MATURATION OF RENAL FUNCTION IN CHILDHOOD:[1, 2] CLEARANCE STUDIES

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Evidence has been presented by several investigators that functional capacity of the kidney in the premature and young infant is lower than in older children and adults. Schoenthal (1) using urea clearance, McCance and Young (2) urea and inulin clearances, Barnett (3) inulin clearance, and Gordon, Harrison and McNamara (4) urea clearance, showed that the infant had a lower glomerular function when compared to the adult on the basis of a unit of surface area. Recently West *et al.* (5) reported a study of renal function in infants during the first two years of life and Barnett *et al.* (6), a study in premature infants. This present study was begun in 1945 to determine the rate of maturation of certain of the kidney functions from the newborn period through childhood. The following functions were estimated: glomerular filtration rate, maximal tubular excretory capacity for para-amino-hippurate, urea clearance, and effective renal plasma flow.[3] Sixty-three normal well children between the ages of two days and 12 years were studied.

METHODS

G.F. was determined as mannitol clearance by the single injection technique. A 20 minute period was allowed for equilibration before the first specimen was collected. The blood levels were plotted against time on semi-logarithmic paper; the blood level at the midpoint of each urine collection period, minus two minutes, read off the resulting curve. The mannitol levels in the blood when so plotted always formed a straight sloping line (a minimum of three and in the majority of instances four levels were determined). There was no evidence of lack of equilibration of mannitol in the body fluids after the period allowed. P.F. was determined simultaneously as the clearance of sodium para-amino-hippurate (PAH) at low plasma levels (between 0.5 and 3 mg. per 100 cc. of plasma); the tubular excretory capacity was determined by the excretion of PAH at high blood levels (between 50 and 100 mg. per 100 cc. of plasma). In several instances the Tm_{PAH} was calculated using the values for glomerular filtration rate determined in previous periods. In 27 instances where the Tm_{PAH} was determined simultaneously with the last period of mannitol clearance, the value for glomerular filtration rate was not influenced by the high concentration of plasma PAH. The blood level of PAH was maintained by a priming injection and a continuous intravenous infusion. The priming solution of PAH for Tm determination was always diluted in the syringe to three to four times its volume, either with the dilute solution remaining in the infusion tubing or with saline, and injected as slowly as possible. In larger children, where the volume might have been too large for a syringe, the priming solution was allowed to run in through the infusion tubing from an open burette flask. When injected rapidly and in concentrated form, this amount of PAH solution may cause a sensation of intense heat, involuntary defecation, nausea, vomiting, abdominal pain or pain in the extremity used for injection. With the technique just described, these reactions were usually mild or absent; with one exception they ceased shortly after completion of the priming injection. They seemed to be milder in infants than in older children. The test was started in the morning, after the child had had a light breakfast or, in the case of infants, a bottle one to three hours previously and was well hydrated.

The laboratory determinations of mannitol and PAH were carried out according to the methods outlined by Smith *et al.* (7, 8). Two modifications were used: (*1*) The deproteinization was performed by the Somogyi

[1] Presented before the Society for Pediatric Research, Stockbridge, Mass., May 1947, and exhibited at the Fifth International Congress of Pediatrics, New York City, July 1947.

[2] The mannitol and para-amino-hippurate used in these studies were kindly furnished to us through the courtesy of Sharp & Dohme, Inc., Glenolden, Pennsylvania.

[3] These abbreviations are used throughout the paper:

G.F. = glomerular filtration rate
P.F. = effective renal plasma flow
Tm_{PAH} = maximal tubular excretory capacity for para-amino-hippurate
F.F. = filtration fraction
PAH = para-amino-hippurate

method (one part plasma or, for mannitol, two parts yeasted plasma dilution, 10 parts distilled water, two parts 0.3 N barium hydroxide solution, two parts 5% zinc sulfate solution). (*2*) For the determination of mannitol the mixtures of plasma filtrate and acid periodate solution were left at room temperature overnight instead of being heated in a boiling water bath for 20 minutes prior to titration.[4]

The standard error of the mannitol clearance determination in a combined series of 75 tests with four periods each plus 60 tests with three periods each was 5.7 cc. with a mean error of 4.73 cc. $\pm$ 0.49. The standard error of 103 determinations of renal plasma flow by PAH clearance with three periods each was 55.2 cc./min. with a mean error of 39.75 cc. $\pm$ 6.44. The standard error of 112 determinations of the tubular excretory capacity for PAH, with three periods in each test, was 5.85 mg./min. with a mean error of 3.75 mg. $\pm$ 0.55. These errors include both the laboratory determination and the bedside technique, such as urine collection, timing of specimens, etc.

The urea clearance was determined simultaneously with the mannitol clearance for three periods in each test. Urea was determined in blood and urine with urease by the aeration method of Van Slyke and Cullen (10), but with boric acid substituted for the standard mineral acid in the receiving flask. Toward the end of this study, Conway's micro-method with urease, as modified by Steinitz (11), was substituted for the Van Slyke and Cullen method. Both methods give identical results.

It must be made clear that these tests were performed with a relatively high urine flow, resulting from the diuresis produced by mannitol and the intravenous infusion. This high urine flow does not alter the clearance rates greatly, with the exception of the urea clearance which may be somewhat higher than under ordinary conditions. Most of the tests were performed on quiet or sleeping children and, therefore, were presumably not unduly influenced by circulatory changes. Prolonged periods of starvation before performing the test were not deemed necessary. We found that the children were much quieter during the test if they were not hungry.

RESULTS

In Figure 1A we have graphically presented the glomerular filtration rates obtained at different ages throughout the first year. In Figure 1B the glomerular filtration rates of the children over one year of age are recorded in a similar fashion. Table I, column 11, gives the actual values for

[4] Note: Incidentally this modification, which in our hands gave more constant results than the original method, may account for the fact that there is no evidence in our figures of the interference of high levels of PAH with the mannitol determination. Other investigators have recently reported such an interference (9).

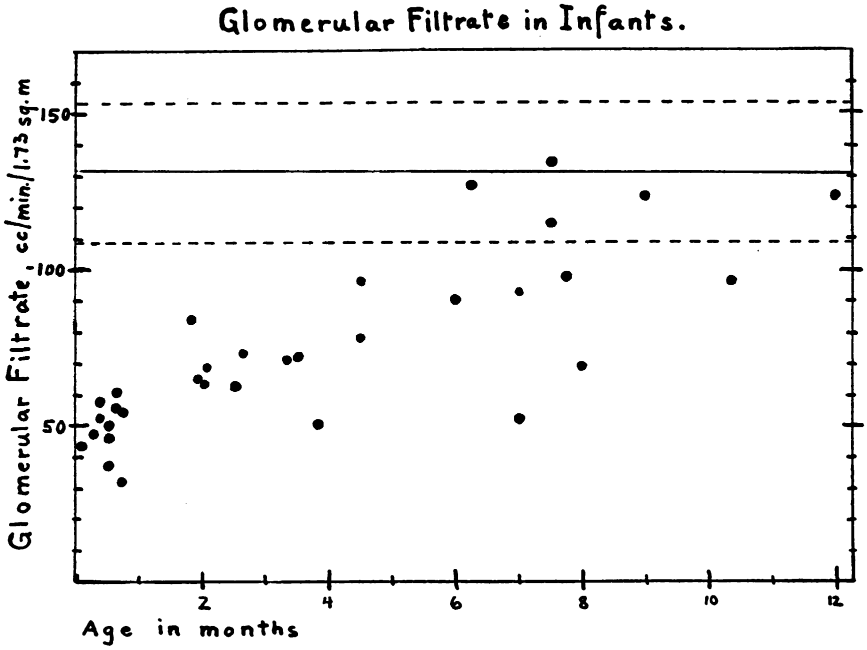

FIG. 1A. GLOMERULAR FILTRATION RATE IN INFANTS

Each dot represents the average value in an individual child. The horizontal line represents the mean adult value of the glomerular filtration rate of an adult with a surface area of 1.73 sq.m. The broken lines represent one standard deviation from this mean, as determined in adults (12).

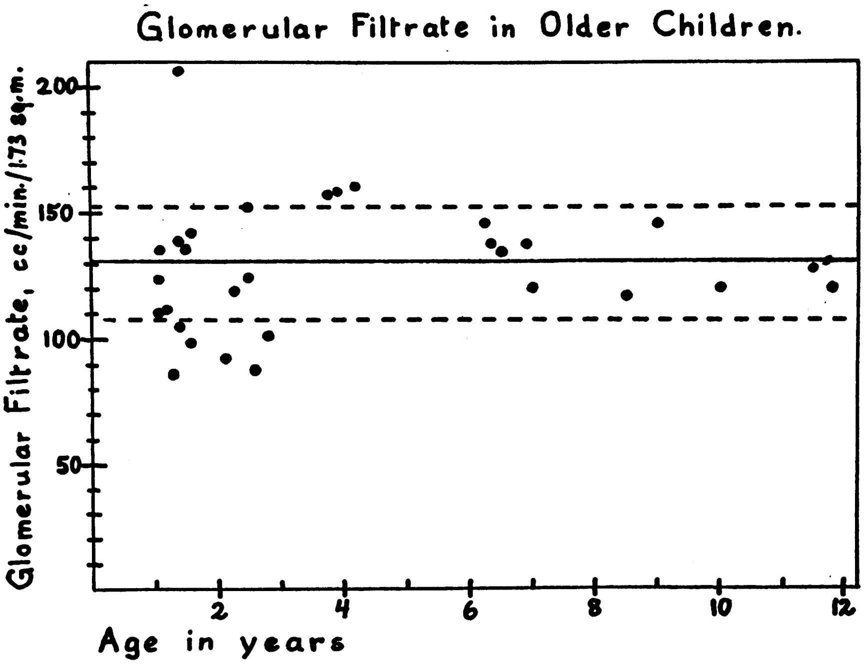

FIG. 1B. GLOMERULAR FILTRATION RATE IN OLDER CHILDREN
Symbols as in Figure 1A.

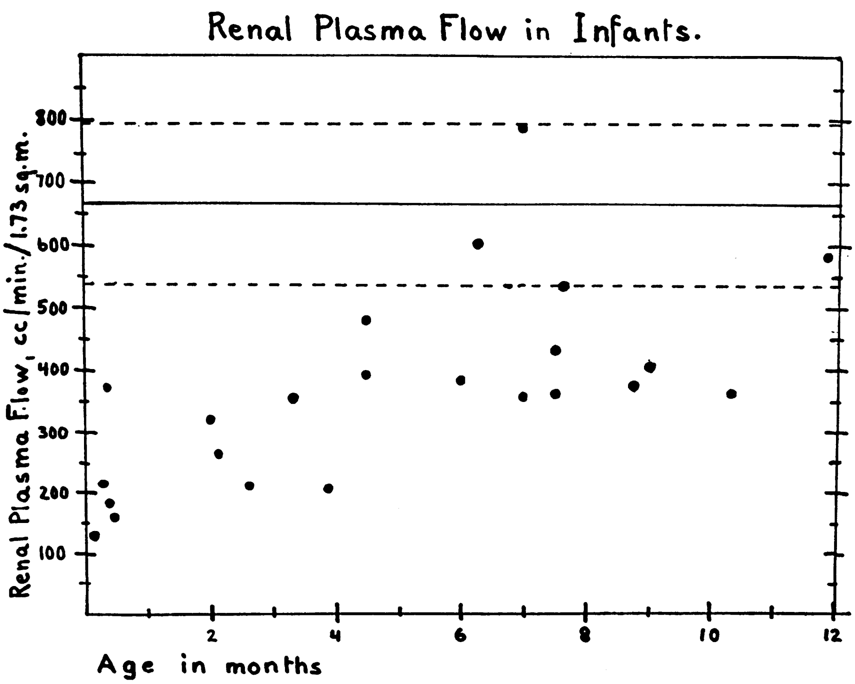

FIG. 2A. EFFECTIVE RENAL PLASMA FLOW IN INFANTS
Symbols as in Figure 1A.

TABLE IA

Renal functions in children, absolute and corrected for surface area, according to age (days)

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
							Urea clearance: (C_M) *cc./min.*		Glomerular filtration (G. F.) *cc./min.*			Effective renal plasma flow (P. F.) *cc./min.*			Tubular excretory capacity (Tm_{PAH}) *mg./min.*				Individual periods *per 1.73 sq. m.*					Plasma level at mid point *mg./100 cc.*	
Patient	Age: *days*	Weight: *Kg.*	Height: *cm.*	Surface area: *sq. m.*	Hematocrit	Blood urea nitrogen: *mg. %*	*per 1.73 sq.m.*	*absol.*	*per 1.73 sq.m.*	*absol.*	Slope: natural log	*per 1.73 sq.m.*	*absol.*	Filtration fraction *per cent* (100×G. F./P. F.)	*per 1.73 sq.m.*	*absol.*	Ratio: P. F./Tm_{PAH}	Ratio: G. F./Tm_{PAH}	C_a	G. F.	P. F.	Tm_{PAH}	Urine flow: *cc./min.*	Mannitol	PAH
L. C. ♂	2	2.4		.208	28	9.7	8.8	1.06	43	5.16	.00598	128	15.4	33.6					8 9.5	40 46	126 130.5		.636 1.33	114 86	1.09 0.54
R. S. ♂	7	3.35		.231		17.1	33	4.40	47	6.28	.00765				38	5.06		1.27	33 33 34	46.5 45 49		37.4 38.7	2.98 2.69 1.55	115 85 62	103 112
E. S. ♂	10	3.0	46	.212		14.1	19.6	2.4	52.5	6.44	.0053	210	25.7	25.0					18 21	51 55	243 178			124 100	4.10 4.07
B. K. ♂	10	3.2		.224	58.5	15.5	33.2	4.3	58	7.51	.00865				57	7.39		1.02	34 31 35	47 62 59		53 56 62	2.30 2.14 2.55	131 108 88	53 56 62
J. K. ♂	14	2.7		.200		11.7	36	4.16	46	5.32	.00487				3.7	0.43		12.5	31 35 37	46 44 47		3.5 3.7 3.9	1.71 2.95 4.53	97 87 79	67 66 53.5
B. M. ♂	14	3.8		.251	44	16.5	22	3.25	37	5.37	.00332				19	2.7		2.05	16.5 20.6 30.3	30 33 49		20 19 17	0.876 1.03 1.50	116 106 97	31 24 19.5
G. K. ♀	15	3.7		.242	47	14.8	37	5.17	50	7.0	.00956				22	3.08		2.27	39 35 37	48 49 52		21 21 23	2.84 3.21 2.96	122 103 88	97 91 110
K. C. ♀	19	2.8		.205	47	13.9	37	4.40	61	7.23	.0136	373	44.2	16.4					36 40 35	54 62 67	344 318 456		5.92 5.60 2.25	123 95 75	1.88 1.44 1.21
A. Y. ♀	19	3.0		.214	48	9.2	51	6.31	56	6.93	.00697	178	22.0	31.5	11	1.36	16.2	5.1	46 55 52	50 58 60 55	185 160 189	10 11 11	8.32 9.87 9.20 3.37 5.43 7.95	118 108 98 69	4.00 4.50 3.45 90 92 94
R. B. ♀	20	3.1		.222	59 ↓ 54	14.0	18	2.28	32	4.11		153	19.6	20.9					17 16 20	26 32 37	130 154 175		.55 .68 .63	130 105 85	2.45 2.04 1.91
E. D. ♀	22	3.0		.208	26	16.7	21.5	2.59	55	6.61	.0073				15.5	1.86		3.55	20 17 23	56 52 57		16 16 15	2.19 1.82 2.05	133 114 96	82 82 82

TABLE IA—*Continued*

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
Patient	Age: *days*	Weight: *Kg.*	Height: *cm.*	Surface area: *sq. m.*	Hematocrit	Blood urea nitrogen: *mg. %*	Urea clearance: (C_M) *cc./min.*		Glomerular filtration (G. F.) *cc./min.*		Slope: natural log	Effective renal plasma flow (P. F.). *cc./min.*		Filtration fraction *per cent* (100×G. F./P. F.)	Tubular excretory capacity (Tm_{PAH}) *mg./min.*		Ratio: P. F./Tm_{PAH}	Ratio: G. F./Tm_{PAH}	Individual periods *per 1.73 sq. m.*					Plasma level at mid point *mg./100 cc.*	
																			C_u	G. F.	P. F.	Tm_{PAH}	Urine flow: *cc./min.*	Mannitol	PAH
							per 1.73 sq.m.	*absol.*	*per 1.73 sq.m.*	*absol.*		*per 1.73 sq.m.*	*absol.*		*per 1.73 sq.m.*	*absol.*									
E. D. ♀	54	3.75		.244	30	12.6	44	6.20	84	11.8	.01065				13.3	1.87		6.32	42	81		13	4.12	83	59
																			44	84		14	3.18	68	57
																			45	87		13	4.67	55	75
B. K. ♂	55	3.5		.237	33	12.0	36	4.94	65	8.9					51	7.0		1.27	35	59		50	2.43	99	54
																			31	71		48	1.83	72	52
																			42	97		54	2.57	57	56
P. C. ♂	61	5.3		.312		15.5	26	4.70	63	11.4	.0134	321	58	19.6	93	16.8	3.46	.68	22	54	231		1.68	152	4.28
																			30	69	342		1.21	120	2.07
																			26	66	301		1.44	97	1.84
																						94	6.04		81
																						92	10.8		88
E. J. ♀	63	4.3		.274		15.5	23	3.64	69	10.9	.0079	263	41.7	26.8	41	6.5	6.4	1.67	21	62	253		1.56	150	5.10
																			24	48	243		1.25	118	3.95
																				99	292		1.65	90	3.63
																						44.5	1.61		44
																						35	1.89		42
																						45	1.00		43
C. P. ♂	75	5.4		.307	34	17.3	39	6.56	62	11.0	.0111				58	10.3		1.07	36	59		57	2.53	122	74
																			41	60		56	3.52	98	84
																			44.5	66		60	6.24	81	86
																			32	62			3.21	65	
																			39				4.89		
																			44				7.33		
J. S. ♀	81	4.15		.266	37	12.9	33	5.08	73	11.2	.0097	211	32.4	29.8					32	63	211		.68	86	0.37
																			34	83			.67	71	
D. K. ♀	101	3.8		.246	39	7.8	47	6.68	71	10.1	.0131	354	50.3	20.0	35	4.98	10.1	2.03	58	81	411		6.48	104	1.82
																			37	64	287		3.48	84	1.45
																			35	70	365		1.25	65	1.25
																						39	9.35		75
																						32	21.4		72
																						35	16.05		64
L. W. ♀	108	5.1		.299	35	7.3	41.5	7.17	70	12.1	.00595								35	59			1.42	85	
																			41	78			2.48	74	
																			42	74			3.64	66	
C. M. ♂	118	3.6		.243	36	31.9	27.5	3.9	50	7.0	.00828	204	28.7	24.5					28	51	201		1.12	120	6.8
																			27	49	206		1.20	84	4.0
J. M. ♂	137	7.2	66	.388	31				96	21.5		480	108	20.7	57	12.8	8.4	1.68		96	464		2.68	102	3.44
																					495		2.41		3.67
																						71	4.05		109
																						43	3.92		108
																						58	3.42		102

TABLE IA—*Continued*

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
Patient	Age: *days*	Weight: *Kg.*	Height: *cm.*	Surface area: *sq. m.*	Hematocrit	Blood urea nitrogen: *mg. %*	Urea clearance: (C_M) *cc./min.*		Glomerular filtration (G. F.) *cc./min.*		Slope: natural log	Effective renal plasma flow (P. F.) *cc./min.*		Filtration fraction *per cent* (100×G. F./P. F.)	Tubular excretory capacity (Tm_{PAH}) *mg./min.*		Ratio: P. F./Tm_{PAH}	Ratio: G. F./Tm_{PAH}	Individual periods *per 1.73 sq. m.*					Plasma level at mid point *mg./100 cc.*	
							per 1.73 sq.m.	*absol.*	*per 1.73 sq.m.*	*absol.*		*per 1.73 sq.m.*	*absol.*		*per 1.73 sq.m.*	*absol.*			C_u	G. F.	P. F.	Tm_{PAH}	Urine flow: *cc./min.*	Mannitol	PAH
E. S. ♂	138	7.1		.388	38	15.5	47	10.5	78	17.5		392	88.0	19.8	68	15.3	5.8	1.15	44 43 53	58 83 94	318 348 510	77 58 69	1.92 1.52 1.92 2.87 2.80 2.68	141 106 81	1.28 0.70 0.60 88 89 85.5
R. M. ♂	181	5.0		.292	33	20	48	8.1	94	15.9	.00765	384	64.8	23.4	46	7.77	8.2.	1.92	50 46	99 81 102	401 366	55 42 40	2.88 1.55 4.84 3.32 2.74	120 89 59	2.51 1.71 64 60 59
A. G. ♂	190	4.2		.260	34	10.8	65	9.75	127.5	19.2	.0109	601	90.5	21.2	22	3.36	26.9	5.7	63 67	124 131	601	23 22	2.62 6.13 2.19 4.95	56 46	0.96 56 54
L. T. ♀	216	8.0		.423	34	17.4	35	8.59	52	12.7	.00865	357	86.5	14.7	64	15.6	5.6	.81	31 36 39	49 51 53 57	276 378 417	78 66 73.5	1.36 1.20 1.43 2.43 2.28 2.52	154 132 116 73	1.77 1.26 1.11 71 73 68
B. S. ♀	223	7.9		.421	34	9.85	49	11.9	94	22.9	.0149	781	190	12.1	88	21.4	8.9	1.06	57 46 45	93 96 93	856 632 855	87 127 66	2.26 1.45 1.18 3.36 4.04 3.07	122 95 72	1.64 1.55 1.28 44 39.5 35
K. M. ♂	225	8.35		.436	37	7.5	76	19.2	114.5	28.9	.0141	365	92	31.4	21	5.3	17.2	5.4	74 77 78	114 110 116 118	379 355 360	22 20 22	1.755 1.86 1.655 2.44 2.42 2.50	164 130 102 45	2.56 2.18 1.70 99 92 92
H. B. ♀	229	7.7	70.5	.413	36	13.3	74	17.65	134	32.0	.01745	430	103	31.2					73 76 74	137 135 129	419 440		2.62 3.53 3.33	141 110 85	2.72 1.53

TABLE IA—*Continued*

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
Patient	Age: *days*	Weight: *Kg.*	Height: *cm.*	Surface area: *sq. m.*	Hematocrit	Blood urea nitrogen: *mg. %*	Urea clearance: (C_M) *cc./min.*		Glomerular filtration (G. F.) *cc./min.*		Slope: natural log	Effective renal plasma flow (P. F.) *cc./min.*		Filtration fraction *per cent* (100×G. F./P. F.)	Tubular excretory capacity (Tm_{PAH}) *mg./min.*		Ratio: P. F./Tm_{PAH}	Ratio: G. F./Tm_{PAH}	Individual periods *per 1.73 sq. m.*					Plasma level at mid point *mg./100 cc.*	
							per 1.73 sq.m.	*absol.*	*per 1.73 sq.m.*	*absol.*		*per 1.73 sq.m.*	*absol.*		*per 1.73 sq.m.*	*absol.*			C_u	G. F.	P. F.	Tm_{PAH}	Urine flow: *cc./min.*	Mannitol	PAH
K. T. ♂	232	8.0		.423	39	19.8	51	12.5	97	23.7	.0144	532	130	18.2	73	17.8	7.3	1.33	49	90	474		1.89	150	1.90
																			50	86	507		1.77	128	1.34
																			54	108	614		1.52	103	1.19
																				104		74	3.32	49	76
																						76	3.94		74
																						68.5	3.48		66
D. M. ♀	268	8.9	72	.459	36	14.8	43.5	11.53	69	18.3	.00935	379	100.5	18.2					42	69	312		1.65	150	2.64
																			45	68	498		1.61	129	1.55
R. L. ♂	275	8.8		.452	33	10.1	55	14.35	124	32.4	.00945	404	105.5	30.7	32	8.35	12.6	3.88	57	128	384		1.995	156	2.42
																			53	117	400		1.14	138	2.01
																			56	123	428		1.277	121	1.84
																				128		32	2.56	75	71
																						30	2.02		69
																						34	1.56		71
J. F. ♀	314	7.7	75	.413	43	13.2	48	11.45	96	22.9	.0104	367	87.6	26.2	49	11.4	7.5	1.96	48	98	359		1.58	133	1.88
																			45	87	352		1.181	109	1.45
																			51	103	389		1.22	88	1.30
																				96		50	2.73	51	89
																						46	2.69		76
																						50	1.91		62
J. L. ♂	356	7.3		.399	34	14.0	74	17.1	124	28.6	.0134	587	135	21.1	55	12.7	10.7	2.26	74	123	569		6.25	132	1.72
																			72	127	574		13.4	108	1.27
																			75	122	617		21.5	87	1.16
																				124		55	2.90	44	74
																						54	3.14		72
																						56	6.55		66

G.F. in cubic centimeters per minute and in column 10 the figures are corrected for surface area. The individual periods are listed in column 21 to show the variability from period to period. It is apparent from these data that the G.F. is very low in the very young infant, averaging about 50 cc./min. per 1.73 sq.m., and slowly rises during the first year, reaching adult values of about 130 cc./min. some time between the first and second year of life. Under six months of age none of the values were within the adult range when corrected for surface area and only a few in the last six months of the first year. In the second year many were found within the adult range, some still below. After the third year all values were found to be within the adult range.

Table I, column 14, shows the actual values obtained for P.F. in cubic centimeters per minute as measured by the clearance of PAH at low blood levels in the same group of infants and children, and column 13 gives the values per 1.73 sq.m. surface area. Figure 2A graphically presents the rate of effective renal plasma flow corrected to standard surface area as the child matures throughout the first year of life, and in Figure 2B the same data are given for the older children. As in the case of G.F., the P.F. (corrected for surface area) is also low in the young infant, increasing gradually and reaching the average adult value around the second year.

Table I, column 17, lists the actual values obtained in estimating the maximal tubular excretory capacity in these children, and in column 16 the values are corrected for standard surface area. In Figure 3A the Tm_{PAH} in mg./min. per 1.73 sq.m. is shown for the first year of life, and in Figure 3B the same data are given for the older children. It is apparent that there is much greater scatter of the values for Tm_{PAH} than of those for G.F. or P.F. While the lowest figures obtained, around 3 to 15 mg./min. per 1.73 sq.m. surface area, are seen in the youngest infants (under one month of age), relatively high values are obtained in other infants of the same age. Several already have adult values within the first six months. After 15 months of age the values are comparable to adult values with very few exceptions.

On casual inspection the graphic charts of the data for G.F. and P.F. appear similar, as if

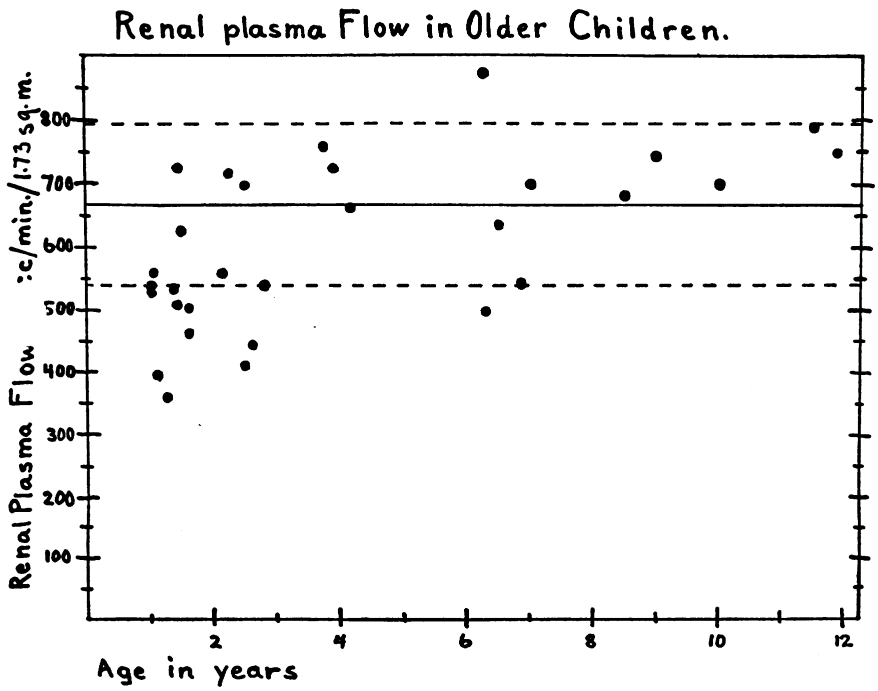

Fig. 2B. Effective Renal Plasma Flow in Older Children
Symbols as in Figure 1A.

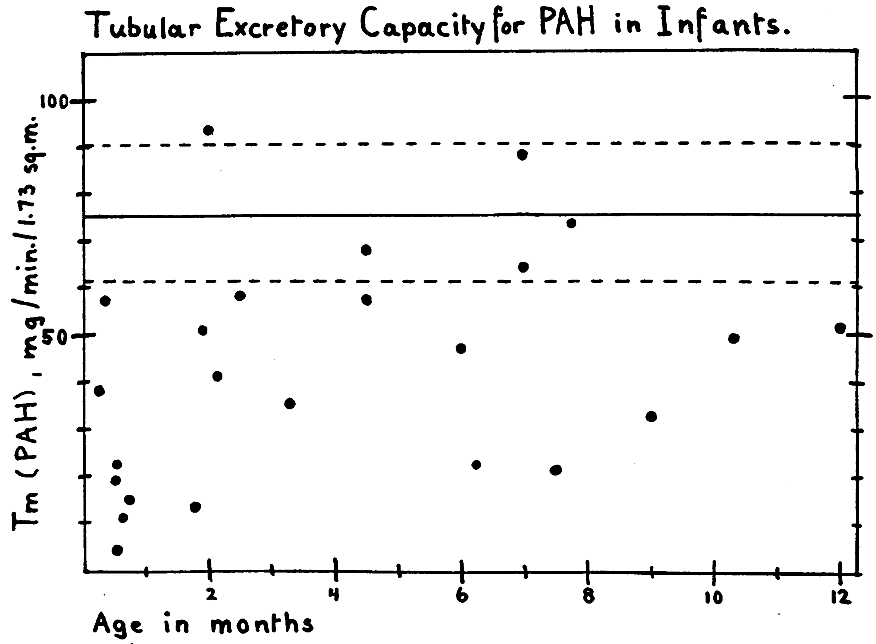

FIG. 3A. MAXIMAL TUBULAR EXCRETORY CAPACITY FOR PAH IN INFANTS
Symbols as in Figure 1A.

the rate of increase of these two physiological factors with aging were identical. Actually, this is not the case as can be seen from the figures on the F.F. (100 × G.F./P.F.) throughout this age span (Figure 4, upper section). If the rate of increase in these two values were identical, then the F.F. would be a constant value and similar to the average adult value of 19.6%. As can

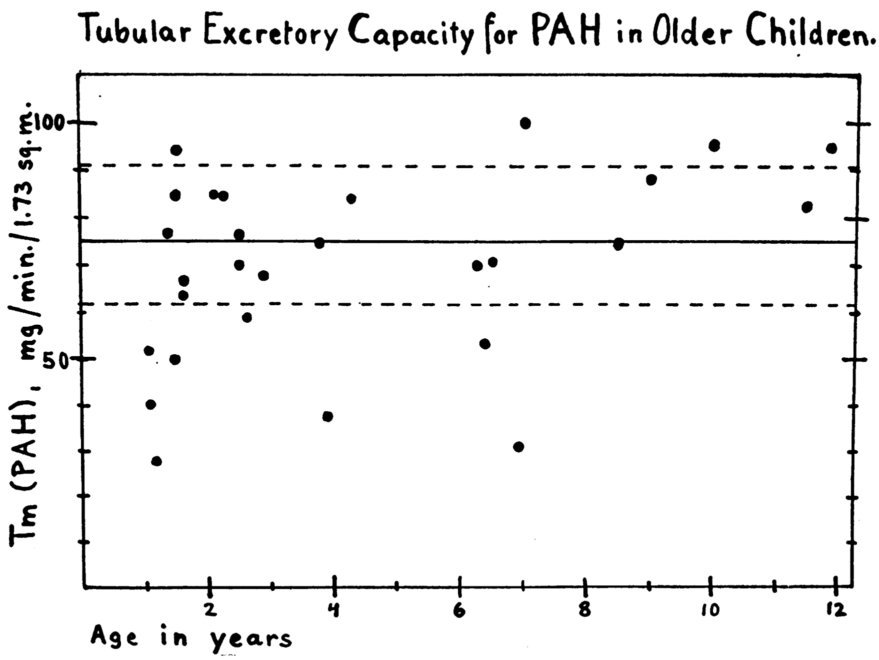

FIG. 3B. MAXIMAL TUBULAR EXCRETORY CAPACITY FOR PAH IN OLDER CHILDREN
Symbols as in Figure 1A.

be seen, this is not the case; for there is a considerable variability of the F.F. throughout the age groups. While several of the values are within the adult range early in life, and occasionally the F.F. is even low in the latter half of the first year, on the average a larger number of higher values are obtained in the first two years. In fact, some high values are found up to the eighth year of life. The average value for the F.F. in children is thus higher than that reported for adults. It might be stated that the fluctuations in rate of P.F. are normally wider than those of G.F., being subject to situations which affect the general circulation, and might thus account for some of the variations of the G.F./P.F. ratio. It must be pointed out that our clearance periods are short and represent "spot" clearances. There remains the possibility of error in estimating the P.F. in the very small infants, an error which would produce false low values. If the blood

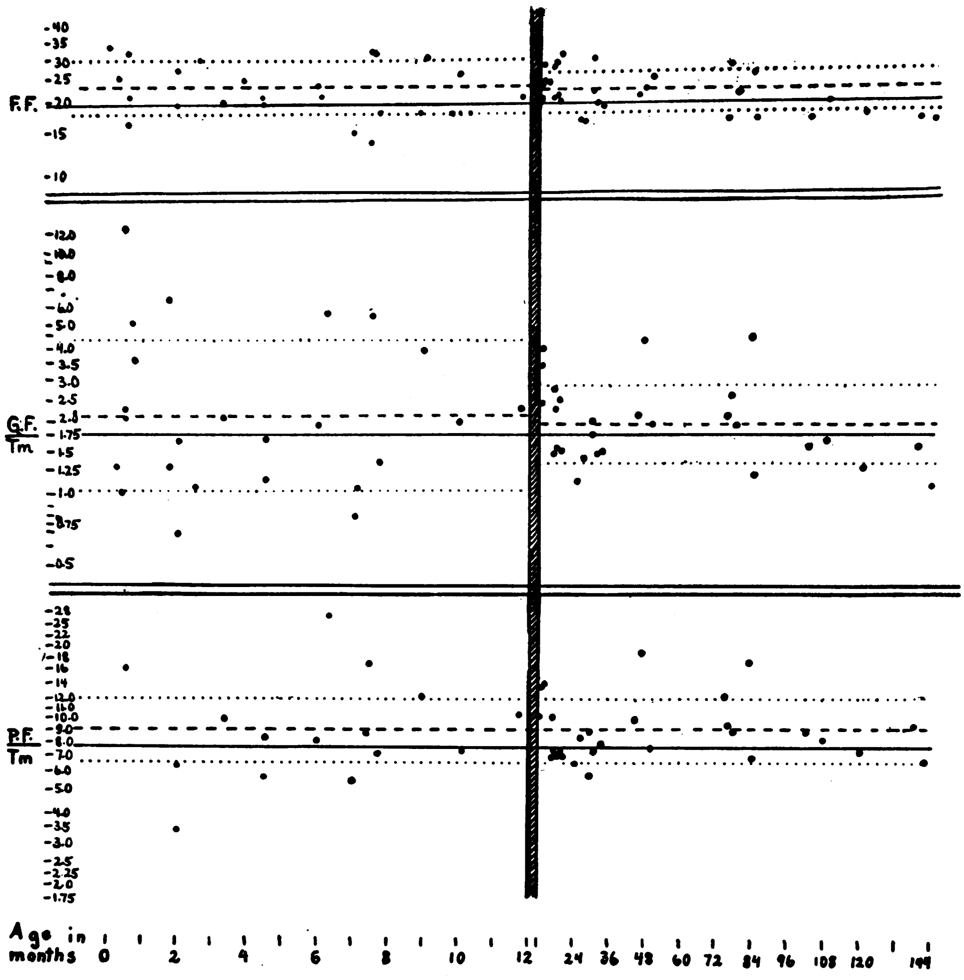

FIG. 4. RATIOS OF RENAL FUNCTIONS TO ONE ANOTHER IN INDIVIDUAL CASES, PLOTTED AGAINST AGE

Upper section: F.F. (100 × G.F./P.F.).
Middle section: G.F./Tm_{PAH}.
Lower section: P.F./Tm_{PAH}.

The ordinate scales are logarithmic, so that equal deviations of the numerator and of the denominator of each ratio from the average will produce equal distances from the line representing the mean. The solid line in each section represents the mean observed in adults (12); the broken line in each section represents the mean observed in the series of children here reported, calculated separately for infants under one year and for children over one year of age. The dotted lines represent one standard deviation from the mean, calculated for the present series.

TABLE IB

Renal functions in children, absolute and corrected for surface area, according to age (months)

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
Patient	Age: *months*	Weight: *Kg.*	Height: *cm.*	Surface area: *sq. m.*	Hematocrit	Blood urea nitrogen: *mg. %*	Urea clearance: (C_M) *cc./min.*		Glomerular filtration (G. F.) *cc./min.*		Slope: natural log	Effective renal plasma flow (P. F.) *cc./min.*		Filtration fraction *per cent* (100×G. F./P. F.)	Tubular excretory capacity (TmPAH) *mg./min.*		Ratio: P. F./TmPAH	Ratio: G. F./TmPAH	Individual periods *per 1.73 sq.m.*					Plasma level at mid point *mg./100 cc.*	
							per 1.73 sq.m.	*absol.*	*per 1.73 sq.m.*	*absol.*		*per 1.73 sq.m.*	*absol.*		*per 1.73 sq.m.*	*absol.*			C_u	G. F.	P. F.	TmPAH	Urine flow: *cc./min.*	Mannitol	PAH
V. A. ♀	12.2	9.25		.467	44	10.5	60	16.2	110	29.8	.0133	538	145.3	20.5					60 60	110 110	535 541		2.24 1.24	124 100	1.87 1.63
M. P. ♂	12.3	11	79	.524		12.0	61	18.5	124	37.6	.0149	529	160	23.5	51.5	15.6	10.3	2.4	62 61 60	114 122 138	517 467 632	52 51	2.03 1.47 1.49 2.61 1.97	124 94 70	2.02 1.67 1.20 64.5 48
E. T. ♂	13	7.5		.405	41	16.2	64	15.0	136	31.8	.01225	557	130.5	24.0	40	9.37	13.9	3.4	75 67 50	134 138	546 590 434	37.5 41 42.5	1.75 1.77 .97 3.02 2.88 4.17	67 53.5	1.37 1.16 1.00 57 58 69
S. P. ♀	13.7	9.6		.479	39	11.2	63	17.45	111.5	30.9	.01095	396	110	28.2	28	7.75	14.1	3.99	64 65 60	107 113 111 115	382 390 415	27 29 27	2.02 1.63 1.40 3.01 2.99 4.17	170 146 124 75	2.40 2.46 1.98 89 97 111
R. M. ♀	15	6.5	76	.387	49		30	6.72	86	19.2		361	80.7	23.8					36 29 26	89 81 89	391 328 364		3.08 1.57 1.20	110 76 58	14 12 5.5
T. Z. ♂	17	11.4	76	.516	43				105	31.4	.0121	510	152	20.6	73	21.8	7.0	1.44		111 105 98	506 511 512	70.5 75.5	1.69 1.72 1.31 2.46 1.56	155 123 97	3.27 2.40 2.09 51.5 35
J. D. ♂	17	10.5		.508	40	9.9	65	19.05	139	40.8	.0129	503	148	27.6	50	14.7	10.1	2.73	65 66 65	137 140 141 137	486 533 489	50 51 49	1.865 1.74 1.545 3.48 3.26 3.25	132 112 94 46	2.08 1.67 1.52 79 75 74
D. M. ♀	17.5	9.5		.477	36	9.4	127	35.0	207	57.1	.0164	724	200	28.6	94	25.9	7.7	2.20	131 126 125	208 204 209	739 696 737	94.8 95.5 92.5	3.84 2.96 2.50 5.41 5.13 3.92	90 71 56	1.14 1.07 0.95 46.5 44 45.5

TABLE IB—*Continued*

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
Patient	Age: *months*	Weight: *Kg.*	Height: *cm.*	Surface area: *sq. m.*	Hematocrit	Blood urea nitrogen: *mg. %*	Urea clearance: (C_M) *cc./min.*		Glomerular filtration (G. F.) *cc./min.*		Slope: natural log	Effective renal plasma flow (P. F.) *cc./min.*		Filtration fraction *per cent* (100×G. F./P. F.)	Tubular excretory capacity (TmPAH) *mg./min.*		Ratio: P. F./TmPAH	Ratio: G. F./TmPAH	Individual periods *per 1.73 sq.m.*					Plasma level at mid point *mg./100 cc.*	
							per 1.73 sq.m.	*absol.*	*per 1.73 sq.m.*	*absol.*		*per 1.73 sq.m.*	*absol.*		*per 1.73 sq.m.*	*absol.*			C_u	G. F.	P. F.	TmPAH	Urine flow: *cc./min.*	Mannitol	PAH
J. M. ♂	18	13.6		.607	38	10.6	81	28.4	135	47.4	.0124	625	219	21.0	85	29.8	7.35	1.55	78 83.5 46	121 131 152	633 617	83 82 91	2.19 2.19 1.14 2.85 3.92 3.56	111 82 47	1.44 2.10 48.5 45 42
D. T. ♂	19	10.0	74	.491	39	15.4	74	21.0	98	27.8	.01245	502	143	19.9	66	18.8	7.6	1.50	66 81 75.5	92 112 94 93	447 597 462	52 76 68	3.68 1.94 3.40 2.35 3.90 2.88	163 107 90 51.5	2.50 2.14 2.03 16 15.8 19.3
A. B. ♂	19	13.2		.593	41	11.75	68	23.3	142	48.6	.0108	463	159	30.7	63	21.6	7.35	2.3	66 70 65	143 149 134	390 545 455	52 68 68	2.53 2.31 1.89 3.33 3.52 3.95	105 90 77	2.88 2.55 2.23 70 66 64
I. R. ♀	25.7	10.3	81	.505	37	15.7	56.5	16.5	92	26.8	.0113	557	162	16.5	84	24.5	6.6	1.10	56 57 57	91 93 92 91	530 559 583	83 85 83.5	2.06 1.86 2.29 3.18 3.18 3.02	143 120 100 56	1.63 1.23 1.20 62 59 57
R. S. ♂	27	10	91	.492	40	8.7	91	25.8	120	34.1	.0159	717	204	16.2	84	23.9	8.5	1.37	79 94 100	105 131 125	820 680 651	72 92 88	1.21 1.61 1.79 3.21 3.31 3.38	110 85 65	1.98 1.73 1.45 44 34 30
K. E. ♀	30	10.6		.503	46	10.1	68	19.8	124.5	36.2	.0153	423	123	29.4	72	20.9	5.9	1.73	68 59 57	120.5 126.5 122.5 127.5	422 345 503	80.5 69.5 65.5	2.10 1.39 1.105 3.02 2.43 2.04	138 106 84 39	1.85 1.65 1.33 58 45.5 39
A. S. ♂	30	11.8	90	.544	38	13.3	53	16.7	152	47.8	.0159	695	218	21.8	77	24.2	9.0	1.97	78 47 34	148 153 156	696 773 617	58 103 70	2.58 1.65 1.49 2.58 3.46 2.45	123 97 74	1.39 1.06 1.23 61 60 58

TABLE IB—*Continued*

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
Patient	Age: *months*	Weight: *Kg.*	Height: *cm.*	Surface area: *sq. m.*	Hematocrit	Blood urea nitrogen: *mg. %*	Urea clearance: (C_M) *cc./min.*		Glomerular filtration (G. F.) *cc./min.*		Slope: natural log	Effective renal plasma flow (P. F.) *cc./min.*		Filtration fraction *per cent* (100×G. F./P. F.)	Tubular excretory capacity (TmPAH) *mg./min.*		Ratio: P. F./TmPAH	Ratio: G. F./TmPAH	Individual periods *per 1.73 sq.m.*					Plasma level at mid point *mg./100 cc.*	
							per 1.73 sq.m.	*absol.*	*per 1.73 sq.m.*	*absol.*		*per 1.73 sq.m.*	*absol.*		*per 1.73 sq.m.*	*absol.*			Cu	G. F.	P. F.	TmPAH	Urine flow: *cc./min.*	Mannitol	PAH
D. G. ♀	31	15.5	96	.679	44	10.9	60	23.5	87	34.1	.0113	445	174	19.6	59	23.1	7.55	1.48	54 64 62.5	69 88 87 93	337 440 451	57 60 59	1.96 1.93 1.595 3.11 2.06 3.50	170 136 110 65	3.10 2.17 1.60 62 61 65
E. M. ♂	34	17	99	.690	40				102	40.7	.0117	544	217	18.7	68	27.1	8.0	1.50		94 102 99 114	541 547	62 74 68	3.16 3.31 2.56 3.46 4.34 3.61	180 150 123 75	2.00 1.75 91 88 93
S. C. ♀	45	17.8	100	.737	40	12.6	70	29.8	158.5	67.5	.01723	754	321	21	75	32	10.0	2.11	70 79 68	157 164 153 160	744 780 737	73.5 77 75	2.35 1.83 1.48 2.40 2.09 2.31	171 135 108 47	1.33 1.16 1.15 51 33 31
J. D. ♂	47	13.6	96	.606	37	9.5	92	32.2	159.5	55.8	.01325	723	253	22.1	37	13	19.0	4.3	94 92 90	156 165 160 157	750 706 713	37 36 37	2.86 2.19 2.06 2.94 1.97 2.96	122 103 88 47	1.07 1.04 1.18 93 97 79
J. C. ♂	50	16.7	101	.670	42	14.3	103	40.6	161.5	62.5	.0145	659	255	24.6	84	32.5	7.85	1.92	100 106 103	164 162 164 156	633 692 652	86.5 82.5 82	3.26 3.55 4.32 4.71 4.05 4.05	122 100 82 39	0.93 0.67 0.67 30.5 25 23.5
H. M. ♂	75	25.9	123	.940	40	8.0	95	51.6	146	79.3	.0129	872	475	16.7	70	38.1	12.5	2.09	97 93 94	147 141 145 151	858 897 861	74 68 68	3.09 2.61 2.16 3.38 2.99 2.80	149 126 108 50	1.10 0.93 0.93 65 63 64
M. W. ♂	76	19.5	124	.83	44	11.3	71	34.1	138	66.2	.01355	497	238	27.8	53	25.4	9.4	2.60	71 71 73	133 140 142 138	495 508 489	52 55 52	2.42 2.32 1.86 2.97 3.08 3.58	172 139 113 58	2.26 1.94 1.77 77 87 75
M. T. ♂	78	18.9	111	.67	45	8.8	68	29.8	135	52.2	.0137	645	250	20.9	72	27.9	8.96	1.88	70 66 66	135 143 141 130	670 604 631	72 69 72	2.96 2.19 1.56 3.39 3.14 3.34	169 142 120 65	2.00 1.81 1.66 65 83 82

TABLE IB—*Continued*

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
Patient	Age: *months*	Weight: *Kg.*	Height: *cm.*	Surface area: *sq. m.*	Hematocrit	Blood urea nitrogen: *mg. %*	Urea clearance: (C_M) *cc./min.*		Glomerular filtration (G. F.) *cc./min.*		Slope: natural log	Effective renal plasma flow (P. F.) *cc./min.*		Filtration fraction *per cent* (100×G. F./P. F.)	Tubular excretory capacity (Tm_{PAH}) *mg./min.*		Ratio: P. F./Tm_{PAH}	Ratio: G. F./Tm_{PAH}	Individual periods *per 1.73 sq.m.*					Plasma level at mid point *mg./100 cc.*	
							per 1.73 sq.m.	*absol.*	*per 1.73 sq.m.*	*absol.*		*per 1.73 sq.m.*	*absol.*		*per 1.73 sq.m.*	*absol.*			C_u	G. F.	P. F.	Tm_{PAH}	Urine flow: *cc./min.*	Mannitol	PAH
J. K. ♂	83	20.9	126	.87	45	8.3	79	39.7	138	69.5	.0139	544	274	25.4	31	15.6	17.5	4.45	75 80 81	130 142 137 143	540 510 583	30 32	3.14 3.49 2.87 3.43 3.38	154 123 101 47	2.08 1.75 1.47 115 115
C. W. ♂	84	22.7	127	.90	34		39	20.3	120.5	62.7		695	362	17.4	100	52	6.95	1.20	37 38 42	117 127 117	765 720 601	126 83 90	3.53 3.97 9.40 5.85 7.06 13.81	146 96 29.5	2.15 1.30 1.11 45.5 33 23
A. R. ♂	102	28.9	132	1.035	52	14.6	75	45	117.5	70.3	.0132	680	407	17.3	75	44.9	9.06	1.57	80 74 72	127 112 121 110	712 650 679	75 72.5 77	5.40 4.78 3.93 4.60 5.75 5.04	201 173 146 94	1.89 1.58 1.17 69 66 69
C. M. ♂	108	24.9	131	.96	40	6.7	100	55.5	146	81.1	.0113	744	413	19.6	88	48.9	8.45	1.66	104 96 95	157 148 135 145	862 751 620	88 90 86	3.96 2.58 1.74 3.67 4.13 4.62	179 133 97 45	1.63 1.30 1.30 76 65 68
B. T. ♂	120	25	136	.99	43	12.2	76	43.5	120	68.8	.0147	701	402	17.1	95	54.5	7.4	1.26	76 79 72	115 122 118 124	733 725 645	96 87 102	5.38 3.66 3.01 3.01 4.94 3.92	163 139 115 53	2.00 1.61 1.68 46 47 51.5
D. M. ♀	138	20	115	.80	43	10.3	99	46.0	128	59.2	.01335	784	362	16.4	82	37.9	9.5	1.56	95 101 100	128 126 138 120	764 805	78.5 81.5 86.5	6.15 8.55 11.30 6.89 7.85 6.55	156 134 116 56	1.65 1.22 60 54 58
M. J. ♀	142	35.5	151	1.24		10.6	53	38.2	120	86	.0126	747	535	15.8	95	68.1	6.8	1.07	51 59 51	109 129 121 120	725 844 672	82 105 98	4.18 3.62 2.78 4.58 5.82 3.71	189 156 131 75	1.38 0.88 0.74 69 64.5 65

level of PAH is too high for complete extraction in one circulation through a kidney with a very low Tm_{PAH}, complete extraction of the PAH circulating through the kidney would not occur, thus the PAH clearance in an immature child may be lower than the actual renal plasma flow. It is possible that in some of our small infants, as well as in some of the cases published by others, the PAH load exceeded the tubular excretory capacity, so that falsely low values for P.F. were produced. Data on the PAH extraction ratio in the very small infant are needed to clear this point. The PAH loads were calculated for the 10 youngest infants on whom the plasma flow has been determined in the present study. All the children older than these ten had a Tm_{PAH} well capable of excreting ordinary loads. The infants, E. S. (ten days old), K. C. (19 days old), and A. Y. (19 days old), had loads which would have required a Tm_{PAH} of at least 10 mg./min. per 1.73 sq.m. to assure complete PAH extraction (assuming that complete extraction occurs when $\frac{\text{load (PAH)}}{Tm_{PAH}}$ is less than 0.5); the loads of L. C. (two days old), R. B. (20 days old), and J. S. (81 days old), were low enough to be excreted with a Tm_{PAH} as low as 2–5 mg./min. per 1.73 sq.m. The remaining four infants in this group had higher loads of PAH, but their Tm_{PAH} was determined and found to be high. Actually, only one infant in the group was observed to have a Tm_{PAH} below 10 mg./min. per 1.73 sq.m.

In order to determine the relative rates of maturation of glomerular and tubular function we have calculated the G.F./Tm_{PAH} ratio on each child (Table I, column 19 and Figure 4, middle section). The scatter of the data is too wide to draw valid conclusions as to the comparative rates of maturation of these two functions. In general, the G.F./Tm_{PAH} ratios (normal for adults taken as 1.72) show a wider variation in the infants under two years of age than seen later. Most of our very high values are seen in this younger age group. After two years of age the values are rarely significantly different from adult values.

The amount of renal plasma flow per unit of tubular excretory capacity as measured by the ratio P.F./Tm_{PAH} is quite variable and evidences

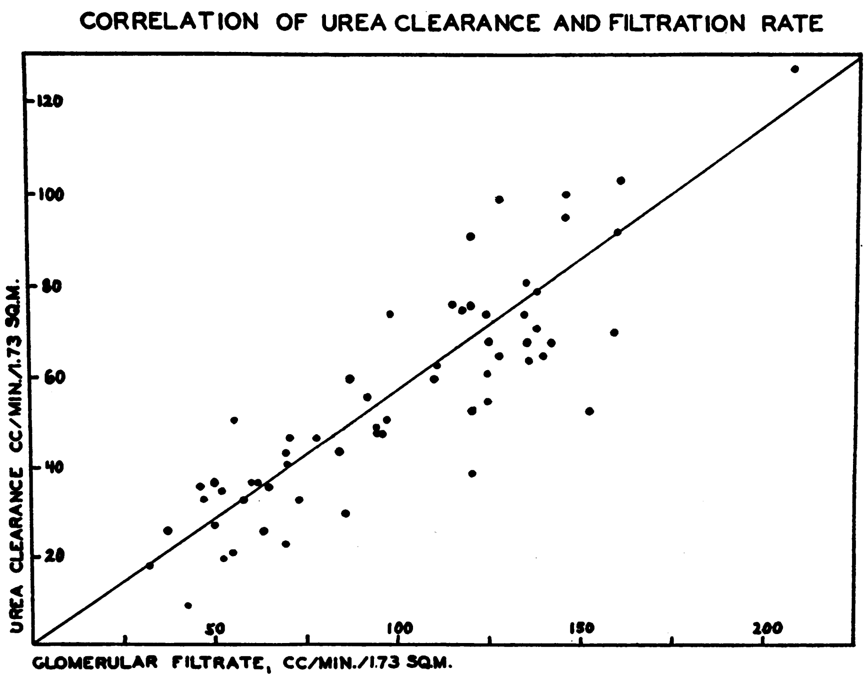

FIG. 5. UREA CLEARANCE, C_M, IN CC./MIN., PLOTTED AGAINST GLOMERULAR FILTRATION RATE

The diagonal line represents a ratio of urea clearance to G.F. of 57.5:100. Each dot represents the average value in an individual child.

the wide variation found in Tm_{PAH} and possibly of the normal fluctuations in P.F. (Table I, column 18 and Figure 4, lower section). In older children the P.F./Tm_{PAH} ratios are more constantly near the adult value.

The urea clearance values of this same group of children are listed according to age in Table I, columns 8 and 9. The wide variation in urea reabsorption accounts for the variable urea clearance values. Figure 5 shows the relationship between urea clearance and glomerular filtration rate with a correlation coefficient of 0.87. In individual cases the urea clearance varied between 34% and 81% of the mannitol clearance. This great variability has also been observed in adults.

DISCUSSION

It is unfortunate that we could not have collected maturation data in the same individual over the span of childhood,[5] so that the comparative rates of maturation of the various functions could be determined more precisely. Our data lend themselves only to comparing the average developmental state of one renal function to that of another at a given age.

While, in general, the G.F., P.F. and Tm_{PAH}, when corrected for surface area, reach adult values somewhere around the second year of life, there are exceptions and, as would be expected, these various functions mature at different rates, so that in one child one function has reached maturity while another is still immature and the reverse may occur in a second child. Examination of the simultaneous ratios for these three variables shows certain trends in comparative maturation. It is apparent from the high F.F. (Table I, column 15 and Figure 4, upper section) that G.F. is at a higher level of maturity than P.F. in many of the younger children, though not all. This tendency toward a high G.F./P.F. ratio persists through the second or third year and in some instances later. West and his group (5) have also shown that this ratio is high in most of their infants under two years of age and Barnett *et al.* (6) in examining premature infants found the F.F. to be even more consistently above that of the normal adult than is apparent in the series of full-term and older infants reported here. Elevation of the intraglomerular capillary pressure (as seen in essential hypertension [12]) may exist in infants to account for the high F.F., but this has not been demonstrated. Whether the low serum protein concentration in the small infant is a factor in the increased F.F. can only be conjectured.

The G.F./Tm_{PAH} ratios (Table I, column 19 and Figure 4, middle section) show a wide scatter. As with F.F., most of the extremely high and low values occurred within the first two years of life. After that time there is less irregularity and only an occasional high value. The few really high values occur in the first eight months of life. However, because of the irregularity of the data one would hesitate to draw a curve to show the trend of relative maturation of G.F. and Tm_{PAH}. The scatter in the ratios is chiefly dependent upon the very variable figures for Tm_{PAH} as the values for G.F. follow a much smoother growth curve. The data obtained by Barnett *et al.* (6) suggest that in premature infants high G.F./Tm_{PAH} ratios may be a more consistent occurrence. The few high figures obtained by West and his co-workers (5) were also observed in the youngest infants. These data suggest that a higher order of maturation of G.F. than of Tm_{PAH} exists in the early months of life but this is by no means constant; for in fact, none of our children under six months of age had a G.F. within the adult range, whereas, several had a Tm_{PAH} within the adult range by this time.

The irregularity in early life of the other ratios discussed is also apparent in the P.F./Tm_{PAH} ratio. No definite trend in relative rates of increase in the P.F. and Tm_{PAH} can be noted from the data (Table I, column 18 and Figure 4, lower section). The data of West *et al.* (5) also show greater variability in the younger infants. Whereas, there is a gross correlation between the rate of increase in P.F. and the maturation of Tm_{PAH}, both reaching adult values at about two years of age, the maturation rate of the plasma flow seems steadier and follows a smoother curve. The tubular function of excreting PAH in the

[5] Two infants in the group were studied on repeated occasions: B. K. at 10 and 55 days of age, and E. D. at 22 and at 54 days of age. In both infants the Tm_{PAH} (absolute values) remained stationary over the interim period, while the G.F. increased slightly in B. K. and considerably in E. D.

young infant does not seem to be limited by an inadequate blood supply.

The urea clearances were done simultaneously with mannitol clearances (under the influence of mannitol diuresis); therefore, the urea clearance values are probably higher than would be usual for these children.

It has been suggested (4) that the low G.F. in the young infant is dependent upon the resistance to filtration offered by the visceral layer of Bowman's capsule, which in the small infant is composed of cuboidal cells in contrast to the thin flat cells of the adult membrane (13, 14). The finding of high F.F.'s in many of these infants indicates that, contrary to the above assumption, a higher proportion of the plasma flow is filtered through the infantile glomerulus than through the adult one and, therefore, the thicker cell of the membrane in itself presumably does not reduce the rate of filtration. It is not unreasonable to postulate that the small size and number of capillary loops in the immature glomerulus (13) may account for the decreased blood flow through the glomerulus and thus the decreased G.F. The smaller number and size of capillary loops also offer a smaller filtering surface than the glomerular tufts of the adult, although in relation to the volume of the capillary bed (which influences the blood flow) the filtering surface in these immature glomeruli may be larger than in mature glomeruli. Whether the anatomical difference is the total or even a prime factor responsible for the low G.F. is not known. It is interesting, nevertheless, that both the functional maturation and the anatomic maturation of the kidney glomerulus occur at about the same time, around the second or third year of life (14). Low blood pressure in the small infant could possibly influence the G.F. but G.F. increases over a period of several months when the arterial blood pressure is more or less constant, indicating a lack of correlation between these two. Salmi (15) and Taussig (16) have shown that the arterial blood pressure in infancy changes very little from one week of age until four years of age. The anatomical fact that throughout childhood, and particularly in infancy, the ratio of the renal cortex to the medulla is lower than in the adult (14) might lead us to expect a low G.F./Tm_{PAH} ratio. However, our figures do not substantiate such an expectation; an indication

TABLE II

Glomerular filtration rate related to various body measurements in individual patients, arranged according to age

Patient	Age	G. F., *cc./min. per*				
		Wt.	Ht.	S.A.	Av. kidney wt.	Av. B.M.R.
	Mo.	*Kg.*	*cm.*	*sq. m.*	*Gm.*	*cal./hr.*
L. C.	1/15	2.15	0.103	24.8	0.224	1.03
R. S.	1/4	1.87	0.123	27.1	0.262	1.1
E. S.	1/3	2.14	0.126	30.3	0.268	1.1
B. K.	1/3	2.35	0.147	33.5	0.313	1.25
J. K.	1/2	1.97	0.104	26.6	0.213	0.88
B. M.	1/2	1.41	0.103	21.4	0.215	0.9
G. K.	1/2	1.89	0.135	28.9	0.28	1.17
K. C.	2/3	2.58	0.137	35.2	0.28	1.17
A. Y.	2/3	2.31	0.13	32.4	0.27	1.15
R. B.	2/3	1.33	0.08	18.5	0.16	0.65
E. D.	3/4	2.20	0.125	31.8	0.25	0.95
E. D.	1.8	3.14	0.207	48.4	0.39	1.3
B. K.	1.8	2.54	0.156	37.5	0.29	0.99
P. C.	2.0	2.15	0.197	36.6	0.37	1.14
E. J.	2.1	2.54	0.188	39.8	0.35	1.10
C. P.	2.5	2.04	0.187	35.8	0.33	1.0
J. S.	2.6	2.70	0.188	42.1	0.34	1.0
D. K.	3.3	2.66	0.165	41.1	0.28	0.77
L. W.	3.5	2.37	0.195	40.5	0.33	0.90
C. M.	3.9	1.94	0.111	28.8	0.18	0.5
J. M.	4.5	2.98	0.326	55.4	0.55	1.41
E. S.	4.5	2.47	0.275	45.1	0.44	1.15
R. M.	6	3.18	0.24	54.5	0.36	0.91
A. G.	6.2	4.56	0.29	73.9	0.44	1.10
L. T.	7.0	1.59	0.19	30.0	0.27	0.69
B. S.	7.3	2.90	0.33	54.4	0.48	1.22
K. M.	7.3	3.46	0.42	66.2	0.60	1.54
H. B.	7.5	4.15	0.454	77.5	0.66	1.7
K. T.	7.6	2.96	0.34	56.0	0.49	1.25
D. M.	8.8	2.06	0.25	39.9	0.35	0.90
R. L.	9.0	3.68	0.45	71.6	0.61	1.6
J. F.	10.0	2.98	0.305	55.5	0.41	1.1
J. L.	11.7	3.92	0.36	71.6	0.47	1.3
V. A.	12.2	3.22	0.38	63.8	0.48	1.35
M. P.	12.3	3.42	0.475	71.9	0.61	1.7
E. T.	13	4.24	0.40	78.5	0.50	1.4
S. P.	13.7	3.22	0.39	64.5	0.48	1.3
R. M.	15	2.95	0.25	49.6	0.28	0.8
T. Z.	17	2.76	0.413	60.9	0.44	1.2
J. D.	17	3.90	0.49	80.5	0.57	1.6
D. M.	17.5	6.00	0.68	119	0.78	2.2
J. M.	18	3.49	0.57	78.0	0.65	1.8
D. T.	19	2.78	0.37	56.6	0.37	1.0
A. B.	19	3.69	0.58	82.0	0.65	1.8
I. R.	25.7	2.60	0.33	53.0	0.31	0.86
R. S.	27	3.41	0.37	69.5	0.39	1.1
K. E.	30	3.41	0.39	72.0	0.40	1.1
A. S.	30	4.05	0.53	88.0	0.53	1.5
D. G.	31	2.20	0.36	50.3	0.375	1.05
E. M.	34	2.40	0.41	59.0	0.43	1.2
S. C.	45	3.79	0.675	91.5	0.66	1.9
J. D.	47	4.10	0.58	92.0	0.53	1.6
J. C.	50	3.74	0.62	93.0	0.59	1.7
H. M.	75	3.06	0.64	84.3	0.63	2.0
M. W.	76	3.39	0.53	80	0.525	1.6
M. T.	78	2.76	0.47	77.8	0.41	1.3
J. K.	83	3.32	0.55	80	0.53	1.7
C. W.	84	2.76	0.49	69.5	0.475	1.5
A. R.	102	2.43	0.53	68.0	0.49	1.65
C. M.	108	3.26	0.62	84.5	0.55	1.9
B. T.	120	2.75	0.505	69.5	0.43	1.6
D. M.	138	2.95	0.51	74.0	0.32	1.3
M. J.	142	2.42	0.57	69.4	0.46	1.9
Adult		2.0	0.8	76	0.44	2.0

that even the mass of tissue in the early months of life is not closely correlated with function.

Throughout these calculations of renal clearance we have correlated the data collected in the infants and children to adult values using surface area as the basis for comparison, as the principle of correlating renal function to surface area has been widely accepted (5, 17–19). Since this may not be the best point of reference, we have also given the absolute values. In order to determine if surface area is the best basis of comparing the G.F. in the growing child to that of the adult, we have related in Table II the G.F. (in cubic centimeters per minute) at different ages throughout childhood to several different measurements of reference: such as (*1*) body weight in Kg., (*2*) body height in cm., (*3*) body surface area in sq.m., (*4*) average kidney weight in Gm., and (*5*) average basal metabolic rate in calories per hour, and have compared these ratios to the adult values. The values for average kidney weight in the different age groups were obtained from the data of Peter (14), and the average values for basal caloric expenditure per hour were obtained from Washburn and Iliff (20). It is apparent that when body weight is used as the measurement of reference, the data are very irregular. In many of the smallest infants the values are above the adult range and after six months of age they are considerably above this level with a gradual decline of the values from a high point during the second and third years of life. When body height is used as reference, there is a gradual increase in the G.F. with growth and the irregularity is less marked than with body weight. However, under these circumstances the values in older children are still much below adult values and this seems unreasonable in the face of other evidence of renal functional maturity in this age group. When surface area is used as standard, occasional adult values are reached around six months of age but the values are not consistently in the adult range until about the second year. Using basal caloric expenditure as reference, there is little change throughout the first six months. After this age the trend is irregularly upward. This increase is slower than the rise seen when surface area correction is used, as might be expected considering the fact that children have a higher basal metabolic rate per sq.m. surface area than adults. When kidney weight is used as reference, there is gradual increase of the G.F. per unit of kidney mass, with maturation being reached between the fourth and fifth months of life. After this age and throughout childhood the values more closely parallel the adult values than when any other measurement of reference is used. This is the more remarkable since the values for kidney weight and basal metabolic rate at different age levels represent average values obtained from the literature, whereas, the weight, height, and surface area were measured in the individual patients, who in many instances deviated considerably from average standards.

It has been shown that the mannitol/inulin clearance ratio may be less than one (21). This fact does not invalidate the above data since the same procedure (mannitol clearance) was used in all the age groups and the values were compared to adult values obtained with the same substance (12).

SUMMARY

1. The glomerular filtration rate, effective renal plasma flow, tubular excretory capacity for PAH and urea clearance have been measured in 63 normal infants and children between the ages of two days and 12 years in order to determine the maturation rate of these individual renal functions.

2. In general, when corrected to standard adult surface area, the clearance values were lowest in the smallest infants and gradually rose to reach adult values around the second year of life. Maturation was most rapid in the first six months, then proceeded more slowly. The youngest child in whom all functions were within the adult range was seven months of age. The average child, however, did not show complete maturation of all functions studied before the end of the second year, although individual functions, particularly Tm_{PAH}, were often found to be mature at a much younger age.

3. G.F. was found to be closely correlated to adult values after the first few months of life when kidney weight is used as the basis for comparison. When body weight and height are used as the basis for comparison, the data are very variable and show no regular maturational trend. When the surface area is the basis of reference, the maturation rate seems slower than when kidney weight is used. Since in the literature the surface area

is most commonly used as the basis for comparison with adult values, our graphic charts have been constructed using surface area correction.

4. Simultaneous ratios of the various functions were calculated to show relative rates of maturation. In general, it might be said that the ratios show wider variability in the early part of life than later on. The data indicate that these individual functions develop at irregular rates; one function might reach maturity in a given child earlier than another, and in a second child the reverse may occur.

a. There is a tendency toward high filtration fractions (G.F./P.F.) in the early months of life which continues through the second and third years.

b. The rate of Tm_{PAH} maturation is extremely irregular, resulting in great irregularity in the ratios in which Tm_{PAH} is involved.

c. Several of the children under two years of age had a rate of P.F. closer to the adult range than was the Tm_{PAH} (high P.F./Tm_{PAH} ratio) but this high ratio was also occasionally seen in older children. In most of the determinations even in the very young infants the P.F./Tm_{PAH} ratio was close to adult values to show roughly parallel rates of maturation.

d. The various ratios estimated would suggest that there is a tendency for G.F. to be more mature in the youngest infants than the other functions measured.

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