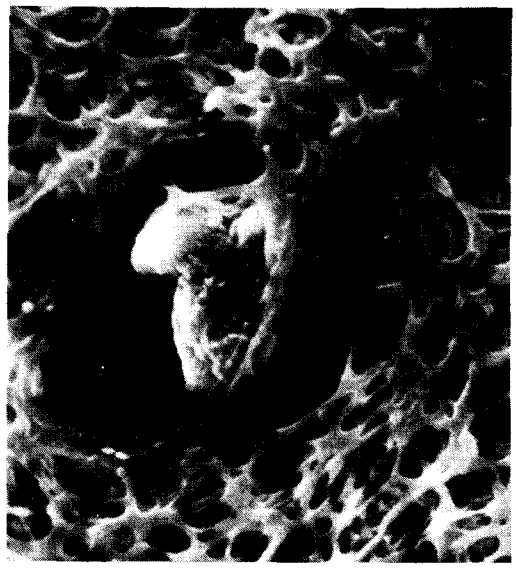

Figure 5. A 30 micron cabisol particle encased in a 45 micron cavity. (Photomicrograph 575X).

a large number of cabisol particles near the surface or a large number of cavities in the media were omitted from the study to avoid inaccurate particle count determinations. (Fig. V)

DISCUSSION

Particles released by the oxygenation systems were effectively trapped by the Harvey H-600 pre-bypass filter. The number of particles reported in this study are far less than the number of particles released from oxygenators noted by Reed[1]. The reason for the sharp reduction is probably due to the recent changes in the manufacturing techniques of oxygenators. Although the oxygenator manufacturers have no Federal standards for oxygenator cleanliness, there is an industrial[2] standard that many manufacturers use for particulate control.

The low particle counts noted with the Sci-Med membrane system demonstrates the positive aspects of fluid flushing the membrane oxygenators during the manufacturing process.

Although the particle counts are relatively low, the data demonstrate a nearly two-fold difference between the Harvey and Cobe oxygenators compared to the Bentley and Shiley units. Additionally, these data show that there is a wide range of particle sizes entrapped in the pre-bypass filter initiating from the oxygenator. Of interest, was the relatively low efficiency of the filters tested as a function of time. It is unknown whether lower flow rates would have resulted in a higher yield over a 15 minute interval, a realistic time period for pre-bypass filtration in clinical practice.

The efficiency of the H-600 pre-bypass filter could be improved by strengthening

the sealed edges of the support structure so that pulsatile flow could be used to increase loose particle dislodgement from the oxygenator and enhance capture by the filter.

This study demonstrates that a significant number of particles exist in four clinical bubble oxygenators. Use of a pre-bypass filter with bubble oxygenators should be considered for infants and children because of their small capillary cross-sectional area, and those patients with preoperative neurologic or vascular complications which could be further magnified by particulate emboli.

BIBLIOGRAPHY

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2. AAMI Oxygenator Standard (Draft) 10/78.

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