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CLINICAL STUDY OF THE CEREBRAL HEMODYNAMICS DURING EXTRACORPOREAL CIRCULATION

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ABSTRACT

The cerebral circulation was studied on 40 clinical cases which underwent open heart surgery under extracorporeal circulation by the low flow rate-hypothermic-hemodilution technique, by means of Kr^{85}, opthalmoscope, blood gas and pH, and cerebral metabolism.

Cerebral blood flow decreased to 65.2 per cent of the control value after the start of extracorporeal bypass, but recovered by the later period of total perfusion, and then exceeded the control value during the rewarming and partial perfusion.

Cerebral metabolism was lowered to 37 per cent of the control value during the total perfusion, but recovered during the rewarming perfusion.

It was pointed out that the findings of the retina were useful to assess the adequacy of the cerebral hemodynamics during the bypass.

The present technique of extracorporeal circulation in this department of surgery was concluded to be adequate for the cerebral circulation.

INTRODUCTION

The development of cardiac surgery in recent years has achieved remarkable improvements in the surgical management of cardiac diseases. The idea of heart-lung machine originating from Gibbon[1] in 1937 has been developed to an entity of research subject and clinical application as the most powerful tool in open heart surgery. Extracorporeal circulation, however, is by itself a condition which induces a living body to an entirely non-physiological environment. It stands to reason that the various influences of this non-physiological environment inevitably brings about major and minor complications and sequelae[2)3)4)].

The organs of a living body respond differently to the altered physiological environment by extracorporeal circulation, and the brain has been shown to be the most susceptible of all the organs. Psychiatric symptoms after cardiac surgery, which should not be overlooked as one of the cerebral sequelae, have been brought up by many reporters. In 1959, Shieds *et al.*[5] reported on the brain symptoms in the animals after extracorporeal circulation combined with hypothermia. Blachly[6], and Egerton and Kay[7] have reported on the

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delirium after open heart surgery using cardio-pulmonary bypass. The frequency of this delirium syndrom was reported by Knox[8] and Fox *et al.*[9] to be between 1 and 19 per cent of the patients treated under cardiopulmonary bypass.

In the 1st Department of Surgery, Nagoya University School of Medicine, very few cases were encountered in which brain sequelae resulted from open heart surgery. Most of the causes were air embolism[10,11], cerebral edema, and unconsciousness associated with postoperative period of hypotension.

There were, also, cases which retarded regaining of consciousness attributable to the prolonged duration of extracorporeal circulation.

The measures to prevent the untoward cerebral effect of extracorporeal circulation are the highly desired thesis of investigation for the safe application of heart-lung machines.

Cerebral blood flow or metabolism associated with extracoporeal circulation has been studied by some authors[12,13], but very few have dealt with those during the perfusion period.

The purpose of the present study is to investigate the cerebral circulatory dynamics during extracorporeal circulation by the low flow rate-hypothermic-hemodilution technique, which is currently in use in this department.

MATERIALS AND METHODS

Fourty individuals were observed for the study of cerebral hemodynamics during open heart surgery. They consisted of 22 males and 18 females, whose ages ranged from 5 to 43 years.

Anesthesia was induced by the intravenous administration of 200 mg of thiamylal sodium, tracheal intubation was performed following the intravenous injection of succinylcholine chloride in the doses of 20 mg or 40 mg, and the ventilation of the lungs was controlled manually throughout the operation, while anesthesia was maintained by the inhalation of 50 per cent of nitrous oxide in oxygen with the addition halothane or ether at the concentration ranging from 0.5 to 2 or 1 to 5 per cent, respectively.

Extracorporeal circulation[14~17] was established using a roller-pump of De Bakey type, a small rotating disc oxygenator into which oxygen containing 2 per cent of carbon dioxide was insufflated, and a double helical heat exchanger.

The heart-lung machine was primed with 5 per cent dextrose in water as much as 30 ml per kilogram of body weight[18,19]. In addition to this, some amount of fluid consisting of 5 per cent dextrose in water in one quarter and heparinized blood in three quarters was added to complete an adequate priming if necessary. Two mg per kilogram of body weight of heparin was given intravenously prior to cannulation, and the same doses to apparatus.

Femoral arterial blood pressure was continuously recorded using a mercury

manometer, and central venous pressure was measured with a water manometer. Body temperature was regulated by the application of a circulating water blanket and a heat exchanger. Esophageal and rectal temperatures were monitored on an electric thermometer.

By a blanket and blood cooling using the heat exchanger, esophageal and rectal temperatures were lowered down to between 25°C to 30°C[19] and total bypass was established by tying up the caval tapes. When intracardiac manipulation was accomplished, rewarming was started with a blanket and assisted circulation. The caval tapes were released and partial perfusion was continued until the body temperature reached 34°C.

Arterial blood samples were drawn from an indwelling femoral arterial catheter anaerobically by means of three-way stopcocks, and from the heart-lung machine. Venous blood samples were drawn from internal jugular vein through a catheter inserted under fluoroscopy.

As a rule, arterial and venous blood samples were obtained after the induction of anesthesia, immediately after the institution of total bypass, during the later half of total bypass, during rewarming and at the end of perfusion. The samples were served for the analysis of oxygen and carbon dioxide content, pH, pCO_2, and pO_2. Oxygen and carbon dioxide content of the blood sample was determined manometrically using Van-Slyke Neill apparatus[20]. pH, pCO_2, and pO_2 of the blood sample were determined by means of Micro-Astrup apparatus[21)22)23)], and the values of base excess was read on the alignment nomogram of Siggard-Anderson[24].

Cerebral blood flow was measured by the method described by Lassen and Ingvar[25] using the clearance rate of Krypton^{85}. After the carotid artery was punctured, a catheter with the external diameter of 0.75 mm was inserted, and from 2 to 5 ml of the saline solution of Kr^{85} (average: 5 mC) was injected. Clearance curve of Kr^{85} was subsequently recorded for 10 minutes using a scintillation detector placed close to the parieto-temporal surface of the skull.

The clearance curve represents the washing out of Kr^{85} from the brain by the arterial blood containg theoretically no recirculating radioactivity. The diffusion of Kr^{85} is sufficiently rapid to maintain the equilibrium between the tissues and the venous blood leaving the same tissues. These factors of Kr^{85} signify that the clearance curve is the reflection only of blood flow[26)27)].

Cerebral blood flow (CBF) was, on the above assumption, calculated from the Lassen and Ingvar fomula[25]:

$$CBF = \frac{I_1 \cdot 0.95\,K_1 + 0.73\,I_2(K_1/K_2) \cdot 1.30\,K_2}{I_1 + 0.73\,I_2(K_1/K_2)} \times 100\ \text{ml}/100\ \text{g}/\text{min}.$$

Cerebral vascular resistance (CVR) was calculated by the formula:

$$CVR = \frac{MABP - MJBP}{CBF}\ \text{mmHg}/\text{ml}/100\ \text{g}/\text{min},$$

where MABP and MJBP represent the mean blood pressures in mmHg of the femoral artery and the internal jugular vein, respectively.

Cerebral metabolic rate for oxygen ($CMRO_2$) was calculated by the formula:

$$CMRO_2 = CBF \times (A-V)O_2 \text{ ml}/100 \text{ g/min},$$

where $(A-V)O_2$ is the arterio-venous oxygen difference in volume per cent.

Cerebral oxygen supply (CDO_2) was calculated by the formula:

$$CDO_2 = CBF \times \frac{AO_2}{100} \text{ml}/100 \text{ g/min}.$$

Cerebral oxygen uptake ratio (ERO_2) was calculaed according to the following fomula:

$$ERO_2 = \frac{CMRO_2}{CDO_2} \times 100\%.$$

Observation of the ocular fundus using an opthalmoscope was performed in 30 cases of open heart surgery. Five per cent of phenylephrine was instilled in the eyes after the induction of anesthesia to dilate the pupils. The camera used in this study was the RC Hand-held Fundus Camera (made by the Kowa Company) incorporating the function for observation of the ocular fundus such as an illumination lamp of 3 watt at 6 volt, an electric flush of 50 watt/sec with flush period of 1/500 sec, magnification at the film plane of $\times 2.4$, finder magnification ratio of $\times 7.2$, and the total magnification ratio of $\times 7.2$, with the compound focus distance of 53.08 mm.

After being processed, the film was enlarged 14 times, and was served for the measurement of diameter of the retinal blood vessels.

RESULTS

Cerebral blood flow

Table 1 gives the measured values of cerebral blood flow at each period. The preperfusion period represents the stabilized stage of anesthesia after its induction and this is used as the control period. After the start of heart-lung bypass, cerebral blood flow decreased significantly to 65.2 per cent of the control level, on the average.

Fig. 1 shows the clearance curves of Kr^{85} obtained during preperfusion and Fig. 2 shows those during initial period of total perfusion. In both of them, the same dose of Kr^{85} was injected. It is obvious that during perfusion both of the initial counting rate and the rate of clearance are lower than during the preperfusion period.

Fig. 3 represnts the actual values of cerebral blood flow. In Fig. 4 the preperfusion levels are designated as 100 per cent to facilitate comparative

TABLE 1. Cerebral blood flow during open heart surgery in 16 cases (ml/100 g/min)

case	name	age and sex	diagnosis	cerebral blood flow (m/100 g/min)				
				before perfusion	total perfusion	total perfusion	rewaming perfusion	after perfusion
1	Y.N.	45 F	A.S.D.	26.5	7.0			
2	K.O.	22 F	P.S.	34.8	13.6		58.5	31.8
3	K.I.	12 M	V.S.D.	18.1	14.2		24.8	23.8
4	M.I.	22 M	TF.	47.9	32.3			
19	Y.M.	24 M	A.I.	47.0	46.5	47.2	48.0	41.0
24	M.H.	24 F	A.S.D.	61.2	19.4	39.2	58.0	67.0
25	M.K.	14 F	T.F.	29.3	22.1	30.0	12.4	15.8
26	H.O.	6 M	T.F.	80.0	42.0	49.7	69.0	64.1
28	H.T.	8 M	T.F.	73.5	23.0	67.2	51.0	55.0
29	H.T.	33 M	M.I.	38.8	22.3	30.4	45.3	43.8
30	K.I.	30 M	A.I.	48.5	31.1	40.0	47.5	
31	H.T.	27 M	M.S.	50.0	23.3	30.6	47.5	44.5
32	N.H.	10 M	V.S.D.	40.0	46.0	50.1	64.4	90.0
33	K.K.	19 M	A.I.	37.1	67.0	51.8	56.0	59.5
39	F.I.	25 F	P.S.	33.0	27.0	43.1	47.5	43.5
40	T.M.	33 F	A.I.	42.3	24.5	32.0	31.2	28.0

A.S.D.: atrial septal defect
V.S.D.: ventricular septal defect
P.S.: pulmonary stenosis
T.F.: tetralogy of Fallot
A.I: aortic insufficiency
M.I.: mitral insufficiency
M.S.: mitral stenosis

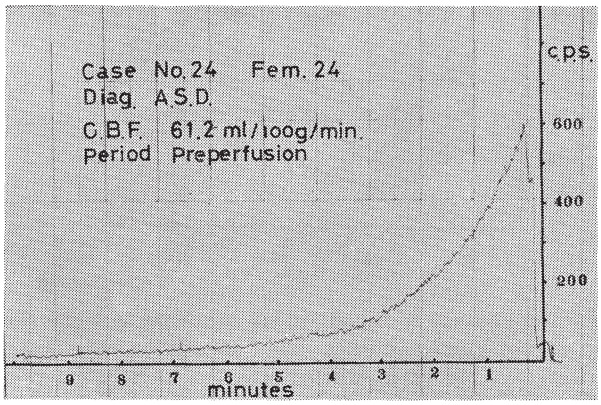


FIG. 1. Clearance curve of Kr^{85} during the preperfusion period. Gamma emission was recorded externally after the intracarotid injection of 5 mC of Kr^{85} dissolved in physiologic saline solution.

analysis of the data. Sixty minutes after the start of total bypass, the cerebral blood flow restored and averaged 95.4 per cent of the control level, although the mean arterial blood pressure remained at 50 mmHg. During rewarming, cerebral blood flow of 47.1 ml per 100 g of brain per minute was obtained, that is, the average increase of 7.3 per cent of the control level. It is also revealed that except in two subjects, cerebral blood flow returned to the preperfusion levels by the postperfusion period.

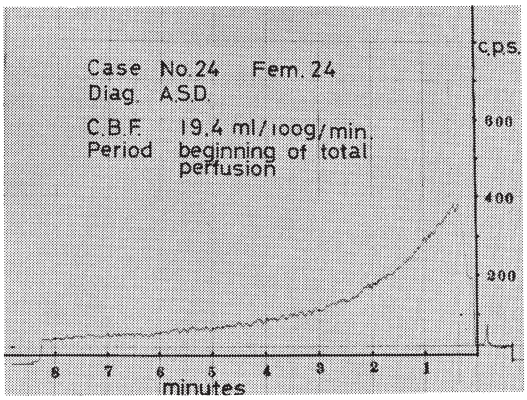


FIG. 2. Clearance curve of Kr^{85} during the beginning period of total perfusion. It is seen that the initial counting rate was lower and the rate of clearance slower than during the preperfusion period.

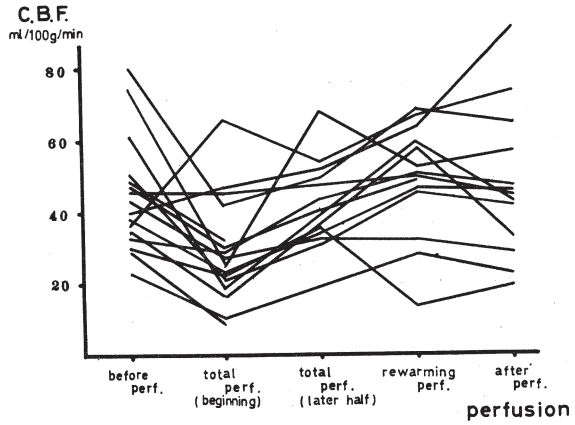


FIG. 3. The changes in actual values of cerebral blood flow during perfusion. It was decreased remarkably during the beginning period of total perfusion, but recovered gradually by the later half period of total perfusion.

Metabolism

pH: Arterial and venous blood pH showed a scatter of certain extent already in the preperfusion period. This is probably because of hypoxia due to bleeding from the operating field or hypocapnea due possibly to positive hyperventilation by the anesthetist.

Arterial blood pH during total perfusion decreased from the preperfusion range of 7.452 to 7.268 (average: 7.375) down to the range of 6.916 to 7.580 (average: 7.264).

During rewarming pH values distinctly increased to the average of 7.394

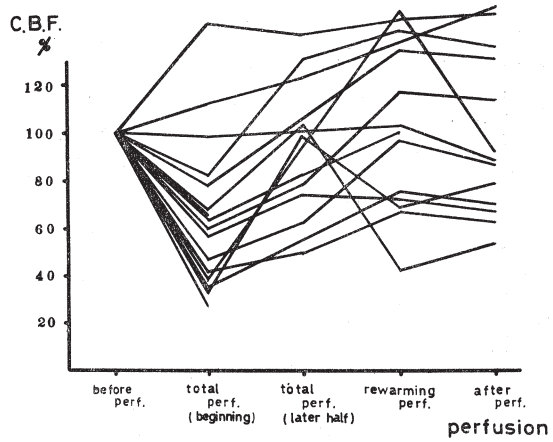


FIG. 4. The changes in cerebral blood flow. Preperfusion levels were designated as 100 per cent.

responding to the adjustment of pH by THAM, sodium bicarbonate and adequate control of ventilation.

During the postperfusion period, the arterial blood pH gradually recovered toward the preperfusion level with the range of between 7.192 and 7.521 (average: 7.350), as shown in Fig. 5.

The jugular venous blood pH followed the pattern similar to that of arterial blood pH.

pCO_2 and base excess: Low arterial pCO_2 was observed already during the preperfusion period owing probably to the positive hyperventilation by the anesthetist. The average arterial pCO_2 was 28.8 mmHg and the average venous pCO_2 was 39.9 mmHg during preperfusion period. During total perfusion, both arterial and venous pCO_2 tended to increase gradually, and their average values were 45.3 mmHg and 52.9 mmHg, respectively. During the postperfusion period, the averages of arterial and venous blood pCO_2 were 31.8 mmHg and 44.5 mmHg, respectively, as shown in Fig. 6.

Base excess values during the perfusion period fell into the average value of −7 mEq/l owing to respiratory and metabolic acidosis, but this average value increased to −4.1 mEq/l during the beginning period of total perfusion. During the later half period of total perfusion it again dropped to −6.2 mEq/l. Not detected is, however, a definite tendency of base excess because of the notable varieties among the individuals, as shown in Fig. 7.

pO_2: Arterial and venous pO_2 changed very little during the perfusion. After the perfusion, arterial pO_2 rose to the average of 268 mmHg, but venous pO_2 remained unchanged, as shown in Fig. 8.

A–V oxygen difference in the brain: The arterio-venous oxygen difference in the brain is shown in Fig. 9. During total perfusion, the arterio-venous

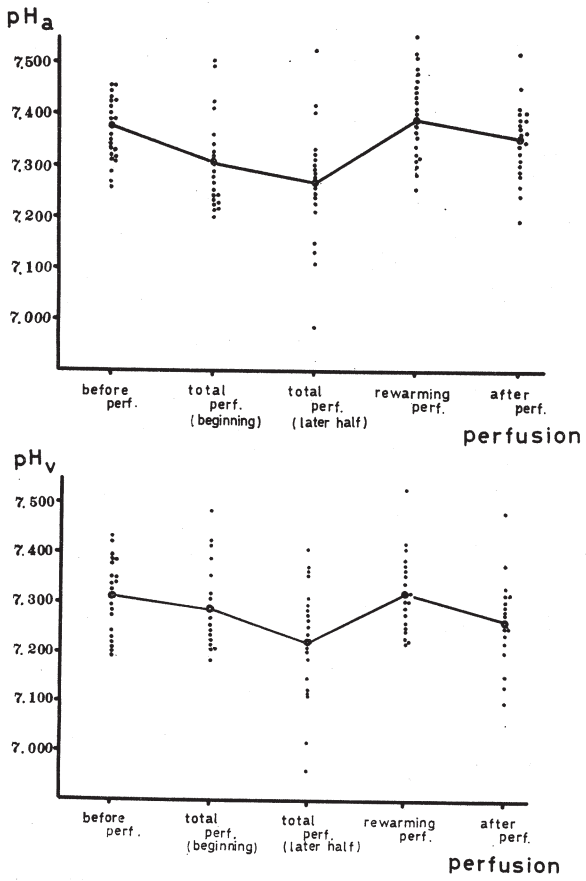


FIG. 5. The changes in arterial and venous blood pH during perfusion. During rewarming, both pH values distinctly increased responding to the ajustment of pH by THAM, sodium bicarbonate, and control of ventilation.

oxygen difference decreased to 3.1 volume per cent on the average. This represents 56 per cent decrease from the control level. During rewarming, the arterio-venous oxygen difference rose to 4.4 volume per cent. After perfusion it restored to 90 per cent of the control level.

Cerebral metabolic rate for oxygen: Cerebral oxygen consumption during total perfusion decreased remarkably to 37 per cent of the control level, and then increased gradually during rewarming. After perfusion cerebral oxygen consumption was 3.5 ml per 100 g of the brain per minute, on the average, as shown in Fig. 10.

Ocular findings

The diameter of the retinal vessels was expressed as its ratio to the diameter of the papilla, since its absolute value differed among different individuals.

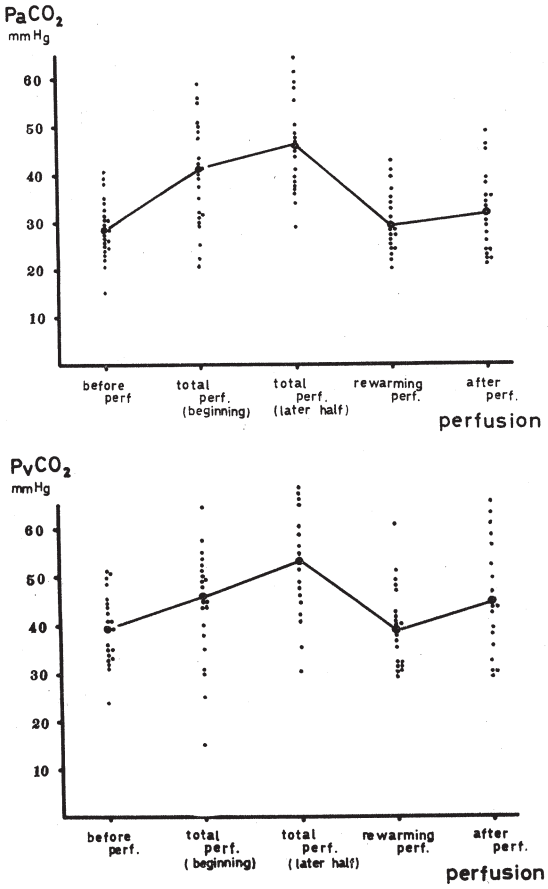


FIG. 6. The changes in arterial and venous blood pCO_2 during perfusion.

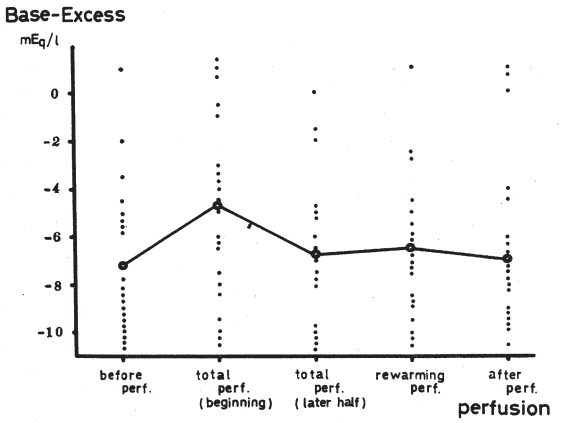


FIG. 7. The canges in base excess during perfusion.

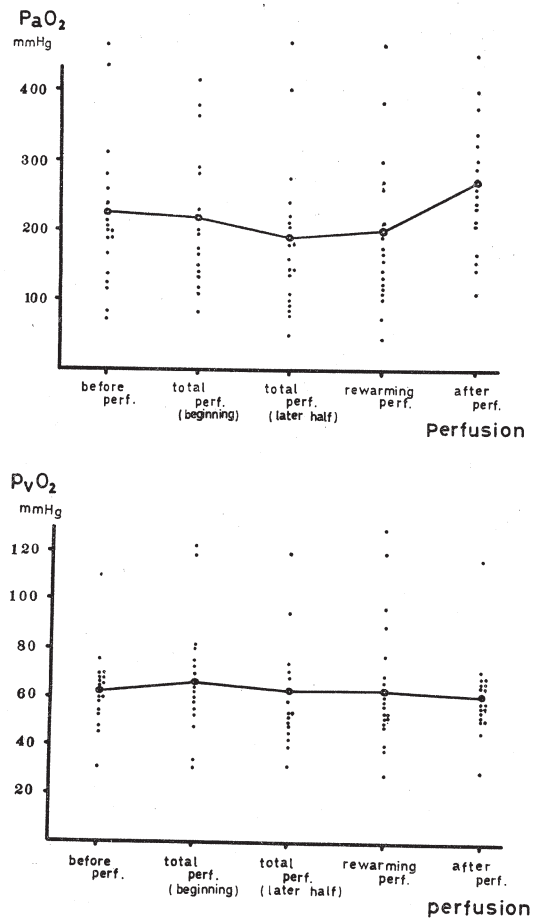


FIG. 8. The changes in arterial and venous blood pO_2 during perfusion. After perfusion arterial pO_2 rose, but venous pO_2 remained unchanged.

Fig. 11 represents a normal fundus photographed after the induction of anesthesia. During cooling, the diameters of both artery and vein were reduced and the papilla became blanched, as shown in Fig. 12.

During total perfusion, the ischemic picture of the arteries became evident while the contour of the peripheral arteries was obscured, as shown in Fig. 13.

The anemic picture of the papilla and the retina were progressively intensified until the later half period of total perfusion when the artery and the vein tended to return to the preperfusion ranges, with the signs of reestablishment of blood flow (Fig. 14).

During rewarming, the diameter of the retinal artery recovered to that during preperfusion period, whereas the veins became dilated (Fig. 15). During this period, the papilla regained almost normal preperfusion tint.

The most marked change in the retinal findings was that of the retinal arteries. To standardize the quantitative expression of the diameters of the blood vessels, the measurement was carried out at the constant distance from the papilla on the central retinal artery and vein.

As shown in Fig. 16, the diameter of the central retinal vessels during cooling, already howed the ischemic narrowing, and it reached to the minimum during the beginning half period of total perfusion. The peripheral circulation was improved during rewarming, and the diameter of the central artery returned to that in the preperfusion period. The veins dilated during rewarm-

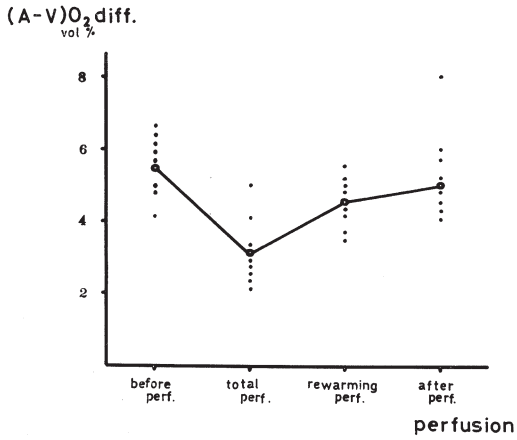
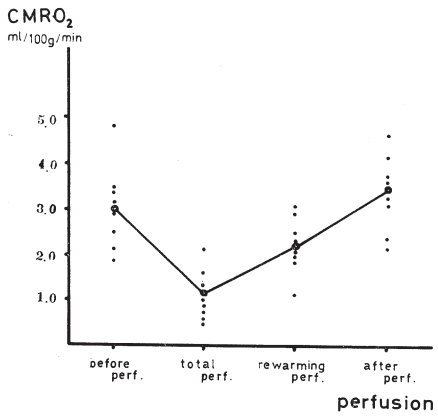


FIG. 9. The changes in arterio-venous oxygen difference in the brain during perfusion. During the total perfusion the arterio-venous oxygen difference decreased significantly to 56 per cent of the mean control level.



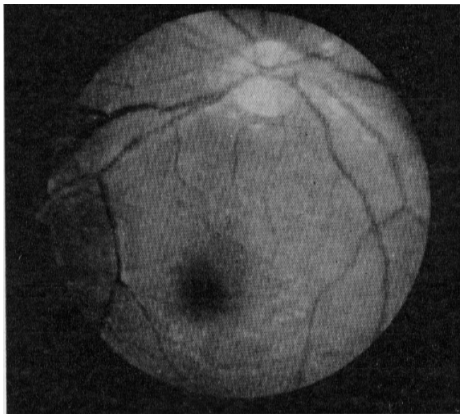


FIG. 10 FIG. 11

FIG. 10. The changes in cerebral metabolic rate for oxygen during perfusion.
FIG. 11. Ocular fundus after the induction of anesthesia.

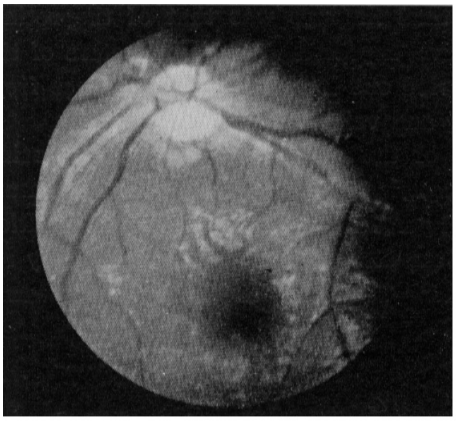


FIG. 12

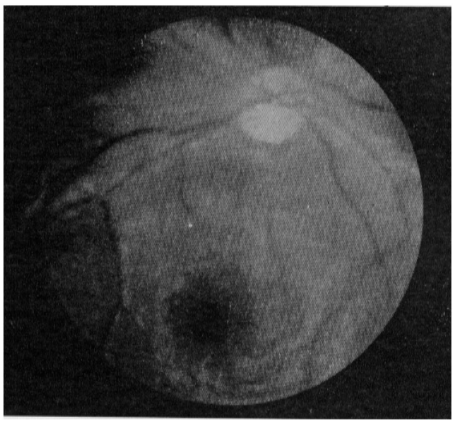


FIG. 13

FIG. 12. Ocular fundus during cooling. The papilla has been blanched.

FIG. 13. Ocular fundus during the beginning of total perfusion. The anemic picture of the papilla and the retinal vessels progressively narrowed and peripheral arteries was obscured.

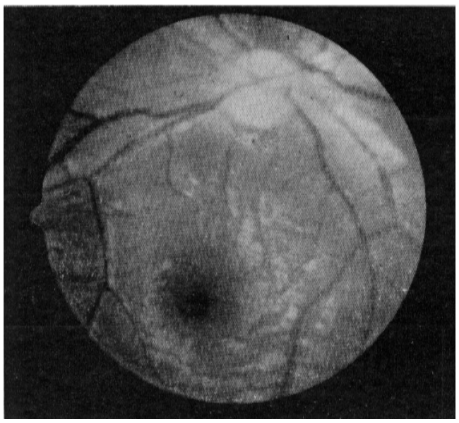


FIG. 14

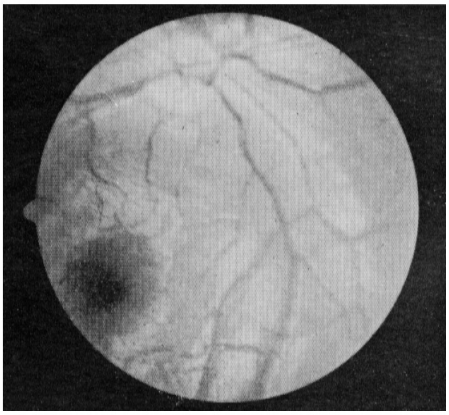


FIG. 15

FIG. 14. Ocular fundus during the later half of total perfusion. It was seen that retinal circulation recovered partly.

FIG. 15. Ocular fundus during rewarming. Retinal arteries recovered, but vein became dilated by congestion.

ing owing to hyperemia due to increased blood flow.

As represented in Fig. 16, both the artery and the vein return to the pre-perfusion state at the end of rewarming and partial perfusion.

DISCUSSION

Method

Since Kety and Schmidt[28] reported in 1945 on the method of quantitative

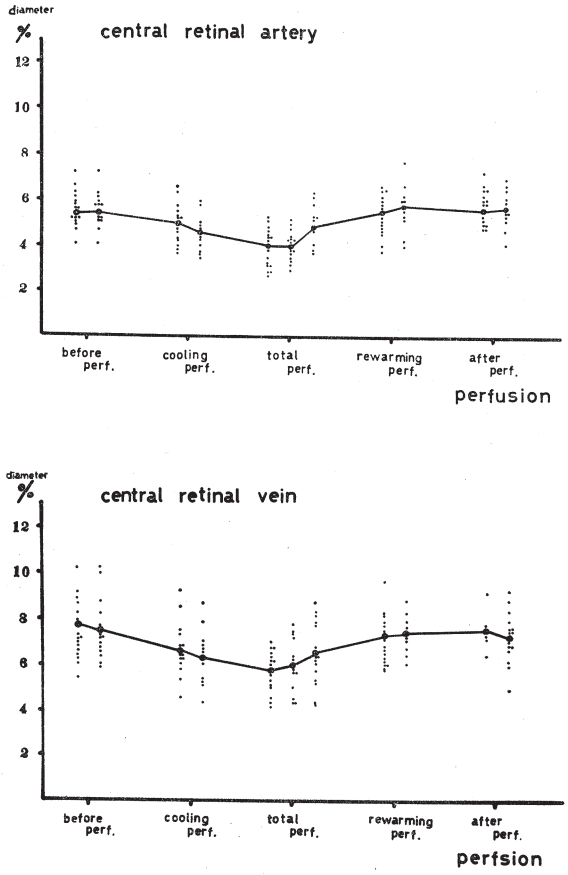


FIG. 16. The changes in diameter of the central retinal artery and vein. Both of them represent ischemic narrowing during total perfusion.

The diameter of the retinal vessels was expressed as its ratio to the diameter of the papilla. Measurement of diameter of retinal vessels was carried out at the constant distance from the papilla.

measurement of cerebral circulation using nitrous oxide, many investigators[29] have utilized this technique in their clinical assessment of cerebral circulation. Aizawa and his associates[29)~32)] in this country have achieved substantial informations using this nitrous oxide method in their investigations on cerebral circulation.

The dye dilution method then became available and has been used in parallel with the nitrous oxide method, since Gibbs and Maxwell[33] reported on Evans Blue dye method in 1947.

The introduction of radioisotopes into the medical methodology provided various ways for extracorporeal assessment of circulation. On cerebral circulation, there have been developed the radioactive inert gas method (Kr^{85}) of

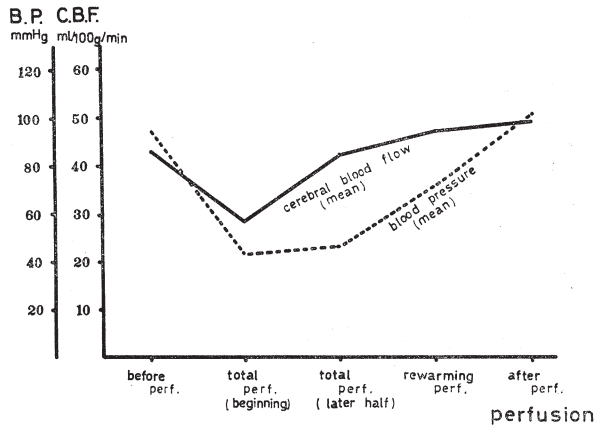


FIG. 17 a. The relationship between cerebral blood flow and mean arterial blood pressure.

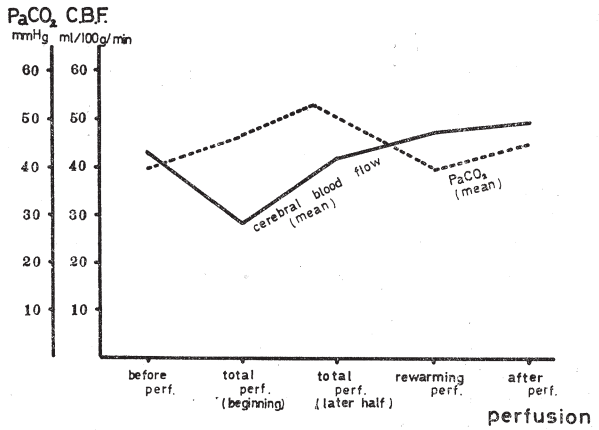


FIG. 17 b. The relationship between cerebral blood flow and $paCO_2$.

Lassen and Munck[34) 35)], the nondiffusive radioisotope method of Oldendorf[36) 37)], Katsuki[38)] and Shin[39)], the indicator fraction technique of Sapirstein[40)], the Kr^{85} injection method of Lassen *et al.*[25)], the blood flow index method of Thompson[41)], and, more recently, the radioactive Xenon method (Xe^{133}) of Harper and Glass[42) 43)].

Owing to the relative inaccessibility to the subject during open heart surgery under extracorporeal circulation and partly to the fact that the use of the nitrous oxide method becomes impracticable because of the inhalation anesthetics, the radioisotope method using Kr^{85} has been used in this department of surgery, according to the technique described by Lassen *et al.* in 1963[25)].

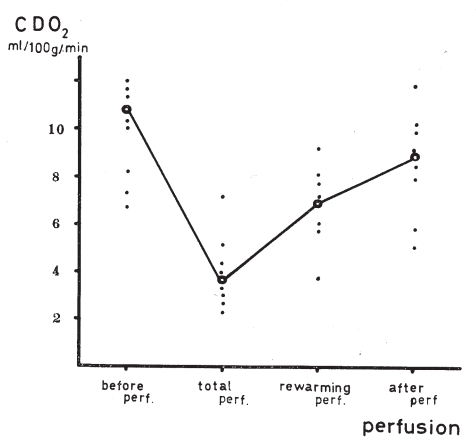


FIG. 18

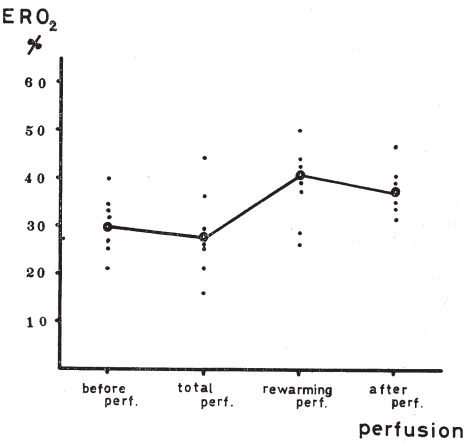


FIG. 19

FIG. 18. The changes in the rate of cerebral oxygen supply/during perfusion.
FIG. 19. The changes in oxygen up-take ratio in the brain.

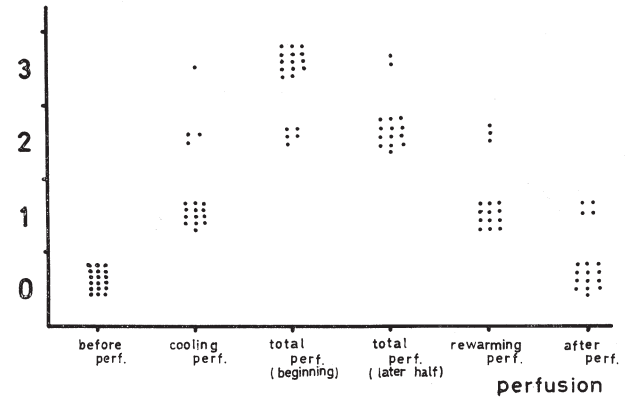


FIG. 20. The changes in the colour of the papilla during perfusion. The colour was classified into three stages.

Degree of changes colour of the papilla grouped as follows:

0: normal colour 2: moderately pale
1: slightly pale 3: very pale

Radioactive innert gas "Krypton" is most useful for our study, because no physical and chemical degradation occured and 95 per cent of this gas passes out through the lungs during each circulation[25)26)]. The exhaled gas from the lungs and the gas diffusing out into the oxygenator have been drained out into the atmosphere outside the room, so that any influence of radiation should not be accumulated in the operating environment. The circulating radioactive krypton was detected from outside of the skull by a scintillation detector and served for the prediction of cerebral blood flow.

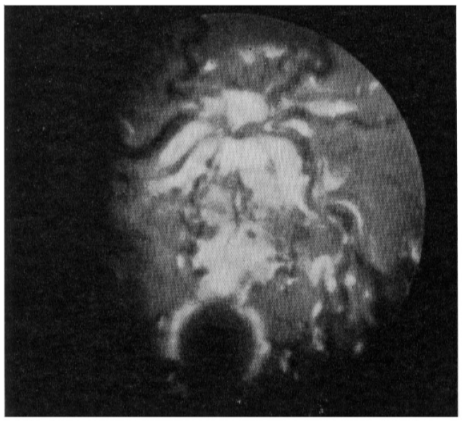


FIG. 21

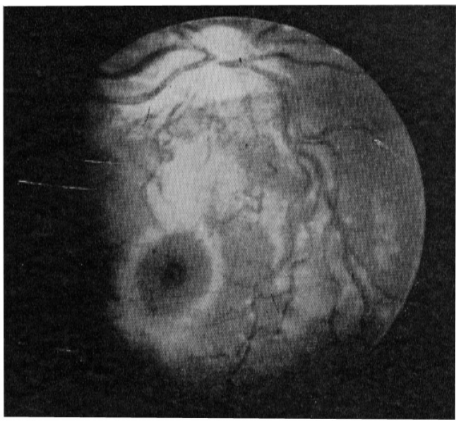


FIG. 22

FIG. 21. Meandering phenomenon of the retinal artery in ocular fundus of tetralogy of Fallot. Preoperation period.

FIG. 22. Meandering phenomenon of the retinal artery in ocular fundus of tetralogy of Fallot. Postoperation period.

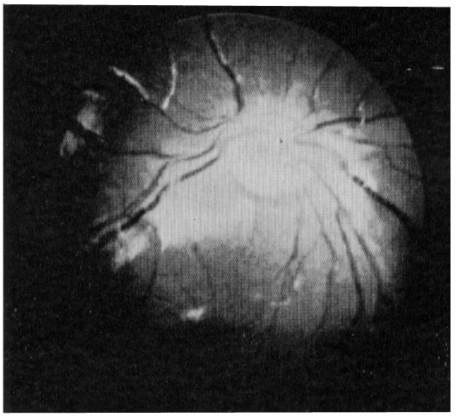


FIG. 23

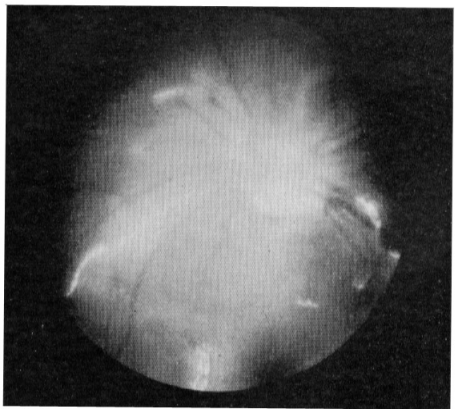


FIG. 24

FIG. 23 and 24. Air embolism is seen as silver wirre like change of the retinal arteries.

The brain metabolism was predicted by combining the cerebral flow with the arterio-venous oxygen difference[44].

Cerebral blood flow and metabolism

Preperfusion brain metabolism and cerebral blood flow of the subjects were studied during the stabilized period of anesthesia. The average cerebral blood flow was 44 ml/100 g/min. which is lower than the values shown by Kety[45] and Aizawa[29], and this is attributable to anesthesia[46].

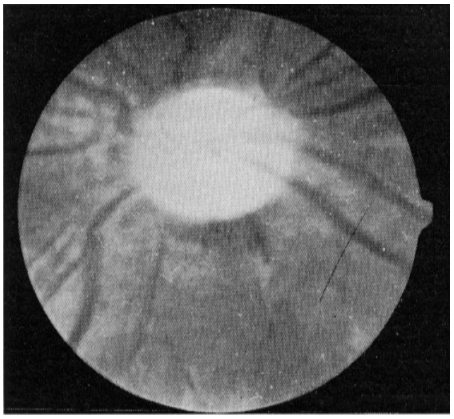


FIG. 25. Spasm of the central retinal artery.

Cerebral blood flow during open heart surgery under extracorporeal circulation was reduced to 28.8 ml/100 g/min., or about 65 per cent of the preperfusion value during the initial period of total perfusion. It recovered to 42.4 ml/100 g/min. by 60 minutes after the start of total perfusion, and then gradually increased to 47.1 ml/100 g/min. during the period of rewarming and partial perfusion and to 48.1 ml/100 g/min. after the end of perfusion. These were, however, general trend of the change in cerebral blood flow during extracorporeal circulation, and there was variation according to the individuals. For example, in the cases with aortic insufficiency, as in the Case 19 and 33, cerebral blood flow showed an increase when the aorta was cross clamped, and maintained normal values during the post-operative period after valvular replacement. The significantly low cerebral blood flow during rewarming and after perfusion in the Case 25 with tetralogy of Fallot was considered to be due primarily to the decreased cardiac output which was intensified by hypovolemia caused by bleeding and an insufficient correction of the right ventricular outflow tract as manifested by the right ventricular pressure of 80 mmHg in systolic and pulmonary arterial pressure of 20/15 (mean: 15) mmHg.

Case 40 died after the perfusion because of an accident in the heart-lung machine, and the cerebral blood flow immediately after the perfusion was significantly low.

All the other cases underwent uneventful postoperative courses.

The factors contributing to the cerebral circulation are manifold. The most important one is its relation with blood pressure, particularly with the mean arterial pressure, since it has been shown by Meyer[47][48] that cerebral blood flow was almost unaltered by a significant rise in the internal jugular vein pressure. McHedlishvili[49] pointed out also that cerebral blood circulation was mostly influenced by the systemic arterial pressure which is the extrinsic mechanism.

Based on their experiments, Halley[3] also reported that the cerebral blood flow was entirely subordinate to the change in the blood pressure. On the other hand, Kety and Schmidt[28] and McCall[50] *et al.* were unable to detect any change in cerebral blood flow with minor degree of hypotension induced by drugs. Aizawa[29,32] reported also that the cerebral circulation and oxygen consumption of the brain were not subjected to the sudden drop of blood pressure to a certain extent, but the only change to be found was the lowered vascular resistance of the brain. Moreover, Finnerty *et al.*[51] stated that the decrease in cerebral blood flow did not take place until the severity of the fall of blood pressure went down to one third of the cerebral value, as hypotension was compensated by the dilatation of cerebral vasculature to maintain the constancy of blood flow.

These autoregulation of the cerebral circulation has been widely admitted, since the mechanism was confirmed under the critical conditions made in the experiments by Meyer[48] and Behrman *et al.*[52]. In 1964, Rapela and Green[53] demonstrated the mechanism of the inhibition of the autoregulation by carbon dioxide. Harper[54,55] also demonstrated that, as long as the arterial carbon dioxide and oxygen tensions were normally maintained, cerebral blood flow was not changed in the range of blood pressure between 155 and 80 mmHg, but it was subjected to change in parallel with the blood pressure when it was below 80 mmHg. Furthermore, he demonstrated that in the presence of hypercapnea the autoregulatory mechanism was abolished rendering the pressure-flow relationship to be linear.

The autoregulation of the cerebral circulation appears to be based on the mutual relationship between blood pressure and partial pressure of carbon dioxide in the cerebral tissues, as pointed out by Lassen[56] (Fig. 17).

The close interrelationship between the cerebral circulation and the carbon dioxide tension has been well understood, as demonstrated by the studies of Meyer[48], Goto[57], and Tazaki[58], on the mechanism of action of carbon dioxide, Wollman[13], in his study of cerebral blood flow during extracorporeal circulation, found that cerebral blood flow was influenced mostly by the factor of arterial carbon dioxide tension and very little by perfusion pressure. Kety and Schmidt[59] observed about 10 per cent increase of cerebral blood flow by the inhalation of 3.5 volume per cent of carbon dioxide regardless of the value of blood pressure.

During the beginning period of total bypass, a marked decrease in cerebral blood flow was observed according to the sudden drop of blood pressure, but the cerebral blood flow recovered remarkably by 60 minutes after the start of the total bypass in spite of the unchanged femoral arterial pressure under a constant flow rate by the apparatus.

This could be explained by a garadual build-up of carbon dioxide in the arterial blood while 2 per cent of carbon dioxide gas was insufflated into the

artificial lung and 5 L/min. of carbon dioxide gas was blown into the operating field, and this triggered the restart of the autoregulatory mechanism during extracorporeal circulation.

The relationship between the cerebral circulation and the oxygen tension has been established. Courtice[60] reported that the influence of oxygen deprivation in the inhaled atmosphere on the cerebral blood circulation did not appear until the oxygen concentration reached below 15 per cent. Kety and Schmidt[59] observed in their clinical experiment that, when 10 per cent oxygen was inhaled, the cerebral vascular resistance as reduced, the blood flow was increased in 35 per cent and cerebral oxygen consumption did not alter.

Noell and Schneider[61], and Aizawa *et al.*[29,32] admitted the similar effect of oxygen deprivation on the cerebral circulation. In the present study, the influence of oxygen tension in the perfused blood may be ruled out, since 5 to 6 l/min. of oxygen was insufflated into the artificial lung.

The influence of blood pH on the cerebral circulation was studied by Kety[59,62]. He made the subjects to inhale 5 to 7 per cent of carbon dioxide to induce respiratory acidosis, and observed the increase in cerebral blood flow, which he attributed to the increase in carbon dioxide content and the decrease in pH in the arterial blood. The metabolic acidosis, on the other hand, induced by Schieve and Wilson[63] with the injection of ammonium chloride, decreased cerebral blood flow.

The direct correlation of cerebral blood flow and pH could not be detected in the present investigation, since the arterial carbon dioxide tension was subjected to change by the addition of carbon dioxide gas into the oxygenator or in the operating field as well as by metabolic acidosis occurring inevitably during total extracorporeal circulation when the average pH was reduced to 7.264.

The influence of temperature on the cerebral circulation was studied by Rosomoff[64], who found the decrease of cerebral blood flow in dogs from 6 to 7 per cent for each degree of centigrade of temperature fall, and observed about 50 per cent decrease of flow at 28°C of body temperature.

Forrester[65] likewise demonstrated that cerebral flow was decreased by the factors as increased blood viscosity and the direct action of cold on the blood vessels, even when the arterial carbon dioxide tension was maintained normal. Temperature is considered to be the main factor contributing to the recovery of cerebral blood flow during the rewarming perfusion.

All the foregoing discussions on the cerebral circulation are aimed for the evaluation of safe and adequate maintenance of the brain tissues during extracorporeal circulation by the technique used in this department of surgery.

The estimation of brain metabolism is most conveniently expressed by oxygen consumption by the brain[29]. For the quantitative evaluation of brain metabolism and its changes oxygen consumption is almost exclusively utilized

clinically.

Fig. 10 illustrates that oxygen consumption by the brain is decreased to 37 per cent of the control level during total perfusion. The degree of diminished brain metabolism here is less than the observation of Horecky[12] that the diminution of the brain metabolism by extracorporeal circulation is 11 per cent during the normothermic period and 94 per cent during the hypothermic period. During rewarming, the metabolism recovers to 77 per cent of the preperfusion values. This recovery rate is still deficient when compared with the recovery rate of the cerebral oxygen supply, as shown in Figs. 18 and 19.

It is probable that the increased demand of oxygen in the brain tissues evokes a secondary regulatory mechanism of the circulation which enhance cerebral blood flow during rewarming. This is exemplified by the fact that the cerebral oxygen uptake ratio recovers during rewarming to 140 per cent of the preperfusion value.

The question of at what extent of lowered oxygen consumption the irreversible brain disfunction results is not yet answered. Schneider *et al.*[66] suggested that 20 per cent of the brain metabolism demanded for the functional activity was sufficient for only the maintenance of the tissues. Weiss *et al.*[67], on the other hand, suggested that oxygen consumption by the heart under extracorporeal circulation diminished to about 40 per cent under the adequate flow. If the brain is to maintain the metabolism of 20 per cent of the normal state, 30 ml/100 g/miu. of cerebral blood flow is calculated to be necessary in the normothermic condition[66]. Viewing from these data, cerebral blood flow obtained by our moderate hypothermic technique of extracorporeal circulaton is apparently sufficient for the requirement. The increase of the cerebral metabolic rate for oxygen to 3.5 ml/100 g/min. during the immediate postperfusion period, which exceeded the value in the preperfusion period, and the elevation of the cerebral oxygen uptake ratio also to 126 per cent of the preperfusion value, suggest that the safe and adequate cerebral blood circulation might have been maintained during the present low flow-hypothermic-hemodilution technique of extracorporeal circulation.

Ocular findings

The cerebral hemodynamics during extracorporeal circulation is currently studied by means of arterial and venous blood pressures and electroencephalogram[67][68]. The only visible blood vessel in the total body is the retinal vessel. In the view-point that the morphological changes of the vessel correspond to the circulatory changes, the retinogram was taken during perfusion and examined later.

Cerebral retinal arteries were observed on the photographs of the fundus by Dimmer already in 1907. The progress in the fundus camera in the recent years has boosted various investigations with this technique. There are some

reports on the measurement of retinal vessels[69)~71)]. There is yet no report on the findings of the blood vessels during extracorporeal circulation.

The relation between the diameter of the retinal artery and blood pressure could be summarized that the diameter of the artery diminished gradually by the beginning half of total perfusion according to the decrease in cerebral blood flow and lowered blood pressure[72)], but in the majority of the cases the increase of the diameter was observed even though the hypotension continued. Combined contribution is considered of the factors as cerebral blood flow, changes in the carbon dioxide tension[73)], and the autoregulatory mechanism[57)]. Significant changes were not observed in the ratio of retinal arteriovenous diameter.

The change in the colour of the papilla was classified into three stages, and the course of the changes during extracorporeal circulation, as su marized in Fig. 20, paralleled to the changes of the diameter of the retinal vessels. The blanched colour represents the lowered blood pressure in the papilla due to the peripheral circulatory insufficiency.

Another significant morphological change of the retinal artery is the meandering phenomenon of the artery observed in the patient with tetralogy of Fallot, as shown in Fig. 21 and 22.

Some other specific changes are demonstrated. Fig. 23 and 24 represent the silver wire appearence of the vessel which was described by Dark *et al.*[74)]. This was most probably caused by the air originating from the aorta when a cross clamp was released. Air embolism is one of the important complications during extracorporeal circulation[10)11)], and this could be detected in the early phase of occurence for the proper countermeasure to be taken, using a fundus camera. Fig. 25 shows the disappearance of vessel contours. This coincides with spasm of the vessels reported by Lemke[75)], corresponding to the migraine syndrom of the patient. This significant syndrom of periphereal circulatory insufficiency was treated with success by an α-adrenergic blocking agent.

The findings of the visible peripheral blood vessels are noteworthy for the accurate understanding of the general circulatory state.

At the same time, the direct influence of local hemodynamics on the brain was detected on the electroencephalogram during perfusion. The changes in electroencephalogram was in parallel with the changes in cerebral blood flow, as has been described by Arfel *et al.*[67)].

The study on the electroencephalogram on the same group of cases during extracorporeal circulation is to be reported elsewhere in detail by Yoshizawa[68)].

SUMMARY AND CONCLUSION

Clinical study was carried out on the cerebral hemodynamics in 40 cardiac patients duuring extracorporeal bypass by the low flow-hypothermic-hemo-

dilution technique which is currently in use in this department. After the analysis of the clinical results and the discussion on the related subjects, the following conclusions were derived:

1) After the start of heart-lung bypass, cerebral blood flow is significantly decreased to the average of 65.2 per cent of the preperfusion control value, but it recovers remarkably during the later half of total bypass in spite of the unchanged arterial blood pressure and flow rate. This was explained by the gradual build-up of carbon dioxide in the blood and the reestablishment of autoregulation mechanism. During rewarming, cerebral blood flow exceeds the preperfusion control value by 7.3 per cent. This is due mainly to the effect of temperature.

2) The arterial carbon dioxide tension tends to increase gradually during total perfusion with concomitant decrease in pH. The correction of the basal deficit is justified by administering THAM or sodium bicarbonate duriug perfusion.

3) The brain metabolism is lowered to 37 per cent of the preperfusion control value during total perfusion, and restores during rewarming.

4) The findings of ocular fundus change in parallel with the changes in cerebral blood flow. Retinography is hence very useful for monitoring cerebral circulation.

There have not been encountered cases with psychiatric syndrom or the sequelae from low cerebral blood flow after undergoing this technique of extracorporeal circulation, except a few cases of air embolism and postoperative hypotension.

It has been revealed by this study that the postoperative cerebral hemodynamics is entirely dependent on the overall result of the repair of cardiac anomalies, and not directly related to the technique of extracorporeal circulation. Hence it is suggested that the present method of heart-lung bypass, *i.e.* low flow-hypothermic-hemodilution technique should be adequate from the point of cerebral circulation.

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