THE DEGREE OF COMPENSATORY RENAL HYPERTROPHY FOLLOWING UNILATERAL NEPHRECTOMY*

I. The Influence of Age

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The gross enlargement of the remaining kidney which occurs after unilateral nephrectomy is called a compensatory hypertrophy.[1] Compensatory hypertrophy of the kidney is a relative term and designates the increase in size of a single kidney over that found when both kidneys are present. It is measured by the increase in the weight of the remaining kidney of an animal from which one kidney has been removed over and above the weight of one kidney of a control animal of the same age and sex maintained under the same conditions and subjected to an operation in which one kidney is exposed but not removed.

By the expression "degree" of compensatory hypertrophy we mean the maximum amount of enlargement which follows unilateral nephrectomy. Our work was done on the albino rat and in this animal the remaining kidney has reached its maximum degree of compensatory hypertrophy 40 days after the removal of the other kidney and the degree of compensatory hypertrophy thereafter remains constant. All the measurements in this paper were made 40 days after operation. But it is essential that some proof that compensatory hypertrophy is

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[1] This enlargement of the remaining kidney is due at least in part to a true hypertrophy of the parenchymal cells of the kidney, but in using the expression compensatory hypertrophy there is no intention to prejudge the question as to the possibility of a hyperplasia of the parenchymal as well as of the vascular and supporting tissue cells.

complete in 40 days be given now because until that point has been established our conclusions as to the relation between age and compensatory hypertrophy cannot be accepted. Without it the possibility would remain that the decrease in the degree of compensatory hypertrophy with advancing age might be only apparent and due to a slowing of the rate of increase in the weight of the remaining kidney in the older rats and not to any lack of ability to attain in the end to as great a degree of increase as is observed in the younger animals. And the necessity of dealing first with this point is the more stringent

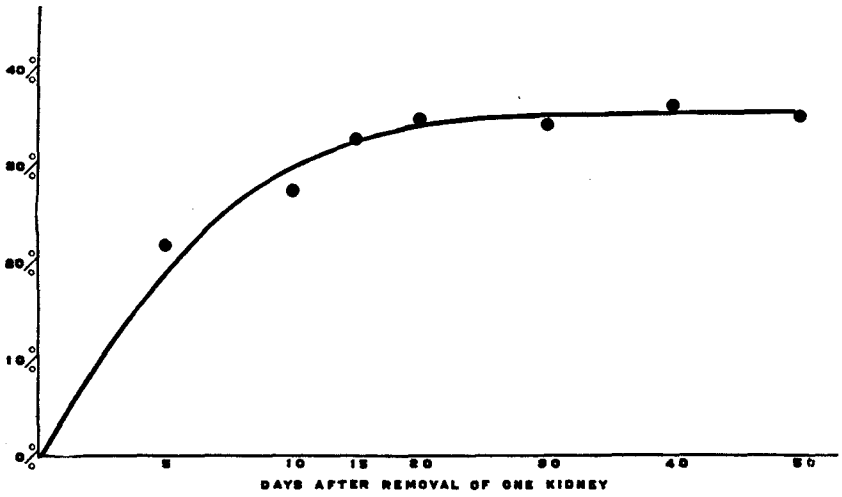

FIG. 1

since Smith and Moise (1) have been led to a different conclusion. They find that compensatory hypertrophy is a process which continues for at least 100 days after nephrectomy and their curve of the rate of compensatory hypertrophy never reaches any clear and definite maximum. However it happens that during the past 8 years we have collected for other purposes than those which concern this paper a large number of observations on the rate of compensatory hypertrophy of the kidney in rats of both sexes and of all ages. The result has been an adequate demonstration that when 40 days have elapsed after the removal of a kidney the remaining kidney has reached its

maximum degree of enlargement. Our results fall into two groups in accordance with differences in diet, in the ages selected for study, in the place where the experiments were carried out, and in the strain of albino rat which was used. We have selected from these two groups all observations in which all ages and both males and females were equally represented and in this way have constructed two graphs which summarize the findings on over 2000 rats. The ordinates represent the percentage increase in the weight of the remaining kidney over the average weight for one kidney of the controls. The difference

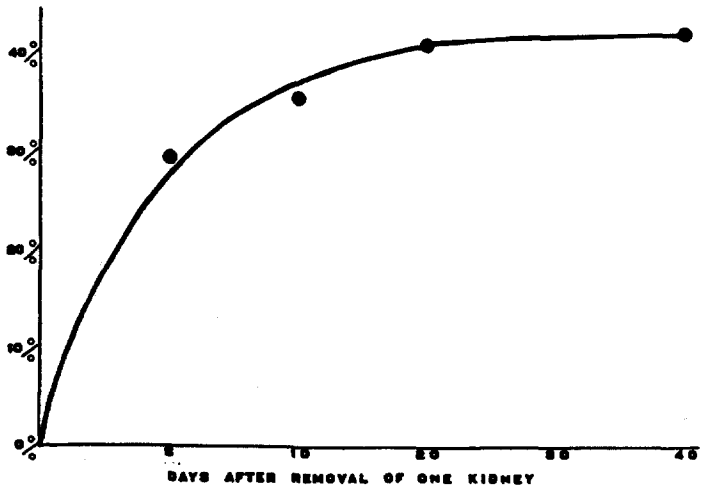

FIG. 2

in the height of the two curves arises from the fact that in the first group (Fig. 1) the study was extended to rats of greater age than in the second group (Fig. 2). It should be noted also that in other experiments, which could not be incorporated in these average curves because both sexes were not represented, observations have been continued to as long as 90 days after operation and that in these instances also the general result indicates that at all ages compensatory hypertrophy is complete in 40 days.

Methods

The general methods used have already been described (2). Male albino rats were divided into control and experimental groups and one kidney was exposed or

TABLE I

Controls			Nephrectomized			Controls			Nephrectomized			Controls			Nephrectomized		
Body weight	Kidney weight	Kidney weight / Body surface	Body weight	Kidney weight	Kidney weight / Body surface	Body weight	Kidney weight	Kidney weight / Body surface	Body weight	Kidney weight	Kidney weight / Body surface	Body weight	Kidney weight	Kidney weight / Body surface	Body weight	Kidney weight	Kidney weight / Body surface
5 days old						15 days old						30 days old					
gm.	*mg.*		*gm.*	*mg.*		*gm.*	*mg.*		*gm.*	*mg.*		*gm.*	*mg.*		*gm.*	*mg.*	
65	410	225	76	676	335	101	541	220	83	764	353	155	675	206	185	1066	289
81	447	210	117	832	324	119	570	208	103	854	343	182	733	201	171	1044	288
67	387	208	64	577	319	98	500	207	99	804	332	158	663	200	157	942	285
105	503	200	111	752	302	125	589	207	122	928	331	159	653	196	178	991	282
79	387	186	65	544	299	143	638	206	152	972	301	174	692	195	158	929	281
75	372	186	89	667	295	146	644	205	124	846	300	173	676	192	177	1002	280
82	393	184	111	731	293	115	518	193	123	844	300	183	695	190	160	912	273
135	547	183	64	525	290	124	542	192	109	769	297	157	625	189	176	971	273
78	373	181	77	584	288	152	621	192	120	820	297	171	657	188	142	834	271
71	347	180	74	569	286	113	507	191	113	769	290	164	639	188	194	1031	271
86	395	178	75	571	285	92	430	185	125	818	288	176	663	187	154	876	269
84	388	178	76	574	284	124	514	182	117	981	287	169	642	186	160	895	268
88	400	178	77	538	263	99	433	179	130	835	286	188	691	185	157	886	268
70	338	177	68	490	261	85	392	178	114	759	285	160	616	184	165	912	267
92	405	174				84	388	178	109	735	284	186	679	184	155	870	266
70	331	173				141	541	177	109	736	284	165	624	183	132	772	262
82	366	171				109	452	174	112	742	282	206	721	182	159	862	259
92	392	169				132	504	171	119	750	274	186	670	181	159	858	258
81	354	167				113	441	166	127	784	273	154	583	179	156	846	258
77	332	163				105	413	164	119	741	270	170	614	176	159	847	254
64	290	160							126	727	254	158	584	176	167	866	252
89	351	155										158	572	173	191	946	251
												159	567	170	183	913	249
												171	583	167	166	845	247
												166	569	166	130	709	243

60 days old						90 days old						180 days old					
220	872	211	165	965	282	267	997	212	289	1425	287	426	1238	193	351	1401	248
209	836	210	199	1045	270	237	895	206	296	1337	265	342	1041	187	318	1274	241
213	785	194	217	1079	263	233	877	204	252	1199	265	361	1050	182	334	1312	240
188	717	193	218	1081	262	301	1037	203	266	1221	260	337	1001	182	389	1444	239
209	744	187	203	1018	260	261	905	195	253	1177	260	373	1052	179	361	1371	238
259	860	186	223	1059	254	259	894	194	298	1289	255	358	1025	179	321	1247	234
214	750	185	245	1126	253	242	814	185	238	1080	248	386	1079	179	327	1259	234
220	761	184	213	1016	251	316	977	185	238	1080	248	345	1001	179	320	1232	232
208	724	182	201	972	250	261	852	184	230	1058	248	395	1067	175	318	1222	231
224	762	182	199	965	249	298	922	182	261	1133	245	354	987	174	335	1266	231
246	808	181	192	943	249	308	917	177	269	1157	245	352	987	174	401	1414	229
194	683	180	222	1032	248	288	874	177	253	1107	244	365	1005	173	345	1280	229
227	752	179	203	973	248	278	849	176	240	1055	241	366	1000	172	317	1187	225
200	694	179	191	929	246	290	875	176	281	1160	238	388	1038	172	332	1220	224
215	729	179	198	945	245	268	829	176	282	1157	237	340	939	170	376	1318	223
225	748	179	176	871	244	231	748	175	290	1162	234	416	1064	168	332	1211	222
286	882	179	182	865	237	397	687	173	246	1033	232	310	858	165	347	1226	219
241	782	178	186	875	237	285	850	173	259	1065	231	349	930	165	343	1214	218
221	735	177	199	917	237	267	807	172	306	1179	228	341	910	164	346	1202	215
209	697	175	215	967	237	262	797	172	256	1038	227	325	883	164	327	1141	212
221	715	172	182	848	232	243	762	172	299	1129	229	333	872	160	321	1125	211
276	805	167	172	799	228	273	805	169	258	1003	219	409	1001	160	322	1120	210
252	749	166	195	861	225	269	796	169	298	1085	214	308	822	159	367	1215	209
222	670	161	157	734	222	208	649	163	257	878	192	392	905	149	326	1086	202
			184	726	198	285	795	162	212	771	191						

TABLE I—*Concluded*

Controls			Nephrectomized			Controls			Nephrectomized			Controls			Nephrectomized		
Body weight	Kidney weight	Kidney weight / Body surface	Body weight	Kidney weight	Kidney weight / Body surface	Body weight	Kidney weight	Kidney weight / Body surface	Body weight	Kidney weight	Kidney weight / Body surface	Body weight	Kidney weight	Kidney weight / Body surface	Body weight	Kidney weight	Kidney weight / Body surface
270 days old						360 days old						540 days old					
gm.	*mg.*		*gm.*	*mg.*		*gm.*	*mg.*		*gm.*	*mg.*		*gm.*	*mg.*		*gm.*	*mg.*	
385	1143	190	379	1394	234	338	1139	207	309	1280	247	380	1233	207	376	1396	236
382	1069	179	289	1158	233	339	1114	202	376	1431	242	452	1321	203	383	1387	231
359	1027	179	345	1299	232	415	1255	199	318	1274	241	361	1092	190	309	1184	228
282	873	179	384	1388	231	367	1136	195	345	1332	238	316	982	186	413	1426	226
357	982	172	343	1263	227	335	1061	194	399	1386	225	472	1222	177	386	1362	226
377	1014	172	381	1348	226	312	1011	194	401	1385	225	472	1192	173	381	1312	220
338	949	172	396	1385	226	414	1216	193	419	1415	222	536	1287	172	403	1328	215
403	1050	170	327	1217	226	303	944	184	377	1306	220	403	1067	172	282	1045	214
441	1115	170	366	1288	222	364	1040	180	516	1594	218	392	1041	171	425	1364	212
388	1019	169	346	1239	221	377	1051	177	352	1231	218	403	1059	171	460	1433	212
422	1071	168	347	1236	220	429	1145	177	255	994	218	426	1087	169	419	1344	211
344	938	168	378	1304	220	439	1152	176	366	1255	216	483	1176	168	378	1255	211
383	988	165	347	1226	219	388	1055	175	339	1192	216	400	1036	168	395	1272	208
354	930	163	326	1180	219	347	969	173	374	1268	215	488	1183	168	496	1464	206
402	1009	163	346	1226	219	354	981	172	284	1047	214	418	1058	167	354	1158	204
334	874	160	359	1250	218	354	970	170	282	1017	209	380	988	166	500	1444	202
433	1122	157	329	1178	218	307	859	166	365	1174	202	427	1054	164	348	1132	202
320	834	157	365	1260	217	401	995	161	406	1192	192	511	1161	160	352	1135	201
359	902	157	325	1153	215	353	913	161	359	1079	188	399	985	160	335	1094	200
424	1006	157	418	1362	214	343	882	158				449	1057	159	380	1173	197
402	966	156	471	1458	212	386	938	156				511	1132	156	379	1163	196
336	854	156	300	1075	211	406	925	149				425	997	155	459	1314	194
487	1092	155	323	1123	210							397	932	152	368	1104	189
371	899	153	339	1128	204												
335	810	148	290	1008	203												
438	957	146	346	1070	191												
428	939	146	438	1244	190												

removed at 5, 15, 30, 50, 60, 90, 180, 270, 540, and 720 days of age. In the groups in which operations were performed at 5 and 15 days of age, it was necessary to clip the incisor teeth of the mother in order to prevent her from eating the young rats after the operation. All other groups received from the first the casein-starch-lard diet described as the experimental male diet (2). Each rat was anesthetized with ether 40 days after operation, exsanguinated, the kidney stripped of its capsule, and cut with a razor into two parts which were pressed between filter paper before weighing.

TABLE II

Age at operation	Age at death	Control group averages						Nephrectomy group averages						Mg. kidney per 100 sq. cm. body surface			Compensatory renal hypertrophy
		No. rats	Initial body weight	Gross body weight at death	Corrected body weight	Body surface	Kidney weight	No. rats	Initial body weight	Gross body weight at death	Corrected body weight	Body surface	Kidney weight	Control group	Nephrectomy group	Difference	
day	*days*		*gm.*	*gm.*	*gm.*	*sq. cm.*	*mg.*		*gm.*	*gm.*	*gm.*	*sq. cm.*	*mg.*				*per cent*
5	45	22	—	89	82	214	387	14	—	84	79	206	617	181	299	118	65.2
15	55	20	25	125	116	269	509	21	26	125	145	271	798	188	296	108	57.5
30	70	25	42	179	170	347	644	26	42	173	164	340	903	185	266	81	43.7
60	100	24	130	235	225	419	759	25	126	206	198	385	944	182	245	63	34.6
90	130	25	166	272	265	468	851	25	169	272	265	467	1118	181	239	58	32.0
180	220	24	290	366	361	575	990	24	281	346	341	554	1249	172	225	53	30.9
270	310	27	322	384	381	596	976	27	324	361	356	569	1239	164	218	54	32.9
360	400	22	318	372	367	581	1035	19	325	365	360	573	1255	178	219	41	23.1
540	580	23	407	437	407	620	1100	23	389	398	390	606	1270	171	210	39	22.8

RESULTS

Table I gives the results. The kidney weight is expressed in miligrams per 100 sq. cm. of body size, since it has been shown that under uniform conditions this value is approximately constant at all ages (3). In calculating the body surface the formula of Carman and Mitchell (4) was used although more recent investigations (5) suggest that the constant should be smaller. However the magnitude of the constant has no effect on our relative figures. The kidney weights tabulated for the control groups are the average of the weights of both kidneys. The degree of compensatory hypertrophy is expressed as the percentage increase in weight of the single kidney over the average

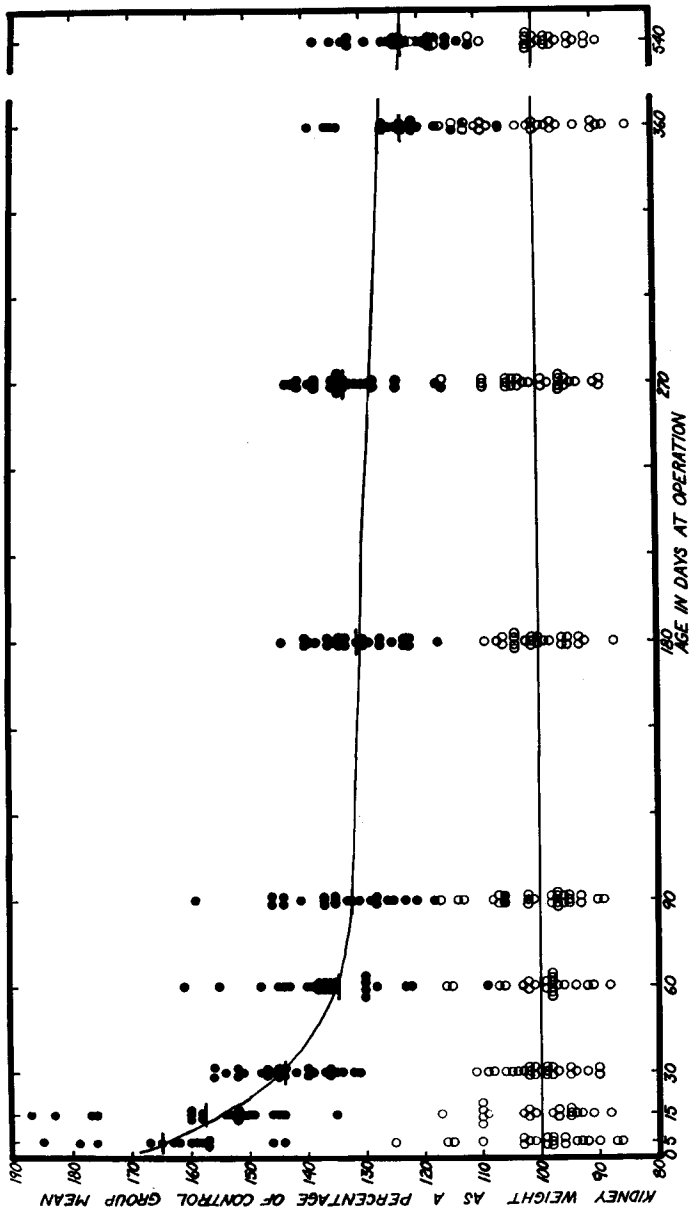
AGE IN DAYS AT OPERATION
0.5
15
30
60
90
180
270
360
540
KIDNEY WEIGHT AS A PERCENTAGE OF CONTROL GROUP MEAN
80
90
100
110
120
130
140
150
160
170
180
190

FIG. 3

weight of both kidneys of the control. In Table II the average results for each age are given. This table and the graphic representation of the individual observations given in Fig. 3, show how the degree of compensatory hypertrophy decreases, rapidly from 5 to 60 days of age, but thereafter very slowly as age advances.

DISCUSSION

Young rats eat a greater amount of food in relation to their size than older rats. With a constant diet such as was given to all but

TABLE III

Age at operation	Control group					Nephrectomized group						
	Intake per sq. dm. per day		*Kidney weight per sq. dm.			Intake per sq. dm. per day		*Kidney weight per sq. dm.			Degree of compensatory renal hypertrophy	
	**Food	Protein	Calculated due to protein intake	As observed	Corrected for protein intake	**Food	Protein	Calculated due to protein intake	As observed	Corrected for protein intake	As observed	Corrected for protein intake
days	*gm.*	*gm.*	*mg.*	*mg.*	*mg.*	*gm.*	*gm.*	*mg.*	*mg.*	*mg.*	*per cent*	*per cent*
30	3.41	0.61	33	185	152	3.30	0.60	66	266	200	43.8	31.5
60	2.41	0.43	23	182	159	2.43	0.44	46	245	199	34.6	26.9
90	2.41	0.43	23	181	158	2.50	0.45	50	239	189	32.0	19.6
180	2.07	0.37	20	172	152	2.11	0.38	42	225	183	30.8	20.4
270	1.59	0.29	16	164	148	1.70	0.31	34	218	184	32.9	24.3
360	2.11	0.38	21	178	157	2.16	0.39	42	219	177	23.0	12.7
540	1.61	0.29	16	171	155	1.71	0.31	34	210	176	22.8	13.5

* One-half the weight of the two kidneys.

** Average of last 10 days of experiment.

the first two groups young rats get proportionally more protein than the older rats. A definite relation has been shown to exist between the amount of protein eaten and the weight of kidney (6). Assuming that the protein-kidney weight formula is applicable to a single kidney it is possible from our food intake data to calculate what would have been the weight of the remaining kidney as well as of the average of the control kidney if the protein intake had been constant at all ages. The results of these calculations are given in Table III. They show that the essential features of the relationship are retained in spite of such corrections and that the decrease in compensatory hypertrophy

as age advances cannot be ascribed to the concomitant changes in protein consumption.

The concentration of water in body tissues decreases with age. Lowrey (7) has determined the water concentration in the kidneys of rats of varying age, and from his data a curve has been constructed which in Fig. 4 has been superimposed on a curve of compensatory hypertrophy derived from our data in Table I.

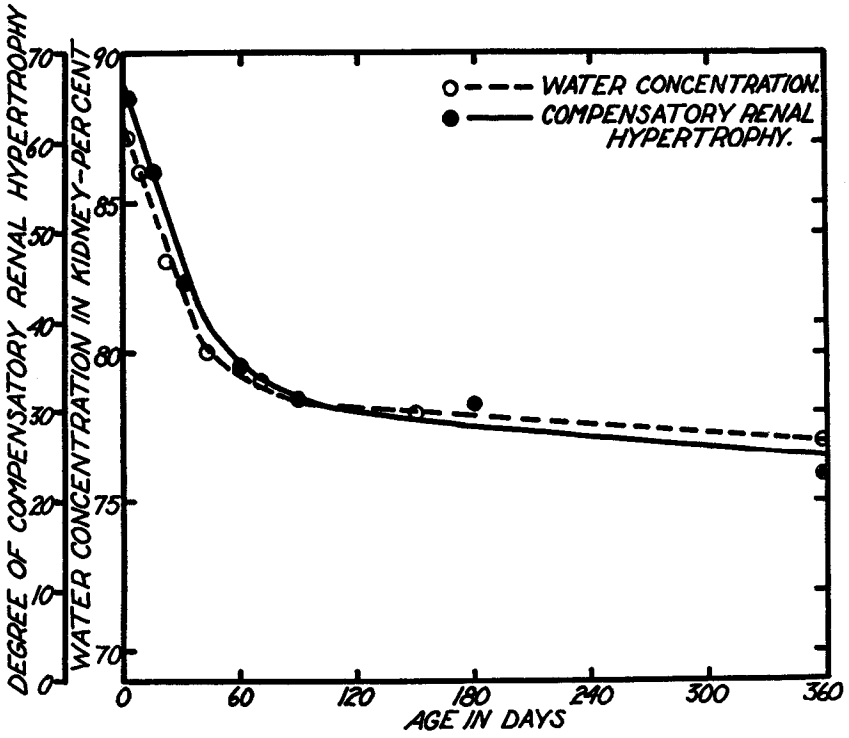

FIG. 4

It is interesting that there should be such a close correspondence between the degree of compensatory hypertrophy and the water concentration of the kidney at the time of nephrectomy. The agreement favors the view that the changes we observe are a special instance of the general decrease in growth capacity in the body as it grows old and that the design of any experiments made in the attempt

to elucidate the mechanism underlying these changes should be based on the general results of the study of senescence.

CONCLUSION

Compensatory hypertrophy of the kidney in albino rats becomes less as age advances. There is a rapid decrease from 5 days to 60 days of age and then a slow diminution throughout adult life.

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