An illustration of the experimental range of variation of blood pressure

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IBERALL, A. S. *An illustration of the experimental range of variation of blood pressure.* Am. J. Physiol. 246 (Regulatory Integrative Comp. Physiol. 15): R516–R532, 1984.—The nominal uniformity of long-term mean pressure (~100 mmHg at heart level) for all mammalian species belies the broad nature of its variance, which is found at many time scales. Such variations should be a useful index of physiologically normal and pathological processes. However, it is dubious whether a scientifically meaningful determination of central blood pressure at its many process scales can be achieved from a few isolated measurements: to cite a common and highly significant instance, measurement made by a physician on a patient during one or two office visits. The data presented here are far from exhaustive (a few reports in the literature and detailed longitudinal data on 1 subj), but they serve to illustrate a protocol and a sample of the physiological results that might be expected if data were gathered for larger populations. The basic scales of interest lie in the lower-frequency domain, involving periods of fluctuations longer than tens of minutes.

mammalian species; blood pressure fluctuations

BACKGROUND OF THE QUESTION

A number of introductory studies on the cardiovascular system (3, 9) and some more general studies of the processes and dynamics of other systems (4, 7, 8, 11–13) provided the author with sufficient background understanding of the characteristics of various physiological systems to expect evidence of vigorous oscillatory behavior (i.e., fairly regular fluctuations) in the blood pressure regulation of the mammal at a great number of time scales. Yet data testing this hypothesis were not easily located in the scientific literature. A decade ago (see Ref. 15 and the discussion following) the author queried whether data existed on ambulatory human patients conducting normal activities for a period of at least 30–60 days. Such data would give some idea of normal patterns of low-frequency blood pressure changes and would probably be the required experimental basis for all pharmacokinetic drug effects. The question drew the response that both Pickering (18) and Meyers (15) had followed outpatients for a long period before treatment. These patients were measuring and recording their own blood pressures. It was suggested that 24 h was the longest period of observation during an indwelling catheter study, but, at that time, there were much longer periods of measurements using a portable automatic blood pressure cuff inflating device, work that Pickering and his associates had also done.

However, from the data available at that time, the totality of dynamic phenomena associated with blood pressure was not clear. Such data was needed if one wanted a frame of reference for a dynamic pharmacology and physiology in which to attempt to look at mechanisms.

The problem of central pressure regulation (and a parallel problem of central flow regulation) in the mammal cannot be solved by some parochial view of its mechanisms. The similarity of the mean level suggests one basic mechanistic design factor influencing long-term pressure regulation in all mammals: given that a mammalian organism has operative organs that sustain the vital signs, a functioning heart delivering a cardiac output, and a functioning nervous system that retains control of its functions, some major mammalian organ system should probably regulate the average pressure level. [In a previous study (10) I attempt to show that the vascular system of the kidney regulates the level of longer-term central pressure.] However, even if such a single regulatory source exists, it would not follow that no variation or fluctuation in pressure would emerge. Many factors are known or are suggested as primary in affecting blood pressure; for example, cardiac output, intravascular volume, and peripheral resistance are commonly listed as a basic physiological litany of such factors (13), and it is often suggested that fluctuations will appear at a circadian and a high-frequency (10s of heart beats) time scale.

Armed with that point of view a decade ago, the author decided to gather some personal longitudinal data. The purpose of this paper is to present those data, particularly as it relates to the lower-frequency components of study, and to complement it with whatever more extensive data have become available. The higher-frequency data—breath to breath, Traube-Hering respiratory waves, and Meyer baroreceptor waves (in the seconds and few-minutes domain)—were not the time scales and data of concern. These higher-frequency components are better known to students of cardiopulmonary coupling.

The data of Pickering et al. (2, 18, 19) as well as some other dynamic pressure data are presented by Meyers et al. (15). It is interesting that a more recent conference (17), devoted to examining the problem of mild hypertension and the question of whether a national program

of identification and treatment is warranted, presented no dynamic pressure data other than Pickering's representation of the data (19). One other comparably recent source (5) is also available.

VARIATION OF THE STATIC AND DYNAMIC REGULATED PRESSURE IN THE LITERATURE

Geddes (6) has written a useful textbook on blood pressure measurement. Among other things, he presents the data of Master et al. (14), generally viewed as the American standard data set for normal blood pressure in the human (see Table 1). Such static statistical data offer little idea of the variation to be expected within an individual. Geddes' discussion, although relevant to the accuracy and likelihood of determining arterial pressure, contributes no other information to this problem.

In addition to the data of Pickering et al. (18) and Clement (5), Meyers et al. (15) offer 48 h of data comprising about 80 measurements on three mildly hypertensive individuals who were not using any antihypertensive medication. Oscillatory processes with a "fast" period of 2–3 h were indicated, but no marked "circadian" periods were evident. There was also a considerable degree of "impulsive" (impulses of pressure lasting about 1 h) irregularity comparable with the salient periodic data. The ranges for each of the three subjects were

Systolic	Diastolic	
111–202	65–148	(Low-salt diet)
105–166	75–145	
107–196	78–132	(Low-salt diet)

Two indications of the character of the dynamic response may be noted in these data. *1*) High (>160 mmHg for 1st subj, >140 mmHg for 2nd subj, and >150 mmHg for 3rd subj) systolic pressures (persisting for 1–4 h) were distributed fairly uniformly over each 24-h period. The second subject exhibited more of these high-pressure readings in the midnight-to-noon hours, whereas the third had more high pressures in the noon-to-midnight hours. There is thus little evidence of a strong common circadian component. *2*) Since it is not apparent that the statements about these range extremes are a fair statistical measure of the distribution function of pressure fluctuations, the number of crossings at given pressure levels was plotted to give an indication of the distribution function. Table 2 illustrates crossings and their cumulative sums, which have been extracted from the data of Meyers et al. (15).

TABLE 1. *Normal pressure distribution in US population*

Age, yr	Pressure, mmHg			
	Systolic		Diastolic	
	Mean	Range	Mean	Range
Males				
25	124	110–137	75	66–85
35	128	111–140	78	68–89
45	130	112–146	80	71–91
55	134	116–155	82	72–93
65	141	120–164	84	73–94
Females				
25	116	103–127	72	62–82
35	121	106–135	75	63–84
45	128	107–148	77	67–88
55	137	113–158	80	71–93
65	147	124–167	83	72–98

Range is for 1 σ; upper and lower normal limits are generally ~ 3–5 mmHg higher or lower. Data from Master et al. (14).

TABLE 2. *Distribution of pressure level crossings*

Pressure, mmHg	No. of Crossings	Cumulative Sum
110	1	1
115	1	2
120	2	4
125	2	6
130	3	9
135	8	17
140	15	32
145	20	52
150	28	80
155	36	116
160	43	159
165	40	199
170	34	233
175	24	257
180	15	272
185	11	283
190	5	288
195	4	292
200	2	294

Values are systolic pressure readings taken from 1 subj over 65 h. Mean: 158 mmHg; ±1 σ range: (143–173) mmHg; ±3 σ range: (113–206) mmHg. Data from Myers et al. (15).

These data would seem to indicate that the nominal "minimum-maximum" range and the ±3 σ range, according to normal statistics, are of the same magnitude. It also appears, however, that the response range of a single individual (e.g., one of these mild hypertensive subjects) is as wide as the entire "normal" response range of a large population of "normal" or "near-normal" subjects. This suggests that the dynamic response of the ensemble of individuals may be basically ergodic. It also suggests that the only way to characterize individuals as distinct from a population (e.g., to test whether they are a part of a normal population) is either to specify the individual's distribution function as a stochastic measure or to isolate specific oscillatory components in the individual record for further investigation of a deterministic nature.

One set of the Pickering et al. (15)[1] data displays a circadian variation in blood pressure in several subjects, indicated as percent change of a 24-h mean (Table 3). Standard errors for each value are included. Only six points are shown, taken at 4-h intervals. The SE of the systolic readings is about ±2.5% and that of the diastolic readings is about ±4%. The circadian range is thus about 15% of the mean range tabulated before, and the data imply a very much stronger circadian cycle (albeit of smaller amplitude than the higher-frequency oscillations) than in the data previously discussed.

[1] Pickering et al. (19) data from Richardson et al. (19) are found in Meyers et al. (15); data from Bevan et al. (2) are found in Perry and Smith (17).

TABLE 3. *Nominal circadian pattern of pressure*

% of Mean, mmHg		Time
Systolic	Diastolic	
102	102	0800
102	103	1200
108	113	1600
110	112	2000
90	85	0000
88	85	0400

Data are from Pickering et al. (18).

Data are also available from Pickering's (15) studies for 8 normal and 22 hypertensive subjects (of unknown etiology) and 8 patients with renal disease (15, 19). The range of systolic means for normal subjects is about 103–120 mmHg, with individual variance ranges of 15–45 mmHg and an average variance range of about 30 mmHg. This is intermediate between the 15 and the 40–60% variance range values previously presented. (Note, however, that the latter range was for hypertensive subjects.) These data present a somewhat unified picture, suggesting that normal subjects are individuals with a mean pressure in the range 90–120 mmHg systolic and 55–80 mmHg diastolic. The hypertensive subjects exhibit much more variation: their means fall in the range 120–210 mmHg systolic and 80–135 mmHg diastolic, with variance ranges of about 50–70 mmHg systolic and 30–40 mmHg diastolic. The variation among patients with renal disease is comparable with that among hypertensive subjects.

The following two other sets of data were presented by Pickering et al. (17): *1*) an actual sample of 24-h data from an indwelling catheter and *2*) a presentation of range data on eight normal, eight "benign-phase" essential hypertensive, and five "malignant-phase" hypertensive individuals. The data taken with a catheter provide some indication of the difficulty involved in determining and comprehending pressure variations. Although the 24-h record appears to show extreme ranges of 50–200 mmHg systolic and 30–100 mmHg diastolic, a fraction of the data are represented by spike-like (15- to 30-min duration) peaks in systolic pressure and dips in diastolic pressure. For example, eight peaks of greater than 20-mmHg and 25 dips of about 10-mmHg amplitude are seen. If those spikes are neglected, the extreme ranges are either 80–130 or 80–150 mmHg systolic (depending on how positional range changes in this experiment are interpreted) and 50–70 or 50–80 mmHg diastolic. An underlying period of 80 min (~10 mmHg double amplitude) seems to exist, as well as a longer 4-h period (~20 mmHg double amplitude). Perhaps there is a weak circadian rhythm present, expressed as higher pressures during the waking hours and lower pressures during sleep.

The second set of data is presented as bar graphs of individuals ranges. (Included in this group is the individual whose data were used to illustrate the 24-h recording; presumably all the data were similarly obtained.) For normal subjects an average variance range of 100 mmHg systolic and 75 mmHg diastolic is indicated, with average pressures of 140 and 85 mmHg. (If we judge by the data in the previous set, these values are a bit high, due to unexplained pressure offsets in the instrumentation record. Thus, although these data may be important ground-breaking results of both qualitative and semiquantitative significance, they are essentially of only preliminary scientific-clinical merit.) The data from benign hypertensive subjects indicate average variance ranges of 150 mmHg systolic and 110 mmHg diastolic and average pressures of 210 and 130 mmHg. The data from malignant hypertensive individuals exhibit average variance ranges of 150 mmHg systolic and 110 mmHg diastolic and average pressures of 250 mmHg systolic and 170 mmHg diastolic.

TABLE 4. *Segment 1: self-administered pressure data on one subject*

Date	Time	Pressure, mmHg	Date	Time	Pressure, mmHg
11/11/79	1800	154/100	1/2/80	1800	138/100
11/12	1900	154/102			150/86
11/14	1900	150/90			130/86
11/19	1930	140/92	1/3	2010	116/78
11/25	1800	138/94			110/70
11/29	2130	145/96			118/80
12/1	1000	134/94	1/4	1200	150/94
12/3	1730	165/100			148/96
12/4	1730	145/104			146/98
12/5	0730	144/96	1/5	1100	128/94
	1730	155/104			124/92
	2000	136/94	1/6	1900	120/80
12/6	0730	132/92	1/7	2100	147/92
	1730	134/94	1/11	2010	160/97
	2030	118/80	1/18	1840	115/84
12/7	0730	132/88	1/21	1700	168/100
	1945	136/98		1830	160/95
	2200	128/80		2000	145/95
12/8	0730	126/92	1/22	0800	160/110
12/9	1200	150/92		1440	190/110
12/10	0715	150/102		1950	160/110
12/12	0730	148/88		2100	130/88
	1730	140/98	1/23	0715	160/94
12/14	0730	132/82		1725	160/104
	1730	150/100		1905	120/84
12/15	0800	134/86	1/24	0720	152/94
12/16	0900	126/94		1655	158/100
	1845	122/84		2045	136/86
12/18	1800	175/100	1/25	0710	140/94
	1900	150/100			

Data are for labile hypertensive subj treated with 50 mg hydrochlorothiazide (Hydro-Diuril) daily.

Unfortunately the rest of the data presented by Perry and Smith (17) fail to provide any other intimation of the existence of extended ranges for individual blood pressure variations and how these might mask individual measurements. Much more typical is the suggestion that a significant increase in mortality is encountered at levels above[2] about 137/88, as determined presumably from a few measurements.

From these data the following a priori estimates of the actual experimental situation may be made (although it overextends the data base). Adult normal subjects are individuals with average pressures of about 100–130/60–85 mmHg and ranges[3] (variation of pressure) of about (30–50)/(20–40) mmHg. Mildly hypertensive adults have

[2] Or, actually, above the narrow range 130/80 to 140/90 mmHg.

[3] Range or variance data are reported in parentheses to distinguish them from mean data.

average pressures of about 130–175/85–110 mmHg and ranges of about (60–80)/(50–80) mmHg. Malignant hypertension lies above these averages (i.e., > 175/110 mmHg). Certain drugs (e.g., diuretics and β-blockers) can be expected to reduce the average pressure of mildly hypertensive individuals by about 10–15/20–30 mmHg; it is far from clear how they might affect the range.

To summarize the major general impressions from Clement (5), after having reviewed the findings of Pickering et al. (18) and Meyers et al. (15) one might conclude the following.

1) There is a broad range of pressure fluctuation (in mmHg) exhibited in individuals over the day: 168–198/80–100 for a hypertensive patient (p. 33); 80–130 variation of mean for a dog (p. 50); 110–240/60–140 total 24-h range, or 150–240/80–140 daily out-of-bed range (p. 63); 90–140/50–90 total 24-h range for a group of normotensive subjects, 120–175/70–110 for a group of uncomplicated hypertensive individuals (p. 70); 115–215/100–150 (p. 83); 115–155/60–85 for a normotensive group, 120–185/80–120 for a mildly hypertensive group, 155–215/100–140 for a moderately hypertensive group, and 230–260/140–160 for a severely hypertensive group (p. 97). The systolic variance averages perhaps about 50 mmHg with a 10- to 100-mmHg range of variance. The diastolic variance averages about 30 mmHg with about a 10- to 50-mmHg range of variance.

2) There is a significant difference in the mean (and variance) range of fluctuations between wakefulness and sleep. This might be considered circadian, or it might be the effect of activity. A circadian component during wakefulness seems to be more doubtful. The mean difference (in mmHg) between the mean waking pressure and mean sleeping pressure seems to be about 25 (p. 38); 45/40 (p. 63); 40/30 (p. 70); 35/25 (p. 74); 45/25 (p. 83); 30 (range 20–40)/15 (range 10–25) (p. 92); and 20/10 in normotensive, 45/24 in mildly hypertensive, and 40/25 in moderately hypertensive individuals (p. 97). The systolic day-night difference is about 40 mmHg; the diastolic day-night difference of about 25 mmHg is a summary.

3) One can draw only informal conclusions about periods (other than the 24 h) or characteristic dynamic patterns. Information on any detailed "high-frequency" patterns shorter than 1 h is not reliable in these data. There is weak evidence for 3- to 6-h (p. 33), 30-min (p. 63), 40-min, and 2-h fluctuations (p. 83) and an 11-s "baroreceptor" fluctuation (p. 86). [For higher-frequency data (at the minutes level) during sleep, see Snyder et al. (21).]

One group, studying dogs, specifically sought to determine the existence of pressure oscillations (20). It is unfortunate that the data presented are only for the mean cyclic pressure, not systolic or diastolic. The data, taken over 8-h periods, showed periodicities of 90 min, comparable with those found in human data (i.e., 1- to 1.5-h cycles). Although not mentioned explicitly by the

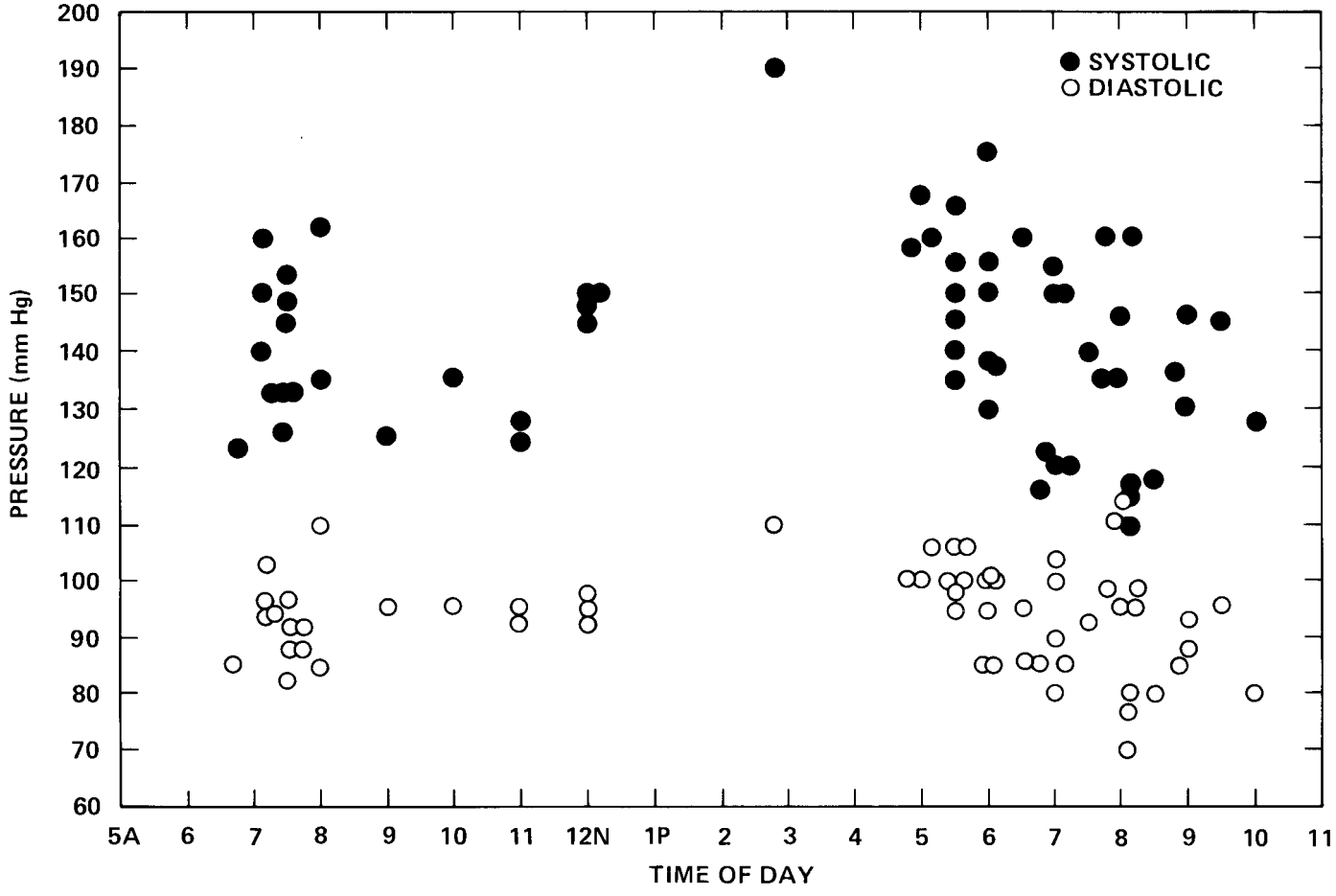

FIG. 1. Daily pressure measurements on subj taken at random times (11/79–2/80).

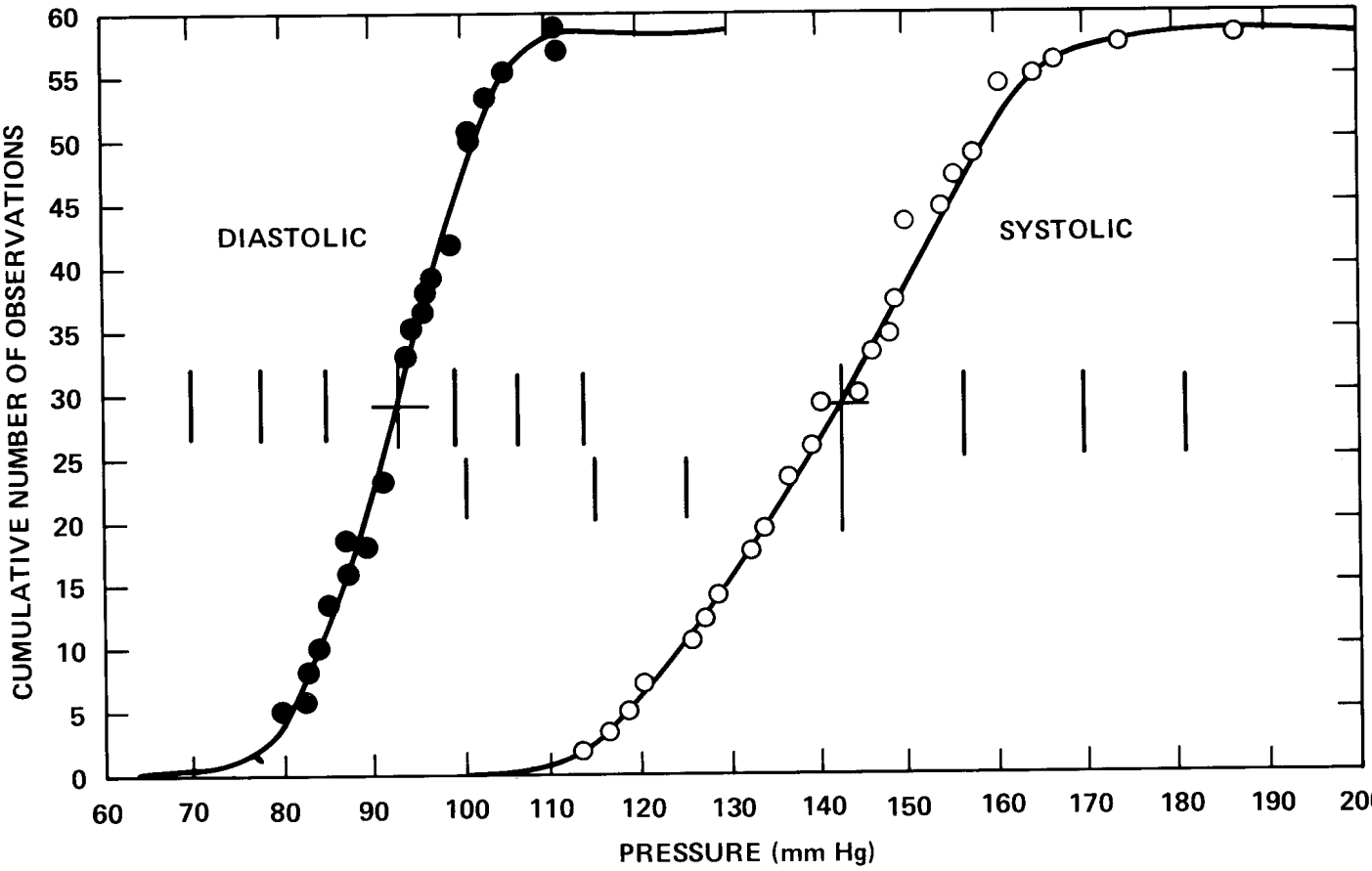

FIG. 2. Cumulative distribution of pressures measured on subj for sample observation period (11/79–2/80). *Small bars* denote ±1 σ, ±2 σ, and ± 3 σ values.

authors, there is weak evidence for faster cycles (e.g., with periods of 1 h, 20–30 min, and perhaps even 5–10 min). Evidence for slower cycles (e.g., 3–6 h) is extremely weak. Spike pressures of about 20 mmHg are found. If these are smoothed over, the pressure range is about ± 20 mmHg. Such a range is comparable with data found in humans.

One additional data set (1) from the same National Institutes of Health group reporting in Meyers et al. (15) verifies the dynamic range suggested here but suggests a much stronger circadian character than found in the other data.

ILLUSTRATING CLINICALLY DERIVABLE LONGITUDINAL DATA AS A PHYSIOLOGICAL BASE

The available research data were not intended to describe an individual experience against a broad diffuse population. As a mild hypertensive who was concerned with a research background for blood pressure regulation, it seemed appropriate to use myself as a subject to underline both the physiological and the clinical problem and to provide a preliminary basis for further research. The specific occasion to prepare a data base presented itself when it became necessary for me to add a β-blocker to a regimen that already included a diuretic. The use of multiple drugs is compatible with the Stepped Care Program (15) being tested and promoted for the National Institutes of Health. Thus this report offers some self-administered measurements of pressure data over a 10-yr period.

Self-administered blood pressure readings were taken with a standard 5.5-in.-wide clinical cuff, a Taylor instrument (Tycos) aneroid manometer, and a 1.5-in. tambour-type stethoscope. The pump-up rate was rapid, and the descent rate was about 3–4 mmHg/s. The systolic pressure noted was the first aural appearance of a crisp beat; the diastolic pressure noted was the cessation of the beat, generally after a moderate degree of muffling. These values seemed to agree within 5 mmHg with those measured with an electronic microphone placed below the cubital fossa at the elbow and recorded on tape.[4] In general, repeated measurements were made to determine an average for systolic and diastolic pressures characteristic of the observed minute in time. Data were taken at random times during the day, with the subject in a sitting resting position, except when otherwise noted, and are presented in a number of temporal segments.

The first such set of data (Table 4) was investigated for the presence of a temporal pattern and the determination of their distribution characteristics (Fig. 1). There is little evidence of a circadian pattern during this waking portion of the day (the only time epoch measured), merely a slight rise toward noon with a corresponding

[4] The recording on tape, purely incidental, permitted occasional checking by ear of the character of the critical sounds.

fall toward evening. Without a more detailed record to detect any cyclic phenomena, one can say only that there is a broad range of about 110–180 (70-mmHg range) systolic and 70–110 (40-mmHg range) diastolic pressure during the wake epoch. A more incisive test of the distribution, given such apparently uniformly "noisy" data, is the cumulative record (Fig. 2). This record exhibits a mean of 142/92 mmHg and a range ($\pm 3\ \sigma$) of about (185–100)/(113–70) = (85)/(43) mmHg. The cumulative result is again somewhat broader than the estimate by eye because of the $\pm 3\ \sigma$ definition of range. By the criteria adduced earlier, such data indicate mild hypertension.

The added effect (if any) of a β-blocker can now be shown. The dose of metropolol (Lopressor) was 50 mg with breakfast at about 0730 and another 50 mg with dinner at about 1800. A preliminary transition period (25 Jan–3 Feb 1980) during which I experimented with the doses, is not included. During this period the mean pressure was about 138/90 mmHg [range (165–100)/(110–60) = (65)/(50) mmHg]. This value is not very different from data of the previous period in which only a diuretic was used. The data collected under the new two-drug regimen are presented in Table 5, and the cumulative distribution is plotted in Fig. 3.

These data exhibit a mean of 137/87 mmHg and a $\pm 3\ \sigma$ range of (185–90)/(114–64) = (95)/(50) mmHg. The effect of the second drug appears to be a reduction of

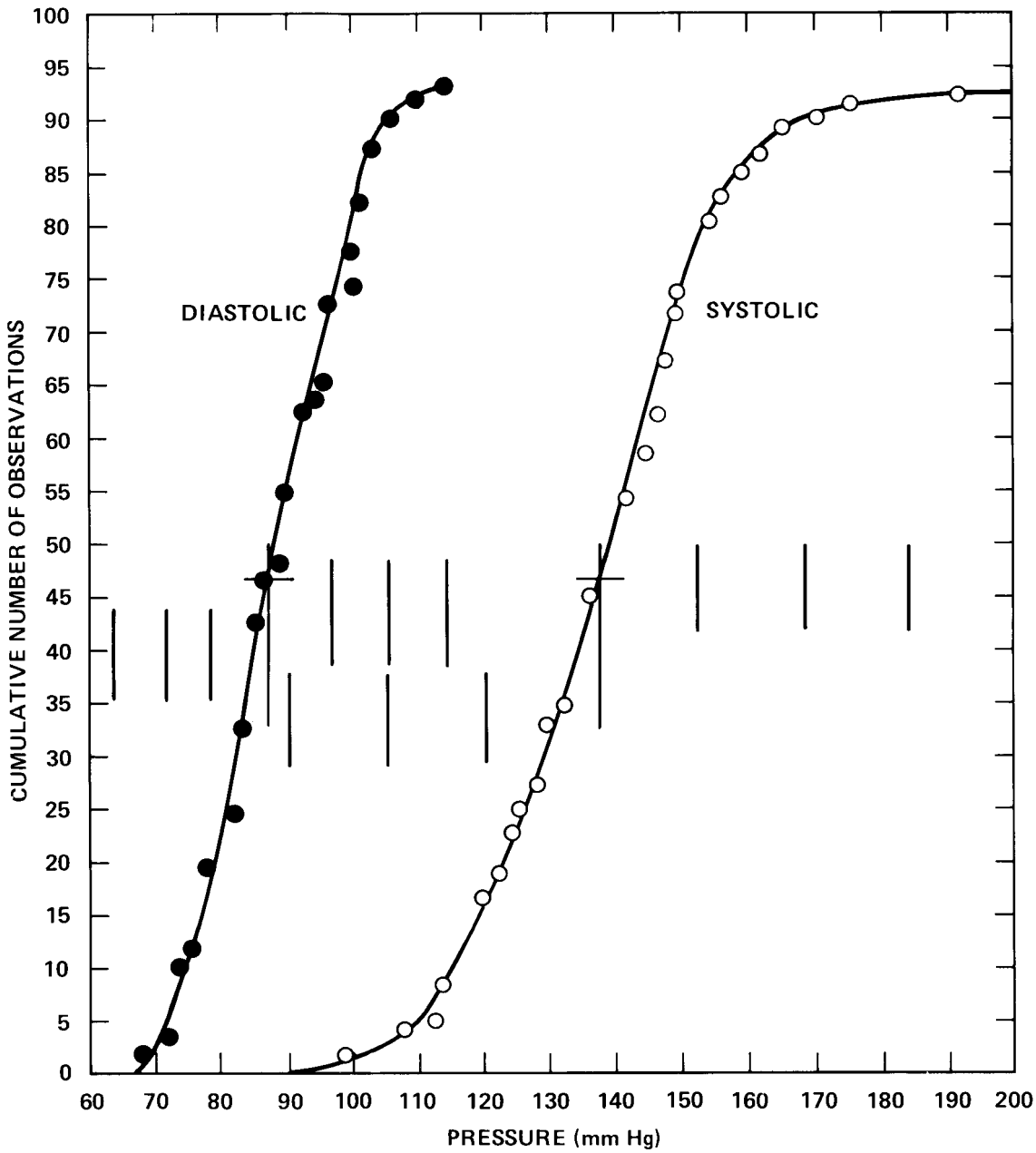

FIG. 3. Cumulative distribution of pressures measured on subj for sample observation period (2/80–5/80).

only about 5 mmHg from the single-drug regimen. This mildly hypertensive individual might now be regarded as approaching an upper limit of normality. Whether this is significant in terms of life expectancy is not really certain. The drugs appear to reduce mild hypertension toward the normal control range.

A more recent set of data is presented in Table 6, and the cumulative distribution is plotted in Fig. 4. These data indicate the more recent status of the subject under the two-drug regimen [mean 133/88, range (168–102)/(112–66) = (66)/(46) mmHg]. The mildly hypertensive subject seems to have stabilized at a point near the lower limit of mild hypertension under the influence of the diuretic and the β-blocker. In fact, at precisely that point, large amounts of data are required to determine whether such regulation has a beneficial effect on mortality rates.

TABLE 5. *Segment 2: self-administered pressure data on one subject*

Date	Time	Pressure, mmHg	Date	Time	Pressure, mmHg
2/12/80	2020	114/76	4/9	2155	124/84
2/13	0710	126/80	4/10	1055	143/100
	1730	140/86		1305	170/102
	2100	120/80		1445	150/92
2/14	0725	130/78		1545	136/84
	0745	140/96		1645	126/86
	1730	154/106		2125	142/98
2/15	0720	150/84	4/11	0825	152/90
	1935	144/96		1035	160/100
2/20	0710	142/92		1150	145/90
	1725	154/96		1320	132/80
	1840	120/76		1510	128/86
2/27	1545	130/84		2005	122/85
3/17	0725	135/95	4/13	1030	156/102
	0825	135/90	5/2	0750	175/100
	1730	145/96		0830	162/106
	1930	120/76		0905	146/92
3/19	0725	150/100		0955	152/88
	0735	140/92		1120	160/100
	0825	146/92		1550	140/84
	0925	140/92		1640	124/82
	1535	140/96		1735	150/90
	1850	124/80		1850	120/80
3/20	0725	140/100	5/7	0830	130/87
	0745	136/88		1110	120/74
4/7	0820	154/102		1155	100/76
	1235	164/106			110/71
	1330	150/88			115/80
	1650	165/112		1330	135/82
	1730	162/102		1500	112/77
	2040	126/82		1615	121/80
4/8	0725	144/88		1655	130/86
	0900	142/94		2125	120/76
	1045	136/95	5/8	0730	128/86
	1535	130/90		0845	154/100
	1615	144/88		0950	136/86
	1650	140/86		1045	134/96
4/9	0730	145/102		1140	130/86
	0840	136/89		1450	124/76
	1050	134/87		1550	120/80
	1200	152/100		1630	124/85
	1355	156/90		1655	140/92
	1525	152/90		1730	146/96
	1705	190/108		2000	120/76
	1745	170/108		2110	116/84
	1900	132/96		2300	130/76
	2115	132/82			

Data are for labile hypertensive subj treated with 50 mg hydrochlorothiazide (Hydro-Diuril) daily and 50 mg metropolol twice daily.

The data in this last set are rather more suggestive of a circadian cycle during the waking hours and are loosely compatible with the other data on the subject. There seems to be a rise in systolic pressure from perhaps 130–150 mmHg at waking to 140–160 mmHg at about 1600–1730, followed by a decay toward 120–130 mmHg after 1900; however, the scatter is quite broad (ca. 30–40 mmHg) at each time. The diastolic rhythm shows a rise from 90 mmHg in the morning to about 100 mmHg in the early evening and then a fall toward 80 mmHg later in the evening. The band width is about 20–25 mmHg.

These recent data may be compared with earlier data on the same subject, before any drugs were used (Table 7 and Fig. 5). The mean of 153/97 mmHg and range of (181–123)/(117–78) = (58/39) mmHg clearly indicated mild hypertension that required treatment. Data recorded at various times subsequently, with the subject receiving 50 mg of the diuretic hydrochlorothiazide daily, are presented in Fig. 6. (The observations include the period Jan through Oct 1974, with a few scattered observations through Jan 1975.)

Except for the high-pressure "tail," the data in Fig. 6 seem to show a Gaussian distribution. This tail may represent a few spikes that were caught during testing of the pressure regulation. Perhaps a better explanation is that the spikes represented escape of the power-limiting system from a lack of complete pressure regulation. [The data in Meyers et al. (15) and Perry and Smith, (17) suggest the frequency with which spiking—presumed to be a nonregulatory response—occurs.] These spikes were observed on 4 days, out of 91 measurements (on 8 and 17 Jan and 1 and 2 Mar, the 1st, 6th, 32nd, and 33rd

TABLE 6. *Segment 3: self-administered pressure data on one subject*

Date	Time	Pressure, mmHg	Date	Time	Pressure, mmHg
2/18/81	0730	150/86		1240	142/102
	1745	160/110		1400	146/85
	1930	124/82		1550	124/86
2/19	0730	128/90		1700	136/100
	1730	140/94	2/27	1040	140/100
	1930	130/90		1150	140/96
2/20	0730	140/90		1610	154/95
2/21	0750	124/86		1730	136/92
	1030	156/94		1915	136/96
2/22	0900	145/96	2/28	1455	122/80
	1010	126/90		2345	126/78
	2020	118/80	3/1	1955	116/83
2/23	0730	132/90	3/2	0745	142/85
	1740	160/100	3/3	0750	140/96
	1845	110/74	3/4	0750	128/90
	1930	124/90		1945	116/78
2/24	1730	143/88	3/6	1200	136/80
	1915	120/76		1835	110/72
2/25	0730	130/88	3/7	0930	125/81
	1750	132/88		1800	132/86
	2130	114/82		2030	131/84
2/26	0730	120/82	3/8	1040	145/96
	0830	146/92		1800	136/82
	0920	136/86		1900	128/86
	1120	172/105	3/9	0745	143/96

Data are for labile hypertensive subj treated with 50 mg hydrochlorothiazide (Hydro-Diuril) daily and 50 mg metropolol twice daily.

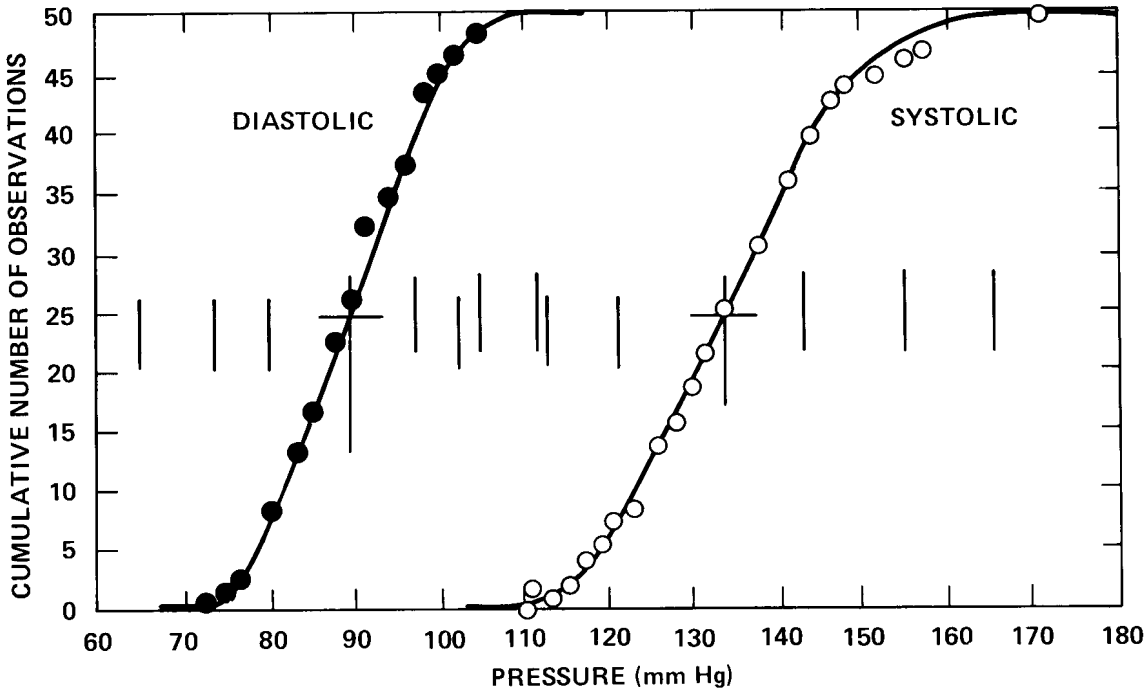

FIG. 4. Cumulative distribution of pressures measured on subj for sample observation period (2/81–3/81).

observations of the series. No significance is attached to these numbers, except to their nonsystematic character. Although it may be reasonable to ignore readings taken on the 1st day of new drug treatment, there is no reason to reject the other data. Thus one might say that perhaps pressure spiking occurs with an estimated upper limit of 3% of the time. This would not be inconsistent with the observations of Iberall and Cardon (11) and Myers et al. (15). Similar observations may be made regarding the low-pressure tail and the "dips" in the diastolic pressure record (on 3 and 14 Feb, 15 May, and 27 July, the 20th, 28th, 57th, and 67th observations). Such values were observed in four readings, an upper limit of about 4% of the time.

If we treat the data as a Gaussian distribution, the mean pressure is 127/87 mmHg (if we include non-Gaussian tails, these numbers would change by about 1 mmHg, a negligible adjustment), and the range is about (165–94)/(110–65) = (71)/(45) mmHg if the presumed spiky tails are included or (154–104)/(110–70) = (50/40) mmHg if the tails are excluded. These data are suggestive of a mildly hypertensive individual who has been brought within the upper limits of normality. One might infer that the difference between this response and a "true" normal response is that the range (whether or not spikes are included) is still somewhat higher than for a normal subject. It is precisely such data, and the effects of such data (e.g., on mortality), that are needed to assign any significance to these absolute values.

As far as historic change is concerned, note that 5–6 yr later the pressure level was found to be 142/92 and (85)/(43) mmHg.

For completeness of the record, the most recent data acquired are shown in Table 8 and Fig. 7, and Table 9 and Fig. 8.

Since the previous (i.e., 1981) regimen seemed to exhibit a satisfactorily low pressure (and range), the treatment was reduced to only a β-blocker. The results (Table 8 and Fig. 7) were a mean pressure of 137/88 mmHg and a $\pm 3\ \sigma$ range of (164–113)/(106–67) = (51)/(39) mmHg. This is essentially the same as the previous regimen with a diuretic and a β-blocker [mean 133/88 mmHg, range (66)/(46) mmHg].

However, on medical examination, cardiograph indications suggested that body weight and blood pressure be reduced. (The subject was ~ 66 in. tall, had a large frame, weighed ~ 190 lb, did not smoke, swam 1 mile/day, and had an average resting heart rate of about 50 beats/min.)

The effect of a 10-lb body weight loss and change of drug treatment is indicated in the last, more recent, segment of data (Table 9 and Fig. 8). The results were a mean pressure of 113/78 mmHg and a $\pm 3\ \sigma$ range of (155–85)/(101–61) = (70)/(40) mmHg, which is quite low. Nominal risk (to be discussed later) is that of a normotensive individual.

The data from Table 9 are also presented as a plot of pressure vs. time (Fig. 9) to examine them for the existence of any particular circadian variation during the wake epoch.

If a circadian rhythm exists during the day, it is hidden in the variance; for example there may be as much as a 5- to 10-mmHg droop in mean systolic pressure (as opposed to the variance) from early morning (0600–0700) to early evening (1900–2000) and a comparable variation (slight concave down arch or droop) in mean diastolic pressure. The magnitude of the possible variation is 50–100% of the values indicated in Table 3 but with a somewhat different temporal tendency. Again one would infer that the circadian component, except possibly

TABLE 7. *Segment 4: self-administered pressure data on one subject*

Date	Time	Pressure, mmHg	Date	Time	Pressure, mmHg
10/14/73		165/90	11/20	1830	155/96
10/19		150/90	11/28	1730	165/102
10/20		150/90	11/29	1900	135/88
10/21	1000	150/90	11/30	1900	134/87
	1600	140/110	12/1	1130	140/83
10/22	1900	158/110	12/2	1930	152/98
		162/106	12/3	1900	154/96
10/23	1740	160/105	12/4	1730	156/108
		164/101	12/5	0730	156/96
10/24	1945	146/98	12/6	1910	135/90
		150/94	12/7	1830	143/93
10/26	1830	170/110	12/8	1015	146/98
		174/106	12/9	1200	152/105
10/27	0915	148/105	12/10	1845	165/110
		165/95	12/12	1830	150/100
	1030	160/100	12/13	1830	146/95
10/28		165/108	12/14	2240	166/100
10/29	2100	155/105	12/15	1830	142/92
10/30	1940	145/96	12/16	1400	150/100
10/31	1800	160/105	12/18	1840	135/100
11/1	0730	150/100	12/19	1930	136/88
	1730	145/105	12/20	1930	154/100
11/2	1930	160/105	12/21	1700	148/105
11/3	1000	140/96	12/22	1000	154/102
		165/105	12/23	1200	150/95
11/4	1100	164/105	12/24	1740	142/94
11/5	1730	150/95	12/25	1200	164/104
11/6	1730	160/100	12/26	1900	140/88
11/7	1730	165/105	12/27	1930	132/86
11/8	2145	158/96	12/28	2300	150/96
11/9	1730	162/104	12/29	2230	148/100
11/10	0930	154/96	12/30	1300	140/98
11/13	1640	152/95	12/31	1645	165/106
11/14	1830	150/95	1/1/74	1300	152/100
11/16	1905	136/90	1/3	1830	162/114
11/17	1530	185/112	1/4	1930	146/94
11/18	1120	173/108	1/5	1100	140/100
	2100	132/85		1330	141/94
11/19	1900	138/92	1/7	1830	146/92

Data are for untreated labile hypertensive subj.

sleep-wake or strenuous activity-rest, is almost indiscernible (cf. Figs. 1 and 9).

Up to this point, the experimental results seem to support the following inferences: the pressure variation is considerable; it may very well be larger for a "labile" hypertensive than for a normotensive individual; it is responsive to diuretics and β-blockers; and it may very well also be responsive to excess or low body weight relative to body weight norms (defined by, e.g., a body with little excess fat), and hence to gain or loss of body weight. However, there was one additional inference, which given these apparent results, seemed as compelling as the others.

It emerged, with considerable clarity (given a 10-yr record of some detail), that the high-pressure readings were largely, if not all, psychosomatic, involving the emotional interaction with people for whom the subject had strong affectional feelings. Such interactions were not particularly "argumentative" or even negative. It just seemed clear that the subject endows his interactions with strong affectional content. Is this component of the psychophysiological response a significant, perhaps even ultimate, driving force for many labile and mildly hypertensive individuals? The author would speculate, "Yes."

The limited evidence indicates that such personal interactions accounted for essentially every pressure measurement of systolic over 130 and diastolic over 90 mmHg. The subject, self-engaged in tasks, with an affectively calm outlook, would almost invariably measure systolic pressures between 97 and 127 mmHg and diastolic pressures between 66 and 84 mmHg. However, these statements can be regarded only as anecdotal and suggestive. To provide at least some experimental evidence for this assertion, I have included Fig. 10, which is based on recent experiences during a day on which considerable data were collected. The two experiences are plotted against the background of recent data accumulated in Sept. 1982. It was possible to observe the spiking of pressure from two short-term emotional experiences and the subsequent course of decay of pressure to normal.

Thus some slight evidence is offered in support of the hypothesis that the spiking response, for both normal and mildly hypertensive individuals, may be a response to stress, largely affective stress in mildly hypertensive individuals.

A BRIEF NOTE ON "STYLE OF LIFE" ASPECTS

Stretching the bounds of physiology to physiological psychology aspects but really implying that the results lie within the domain of endocrine and neuroendocrine physiology, the author is inclined to consider what is referred to as life-style. The author is a physicist and intellectual, by election. He suspects that this choice was made because he cannot handle well his affective relationships with people. Related choices make him a driver, the type of personality who tends toward mild hypertension. It is quite possible that choices of this sort tend to influence and direct the course and election of a life trajectory, and the data under study support that notion. The common suggested treatment for a mildly hypertensive individual is a change in one's life-style, which most people find essentially impossible. The author, for example, gave up smoking after 30 yr as a heavy smoker. This was feasible (in his mid-40s), although it was difficult and many earlier attempts had failed. The author began appreciable exercise at the same time and has persisted for the past two decades. This was not difficult, although various studies have indicated that only a small percentage of a population will persist in significant exercise for more than a few years. The author has confronted the problem of weight control for the past 20 yr. The following yearly averages are indicative

Yr	Avg Wt, lb	Variance, lb
1967	208	199–216
1968	214	203–223
1969	207	199–214
1970	203	195–218
1971	192	179–213 (strict wt-reduction diet)
1972	185	175–194
1973	188	173–187
1974	178	172–182
1975	181	174–185

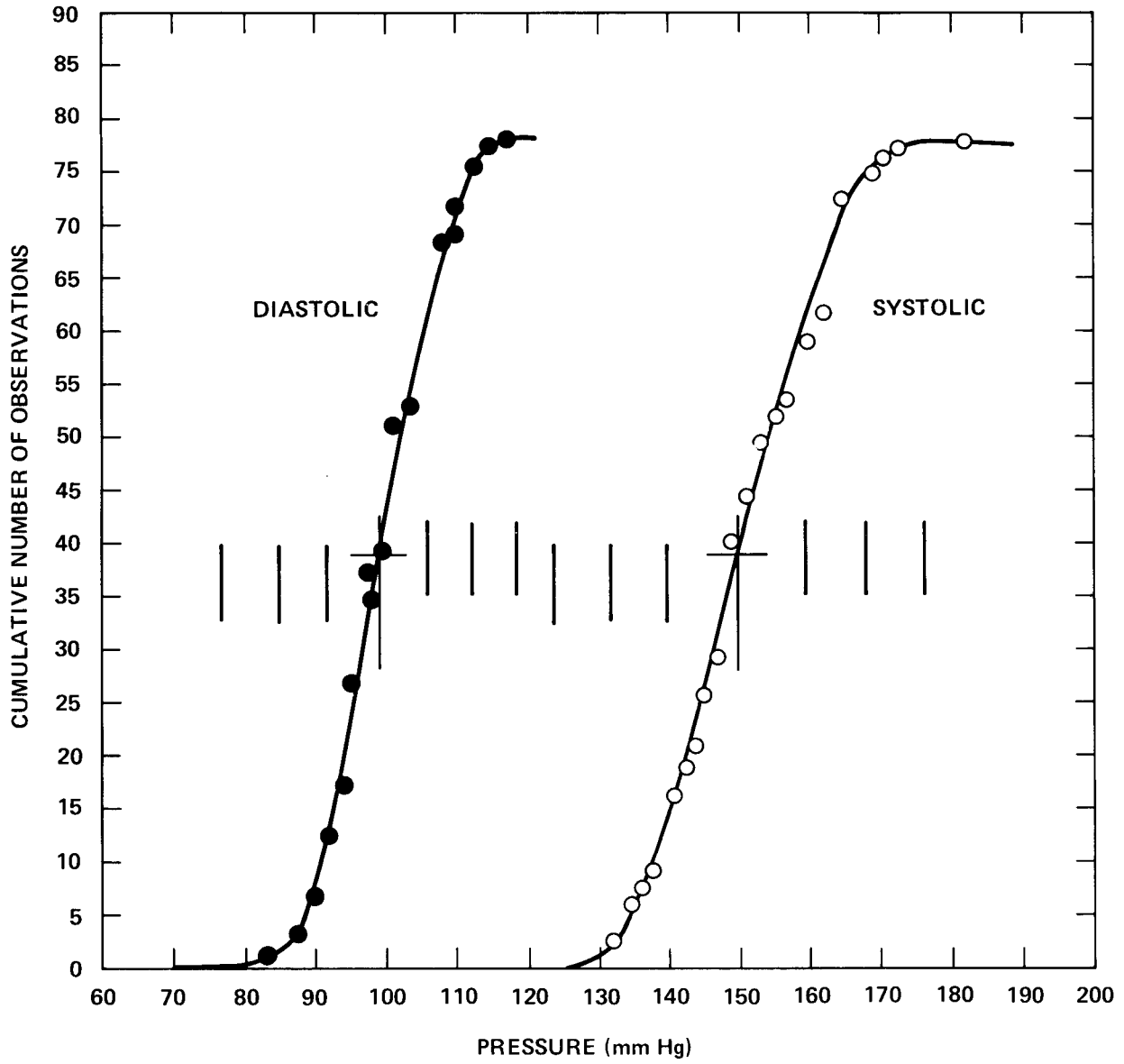

FIG. 5. Cumulative distribution of pressures measured on subj for sample observation period (10/73–1/74).

Yr	Avg Wt, lb	Variance, lb
1976	181	175–185
1977	184	181–191
1978	183	174–190
1979	184	181–189
1980	189	180–194
1981	191	183–194
1982	182 (est)	170 (est)–194 (strict wt-reduction diet)
1983	176	170–182

At about 165 lb, the author would be very lean. These data indicate a weight reduction from perhaps 220 (35% extra wt) to 185 lb (12% extra wt) one decade ago, and a loose maintenance of that weight for the past decade. The problem now, to strip that extra 10–15% and maintain the weight, is very difficult. Perhaps it is a problem that one can deal with in the seventh decade of life. This provides the foreground for the most difficult problem of all, change in life-style. Perhaps it is only in the seventh decade of life that one acquires enough experience to undertake the self-control. Self-control of the details of a life-style apparently involves a great deal of disengagement from immediate interactions, one not easily gained by such methodologies as transcendental meditation or biofeedback. Perhaps the training regimen for psychiatrists is somewhat helpful to them in learning how to avoid self-inflicted stress. The data acquired in this longitudinal study provide no strong support for the case that weight reduction in a moderately obese range will result in significant reduction in central pressure. At most, perhaps, one may infer that weight reduction does not seem to exacerbate a mild hypertension.

In any case, the final conclusion is that physiology, particularly neurophysiology, cannot withdraw its concerns from the various psychosomatic couplings.

A complete log of all available data is presented below

Log of Pressure Records of One Subject

Dates	Pressure, mmHg		Treatment
	Means	Ranges	
2/72–6/72	124/80	(155–118)(100–76)	None
Comments. Normal response. Some very weak evidence for about a 5-day cycle with a double amplitude of about 20 mmHg systolic and 10 mmHg diastolic.[5]			
10/13/72 1/25/73	140/92 140/88		
Comments. Still a normal response (2 isolated observations).			
10/73–1/74	153/97	(181–123)/(117–78)	None
Comments. Mild hypertensive response. Weak evidence of a 3- to 4-day cycle with a double amplitude of about 20 mmHg systolic, 10 mmHg diastolic. Possibly a weaker cycle in the 20- to 40-day range. No circadian cycle detectable.			
1/74–12/75	127/87	(165–94)/(110–65)	50 mg hydrochlorothiazide daily
Comments. Mild hypertension reduced to normal by a diuretic (hydrochlorothiazide, Hydro-Diuril). Some weak evidence for a 3.5- to 5-day cycle with a double amplitude of 10–20 mmHg systolic and 10 mmHg diastolic. Possibly a weaker 20- to 40-day cycle. No detectable circadian rhythm.			
2/76–12/76	139/94	(173–113)/(121–69)	50 mg hydrochlorothiazide daily
Comments. Mild hypertension has drifted upward in spite of a diuretic. Insufficient density of observations to indicate any high-frequency cycles (e.g., 3–5 days). May be weak evidence of an intermediate cycle. No detectable circadian rhythm. Possibly elevated pressures (10–15 mmHg) between 1600 and 1800; relaxation toward the norm by ~ 1900 (i.e., ~ 2-h relaxation time).			
11/79–1/25/80	142/92	(185–100)/(113–70)	50 mg hydrochlorothiazide daily
Comments. Mild hypertension has drifted upward (and stabilized?) in spite of diuretic. Weak evidence of ~ 3.5- to 5-day cycle with a double amplitude of 10–20 mmHg systolic and 10 mmHg diastolic. Very weak evidence for ~ 10-day cycle. Some evidence for a weak circadian cycle, rising between 1200 and 1400, peaking at ~ 1600–1800, and falling off toward normal by ~ 2000.			
1/25/80–2/3/80	139/90	(165–100)/(110–60)	Transition: introducing a β-blocker (metropolol)
Comments. Attempt to stabilize this mild hypertensive using a diuretic and a β-blocker, without side effects. Weak evidence of a 5-day cycle with a double amplitude of 20–25 mmHg systolic and 10–15 mmHg diastolic. Very weak evidence for about a 20-day cycle with about 5 mmHg double amplitude. (Data were taken in daily clusters and averaged for each day of observation.)			
2/80–5/80	137–87	(185–90)/(114–64)	50 mg hydrochlorothiazide 100 mg metropolol daily
Comments. Mild hypertension reduced to near normal with a β-blocker in addition to a diuretic. Data was insufficiently dense to demonstrate any temporal periodicities. Daily clustering indicates possible circadian cycle ranging from 140 to 150 mmHg waking to 130–140 mmHg in midmorning, and rising again to 150–160 mmHg at midday; second similar drop and rise to about 150 mmHg and a final decay to 120–130 mmHg between 1900 and 2300. "Noise" level of about 10 mmHg.			
2/81–3/81	133/88	(168–102)/(112–66)	50 mg hydrochlorothiazide 100 mg metropolol daily
Comments. Second-year check on ability of β-blocker and diuretic to stabilize mild hypertension at near-normal levels. Weak evidence for a 5-day cycle with a double amplitude of 20–25 mmHg systolic and 10–15 mmHg diastolic. Very weak evidence of ~ 20-day cycle with ~ 5-mmHg double amplitude. (Data again averaged for each day of observation.)			
5/82–8/82	137/88	(164–113)/(106–67)	100 mg metropolol daily
Comments. A change in career, climate, exercise regime (swimming 8 h/wk instead of 3 h/wk) suggested reevaluating need for hypertension drugs. With no drugs, pressure was high. Subject elected to try a β-blocker only (diuretic did not seem to be useful). These are the results after a year of such management. Given the size of the observed variance, the data are insufficient to note any significant cycles, including a circadian.			
9/82	113/78	(155–85)/(101/61)	Three changed drug regimes: *a*) 50 mg atenolol (Tenormin), 50 mg hydrochlorothiazide (Moduretic) daily *b*) 100 mg metropolol, 50 mg hydrochlorothiazide (Moduretic) *c*) 50 mg metropolol, 50 mg hydrochlorothiazide (Moduretic)
Comments. A change in drug regime and weight loss produced a lowering of the distribution of observed pressures. It did not reduce the affective pressure spiking. At most there might be a circadian droop of ~ 5 mmHg diastolic pressure from morning to afternoon and an additional 10 mmHg into the evening, or a droop in the systolic pressure of ~ 5 mmHg from a daytime value toward an evening value.			
12/81–3/82			
Comments. In addition to these randomly taken data, some data were acquired during waking hours with a pressure recorder. The data segments, taken with the subject in a sitting position while doing desk work, were up to 8 h in duration and consisted of recordings obtained every minute with an automatically inflating cuff. Not only were the systolic and diastolic pressures indicated but also the individual heart beats during that dropping pressure interval. Data on two subjects were taken, one the author, and the other a normotensive "calm" young man. In both instances, there appeared to be a few pressure fluctuations per hour; that is, data that may be interpreted as waxing and waning cycles or constant pressure spikes of 10- to 15-min and perhaps 30- to 50-min duration [e.g., compatible with the data in (18)]. However, the amplitude of the fluctuations appear quite variable (5–20 mmHg). Some evidence also exists for weak cycles centered perhaps about a 3-h period. Spiking, perhaps, represents more isolated fluctuations at this time scale of even greater amplitude.			

[5] Also examine Shimada and Marsh (20) for comparably weak evidence of a cycle with a several-day period.

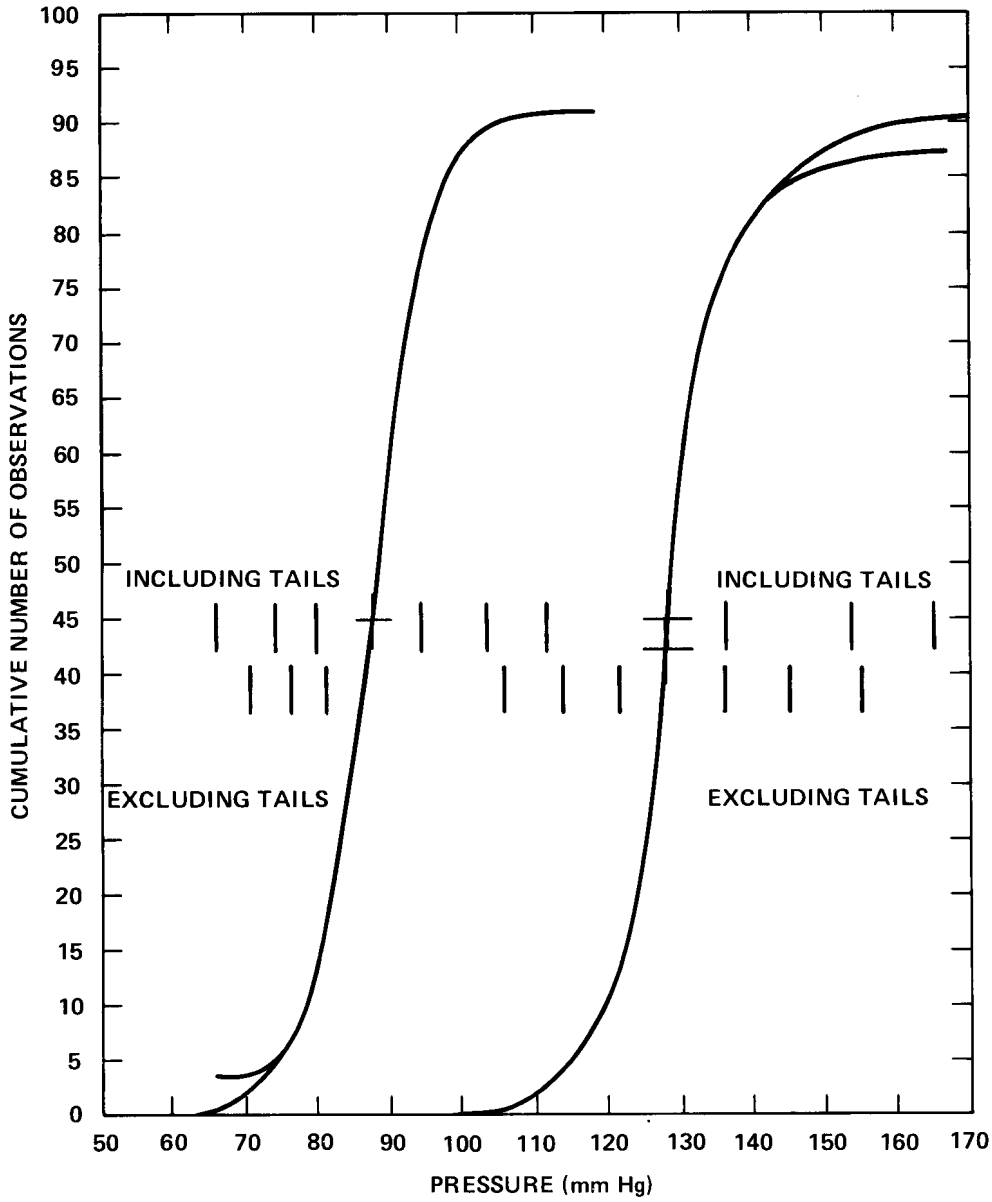

FIG. 6. Cumulative distribution of pressures measured on subj for sample observation period (1/74–10/74; a few scattered observations through 1/6/75).

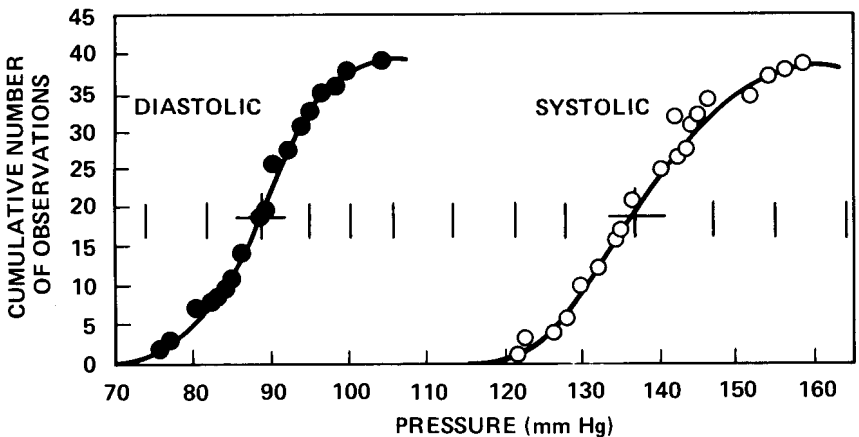

FIG. 7. Cumulative distribution of pressures measured on subj for sample observation period (5/82–8/82).

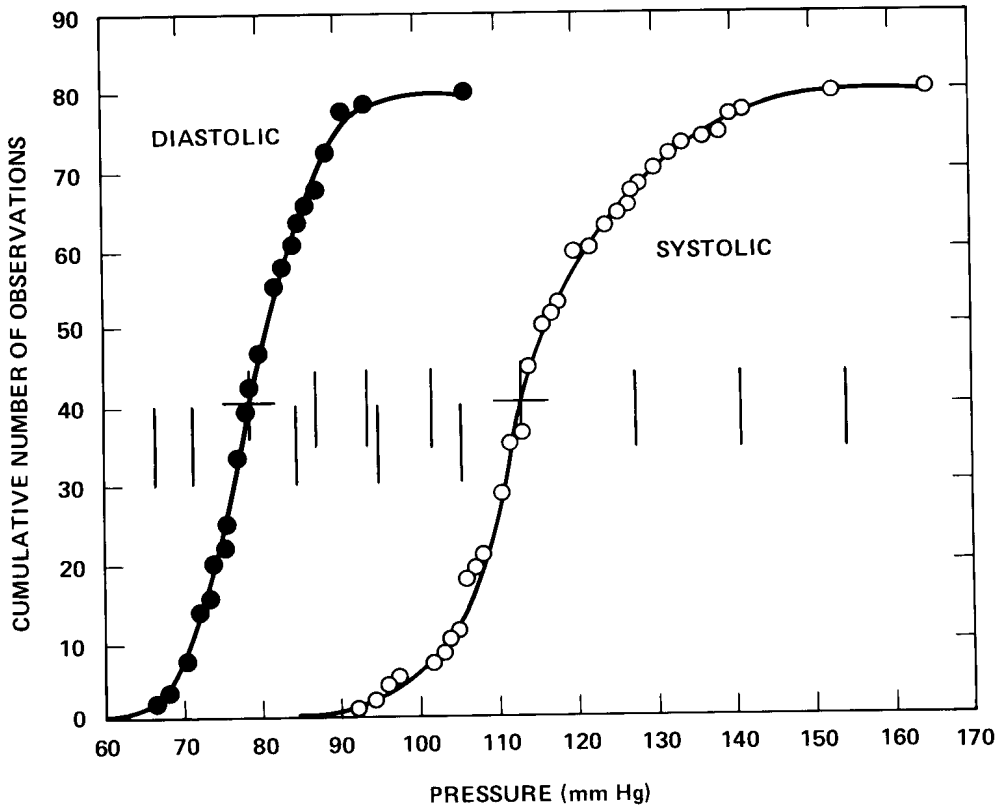

FIG. 8. Cumulative distribution of pressures measured on subj for sample observation period (8/82–9/82).

TABLE 8. *Segment 5: self-administered pressure data on one subject*

Date	Time	Pressure, mmHg	Date	Time	Pressure, mmHg
5/3/82	1535	130/82	7/1	0905	140/84
5/4	0905	126/92	7/2	1030	122/85
	0907	132/88	7/6	0850	154/100
	1120	136/92	7/7	1200	140/96
		136/95	7/8	1020	156/90
	1400	142/88	7/19	1100	134/90
5/5	1040	122/76	7/21	1030	158/104
5/6	1100	146/90	7/22	1000	140/88
	1430	121/77	7/23	1050	136/88
5/7	1045	128/80	7/26	1015	135/80
	1125	130/86		1155	132/90
5/10	1445	143/89	7/27	1120	144/94
6/15	0910	140/100	7/29	1110	136/94
	1050	132/80	7/30	1200	134/94
6/21	0905	144/88		1415	130/86
	1155	152/98	8/24	1105	154/96
	1340	128/76		1250	144/86
6/22	1040	145/90	8/25	1030	134/83
6/23	1015	144/90			
	1140	146/96			
6/25	0920	130/80			

Data for labile hypertensive subj treated with 50 mg metropolol twice daily.

DISCUSSION AND SUMMARY

Based on theoretical ideas (3, 8, 9), I expected to find an extended dynamic range in the regulation of mammalian blood pressure. Data obtained by Pickering et al. (18) with an indwelling catheter, data presented by Clement (5), and 48-h clinical data reported by Meyers et al. (15) provided basic evidence for the extent of the range, as well as some indication of the various frequency components of the dynamic spectrum of pressure variations (2, 5, 15, 17–19). Confirmation of the range and some of the low-frequency components are indicated by Bartter (1). Shimada and Marsh (20) demonstrated similar results for the range as well as some of the higher-frequency components in another mammalian species.

It has been shown that by careful self-made measurements, clinical data can be obtained that rivals, in dynamic quality, low-frequency data provided from indwelling catheters. This is not a claim that a catheter and dynamic pressure gauge cannot provide greater accuracy than a cuff, particularly at high frequency, but that the dynamic noisiness of central pressure is so extensive—and at low frequency, to a certain extent arbitrary—that no gain in quality of the data set is obtained from the greater precision. The basic scientific principle revealed by the data set is that of ergodicity. "Random" measurements taken over an extended period of time have essentially the same statistical properties as a carefully selected sequence of data taken over a period of known closure (e.g., 1 or more typical days exhibiting the normal rhythms of living). The only processes not revealed by the random clinical measurements are high-frequency phenomena (e.g., data in the seconds and minutes range). Such measurements may provide some idea of the amplitude and duration of pressure spikes, as well as higher-frequency data usually associated with respiratory processes and baroreceptors. If the observer attends very carefully to all the instances of spiking in the low-frequency cuff measurements, he may be able to advance

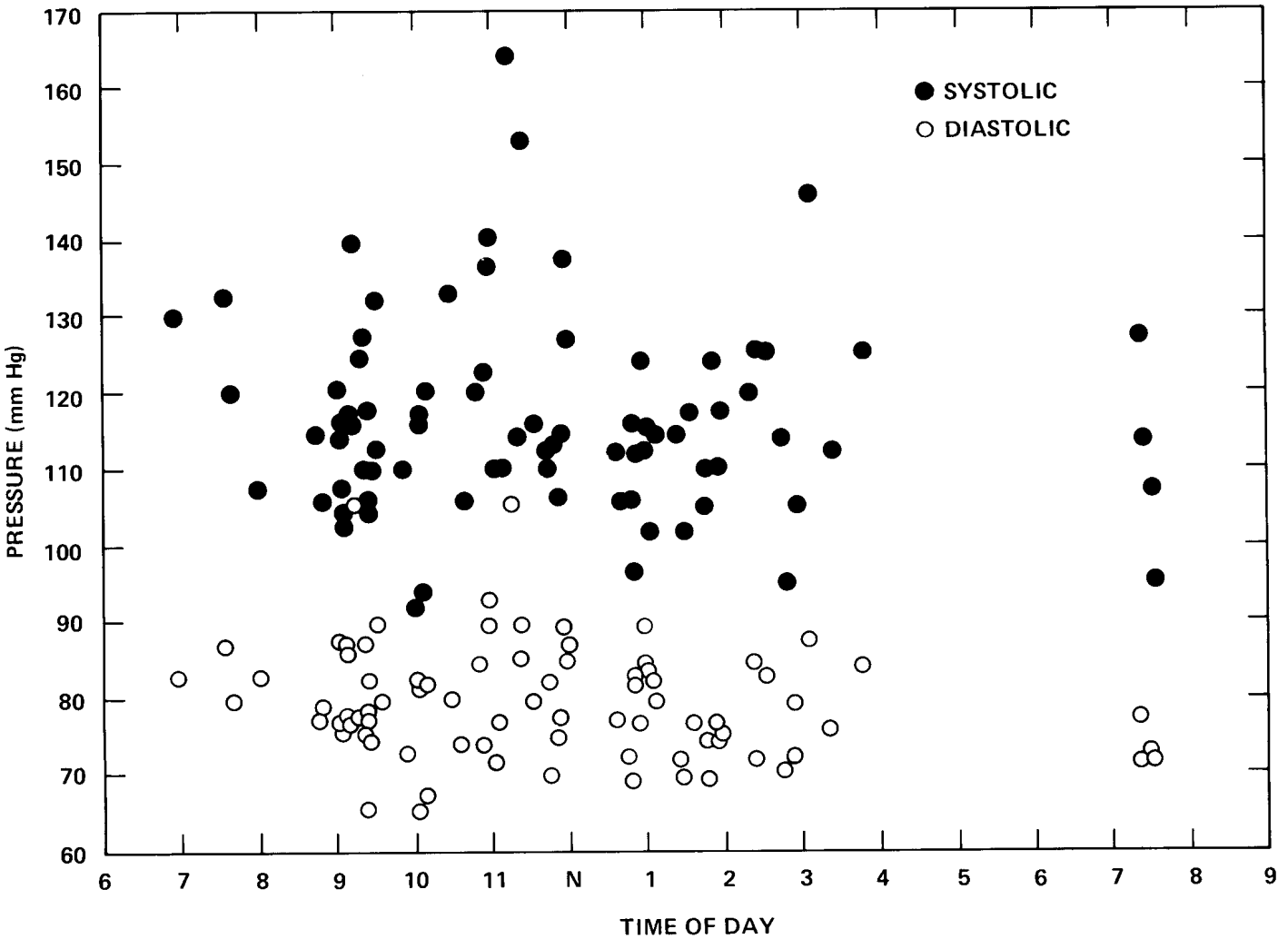

FIG. 9. Daily pressure measurements on subj taken at random times (8/82–9/82).

TABLE 9. *Segment 6: self-administered pressure data on one subject*

Date	Time	Pressure, mmHg	Position	Date	Time	Pressure, mmHg	Position	Date	Time	Pressure, mmHg	Position	Date	Time	Pressure, mmHg	Position
8/27/82*	0905	114/76	A	9/9	1100	140/90	C	9/1	0915	140/106	A		1445	96/72	B
	0909	104/78	B			137/93	A		1137	116/80	B		1544	125/84	B
	1300	112/85			1243	116/82	A		1337	118/77	B	9/14†	0920	106/77	A
	1305	102/82	B		1245	106/82	A	9/2	1115	164/106	C		0923	104/78	B
	1425	126/85	B		1343	105/70	B		1300	124/84	B		1005	92/66	B
	1920	114/72	C		1355	118/75	B		1355	110/74	B		1007	94/68	B
	1922	96/72	B	9/10	0926	110/66	A	9/3†	0915	116/78	A		1121	114/86	A
	1924	108/78	A		0927	110/74	A		1010	116/82	A		1152	106/77	B
8/28	0743	120/80	C		0955	110/73	B		1105	110/72	B		1243	106/72	B
	0803	108/83	A		1142	113/76	B		1200	127/87	B		1340	110/74	B
	0935	132/90	B		1158	114/86	B	9/7	0907	116/87	A	9/15‡	0849	106/79	A
8/29	0942	112/80	A		1318	114/72	B		0922	124/76	B		0906	107/77	B
	1012	117/82	B		1455	106/79	B		1040	106/74	B		1102	110/78	B
	1432	130/83	C	9/13‡	0912	116/86	A		1146	112/82	B		1350	124/77	B
	1917	127/78	C		0924	118/82	B		1240	97/70	A	9/16‡	0840	114/78	A
8/30	0700	130/83	C		1040	120/85	B		1328	102/70	B		1055	122/74	B
	0740	132/88	B		1153	138/90	B		1510	146/88	B		1123	153/90	B
	0923	128/88	B		1240	112/77	A	9/8	0906	103/77	A		1253	112/77	A
	1517	112/76	B		1256	120/90	B		1031	133/80	B		1445	114/71	B
8/31	0910	120/88	A		1310	114/80	B		1146	110/70	B				
	1011	120/82	B		1418	120/72	B								

Data are for labile hypertensive subj adhering to strict wt-reduction diet. Blood pressure was measured while subj was standing (A), sitting (B), or lying down (C). Subj was treated with *50 mg atenolol (Tenormin) at breakfast and 55 mg hydrochorothiazide (Moduretic) at lunch, †50 mg metropolol twice daily and 55 mg Moduretic at lunch, and ‡25 mg metropolol twice daily and 55 mg Moduretic.

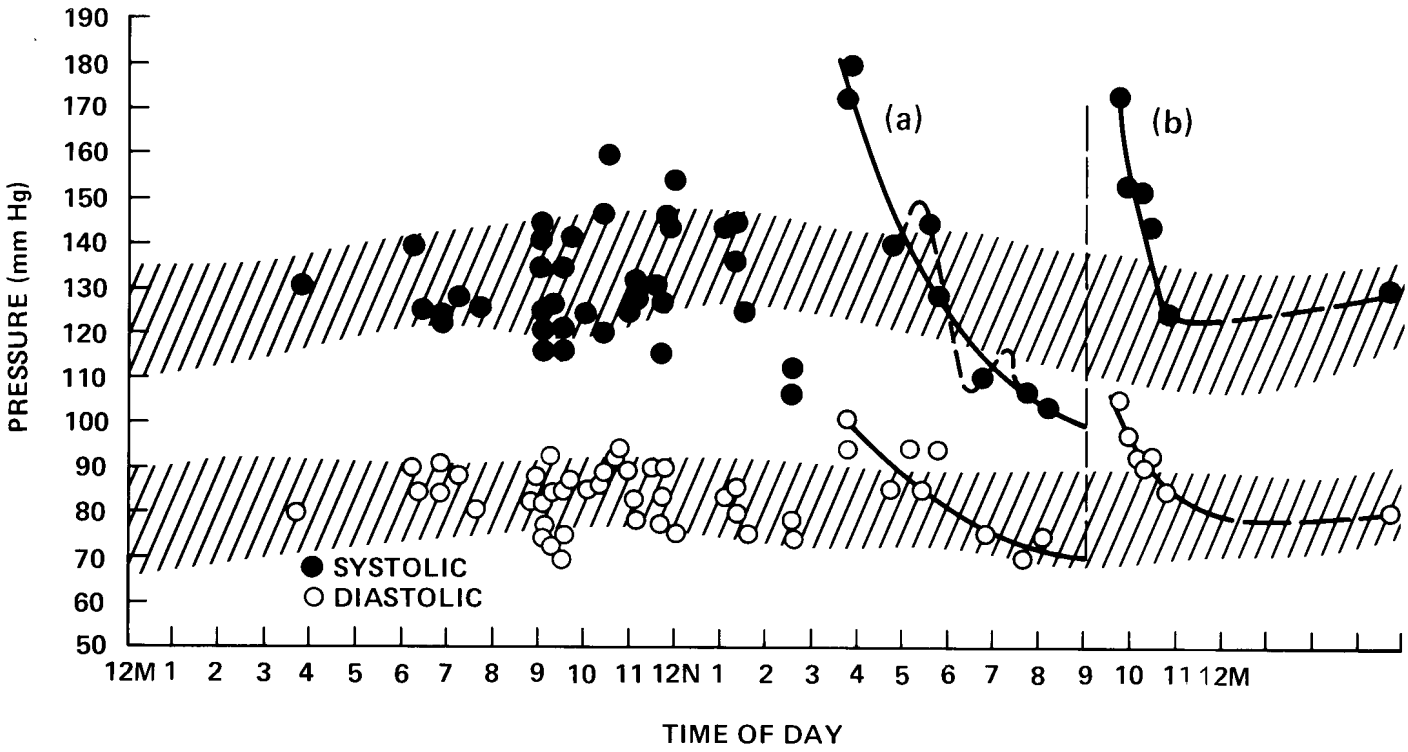

FIG. 10. Effect on pressure of 2 short-term emotional incidents of different severities (data from 9/82). a, Brief intense internal conflict; b, long (1.5 h) extremely friendly telephone call.

some conjecture as to their cause (e.g., that they arise from some affective process). Specifically, 50–100 random measurements made over a period of approximately 2 mo provide sufficient data for a rather precise normal distribution function. From this the mean (systolic and diastolic) pressures and measured estimates of 1 and 2 σ can be determined. (See APPENDIX for some details on the mathematical methodology for treating the data.)

High-frequency records (17, 20) show pressure spikes and other fluctuations with periods on the order of 5–15 min, cyclic fluctuations within the 30- to 50-min and the 1.5- to 4-h range, and perhaps some circadian rhythm even during the wake portion of the day-night cycle. (Literature indicates a generally strong circadian rhythm over the entire day-night cycle.) The self-recorded random data can suggest the form of the circadian rhythm. However, that form is better delineated if the data are sometimes clustered in a few days of observation (e.g., 6 observations spaced out over 1 waking day). Data that distort the range extremes seem to constitute only a small percentage of the total number of measurements. They are suggestive of the fraction of recorded data represented by spiking.

The data acquired here over a period of about 10 yr exhibit certain fairly stable characteristics. There seems to be a 3.5- to 5-day cycle (noted in the log) with about a 20-mmHg systolic and 10-mmHg diastolic double amplitude. Weaker evidence suggests a 20- to 40-day cycle with about a 5-mmHg double amplitude. A circadian variation (for the waking portion of the day, the only period tested), which may be somewhat characteristic of the individual, is possible. In the one case investigated, pressure rose toward midday, with perhaps one or two dips, peaked at the end of the work day (and the drive home), and then dropped toward evening. It might be thought that a change in life-style (and outlook) could change that pattern. However, the actual experimental evidence is that such changes are not easily effected. For example, neither mild daily exercise nor mild restraint in dietary patterns would produce such changes.

Such data seem to have a great deal of reliability and stability as measures of the status of the individual, much more so than could possibly be assigned to an individual random measurement. Although I have an extensive background and experience in measurement and analysis from which to draw, it appears that self-made clinical measurements are within the scope of the lay person if careful instructions and cautions are provided. The measurement equipment is neither elaborate nor expensive.

The purpose of this note is to stress that the acquisition of a considerable data base on the commonly expected blood pressure range of normal and abnormal individuals is of prime importance. Only then can correlations between such records and clinical aberrations and treatment be established.

There is another issue of importance here. Earlier [see (17)], an effort had been made to extract some physiological meaning from such data. The following table of results was proposed as an a priori estimate.

Significance of Pressure Levels

Status	Pressures, mmHg	
	Means	Ranges
Normal	100–130/60–85	(20–40)/(20–30)
Mild hypertensive	130–175/85–110	(60–80)/(50–80)
Malignant hypertensive	>175/110	

According to these a priori criteria, the data set presented herein for one subject appears to be that of an individual who, with the aid of drugs, was able to stabilize his pressure at the upper limits of the normal range (or the lower limits of mild hypertension). But what does that mean? Again, a priori, some idea of the risk associated with such status may be inferred. No claim is made for the accuracy of the results, only that the analysis is provocative and worth exploration in large samples.

In an article in Perry and Smith (17) on the "Problems in Definition of Mild Hypertension," Labarthe presents a table (Table 6) of the variations in mortality among men and women 15–69 yr of age, according to systolic and diastolic pressures. The result is expressed as a mortality ratio (i.e., ratio of an actual to an expected mortality). The data are adapted from Lew and were apparently acquired from life insurance experience.

The data for males have been abstracted from the above-mentioned table and are expressed as a contour graph (Fig. 11). The points plotted against these contours are the data obtained for this study from various epochs. An inferred model may not be precise, but it captures the broad characteristics of the data, which suggest a hypothetical trajectory in mortality space variables. If these were the true facts (as indeed they may be), they would indicate the value of drug treatment for mild hypertension, the lability of the actual regulatory processes, and the potential merit of procuring data of such quality for blood pressure and for mortality.

It seems, then, that this kind of data and methodology, a combination of research and clinical techniques, may be required so that medical diagnosis and treatment can be based on quantitative scientific inference. It is through the use of such methods that an understanding of the complex human machinery and its (homeokinetic) dynamic regulatory processes can be achieved, as it operates in both normal and various abnormal states.

Even though these data defining a systolic-diastolic pathway in mortality space are derived from a single

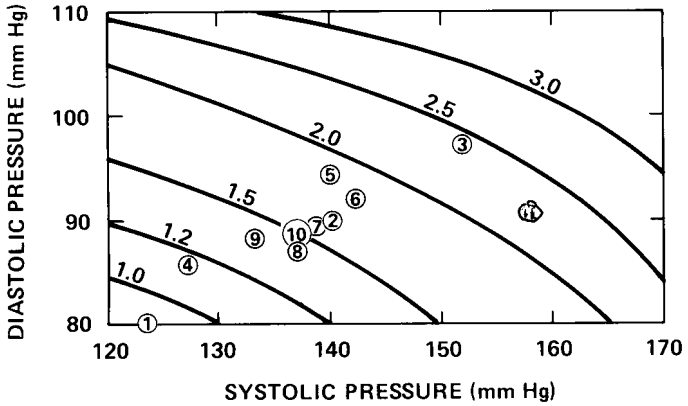

FIG. 11. Increased mortality risk factor due to elevated mean pressures (male). Nos. on *curves* are mortality risk relative to population of normotensive individuals. 1, Originally normal (2/72–6/72); 2, still diagnosed normal (10/72–1/73); 3, hypertensive (10/73–1/74); 4, diuretic (1/74–12/75); 5, diuretic, but drifting upward (2/76–12/76); 6, diuretic, still elevated (11/79–1/80); 7, begin additional β-blocker (1/80–2/80); 8, diuretic plus β-blocker (2/80–5/80); 9, diuretic plus β-blocker (2/81–3/81); 10, β-blocker only (5/82–8/82); 11, diuretic plus β-blocker plus weight reduction (off curve) (8/82–9/82). [From Labarthe (15); adapted from Lew.]

TABLE 10. *Hypothetical pressure measurements on one subject*

Pressure Range, mmHg	Diastolic		Systolic	
	n	Cum	*n*	Cum
60–61				
62–63	1	1		
64–65	2	3		
80–81	12	64		
82–83	16	80		
110–111	2	93		
112–113	1	94		
114–115				
120–121			1	1
160–161			7	8
162–163			11	19
188–189			2	93
190–191			1	94
192–193				

n, No. of observations; cum, cumulative sum.

individual, spot checks of a variety of other data suggest that the track is quite usual (not the time course, only the curve of points explored). Thus it might be inferred that this reveals the standard regulatory pathway for systolic-diastolic correlation in both health and disease. The functioning regulation has one course, whether the system survives for a long or a short time. If this is so, it becomes an interesting path to pursue in cardiovascular systems research.

In contrast to these data, according to the recent multiple-risk-factor intervention trial study (16), *1*) cardiovascular death rates dropped to much lower levels in an American male population than had been anticipated from the statistical results known 10 yr ago and *2*) management of hypertension by drugs and advice resulted in cardiovascular mortality that did not differ significantly from a matched male population that was not so managed. The risk problem and the physiological factors involved are still open for study.

APPENDIX

Obtaining and Treating Data

Data are carefully recorded, and date, time of day, and any ususual conditions are noted. These data are then transcribed into a distribution function and a cumulative distribution function (Table 10). These two distributions are then carefully plotted as cumulative sums ("cums") (Fig. 12).

The mean pressure is plotted at the number of observations (n) divided by 2 (e.g., 47). $\pm 1\ \sigma$ specifies an area under a normal Gaussian distribution within the region $(0.5 \pm 0.341)\ n = (0.841n, 0.159n) = 89, 15$. Similarly, $\pm 2\ \sigma$ specifies the region within $(0.5 \pm 0.477)\ n = (0.977n, 0.023n) = 92, 2$. These four estimates give $\pm 1\ \sigma$ and $\pm 2\ \sigma$, which represent four independent estimates of the standard deviation, σ. If these four independent estimates have essentially the same magnitude, they may be adjusted (averaged) to obtain the best single mean estimate. That mean estimate of 1 σ is then extended to estimate the $\pm 3\ \sigma$ values. Note that it is a waste of time to try to compute the $\pm 3\ \sigma$ points from the cums for such a small distribution (e.g., < 100 points). The range, then, is the difference between the $\pm 3\ \sigma$ values of pressure.

Regarding the spiking discussed earlier, if the tails of the two distributions, i.e., those data beyond the $\pm 2\ \sigma$ estimates, are not good

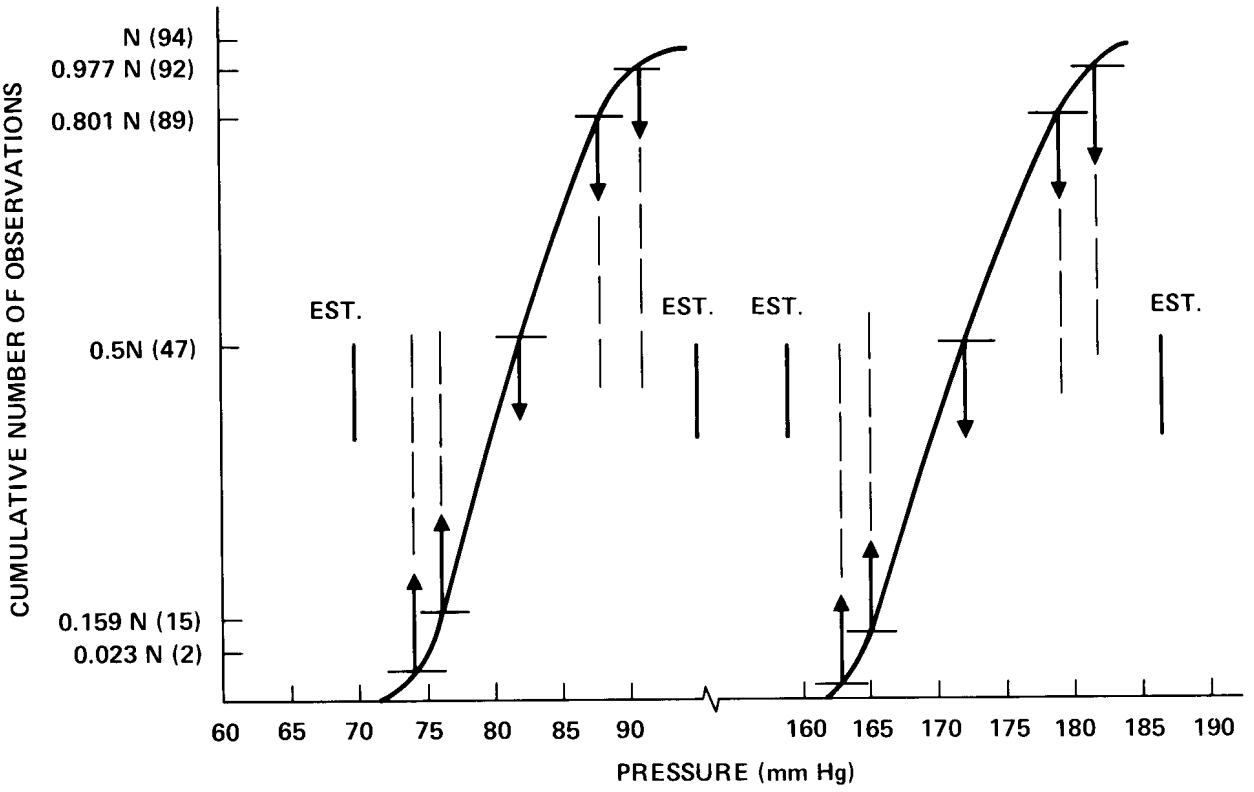

FIG. 12. Hypothetical plot of cumulative pressure measurements.

respresentations of Gaussian tails, one may be able to infer from them the fraction of the distribution that is "abnormal," which may represent upper systolic spikes at one end of the distribution and lower diastolic spikes at the other end.

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REFERENCES

1. BARTTER, F. Periodicity and medicine. *Chronobiologia* 1: 137–144, 1974.
2. BEVAN, A., A. HONOUR, AND F. STOTT. Direct arterial pressure recording in unrestricted man. *Clin. Sci.* 36: 329–344, 1969.
3. BLOCH, E., S. CARDON, A. IBERALL, D. JACOBOWITZ, K. KORNACKER, L. LIPITZ, W. MCCULLOCH, J. URQUHART, M. WEINBERG, AND F. E. YATES. *Introduction to a Biological Systems Science.* Springfield, VA: NTIS, 1971. (NASA Contractors Rep. CR-1720).
4. CARDON, S., AND A. IBERALL. Oscillations in biological systems. *Curr. Mod. Biol.* 3: 237–249, 1970.
5. CLEMENT, D. (Editor). *Blood Pressure Variability.* Baltimore, MD: University Park, 1978.
6. GEDDES, L. *The Direct and Indirect Measurement of Blood Pressure.* Chicago, IL: Year Book, 1970.
7. IBERALL, A. New thoughts in biocontrol. In: *Towards a Theoretical Biology. 2 Sketches*, edited by C. Waddington. Chicago, IL: Aldine, 1969.
8. IBERALL, A. On the general dynamics of systems. *Gen Syst.* 15: 7–13, 1970.
9. IBERALL, A. Flow and pressure regulation in the cardiovascular system. In: *Flow, Its Measurement and Control in Science and Industry*, edited by W. Vannah and H. Wayland. Pittsburgh, PA: Instr. Soc. Am., 1974, vol. 1, part 3.
10. IBERALL, A. A system's theoretic for cardiovascular flow and pressure in mammals. *Am. J. Physiol. (Regulatory Integrative Comp. Physiol.)* In press.
11. IBERALL, A., AND S. CARDON. Control in biological systems—a physical review. *Ann. NY Acad. Sci.* 117: 445–518, 1964.
12. IBERALL, A., S. CARDON, A. SCHINDLER, F. YATES, AND D. MARSH. *Progress Toward the Application of Systems Science Concepts to Biology.* Springfield, VA: Ref. Doc. Center, 1972. (Contractors Rep. Army Res. Off. AD-750174).
13. IBERALL, A., AND W. MCCULLOCH. The organizing principle of complex living systems. *Trans. ASME J. Basic Eng.* 91: 290–294, 1969.
14. MASTER, A., C. GARFIELD, AND M. WALTERS. *Normal Blood Pressure and Hypertension.* Philadelphia, PA: Lea & Febiger, 1952.
15. MEYERS, W., C. DELEA, AND F. BARTTER. Chronopharmacology in the treatment of hypertension with diuretics. In: *Temporal Aspects of Therapeutics*, edited by J. Urquhart and F. Yates. New York: Plenum, 1973.
16. PAUL, O. Multiple risk factor intervention trial. *J. Am. Med. Assoc.* 248: 1465–1477, 1982.
17. PERRY, H., AND W. SMITH (Editors). Mild hypertension, to treat or not to treat. *Ann. NY Acad. Sci.* 304: 1–485, 1978.
18. PICKERING, G. Hypertension, definitions, natural histories, consequences. *Am. J. Med.* 52: 570–583, 1972.
19. RICHARDSON, D., A. HONOUR, G. FENTON, F. STOTT, AND G. PICKERING. Variations in arterial pressure throughout the day and night. *Clin. Sci.* 26: 445–460, 1964.
20. SHIMADA, S., AND D. MARSH. Oscillations in mean arterial blood pressure in conscious dogs. *Circ. Res.* 44: 692–700, 1979.
21. SNYDER, F., J. HOBSON, D. MORRISON, AND F. GOLDFRANK. Changes in respiration, heart rate, and systolic blood pressure in human sleep. *J. Appl. Physiol.* 19: 417–422, 1964.