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A SYSTEM FOR HYPOTHERMIC PERFUSION

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A new type of hypothermic low flow perfusion apparatus was devised in our clinic. The apparatus consists of two heat exchangers and a disc-oxygenator. It was applied for five cases of congenital heart diseases and all cases were recovered successfully. It is aimed as a next plan to minimize the volume of heparinized blood by adapting the apparatus smaller in its capacity.

Artificial lowering of body temperature in order to facilitate surgical treatment is now practiced in many centres. The technique varies from place to place, some prefer to cool their patients by exposing the body surface to ice packs or cold water, *i.e.* surface cooling, and others prefer to bypass a proportion of the circulatory blood through a heat exchanger, *i.e.* blood stream cooling.

Since March 1954, the experimental study on deep hypothermia for open heart surgery has been investigated in our clinic. Adult mongrel dogs were used; deep hypothermia was obtained by means of surface cooling; E.C.G. and E.E.G. were recorded; and histopathological findings were studied.

From this study the authors confirmed that the causes of death in deep hypothermic dog depended mainly on cardiac failure in the rewarming course. To avoid the cardiac failure during rewarming, the intrathoracic rewarming method was established.[1]

It would be reasonable to keep the tempprature of the intrathoracic region higher than that of the body surface under hypothermia. This consequently exerts a favorable influence on the general circulatory condition.

By intrathoracic rewarming, the contraction of the heart muscle becomes stronger, and higher arterial pressure is maintained in spite of lower body temperature. The body temperature rises rapidly because rewarming is carried out through a large surface of lungs.

We have led this method to the clinical use.[2] Those are shown in Table 1. The conclusions of the clinical experiences were as follows:

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TABLE 1. Open Heart Surgery under Simple Hypothermia

	Operation	Death
P.S.	8	2
A.S.D.	29	2
A.S.D. (prim.)	1	0
V.S.D.	27	4
V.S.D.+P.H.	7	1
V.S.D.+P.S.	5	2
A.S.D.+M.I.	1	0
A.S.D.+M.S.	1	0
V.S.D.+P.S.	5	0
V.S.D.+Aneurysm of Sinus Valsalva	1	1
V.S.D.+A.S.D.+Aneurysm of Sinus Valsalva	1	0
Tetl. of Fallot	3	3
A.S.	1	0
P.D.A.	1	0
Total	91	15 (16.5%)

1. The safety limit of cardiac occlusion time under intermediate hypothermia is believed to be about 15 minutes.

2. It is possible to prolong the occlusion time by employing coronary perfusion and intrathoracic rewarming because of prompt restoration of effective cardiac output after releasing cardiac occlusion.

3. Ventricular fibrillation does not happen frequently and, if it occured, can be defibrillated easily by electric shock owing to the method of intrathoracic rewarming.

4. Because of the time limitation of cardiac occlusion, immersion hypothermia has disadvantage in some cases. For example, radical treatment on Fallot's tetralogy must be expected against indication to intermediate simple hypothermia.

According to those conclusions, we decided to design further experimental study in order to prolong the cardiac occlusion time more than half an hour under intermediate hypothermic state.

Therefore the low flow rate hypothermic perfusion using 5 per cent dextrose in water as the priming fluid was carried out experimentally and clinically according to the principle of the work of Zuhdi *et al.*[3)-7)]

This is a preliminary report to describe these results.

APPARATUS

The apparatus consists of a rotating disc-oxygenator and two heat exchangers inlying a small stainless-steel herical coil (Fig. 1).

One of the heat exchangers has been designed to cool the blood after the disc-oxygenator, and the other to warm the blood before oxygenator avoiding bubble formation.

According to Drew's information,[8) 9)] we considered that bubble formation

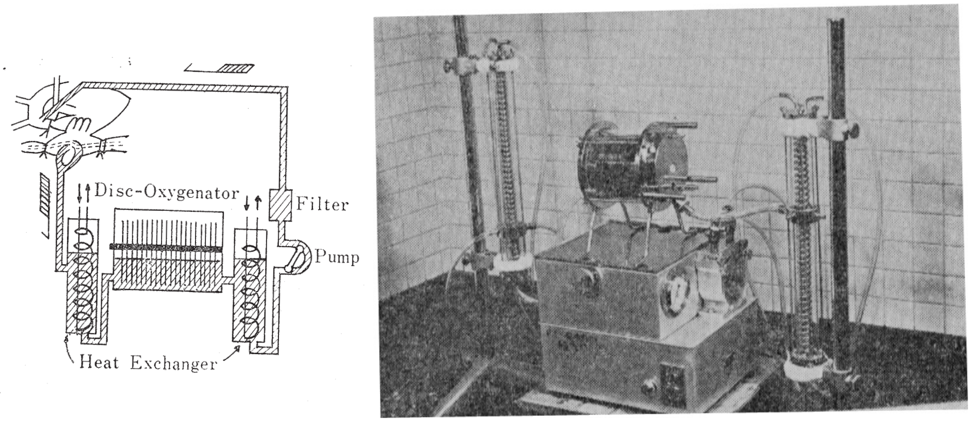

FIG. 1. The low flow rate hypothermic perfusion system.

may be avoided more easily by rewarming the perfusing blood before the oxygenator rather than after it.

But in recent clinical series two heat exchangers are used synchronously for cooling or rewarming without any air embolism.

EXPERIMENTAL RESULTS

Thirty-one adult mongrel dogs were anesthetized and circulated as shown in Table 2. Minimal esophageal temperature was ranged from 20° to 28°C

TABLE 2. Hypothermic Perfusion Data (Dog)

	No.	1	2	3	4	5	6	7	8	9	10	11	18	19
	Body Weight (kg)	19	16	16	23	16	11.5	11.5	11.5	16.5	19.5	19	15	8
Priming Volume	5% Dextose (ml)	550	500	500	600	500	440	410	410	470	480	470	400	300
	Heparinized Blood (ml)	650	700	700	600	700	760	690	690	630	520	530	400	500
	Minimum Esophag. Temp (°C)	23.4	22.4	20.0	22.2	23.5	23.1	24.2	23.4	24.0	25.0	24.5	21.5	20.5
	Minimum Rectal Temp (°C)	18.8	16.5	15.8	21.7	23.3	24.3	19.5	24.5	22.1	23.9	22.4	25.5	24.3
	Flow Rate (ml/kg/min.)	21.0	21.0	26.0	17.4	25.0	26.0	34.0	43.0	27.0	25.0	26.0	27.0	37.0
Duration of Perfusion	Cooling (minute)	40	35	29	33	11	14	11	7	20	8	11	11	7
	Complete Bypass (minute)	—	31	38	19	20	29	33	39	23	33	32	18	32
	Rewarming (minute)	32	90	18	27	24	18	14	17	19	32	19	17	9
	Outcome	Survived	Dead Bleeding	Dead Bleeding	Survived	Survived	Survived	Dead Cardiac Failure	Survived	Survived	Survived	Survived	Survived	Dead Vent. Fibrill.

TABLE 2. (*continued*)

		20	21	22	23	24	25	26	27	28	29	30	31
No.		20	21	22	23	24	25	26	27	28	29	30	31
Body Weight (kg)		10	12.5	10	19	12	18	11	18.5	14	17	18	9
Priming Volume	5% Dextrose (ml)	500	400	350	450	450	530	400	525	424	530	450	450
	Heparinized Blood (ml)	500	400	450	500	500	470	700	675	776	670	650	850
Minimum Esophag. Temp (°C)		27.0	28.0	23.0	24.5	23.2	24.5	25.1	24.5	27.5	27.6	28.0	28.1
Minimum Rectal Temp (°C)		26.5	26.0	26.0	21.2	24.9	26.4	20.9	28 0	27.5	25.5	27.5	25.0
Flow Rate (ml/kg/min).		40.0	30.0	35.0	33.0	30.0	28.0	38.0	32.0	28.0	29.0	33.0	30.0
Duration of Perfusion	Cooling (minute)	6	7	11	7	5	7	7	7	6	6	15	15
	Complete Bypass (minute)	37	31	30	38	31	31	35	39	31	32	30	30
	Rewarming (minute)	28	32	26	31	11	20	39	38	22	25	30	45
Outcome		Survived	Survived	Dead Cerebral edema	Dead Cerebral edema	Dead Filaria	Dead Cerebral Damage	Survived	Survived	Dead Cardiac Failure	Survived	Survived	Survived

and cardio-pulmonary bypass was maintained at a flow rate of 20 to 40 ml per kilogram per minute. Cardiac cavity was opened for about 30 minutes. Sixteen dogs survived in good health but the others died from cardiac failure or cerebral complication. Autopsy findings clarified that severe hypotension during perfusion led the dogs to cardiac failure or the cerebral complication, and the cerebral damage was not due to air embolism but to perfusing technique.

From the experimental study, it was concluded that blood pressure during hypothermic perfusion must be maintained more than 50 mmHg.

METHOD

The apparatus was primed with a certain amount of 5 per cent dextrose in water and donor blood which were roughly calculated from the formula described below. The priming volume of the apparatus was about 1 500 ml.

$$\text{5 per cent dextrose in water} = B + \frac{A-B}{4}$$

$$\text{Blood} = \frac{3}{4}(A-B)$$

A: priming volume = 1 500 ml
B: a third of the patient's daily fluid requirement

The patient was given a 2 mg of heparin sodium per kilogram of body weight immediately before cannulations. The venae cavae then were cannulated in the usual fashion followed by the introduction of the arterial cannula directly into the aortic arch. The cannulae were connected to the apparatus and then perfusion started.

During the cooling period, care must be taken to maintain a good cardiac output and pressure. Assisted blanket cooling was used together avoiding severe temperature gradient between the peripheral and central tissue. At 32° to 30°C of rectal temperature or 29° to 25°C of esophageal temperature, cardiac occlusion was made and cardiac cavity opened. It took about 10 minutes for cooling usually.

Every ten minutes the clamp occluding the aorta was released to perfuse the coronary arteries for a short period.

Intracardiac manipulation was performed very easily because of hypothermic soft myocardium with blood less field. Ventricular fibrillation did not occur and, if it occured, a single electric shock was enough to restore the heartbeat.

During the rewarming period, care must be taken for changes of blood pressure also. Generally, when the temperature reached 33° or 34°C by esophagus, perfusion was stopped.

Most of the patients in this series were perfused at a rate of 30 ml per minute per kilogram of the body weight.

Mean arterial pressure varied from 30 to 60 mmHg during complete bypass and intracardiac repair.

CLINICAL DATA

Clinical data are shown in Table 3 and 4. Five cases were operated on

TABLE 3. Hypothermic Penfusion Data (Clinic)

No.	1	2	3	4	5
Age	9	9	4	14	6
Body Weight (kg)	21.5	21.5	15.5	42.0	31.0
Diagnosis	P.S.	A.S.D.	V.S.D.	V.S.D.	V.S.D.
Minimum Temp Rectal (°C)	24.0	26.5	31.0	32.7	31.2
Minimum Temp Esoph (°C)	28.5	27.5	26.5	25.2	26.9
Total Pump Time	52′50″	43′15″	35′15″	38′50″	34′30″
Vent. Fibhill	+ spont. defibrill	—	—	—	—
Outcome	Survived	Survived	Survived	Survived	Survived

TABLE 4. Hepothermic Perfusion Data (Clinic)

	No.	1	2	3	4	5
Priming Volume	5% Dextrose (ml)	500	500	550	800	700
	Heparin Blood (ml)	1000	1000	1200	900	1000
Flow Rate (ml/kg/min.)	Cooling	35	32	32	24	26
	Complete Bypass	37	36	38	20	28
	Rewarming	37	35	32	29	24
Arterial Pressure During Complete Bypass (mmHg)		60	30~40	30~40	40~50	30~40
Duration of Perfusion (′: minute)	Cooling	10′	3′30″	3′	3′55″	5′
	Complete Bypass	15′20″	15′55″	16′30″	13′00″	11′40″
	Rewarming	43′00″	22′55″	21′00″	21′05″	17′30″
Body Temp When Complete Bypass Start.	Rectal (°C)	25.0	27.8	34.0	35.1	32.0
	Esophag. (°C)	31.0	31.5	30.0	26.3	28.5

and all of them were repaired successfully.

The total pump time was varied from 35 to 53 minutes. The cardiac occlusion time was about 15 minutes. The total heparinized blood requirement was about 1 000 ml. The temperature curves and the blood pressure curve during the procedure of the Case No. 5 (6-year-old male, Ventricular Septal Defect) are shown in Figure 2. E.C.G. and E.E.G. findings in the same case are shown in Figure 3.

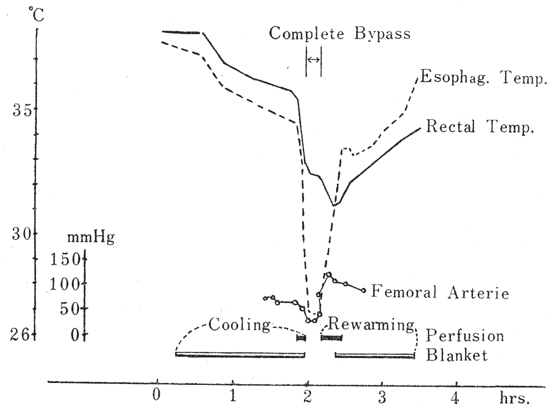

FIG. 2. Temperature and blood pressure
Case No. 5 (6-year-old male V.S.D.)

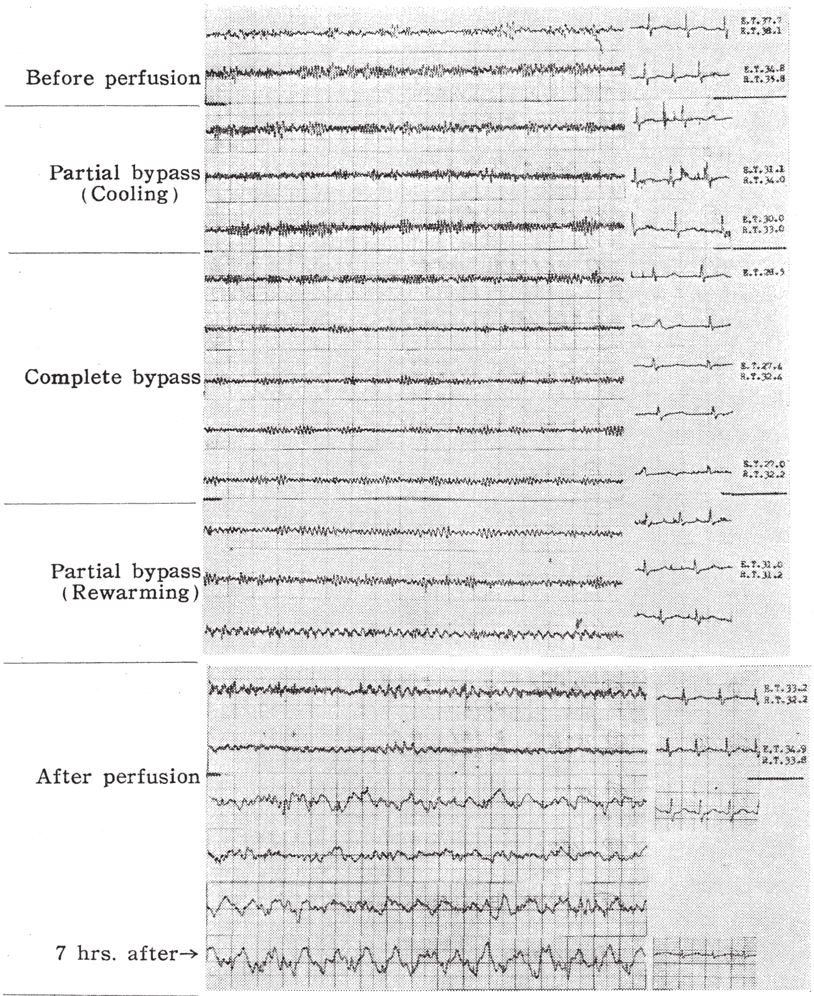

FIG. 3. E.E.G. and E.C.G. Case No. 5. (6 year old male V.S.D.)

DISCUSSION

Considering the disadvantages of intermediate simple hypothermia, which has the time limitation for the permissible cardiac occlusion and requires longer period of time to cool or warm patients, the combination of extracorporeal circulation with hypothermia became necessary.

Gollan,[10] one of the first users of this combination, summarized many of the early experimental studies in his monograph in 1959.

The clinical combination of these methods was stimulated greatly by the development of a simple, efficient heat exchanger by Brown[11] in 1958.

And Drew found a correlation between the frequency of neurologic injury and the type of heat exchanger used, and suggested that bubbles formed in the perfusing blood might be the cause of injury.

Our newly devised apparatus (Fig. 1) has two heat exchangers inlying small stainless steel herical coil. One of them, placed before the oxygenator, is only used for warming the perfusate to avoid air embolism. And the other is for cooling only. But clinically both heat exchangers were used simultaneously for cooling and rewarming patients without any disadvantages.

In rewarming course, care was taken to warm the perfusate within the temperature gradient of 15°C.

Most of the patients in this series were perfused at a rate of 30 ml per minute per kilogram of the body weight, and none of them showed cerebral air embolism, hematuria etc. postoperatively.

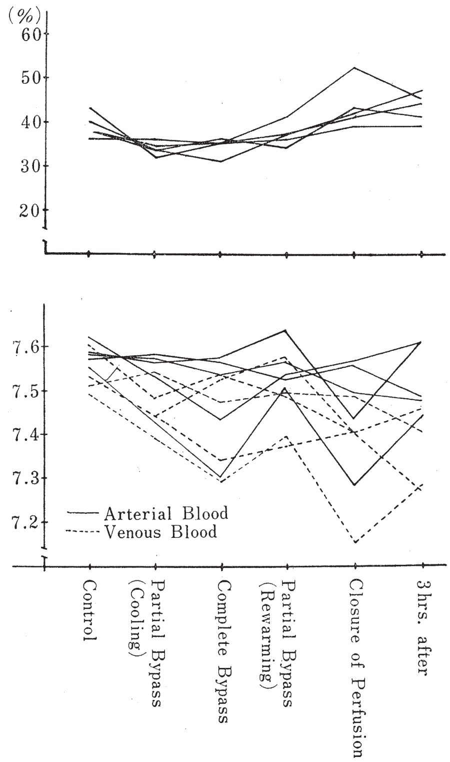

FIG. 4. Hematocrit and pH.

Blood pH, hematocrits, blood platerets, pCO_2 and oxygen consumption were measured immediately before perfusion, at various intervals during perfusion, during chest closure and after operation. Fully description about those data will be presented elsewhere.

The changes of hematocrits and pH are shown in Figure 4. It is apparently recongnized from the data that the blood was not diluted remarkably in perfusing period and the original state was restored postoperatively. The heparinised blood primed in the apparatus was 1 000 ml in every case. It is expected to increase the priming volume of 5 per cent dextrose in water replacing rather large volume of heparinised blood.

As the field of open heart surgery grows, more and more donor blood is generally required for extra-corporeal perfusion. The cost of collection and storage of donor blood on large amount is very expensive.

When blood expenditure is kept to a minimum the program becomes practical and feasible.

The apparatus devised in our clinic must be minimized in its priming capacity.

CONCLUSION

1) A new type of hypothermic low flow perfusion apparatus was devised in our clinic.

2) The apparatus consists of two heat exchangers and a disc-oxygenator.

3) It was applied for five cases of congenital heart diseases and all cases were repaired successfully.

4) It is aimed as a next plan to minimize the volume of heparinised blood by adapting the apparatus smaller in its capacity.

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REFERENCES

1. Kato, S. *J. Jap. Assoc. Thoracic Surgery* **7**: 1201, 1958 (in Japanese).
2. Fukukei, I., Y. Iyomasa and S. Kato. *Arch. Surg.* **85**: 371, 1962.
3. Zuhdi, N., B. McCollough, J. Carey and C. Krieger. *J. Int. Coll. Surg.* **35**: No. 3, 1961.
4. Zuhdi, N. *et al.* *J. Thor. Card. vasc. Surg.* **39**: 629, 1961.
5. Zuhdi, N. *et al.* *Arch. Surg.* **82**: 320, 1961.
6. Zuhdi, N. *et al.* *J. Okl. Med. Ass.*, July, 514, 1960.
7. Zuhdi, N. *et al.* *J. Okl. Med. Ass.*, October, 671, 1959.
8. Drew, C. E., G. Keen and D. B. Benazon. *Lancet* **1**: 745, 1959.
9. Drew, C. E. and I. M. Anderson. *Lancet* **1**: 748, 1959.
10. Gollan, F. *Physiology of Cardiac Surgery*. Illinois: Charles C. Thomas, 1959.
11. Brown, I. W., W. W. Smith and W. O. Emmons. *Surgery*. **44**: 372, 1958.
12. Spencer, E. C. and H. T. Bahnson. *Circulation* **26**: 292, 1962.