A STUDY OF BLOOD FLOW, VENOUS BLOOD OXYGEN SATURATION, BLOOD PRESSURE AND PERIPHERAL RESISTANCE DURING TOTAL BODY PERFUSION

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CORRECTION of certain congenital cardiac anomalies by open intracardiac surgical procedures is now possible through the development of means for bypassing the heart and lungs.[1-4] Since March, 1955, a pump-oxygenator based on the principles proposed by Gibbon[5] has been used clinically for open intracardiac operations at the Mayo Clinic. Details of its construction and operation[6] and its use in the experimental laboratory[7] and in earlier series of cases[8-10] have been reported. The perfusions in these early cases, which supplied the data for this analysis, were in a number of particulars different from those employed by us in the past 24 months. Flow rates, for example, were lower in the early cases probably because of imperfect venous cannulation and hypovolemia. Heat loss in the extracorporeal apparatus was not actively combated. Recirculation through the oxygenator occurred during the perfusion. Nonetheless, physiologic data obtained during these early and, by present standards, imperfect perfusions are worthy of reporting and interpreting.

This paper represents, then, a study of certain physiologic variables during total body perfusion in 45 of the first 90 patients in whom the Gibbon-type pump-oxygenator was used in 1955 and 1956. These variables include: (1) flow of arterialized blood to the patient, (2) oxygen saturation of the mixed venous blood, (3) arterial and venous blood pressure, and (4) body temperature.

"Peripheral resistance" was calculated from certain of these data.

An objective was to examine the relation-ships between the above factors during total body perfusion. Also, in 31 of these patients, the values for these physiologic variables during total perfusion were compared with the determinations of the same variables made prior to operation at cardiac catheterization.

The Gibbon-type pump-oxygenator functioned in the following manner. Blood from the superior and inferior venae cavae was drawn by controlled suction to a "venous" reservoir. From there it was pumped to the top of a vertical multiscreen oxygenator. After it flowed by gravity in a thin film down the screens, it was pumped back to the aorta via the left subclavian artery. In this series of patients the venous inflow was not restricted and arterial flow was not predetermined, but the volume of venous return determined arterial flow per unit of time. In the oxygenator the blood was exposed to a mixture of 95 per cent oxygen and 5 per cent carbon dioxide, these gases flowing at 10 liters per minute. Automatic level-sensing devices incorporated in the pump-oxygenator assembly permitted the maintenance of a constant blood volume in the extracorporeal circuit.

Blood accumulating in the heart during perfusion was collected by a specially constructed aspirator and returned to the venous reservoir. The interval between the time of insertion and the time of removal of this intracardiac aspirator has been designated the time of total body perfusion. All measurements and calculations reported in this study were confined to this period during which the pump-oxygenator alone was supporting the patient. For this series of patients, induced cardiac asystole was not used.

METHODS

General. Anesthesia and supportive care of these patients have been described previously by Patrick, Theye and Moffitt.[11] Pa-

tients were premedicated with a barbiturate and morphine. After induction of anesthesia, endotracheal intubation was carried out. All patients were maintained in a light state of anesthesia with ether (level 1) as monitored by means of the electroencephalogram.[12] Manually controlled respiration by hyperventilation was employed.

Measurement of Arterial Flow Rate. During perfusion the rate of rotation of the arterial pump was continuously recorded by use of a photokymographic assembly mounted on a cart. This cart was a modification of the assembly described by Hallenbeck, Wood and Clagett.[13] After each perfusion the pump was calibrated by measuring the volumes of blood pumped at the speeds of rotation seen during perfusion. During calibration, pressure in the arterial line was adjusted to the levels observed during perfusion.

Arterial blood flow was measured in liters per minute at intervals of 1 minute during total perfusion. These values were converted to a "perfusion index" by dividing total flow per minute by the patient's surface area (calculated by the DuBois[14] method).

Nineteen of the patients undergoing cardiac catheterization were anesthetized with tribromoethanol (avertin) administered rectally and all were breathing room air. In all patients, cardiac output was determined by the Fick method.

Oxygen Saturation of Venous Blood. Venous oxygen saturation was determined by a cuvette oximeter[15] attached to the line returning blood from the patient to the pump-oxygenator. Because of the presence of anesthetic gases in the blood, use of chemical methods was not attempted.

The deflection of the cuvette was measured from the photographic record at intervals of several minutes during total perfusion. This was converted by means of a calibration scale to oxygen saturation in per cent. Changes in oxygen saturation showed a time lag of 1 to 3 minutes, due mainly to the presence of a long tube of small bore between the main venous flow line and the oximeter. In each case the initial deflection of the oximetric record was equated in time to the beginning of total perfusion to correct for this time lag.

During cardiac catheterization, oxygen saturation of the mixed venous blood was estimated both by oximetry and by the Van Slyke method.

Determination of Arterial and Venous Blood Pressure. Blood pressure in the lower part of the abdominal aorta (42 cases) and in the radial artery (three cases) was recorded continuously by means of a strain-gauge manometer[16] with catheter and needle systems respectively. Pressure was also recorded continuously from a large central vein during perfusion by the same method. At intervals, calibrations were inscribed on the photographic record with known pressures from a Tycos aneroid manometer applied to both strain gauges. The reference zero was a point equidistant from the sternal and back levels at the third intercostal space. The intravascular pressures were measured from the photographic record at 1-minute intervals during total perfusion. Mean pressures were calculated by adding one third of the pulse pressure to the diastolic pressure. Pressures in the right side of the heart, pulmonary arteries and radial arteries were measured during cardiac catheterization by a strain-gauge manometer in 31 of the cases.

Calculation of Peripheral Resistance. Pressure-flow ratios were calculated as an expression of vascular resistance (R) in dynes seconds centimeters^{-5}. The difference between mean aortic and mean central venous pressures was used as effective perfusing pressure (P) in the formula R = P/F, in which F equals flow.

Determination of Body Temperature. An intrarectal thermistor measured body temperature, which was recorded in degrees centigrade periodically during total perfusion. To minimize falling body temperature the patient lay on a heated blanket which was attached to a Thermorite heating unit.

RESULTS

Material. The 45 patients varied in weight from 3.7 to 84.1 kg. and in surface area from 0.21 to 2.11 square meters. In the total group were 10 patients who weighed less than 10 kg. and eight who weighed 50 kg. or more (table 1). The 25 males and 20 females varied in age from 2.5 months to 40 years. Eight patients were less than 1 year and 27

TABLE 1

BLOOD FLOW AND VENOUS OXYGEN SATURATION BY GROUPS ACCORDING TO WEIGHT

Weight (kg.)	During Total Body Perfusion			During Cardiac Catheterization		
	Cases	Average of Mean Perfusion Index (l./minute/m.²)	Average of Mean Venous Oxygen Saturation (per cent)	Cases	Average Cardiac Index (l./minute/m.²)	Average Venous Oxygen Saturation (per cent)
<10	10	1.50	74	5	4.20	61
10–19.9	15	1.90	75	10	5.10	68
20–29.9	6	1.40	69	4	5.10	70
30–49.9	6	1.45	72	4	3.80	77
50–84.9	8	1.77	75	8	2.90	68

were less than 10 years of age. Final operative diagnoses are listed in table 2. The largest single group consisted of 16 patients with ventricular septal defect. The average time of total perfusion for all patients was 35 minutes (range 11 to 70 minutes).

Blood Flow Values (Table 1). Average of the mean perfusion index for the 45 patients was 1.69 liters per minute per square meter (range 0.62 to 2.95 l./minute/m.²). An average flow of 1.50 l./minute/m.² was found in the babies weighing less than 10 kg., whereas 1.77 l./minute/m.² was the average for the adults weighing 50 kg. or more.

At preoperative cardiac catheterization in 31 of the patients, the average cardiac index was 4.2 l./minute/m.² (range 1.7 to 7.6). Five patients weighing less than 10 kg. had an average flow of 4.2 l./minute/m.² The eight patients who weighed 50 kg. or more had an average cardiac index of 2.9 l./minute/m.²

Venous Oxygen Saturation (Table 1). The average of the mean oxygen saturation of the venous blood returning from the patient in 45 cases proved to be 73 per cent (range 54 to 88 per cent). The average saturations in the different weight groups were similar. The patients weighing less than 10 kg. and those weighing 50 kg. or more had almost identical averages of the mean venous oxygen saturations, namely 74 and 75 per cent.

At preoperative cardiac catheterization the average mixed venous oxygen saturation was 70 per cent (range 46 to 85 per cent). In five patients weighing less than 10 kg. the average oxygen saturation of venous blood was

TABLE 2

NATURE OF CLINICAL MATERIAL INCLUDED IN THIS STUDY

Cases	Final Operative Diagnosis
16	Ventricular septal defect
4	Tetralogy of Fallot
3	Common ventricle (predominant lesion)
3	Atrial septal defect with total anomalous pulmonary venous drainage
3	Ventricular septal defect with mitral stenosis
2	Ventricular septal defect, atrial septal defect
2	Ventricular septal defect with patent ductus arteriosus
2	Atrial septal defect with partial anomalous pulmonary venous drainage
2	Atrial septal defect with pulmonary stenosis
1	Atrial septal defect
7	Miscellaneous lesions

61 per cent while in the group of eight patients weighing 50 kg. or more it was 68 per cent.

Values for Arterial and Venous Blood Pressures. In 44 cases during total perfusion, the average of the mean arterial blood pressure was 45 mg. of mercury, and of the mean central venous pressure, 14 mm. of mercury (table 3).

For the first 10 minutes of total perfusion, the average of the mean arterial pressure was 41 mm. of mercury, and for the last 10 minutes this figure rose to 47 mm. For these same periods the average of the mean central venous pressures were 14 and 13 mm. of mercury respectively (table 4).

TABLE 3

BLOOD PRESSURE, BLOOD FLOW AND PERIPHERAL RESISTANCE BY GROUPS ACCORDING TO WEIGHT

Weight (kg.)	During Total Body Perfusion				During Cardiac Catheterization			
	Average of Mean Arterial Pressure (mm. Hg)	Average of Mean Central Venous Pressure (mm. Hg)	Average of Mean Arterial Flow (l./minute)	Average Peripheral Resistance (dynes sec. cm.$^{-5}$)	Average Radial Pressure (mm. Hg)	Average Central Venous Pressure (mm. Hg)	Average Arterial Flow (l./minute)	Average Peripheral Resistance (dynes sec. cm.$^{-5}$)
<10	45	17	0.52	4,650	58	4	1.43	3,560
10–19.9	45	14	1.29	2,010	73	6	3.30	1,730
20–29.9	32	11	1.28	1,380	70	7	4.60	1,110
30–49.9	49	12	1.96	1,600	83	6	5.30	1,300
50–84.9	51	13	3.08	1,040	83	6	5.20	1,270

TABLE 4

BLOOD PRESSURE, BLOOD FLOW AND PERIPHERAL RESISTANCE DURING PERFUSION BY GROUPS ACCORDING TO WEIGHT

Weight (kg.)	During Initial 10 Minutes				During Final 10 Minutes			
	Average of Mean Arterial Pressure (mm. Hg)	Average of Mean Central Venous Pressure (mm. Hg)	Average of Mean Arterial Flow (l./minute)	Average Peripheral Resistance (dynes sec. cm.$^{-5}$)	Average of Mean Arterial Pressure (mm. Hg)	Average of Mean Central Venous Pressure (mm. Hg)	Average of Mean Arterial Flow (l./minute)	Average Peripheral Resistance (dynes sec. cm.$^{-5}$)
<10	45	17	0.61	4,080	46	16	0.46	5,800
10–19.9	40	15	1.39	1,540	48	14	1.23	2,500
20–29.9	27	10	1.35	1,090	34	7	1.26	1,550
30–49.9	48	11	2.10	1,460	49	11	1.84	1,880
50–84.9	45	13	3.13	870	56	9	2.99	1,260

At cardiac catheterization in 31 of these patients the mean pressure in the radial artery averaged 74 mm. of mercury. Mean central venous pressure averaged 6 mm. (table 3).

Peripheral Resistance. The average peripheral resistance in 44 cases during total perfusion was 2250 dynes seconds centimeters^{-5} (table 3).

In the 31 patients at preoperative cardiac catheterization, the average systemic peripheral resistance was 1770 dynes seconds centimeters^{-5} (table 3).

For the initial 10 minutes of total perfusion the average peripheral resistance was 1860 dynes seconds centimeters^{-5}. During the final 10 minutes of perfusion the average value was 2840 dynes seconds centimeters^{-5} (table 4).

Body Temperature During Total Perfusion. The average decrease in intrarectal temperature during total perfusion was 1.7 C. (range

0.1 to 4.7 C.) in 43 patients. In two patients small increases in body temperature occurred.

COMMENT

Blood Flow Values. The arterial blood flow was determined at one period during cardiac catheterization by the direct Fick method and during total perfusion was metered continuously by the output of the arterial pump. It is believed that each method was sufficiently accurate to yield comparable results.

As would be expected, total blood flow to the patient during perfusion increased as the surface area of the patient became greater (fig. 1).

Blood flow per unit of surface area, that is, perfusion index, was variable but apparently was independent of body weight. Indices in the different weight groups were similar. This relative independence of cardiac index and
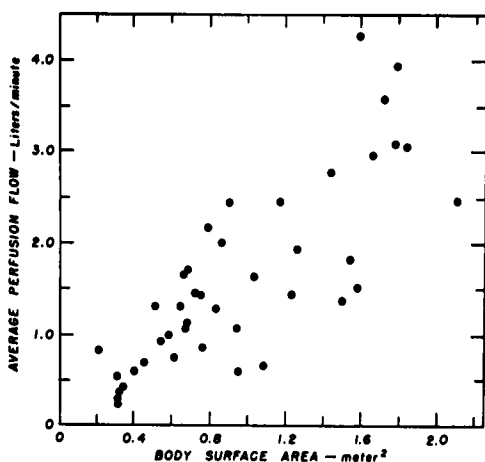
FIG. 1. Relation of average perfusion flow to body surface area in 45 patients undergoing total body perfusion. Note the direct correlation despite considerable scatter of the data.

body weight was also evident at cardiac catheterization.

The data indicate that the arterial blood flow during these total body perfusions was approximately one half as great as at cardiac catheterization of the same patients.

Venous Oxygen Saturation. The oxygen saturation of venous blood during total body perfusion was continuously determined by a cuvette oximeter, while during cardiac catheterization a single determination was done by the Van Slyke method. The venous blood returning from the patient during perfusion differed from that of the same patient during catheterization in that the coronary return was not included.

When the patients were considered in groups according to weight, the venous oxygen saturation during perfusion was comparatively constant and was as high as during cardiac catheterization, but within the groups there was wide variability, and no relation to the values obtained at cardiac catheterization could be demonstrated.

The oxygen saturation of arterial blood was maintained at 100 per cent throughout the period of perfusion. The oxygen content of arterial blood during perfusion was, however, unknown because of lack of a direct measurement of oxygen tension and the unsuitability of manometric technics during use of a volatile anesthetic agent. Quantities of oxygen up to 1.5 cc. per 100 cc. of blood might be present in the dissolved form and this factor could influence oxygen saturation of the venous blood in an upward manner during perfusion.

For all patients, the average of the values for oxygen saturation of venous blood was found to be higher during perfusion (table 1) than during catheterization despite a reduction in average blood flow of more than 50 per cent.

Because of lack of a value for the oxygen content of arterial blood, data on oxygen consumption for the perfusion period could not be calculated with accuracy, but a reduction in oxygen consumption to approximately 65 per cent of the value for the normal waking patient appears likely. Possible reasons for a reduction in oxygen consumption during these perfusions include: (1) anesthesia,[17, 18] (2) reduced body temperature,[19] (3) lessened oxygen requirements of the heart, lungs and muscles of respiration, and (4) incomplete perfusion of certain parts of the body.

Relation of Venous Oxygen Saturation to Arterial Blood Flow. The oxygen saturation of mixed venous blood during perfusion was found to be directly related to blood flow expressed as a perfusion index (fig. 2). This direct relationship was also found during individual perfusions in patients of different weights (fig. 3).
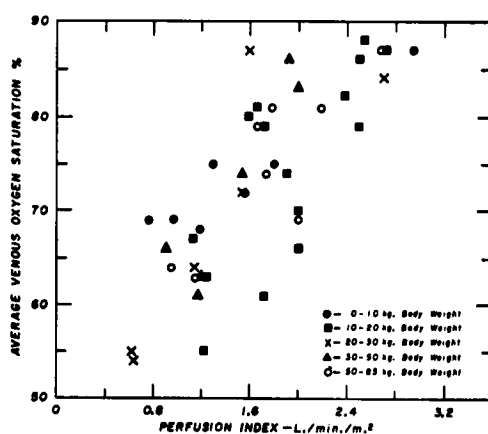

FIG. 2. Relation of average oxygen saturation of mixed venous blood to average perfusion index (perfusion flow divided by body surface area). Note the direct correlation between these variables. This relation is not significantly affected by body weight.

Patient 22 (fig. 3) underwent total body perfusion on two occasions separated by an interval of 14 minutes. For the first period of 24 minutes venous oxygen saturation varied with blood flow, with the average flow being 1.47 l./minute/m.² and the average venous saturation being 54 per cent. After an interval of 14 minutes she was again perfused for 22 minutes. The average flow during the second perfusion was 2.05 l./minute/m.² and the average venous saturation was 74 per cent.

Figure 4 compares this relation in two patients of identical weights. Patient 39 was maintained at an average flow of 1.78 l./minute/m.² and had an average venous oxygen saturation of 81 per cent. Patient 40 had a lower average blood flow of 0.96 l./minute/m.², and an average venous oxygen saturation of 64 per cent resulted.

The direct relation between the oxygen saturation of mixed venous blood and the blood flow is implicit in the Fick equation:

$$Flow = \frac{O_2 \text{ consumption}}{\substack{O_2 \text{ content of arterial blood} \\ - O_2 \text{ content of mixed venous blood}}}$$

If one assumes that oxygen consumption and oxygen content of the arterial blood are con-

FIG. 4. Correlation of venous blood oxygen saturation with blood flow in two patients of identical weights who were perfused at markedly differing average blood flows.

stant during perfusion, the direct relationship between blood flow and venous oxygen saturation can readily be seen.

When the oxygen saturation of the mixed venous blood is at or above the range of normal, it is likely that the oxygen tension of the tissues will be maintained within a roughly normal range. If the oxygen saturation of the mixed venous blood is below normal, the oxygen tension in certain regions of the body may be extremely low, to the extent of causing tissue damage due to hypoxia.

A normal venous oxygen saturation is a desirable goal during total body perfusion and is directly related to the magnitude of the blood flow.

Blood Pressure and Peripheral Resistance. Mean arterial blood pressure decreased rapidly after the institution of total perfusion and increased slowly during the perfusion period. Central venous pressure during perfusion was higher than at preoperative cardiac catheterization but remained at the same level for the duration of perfusion.

There appeared to be no significant difference between peripheral resistance at perfusion and at cardiac catheterization in the same patients. The decrease in arterial blood
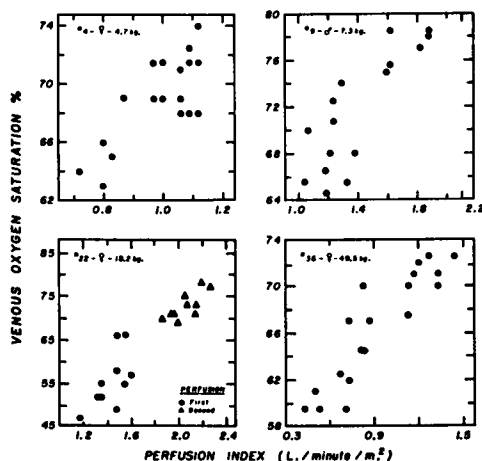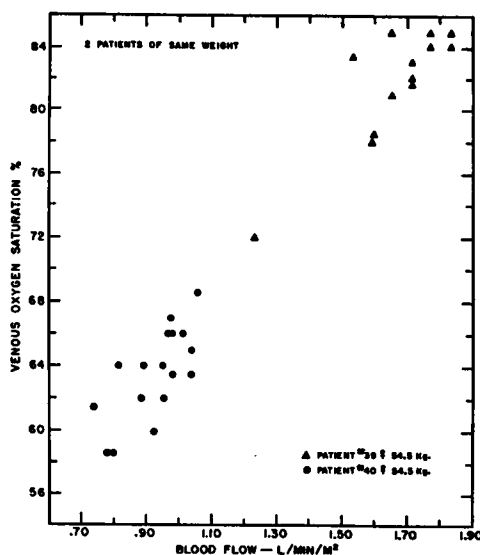

FIG. 3. Relation of oxygen saturation of venous blood to perfusion index in four patients of differing body weights. Values for flow and saturation were obtained simultaneously at intervals of approximately 3 minutes. Note in each the direct correlation between the variables. In the lower left panel (case 22) the correlation is maintained during two periods of perfusion (see text). Case 36 shows an unusually severe decline in flow during perfusion.
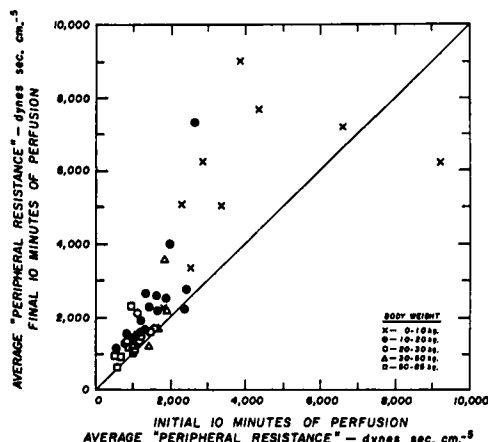
FIG. 5. Relation of average peripheral resistance determined during initial 10 minutes of perfusion to average peripheral resistance determined during final 10 minutes of perfusion. Note the increase in calculated resistance that occurs in the majority of patients during perfusion. As would be expected, higher resistance values were obtained in the smaller subjects.

pressure was due to the approximately 50 per cent reduction in blood flow during perfusion.

During the time of total perfusion, peripheral resistance increased in 41 of 44 patients. This was demonstrated by comparing the initial and final 10-minute periods on perfusio: (fig. 5) and by calculating resistance in rep resentative cases at intervals during perfusio: (fig. 6). The patients who weighed less tha: 10 kg. showed the greatest increases an(most variability in this respect. The larges patients showed at least small increases i: peripheral resistance which appeared to pro gress as perfusion continued.

Possible explanations for the increase i: peripheral resistance during these whole bod: perfusions include: (1) the direct effect o circulating vasopressor substances, (2) ac tivity of the sympathetic nervous system, (3 local veno-arterial reflexes and (4) change in viscosity of the perfusing medium due t(loss of water from the vascular system o changes in temperature.

Body Temperature During Total Perfusion
All but two patients in the series underwen a decrease in body temperature during tota perfusion. General factors involved in chang(in body temperature in the operating roon include: room temperature and air movement anesthesia, temperature of the heating uni on which the patient was lying, and status o: the patient's draping.
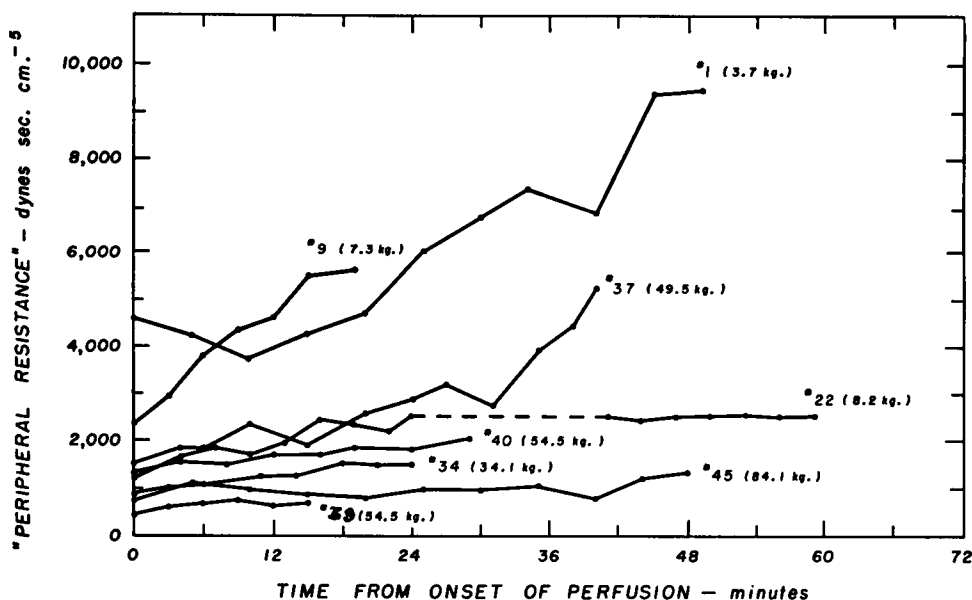

FIG. 6. Change in calculated peripheral resistance during period of perfusion in eight patients. In most cases a steady increase in resistance occurs as the perfusion proceeds (see text).

During this series neither the perfusing blood nor the gases in the oxygenator were heated. The data suggest that arterial flow rate and perfusion time directly, and surface area inversely, influenced decrease of body temperature. Temperatures in the small patients with low blood volumes perfused with a proportionally larger volume of blood from the machine decreased more than those of the adults.

The main factor affecting a decrease in body temperature appeared to be the temperature of the perfusing blood.

CONCLUSIONS AND SUMMARY

From a study of 45 patients during total body perfusion, arterial blood flow, calculated on a basis of surface area, averaged approximately one half as great during these perfusions as at preoperative cardiac catheterization. No demonstrable relationship was found to exist between perfusion index and body weight.

Despite the reduction in blood flow during perfusion, venous oxygen saturation was maintained approximately at, or higher than, saturation preoperatively. This must have been due to a reduction in oxygen consumption during whole body perfusion.

Oxygen saturation of the mixed venous blood varied directly with perfusion (that is, cardiac) index.

Mean arterial blood pressure was maintained at a lower level and mean venous blood pressure at a higher level during whole body perfusion than at preoperative cardiac catheterization. Mean arterial blood pressure rose as perfusion progressed.

No significant difference was seen between total peripheral resistance during perfusion and at cardiac catheterization.

As perfusion continued, peripheral resistance increased, most markedly in the smaller patients.

Almost all patients had a decrease in body temperature during perfusion, with the temperature of the perfusing blood being the dominant factor.

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