Hemodynamic findings in severe protein-calorie malnutrition[1]

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ABSTRACT This study was undertaken because circulatory disturbances had been advanced as a possible cause of death during initial renourishing of protein-calorie deprived children. Body weight, plasma albumin concentration, intravascular volumes (radiochromium), cardiac index (dye dilution technique), intravascular pressures (flow-guided catheterization), and related hemodynamic parameters were determined at rest in 43 infection-free African children with a form of protein-calorie malnutrition known as marasmic kwashiorkor, and were compared with values observed in 24 convalescent children. The malnourished children showed a prolonged circulation time with a tendency to bradycardia and hypotension; cardiac index, stroke index, and heart work were significantly reduced, as were the intravascular volumes. Hemodynamic data correlated with either body weight or plasma albumin and cardiac index bore a direct relation to red cell volume. In the most severely malnourished subjects, ventricle filling pressures were low and vascular resistances were high. It is inferred that most patients were in an adaptive hypocirculatory state comparable to hypothyroidism, while the most severely malnourished children showed frank peripheral circulatory failure comparable to hypovolemic shock. Circulatory failure on admission was associated with high death rate during treatment but the relation between cause and effect could not be clearly demonstrated. *Am. J. Clin. Nutr.* 30: 334–348, 1977.

The diet of the Shi peasants, who live in a subsistence economy on the Western shore of Lake Kivu (Zaïre, Central Africa), is characterized by chronic energy deficiency, aggravated by periodical protein deficiency (1, 2). Ten to 15% of the general population show clinical or biological signs of malnutrition, and the women's milk production is generally insufficient (3). Shi children are breast fed up to the age of 2, but very soon after birth the mother has to introduce a supplementary vegetable diet that is lacking in proteins. Later on, 10 to 20% of the children develop, mostly between 1 and 6 years, a condition of malnutrition midway between pure protein and pure calorie malnutrition (3, 4). This particular form of undernourishment is one of the facets of protein-calorie malnutrition (PCM) and is classically labeled as marasmic kwashiorkor (1, 5).

Lwiro Pediatric Unit has been set up at the very center of the food-shortage zone, and all severely malnourished children are treated there. Despite intensive classical treatment (6–8), we have to deplore a 20 to 30% mortality, a rate that compares with that registered in numerous other centers working, as we do, without restrictive hospitalization criteria (9–15). Death generally overtakes young patients in the early stages of realimentation. More than half the number of therapeutic failures can be attributed to intractable infections or hydroelectrolytic disturbances (5); the cause of death itself, however, remains unexplained in a number of cases, and notably in patients who die suddenly and unexpectedly.

Early death in children in the refeeding period has often been observed (7), but has never been the subject of a pathogenic study. Because they noticed in malnourished children clinical signs of a low output

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state, some authors have proposed the hypothesis of a cardiovascular process (16, 17). Others have observed in marasmic kwashiorkor electrocardiographic anomalies suggestive of myocardial atrophy (16, 18, 19); this atrophy may be responsible for the modifications of the radiographic image of the heart (20) and might be the cause of the heart failure episodes sometimes registered in the early stages of refeeding (21). However, the few anatomical studies available (21, 22) do not mention any specific myocardial lesion in the acute state of PCM; moreover, the histological anomalies recorded in the heart muscle appear to be proportionally less important than those observed in the skeletal muscle (22). The absence of hemodynamic studies still makes it impossible to reach any valuable conclusion about the functional consequence of the observed anomalies.

The high mortality rate observed in the early stages of the treatment of marasmic kwashiorkor cannot be tolerated, and a thorough study of the causes of death is obviously necessary. This being accepted, a more invasive study of the repercussions of malnutrition on the cardiovascular function was one of the required preliminary steps. The acquisition of a simple, safe technique for monitoring the pressure in the pulmonary circulation, requiring neither radioscopy nor rigid catheter (23), provided a good opportunity to undertake such a study.

Before analyzing the function of the heart muscle, it was essential to establish the characteristics of blood circulation in children with marasmic kwashiorkor. This is our aim in the present work, where the results obtained in 43 cases of marasmic kwashiorkor are collected. The clinical features of those patients have been described in detail in another paper (24) on circulating volumes in malnutrition.

Materials and method

Patients

For our study 43 Shi children with marasmic kwashiorkor were investigated at the Lwiro Children's Unit[3] (altitude 1,700 m or 5,000 feet). Their age ranged from 1.42 to 11.75 years, with a mean of 3.92 years. The main selection criteria were the absence of clinical infection apart from diarrhea, and the presence of at least one clinical sign of marasmic kwashiorkor: edema, hair changes, skin lesions, and weight retardation (Table 1 in (24)). Edema was generalized in 25 patients, moderate in 13, and absent in five. Ten patients had no skin lesion and none had normal hair. Hepatomegaly was a rare finding. According to the local reference curve, height was below the 5 percentile in 20 children, between the 5 and 25 percentiles in 15, and above the 25 percentile in 8; in all but five patients, height was below the 3 percentile of the Boston reference curve. Body weight ranged from 65 to 108% (mean 81%) of the expected weight for height according to the local reference curve, and was far below the 3 percentile of the Boston curve for age in all patients. The plasma albumin concentration ranged from 0.43 to 3.27 g/dl, with a mean of 1.57 g/dl. The venous hematocrit averaged 30.2 vol/100 ml with a 19.7 to 38.7 range, and the blood hemoglobin averaged 9.7 g/dl with a 6.1 to 13.9 range. Figures for serum urea, ionogram, and acid-base equilibrium were unremarkable apart from a slight compensated, hyperchloremic acidosis (1).

Clinical and biological signs of hepatic failure were absent. Hemoglobin electrophoresis was normal and none of the children suffered from malaria, but relatively benign parasitosis (ascaris, *Giardia lamblia*, strongyloides, and trichuris) were common. None of the patients presented evidence of either congenital or acquired heart disease. High values obtained for plasma albumin concentration and body weight belonged to two borderline cases of protein malnutrition (D 450 and 1762) and to a recently cured case of marasmic kwashiorkor (D 1539). The remaining 40 patients showed both clinical and biological features of a long-standing calorie deficiency with superimposed protein deficiency, i.e., of marasmic kwashiorkor.

Malnutrition ranged from slight to severe; with a view to correlating hemodynamic data with the severity of the disease, mild or borderline cases were not rejected, however. For ethical and epidemiological reasons, children with mild malnutrition were fewer and older than the severely malnourished subjects.

The patients were managed from admission in accordance with the routine realimentation scheme established by De Maeyer (8) and Vis (25). Any undesirable interference with this scheme was carefully avoided throughout the study. The diet comprised mainly skimmed milk and local foods (beans, palm-oil, peanuts, rice, bananas, fish, and meat) with neither vitamin nor iron supplement. During the first 24 hr, the children received sufficient amounts of water, electrolytes and glucose to fulfil their requirements by mouth or by feeding-tube. Thereafter foods were progressively introduced, so that 130 cal/kg, 4.5 g/kg of pro-

[3] The Lwiro Children's Unit belongs to the Département de Nutrition de l'Institut pour la Recherche Scientifique en Afrique Centrale (IRSAC), Kivu, Zaïre, and is run in collaboration with the Centre Scientifique et Médical de l'Université Libre de Bruxelles en Afrique Centrale (CEMUBAC). The CEMUBAC is sponsored by the Pediatric Department of the University of Brussels, Belgium.

tein, an 2 mEq/kg of sodium were given daily by the 10th realimentation day. When necessary, potassium supplement and sodium bicarbonate were given to replace actual losses. Parasitosis and acquired infectious episodes were treated specifically. No blood transfusion was given, except later during treatment in a case of severe anemia (D 1754) or when severe circulatory failure seemed imminent (D 1525, 1727, 1734, 1738, 1744, 1747, 1750, 1758). A transient period of parenteral fluid administration was necessary in four curable and 14 incurable patients to maintain their water and electrolyte balance. Preventive antibiotic therapy was given routinely to patients requiring intravenous therapy. Twenty-eight of the 43 subjects recovered and 15 died during realimentation.

The 15 incurable cases (Table 2 in (24)) were the youngest patients (mean age, 2.50 years), and were on admission the most severely malnourished and anemic. Thirteen patients presented generalized edema, and dehydration, if present, was not clinically detectable. Body weight ranged from 65 to 90% (mean, 77%) of the local expected weight for height, and height was below the 5 percentile of the local reference curve for age in 11 patients. Plasma albumin concentration ranged from 0.43 to 1.78, with a mean 1.18 g/dl, and the venous hematocrit averaged 28.6 vol% with a 19.7 to 33.8 range. Serum electrolyte values were not significantly different from values obtained in curable cases. All the incurable patients showed in addition clinical features of a hypocirculatory state: hypothermia, cold extremities, decreased peripheral pulsations, collapsed veins, quiet precordium, and a tendency to bradycardia and low blood pressure. They also exhibited low physical and mental activity; those classical signs of PCM (5–7) could have been ascribed to circulatory failure as well. Until completion of the present study, we were obliged to believe from other sources (21)—not without reserve, however (25)—that severely malnourished patients presented an increase in blood volume with threatening heart failure. The refeeding was therefore carefully conducted and a special effort was made to avoid excess fluid administration; likewise, blood transfusion was postponed, being held as a last, hopeless, remedy. Development of intractable lung infection was regarded as the ultimate cause of therapeutic failure in five patients (D 1203, 1744, 1747, 1750, 1758), who died after 10 to 59 days of treatment. In the other 10, realimentation was hampered by anorexia and diarrhea, and no improvement was noted in spite of tube-feeding, fluid and electrolyte perfusion, and antibiotherapy. In all but two (D 1520 and 1510) of those 10 patients edema and signs of hypocirculatory state remained unchanged throughout the treatment period, without evidence of either dehydration or congestive heart failure, and death supervened after 1 to 16 days of treatment. Biological data were obtained 1 to 24 hr before death in most patients (Table 2 in (24)): there was a further decrease in both venous hematocrit (mean = 24.4 vol/100 ml) and plasma albumin concentration (mean = 0.90 g/dl); mean values for serum potassium, sodium, chloride, and bicarbonate were respectively, 4.3, 144, 109 and 19.0 mEq/liter. Death occurred generally after a progressive slowing-down of heart rate with final cardiac arrest unresponsive to classical resuscitation methods; more particularly, external cardiac massage, blood transfusion, and intravenous injection of atropine sulfate, sodium bicarbonate, and isoproterenol had no effect on the circulatory state of the dying children.

Twenty-four apparently well-nourished Shi children, 9 girls and 15 boys, formed the control group. Their age ranged from 3.42 to 14.00 years, with a mean of 6.84 years. The healthy subjects were chosen on a clinical basis only: absence of acute malnutrition signs and weight above 85% of the expected weight for height. In most of them, however, height was below the 50 percentile of the local reference curve for age; moreover, the plasma albumin concentration was below 3.00 g/dl in 10 subjects and below 2.70 g/dl in five subjects. The control group was therefore not exactly representative of the optimal nutritional status; 15 subjects had in fact been treated for mild malnutrition, more than 1 year before, in the outpatient department. For ethical reasons, age, and sex discrepancy between recovered and sick children was unavoidable. Once informed of the nontherapeutic and uncomfortable aspect of the study, most parents who were asked to give consent refused to collaborate; furthermore, those who finally agreed were reluctant to part from their recovered daughters and never consented to participation of their younger children. The parents interviewed were of course informed that they were free to refuse and that there would be no reward if they gave consent.

Method

The aim of the study was the measurement at rest of both cardiac output and intravascular pressures in children with marasmic kwashiorkor, with intent to correlate the results with both malnutrition criteria and intravascular volumes.

The children were investigated in the morning of the day after admission. They had received from the admission time the routine dietary management, and the usual nocturnal fasting period (6 hr) had been respected. Weight, height, and rectal temperature were measured, and the child was placed in the catheterization room, where the mean ambient temperature was 22.4 C. Either the basilic vein (13 patients) or the saphenous vein (30 patients) was exposed according to classical procedure (26), and a 10-ml venous blood sample was drawn for laboratory determinations and manipulations. The red cell volume was measured first. A right-heart catheterization was then performed; when the flow-guided catheter had entered the pulmonary artery, a teflon needle was inserted into the brachial (13 patients) or femoral artery (30 patients) and pressures were recorded in both pulmonary circulation and systemic artery. The cardiac output was determined by a dye dilution technique between periods of pressure recording. At the end of the procedure, a blood transfusion equal to blood losses (maximum 20 ml) was given and both catheters were removed. However, in very sick patients with catheterization data showing evidence of circulatory failure, the venous catheter was maintained and intravenous therapy was immediately started (D 1511, 1525, 1531, 1532, 1744). As values for both cardiac output and intravascular volumes were not immediately available, no further change was introduced in the dietary routine. The

investigations were conducted under uninterrrupted cardiac monitoring and lasted 1 to 4 hr; the malnourished children slept most of the time and required no sedation; all patients received a 3-day preventive antibiotic treatment. No untoward effect was encountered except in two cases (D 1727 and 1738) showing an abnormally prolonged arterial bleeding after removal of the teflon needle from the femoral artery. Both children required a further blood transfusion to replace losses, and the bleeding stopped after prolonged compression of the vessel; on recovery, about 2 months later, both children had normal arterial pulses, and no arteriovenous fistula was subsequently noted. The elapsed time between investigation and death was 12 hr in one patient (D 1525), 24 hr in two (D 1531 and 1532), and a 5 to 58 day range (mean, 15 days) in the remaining 12. The 21-month-old girl who died early had on admission generalized edema and severe skin lesions; rectal temperature was 35 C and heart rate averaged 56 beats/min; weight was 71% of the local expected weight for height, and height was below the local 5 percentile for age; the plasma protein and albumin concentrations were 2.42 and 0.43 g/dl, respectively; the venous hematocrit was 19.7 vol/100 ml and hyponatremia was present without acidosis. The catheterization data showed a low central venous pressure (−2 mm Hg) with marked systemic hypotension (58/24 mm Hg). The oral diet was immediately replaced by intravenous therapy and a 10 ml per kilogram of blood transfusion was given, but the condition of the child did not improve significantly. However, as shown by the low figures obtained for both total blood volume (50.5 ml/kg) and cardiac index (0.90 1/min m^2) in this case, the therapeutic implications of the catheter study seemed correct. The two children who died 24 hr after the catheter study were also severely malnourished and found to be in circulatory failure; they were given adequate amounts of fluid and electrolytes intravenously to achieve "rehydration," but, again, without any benefit. It is clear that the pressure-monitoring technique per se did not cause death in any patient. On the contrary, it gave accurate information on the circulatory state.

A catheter study was performed in 20 healthy children, and cardiac output was measured in 11. The left basilic vein and the left brachial artery were chosen for catheter and needle insertion. The subjects received a light sedation (chlorpromazine 1 mg/kg by oral route) and blood losses (maximum 20 ml) were not replaced. No untoward effect was encountered; more particularly, heart rhythm disturbances, vessel thrombosis, arterial lesion, and septic complications were not observed.

Techniques

The malnutrition criteria adopted in this study were the plasma albumin concentration determined according to Wolfson et al. (27) and Sonnet and Rodhain (28), and the body weight expressed in percent of the expected weight for height according to local standards (24). In edematous children, the weight taken into account was the "edema-free body weight," i.e., the lowest weight observed during realimentation.

The red cell volume and the total blood volume were determined using a radiochromium technique already described (24) and were expressed in milliliters per square meter of body surface area calculated from height and body weight (29).

The pressures were safely measured in the pulmonary circulation, using a flow-guided catheter technique requiring no fluoroscopic equipment (23). A flexible thin catheter (internal diameter 0.6 mm), a statham P23 Db pressure transducer, and a Philips electromanometer (type 133-4-452) were used. The systolic-diastolic and mean pressures were measured in pulmonary artery wedge, pulmonary artery, right ventricle, and right atrium, according to classical procedure (26). Sixty-three right heart catheterizations were performed. The catheter entered the pulmonary artery in 45 instances (70%) and the pulmonary artery wedge in only 26 instances (41%); preferring a systematic error, we replaced the pulmonary artery wedge pressure by the pulmonary artery diastolic pressure in calculating the vascular resistances. The pulmonary artery wedge pressure, and—failing this—the pulmonary artery diastolic pressure were considered as the indices of the left atrium pressure, and thus of the left ventricle filling pressure (30). The right ventricle filling pressure was the right ventricular end-diastolic pressure. The systolic-diastolic and mean pressures were measured in the systemic artery using the above device connected to a thin teflon needle. The pressures were expressed in millimeters of mercury.

The cardiac output was measured by a classical dye-dilution technique (26, 31) adapted to children and infants according to Hanson and Tabakin (32) and Arcilla et al. (33). The indocyanin-green solution (cardiogreen; Hyson, Westcott and Dunning, Baltimore, Md.) was injected through the venous catheter in either the superior or the inferior vena cava, and arterial blood was withdrawn through the sterilized cuvette of a Philips densitometer (Hb-Oximeter XO-100) by means of a Gilford constant-rate (10.2 ml/min) withdrawal pump (type 1055). The dead space of the sampling system was 0.43 ml. A sequence of six curves was recorded on a 15-min period, blood being returned to the child after inscription of each curve. The densitometer was calibrated with patient's blood and with the dye solution used for injections. The response of the densitometer was linear over the low dye concentrations used in this study and was not affected by either the plasma albumin concentration or the blood hemoglobin concentration. Dilution curves, pressure curves, and electrocardiogram were recorded on a Philips uv oscillograph (Oscilloport E). Cardiac output was measured on each curve according to Kinsman et al. (34) and Hamilton et al. (35), and the results were averaged in each set of curves. The standard deviation of the mean difference between extreme values obtained in each set of curves amounted to 12.4% of the mean output in malnourished children, and to 8.5% in the convalescent group; the standard error of a single measure amounted to 4.1% of the mean output in malnourished patients and to 3.6% in the convalescent children.

The heart rate was averaged on the set of first circulations of dye. The stroke volume was calculated from cardiac output and heart rate, and was converted

TABLE 1

Patients	Age	Weight	Expected weight for height	Weight in percentage of value expected for height	Height	BSA	Plasma albumin concentration	Hematocrit	Right atrium mean pressure	Right ventricle end-diastolic pressure	Pulmonary artery wedge	Pulmonary artery pressure systolic/diastolic (mean)	Systemic artery pressure systolic/diastolic (mean)	Heart rate	Appearance time	Cardiac output	Stroke volume	Total blood volume	Red cell volume
	year/mo	*kg*	*kg*	*%*	*cm*	*m²*	*g/dl*	*vol/100 vol*				*mm/Hg*		*beat/min*	*sec*	*liter/min*	*ml/beat*	*ml/m²*	
Malnourished children																			
D. 003	8.4	12.8	17.5	73	107	0.625	1.93	34.5	1.0	2.1			100/48 (68)	95	8.0	1.69	17.8	1,335	414
D. 450	11.9	21.5	20.3	105	115	0.820	2.53	28.6	6.5	7.5	11.0	28.0/10.3 (17)	124/64 (90)	106	9.0	1.86	17.6	1,812	465
D. 987	8.1	15.3	18.1	84	109	0.685	2.41	33.4	0.5	2.0	8.0	23.0/7.7 (14)	114/62 (78)	109	7.0	1.49	13.6	1,384	416
D. 1203[a]	2.11	5.3	8.1	65	71	0.310	1.25	24.7	−4.0	1.2			94/50 (70)	141	6.0	0.47	3.2	1,041	231
D. 1510	1.10	7.7	9.6	76	76	0.390	1.73	30.7	2.5	5.5	6.5	29.8/7.2 (15)	94/40 (60)	77	7.8	0.61	7.9	1,287	356
D. 1511	1.9	5.5	7.7	71	67	0.312	0.99	29.2	−2	−1			98/54 (74)	99	7.1	0.32	3.2	1,020	268
D. 1512	?	9.3	10.3	90	80	0.443	1.15	27.3		2.7			109/54 (84)	110	6.4	0.74	6.6	1,080	266
D. 1514	6.0	12.1	14.0	86	98	0.580	1.47	30.2	2.5	2.4	6.0	17.2/7.5 (12)	112/65 (88)	109	7.0	1.07	9.7	1,149	313
D. 1518	7.2	10.6	13.3	80	94	0.527	1.76	31.7	2.0	3.4	5.0	20.8/5.0 (14)	118/62 (90)	150	6.6	0.58	3.8	1,205	343
D. 1520	1.8	7.6	8.7	87	72	0.378	1.40	24.0	3.0	6.0		22.5/7.2 (13)	94/38 (62)	134	7.5	0.69	5.1	1,110	266
D. 1522	4.0	9.0	12.5	72	90	0.477	0.93	26.0	0.0	0.0		20.0/2.2 (12)	88/44 (70)	104	6.9	0.59	5.6	1,049	246
D. 1525	1.9	5.6	7.9	71	70	0.323	0.43	19.7	−1.8				58/24 (44)	56	8.3	0.29	5.2	876	156
D. 1527	1.10	6.5	8.1	80	71	0.350	1.69	33.9	0.6	−1.0			82/44 (68)	129	6.9	0.56	4.3	1,034	315
D. 1530	3.0	8.5	9.9	85	77	0.415	2.68	30.8	0.0	3.3	5.0	23.3/6.6 (14)	82/38 (60)	109	8.2	0.69	6.3	1,320	352
D. 1531	3.6	7.0	9.9	71	77	0.382	1.54	33.8	−2.0	0.0			74/26 (50)	65	11.3	0.18	2.8	1,062	323
D. 1532	2.6	6.4	8.8	72	74	0.357	0.80	24.5	–	−3.6			86/34 (60)	95	7.6	0.37	3.8	894	197
D. 1533	11.5	27.7	29.2	94	134	1.000	2.60	32.0	8.0	10.2		24.0/13.4 (19)	122/74 (101)	101	10.3	2.15	21.2	1,557	448
D. 1537[a]	4.0	8.1			87	0.443	2.46	26.0	1.5	7.0				104	7.9	1.15	11.0	1,139	267
D. 1538	5.9	10.4	12.4	84	88	0.495	2.09	31.2	4.0	5.3			100/38 (64)	106	8.7	0.90	8.5	1,287	362
D. 1539	1.8	9.8	9.0	108	75	0.430	3.27	38.7	0.0	4.6			100/56 (80)	137	7.4	1.05	7.6	1,478	514
D. 1540	3.0	10.8	11.3	95	83	0.485	1.59	30.8					104/54 (78)	123	6.4	1.56	12.6	1,443	415
D. 1713	8.0	13.2	16.5	80	104	0.620	1.47	36.4	3.5	3.4		22.7/6.7 (13)	120/60 (90)	107	7.0	1.22	11.5	922	302
D. 1716	8.0	13.5	17.3	78	107	0.640	1.15	31.2	1.5	1.5		28.0/9.0 (19)	80/34 (54)	110	6.8	1.20	10.8	1,245	350
D. 1718	3.7	10.0	12.5	80	90	0.495	1.29	39.7	−1.5	0.0			76/36 (54)	103	6.9	1.01	9.7	1,250	447
D. 1720	7.0	11.9	14.7	81	100	0.580	1.26	29.5	1.5	2.8	6.0	18.7/6.8 (11)	110/44 (72)	83	8.0	1.49	17.6	1,111	295
D. 1721	5.1	9.9	13.5	73	96	0.515	0.56	35.7	1.0	1.0		28.0/7.2 (14)	106/50 (82)	108	7.9	0.61	5.5	921	296
D. 1724	3.0	8.0	9.5	84	75	0.395	1.31	23.5	3.0	6.3		29.3/9.7 (17)	110/56 (84)	107	6.2	0.97	8.9	1,261	267
D. 1725	1.6	6.3	8.7	72	72	0.348	1.52	27.7	0.0	2.8		25.1/7.2 (15)	100/54 (72)	101	7.2	0.54	5.2	1,187	296
D. 1727	4.0	8.8	11.6	76	84	0.450	0.96	23.5	3.0	4.3			111/56 (85)	96	6.9	0.82	8.5	1,050	222
D. 1730	3.4	10.2	11.4	89	84	0.475	1.32	31.0	0.5	2.1	3.5	17.1/3.9 (10)	88/38 (60)	98	7.0	0.86	8.7	1,239	346
D. 1734	4.6	9.3	12.0	77	86	0.465	1.31	30.2	−1.0	1.4	3.0	22.9/7.0 (14)	94/44 (68)	115	5.1	0.80	6.8	1,143	311
D. 1738	1.6	4.4	6.2	71	60	0.262	1.47	27.7	1.0	−0.3			106/46 (75)	96	5.8	0.62	6.4	908	287

TABLE 1—*Continued*

D. 1740	3.0	8.0	9.2	87	76	0.388	1.51	29.0	1.0	3.9	8.0	22.6/5.7	(14)	100/48 (68)	108	5.2	0.85	7.8	1,214	317
D. 1742	1.11	9.4	9.9	95	77	0.433	2.35	36.2	1.0	1.8	6.0	22.0/9.6	(16)	96/52 (72)	125	6.1	1.19	9.4	1,451	474
D. 1744	2.0	6.0	8.7	69	72	0.340	1.78	29.7	−3.0	−2.0		18.0/4.0	(9)	76/36 (56)	118	6.3	0.48	3.9	1,150	310
D. 1745	?	6.4	8.2	74	71	0.334	1.45	30.7	1.5	4.5				86/44 (60)	107	5.4	0.68	6.3	1,176	325
D. 1747	4.6	8.8	11.7	75	85	0.450	1.18	25.0	−1.0	0.5	0.0	20.0/4.0	(12)	76/30 (50)	117	4.9	0.69	5.8	1,169	263
D. 1750	1.8	7.0	8.9	84	73	0.368	1.20	27.7	−1.0	1.0	3.0	26.4/8.2	(16)	92/43 (64)	95	6.2	0.87	9.1	1,062	265
D. 1752	2.6	8.0	9.9	80	77	0.405	1.14	37.5	−2.0	−0.2	5.0	20.4/6.2	(12)	100/42 (66)	114	6.9	0.75	6.5	1,070	361
D. 1754[a]	2.6	9.4			86	0.466	0.95	32.0	0.0	−0.2		18.5/6.2	(10)	96/46 (68)	123	6.1	1.34	10.9	1,130	325
D. 1757	4.4	8.9	12.0	74	86	0.460	1.88	30.7	3.0	5.4				116/50 (76)	97	5.8	1.12	11.5	1,337	370
D. 1758	1.5	7.5	8.5	88	71	0.370	0.85	31.5	−1.0	0.3		17.3/6.3	(10)	106/50 (80)	116	6.3	0.65	5.5	983	279
D. 1762	3.2	10.6	11.3	93	83	0.480	2.79		2.0	4.0		26.5/8.2	(16)	116/60 (84)	86	5.7	1.13	13.1		
Convalescent children																				
CQ 221	5.10	15.3	16.4	93	104	0.660	3.02	35.3	2.0	5.7		26.2/10.0	(17)	130/60 (90)	105	6.4	2.01	19.0	1,819	577
D. 528	11.0	23.6	26.0	90	126	0.920	3.30	44.0	3.0	4.0	9.0	25.0/8.2	(18)	18/86 (114)	96					
D. 760	?	15.8	17.4	90	107	0.687	2.73	40.0	4.0	7.0	9.0	29.0/9.0	(20)	136/66 (100)	100					
CM 914	6.0	16.3	15.8	103	103	0.680	3.29	38.0	−1.0	0.5		31.5/9.5	(19)	122/74 (98)	100					
D. 934	7.0	15.5	16.1	96	106	0.675	3.47	40.0	0.0	2.0		30.5/9.0	(21)	114/68 (90)	150					
D. 936	5.0	18.0	17.5	103	108	0.726	3.36	39.3	4.0	4.0				114/54 (78)	150				1,720	609
D. 965	3.6	12.7	12.0	106	87	0.539	3.39	33.0											1,773	527
CM1011	6.0	17.5	16.6	105	105	0.703	3.82	40.0	5.5	7.0	11.0	31.0/14.0	(21)	134/84 (104)	125				1,681	605
D. 1085	3.6	13.0	12.5	104	88	0.550	2.79	34.0	1.5	3.0	6.0	29.0/8.0	(18)	110/54 (76)	101	6.3	1.58	15.6	1,645	503
D. 1089	5.10	15.6	14.8	105	99	0.645	2.94	33.3	3.0	1.5		30.0/9.0	(16)	140/76 (102)	138	5.4	2.86	20.5	1,534	459
D. 1093	3.8	12.1	12.7	95	89	0.538	3.10	41.0	0.0	2.7	8.5	30.0/7.0	(16)	100/50 (70)	83	7.1	1.25	15.0	1,507	556
D. 1128	6.2	13.1	14.4	90	98	0.593	2.76	35.0	2.5	2.5	8.0	330/14.0	(24)		126	5.5	1.92	15.2	1,557	490
D. 1168	5.10	12.0	13.7	86	98	0.570	2.49	35.0	1.0	2.0	4.0	31.0/8.0	(16)	113/66 (84)	127	6.4	1.63	12.8		
D. 1276	5.7	13.8	12.7	108	91	0.559	2.43	31.0	2.5	4.6	7.0	25.0/12.0	(19)	120/60 (86)	126	5.5	2.01	15.9		
D. 1336	11.0	27.0	26.0	104	127	0.960	3.90	48.0											2,071	895
D. 1468	4.7	11.8	13.7	84	95	0.535	2.60	32.0	−1.0	3.6		32.0/11.0	(20)	112/52 (80)	123	6.0	1.74	14.0		
D. 1504	10.0	23.1	21.4	108	117	0.860	3.91	48.0											1,961	847
D. 1546	8.0	17.0	19.6	85	114	0.740	3.55	39.0	5.0	7.0	8.0	29.0/12.0	(20)	124/68 (90)	110					
D. 1548	14.0	30.8	34.5	88	143	1.130	3.37	42.2	6.0	9.0	13.0	38.0/17.0	(27)	126/66 (102)	105				1,926	732
D. 1550	3.5	11.6	11.5	101	85	0.508	3.09	?	0.0	3.5		31.0/12.5	(22)	134/64 (86)						
D. 1560	6.6	16.6	16.6	100	105	0.690	2.64	36.5	2.0	4.0	4.0	18.0/7.0	(12)	110/60 (84)	105	7.1	2.38	22.6	1,666	547
D. 1611	5.8	12.2	12.8	95	90	0.540	2.76	38.8	0.5	2.5	6.0	30.0/11.0	(18)	120/80 (100)	125	7.1	2.41	19.1	1,738	607
D. 1693	5.10	14.4	13.4	107	95	0.603	2.45	35.0	3.0	4.0		23.0/11.0	(17)	112/70 (88)	102	5.8	1.55	15.1		
KT[b]	12.0	29.0	?	?	147	1.128	4.02	46.0											2,189	906

[a] Underlined figures show incurable cases. [b] Tutsi child.

into stroke index, in milliliters per beat and m^2 body surface area (BSA). The appearance time of the dye, in seconds, was averaged on each set of curves and was taken as an index of the circulation time after correction was made for sampling distorsion (36). The left ventricle work (LVW) was calculated from LVW = 0.0135 × cardiac output × systemic artery mean pressure, and was expressed in kilogram-meters; it was converted into LVW index, in kilogram-meters per m^2 BSA. The left ventricle stroke work (LVSW) was calculated from: LVSW = 0.0135 × stroke volume × systemic artery mean pressure, and was expressed in gram-meters. It was converted into LVSW index, in gram-meters per m^2 BSA. The systemic vascular resistances (SVR) were calculated from:

$$SVR = \frac{\text{systemic artery mean pressure} - \text{right ventricular end-diastolic pressure}}{\text{cardiac output}}$$

and were expressed in arbitrary units (mm Hg min/1). The pulmonary vascular resistances (PVR) were calculated from:

$$PRV = \frac{\text{pulmonary artery mean pressure} - \text{pulmonary artery diastolic pressure}}{\text{cardiac output}}$$

and were also expressed in arbitrary units.

Presentation of the data

Individual data of both malnourished and convalescent children are listed in table 1[4]. The data obtained in malnourished patients were averaged and were compared with values obtained in the control group, using the Student's *t* test (Table 2). The data obtained in two subgroups of patients of similar height were also analyzed (Table 3). The heart rate of malnourished patients was graphically compared with American standards for age (37 to 39) and also with heart rates observed in 90 well nourished Shi children belonging to an electrocardiographic survey (P. Viart, A. Gallez, unpublished observations) (Fig. 1). The blood-pressure values were similarly compared with American Standard for age (Fig. 2) (37 to 39). The pressures in the pulmonary circulation of convalescent children were compared with the pressures obtained, using an identical technique, in healthy sea-level-resident Belgian children (23). Correlation coefficients were calculated for linear relationship between cardiac or stroke indices on the one hand, and either malnutrition criteria or intravascular volumes on the other (Table 4).

Results

Convalescent children (Tables 2 and 3).

The convalescent Shi children showed a slight pulmonary hypertension (mean pressure was 18.9 ± 2.2 mm Hg[5] in the pulmonary artery) in comparison with sea-level-resident Belgian children (12.5 ± 1.9 mm Hg[5], $P < 0.001$). The systemic blood pressure was also above range for normal American children (Fig. 2). Heart rate (Fig. 1) and figures for other hemodynamic data were within accepted normal range.

Malnourished patients (Tables 2 to 4)

The hemodynamic data were as a whole abnormal in malnourished children when compared with those obtained in convalescent subjects (Tables 2 and 3). The red cell volume averaged 51%, and the total blood volume 66% of the values observed in convalescents; systemic hypotension (Fig. 1) and bradycardia (Fig. 2) were a frequent but not systematic finding; the appearance time of dye was prolonged; cardiac and stroke indices averaged 58 and 62%, respectively, of the values found in convalescents, and both ventricle filling pressures were low; the lowest figures were obtained for the indices of the heart physical work; the systemic and pulmonary vascular resistances were elevated in the same proportion. The differences in absolute values observed between malnourished and convalescent children of the same height (Table 3) were equally significant.

There was a positive correlation between cardiac index and either body weight or plasma albumin concentration, but not between stroke index and both malnutrition criteria (Table 4). The correlation between cardiac index and red cell volume was positive and significant, while no relation was found to exist between cardiac index and venous hematocrit (Fig. 3). An inverse relation existed between systemic vascular resistances and total blood volume; however, a direct relation existed also between total blood volume and either body weight or plasma albumin concentration (Table 4).

[4] Table 1 has been filed with the National Auxiliary Publication Service of the American Society for Information Science, care of CCM Information Sciences Incorporated, 22 West 34th Street, New York City, 10001 U.S.A.

[5] Mean and interval of confidence of the mean. ($P < 0.01$)

TABLE 2
Hemodynamic parameters (mean ± standard error of the mean) in malnourished and convalescent children[a]

	Malnourished children	Convalescent children
Age range (years)	1.42 - 11.75	3.50 - 14.00
Weight in percent of expected weight for height	81 ± 2	98 ± 2
Plasma albumin concentration (g/dl)	1.57 ± 0.10	3.13 ± 0.13
Red cell volume (ml/m²)	323 ± 12	633 ± 40
Total blood volume (ml/m²)	1179 ± 29	1771 ± 54
Pressures (mm Hg)		
Right atrium (mean)	0.9 ± 0.4	2.2 ± 0.5
right ventricle: systolic	25.0 ± 0.8	31.3 ± 0.7
end-diastolic	2.5 ± 0.4	4.0 ± 0.5
pulmonary artery: systolic	22.7 ± 0.7	28.9 ± 1.0
diastolic	7.0 ± 0.4	10.4 ± 0.6
mean	13.7 ± 0.5	18.9 ± 0.8
pulmonary artery wedge (mean)	5.4 ± 0.7	7.8 ± 0.8
systemic artery: systolic	94 ± 2	122 ± 3
diastolic	47 ± 2	66 ± 3
mean	71 ± 2	91 ± 3
Heart rate (beat/min)	107 ± 3	115 ± 5
Appearance time (sec)	7.1 ± 0.2	6.1 ± 0.2
Cardiac index (1/min m²)	1.90 ± 0.09	3.27 ± 0.20
Stroke index (ml/beat m²)	17.7 ± 0.9	28.3 ± 1.1
Left ventricle work index (kg/m²)	1.8 ± 0.1	3.9 ± 0.6
Left ventricle stroke work index (g/m²)	17 ± 1	34 ± 3
Ratio pulmonary/systemic vascular resistances	0.09	0.10

[a] Differences between malnourished and convalescent children are all statistically significant ($P < 0.01$), except for underlined figures ($0.01 < P < 0.05$)

TABLE 3
Hemodynamic parameters (mean absolute values) in malnourished and convalescent children of the same height[a]

	Malnourished children	Convalescent children
Number of patients	10	10
Age (years)	5.90	5.24
Height (cm)	95	95
Body surface area (m²)	0.539	0.579
Weight,[b] in percent of the expected weight for height	79	97
Plasma albumin concentration (g/dl)	1.33	2.73
Total blood volume[c] (ml)	608	960
Right ventricle end-diastolic pressure (mm Hg)	2.1	3.2
Pulmonary artery diastolic pressure (mm Hg)	6.4	10.1
Systemic artery mean pressure (mm Hg)	73	86
Heart rate (beat/min)	110	115
Appearance time (sec)	7.1	6.1
Cardiac output (1/min)	0.95	1.90
Stroke volume (ml/beat)	8.9	16.2
Left ventricle stroke work (gm/beat)	8.7	19.1
Systemic resistances (mm Hg min/liter)	86.7	42.3

[a] Differences between malnourished and healthy children are all statistically significant ($P < 0.01$), except for underlined figures. [b] Weight for malnourished children is the edema-free body weight. [c] The number of control values for total blood volume is 7 instead of 10.

Correlation between cardiac output and body surface area

The linear correlation between cardiac output (CO) and BSA was not very significant in convalescent children ($r = 0.54, n = 11$; $CO = 4.60 \times BSA - 0.77$), owing to the narrow range of body surface area (0.535 to 0.690 m²), and the rather large coefficient of variation (20.8%) of the cardiac index in this group.

The correlation coefficient amounted to

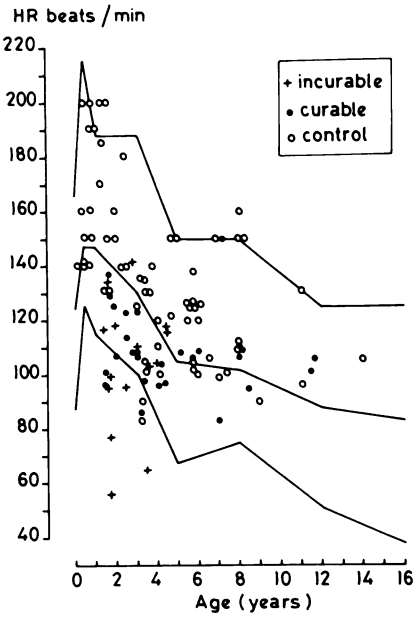

FIG. 1. Heart rates (HR) versus age, observed at rest in 43 malnourished (curable and incurable cases), and in 90 healthy (control) Shi children. *Continuous lines* show the average heart rate (*middle line*), and the upper limit (*upper line*), and lower limit (*lower line*) of the heart-rate range obtained in normal American children at rest (37).

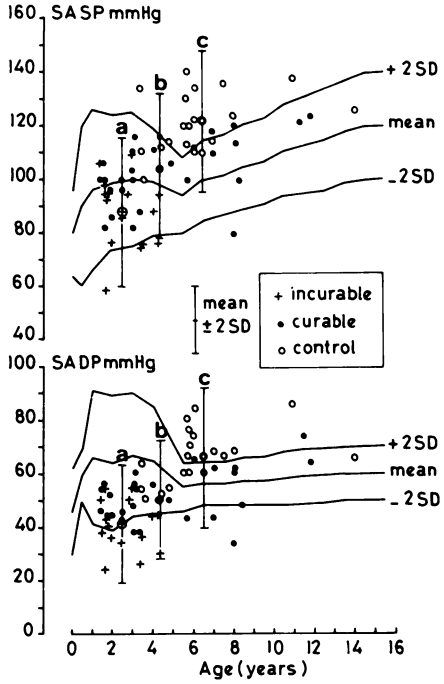

FIG. 2. Intraarterial systolic blood pressure (SASP) and diastolic blood pressure (SADP) observed as a function of age in 43 malnourished (curable and incurable cases) and in 20 recovered (control) Shi children. *Vertical lines a, b* and *c* show the blood pressure range (mean ± 2 SD) observed in incurable, curable, and control patients, respectively. *Continuous lines* show the blood pressure range (mean ± 2 SD) obtained by indirect measurement in normal American children (38, 39).

0.82 (n = 28) in curable children, and the mean cardiac index in this subgroup (2.13 1/min m^2) did not differ significantly from the slope of the regression line relating cardiac output to body surface area (CO = 2.21 × BSA − 0.03). The correlation was also significant in incurable patients (r = 0.66, n = 15), but the mean cardiac index (1.46 1/min m^2) in this subgroup was different from the slope of the regression line (CO = 2.46 × BSA − 0.38).

Discussion

Significance of hemodynamic parameters related to BSA

Although desirable, it was not possible to establish a multiple regression equation for prediction of cardiac output (40) in the present study. Consequently, the cardiac output and derived parameters were related to the anthropometric reference most commonly used, namely the body surface area (40–42). As the relationship between cardiac output and BSA is not a linear function of growth (41–43), such related values are not wholly suitable for strict interpretation. Moreover, the BSA-prediction formula (29, 44) proved less accurate in the 0.30 to 0.60 m^2 range (41, 42), to which belonged most of the patients investigated in this study.

In spite of this, the correlations found between cardiac output and BSA were highly significant in our patients. Furthermore, as indicated by the analysis of data obtained in subgroups of patients of similar morphology (Table 3), the bias introduced was insufficient to alter the significance of the results.

This does not mean, however, that BSA was the reference parameter of choice for interpretation of hemodynamic changes in malnutrition. The unit of surface area corresponds to fewer active cells in marasmic kwashiorkor because of changes in the body

composition (5, 45, 46). Consequently, an underestimation of the circulatory function per unit of active-cell mass was introduced when hemodynamic data of malnourished children were related to BSA. As the size and the metabolism of the active-cell mass were not determined in this study, the changes observed were only significant in comparison with age, and not necessarily in comparison with the actual circulatory load.

Convalescent children

An increase in pulmonary vascular resistances is known to persist in children living in an environment of chronic hypoxia (47–49). As the Shi territory lies about 2,000 m (6,000 feet) above sea level, the moderate increase in pulmonary artery pressure found in our convalescent subjects was predictable. The figures for pulmonary vascular resistances were even slightly underestimated, as pulmonary artery diastolic pressure was substituted for the left atrium pressure in calculating resistances. There was in addition a definite tendency to systemic hypertension in the convalescent group (Fig. 2). This was true not only in comparison with indirectly established standards (37–39, 50), but also in comparison with normal figures given for intra-arterial measurement of blood pressure (51). It is likely that in the present study incomplete relaxation of the

TABLE 4
Correlation coefficient values[a]

	Weight, in percent of the expected weight for height	Plasma albumin concentration	Red cell volume	Total blood volume
		g/dl	*ml/m²*	
Cardiac index, in liter/min m²	0.68 (n = 54)	0.64 (n = 54)	0.68 (n = 53)	0.70 (n = 53)
Stroke index, in ml/beat m²	0.59 (n = 54)	0.33 (n = 54)	0.63 (n = 53)	0.65 (n = 53)
Total blood volume, in ml/m²	0.80 (n = 56)	0.90 (n = 56)		

[a] Control values were included in calculation, n = number of paired data.

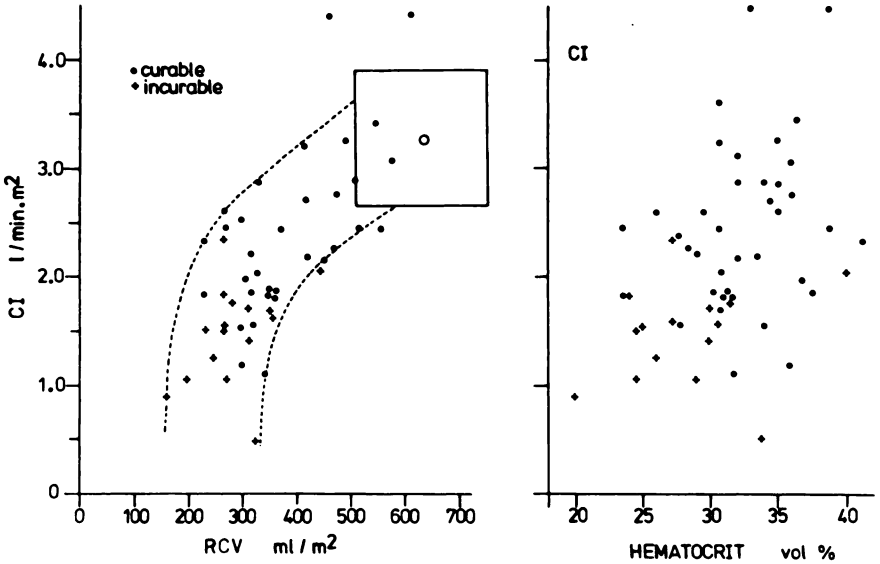

FIG. 3. Relationship between cardiac index (CI) and red cell volume (RCV) (*left*), and between CI and hematocrit (*right*) in 42 Shi children suffering from marasmic kwashiorkor (curable and incurable cases). The *framed area* represents the confidence limits of the mean control values. As suggested by the *dotted lines*, the relationship between CI and RCV is no longer linear for the lowest values, although the linear correlation coefficient obtained for all the data was significant (r = 0.68, n = 49).

patients was responsible for the fact. On the other hand, the figures for other hemodynamic parameters in convalescents compare with figures given for healthy American children (41, 42, 52–58).

Malnourished children

The results clearly show that children suffering from marasmic kwashiorkor exhibit a hypocirculatory state for age. The influence of calorie malnutrition on the circulation has been studied in adult prisoners of war (59–67). Bradycardia, prolonged circulation time, low central venous pressure, systemic hypotension, and a decreased cardiac output were the main findings in those patients.

In their exhaustive experiment on adult volunteers, Keys et al. (68) likewise demonstrated that both the blood volume and the ventricle ejection fraction were normal in marasmic patients, and that the decrease in physical work of the heart was proportional to the decrease in circulatory load; from this, they concluded that hemodynamic changes were for the greater part an adaptive phenomenon in marasmus. Recent experimental data corroborated this opinion (69, 70). Hemodynamic studies are fewer in infantile malnutrition. The circulation of marasmic infants was studied by Kerpel-Fronius and Varga (71): these authors found that both cardiac output and ventricular performance were lowered in their patients but they were aware of the difficulty of interpretation arising from the changes in body composition. Alleyne (72) recently measured the cardiac output in protein calorie-depleted children; although his finding of a low output with prolonged circulation time was significant, the study was not conclusive for want of correlation with either malnutrition criteria or other hemodynamic parameters. It also appears from these various observations that global malnutrition—whatever its pattern—tends to depress the circulatory function. The results of the present study show that marasmic kwashiorkor does not escape that general tendency.

The hemodynamic characteristics of the malnourished subjects were as a whole comparable with the changes described in hypothyroidism (73–75): bradycardia, prolonged circulation time, low cardiac output, and elevated vascular resistances with normal ventricle filling pressures are indeed well-documented features in myxedematous patients. The presence of a lowered oxygen consumption in protein calorie malnutrition (76, 77) reinforces the analogy. Moreover, cardiac output classically bears an inverse relation to both the red cell volume and the hematocrit in anemic well-nourished subjects (78–80); if marasmic kwashiorkor anemia proves adaptive (45, 81) the red cell volume is then an index of the residual active cell mass, and the direct relation that cardiac index bore to red cell volume in this study (Fig. 3) suggests that the circulation was adapted to a lowered circulatory load in most patients. However, the relationship depicted in Figure 3 is not perfectly linear, and the reduction of cardiac index tends to be greater than the reduction of red cell volume for the lowest values. Consequently, it is not impossible that the circulatory function was unadapted to metabolic requirements in a few subjects. Confirmation of this would of course require oxymetric determinations, especially as the function of residual "active" cell mass could be impaired in severe malnutrition (82). On the other hand, the lack of correlation between hematocrit and cardiac index (Fig. 3) is not surprising and again lays emphasis on the plasma volume changes induced by the malnutrition process (24).

That the circulation really was insufficient in a few patients is further suggested by data obtained in children who subsequently died (Table 5). Not only were those subjects severely malnourished, but they also showed on admission clinical and hemodynamic features of severe peripheral circulatory failure, as seen in endotoxic (83, 84) or hypovolemic (85, 86) shock: low cardiac and stroke indices, high vascular resistances, and collapsed ventricle filling pressures. The inverse relation that systemic resistances bore to total blood volume suggests that hypovolemia is involved in marasmic kwashiorkor. On the other hand, as most incurable children showed no improvement after intravenous fluid therapy was begun, hypovolemia could hardly be regarded as the single cause of the circulatory impairment, and the possible role of inconspicuous septi-

TABLE 5
Hemodynamic parameters (mean values) in curable and incurable malnourished patients at time of admission to the hospital[a]

	Incurable patients	Curable patients	Convalescent children
Number of patients	15	28	11-24[b]
Age (years)	2.50	4.58	5.33-6.83
Weight, in percent of the expected weight for height	77	84	98
Plasma albumin concentration (g/dl)	1.18	1.71	3.13
Total blood volume (ml/m²)	1059	1236	1771
Right ventricle end-diastolic pressure (mm Hg)	0.7	(3.4)	(4.0)
Pulmonary artery diastolic pressure (mm Hg)	6.1	7.5	10.4
Cardiac index (l/min m²)	1.46	2.13	3.27
Left ventricle stroke work index (g/beat m²)	12	21	34
Systemic vascular resistances (mm Hg min/liter)	124	79	47

[a] Differences between incurable and curable children are all statistically significant ($P < 0.01$), except for underlined values; differences between convalescent children and either curable or incurable children are all significant ($P < 0.01$), except for values in parentheses. [b] According to the parameter studied, the number of available control data ranged from 11 to 24.

cemia has also to be considered. Furthermore, both vascular resistances and total blood volume correlated with malnutrition criteria as well (Table 4), so that the exact cause of the circulatory failure remains unclear. The difficulty of interpretation is further reinforced by the changes in body composition that altered the physiological meaning of the data related to body surface area.

While the mechanism leading to circulatory failure is probably complex in marasmic kwashiorkor, there appears to be a threshold of malnutrition at which it comes into action. This is supported by the relationships depicted in Figure 4, in so far as the plasma albumin concentration was a reliable index of the nutritional status (87, 88) in our patients: in that graph, data obtained in the 43 malnourished and the 24 convalescent children were grouped and averaged in eight class-intervals of plasma albumin concentration, and the averages were replotted against the midpoints of each class interval: hemodynamic changes associated with a decreasing plasma albumin concentration were thus illustrated. As long as plasma albumin concentration remained above 1.5 g/dl, cardiac output and red cell volume decreased in the same proportion, while vascular resistances and central venous pressure (i.e., right atrium mean pressure) remained near normal. Below 1.5 g/dl, a drop in central venous pressure and a rise in resistances took place, while the decrease in cardiac output finally exceeded the decrease in red

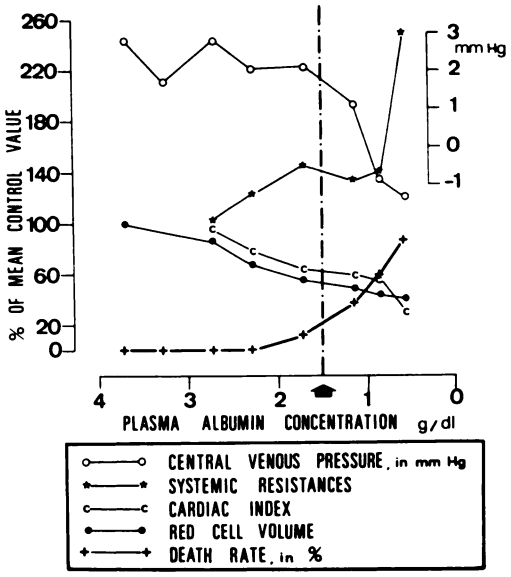

FIG. 4. Relationships between plasma albumin concentration and hemodynamic parameters observed before treatment in 43 malnourished and 24 convalescent Shi children. The death rate observed during treatment is also shown. See text.

cell volume. It thus appears that the transition from an adapted circulatory state to frank circulatory failure took place when the albumin concentration reached a crucial level of 1.5 g/dl. In addition, circulatory failure in the acute state of the disease was associated with poor prognosis, as shown in Figure 5 by the rise in the death rate. This does not mean, however, that circulatory failure was the cause of death, especially as

a rather long period of time elapsed in most cases between the time of the catheter study and the time of death. In fact, the real cause of death remained unknown in patients who received continuous intravenous therapy and prophylactic antibiotherapy—although clinically free of infection. One hypothesis is that the impairment of the blood flow before the start of treatment had produced a breakdown of adaptation, resulting in irreversible metabolic changes at tissular level. If this proves true, the condition would be beyond available therapeutic means, and further study dealing with the exact cause of the circulatory failure in marasmic kwashiorkor should be undertaken before a more effective treatment can be proposed.

The myocardial function was not studied in the present work. It is clear, however, that the heart played no direct role in the circulatory disturbances observed before treatment: its functional reserve indeed was sufficient to meet the very low circulatory load encountered in marasmic kwashiorkor. This does not prove that the contractility of the malnourished myocardium was normal. Furthermore, nothing can be said about the response of the heart muscle during the stress of realimentation, and above all, of intravenous therapy; although we observed no clinical sign of heart failure in children who died, the possibility of a myocardial inadequacy has not been ruled out. This would require, in fact, sequential hemodynamic and myodynamic investigation throughout the refeeding period.

Summary

Cardiac output, intravascular pressures, and circulating volumes were determined at rest and before the start of realimentation in 43 African children with a form of PCM known as marasmic kwashiorkor, and were compared with data obtained in 24 convalescent subjects. When related to the body surface area, the results showed that a progressive transition from an adaptive hypocirculatory state to a frank peripheral circulatory failure took place in malnourished children as their nutritional condition worsened. Although hypovolemia might have been responsible, the exact cause of the circulatory failure remained unclear, but it was evident that the heart played no direct role. The children with circulatory failure on admission were also the most severely malnourished; most of them died despite intravenous therapy, suggesting that irreversible metabolic changes had taken place at cellular level before treatment, through breakdown of adaptation.

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