MASSIVE HEMOLYSIS IN EXTRACORPOREAL CIRCULATION

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Massive hemolysis has been feared as a complication of operations involving an extracorporeal pump-oxygenator for cardiopulmonary bypass but this complication has not been reported. After successful use of the De Wall-Lillehei pump-oxygenator in 26 patients at this center, massive hemolysis was encountered in the next 2 patients. The purpose of this communication is to record these instances of excessive hemolysis and to report the nature and results of laboratory efforts to determine the cause of this complication.

CASE REPORTS

Case 1.—D. L. M. A 12-year-old white boy, weighing 35 kilograms, with aortic stenosis underwent open-heart correction with the use of cardiopulmonary bypass on Aug. 5, 1959. The duration of bypass was 12 minutes with a perfusion rate of 2,500 c.c. per minute. Immediately following completion of the operation, the patient was noted to have gross hemoglobinuria. Serum hemoglobin at that time was 1,400 mg. per cent. Consultation was obtained from the medical service and Solu-Cortef was administered for approximately 24 hours. In addition, 4 per cent urea (1, 2, 3, 4) and M/6 sodium lactate were administered intravenously at a rate of 3 c.c. per minute to obtain diuresis and alkalinization of the urine. Within 24 hours the urine was clear and the remainder of the hospital course was uneventful.

Case 2.—E. M. L. A 5-year-old white girl, weighing 30 kilograms, with pulmonary valvar stenosis and patent ductus arteriosus underwent open-heart correction of pulmonary valvar stenosis and division and suture of the patent ductus arteriosus using cardiopulmonary bypass with a bubble oxygenator (Aug. 12, 1959). The patient was on bypass for 30 minutes with a perfusion rate of 2,000 c.c. per minute. Following completion of the surgery the patient was noted to have hemoglobinuria and plasma hemoglobin of 2,000 mg. per cent. Medical consultation was obtained and exchange transfusion was done through the right saphenous vein with approximately 2,000 c.c. of whole fresh blood. The patient was given Solu-Cortef, and 4 per cent urea and M/6 sodium lactate were administered intravenously to promote diuresis and alkalinization. After approximately 24 hours the urine had cleared and the patient recovered satisfactorily.

Case 3.—S. K. H. A 17-year-old white girl, weighing 45 kilograms, with a ventricular septal defect had this defect closed on Aug. 19, 1959, using cardiopulmonary bypass with a bubble oxygenator with only one change from the previous 2 cases in that large helix tubing
MASSIVE HEMOLYSIS

Following each instance of severe hemolysis, consideration was given to possible causes of this alarming occurrence. The surgical and technical personnel of the operating team had not changed and there had been no recognized change in surgical technique. The pump-oxygenator used was a bubble oxygenator as described by De Wall and his co-workers and was not changed from that used in previous successful cases. The flow rates and duration of bypass were within the limits previously used without hemolysis.

The possibility of transfusion reaction was investigated by rematching all of the blood used and no incompatibility was found. An hemagglutination test was made on both donor and recipient's blood but no abnormal antigen was present. These results appear to prove that transfusion reaction was not responsible for the observed hemolysis.

In the laboratory the pump was assembled exactly as it was in surgery and, using fresh heparinized dog blood, within one minute after starting the pump grossly noticeable hemolysis was present. The pump was adjusted to make it barely occlusive. The fingers of the pump were working correctly and it was not felt that pump trauma could be the cause of the hemolysis. A different Sigmamotor pump was used as a check with the same results.

The process of cleaning tubing was carefully checked, as a known hemolytic agent, Alconox, had been used. However, hemolysis resulted whether the tubing was cleaned with Alconox, with plain water, or even if it was not cleaned prior to use. Osmolarity changes during the run were checked with Fiske osmometer and there were no significant changes. All metallic parts were resiliomized and again the hemolysis occurred. It was felt that the remaining probable source of hemolysis was the plastic tubing. Pieces of tubing approximately one foot in length were filled with 50 c.c. of whole, fresh, heparinized dog blood and incubated in a water bath at 38° C. Grossly evident hemolysis occurred in the small helix tubing after 15 minutes and there was no gross hemolysis in the other sizes of tubing. Plasma hemoglobin was not obtained during this part of the experiment. The bubble oxygenator was again assembled as in the previous experiment and when the small helix tubing was bypassed no gross hemolysis was apparent. When the small helix was incorporated hemolysis began to appear.

Two bubble oxygenators were then set up using a segment of the small helix tubing in question in one and a different piece of large helix tubing in a second. Fresh heparinized dog blood was then drawn and one half of the blood was used in the small helix pump-oxygenator and the other half of the blood from the same dog in the large helix pump-oxygenator. At flows of 1,140 c.c. per minute for 60 minutes, there was a rather marked difference in the amount...
of hemolysis with the large helix as compared to the small helix (Table 1). The small helix had at least 5 times as great amount of hemolysis as the large helix after identical flow volumes.

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<th>TABLE I. PUMPING THROUGH LARGE AND SMALL HELIX</th>
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<tbody>
<tr>
<td>BLOOD FLOW (1,140 C.C./MIN.)</td>
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<tr>
<td>TIME (MIN.)</td>
</tr>
<tr>
<td>1  5  10  15  20  25  30  60</td>
</tr>
<tr>
<td>Large helix  0  0  0  3  5  9  12  27</td>
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<tr>
<td>Small helix  2  5  12  35  38  75  86  165</td>
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*Values reported in mg. % of plasma hemoglobin.

DISCUSSION

Hemolysis of blood in the small helix tubing was successively reproduced but with serial tests of the small helix tubing there was progressively less hemolysis evidenced, both grossly and by plasma hemoglobin determinations. It was believed on this basis that the agent in the tubing causing the hemolysis was slowly deactivated or dissipated. Hemolysis had not been a problem prior to these 2 cases and Case 3 demonstrates that after changing only the helix tubing in our setup that massive hemolysis was not obtained. Subsequently 36 patients have been operated upon employing the bubble oxygenator (3 patients) or the rotating disc oxygenator (33 patients) without significant hemolysis. The tubing used in the two clinical cases demonstrating massive hemolysis and the tubing used in the laboratory were all from a single 60 foot piece of helix tubing and the hemolysis could not be demonstrated from other lots of small helix tubing. We were unable to identify the actual hemolytic factor in the tubing. In reviewing the literature, no previous reports of hemolysis from this cause were found and this is submitted as a new cause of massive hemolysis and a rare complication of extracorporeal circulation.

Since the substance causing hemolysis appeared to be unstable, becoming less evident with each subsequent exposure to blood in the laboratory, it is suggested that batches of new tubing be tested with blood to observe hemolysis.

A detailed discussion of the treatment of massive hemolysis is beyond the scope of this communication. In these patients a regimen consisting of rapid alkalization, early administration of cortisone, osmotic diuresis using urea, and exchange transfusion have been effective.

CONCLUSIONS

1. Massive hemolysis following cardiopulmonary bypass has been encountered in 2 consecutive patients.
2. Laboratory investigation indicates the presence of an unstable hemolytic agent in a single segment of plastic tubing.
3. This experience suggests the need for routine testing of new segments of plastic tubing.
4. Treatment of these patients with cortisone, sodium lactate, urea, and exchange transfusion has been effective.
small helix (Table I). The hemolysis as the large helix

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<th>SMALL HELIX</th>
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<td>25</td>
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<td>5</td>
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