THE SYSTOLIC BLOOD PRESSURE OF THE NORMAL RABBIT MEASURED BY A SLIGHTLY MODIFIED VAN LEERSUM METHOD.

FINAL REPORT.

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In this report it is intended to complete and extend my previous publication (1) on the systolic blood pressure of the rabbit. An account of the method used, together with the technique both of the loop operation and of the measurements, is to be found in the first report and will not be given here.

The number of loops made has been 186, the first one on April 4, 1923, the last one on July 30, 1926. Good loops, that is, even, soft and of convenient length, were obtained in 97 (52.2 per cent), of which 4 were lost before any measurement was made (trauma, pneumonia) and 3 are omitted now because the measurements were started in the course of an experiment. The majority of failures is due to necrosis or infection of the loop. From March 31 to April 16, 1925, 23 loops were made, of which only 3 were satisfactory (13 per cent), 18 being spoiled by necrosis or infection (78.3 per cent). On the other hand, from September 25 to September 30 of the same year, 22 loops were made, of which 16 were good (72.7 per cent), only 5 being ruined by infection or necrosis (22.8 per cent). On July 29 and 30, 1926, 7 loops were made, all good. These figures show the extremes of failure and success which have been met in this work. The success of the other series falls between 50 and 60 per cent, so that the poor result with the loops made in April, 1925, seems to have been due to some extraneous factor not determined. The other causes of failure are general, such as pneumonia, pleurisy, otitis media, etc., and are not peculiar to this plastic operation. There is still another complication which may

TABLE I.

No. of rabbit	Sex	Observation period	No. of days on which blood pressure was taken	Mean of blood pressure 1st day	Maximum blood pressure whole period	Minimum blood pressure whole period	Pulse rate 1st day	Fastest pulse rate whole period	Slowest pulse rate whole period	Body weight		Remarks
										Initial	Final	
		1923		*mm. Hg*	*mm. Hg*	*mm. Hg*				*kg.*	*kg.*	
37-2	F	May 15–Sept. 12	92	126	165	102		272	172	2.110		Weight Apr. 4. Snuffles
39-6	F	May 15–June 1	11	125	136	90						Snuffles. Ear canker
39-7	F	May 16–June 5	15	130	170	125						Snuffles
42-0	F	July 25–Oct. 17	48	118	147	90	228	264	176		2.275	Albino. Litter of 10 Aug. 1
42-1	M	Aug. 3–Sept. 10	31	103.6	132	72	204	224	120	2.675		Weight June 5
46-1	M	Aug. 4–Oct. 17	40	104.1	130		208	256	160	2.390	2.600	Constriction. Snuffles
46-9	M	Oct. 16–Dec. 3	35	136.6	157	105	232	264	160	2.350	2.390	White Angora
		1923–24										
47-0	M	Aug. 4–Jan. 16	103	102.4	149	90	194	248	128	2.375	2.805	
		1923										
47-3	M	Aug. 18–Aug. 20	2	129.5	143	119	204	264	200	1.702		Weight July 24. Trauma
47-4	M	Oct.–Dec. 1	37	105.9	138	82	248	264	112	1.895	1.905	
47-7	M	Oct. 18–Nov. 26	31	101	133		162	236	136	2.120		Weight Oct. 27. Constriction. Abscess at angle of left lower jaw
48-2	M	Oct. 9–Dec. 1	44	111.9	129	75	242	264	156		2.060	
		1923–24										
48-3	M	Oct. 8–Oct. 13	266	109.5	144	77	222	280	112	2.290	3.145	Sciatic injury, Oct. 18, 1923
		1923										
48-4	M	Aug. 21–Oct. 12	16	114.1	127		240	300	208			Resistance. Abscess (flank). Constriction

48-5	M	Oct. 18–Dec. 1	35	139.5	156	92	253	296	160		2.120	Sciatic injury
48-7	M	Aug. 15–Dec. 1	58	128.1	172	103	296	300+	192	2.285	2.610	Albino. Mediastinal abscess during experiment
48-8	F	Aug. 14–Sept. 8 *1923–24*	23	110	143	94	156	240	148		2.585	Abscesses in abdominal wall
48-9	M	Aug. 14–Oct. 13 *1924*	301	134.5	201	116	248	300+	144	2.890	3.015	
D 1	M	Jan. 7–Feb. 26	44	99.2	135		200	220	136	2.310	2.855	Constriction
D 3	F	Jan. 7–Feb. 11	31	126.8	140	95	200	280	132	2.290	2.000	Purulent pleurisy
D 6	F	Jan. 7–Feb. 26	45	128.1	140		176	232	152	2.065	2.495	Constriction, marked
D 8	F	Jan. 7–Mar. 27	39	144.8	160	103	192	300+	176	2.795	2.610	
D 10	F	Jan. 7–Feb. 26	44	140.4	150		264	280	188	2.465	2.705	Constriction
D 12	F	Jan. 7–Feb. 26	44	129.3	132		224	224	152	1.970	2.435	Albino
D 13	M	Feb. 1–Mar. 27	46	138.7	157	95	192	240	136	2.345	2.275	
D 16	F	Apr. 15–Apr. 29	10	136	159	124	240	256	216	2.275	2.305	
D 19	M	Apr. 15–Apr. 29	10	143.6	162	125	232	256	184	2.060	2.050	
D 21	F	Apr. 15–Apr. 29	9	154.6	162	135	216	216	176	2.175	2.200	
D 22	F	Apr. 15–June 17	19	126.7	168	111	192	232	176	2.280	2.480	
D 23	F	Apr. 15–May 15	12	115.3	133		184	216	144	2.080	2.150	Constriction
D 24	M	May 1–May 15	10	121	129		208	232	168	1.845	1.915	Constriction
D 25	F	May 20–July 17	28	84.6	110	72	216	248	160	1.840	2.085	Resistance
D 26	F	May 1–May 28	21	128.2	148		200	220	168	1.975	2.225	Constriction
D 27	F	Apr. 22–May 20	20	122.9	135		216	240	184	1.815	2.000	Constriction
D 28	F	June 13–July 11	23	109.9	131	91	168	224	144	2.055	2.310	
D 31	F	Apr. 22–May 20	18	108	119		176	224	160	1.920	1.975	Constriction
D 33	M	Apr. 23–Apr. 28	5	109.6	120	87	200	224	168	1.885	1.865	Trauma
D 34	F	May 30–June 17	16	125.6	133	97	184	200	136	2.370	2.635	
D 41	M	June 12–July 10	23	137.1	145	96	192	232	164	2.325	2.290	
D 42	M	June 12–July 10	22	108	120	90	224	240	192	1.820	1.965	
D 45	M	June 5–July 11	29	107	122	89	208	240	152	2.125	2.060	

TABLE I—*Continued.*

No. of rabbit	Sex	Observation period	No. of days on which blood pressure was taken	Mean of blood pressure 1st day	Maximum blood pressure whole period	Minimum blood pressure whole period	Pulse rate 1st day	Fastest pulse rate whole period	Slowest pulse rate whole period	Body weight		Remarks
										Initial	Final	
		1924		*mm. Hg*	*mm. Hg*	*mm. Hg*				*kg.*	*kg.*	
D 46	M	June 12–July 11	23	135.1	149	105	184	232	160	2.184	2.115	
D 49	F	June 30–July 19	16	116.7	140	97	184	232	168	2.140	2.365	
D 53	F	June 30–July 19	17	95.6	116	89	208	252	176	1.970	2.050	
D 55	F	June 30–July 19	17	123.1	155	107	216	248	168	2.425	2.215	Litter of 3 July 6
D 56	M	June 30–Aug. 22	43	101.7	132	84	208	248	160	1.955	2.165	Ear canker
D 59	F	June 30–July 19	17	115.8	145	98	196	232	176	1.910	1.965	
D 61	M	Aug. 11–Sept. 30	15	95.8	131	90	224	256	208	2.095	1.705	Sciatic injury
D 62	F	July 8–Sept. 10	28	129.6	154	102	216	256	168	2.415	2.315	Litter of 8 July 16
D 65	M	Aug. 12–Sept. 10	25	138.2	170	112	192	240	168	2.150	2.325	
D 66	M	Aug. 11–Oct. 27	61	100	125	70	208	280	144	1.945	2.460	Large abscess in thigh
D 67		Aug. 1–Sept. 10	25	97.6	129	92	248	264	176	2.420	2.635	
		1924-25										
D 69	F	Sept. 25–Feb. 10	76	145	174	126	224	248	160	2.825	3.460	
D 77		Nov. 10–Feb. 5	40	120.4	140	98	200	288	152	2.815	3.580	
D 78	M	Nov. 10–Feb. 5	39	114.5	156	91	264	280	168	3.115	3.730	Resistance. Constriction
D 80	M	Nov. 10–Mar. 24	69	144.4	168		216	240	152	2.965	3.040	Otitis media. Constriction
D 82	F	Nov. 10–Feb. 10	43	110	135	90	224	248	168	2.325	3.355	
		1924										
D 83	F	Nov. 10–Nov. 29	6	113.1	130	110	248	256	144	2.725	2.875	Chewed loop

		1924–25										
D 84	F	Nov. 24–Feb. 10	35	121.1	152	106	248	296	216	2.780	3.320	
D 85	M	Nov. 24–Feb. 10	33	103.7	141	99	200	248	144	2.820	3.350	
		1925										
D 87	M	Jan. 8–Mar. 24	59	110.8	130	82	264	264	148		3.625	Weight Oct. 24, 1924, 2.270 kg.
		1924										
D 88		Nov. 24–Nov. 26	3	109.6	115	94	200	200	176	2.480		Death from diarrhea
		1925										
D 89		Jan. 8–Mar. 26	60	118	142	97	224	248	160		3.195	Weight 2.300 kg. Nov. 22, 1924
		1924–25										
D 91	F	Nov. 24–Feb. 14	38	128.5	142		216	224	168	2.220	2.945	Constriction
		1924										
D 92	F	Nov. 24–Nov. 25	2	121.1	125	102	288	300	288	2.320		Accidental death
		1924–25										
D 94	F	Nov. 24–Feb. 10	34	126.3	167	112	232	288	200	2.310	2.460	
D 96	M	Nov. 24–Mar. 24	62	114.5	152		240	272	184	2.150	2.880	Constriction
		1925										
D 97	F	Apr. 15	1	133.5	140	130	248			3.480		
D 98	F	Apr. 15	1	131.1	138	124	272			2.550		
D 116	F	Sept. 24–Oct. 30	17	124.4	133	107	224	256	216		3.010	Constriction
D 118	F	Sept. 24–Oct. 30	16	123.9	138	95	232	256	208		2.330	
D 119	F	Sept. 24–Oct. 30	16	100.6	122	92	264	288	224		2.670	
D 123	F	Oct. 19	1	84.3	90	80	240			2.250		Weight Sept. 25, 1925. Trauma
D 125	M	Oct. 19–Oct. 30	10	101.7	119	89	232	240	216		2.320	Constriction (late appearance)
D 127	M	Oct. 19–Oct. 30	10	122.9	134	85	232	248	200		2.160	
D 131	M	Oct. 19–Oct. 30	10	97.4	112	72	232	240	184		2.080	
D 134	M	Oct. 20	1	71.3	75	69	208			1.720		Trauma. Weight Sept. 29, 1925
D 135	F	Oct. 19–Oct. 30	10	73.4	89	68	184	232	184		2.590	
D 136	M	Oct. 19–Oct. 30	10	82	105	80	176	208	176		2.510	
		1926										
D 137	F	June 10–June 22	9	114.2	129	102	192	208	176		2.920	

TABLE I—*Concluded.*

No. of rabbit	Sex	Observation period	No. of days on which blood pressure was taken	Mean of blood pressure 1st day	Maximum blood pressure whole period	Minimum blood pressure whole period	Pulse rate 1st day	Fastest pulse rate whole period	Slowest pulse rate whole period	Body weight		Remarks
										Initial	Final	
		1925–26		*mm. Hg*	*mm. Hg*	*mm. Hg*				*kg.*	*kg.*	
D 138	F	Oct. 19–Apr. 22	103	91.9	112	77	216	280	192	2.475	2.650	Constriction
		1926										
D 139	F	June 10–June 22	9	102.2	129	98	216	272	200		3.140	
		1925–26										
D 140	M	Oct. 19–June 22	111	101.7	132	74	200	264	184	2.065	3.410	
D 141	M	Oct. 19–Apr. 22	92	91	126	79	208	280	184	1.885	3.060	Sciatic injury, Nov. 21, 1925
		1926										
D 142	M	June 10–June 23	10	132.9	136	105	224	272	224		2.980	
		1925–26										
D 143	F	Oct. 19–June 22	107	106.3	138	85	240	288	216	2.310	3.470	
		1926										
D 144	F	Aug. 24–Oct. 4	10	100.7	115	90		240	208		2.565	
D 145	M	Aug. 24	1	90.4	92	89						Trauma
D 146	M	Aug. 24–Oct. 4	10	91.9	103	84	208	224	184		2.365	Accidental death
D 148	F	Aug. 24–Oct. 4	10	77.4	98	70	208	240	200		2.835	

appear when the animal kicks within the controlling box, and to which young animals, very quick in their actions and with soft bones, are specially susceptible. This is referred to below as "spinal trauma" and in Table I as "trauma." In some instances, under the same circumstances, instead of a complete paraplegia, there appears a partial

TABLE II.

Blood pressure	No. animals	Per cent
mm. Hg		
150–	1	1.1
140–149	6	6.7
130–139	13	14.4
120–129	20	22.2
110–119	18	20.0
100–109	16	17.8
90–99	10	11.1
80–89	3	3.3
70–79	3	3.3
	90	99.9

TABLE III.

Pulse rate per min.	No. animals	Per cent
280–299	2	2.3
260–279	5	5.9
240–259	13	15.3
220–239	17	20.0
200–219	29	34.1
180–199	13	15.3
160–179	5	5.9
140–159	1	1.2
	85	100.0

paralysis of one or both of the hind legs, without disturbance of the sphincters, and the animal recovers completely. This is referred to as "nerve injury." This complication is caused by the use of a controlling box and is not inherent in the loop method. One complication peculiar to the method is that some animals chew the loop. Five

did this: four (D 65, D 80, D 83 and D 96) during an interval in which no measurements were taken; and one (D 142) during a period of daily readings (March, 1927). The last one has not done it again so far, and three of the other four did not persist, so that in these animals the loop healed again and remained in good condition. But D 83 kept on chewing it until it became so scarred and so hard, that no more measurements could be taken. Eventually the animal died of hemorrhage. The reason for this is not clear, because repeated examination shows that there is no anesthesia or analgesia in the loop. Finally, one animal (D 25), on being lifted from the cage, caught its claw under the loop, kicked and tore it. This last accident (1 out of 97 good loops) and the "spinal trauma" are avoidable. The latter occurs in general on the first measurement and only in young animals, so it can be avoided by using full grown animals. This is preferable to packing the animal so tightly in the box that it cannot move. These are the only complications I have seen, which can be directly or indirectly attributed to the loop method. I have never seen thrombosis of the carotid or inflammation of the loop in animals under observation, which Van Leersum (2) reported having seen in one animal, or in fact any ill effects on the general condition of the rabbit. I have measured the blood pressure for as long as 15 months, with almost daily readings (1), and I am still measuring one rabbit 18 months after the first reading.

The data to be discussed now have been arranged in tabular form. They represent routine observations only, and not the results of any experimental condition imposed upon the animal, excepting of course the actual procedure of measuring the blood pressure and also a period of inanition of a few days to which several animals were subjected early in the work. Only one animal (No. 48-9) showed any effects of inanition, and the variations observed were not the extremes of the total variation recorded (1). On the other hand several of the animals developed diseases of various kinds, or were found to be pregnant or were the victims of some accident. These appear in Table I under "Remarks" and will be discussed later on. The blood pressure of a total of 90 rabbits (including the first 63 reported before) on the 1st day of observation is seen in Table II. The figures represent the arithmetic mean of the first 10 consecutive readings. The difference

between this table and the first one published (1) is partly due to better statistical treatment (a more careful distribution of the means). Three rabbits appear between 70 and 80 mm. Hg and none beyond 150 mm. The table, as it stands now, shows that on the 1st day of the examination, 60 per cent of the rabbits had a systolic blood pressure between 100 and 129 mm. Hg, and 85 per cent between 90 and 139 mm. Hg. The table, small as it is, compares in a general way with similar compilations made on men and women on the 1st day of examination. Concerning the published data on the blood pressure of the rabbit (direct measurement) it will be enough to quote the following: Volkmann (3) gives 90 and 108 mm. Hg. Meyer (4), after compiling the literature up to 1881, 51 experiments, comes to the following conclusion: "Dannach kann man als Grenzwerthe des mittleren Blutdrucks normalen Kaninchen ca. 70 und 140 mm. Hg annehmen." A remarkable conclusion, I think. Tigerstedt (5) says: "Beim Hunde schätzt man den Blutdruck auf 130–180 mm. Hg, beim Kaninchen auf 80–120."

The pulse rate of the rabbits reported in the present paper, counted on the loop itself at the end of each set of blood pressure readings, is shown in Table III. The pulse rate of the 1st day only has been given. By counting every other beat in a quarter of a minute, and multiplying by 8, it was possible to obtain the fast rates recorded. The error in these figures is at most ± 8, small for the purpose. It appears that the pulse rate of 84.7 per cent of these rabbits ranged, during the first measurement, between 180 and 259 beats per minute. Tigerstedt (5) quotes the figures of Colin (1888), 120–150 per minute, and Ellinger (1894), 120–160 per minute, as the pulse rate of the rabbit. I have had no access to the original works quoted by Tigerstedt, so I do not know under what conditions Colin and Ellinger counted the pulse rate. But since it is much simpler to count the pulse than to measure the blood pressure, and since it can be done with very little disturbance to the animal, the pulse rate becomes an invaluable index of the presence of psychic or other factors which may have at the same time some effect on the blood pressure.

It is important to note that neither the mean of blood pressure nor the pulse rate of the *first* observation is in general the highest recorded during the whole period. Thus, for instance, only five

showed on the 1st day as fast a pulse rate as the fastest during the entire interval of observation of the respective animals (D 12, D 21, D 87, D 88, 48-7), and of these only one was near the maximum of the whole series (No. 48-7, 296 per minute), discarding of course those animals in which only one observation was made. With regard to the blood pressure, the number of animals in which the highest single reading of the corresponding period of observation was at most 10 mm. Hg higher than the mean of the 1st day, was sixteen, and of these eight were examined during less than 1 week. The remaining eight are D 10, 12, 21, 24, 34, 41, 116, 142. The distribution of the

TABLE IV.

Blood pressure	No. animals	Per cent
mm. Hg		
200–	1	1.2
170–179	4	4.9
160–169	7	8.5
150–159	10	12.2
140–149	15	18.3
130–139	22	26.8
120–129	12	14.6
110–119	7	8.5
100–109	2	2.5
90–99	0	
80–89	2	2.5
	82	100.0

maximum blood pressure by animals is seen in Table IV. By maximum is meant the highest blood pressure recorded *at least once* during the whole period of observation of the corresponding animal. Eight animals have been omitted because they were examined only during 1, 2 or 3 days. The table shows that on prolonging the observation period, 71.9 per cent reached 130 mm. Hg, 45.1 per cent reached 140, and 26.8 per cent reached 150, at least once, whereas on the first examination only 22.2 per cent were at or above 130 mm. Hg (see Table II).

I shall consider in more detail those which reached or passed 160 mm. Hg. D 8, D 19, D 21, D 65 and D 80 had only isolated high

figures, so that in their protocols there is no *mean* of 10 readings at or above 160. Nos. 37-2, 48-7 and D 94 had only one *mean*, and Nos. 39-7 and D 22 two *means* above 160 mm. Hg. D 69 showed *means* between 160 and 173, 11 times out of 76 (14 per cent), *scattered* throughout the period of observation. There remains one rabbit, No. 48-9, whose graph was reproduced in the first report (1). The number of *means* at or above 160 is 92, out of 516 (18 per cent), but what makes this observation noteworthy is the fact that, excepting scattered high means in October and December, 1923, practically

TABLE V.

Blood pressure	No. daily averages		Per cent	
	No. 48-3	No. 48-9	No. 48-3	No. 48-9
mm. Hg				
190–199		1		0.3
180–189		3		1.0
170–179		15		5.0
160–169		33		11.0
150–159		76		25.2
140–149		84		27.9
130–139	6	57	2.2	18.9
120–129	12	31	4.5	10.3
110–119	34	1	12.7	0.3
100–109	117		43.8	
90–99	79		29.6	
80–89	19		7.1	
Total.....	267	301		

all the readings made in September and the first third of October, 1924, were at or above 160 mm. Hg.

What is the behavior of the pulse rate? In general, when the blood pressure rises in a normal rabbit, the pulse rate increases, but the converse is not true: an increase in pulse rate is not necessarily acompanied by a rise in blood pressure. If the animal resists, whether the blood pressure rises or not, the pulse rate increases. In Table I the exceptional animals from the point of view of resistance are referred to by the word "resistance" under "Remarks." Under conditions of "excitement" there may be no effect on pulse rate or

blood pressure, or a marked increase in both or only in the pulse rate. Excitement is an unsatisfactory word to use, because it involves so much which is subjective. Without attempting to define it, I shall give a list of the observations included under this heading: tickling the animal's nose or closing its nostrils for a few seconds during a set of measurements; after a few days of inanition putting a piece of carrot under its nose, while measurements are being taken; placing adult male rabbits, after several months confinement, with females, both in heat and not in heat, and taking the blood pressure and pulse rate before and after copulation. Under these conditions "excitement" is expected to be produced, and the animals show, indeed, signs which can be interpreted as such. Yet the results on blood pressure or pulse rate are not consistent or uniform in all the rabbits examined. A few examples may be seen in the first paper (1). The meaning of "an increase in pulse rate" will be understood from an examination of the figures of the two animals which exhibited the highest blood pressure, D 69 and No. 48-9.

TABLE VI.

Pulse rate	Daily averages		Per cent	
	No. 48-3	No. 48-9	No. 48-3	No. 48-9
280–299		2		0.7
260–279	1	12	0.3	4.0
240–259		59	0.0	19.7
220–239	8	77	3.0	25.8
200–219	25	94	9.5	31.4
180–199	42	41	16.0	13.7
160–179	110	12	41.7	4.0
140–159	57	2	21.6	0.7
120–139	20		7.6	
100–119	1		0.3	
Total.....	264	299		

D 69, as stated above, showed 11 means between 160.2 and 173 mm. Hg (with a mean of the means of 165) and the pulse rate of the corresponding days was between 208 and 248 per minute (mean 229). No. 48-9 showed 29 consecutive means between 155 and 193 mm.

Hg, with a mean of the means of 174, and the pulse rate of the corresponding days varied between 212 and 272 (mean 245).

The totals of the data from Nos. 48-9 and 48-3 are seen in Tables V and VI. Their graphs may be seen in the first paper (1). They represent the limiting cases found in this investigation. A few animals had a lower blood pressure than No. 48-3, but they were examined for a much shorter time, or their pulse rate was higher, or their figures were more scattered in distribution, or their behavior was not quite so good. Again, no other animal had a higher blood pressure than No. 48-9. So that these observations help in determining what might be called the boundary conditions of experimental hypertension in rabbits.

It is not practicable to present all the data in detail. If ever a compilation on the "normal" rabbit were attempted (and such a compilation is an urgent need of laboratory workers),[1] then this material would find its proper place there. It is only necessary here to show the salient facts observed on which a criterion for a pathological rise in blood pressure in the rabbit may rest. It must be borne in mind, that by "normal blood pressure of the rabbit" is meant the systolic blood pressure of a healthy looking rabbit *under the conditions of the measurement.* The practice of taking the blood pressure of the rabbit a few days before the experiment, *as control,* has less value than is generally conceded. 1 week, or 1 month of observation, is not sufficient to characterize completely the blood pressure curve of a rabbit, and does not guarantee that the pressure will behave in the same way in a subsequent interval of time. Finally, the purpose of the investigation must be considered. For acute experiments, there is little need of a carotid loop. On the other hand, a method like this is indicated for the study of prolonged alterations in blood pressure, which may simulate either the clinical picture of hypertension or Addison's syndrome. With these reservations in mind, a criterion could be formulated as follows:

(*a*) Under the conditions of the measurement, a rabbit may be said to have a pathologically high blood pressure, if the blood pressure

[1] The recent work of Brown, Pearce and Van Allen is an excellent beginning in this direction (11).

oscillates *above 180 mm. Hg* and does not fall below that figure during a length of time dependent on the nature of the experiment.

(*b*) Under the same conditions, the blood pressure may be considered pathologically high if it oscillates *about 170 mm. Hg* with a concomitant pulse rate *below 200 beats per minute.*

The introduction of the pulse rate in (*b*) allows the avoidance of consideration of resistance, "excitement," and the like, and makes unnecessary the discarding of any figure in the course of the investigation. It seems superfluous to add that these criteria are provisional. Strictly speaking they rest on observations made on 90 "normal" animals (over 30,000 blood pressure readings, about 2,900 pulse rate counts), but they are reinforced by the subsequent experience with these animals under several pathological conditions. Since these observations, moreover, spread over 4 years, and since the animals were obtained from different dealers in different years, it is expected that future experience with the method here adopted will not differ grossly from that described in the present report. The observations of Van Leersum himself (1911, 1912) on twelve rabbits, agree very well with mine.

An Important Source of Error of the Method.—The following phenomenon has been observed in several rabbits.

D 138, Feb. 4, 1926, 3.09 p.m.* 100–101–79–82–84 = 93–98–98–100 = 103–97–100–99 = 102–101–103–103 = 103–92–92 (pulse rate 232).

D 80, Jan. 21, 1925, 10.55 a.m.* 152–102–112–108–112–118–126 = 141–132–132–136 = 146–143–143–145 = 145–143–142 = 141–142 (pulse rate 224).

Jan. 30, 1925, 11.36 a.m.* 144–140–140–138 = 139–139–140–105 = 102–108–116–120 = 130–131–130–135 = 130–132–128–132 (pulse rate 224).

* Cuff adjusted to loop.

This abrupt fall in blood pressure occurs at any time in a given rabbit. If observed once in an animal it may be observed many times. No sign of a more general character accompanies this phenomenon: no alteration in pulse rate, no change in behavior, no respiratory disturbance, no pupillary effect. It may probably be explained by a local constriction of the carotid under the influence of

the pressure applied on the cuff. The fact that it does not appear in all animals is not an objection to this explanation, because the carotid is subjected to this stimulus intermittently for a short time (3 to 5 minutes), and it is not to be expected that all carotids will react in the same way to a given stimulus. It is clear that the change must be local and not the expression of an actual fall of arterial pressure, which would be accompanied by a change of pulse rate. In Table I it appears under "Remarks" as "constriction." In some animals it is very slight, for instance:

D 78, Nov. 17, 1924, 3.18 p.m.* 138–132–133–132 = 132–130–96 = 129–128–127–127.

In others it is frequent and becomes disturbing, as in the following example:

D 6, Jan. 26, 1924, 10.27 a.m.* 115–110–104–89–88 = 112–113–115 = 114–112– (pulse rate 184).
114–112–113–97 = 106–112–106–108 = 112–116 (pulse rate 176).

*Cuff adjusted to loop.

I have discarded no animal on this account, but the "minimum blood pressure" has no meaning under these conditions, and has been omitted from the table. It is enough to recognize this phenomenon to avoid the error produced by it.

Changes in the Carotid within the Loop.—The majority of the carotids enclosed in a loop showed after the death of the animal a marked transverse striation of the intima. The striations are due to a slight thickening of the intima. Under the microscope the lesion is not well defined: a slight sclerosis of the subintimal tissues and here and there a moderate vacuolization of the muscular coat. This striation has been observed in the remaining parts of several carotids, a long time after the loop had been severed on account of necrosis; that is, in arteries to which *no cuff had ever been applied.* It has been found absent in arteries in which measurements had been taken for a considerable time. In a few animals which died immediately after the operation (possibly ether death), the examination of the carotid revealed sharp transverse lines of intimal tearing, very probably produced by stretching the artery during dissection. Before this injury was recognized and avoided, it was not uncommon to see, before the final suture of the loop, small extravasations of blood on the muscular layer of the carotid, which gave to the artery a slightly beaded appear-

ance, the more noticeable since the artery at the end of the operation contracts down through exposure. With more care in the manipulation of the artery this lesion may be reduced in extent, and possibly eliminated altogether. The fact is, the rabbit's carotid is a very thin and delicate object and must be treated accordingly. I think that the lesion observed in a good number of the carotids is due to the cicatrization of these intimal operative injuries.

Shapiro and Seecof (7), reviewing some of the methods of blood pressure measurement in the rabbit, say that Van Leersum's would be an excellent one "provided the artery could be thus isolated without altering the compressibility of its walls through inflammatory reactions. This objection seems to render the method both impractical and prohibitive." The authors fail to realize that the method is not sensitive enough to detect small changes in the thickness of the artery. The cuff effect in this method consists of several parts, the cuff proper (a piece of cotton fabric and of rubber tubing), the skin with and without hair, subcutaneous tissue and the vessel wall. Of these, the first three become softer and more supple in time, which, theoretically at least, would lower the value of the total effect, whereas the thickening of the intima is not progressive as far as I have been able to ascertain. Under these conditions, fluctuations of 40 mm. Hg *in one animal* several days, or several weeks apart, or occasionally in 1 day, cannot be due to variation in compressibility of the arterial wall. Finally, in experiments on arteriosclerosis (to be reported soon) where *calcification* was found in the media of the carotid within the loop, as well as in other large vessels, and in the aorta, no constant elevation of the blood pressure was observed.

MacWilliam in his review (8) on the blood pressure of man says: "It may be taken as established that high blood pressure readings, when carefully taken, represent approximately correct measurements of the actual intra-arterial pressures as a rule. It is only in a small minority of abnormal cases of thickened arteries with excessive tonic contraction, etc., that serious discrepancy may occur, sclerotic conditions without muscular contraction having no important influence. Digital compression for 3 or 4 minutes or massage of the artery are useful in removing abnormal resistance and have the advantage of not causing congestion of the limb which may arise from repeated compressions by the armlet." The lesion in the carotid of my rabbits is of the type considered by MacWilliam as having no important influence, and the method, as actually used, amounts to a digital massage of the artery, so that, if this massage were as efficacious as MacWilliam believes and such "excessive tonic contraction" were ever present in the rabbit, the method would automatically eliminate this source of error.

Blood Pressure in Pathological Conditions.—After what has been said before it will be easy to see the difficulty of attaching importance

to small variations in blood pressure, within the range of figures between 80 and 170 mm. Hg. Their importance increases as the pressure approaches these limiting values. The diseases that have occurred in animals under observation (not experimented upon, excepting the blood pressure readings) are, in order of decreasing frequency: coryza, ear canker, pneumonia (with or without pleurisy), purulent pleurisy, subcutaneous abscesses, meningitis (drooping and rotation of head). Diseases found at autopsy, not diagnosed during life: coccidial cysts in abdomen, otitis media (one or both sides, without meningeal involvement), scarred kidneys, arteriosclerosis of aorta (slight), pulmonary abscesses (discrete), pulmonary mycosis, mediastinal abscess. Accidental injuries: "spinal trauma," "sciatic injury," total infarction of kidney (ligature of renal vein during adrenalectomy).

Of all these conditions only two deserve special mention: "Spinal trauma" and meningitis. During the terminal coma of the latter the blood pressure is low, 70–80 mm. Hg. Occasionally, however, the pulse is slow and irregular, and the actual blood pressure readings are not reliable. Concerning "trauma," the observation is as follows: the animal is within the box, quiet; blood pressure is taken as usual. Suddenly the animal moves within. The motion may not appear to be of excessive violence. The blood pressure rises abruptly (140–150 mm. Hg) and the pulse is very slow and strong. Soon afterwards (1 minute or so) the pressure gradually falls and the pulse rate increases. Greater details cannot be given because the occurrence fortunately is rare and takes place within a very short time.

In the other conditions the blood pressure findings are discordant. In one rabbit suffering from a large unnoticed abscess of the thigh, the blood pressure was low (the graph has been reproduced in another paper (9)). During the course of pleuropneumonias the blood pressure may lie between 80 and 90 (see graph for No. 47–0 (10)), or between 90 and 110 mm. Hg. In No. 48-7 the mediastinal abscess, a large mass twice as large as the heart, situated on the right side, anteriorly, and adherent to the pericardium, showed a certain effect on the blood pressure, the more interesting since it was completely misunderstood during life. The observation is so unusual, that an abstract of the protocol is presented.

No. 48-7, albino, male rabbit. July 31, 1923, carotid loop is made, weight 2.440 kilos. Partial necrosis of distal portion of loop. Healed completely.

Aug. 15, first blood pressure readings (see Table I). Aug. 18– Sept. 8, blood pressure between 120 and 129 mm. Hg (74 per cent of daily means). Oct. 6 and Dec. 2, 1923, blood pressure between 130 and 149 (72.5 per cent of daily means.)

Dec. 3, lead carbonate smeared in carrot, fed by hand, about 25 mg. daily. Dec. 8, weight 2.550 kilos; Dec. 23, best weight, 2.675 kilos. Dec. 24, daily dose of lead carbonate increased to 78 mg.

Jan. 4, 1924, diminished appetite; Jan. 12, weight 2.480 kilos; Jan. 17, weight 2.190 kilos. Jan. 20, little appetite. Jan. 26, lowering of blood pressure; blood pressure from Dec. 3, 1923, to Jan. 24, 1924, between 120 and 139 (78.4 per cent of daily means). Feb. 6, lowest weight, 2.120 kilos.

The loss in weight and the lowering of blood pressure (see below) were thought to be due to lead carbonate, and the latter was interrupted until Feb. 18, 1924. From Feb. 18 to May 31, lead was given daily in increasing dose, from 40 up to 300 mg. Feb. 16, weight 2.260 kilos. Weight increases slowly in spite of increasing dose of lead.

Feb. 20, symptoms while drinking water, as if water had entered the trachea. Abundant râles. Bronchial (or tracheal) moisture persisted until Mar. 19. On Mar. 1, it was thought that the animal had a foreign body in the trachea. Apr. 11, weight 2.480 kilos; May 26, weight 2.285 kilos. June 2, animal looks sick. Blood pressure from Jan. 26 to May 31, 1924, between 100 and 119 mm. Hg (87 per cent of daily means). Concerning the pulse rate the only thing at all remarkable is the fast rate in the second half of May, between 240 and 280 per minute (mean 258). Blood pressure on June 2, between 74 and 78 mm. Hg, pulse rate 208. June 3, lies on side, does not move. June 4, dead.

The beginning of this disease may have been concomitant with the first fall in weight in the latter part of Dec., 1923, and the formation of a mass in the mediastinum (probably from lymph nodes) may account for the spell on Feb. 20 and the slow recovery from it. The increase in weight in spite of increasing dose of lead carbonate militates strongly against lead poisoning. Lead given in this fashion to a group of animals (of which No. 48-7 is one) has shown no deleterious action (experiments to be reported later). The animal was in excellent physical condition up to June 2, 1924. It had been mated repeatedly during the whole observation, the last copulation having occurred on May 20.

Carotid Loop in Dogs.—As a further check on the method, loops were made in two dogs. Here it was possible to use the stethoscope and find auscultatory criteria for systolic and diastolic pressure similar to those used in man. The daily means of one of the dogs ranged from 123 to 165 mm. Hg, 77.7 per cent lying between 130 and 149 (85 days), for the systolic pressure, and from 69.1 to 103 mm. Hg, 87 per cent between 80 and 99, for the diastolic. The pulse rate oscil-

lated between about 60 and 184 per minute, 87 per cent of the counts being between 80 and 139. The other dog was examined during a much shorter time: systolic between 125.8 and 164.5 mm. Hg (10 daily means), diastolic 80–103, pulse rate 104–160. Both these dogs were subjected later on to double adrenalectomy. A complete report will appear shortly in collaboration with Dr. J. M. Rogoff.

SUMMARY.

The blood pressure and pulse rate of 90 normal rabbits have been studied for various periods of time, from 1 day (accidental death interrupting the observation) to 15 months. The main data are presented in a table containing the blood pressure and pulse rate on the 1st day of observation, the maximum and minimum of both during the entire period of observation of each animal, together with the sex and weight of the animal. Separate tables are given showing the distribution of blood pressure, pulse rate and the "maximum" blood pressure by animals. Detailed data on two animals observed for the longest time are given in tabular form. The anatomical changes that occur in some carotids enclosed in a loop are described and discussed. Considerations on "excitement" and pathological conditions which arise spontaneously in rabbits are given. A criterion for a pathologically high blood pressure in rabbits is proposed.

The blood pressure of the normal rabbit ranges between 70 and 170 mm. Hg. The pulse rate, taken simultaneously with the blood pressure, fluctuates between 112 and 300 per minute.

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