The mechanical causes of hemolysis during cardiopulmonary bypass (CPB) for open heart surgery have been noted for many years. The major factors involved include trauma to erythrocytes from mechanical compression by pumping devices, the turbulent mixing of air and blood in the intracardiac suction lines and more recently the flow characteristics of artificial systems which include changes in velocity, pressure, angulation, deformation and other physical causes. Recently the concept of denaturation of blood has been pursued by some groups. The nature of the causes of blood alterations has commonly been assigned to physical variation modification. Recent work in this laboratory by Vasko, Riley and DeWall is highly suggestive of the role of non-mechanical factors as a cause of blood alteration during CPB. This report deals with hemolysis and control. Other facts will be reported in a subsequent paper.

**EXPERIMENTAL DESIGN:**

In both laboratory experiments with dogs and clinical evaluations the same basic (extracorporeal) circuit was utilized. The extracorporeal circuit was gravity venous return to a conventional bubble oxygenator from cannulae placed in the vena cavae or the right ventricle. The gas exchange was accomplished by the introduction of a mixture of 98% O\textsubscript{2} and 2% CO\textsubscript{2}. The "arterialized" perfusate was returned using a conventional double roller pump through a single cannula placed in the ascending aorta as described by DeWall. Intracardiac blood was returned to the system by pump suction to a cardiotomy reservoir.

In laboratory experiments two different filters were incorporated between the reservoir and the oxygenator. In a third group and in clinical procedures no filter was utilized.

The priming solution for both laboratory experiments and clinical cases was pasteurized plasma protein solution (PPS). The PPS used in canine experiments was of canine origin and in patients plasmanate R was utilized.

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* Temprol, Bentley Laboratories, Santa Ana, California
+ Cannalb, Pitman-Moore Laboratories
SAMPLING SITES
1. PERICARDIAL SAC
2. CARDIOTOMY RESERVOIR
3. POST FILTER
4. ARTERIAL LINE
5. VENOUS LINE

Figure 1. Illustrates the sampling sites used in laboratory experiments; the clinical cases were the same with the exception that no filter was used.

ized. Total bypass was achieved by occluding snares about the caval cannulae or by cross clamping the pulmonary artery when right ventricular cannulation was employed.

Determinations of arterial and venous $pO_2$, $pCO_2$, and pH were carried out at control and every 20 minutes during bypass to assure normal acid-base balance. The perfusion technique has been previously described by Vasko and DeWall6. The duration of perfusion was 4 hours in laboratory experiments and 2 to 4 hours in clinical cases depending on the procedure.

Blood samples for measurement of plasma hemoglobin were taken from pericardial blood prior to and during CPB, cardiotomy reservoir, post-filter (when employed), venous blood before entering the oxygenator, arterial blood emerging from the reservoir and intrathoracic blood accumulations. See Figure 1.

RESULTS:

In Group I dogs (no filter) the plasma hemoglobin levels at initial sampling were severely elevated in pre-perfuson samples of blood from the pericardial sac and thoracic cavity prior to onset of bypass (145 (145 mg%±12) while control venous samples had no demonstrable plasma hemoglobin levels. This is of high statistical significance (P<.002).

During perfusion the plasma hemoglobin levels rose slowly over a 4 hour period in venous blood (from 0-115 mg%±20) and in post-oxygenator arterial blood (0-90 mg%±12). The blood returned to the cardiotomy reservoir had considerable variation as would be expected (mean 1 hour sample 420±92 mg%).

Mean values of samples at 2, 3, 4 hour periods were also highly elevated. No linear or exponential increase could be noted. Blood samples taken from the site between the reservoir and oxygenator were elevated consistent with the cardiotomy reservoir samples but were 22% less than the reservoir sample taken at the same time.

Group II dogs, which had a filter between the reservoir and the oxygenator, had elevations in plasma hemoglobin the same as those in Group I with one exception. That was a mean increase of 12% ± 5 in plasma hemoglobin in samples taken after the filter over those taken between the cardiotomy reservoir and the filter.

In clinical patients the increases were similar to those of the Group I dogs. When intracardiac blood was returned to the cardiotomy reservoir, increases in cardiotomy blood were much higher than arterial or venous blood.

In four clinical cases the cardiotomy blood was drawn back by a vacuum method rather than the roller pump in the hope this would decrease the plasma hemoglobin from suction. Laboratory findings were almost identical to amounts found when roller pumps are used.

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In another group of seven patients no blood was returned to the circuit by suction and the arterial and venous plasma hemoglobin levels were increased only slightly (from 0 to 30 mg% ± 3) in perfusions lasting up to 2½ hours.

There was, however, a phenomenon encountered in five patients in which the plasma hemoglobin levels rose only slightly until the administration of 4 or 5 units of banked ACD blood, 20 days or older, was completed. At this time the levels of plasma hemoglobin increased rapidly up to 3-4 times the control value. This was not time related as one patient developed a plasma hemoglobin of 320 mg% and frank hematuria after 42 minutes of perfusion.

**DISCUSSION:**

Although it is impossible to eliminate increases in plasma hemoglobin during CPB, the results in the experiment have shown some basic changes can reduce the amount of rise.

It has been demonstrated that blood found in the pericardial sac and thoracic cavity following thoracotomy but prior to perfusion itself is a source of severe hemolysis, and the blood should not be returned to the extracorporeal circuit under any circumstances. Further, thoracic blood accumulation over a period of 10 or more minutes would be best discarded, or if reinfused, suctioning is best done leaving the top "layer" with its accumulation of fat, etc. for the discard suction.

Sampling from the cardiotomy reservoir indicated an elevated plasma hemoglobin as would be expected, but it was interesting to note that post reservoir samples taken at the same time show this reservoir to provide some reasonable degree of filtration.

Filters added into the line between the reservoir and oxygenator also proved to be of great interest. In this experiment, not only did they not reduce the hemolysis, but did, in fact, show an increase in plasma hemoglobin levels, suggesting it is more beneficial to the extracorporeal circuit to eliminate filters.

Following the laboratory experiments, the clinical cases were also sampled (in these we did not utilize filters). However, in an attempt to reduce the cardiotomy suction damage, a system was set up whereby the cardiotomy suction was created by a vacuum rather than by roller pump in four cases, but laboratory data was almost identical to the roller pump system and did not warrant the extra materials and details of setup involved.
SUMMARY:
The results are suggestive of an improvement in reduction of hemolysis would be the discard of all blood loss and replacement with banked blood. The results obtained were satisfactory in that there were only slight plasma hemoglobin increases, unless the replacement blood exceeded 4-5 units of blood in which case the levels rose rapidly. Blood stored 10 days or more seemed to be the greatest offender. Length of perfusion was relatively unimportant. Consequently, our present practice is to discard blood unless loss is unusually high and then it is judiciously returned to the circuit. Suction is always kept off when not in use and the RPM kept at the lowest possible level. The hemolysis seen following large amounts of ACD blood suggests that there must be some incompatibility, not necessarily between donor and recipient, but perhaps between donor and banked blood.

CONCLUSIONS:
Mechanical factors are not necessarily the prime offenders in hemolysis, and the addition of filters does not solve the problems of hemolysis in CPB. Technique appears to play a most important role; technique of perfusion and surgery alike. Judicious use of suctioning, and the source of blood being returned to the extracorporeal circuit have a direct bearing on the plasma hemoglobin values. Decreased usage or elimination of banked ACD blood during CPB also produces low plasma hemoglobin values.

REFERENCES