

Chalk in the prime

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ABSTRACT After observations of cloudiness in the perfusion circuit at open intracardiac operations, laboratory experiments showed a precipitate in a Hartmann's solution (compound sodium lactate solution, Ringer-lactate) and sodium bicarbonate based priming fluid used for cardiopulmonary bypass. The precipitate was found to consist of calcium carbonate crystals. The crystals were not dissolved by adding plasma proteins, nor were they sufficiently cleared from the extracorporeal circuit by a 40 μm filter in the arterial line. The crystals may embolise in microvascular beds and thus be a cause of postoperative morbidity. The practice of adding sodium bicarbonate to the pump prime may be unnecessary.

In most open intracardiac surgery in adults a non-blood priming solution is used to fill the extracorporeal circuit before operation. The omission of homologous blood leads to improved tissue perfusion¹ and improved haemostasis^{2,3} and has simplified the logistics of open heart surgery. In 1982 72% of cardiopulmonary bypass operations in the United States were performed with physiological saline solution as a priming fluid and in 18% of these sodium bicarbonate was used as an additive.⁴ Only a few centres in the United Kingdom have used a prime containing sodium bicarbonate.

We wish to report an adverse chemical reaction, which occurs in a prime containing Hartmann's solution (compound sodium lactate solution, Ringer-lactate) and sodium bicarbonate and which may have important physiological consequences. From 1979 until December 1984 we used a prime based on Hartmann's solution (the composition of which is given in table 1). When we recently changed to a completely clear tubing (Portex) for use with the extracorporeal circuit, we noticed cloudiness in the priming fluid.

From the ion content of the constituents of the prime it seemed possible that the cloudiness was due to the formation of calcium carbonate crystals, the calcium being provided by the Hartmann's solution and the carbonate component by sodium bicarbonate. The aim of this study was to identify the cause and chemical and physical characteristics of the cloudiness in the priming fluid.

Methods

The priming fluid (A) prepared in the laboratory was the same as the one used clinically. It consisted of a mixture of Hartmann's solution, sodium bicarbonate, mannitol, and heparin in the quantities given in table 1. As a control (B) we used a mixture described in table 2. This contained the same amounts of sodium bicarbonate, heparin, and mannitol as fluid A, but instead of Hartmann's solution the same volume (2000 ml) of Plasmolyte 148 (Travenol) was used. This has an ion content similar to that of Hartmann's solution, but does not contain calcium. All experiments were performed at room temperature (23°C) with 1/100 of the quantities of the fluids.

Sediment for microscopic examination was obtained by allowing the prepared samples of prime to stand for 30 minutes. They were then centrifuged at 2500 rev/min for 10 minutes and the supernatant was aspirated until 0.5 ml of fluid was left with any sediment. The sediment was mixed with the remaining supernatant and examined microscopically (magnification $\times 10$).

To determine the chemical nature of the precipitate the Hartmann's based prime was prepared and stirred for five minutes, and the precipitate was allowed to settle. From the bottom of the flask 2 ml were aspirated and centrifuged at 2000 rev/min for five minutes and the supernatant was aspirated. A few drops of normal hydrochloric acid were added to the remaining precipitate. To determine whether the precipitate dissolved when physiological quantities of protein were added, priming fluids A and B were prepared; after they had stood for 30 minutes 50 ml of pooled plasma were added and mixed with a vortex mixer.

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Accepted 10 September 1985

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Table 1 *Priming fluid A: composition and ion content of Hartmann's solution and sodium bicarbonate based prime (2000 ml Hartmann's solution)*

	Ion content (mmol/l)
Sodium	131
Potassium	5
Chloride	111
Calcium	2
Lactate	29
100 ml mannitol 20%	
100 ml sodium bicarbonate 8.4%	
1.6 ml heparin 5000 IU/ml	

Table 2 *Priming fluid B (control): Composition and ion content of Plasmolyte 148 and sodium bicarbonate based prime used as control (2000 ml Plasmolyte 148)*

	Ion content (mmol/l)
Sodium	140
Potassium	5
Chloride	98
Magnesium	1.5
Acetate	27
Gluconate	23
100 ml mannitol 20%	
100 ml sodium bicarbonate 8.4%	
1.6 ml heparin 5000 IU/ml	

The mixtures were then centrifuged at 2500 rev/min for 10 minutes and the precipitate and supernatant of both mixtures were examined under a low power microscope to detect the presence of crystals.

To determine whether the crystals were cleared by a 40 μ m arterial filter, a circuit was set up in the laboratory (fig 1), consisting of a pump (American Optical, 7 inch (17.5 cm) shoe), arterial filter (Pall extracorporeal filter, 40 μ m), and cardiotomy bag (standard Polystan cardiotomy bag). The tubing consisted of 1/4 inch (0.6 cm) and 3/8 inch (1 cm) Portex PVC tubing and Dow Corning silicone pump tubing (1/2 inch (1.3 cm) internal diameter). The circuit was filled with the priming fluid under test and circulated at 3 l/min.

Samples were taken from both prefilter and post-filter sampling ports (fig 1) at 10 minute intervals. After 90 minutes the arterial filter was cut open and washed into 400 ml of distilled water. A sample was taken from this fluid. The experiment was repeated with fluid B as the control. The turbidimetry of all samples was measured at 580 nm against a water standard.

To determine the minimal concentration of sodium bicarbonate that caused precipitation when the calcium concentration was kept constant, samples of priming fluid were prepared that contained Hartmann's solution, mannitol, and heparin in the amounts given in table 1. To this decreasing amounts of bicarbonate were added (100, 75, 50, and 25 ml). The volume difference was corrected by adding dis-

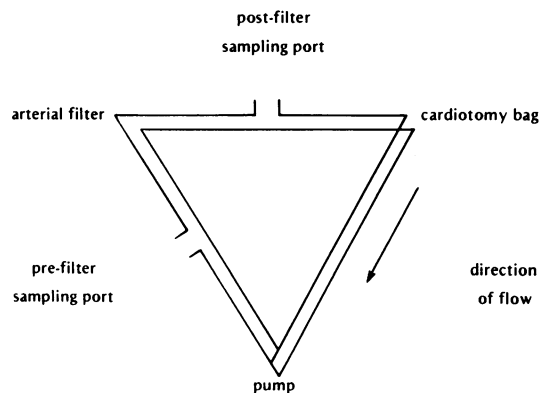


Fig 1 *Extracorporeal circuit set up in the laboratory to determine the optical density of the priming fluid.*

tilled water to keep the final calcium concentration constant at 1.8 mmol per litre of priming fluid.

The samples were centrifuged and the sediment was examined under the microscope.

Results

MICROSCOPY

When the Hartmann's bicarbonate based prime (fluid A) was examined in a low power field, numerous hexagonal and rhomboid crystals were present. If a solution of washed erythrocytes was added, these crystals were found to be about the same size as erythrocytes (fig 2). Given that the erythrocyte has to change shape to pass through small capillaries, the crystals could probably obstruct microvascular beds.

No crystals could be seen under the microscope when samples of Plasmolyte based prime (fluid B) were examined.

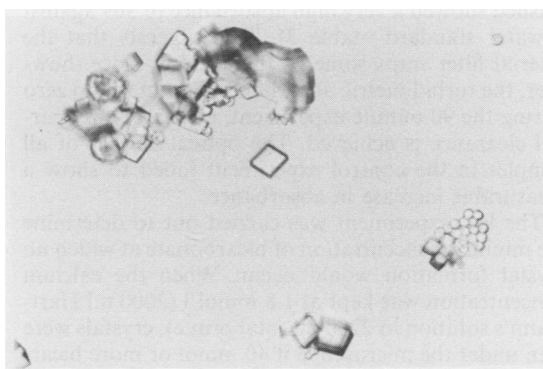


Fig 2 *Calcium carbonate crystals (below) and crystals seen in the priming fluid (above).*

CHEMISTRY

The addition of hydrochloric acid to the sediment obtained from fluid A produced bubbling and seemingly dissolved the precipitate. The chemical reaction which takes place is:



Hydrochloric acid freed carbon dioxide, which indicates the presence of a carbonate salt. Atomic absorption spectroscopy performed by the University of Sheffield department of chemistry confirmed that calcium formed the cation component of the precipitating crystals. We conclude that the crystals that were observed under the microscope and caused the clouding in fluid A are composed of calcium carbonate.

Adding plasma proteins in physiological concentration to the priming fluid (volume relation of priming fluid to pooled plasma 2:5) could conceivably reduce crystal formation, as calcium is bound by albumin in the blood. When a mixture of fluid A and plasma was examined under the microscope, however, this mixture was found to contain crystals. Plasma alone and the control prime-plasma mixture did not contain crystals.

PHYSICAL CHARACTERISTICS

The turbidimetric measurement of priming fluid taken at intervals during circulation in the pump gave an indication of the clearance of crystals by an arterial filter. The results of this experiment are shown in table 3. The absorbance of the prime remained high throughout the 90 minute experiment, indicating the presence of calcium components—that is, crystals. This was confirmed by microscopic examination of a sample of the priming fluid taken at 90 minutes, which showed that crystals were still present, although somewhat smaller and more ragged than those observed in the freshly prepared prime.

Samples of the fluid in which the arterial filter was washed showed a very high absorbance (0.369 against a water standard—table 3). This suggests that the arterial filter traps some of the crystals; since, however, the turbidimetric absorbance did not fall to zero during the 90 minute experiment, evidently only partial clearance is achieved. The optical density of all samples in the control experiment failed to show a measurable increase in absorbance.

The last experiment was carried out to determine the minimal concentration of bicarbonate at which no crystal formation would occur. When the calcium concentration was kept at 1.8 mmol/l (2000 ml Hartmann's solution in 2200 ml total prime), crystals were seen under the microscope if 40 mmol or more bicarbonate were added per litre of prime. If only 20 mmol bicarbonate were added per litre of prime no crystals

could be seen.

SUMMARY

These experiments show that using Hartmann's solution with bicarbonate in priming fluid results in the formation of calcium carbonate crystals. These crystals do not dissolve when plasma proteins are added, and are only partly cleared by a 40 μm arterial filter.

Discussion

Extracorporeal cardiopulmonary bypass is physiologically inferior to the normal circulation, and with careful appraisal of function many organs will show impairment. Although compensatory mechanisms will often restore function, permanent damage to the brain may nullify any beneficial results of open heart surgery.

Many causes of organ dysfunction have been identified and among these obstruction of small vessels by microemboli plays a major part. Many sources of such microemboli have been described but, to our knowledge, no previous studies have found crystals forming in a non-blood prime as a source of microemboli. In this study, which is only an *in vitro* experiment, we have shown that calcium carbonate crystals form, but so far we have not attempted to prove that they play a part in postoperative organ dysfunction; it is, however, difficult to conceive how their presence could be beneficial.

This leads to the question whether sodium bicarbonate should be used at all as a constituent of priming fluids. Since cardiopulmonary bypass became an established procedure the fear of metabolic acidosis has been ever present. Originally, when only a blood prime could be used, the "homologous blood syndrome"¹ caused profound acidosis owing to impaired tissue oxygenation. It had already been shown that dextrose 5% could be used as a blood free prime.⁵ Dextrose 5%, however, is acidic (pH 4) and, unlike

Table 3 Optical density of priming fluids at 580 nm against water standard

Time (min)	Hartmann's/bicarbonate prime (Priming fluid A)		Plamolyte/bicarbonate prime (Priming fluid B)	
	Prefilter	Postfilter	Prefilter	Postfilter
2	0.278	0.228	0.0	0.0
10	0.239	0.220	"	"
20	0.193	0.173	"	"
30	0.150	0.145	"	"
60	0.109	0.109	"	"
90	0.092	0.082	"	"
Arterial filter	0.369		0.0	

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the modern electrolyte solutions, does not provide bicarbonate precursors.

Adding bicarbonate therefore seemed sensible. Currently, at least in the United States, most perfusions are performed with a physiological saline solution⁴; but various other fluids, including bicarbonate, are often added. A symposium on cardiac surgery in 1980⁶ recommended a prime that among other component contains Hartmann's solution and sodium bicarbonate.

A review of published reports has failed to provide any evidence on why it should be necessary to add sodium bicarbonate to the priming fluid if this is mainly composed of an electrolyte solution. If during bypass metabolic acidosis occurs, it should be corrected appropriately. If bicarbonate is added to the prime, only calcium free electrolyte solutions should be used.

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