Diastolic Hypertension Produced by High Fat Diets and Dietary Stresses.* (23368)

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Four normal healthy dogs that were subjected to high fat diets and severe dietary stresses and irregularities over a prolonged period of time gradually developed a highly significant diastolic hypertension of long duration. Previous publications have described by graphic illustration, the first circulatory abnormality to appear(1) and the genesis and development of the hypertension(2). It is the purpose of the present communication to present a statistical evaluation of the fully developed hypertension.

Methods and procedure. The 4 dogs (2 males and 2 females) had been used in blood pressure studies for approximately 5 years. During that time blood pressure had been determined 5 to 6 days each week with almost no interruption, consequently, the animals were well trained and standardized. They were mature adult animals of approximately the same age and the 2 females were still having regular estrous cycles.

Blood pressure was determined by the auscultatory method of Allen(3) with certain modifications(4,5). During the present studies, blood pressure and heart rate were determined by the same observer, 5 to 6 days weekly between 6 and 10 a.m., with a specific time for each dog. The daily blood pressure values were the mean of from 10 to 15 consecutive readings.

The normal kennel diet consisted of a weighed amount of Nutrena dog food which kept each animal at an optimal body weight and the amount fed was the same during the control and the hypertensive periods. During all phases of the study the animals were fed at 3:00 p.m.

The first period of dietary stress (Experimental Period I) consisted of the following dietary manipulations done consecutively in the order given:

(A) A long preliminary fast (29 to 33 days) followed by realimentation with diets containing 50% of the calories from equal amounts of beef suet and salt free butter and 50% from cracker meal or horse meat, usually the former. These diets were fed at the level of 120 cal/M^2/hr. The preliminary fast and realimentation with the high fat diets will be referred to as "fat episodes." In Experimental Period I these were repeated 6 times in 14 months. There was little or no gain in weight on the high fat diets.

(B) A diet containing one-half cracker meal and one-half raw horse meat fed at the level of 120 cal/M^2/hr for 3 months. This diet caused very marked obesity. (C) The normal kennel diet for 3 months during which time weight loss was minimal. (D) A very low calory diet of raw horse meat for 5½ months which caused marked weight loss. (E) The normal kennel diet for 2 months. (F) The same low calory diet of raw horse meat for 2 months. (G) The usual kennel diet for 1½ months. (H) A diet of raw horse meat fed at the level of 120 cal/M^2/hr for 39 days. This diet caused a rapid gain in weight. (I) The normal kennel diet for 3 months. This period terminated approximately 22 months after the end of the last fat episode. The blood pressure and heart rate during the final 3 months on kennel diet are shown in the Table as Experimental Period I.

The second period of dietary stress consisted of 3 "fat episodes" in 10 months. The duration of the preliminary fasts varied from 20 to 36 days. These differed from those in the first period of dietary stress in that the realimentary diet contained 70% of the calories from animal fat and in each "fat episode" the high fat diets were alternated ir-

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regularly between the levels of 60 cal/M^2/hr and 120 cal/M^2/hr. Each fat episode was followed by a period on the low calory meat diet. At the end of this second period of dietary stress the animals were placed on the normal kennel diet for 84 days. The blood pressure and heart rate during the final 84 days on kennel diet are shown in the table as Experimental Period II.

The theoretical reasons for the use of the experimental design described above have been discussed(1,6).

(A) *Control blood pressure.* These 4 animals had been used in studies of the effect of protein and carbohydrate on blood pressure and heart rate(6). The control blood pressure and heart rate on the normal kennel diet were determined several times before, during and after these previous studies. It was found that protein and carbohydrate caused no permanent circulatory abnormalities and no change in the control blood pressure values on the kennel diet(7). The last control period was just before starting the present studies on animal fat. The number of control days on which blood pressure was determined varied from 89 to 168 for the 4 dogs. Since the value for each control day was the mean of from 10 to 15 readings, the number of determinations is large. The individual daily control values were combined statistically for each dog to give a single mean and standard deviation and from these the coefficients of variation and standard errors of the control mean value were calculated.

(B) *Blood pressure and heart rate after first period of dietary stress (Experimental Period I).* In Dogs I, III and IV elevations of the systolic and diastolic pressures above the control values were of about the same order of magnitude and were sufficiently great to be considered physiologically significant. Statistically the probability of these elevations calculated from t was <0.01. In Dogs I and IV the pulse rates were significantly lower than the control value but significantly higher than the control in Dog III.

In Dog II the actual elevation of the pressure above the control value was too small to be considered physiologically significant but the high statistical significance suggests that the basic trend in this animal was the same as in the others. The pulse rate in this dog is significantly lower than the control value. The small number of readings made on this dog was due to the fact that while the experiment was in progress, before the statistical study was made, we considered this animal to be refractory to the dietary stresses and temporarily discontinued the daily determinations of blood pressure.

(C) *Blood pressure and heart rate after second period of dietary stress (Experimental Period II).* In Dogs I, III and IV the systolic and diastolic pressures were again significantly above the control values. The heart rate in Dogs I and IV was again significantly below the control values but was again higher in Dog III.

In Dog II the systolic and diastolic pressures became markedly elevated above the control values while pulse rate was significantly slower.

Discussion. Throughout the entire experimental period the various dietary changes were always made simultaneously on the 4 dogs so that the dietary stresses were of the same duration and intensity. In view of this it is interesting to note the tendency to individual susceptibility of the animals. The first experimental period resulted in a near maximal elevation of blood pressure in Dogs I and III, while Dog II showed little effect. The second experimental period caused a marked rise in the pressure of Dog II and additional elevation in Dog IV.

During Experimental Period I the stress of the "fat episodes" caused a number of complications such as jaundice, vomiting, anorexia, convulsions, tarry stools and high retention of bromsulphthalein. During the second experimental period, the "fat episodes" were well tolerated and the only abnormal sign noted was occasional tarry stools.

During Experimental Period I the first circulatory abnormality to appear was failure of the blood pressure to decline during fasting; it either rose and plateaued at high levels or more frequently rose progressively during fasts of several weeks' duration. This abnormality appeared gradually and was not fully developed in all dogs until after the

TABLE I. Effect of 2 Periods of Dietary Stresses on Blood Pressure and Heart Rate of 4 Normal Dogs.

Dog		Control on kennel diet			Exp. period I			Exp. period II			Difference from control and significance of difference: Exp. I			Exp. II		
		S	D	P	S	D	P	S	D	P	S	D	P	S	D	P
I	M	114	44	82	141	76	62	133	79	56	+27	+32	−20	+19	+35	−26
	S.D.	13.21	9.42	14.64	6.81	5.49	9.18	7.09	5.00	5.39	<.01	<.01	<.01	<.01	<.01	<.01
	C.V.	11.5	21.4	17.8	4.8	7.2	14.8	5.3	6.3	9.6						
	S.E.	1.18	.84	1.31	.87	.70	1.18	1.00	.70	.76						
	N	124	124	124	60	60	60	50	50	50						
II	M	130	61	68	140	67	55	166	102	51	+10	+6	−13	+36	+41	−17
	S.D.	14.7	12.50	11.36	5.70	3.16	1.22	20.91	21.97	5.33	<.01	<.01	<.01	<.01	<.01	<.01
	C.V.	11.3	20.4	16.7	4.07	4.7	2.2	12.5	21.5	10.4						
	S.E.	1.38	1.18	1.06	2.55	1.41	.54	2.95	3.13	.76						
	N	113	113	113	5	5	5	50	50	50						
III	M	104	60	73	144	104	87	133	100	82	+40	+44	+14	+29	+40	+9
	S.D.	6.71	7.04	13.8	11.89	9.49	10.14	10.38	9.79	9.56	<.01	<.01	<.01	<.01	<.01	<.01
	C.V.	6.4	11.7	18.9	8.3	9.1	11.6	7.8	9.7	11.6						
	S.E.	.71	.74	1.46	1.54	1.23	1.32	1.48	1.39	1.36						
	N	89	89	89	59	59	59	49	49	49						
IV	M	114	59	79	143	96	67	153	105	71	+29	+37	−12	+39	+46	−8
	S.D.	10.40	9.15	10.86	10.22	10.83	6.92	15.45	12.79	9.91	<.01	<.01	<.01	<.01	<.01	<.01
	C.V.	9.1	15.5	13.7	7.1	11.6	10.3	10.0	12.1	13.9						
	S.E.	.80	.70	.83	1.32	1.39	.89	2.20	1.82	1.45						
	N	168	168	168	60	60	60	49	49	49						

S, D, and P = Systolic and diastolic pressure and pulse rate.

M = Mean; S.D. = Stand. dev. of mean; C.V. = Coefficient of variation; S.E. = Stand. error of mean; N = No. of days on which blood pressure and heart rate were determined.

Identifying dog numbers are the same as in references 1 and 2.

sixth "fat episode." At this time the blood pressure would return to and remain at the control level for 51 days or more, if the animals were placed on the normal non-stress kennel diet; however, the abnormality was latent and would become overt as soon as fasting was started(1).

The above findings led to the hypothesis that the homeostatic mechanisms which tend to oppose the fall in blood pressure during caloric restriction had become hypereffective. If this hypothesis was correct it appeared that a prolonged period on a very low caloric intake might strengthen these homeostatic mechanisms and cause them to become permanently over-active even when the animals were on the non-stress, calorically sufficient kennel diet, and thus result in hypertension as a disease of adaptation as defined by Selye (8).

This hypothesis was tested experimentally and resulted in a significant hypertension while on the usual kennel diet. The condition now resembles benign essential hypertension since there is no retinopathy, albuminuria or azotemia.

The question may be raised as to whether the elevation of blood pressure of these 4 dogs may not have been spontaneous, due to ageing. This is obviously rather difficult to answer in a prolonged experiment of this kind, but the following points argue against this explanation: (1) The high pressure on the kennel diet became evident rather promptly after Experimental Period I in Dogs I, III and IV and after Experimental Period II in Dog II. (2) Two trained standardized dogs of approximately the same age as the 4 experimental dogs have been used in other phases of our blood pressure studies for a period of time approximately one year less than the 4 dogs reported here and have shown no spontaneous rise in blood pressure on the kennel diet. (3) Blood pressure of 2 other dogs of approximately the same age was previously found to be practically unaltered when on the kennel diet, after 4 years of observation.

It is provocative to note that these experiments unintentionally resemble the dietary habits of many inhabitants of countries where hypertension is common, *i.e.*, over-indulgence in high fat-high calory diets resulting in obesity and followed by strenuous and irregular attempts to reduce—failure of the will power to continue the reducing regimen and a renewal of the cycle.

Summary. Four normal adult dogs were subjected to rather intense dietary stresses and irregularities over a prolonged period of time. Basically these dietary manipulations consisted of the following: (1) A prolonged preliminary fast followed by realimentation with diets containing 50 to 70% of the calories from beef suet and butter and fed at a level of from 60 to 120 cal/M^2/hr. These "fat episodes" were repeated 6 times in 14 months in the first experimental period and 3 times in 10 months during the second experimental period. (2) The production of marked obesity by a high calory diet. (3) A long period on a low calory diet of raw horse meat which caused marked weight loss. (4) Return to the normal kennel diet. As a result of these dietary manipulations, the animals gradually developed a highly significant diastolic hypertension which is still present while on the normal kennel diet approximately 34 months after the end of the last fat episode of Experimental Period I.

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