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Experimental and Clinical Investigation of Closed Circuit Extracorporeal Circulation for Open Heart Surgery in Infants

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Introduction

In 1953, GIBBON and his associates[11)16)18)30)] reported the first successful case of open heart surgery using a heart-lung (H-L) bypass. Subsequent improvements in the H-L bypass technique and surgical procedures[22)28)] reduced operative mortality[42)] of open heart surgery to a level similar to other major surgical procedures. None the less, in infants of less than 7 to 8 kg of body weight, open heart surgery is more often carried out under profound hypothermia with induced circulatory arrest[4)24)38)] rather than by normothermic extracorporeal circulation. Many surgeons prefer the former chiefly because the problems in control of circulating blood volume and decreased operative field are reduced, especially in neonates and infants, as compared to the latter. Open heart surgery under profound hypothermia, however, has to be completed within about an hour, and the profound hypothermia which is markedly unphysiologic has various pathophysiological problems yet to be solved[6)7)14)29)36)39)].

Difficulty in the control of the circulating blood volume in H-L bypass[15)31)] can be avoided by use of a closed circuit system rather than an open one[8)]. We have developed a new closed circuit extracorporeal circulation which maintains the circulating blood volume. The circuit includes an auxiliary pump which is controlled by electric signals induced from the central venous pressure (CVP) through an electronic control unit.

The results of the experiment and its clinical application in an infant undergoing open heart surgery will be discussed in this paper.

Materials and Methods

A closed circuit extracorporeal circulation system was employed in this study since maintenance of the total circulating blood volume in experimental animals using an open circuit extracorporeal circulation system is difficult.

Continuous monitoring of the circulating blood volume is technically inapplicable. Instead,

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the CVP was employed as a practical approximation of the volume.

A diagram of the closed circuit extracorporeal circulation system which is applied to a dog is shown in Fig. 1. The venous blood was drained through catheters inserted in the superior

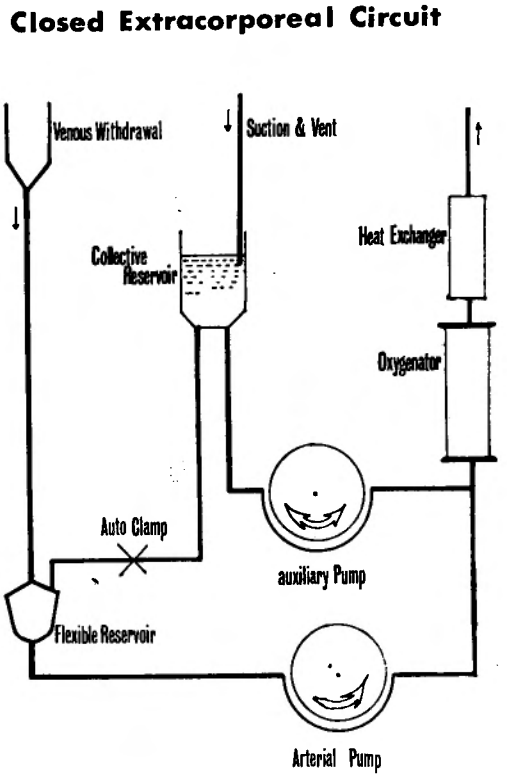

Fig. 1

and inferior vena cava by gravity into a flexible reservoir 60 cm below from the right atrial level[27]. The blood was then pumped through a membrane oxygenator and a heat exchanger back into the femoral artery. To maintain the CVP at an optimal level, an auxiliary pump circuit from a collective reservoir was arranged to bypass the arterial pump circuit.

Constant and stable venous drainage is especially important in the closed circuit circulation. Slight dislodgement of the catheters can easily cause a decrease or even stoppage of the drainage. In an ordinary closed circuit without an auxiliary pump circuit, disturbance to the drainage results in evacuation of the blood in the flexible reservoir within about 20 seconds and arterial supply to the experimental animal has to be stopped.

The bypass circuit has an automatically controlled clamp which is activated by an electric sensor[9] that detects the blood volume in the flexible reservoir. When the blood volume in the flexible reservoir is decreased, the clamp opens automatically, the blood in the collective reservoir is transfered into the flexible reservoir and the blood volume in the flexible reservoir is maintained as much as it can keep.

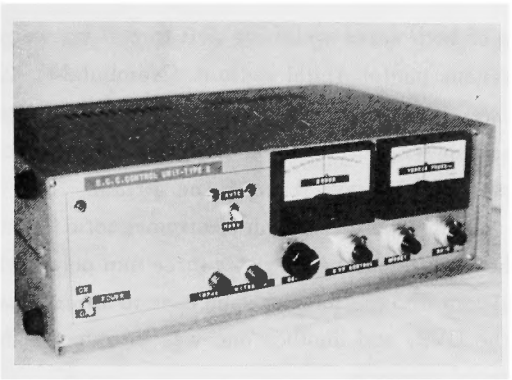

Fig. 2

The auxiliary pump has a control unit (Fig. 2) for maintenance of the CVP. The pressure level is introduced into the control unit through a polyethylene tube 3 mm in diameter. A strain gauge transducer in the control unit changes the pressure to an electric signal, which is introduced into a differential amplifier. The desired level for the CVP has been programed into the control unit as reference voltage and the unit detects the difference between the reference and the input (Fig. 3). When a positive difference is detected (or

Functional Diagram of Control Unit

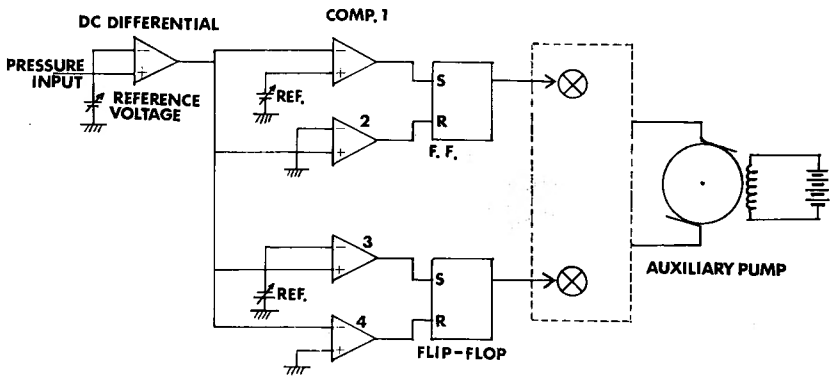

Fig. 3

the CVP is elevated), the control unit activates the auxiliary pump to rotate in a direction so that a part of the arterial pump output is removed to the collective reservoir. When the difference is negative (or the CVP is lowered), the auxiliary pump is driven in the reverse direction and adds to the arterial pump output. In either case, the auxiliary pump is worked off as the CVP resumes a given level and the difference is no longer detectable. As a result, the CVP is maintained at the desired level programed into the control unit as reference voltage.

Adult mongrel dogs of both sexes weighing 5.0 to 8.0 kg were used. The dogs were anesthetized with intravenous pentobarbital sodium (Nembutal®) 25 mg/kg and controlled respiration on room air was instituted by use of a Harvard respirator. Through a bilateral thoracotomy, the right atrium was reached and a pair of drainage catheters were introduced into the superior and inferior vena cava through the atrium. The catheters were connected to a 5/8 inch Tygon tube interposed with an electromagnetic flowmeter probe. An arterial cannula was placed in the right femoral artery. A three mm polyethylene tube was introduced through the right femoral vein into the inferior vena cava to approximately the level of the renal veins so as to monitor the CVP, and another one was introduced through the left femoral artery to minitor the arterial pressure.

Through a laparotomy the portal vein was reached and a polyethylene tube was inserted to monitor the portal venous pressure. The external jugular vein was also cannulated to monitor the cerebral venous pressure. Two dogs were exsanguinated as blood donors and the priming blood was diluted with 5% glucose and Ringer's lactate solution to yield hematocrit values of 24 to 30%. A Travenol heat exchanger was adjusted to maintain the temperature between 34 and 36°C. A Kolobow membrane artificial lung was used because it tolerated the high arterial pressure produced in our closed circuit. The extracorporeal circulation was started as partial perfusion until the desired CVP was reached and a stable arterial pump output of 100 ml/kg/min was obtained[48]. It then was switched to total perfusion[12].

Initial doses of heparin were 3 mg/kg, and activated coagulation time was periodically measured during the experiment[23)25)32)33)34)35)]. When it became 300 seconds or less, an additional 1 mg/kg was given into the circuit.

The perfusion was maintained for about three hours. Oxygen consumption, venous drainage ratio between the inferior and superior vena cava, cerebral venous pressure, portal venous pressure and total peripheral resistance were measured throughout the course of the experiment, and energy charges of the ATP-ADP-AMP system in heart muscle, liver and kidney tissues were also examined at the end of the experiment.

Results

1. *Determination of the Optimal Venous Pressure*

A closed circuit extracorporeal circulation requires adequate venous drainage to maintain the constant arterial pump output. Correlation between the CVP and the venous drainage was studied as a preliminary experiment. As shown in Fig. 4, a good correlation was observed between these two parameters. Arterial pump output of one hundred ml/kg/min, which in the closed circuit should be equal to the venous return, was obtained when the CVP was 5 cmH_2O or higher. With a safety margin, 6 cmH_2O of the CVP or higher was employed throughout the rest of the experiment.

2. *Determination of the Optimal Auxiliary Pump Output*

The response of the control unit to the CVP was shown in Fig. 5. In this experiment,

output of the arterial pump was 100 ml/kg/min, auxiliary pump output was 25% of the

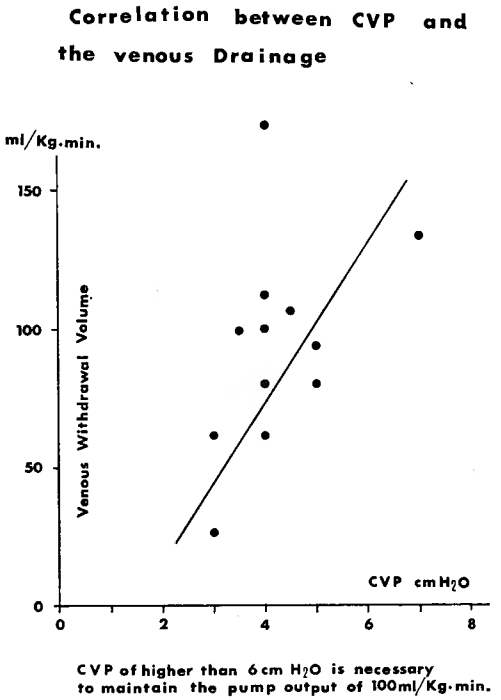

Fig. 4

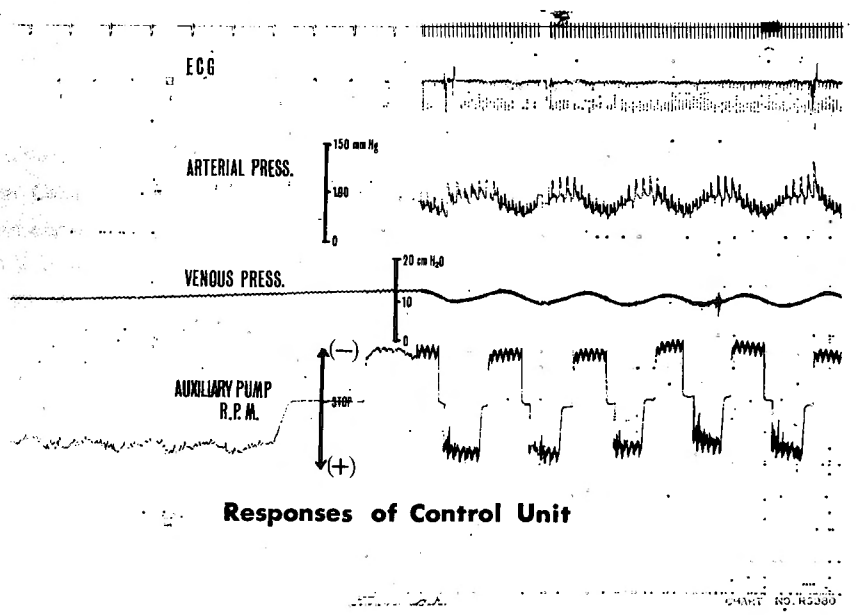

Fig. 5

arterial pump output and reference voltage was equivalent to 10 cmH_2O of the CVP. The control unit yielded a good response to the changes in the CVP as shown on the graph.

However, continued fluctuation in the CVP suggests excessive exsanguination and infusion due to high output of the auxiliary pump. The output of the auxiliary pump was reduced to 10% of the arterial pump output in a subsequent run. As shown in Fig. 6, a more stable

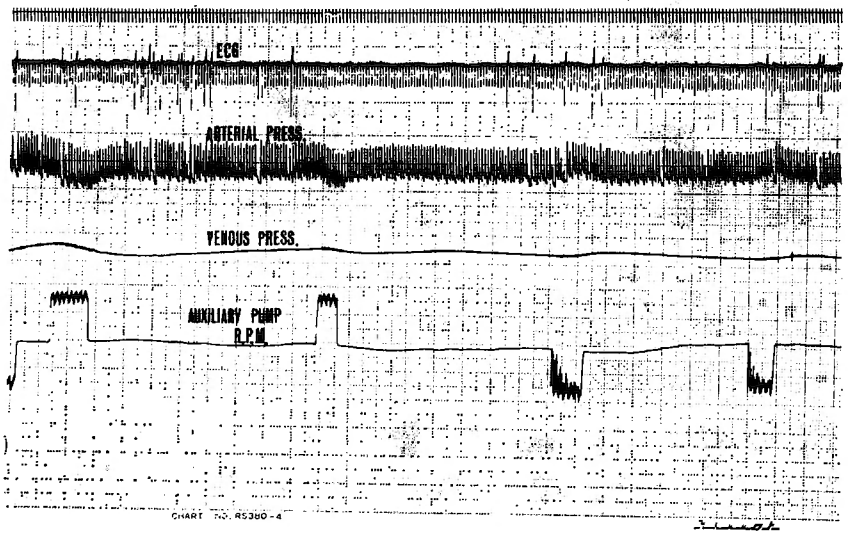

Fig. 6

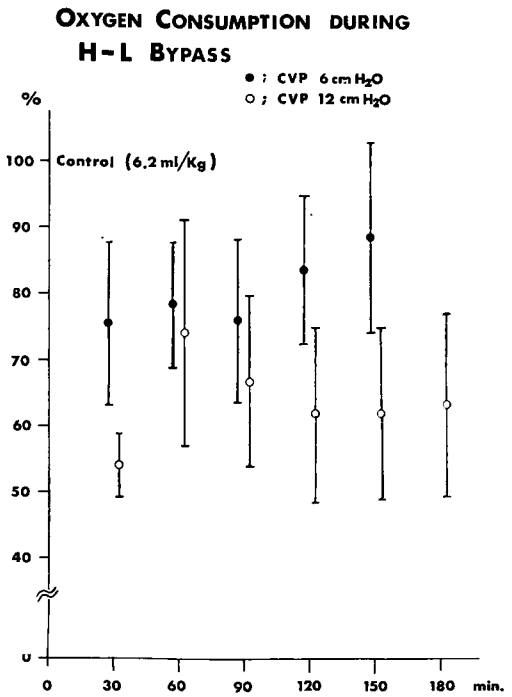

Fig. 7

Table 1 Oxygen consumption during H-L bypass

case	30	60	90	120	150	180min.
CVP; 6cmH_2O						
1)	98	92	95	102	114	
2)	80	85	90	72	102	
3)	67	63	60	69	80	
4)	69	69	63	84	85	
5)	58	85	69	80	89	
6)	69	79	72	90	94	
7)	80	75	79	94	72	
8)	83	80	80	78	73	
Mean	75.5	78.5	76.0	83.6	88.6	
±S.D.	±12.3	±9.4	±12.4	±11.2	±14.4	
CVP; 12cmH_2O						
1)	59	103	90	85	88	92
2)	62	85	82	62	62	64
3)	48	83	65	63	60	60
4)	49	84	74	80	76	78
5)	54	61	62	45	50	52
6)	56	63	60	49	49	51
7)	58	62	49	51	51	55
8)	52	59	58	60	62	58
9)	50	68	60	62	59	58
Mean	54.2	74.2	66.7	61.9	61.9	63.1
±S.D.	±4.9	±15.2	±12.9	±13.4	±12.8	±13.5
Student's t-test	$p<0.01$	$p>0.05$	$p>0.05$	$p<0.05$	$p<0.05$	

All p values were calculated with the Student's t-test paired experiment at each time of H-L bypass.

CVP was obtained in this set-up, which became a routine in this study.

3. *Oxygen Consumption under Different CVP*

Oxygen consumption was obtained in two groups of dogs, in which the CVP settings were 12 cmH_2O and 6cmH_2O respectively. The oxygen consumption[1] was calculated by Fick's principle[21)26)37)43)] from arterial and venous blood oxygen saturation and arterial pump output[5)]. Oxygen consumption prior to the extracorporeal circulation was measured by Scholander's method from expiratory gas analysis and was used as a control value (Fig. 7, Table 1, 100% or $\dot{V}o_2/kg = 6.2 \pm 0.2$ ml/kg).

In the higher CVP group, the initial drop in oxygen consumption was statistically significant ($p<0.01$) and remained at a similar level through the 3 hour period of the experiment. In the lower CVP group, oxygen consumption increased ($p<0.05$) after 2 hours under the extracorporeal circulation.

4. *Venous Drainage Ratio between the Superior and Inferior Vena Cava*

Venous drainage from the superior and inferior vena cava was monitored with

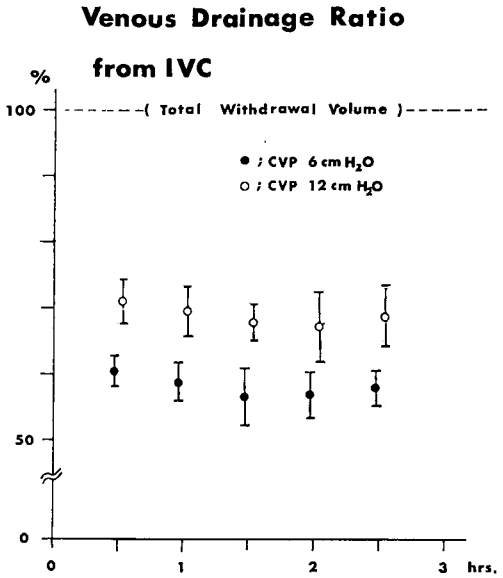

Fig. 8

Table 2 The percentage of the drainage volume from the inferior vena cava to the entire venous drainage

case	30	60	90	120	150	180min.
CVP; 6cmH_2O						
1)	63	60	58	55	58	
2)	58	54	48	51	54	
3)	57	59	58	58	57	
4)	62	62	58	60	62	
5)	60	59	58	60	58	
6)	62	59	60	58	59	
Mean	60.3	58.8	56.7	57.0	58.0	
± S. D.	±2.4	±2.6	±4.3	±3.5	±2.6	
CVP; 12cmH_2O						
1)	74	72	71	71	74	
2)	67	62	64	56	60	
3)	75	72	68	72	70	
4)	68	70	70	68	70	
5)	70	71	69	68	68	
6)	72	71	65	68	70	
mean	71.0	69.7	67.8	67.2	68.7	
± S. D.	±3.2	±3.8	±2.8	±5.7	±4.7	
Student's t-test	$p<0.01$	$p<0.01$	$p<0.01$	$p<0.01$	$p<0.01$	

All p values were calculated with the Student's t-test paired experiment at each time of H-L bypass.

electromagnetic flowmeters installed in drainage cannulae. Fig. 8 illustrates the percentage of the drainage volume from the inferior vena cava to the entire venous drainage (Table 2). The lower CVP group (6 cmH_2O) yielded a decrease in the ratio or an increase in the venous return from the superior vena cava compared to the higher CVP group (12 cmH_2O) throughout the course of the experiment ($p<0.01$).

5. *Cerebral Venous Pressure*

A catheter was inserted cephalad through the external jugular vein of the dogs in 4 different CVP ranges; 1.5-5, 5-7, 7-9 and 10-15 cmH_2O respectively. As shown in Fig. 9, the average cerebral venous pressure before the extracorporeal circulation was 17.2 ± 1.4 cmH_2O (Table 3).

Table 3 Cerebral venous pressure during H-L bypass

case	control	30	60	90	120	150	180min.
CVP; 1.5−5cmH_2O							
1)	17	22	24	25	25	24	23
2)	14	24	23	24	25	24	23
Mean		23	23.5	24.5	25	24	23
± S. D.		±1.4	±0.7	±0.7	0	0	0
CVP; 5−7cmH_2O							
1)	19.5	24	23	23	22	21	21
2)	17	22	24	22	21	20	20
3)	19	25	23	21	21	20	20
4)	15	20	19	19	20	19	18
5)	17.5	21	20	20	19	19	18
Mean		22.4	21.8	21	20.6	19.8	19.4
± S. D.		±2.1	±2.2	±1.6	±1.1	±0.8	±1.3
CVP; 7−9cmH_2O							
1)	18	19	19	18	17	16	16
2)	17	20	19	16	18	17	16
3)	18	16	16	16	18	18	18
4)	16	16	15	13	15	17	17
Mean		17.8	17.3	15.8	17	17	16.8
± S. D.		±2.1	±2.1	±2.1	±1.4	±0.8	±1.0
CVP; 10−15cmH_2O							
1)	7	18	20	21	20	23	20
2)	18	15	16	14	12	12	13
3)	18	16	15	18	16	15	13
4)	17	15	10	14	16	15	15
Mean		16	15.3	16.8	16	16.3	15.3
± S. D.		±1.4	±4.1	±3.4	±3.3	±4.7	±3.3
Mean	*17.2						
± S. D.	±1.4						

*Mean ± S.D. of control values of all cases

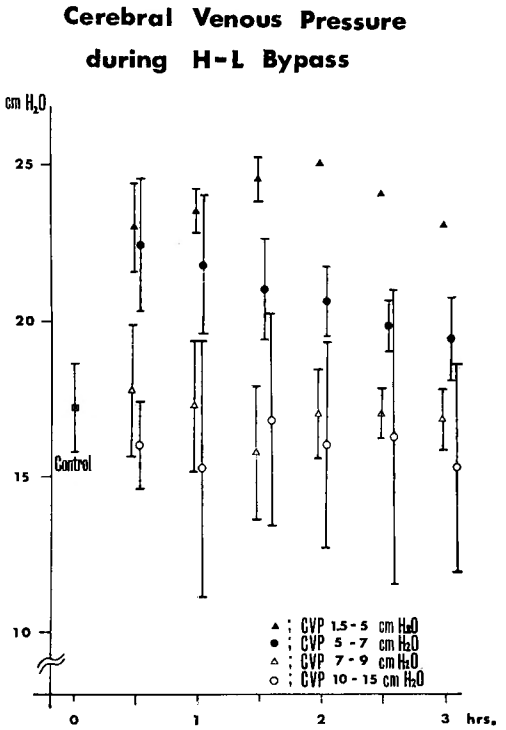
Cerebral Venous Pressure
during H-L Bypass
cm H2O
25
20
15
10
Control
CVP 1.5-5 cm H2O
CVP 5-7 cm H2O
CVP 7-9 cm H2O
CVP 10-15 cm H2O
0
1
2
3 hrs.

Fig. 9

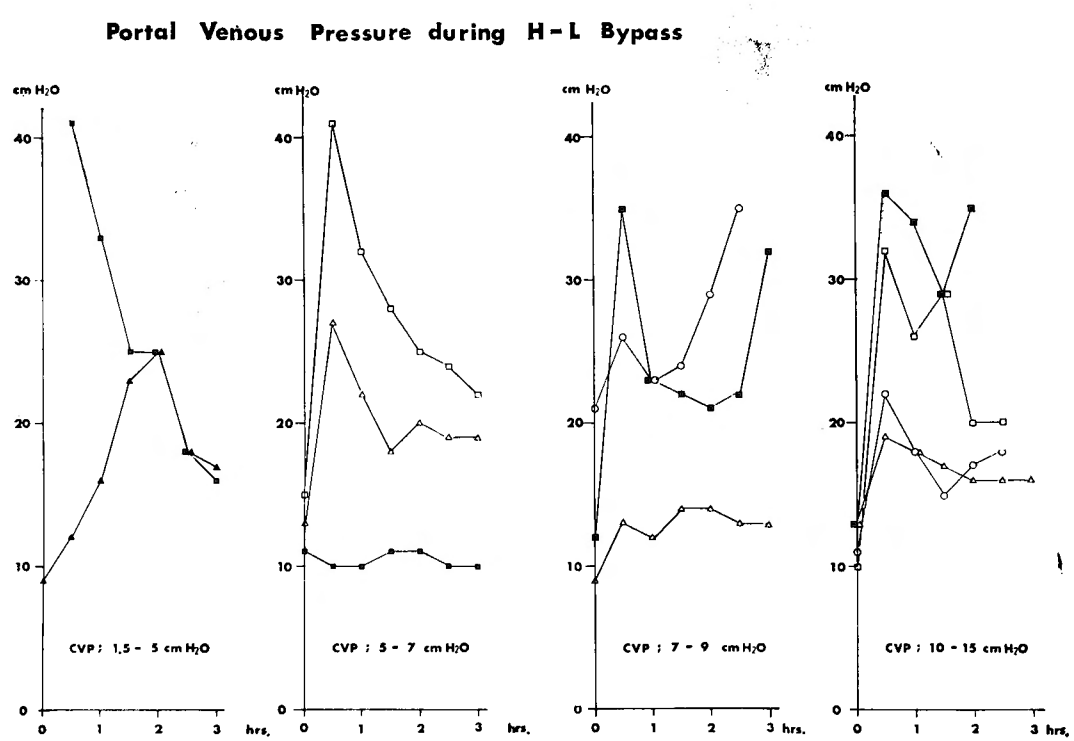
Portal Venous Pressure during H-L Bypass
cm H2O
40
30
20
10
0
CVP ; 1.5 - 5 cm H2O
CVP ; 5 - 7 cm H2O
CVP ; 7 - 9 cm H2O
CVP ; 10 - 15 cm H2O
0
1
2
3 hrs.

Fig. 10

Table 4 Portal venous pressure during H-L bypass

case	control	30	60	90	120	150	180min.
CVP; 1.5−5cmH_2O							
1)		41	33	25	25	18	16
2)	9	12	16	23	25	18	17
Mean		26.5	24.5	24	25	18	16.5
± S. D.		±20.5	±12.0	±1.4	0	0	±0.7
CVP; 5−7cmH_2O							
1)	15	41	32	28	25	24	22
2)	13	27	22	18	20	19	19
3)	11	10	10	11	11	10	10
Mean		26	21.3	19	18.7	17.7	17
± S. D.		±15.5	±11.0	±8.5	±7.1	±7.1	±6.2
CVP; 7−9cmH_2O							
1)	12	35	23	22	21	22	32
2)	21	26	23	24	29	35	
3)	9	13	12	14	14	13	13
Mean		24.7	19.3	20	21.3	23.3	22.5
± S. D.		±11.1	±6.4	±5.3	±7.5	±11.1	±13.5
CVP; 10−15cmH_2O							
1)	13	36	34	29	35		
2)	10	32	26	29	20	20	
3)	11	22	18	15	17	18	
4)	13	19	18	17	16	16	16
Mean		27.3	24	22.5	22	18	
± S. D.		±8.1	±7.7	±7.5	±8.8	±2.0	
Mean	*12.5						
± S. D.	±3.4						

* Mean ± S. D. control values of all cases

During the experiment, the cerebral venous pressure had an inclination to rise higher in the groups with lower CVP than in the groups with higher CVP, but it was not much affected by the duration of the bypass.

6. *Portal Venous Pressure*

Portal venous pressure was measured in dogs with the same CVP ranges as in the previous experiment. As shown in Table 4, the average portal pressure before the bypass was 12.5 ± 3.4 cmH_2O. In some cases of any groups, the pressure was found to peak at 45-50 cmH_2O and caused an apparent congestion in the portal system (Fig. 10).

7. *Energy Charge of the ATP-ADP-AMP System*

Energy charges[2)3)10)] calculated from the formula ; $\frac{(ATP+\frac{1}{2}ADP)}{(ATP+ADP+AMP)}$ were determined of the heart muscle, the liver and kidney tissures following 3 hours of extracorporeal circulation

with lower (7 cmH_2O) and higher (14 cmH_2O) central venous pressures (Table 5). As shown in Fig. 11, in heart muscle tissures, the energy charges are little affected by the bypass of either modes as compared to pre-circulation control values. A decrease in energy charge is dominant in the liver and kidney tissures after the bypass, the decrease being larger in the higher CVP group than in the lower one ($p<0.005$).

8. *Changes in the Total Peripheral Resistance (TPR)*

The ratio of the TPR[41] during the extracorporeal circulation is shown in Table 6. The TPR is indicated by $\frac{\text{(mean arterial pressure)} - \text{(central venous pressure)}}{\text{(arterial pump output)}}$ and is shown in Fig. 12 as percentage to pre-bypass value (6.1 mmHg·sec/ml). A CVP of 7-9 cmH_2O yielded more constant TPR values as compared to the CVP of 10-15 cmH_2O, which showed a larger decline and fluctuation.

Clinical Experience

A two-year-old male with VSD (infracristal) + pulmonary hypertension weighing 6.5 kg underwent open heart surgery under closed circuit extracorporeal circulation described in this paper. The circuit was primed with routine ACD-blood and low molecular weight

Table 5 Energy charge of the ATP-ADP-AMP system after 3 hours H-L bypass

case	control	CVP; 7cmH_2O	CVP; 14cmH_2O	Student's t-test
A) HEART				
1)	0.930	0.929	0.924	
2)	0.925	0.922	0.920	
3)	0.929	0.926	0.920	
4)	0.926	0.924	0.918	
Mean	0.928	0.925	0.921	$p>0.05$
± S. D.	±0.0024	±0.0030	±0.0025	
B) LIVER				
1)	0.870	0.837	0.807	
2)	0.880	0.830	0.814	
3)	0.865	0.832	0.808	
4)	0.875	0.840	0.804	
Mean	0.873	0.835	0.808	$p<0.005$
± S. D.	±0.0065	±0.0046	±0.0042	
C) KIDNEY				
1)	0.883	0.830	0.794	
2)	0.890	0.840	0.801	
3)	0.879	0.835	0.792	
Mean	0.884	0.835	0.796	$p<0.005$
± S. D.	±0.0056	±0.0050	±0.0047	

All p values refer to the lower CVP group vs. the higher CVP group.

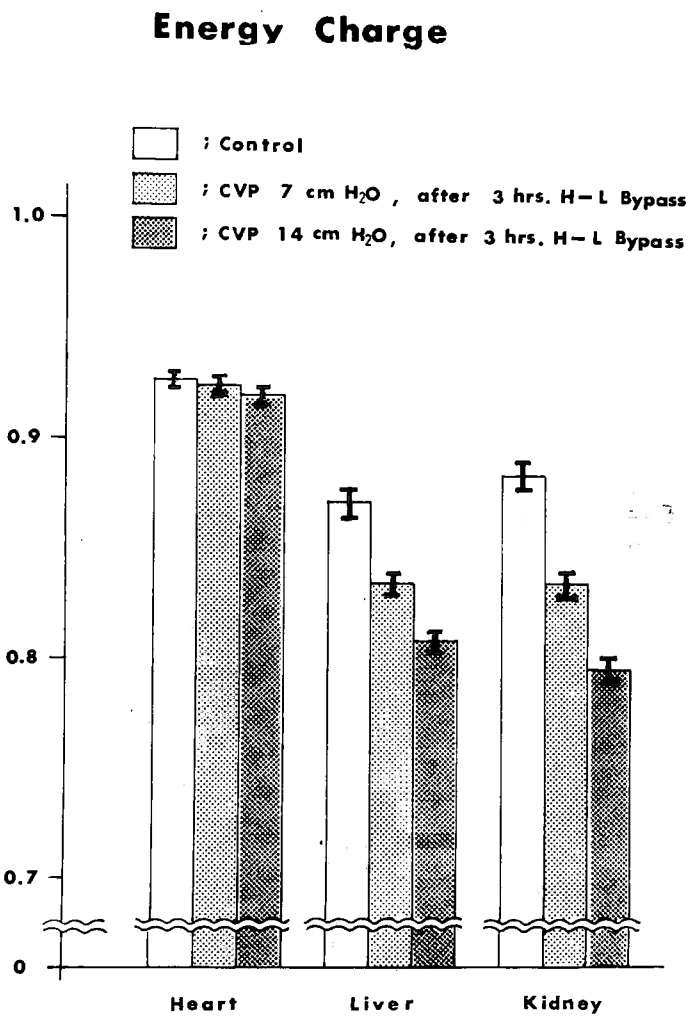

Fig. 11

dextran. The effective priming volume for the extracorporeal circulation, the collective reservoir excluded, was approximately 800 ml (Fig. 13). Arterial pump output was 150 ml/kg /min the auxiliary pump output was 20 ml/kg/min and the CVP was maintained at 7-9 cmH_2O during the bypass. Manual increase of the auxiliary pump output was occasionally required as was suction from the operative field and the intracardiac cavity increased during the surgery. Otherwise, the extracorporeal circulation was beautifully controlled with the automatic control unit mechanism. The H-L bypass lasted for as long as 70 minutes and the patient left the operating room in good condition.

Discussion

Extracorporeal circulation for open heart surgery in infants weighing less than 7 to 8 kg

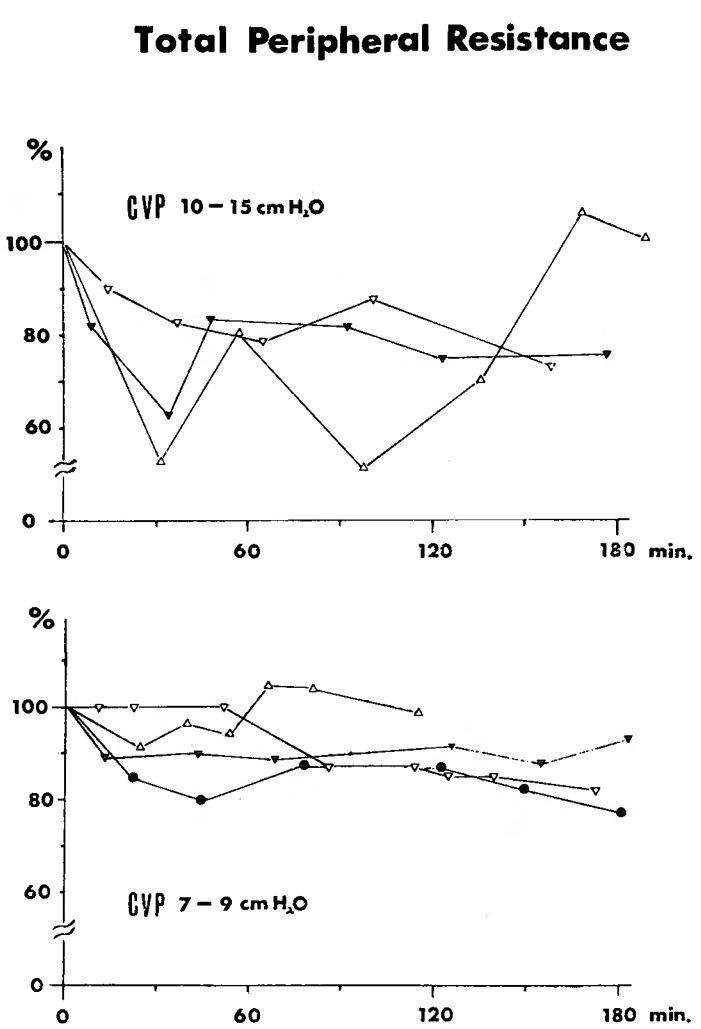

Fig. 12

is not popularly employed due to a decreased operative field and difficulty in controlling the circulating blood volume[45].

In 1974, SENNING and his co-workers[46] reported on a closed circuit extracorporeal circulation. The circuit employed in the report involved feed-back of the pressure of the venous drainage tube into the arterial pump output. In this system, changes in the pump output directly affects the drainage tube pressure, which again is fed back to the pump, and results in abrupt changes of the venous tube pressure over the area the system can potentially control. Senning's system was partially reproduced in our preliminary experiments by pumping out venous blood and +20 to −60 mmHg of drainage tube pressure deviation was frequently disclosed. When a roller pump was employed for venous drainage, the wedged pump head sometimes built up a venous pressure as high as 50 mmHg which was inadequate

Table 6 Total peripheral resistance

case	control	30	60	90	120	150	180min
CVP; 7−9cmH_2O	%						
1)	100	100	96	87	85	84	82
2)	100	93	99	102	99		
3)	100	83	83	87	87	82	78
4)	100	89	89	90	91	88	93
Mean		91.3	91.8	91.5	90.5	84.7	84.3
± S. D.		±7.1	±7.2	±7.1	±6.2	±3.1	±7.8
CVP; 10−15cmH_2O							
1)	100	83	79	85	83	75	
2)	100	53	79	56	62	85	102
3)	100	66	83	81	75	75	75
Mean		67.3	80.3	74	73.3	78.3	88.5
± S. D.		±15.0	±2.3	±15.7	±10.6	±5.8	±19.1

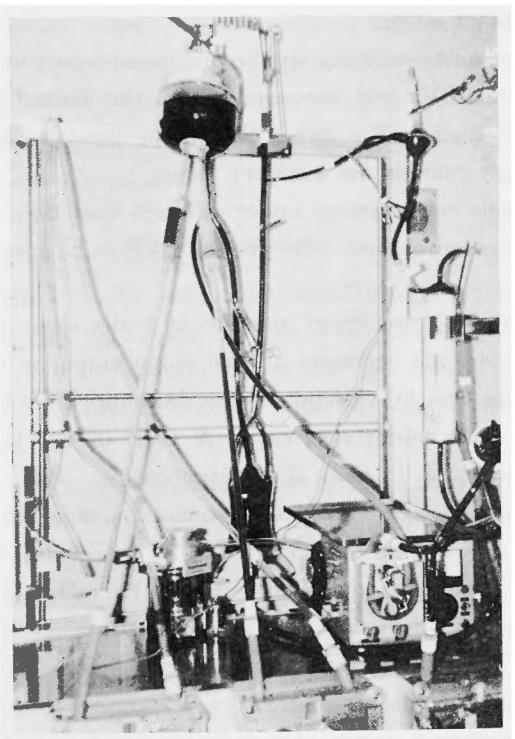

Fig. 13

for controlled perfusion.

The basic design of our circuit consisted, from the experiences, of gravity drainage of venous blood into a closed-circuit flexible reservoir instead of pump drainage.

Control of circulating blood volume constitutes the principal consideration in our extracor-

poreal circulation circuit. Constant monitoring of the circulating blood volume and its direct feed-back to the pump output should be theoretically ideal, but the monitoring is still not feasible for the currently available technology.

The CVP was substituted for the circulating blood volume as a most practical approximation[40]. Mean systemic pressure (Pms)[19] advocated by GUYTON[17)20)] indicates that circulating blood volume is a direct function of the CVP, providing that the TPR is not affected by vasomotor reflex and that cardiac output remains constant.

In extracorporeal circulation, pump output represents cardiac output and the output can be controlled at any desired level. If TPR changes could be minimized, the CVP might be used as a good indicator of the circulating blood volume in an extracorporeal circulation.

In an open circuit system, however, the priming blood volume in the circuit would be too large to allow adequate control of the circulating blood volume.

We have employed a closed circuit system with an auxiliary pump circuit which includes a collective reservoir for the return of blood sucked from the operative field and the vent. Use of this additional circuit helps mantain both circulating blood volume and priming volume in the entire circuit stable.

An electronic control unit constitutes another important aspect in our circulation system[47]. The unit senses the actual CVP and compares it with the desired pressure programed into the unit as a reference voltage. The unit picks up any possible difference between the two pressures and accordingly controls the auxiliary pump.

The circulation system was operated under different conditions and various parameters were studied to determine an optimal value for the CVP to be programed into the control unit.

The CVP below 6 cmH_2O was found to result in a decrease of venous drainage and was insufficient to maintain the necessary arterial pump output in our circuit. The insufficiency became apparent first by vibration of the draining tubes and then by a complete collapse of the inferior and superior vana cava. A CVP of not less than 6 cmH_2O was programed into the control unit in most of the experiments.

Measurements of oxygen consumption and venous drainage ratio between the superior and inferior vena cava showed that the CVP setting in the control unit at 6 cmH_2O yielded a better extracorporeal circulation than did the setting at 12 cmH_2O. Cerebral venous pressure monitoring indicated the least deviation from pre-operative values when the CVP was maintained at 7-9 cmH_2O. The cerebral venous pressure became reciprocally higher as the CVP was set lower. Cerebral circulation is controlled as a terminal consequence of information regarding systemic physiological changes for maintenance of the most stable homeostasis in the entire living organism[44].

Portal venous pressure increased in some cases regardless of the CVP settings. Portal bed pooling observed in some cases may indicate the hazard of inadvertent obstructions of the hepatic venous outflow especially in smaller sized animals.

Energy charge of adenine nucleotide studies also indicated that 7 cmH_2O CVP is more

optimal for the extracorporeal circulation than higher pressure levels.

TPR deviation was also minimal, being 80-105% of the control value, with the CVP at 7 cmH_2O. Conclusively, the CVP setting at 7-9 cmH_2O gave the most stable extracorporeal circulation with the minimum TPR changes in our closed circuit system.

The same CVP setting also offered the least amount of physiological deterioration as assessed by energy charges, cerebral venous pressure, oxygen consumption and venous drainage ratio between the superior and inferior vena cava.

The priming volume which was already small in our system, could be still reduced by improvement of the circuit. The oxygenator and other components were chosen from commercially available models and the use of specially desired ones should reduce the priming volume at least by 100 ml.

Use of forced vacuum drainage which is applied externally to the flexible reservoir is now under development. This will further reduce the priming volume and will also make access of the entire circulatory system to the immediate neighborhood of the operating table possible.

Application of our closed circuit extracorporeal circulation system to an assist circulation system[13] at a lower flow rate is now under consideration and seems safer than the presently available circuit.

We are now trying to get the circuit improved in its safety and reliability and are going to apply it further to more clinical cases.

Summary

1) Difficulty in the control of the circulating blood volume in extracorporeal circulation in infants and neonates could be avoided by use of our closed circuit.

2) We monitored the central venous pressure for the control of the circulating blood volume which could not have been technically done to monitor and to immediately reflect its alteration.

3) The closed circuit system has a control unit by monitoring the central venous pressure which activates an auxiliary pump in order to maintain the central venous pressure at a desired level.

4) Our reseach for determination of optimal central venous pressure programed into the control unit in our closed circuit system was carried out, and the optimal pressure was found to be 7-9 cmH_2O on the physiological and biochemical studies.

5) With this system, clinical application to one patient was performed safely, and further efforts to improve the circuit and to apply it to more clinical cases are now being undertaken.

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References

1) Andersen MN, Senning A: Studies in oxygen consumption during extracorporeal circulation with a pump-oxygenator. Ann Surg **148**: 59-65, 1958.
2) Atkinson DE : The energy charge of adenylate pool as a regulatory parameter. Interaction with feedback modifiers. Biochemistry **7** : 4030-4034, 1968.
3) Atkinson DE and Walton GM : Adenosine triphosphate conservation in metabolic regulation. J Biol Chem **242** : 3239-3241, 1967.
4) Barrat-Boyes BG and Simpson M : Intracardiac surgery in neonates and infants using deep hypothermia with surface cooling and limited cardiopulmonary bypass. Circulation **43**: 25-30, 1971. (suppl.)
5) Bartels H, Harms H: Sauerstoffdissoziationskurven des Blutes von Säugetieren. Pflügers Arch. **268**: 334-365, 1959.
6) Bigelow WG and Lindsay WK: Hypothermia; its possible role in cardiac surgery, an investigation of factors governing survival in dogs at low body temperatures. Ann Surg **132** : 849-866, 1950.
7) Björk VO et al: Contraindications to profound hypothermia in open-heart surgery. J Thorac Cardiovasc Surg **44** : 1-13, 1962.
8) Brazhnikov EM and Mamlina VI et al : New method of complete and auxiliary extracorporeal blood circulation. Biomed Eng (NY) **8** : 73-75, 1975.
9) Clark RE, Ferguson TB et al : Experimental and clinical use of an automated perfusion system and membrane oxygenator. Suppl. II to Circulation. 49 and 50: 213-218, 1974.
10) Daitoh N et al: The effects of nonpulsatile perfusion on the renal energy metabolism (energy charge). Artificial Organs **7** : 444-447, 1978.
11) DeBakey ME, Cooley DA and et al: Aneurysm of the aorta treated by resection. JAMA **163** : 1436-1443 1957.
12) DeWall R : What constitutes adequate perfusion? J Cardiovasc Surg **16**: 458-464, 1975.
13) Dow JW and Dickson JF et al: Experimental evaluation of veno-arterial pumping, a proposed technique for circulation support. J Thorac Surg **38**: 323-331, 1960.
14) Fuhrman GJ and Fuhrman FA: Metabolism of rat heart slices, with special reference to effects of temperature and anoxia. Amer J Physiol **163**: 642-647, 1950.
15) Giannelli Jr S, Ayres SM et al: Peripheral vascular volumes and whole body hematocrit during human heart lung bypass. Circul **41**: 629-640, 1970.
16) Gibbon Jr JH and Miller BJ : An improved mechanical heart and lung apparatus. Med Clin North America **37** · 1603-1624, 1953.
17) Guyton AC: Determination of cardiac output by equating venous return curves with cardiac output response curves. Physiol Rev **35** : 123-129, 1955.
18) Gollan F and Blos P: Studies on hypothermia by mean of a pump-oxygenator. Amer J Physiol **171**: 331-340, 1952.
19) Guyton AC: Circulatory Physiology : cardiac output and its regulation. Saunders, Philaydelphia 1963 b.
20) Guyton AC and Lindsey AW et al : Venous return at various right atrial pressures and the normal venous return curve. Am J Physiol **189** : 609-615, 1957.
21) Hamilton WF and Moore JW : Studies on the circulation IV. Am J Physiol **99**: 534-551, 1932.
22) Harshbarger HG et al: Studies in extracorporeal circulation. 4. Surgical Techniques. Surg Gynecol Obstet **106**: 111-118, 1958.
23) Hattersley PG: Activated coagulation time of whole blood. JAMA **196**: 436-440, 1966.
24) Hikasa Y et al: Open heart surgery in infants with an aid of hypothermic anesthesia. Arch Jap Chir **36**: 495-508, 1967.
25) Hill JD et al : A simple method of heparin management during prolonged extracorporeal circulation. Ann Thorac Surg **17**: 129-134, 1974.
26) Kinsman JM, Moore JW, Hamilton WF and Spurling RG : Studies on the circulation I. Am J Physiol **89**: 322-330, 1929.

27) Kirby CK, Gianelli Jr S et al: Simple automatic method of blood volume control during cardiac bypass for open heart surgery. Arch Surg **78**: 193-196, 1959
28) Kuroiwa T: Clinical studies on extracorporeal circulation considerations on the perfusion data by Nagoya Model VI Pump-oxygenator. J Jap Assoc Thorac Surg **14**: 1153-1195, 1966.
29) Lee Jr WH, Krumhaar D et al: Denaturation of plasma proteins as a cause of morbidity and death after intracardiac operations. Surg. **50**: 29-39, 1961.
30) Lewis FJ and Taufic M: Closure of atrial septal defect with the aid of hypothermia; experimental accomplishments and the report of one successful case. Surgery **33**: 52-59, 1953.
31) Litwak RS, Gilson AJ et al: Alteration in blood volume during "normovolemic" total body perfusion. J Thorac Cardiovasc Surg **42**: 477-488, 1961.
32) Mattox KL et al: Use of the activated coagulation time in intraoperative heparin reversal for cardiopulmonary operations. Ann Thorac Surg **19**: 634-638, 1975.
33) Matsuda M et al: Activated coagulation time (Hemochron time) during extracorporeal circulation. Artificial Organs **6**: 93-97, 1977.
34) Matsuda M et al: Activated coagulation time under heparin therapy in surgical diseases. Arch Jap Chir **46**: 113-120, 1977.
35) Maureen HB, Wilfred MH and Brian SB: Evalution of tests used to monitor heparin therapy during extracorporeal circulation. Anesthesiol **43**: 346-353, 1975.
36) Messmer BJ et al: Psychomotor and intellectual development after deep hypothermia and circulatory arrest in early infancy. J Thorac Cardiovasc Surg **72**: 495-502, 1976.
37) Moore JW, Kinsman JM, Hamilton WF and Spurling RG: Studies on the circulation II. Am J Physiol **89**: 331-339, 1929.
38) Mori A et al: Deep hypothermia combined with cardiopulmonary bypass for cardiac surgery in neonates and infants. J Thorac Cardiovasc. Surg **64**: 422-429, 1972.
39) Okamura H et al: Experimental and clinical studies on the cardic resuscitation after long cardiac circulatory arrest under the ultrahypothermic anesthesia. Thorac Surg (Jap.) **13**: 174-180, 428-432, 705-712, 1960.
40) Herron PW, Jesseph JE et al: The effects of arterenol on blood pressure and venous return during extracorporeal circulation. Surg **44**: 398-401, 1958.
41) Read RC, Kuida H et al: Venous pressure and total peripheral resistance in the dog. Am J Physiol **192**: 609-612, 1958.
42) Sloan H, Mackenzie J et al: Open-heart surgery in infancy. J Thorac Cardiovasc Surg. **44**: 459-476, 1962.
43) Stewart GN: The pulmonary circulation time, the quantity of blood in the lungs, and the output of the heart. Am J Physiol **58**: 20-52, 1921.
44) Terrence Reidy BS, Büky B et al: Improved hemodynamics for partial extracorporeal bypass. Am Surg **40**: 680-687, 1974.
45) Turina M, Housman LB et al: An automatic cardiopulmonary bypass unit for use in infants. J Thorac Cardiovasc **63**: 263-268, 1972.
46) Turina M, Gattiker R: Total korrektur von angeborenen Herzfehlern im Säuglingsalter. Thoraxchirur **21**: 428-433, 1973.
47) Weissbach G, Emmrich K und Herbst M: Entwicklung einer automatisierten Herz-Lungen-Maschine zur Langzeit- und Säuglings-perfusion. Z Exper Chirur. **7**: 240-249, 1974.
48) Woodward K, Berman AS and Odland L: Plasma, erythrocyte and whole blood volume in the normal beagle. Am J Vet Res **29**: 1935-1941, 1968.

和文抄録

閉鎖回路を使用した乳幼児の常温下体外循環に関する研究

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乳幼児の常温下体外循環に関しては,一定の循環血液量の維持方法の困難性の問題がある.しかしながら,循環血液量を逐次知り,これを制御することは,現在のところ,なお困難であるので,中心静脈圧をこれに代わるものとして採用し,その方法を研究した.そして,これを一定に保つ為の Control Unit を作り,その作動の安全性,回路の安全性についての実験を行った.さらに,この装置に設定する"設定静脈圧"の高低につき,生理的,生化学的な考察を行い,臨床応用に供した.