MEDICAL GRAND ROUNDS

PARKLAND MEMORIAL HOSPITAL

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# ESSENTIAL HYPERTENSION: NATURAL HISTORY AND RESULTS OF TREATMENT

## I. Definitions

A. Recording of blood pressure:

1. American Heart Association (1951):

Pressure in the sphygmomanometer should be increased quickly to a level about 30 mm Hg above the point at which the radial pulse disappears and then be reduced slowly at a rate of about 2 to 3 mm Hg per heart beat. Systolic pressure: the point at which a sound is heard with each heart beat is taken as systolic pressure. If the pressure obtained by palpation is higher than the pressure obtained by the auscultatory method, the pressure obtained by palpation should be accepted as systolic pressure. Diastolic pressure: the point at which the sounds of Korotkoff completely disappear is taken as diastolic pressure. If no cessation of sounds occurs, the point of muffling should be taken as diastolic pressure and recorded as "the point of muffled sounds." (1).

(1) Bordley, J., III, Connor, C.A.R., Hamilton, W.F., Kerr, W.J., and Wiggers, C.J. Recommendations for human blood pressure determinations by sphygmomanometers. Circulation, 4: 503, 1951.

2. World Health Organization (1963):

Recommends recording of both point of muffling and point of disappearance of sounds, as 220/120/108.

(2) Arterial hypertension and ischaemic heart disease: comparison in epidemiological studies. 3. The background to WHO's present work on comparable methodology. WHO Chron., 17: 15, 1963.

B. Casual blood pressure: a blood pressure recorded under non-basal conditions.

C. Basal blood pressure: a blood pressure best recorded early in the morning before arising or after at least 30 minutes in the supine position in a comfortably warm room (1).

D. Supplemental blood pressure (Smirk): the difference between basal and casual blood pressure, a labile increment usually attributed to stress, exercise, anxiety, etc. Mortality rates are reported to correlate well with basal blood pressure but not at all with supplemental blood pressure (3).

(3) Smirk, F. H., Veale, A.M.O., and Alstad, K.S. Basal and supplemental blood pressures in relationship to life expectancy and hypertension symptomatology. New Zealand Med. J., 58: 711, 1959.

## I. Epidemiological Studies of Blood Pressure

Problems in epidemiological studies (2, 4-6):

(4) Geiger, H. J. and Scotch, N.A. The epidemiology of essential hypertension. A review with special attention to psychologic and sociocultural factors. I. Biologic mechanisms and descriptive epidemiology. II. Psychologic and sociocultural factors in etiology. J. Chron. Dis. 16: 1151, 1963.

(5) McKeown, T., Record, R.G., and Whitfield, A.G.W. Variation in casual measurements of arterial pressure in two populations (Birmingham and South Wales) re-examined after intervals of 3-4 1/2 years. Clin. Sci., 24:437, 1963.

(6) Build and Blood Pressure Study, Vol. I and II. Society of Actuaries, Chicago, Illinois, 1959.

A. Age:

1. Many cross-sectional surveys have shown that the blood pressure of the population (particularly in urbanized cultures) increases with age. There is also increased skewing of the frequency distribution curve to the right as age increases (4-14).

(7) Bechgaard, P. Arterial hypertension. A follow-up study of one thousand patients. Acta med. scand., Supplement 172: 1, 1946.

(8) Hamilton, M., Pickering, G.W., Roberts, J.A.F., and Sowry, G.S.C. The aetiology of essential hypertension. I. The arterial pressure in the general population. Clin. Sci., 13: 11, 1954.

(9) Master, A.M., Garfield, C.I., and Walters, M.B. Normal blood pressure and hypertension: new definitions. Philadelphia, Lea & Febiger, 1952.

(10) Bøe, J., Humerfelt, S., and Wedervang, F. The blood pressure in a population. Blood pressure readings and height and weight determinations in the adult population of the city of Bergen. Acta med. scand. 157: supplement 321: 1, 1957.

(11) Humerfelt, S. BJ. An epidemiological study of high blood pressure. Acta med. scand., Supplement 407: 1, 1963.

(12) Comstock, G.W. An epidemiologic study of blood pressure levels in a biracial community in the Southern United States. Amer. J. Hyg. 65: 271, 1957.

(13) Kagan, A., Gordon, T., Kannel, W.B., and Dawber, T.R. Blood pressure and its relation to coronary heart disease in the Framingham study. Proc. Council for High Blood Pressure Research, Vol. VII, 53, 1958.

(14) Hoobler, S.W., McDonough, J., and Ostfeld, A. Hypertension, pregnancy toxemia, and renal disease--community services. The Heart and Circulation, Second National Conf. of Cardiovascular Diseases, Vol. II, Community Services and Education, pp. 56, 1964.

(15) Stark, N.W. Basal blood pressure and pulse rate in adolescent. Am. J. Dis. of Children, 68: 16, 1944.

2. However, primative populations tend to show little increase in blood pressure with age (15-17).

(15) Lowenstein, F.W. Blood-pressure in relation to age and sex in the tropics and subtropics. Lancet, I: 389, 1961.

(16) Cruz-Coke, R., Etcheverry, R., and Nagel, R. Influence of migration on blood pressure of Easter islanders. Lancet, I: 697, 1964.

(17) Clifford, N.J., Kelly, J.T., Jr., Leo, T.F., and Eder, H.A. Coronary heart disease and hypertension in the White Mountain Apache tribe. Circulation, 28: 926, 1963.

3. It is not clear whether all adults tend to have an increase in BP with age (8, 9, 18) or whether this increase is limited to a "hypertensive" fraction of the population (19, 20).

(18) Harlan, W.R., Osborne, R.K., and Graybiel, A. A longitudinal study of blood pressure. Circulation, 26: 530, 1962.

(19) Robinson, S.C. and Brucer, M. Range of normal blood pressure: A statistical and clinical study of 11,383 persons. Arch. Int. Med., 64: 409, 1939.

(20) Stamler, J., Lindberg, H.A., Berkson, D.M., Shaffer, A., Miller, W., and Poindexter, A. Epidemiological analysis of hypertension and hypertensive disease in the labor force of a Chicago utility company. Proc. Council for High Blood Pressure Research, Vol. VII, pp. 23, 1958.

B. Sex

1. In general, BP in men is slightly higher than in women until about age 45, when the reverse is true.

2. All studies confirm that mortality rates from hypertensive diseases are higher in the male.

C. Race

1. Negroes (both male and female) have a higher incidence of hypertension and higher mortality rate from hypertensive diseases than do whites (12, 21-23).

(21) Lennard, H.L. and Glock, C.Y. Studies in hypertension. VI. Differences in the distribution of hypertension in Negroes and whites: an appraisal. J. Chron. Dis. 5: 186, 1957.

(22) Moser, M. Epidemiology of hypertension with particular reference to racial susceptibility. Ann. New York Acad. Sci., 84: 989, 1960.

(23) Phillips, J. H., Jr. and Burch, G.E. Review of cardiovascular diseases in white and Negro races. Medicine, 39: 241, 1960.

D. Genetic factors

1. There is general agreement that the blood pressures of family members tend to resemble one another; i.e., that hypertension is clustered in families (24-32).

(24) Thomas, C.B. and Hirschhorn, B. The familial occurrence of hypertension and coronary artery disease, with observations concerning obesity and diabetes. Ann. Int. Med., 42: 90, 1955.

(25) Hamilton, M., Pickering, G.W., Fraser Roberts, J.A., and Sowry, G.S.C. Arterial pressures of relatives of patients with secondary and malignant hypertension. Clin. Sci., 24: 91, 1963.

(26) Miall, W.E. and Oldham, P.D. The hereditary factor in arterial blood-pressure. Brit. Med. J., I: 75, 1963.

(27) Cruz-Coke, R. The hereditary factor in hypertension. Acta genetica et statistica medica, 9: 207, 1959.

(28) Ostfield, A.M. and Paul, O. The inheritance of hypertension. Lancet, I: 575, 1963.

(29) Platt, R. The nature of essential hypertension. Lancet, II: 55, 1959.

(30) Platt, R. Heredity in hypertension. Lancet, I: 899, 1963.

(31) Morrison, S.L. and Morris, J.N. Nature of essential hypertension. Lancet, II: 829, 1960.

(32) McKusick, V.A. Genetics and the nature of essential hypertension. Circulation, 22: 857, 1960.

2. Relatives of hypertensive subjects, although still normotensive, may be hyperreactive to norepinephrine (33) and to angiotensin (34).

(33) Doyle, A.E. and Fraser, J.R.E. Essential hypertension and inheritance of vascular reactivity. Lancet, II: 509, 1961.

(34) Wood, J.E. Genetic control of neutralization of angiotensin and its relationship to essential hypertension. Circulation, 25: 225, 1962.

3. Controversy continues over whether the genetic component of the blood pressure is inherited as a graded polygenic characteristic (25-28) or as a Mendelian dominant (29-31).

E. Non-genetic factors.

1. All authors agree that genetic factors are less important than certain environmental factors in determining the BP of an individual: psychological and social factors (4, 15, 39), obesity (4, 6, 7, 10), salt intake (35-38), occult renal disease (40-42), toxemia of pregnancy (43-45), etc.

(35) Dahl, L.K. Possible role of salt intake in the development of essential hypertension. Essential Hypertension: An International Symposium, (F.C. Reubi, ed.), Springer-Verlag, Berlin, 1960, pp. 53-65.

(36) Johnson, B.C. and Remington, R.D. A sampling study of blood pressure in white and Negro residents of Nassau, Bahamas. J. Chron. Dis., 13: 39, 1961.

(37) Schneckloth, R.E., Stuart, K.L, Corcoran, A.C., and Moore, F.E. Arterial pressure and hypertensive disease in a West Indian Negro population. Report of a survey in St. Kitts, West Indies. Am. Heart J., 63: 607, 1962.

(38) Whyte, H.M. Body fat and blood pressure of natives in New Guinea: Reflections on essential hypertension. Australasian Ann. Med., 7: 37, 1958.

(39) Cruz-Coke, R. Environmental influences and arterial blood-pressure. Lancet, II: 885, 1960.

(40) Roland, A.S., Hildreth, E.A., and Sellers, A.M. Occult primary renal disease in the hypertensive patient. Arch. Int. Med., 113: 101, 1964.

(41) Kleeman, C.R., Hewitt, W.L., and Guze, L.B. Pyelonephritis. Medicine, 39: 3, 1960.

(42) Merriam, J.C., Sommers, S.C., and Smithwick, R.H. Clinicopathologie correlations of renal biopsies in hypertension with pyelonephritis. Circulation, 17: 243, 1958.

(43) Epstein, F.H. Late vascular effects of toxemia of pregnancy. New Eng. J. Med., 271: 391, 1964.

(44) Adams, E.M. and MacGillivray, I. Long-term effect of pre-eclampsia on blood pressure. Lancet, II: 1373, 1961.

(45) Chesley, L.C., Cosgrove, R.A., and Annitto, J.E. A follow-up study of eclamptic women: fourth periodic report. Am. J. Obst. and Gyne., 83: 1360, 1962.

III. Natural History of Hypertensive Disease.

A. Conflicting viewpoints:

1. "The term hypertensive disease is synonymous with essential hypertension and should properly be restricted to designate the as yet unidentified physiological disturbance (or disturbances) characteristic of this disease and which leads ultimately to elevation of diastolic and systolic blood pressures, anatomical changes in the vascular tree, and functional impairment of the involved tissues. . . . Hypertensive disease is considered to be a clinical entity in which an unknown pressor mechanism initiates arteriolar vasoconstriction, elevated blood pressure and vascular sequelae. Hypertension, as such, like arteriolar changes, is conceived to be a sequela appearing during the progressive development of the disease."--Definition of Goldring and Chasis, adopted by WHO (2).

2. "The new view. . . . is that essential hypertension represents a quantitative and not a qualitative deviation from the norm; that there is no natural dividing line between normal and abnormal pressures; and that any attempt to divide pressures sharply into normal and abnormal is artificial." (46)

(46) Oldham, P.D., Pickering, G., Roberts, J.A.F., and Sowry, G.S.C. The nature of essential hypertension. Lancet, I: 1085, 1960.

B. "Official" definition of hypertension by WHO (2).

1. Normotension: systolic BP < 140 and diastolic BP < 90.

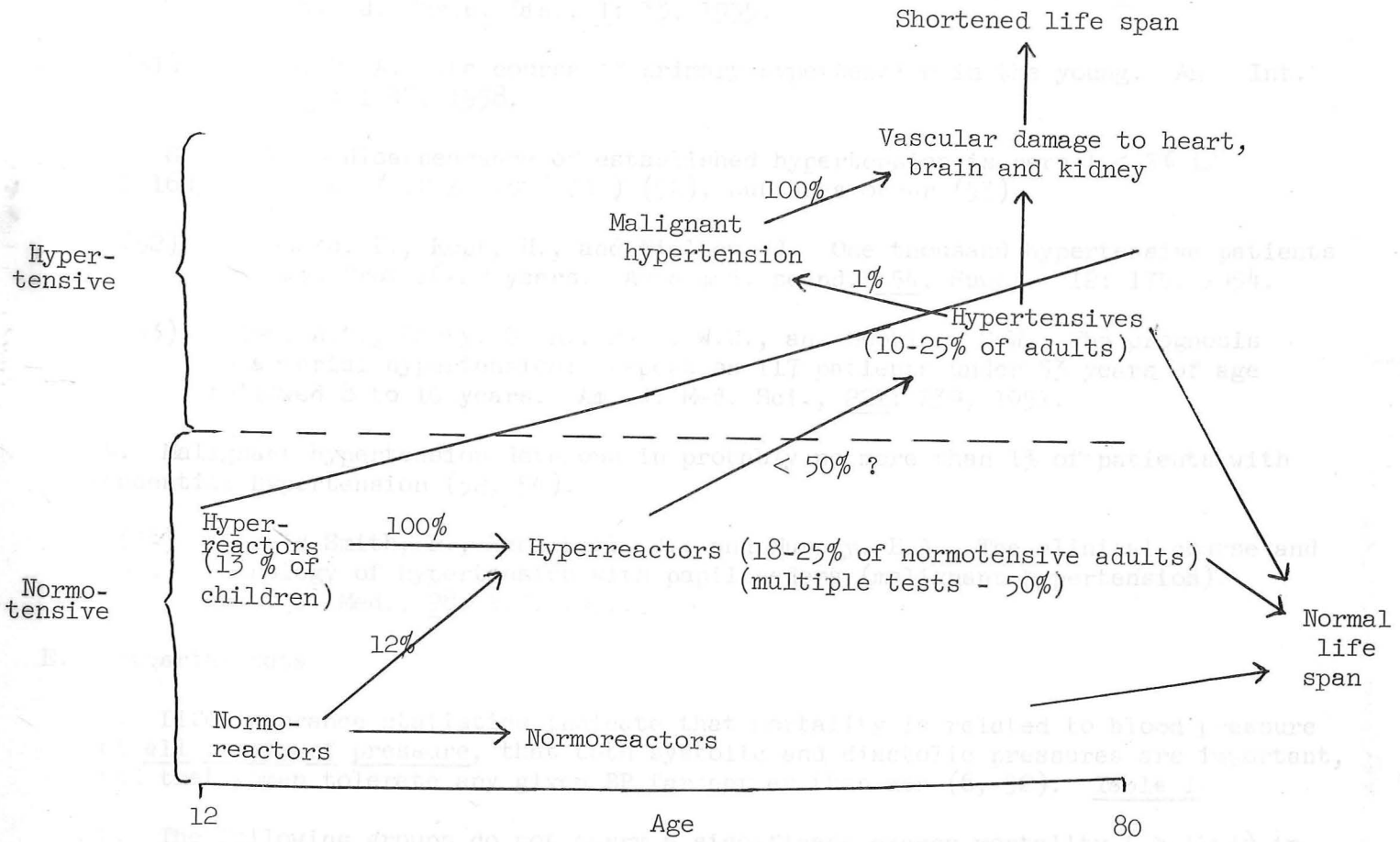
2. Hypertension: systolic BP > 160 and/or diastolic BP > 95.

3. Borderline hypertension: any BP reading between the above limits.

C. Prevalence of hypertension.

| Population | Sex | No. | Criteria | % | Reference |
|---|---|---|---|---|---|
| Framingham | M | 1882 | > 160 systolic | 10% | 13 |
| " | " | " | > 86 diastolic | 33% | " |
| " | F | 2294 | > 160 systolic | 13% | " |
| " | " | " | > 86 diastolic | 27% | " |
| Western Elec. Co. | M | 2000 | > 160/95 | 11% | 28 |
| Bergen, Norway | M | 17,901 | > 90 diastolic | 14% | 10 |
| " | F | 26,281 | " | 16% | " |
| Evans Co., Ga. | M & F | 3102 | > 100 diastolic | 28% | 13a |

D. Overall pattern




1. The available evidence suggests that hyperreactivity to the cold pressor test is life-long, that most of the hypertensive population develops hyperreactivity, but that no more than one-half of all hyperreactors eventually develop hypertension (47, 48). When three different tests for hyperreactivity were done, 50% of 204 adults responded to one or more, but only 2.7% responded to all three (49).

(47) Hines, E.A., Jr., and Brown, G.E. The cold pressor test for measuring the reactibility of the blood pressure: data concerning 571 normal and hypertensive subjects. Am. Heart J., 11: 1, 1936.

(48) Barnett, P.H., Hines, E.A., Jr., Schriger, A., and Gage, R.P. Blood pressure and vascular reactivity to the cold pressor test. Restudy of 207 subjects 27 years later. J.A.M.A., 183: 845, 1963.

(49) Glock, C.Y., Vought, R.L., Schweitzer, M.D., Clark, E.G., and Katz, J. Studies in hypertension. IV. Comparison of reaction to three tests for hyperreactivity among 204 volunteers. J. Chron. Dis. 4: 490, 1956.

2. In a group of 500 hypertensives ( > 90 diastolic ) followed from onset to death, Perera (50) has found mean age of onset to be 32 (range 9-48); mean age of death was 52 (range 27-83); mean survival was 20 years (range 1-44 years). Mean survival time after onset of LVH or grade II eyegrounds was 6 years. The overall course was similar in patients with onset under age 25 (51).

(50) Perera, G. A. Hypertensive vascular disease: description and natural history. J. Chron. Dis., I: 33, 1955.

(51) Perera, G. A. The course of primary hypertension in the young. Ann. Int. Med., 49: 1348, 1958.

3. Spontaneous disappearance of established hypertension is rare ( < 5% if BP 160/100 and < 1% if BP 180/100 ) (52), but does occur (53).

(52) Bechgaard, P., Kopp, H., and Nielsen, J. One thousand hypertensive patients followed from 16-22 years. Acta med. scand. 154, Suppl. 312: 175, 1954.

(53) Griep, A.H., Barry, G. R., Hall, W.C., and Hoobler, S.W. The prognosis in arterial hypertension: report on 117 patients under 53 years of age followed 8 to 10 years. Am. J. Med. Sci., 221: 239, 1951.

4. Malignant hypertension develops in probably no more than 1% of patients with essential hypertension (52, 54).

(54) Kincaid-Smith, P., McMichael, J., and Murphy, E.A. The clinical course and pathology of hypertension with papilloedema (malignant hypertension). Quat. J. Med., 28: 117, 1958.

E. Actuarial data

1. Life insurance statistics indicate that mortality is related to blood pressure at all levels of pressure, that both systolic and diastolic pressures are important, and that women tolerate any given BP far better than men (6, 52). Table 1.

2. The following groups do not carry a significant excess mortality ( > 125%) in actuarial studies:

--White women age 50 and over with blood pressure less than 200/120 and no cardiovascular complications (52).

--White women at any age with BP less than 160/90 (6).

--White men age 50 and over with BP less than 140/90 (6).

--White men at any age with BP less than 135/80 - 125/85 (6).

F. Malignant Hypertension (papilledema).

1. Course is almost always fatal. Table 2.

(55) Keith, N.M., Wagener, H.P., and Barker, N.W. Some different types of essential hypertension: Their course and prognosis. Am. J. Med. Sci., 197: 332, 1939.

(56) Sokolow, M. and Perloff, D. The prognosis of essential hypertension treated conservatively. Circulation, 23: 697, 1961.

(57) Palmer, R.S. Treatment of hypertension. A 23-year follow-up of 453 patients with a selected review and report of current experience. J. Chron. Dis., 10: 500, 1959.

(58) Peet, M.M. and Isberg, E.M. The surgical treatment of essential hypertension. J.A.M.A., 130: 467, 1946.

(59) Thorpe, J.J., Welch, W.J., and Poindexter, C.A. Bilateral thoracolumbar sympathectomy for hypertension. A study of 500 cases. Am. J. Med., 9: 500, 1950.

(60) Newborg, B. and Kempner, W. Analysis of 177 cases of hypertensive vascular disease with papilledema. One hundred twenty-six patients treated with rice diet. Am. J. Med., 19: 33, 1955.

(61) Simpson, F.O. and Gilchrist, A.R. Prognosis in untreated hypertensive vascular disease. Scot. Med. J., 3: 1, 1958.

(62) Björk, S., Sannerstedt, R., Angervall, G., and Hood, B. Treatment and prognosis in malignant hypertension. Clinical follow-up study of 93 patients on modern medical treatment. Acta med. scand., 166: 175, 1960.

(63) Dustan, H.P., Schneckloth, R.E., Corcoran, A.C., and Page, I.H. The effectiveness of long-term treatment of malignant hypertension. Circulation, 18: 644, 1958.

(64) Perry, H.M., Jr. and Schroeder, H.A. The effect of treatment on mortality rates in severe hypertension. A comparison of medical and surgical regimens. Arch. Int. Med., 102: 418, 1958.

(65) Mohler, E.R., Jr. and Freis, E.D. Five-year survival of patients with malignant hypertension treated with antihypertensive agents. Am. Heart J., 60: 329, 1960.

(66) Harington, M., Kincaid-Smith, P., and McMichael, J. Results of treatment in malignant hypertension. A seven-year experience in 94 cases. Brit. Med. J., 2: 969, 1959.

(67) Farmer, R.G., Gifford, R.W., and Hines, E.A. Effect of medical treatment of severe hypertension. Arch. int. med., 112: 118, 1963.

(68) Sokolow, M. and Perloff, D. Five year survival of consecutive patients with malignant hypertension treated with antihypertensive agents. Am. J. Cardiol., 6: 858, 1960.

(69) Hodge, J.V., McQueen, E.G., and Smirk, H. Results of hypotensive therapy in arterial hypertension, based on experience with 497 patients treated and 156 controls, observed for periods of one to eight years. Brit. Med. J., 1: 1, 1961.

2. Spontaneous remission (70) and even apparent spontaneous cure (54) have been reported.

(70) Keith, N.M. and Wagener, H.P. Recession of neuroretinopathy during the course of malignant hypertension. Its occurrence in fifteen patients who did not receive directed therapy. Arch. Int. Med., 87: 25, 1951.

3. Malignant hypertension is reported to be due to essential hypertension in 42-90% of cases, to chronic pyelonephritis or glomerulonephritis in 6-35% of cases, and to other causes in 5-10% of cases (54, 63). Wilson states that 50% of cases of chronic glomerulonephritis will have malignant hypertension terminally (71).

(71) Wilson, C. Experiment and therapy in hypertension. Proc. Royal Soc. of Med., 48: 279, 1955.

G. Non-malignant hypertensive disease.

1. Mortality increases directly with the level of blood pressure and the degree of organ involvement. Table 3 -- (applies only to white population) (55-57, 61, 72, 73).

(72) Hammarström, S. and Bechgaard, P. Prognosis in arterial hypertension. Comparison between 251 patients after sympathectomy and a selected series of 435 non-operated patients. Am. J. Med., 8: 53, 1950.

(73) Leishman, A.W.D. Merits of reducing high blood-pressure. Lancet, I: 1284, 1963.

2. Hypertension is a major factor predisposing to coronary heart disease (74, 75) and to cerebral vascular disease (75-77).

(74) Kannel, W.B., Dawber, T.,R., Kagan, A., Revotskie, N., and Stokes, J. III. Factors of risk in the development of coronary heart disease: six-year follow-up experience--the Framingham study. Ann. Int. Med., 55: 33, 1961.

(75) Roberts, J.C., Moses, C., and Wilkins, R.H. Autopsy studies in atherosclerosis. I. Distribution and severity of atherosclerosis in patients dying without morphologic evidence of atherosclerotic catastrophe. Circulation, 20: 511, 1959.

(76) Low-Beer, T. and Phear, D. Cerebral infarction and hypertension. Lancet, I: 1303, 1961.

(77) Baker, A.B. and Iannone, A. Cerebrovascular disease. VII. A study of etiologic mechanisms. Neurology, 11: 23, 1961

H. Causes of death in untreated hypertensive disease.

1. Approximately 70-90% of patients with established hypertension die of cardiovascular-renal disease (78, 79). See Table 4.

(78) Smith, D.E., Odel, H.M., and Kernohan, J.W. Causes of death in hypertension. Am. J. Med., 9: 516, 1950.

(79) Mathison, H.S., Jensen, D., Löken, E., and Löken, H. The prognosis in essential hypertension. Am. Heart J., 57: 371, 1959.

IV. Results of Treatment

A. Malignant hypertension.

1. This is the only form of hypertension is which there is nearly unanimous agreement that treatment substantially improves survival. See Table 2.

2. Lowering of blood pressure may be expected to reverse the papilledema and retinitis (over a period of weeks to months) in about 75% of cases, and to improve the ECG in about 25% of cases (deterioration will continue in another 20% and no change will occur in the remainder) (66, 68).

3. Azotemia sharply limits survival. Patients with a BUN higher than 80 mg% tend to deteriorate; those with a BUN of 40 mg% or less tend to stabilize or improve. Malignant hypertension due to chronic renal disease is reported to, if anything, respond better to treatment than azotemic malignant hypertension due to essential hypertension (66).

4. Healing of renal lesions during treatment has been observed (80).

(80) McCormack, L.J., Beland, J.E., Schenckloth, R.E., and Corcoran, A.C. Effects of antihypertensive treatment on the evolution of the renal lesions in malignant nephrosclerosis. Am. J. Path., 34: 1011, 1958.

5. Treated patients continue to die of uremia and strokes. Heart failure as a cause of death has been largely replaced by an increasing incidence of atherosclerotic complications such as cerebral vascular accidents, myocardial infarction, dissecting aneurysms, etc. (63-66).

B. Non-malignant hypertensive disease.

1. Vital statistics indicate that in the decade from 1950 to 1960 mortality from hypertensive disease in the U.S. has fallen by 30-40% (13a).

2. Several groups have reported that drug treatment of K-W Grade II & III hypertensives prolongs survival (64, 67, 69, 73). The most dramatic results are those of Leishman (73) - Table 5. There are no well documented reports of drugs failing to alter survival except that of Perera (K-W Grade II patients) (81).

(81) Perera, G.A. Antihypertensive drug versus symptomatic treatment in primary hypertension. Effect on survival. J.A.M.A., 173: 11, 1960.

3. Several surgical groups have reported increased survival after sympathectomy in hypertensive disease (58, 72, 82-84).

(82) Smithwick, R.H., Bush, R.D., Kinsey, D., and Whitelaw, G.P. Hypertension and associated cardiovascular disease. Comparison of male and female mortality rates and their influence on selection of therapy. J.A.M.A., 160: 1023, 1956.

(83) Kinsey, D., Sise, H.S., and Whitelaw, G.P. Changes in mortality rates of treated hypertensive patients in a decade. Geriatrics, 16: 397, 1961.

(84) Saare, H. Late results of surgical therapy (sympathectomy and adrenalectomy), Essential Hypertension, An International Symposium, Springer-Verlag, Berlin, 1960, pp. 332-346.

A complicating factor in evaluating results is that survival rates in patients graded by the systems of Smithwick (82), of Hammarström and Bechgaard (72), and of Palmer (57) tend to resemble those of the next lower grade in the Keith-Wagener-Barker system (55). See Hood et al. (85) and Table 3.

(85) Hood, B., Björk, S., Sannerstedt, R., and Angervall, G. Analysis of mortality and survival in actively treated hypertensive disease. Acta med. scand., 174: 393, 1963.

Thorpe et al. (59) found sympathectomy of clear benefit only in severe hypertension. Independent evaluation of Smithwick's patients by White (86) and Evelyn et al. (87) have yielded conflicting opinions.

(86) White, P.D. Severe hypertension--study of one hundred patients with cardiovascular complications. Follow-up results in fifty controls and fifty patients subjected to Smithwick's lumbodorsal sympathectomy, 1941 to 1946. J.A.M.A., 160: 1027, 1956.

(87) Evelyn, K.A., Singh, M.M., Chapman, W.P., Perera, G.A., and Thaler, H. Effect of thoracolumbar sympathectomy on the clinical course of primary (essential) hypertension. A ten-year study of 100 sympathectomized patients compared with individually matched, symptomatically treated control subjects. Am. J. Med., 28: 188, 1960.

4. Treatment has been reported to decrease the rate at which renal function deteriorates, but the data are convincing only for patients with rapidly progressive or malignant hypertension (88, 89).

(88) Moyer, J.H., Heider, C., Pevey, K., and Ford, R.V. The effect of treatment on the vascular deterioration associated with hypertension, with particular emphasis on renal function. Am. J. Med., 24: 177, 1958.

(89) Reubi, F.C. The late effects of hypotensive drug therapy on renal function of patients with essential hypertension, Essential Hypertension, An International Symposium, Springer-Verlag, Berlin, 1960, pp. 317-331.

5. Treated hypertensive patients who die still succumb largely to cardiovascular-renal disease. Treatment reduces the incidence of congestive heart failure and of strokes (73, 85, 90) and probably reduces the incidence of uremia (73, 85). The incidence of myocardial infarction is probably not reduced (85, 90). Table 6.

(90) Smirk, H. and Hodge, J.V. Causes of death in treated hypertensive patients. Based on 82 deaths during 1959-61 among an average hypertensive population at risk of 518 persons. Brit. Med. J., 2: 1221, 1963.

V. Guidelines for Therapy.

A. Treatment indicated:

1. Patients with malignant hypertension of any cause, with or without azotemia.

2. Patients with acute hypertensive emergencies--encephalopathy, acute heart failure, etc.

3. Hypertensive patients with <u>any</u> of the following:

--retinal hemorrhages and exudates
--initial diastolic BP > 130 in males or 150 in females
--diastolic BP in the hospital > 110 in males or 130 in females
--cardiac enlargement of 20% or more on x-ray and/or ECG signs of LVH and strain
--early renal failure

4. Patients who are symptomatic (headaches) or who have heart failure and uncontrolled hypertension.

B. Treatment probably indicated:

1. Males with diastolic BP > 100 and females with diastolic BP > 110, who <u>also</u> have any one of the following:

--K-W Grade I eyegrounds in the male or Grade II in the female.
--Clear evidence of cardiac enlargement (more than rounding of the left border) on x-ray
--ECG evidence of LVH

2. Males with diastolic BP > 110 and females with diastolic BP > 120, even in absence of any cardiac or renal involvement.

C. Treatment optional (no proven benefit or harm):

1. Males with BP 140/80 - 200/110 and no organ involvement.

2. Females under age 50 with BP 160/90 - 200/120 and no organ involvement.

D. Treatment not indicated:

1. Hyperreactors.

2. Females over age 50 with BP < 200/120 and no organ involvement.

E. Comments:

1. History of stroke is an indication, not a contraindication, for treatment.

2. Early renal failure due to nephrosclerosis is a prime indication, not a contraindication, for therapy.

3. Hypertension due to renal disease should probably be considered, from the standpoint of drug therapy, as equivalent to essential hypertension.

4. Although no data are available that pertain specifically to therapy in the Negro, the very high mortality rate from hypertensive disease in this race suggests that Negro patients (both male and female) should be treated at an earlier stage of the disease than is recommended for whites.

5. Bechgaard has reported that women who develop hypertension as a sequela to toxemia of pregnancy carry a mortality risk comparable to men of the same age and level of blood pressure (91).

(91) Bechgaard, P. The natural history of benign hypertension, Essential Hypertension, An International Symposium, Springer-Verlag, Berlin, 1960, pp. 198-213.

Table 1
RATIO (PERCENT) OF ACTUAL TO EXPECTED MORTALITY (Ref. 6)

Men - Age 15 to 69

| Systolic BP | Diastolic BP 48-67 | 68-82 | 83-87 | 88-92 | 93-97 | 98-102 |
|---|---|---|---|---|---|---|
| 98 - 127 | 80 | 86 | 106 | 116 | 114 | |
| 128 - 137 | 100 | 109 | 127 | 140 | 168 | 197 |
| 138 - 147 | 151 | 141 | 153 | 170 | 199 | 224 |
| 148 - 157 | | 166 | 196 | 191 | 224 | 269 |
| 158 - 167 | | 233 | 197 | 240 | 268 | 289 |

Women - Age 15 to 69

| Systolic BP | Diastolic BP 48-67 | 68-82 | 83-87 | 88-92 | 93-97 | 98-102 |
|---|---|---|---|---|---|---|
| 98 - 127 | 57 | 56 | 55 | 58 | | |
| 128 - 137 | 62 | 60 | 64 | 74 | 65 | |
| 138 - 147 | | 71 | 73 | 72 | 117 | 132 |
| 148 - 157 | | 61 | 83 | 96 | 98 | 139 |
| 158 - 167 | | 97 | 150 | 125 | 172 | 205 |

Table 2

MORTALITY OF PATIENTS WITH MALIGNANT HYPERTENSION-UNTREATED AND TREATED

| Reference | Date | Sex | Controls No. | Controls Type | Treated No. | Treated Treatment | Percent Survivors 1 yr. C | 1 yr. T | 2 yrs C | 2 yrs T | 5 yrs C | 5 yrs T |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Keith et al. (55) | 1939 | M & F | 146 | F | | | 20 | | 12 | | 1 | |
| Sokolow & Perloff (56, 68) | 1960 | M & F | 76 | F | 26 | Drug | 36 | 40 | 26 | 27 | 18 | |
| Palmer (57) | 1959 | M & F | 54 | F | | | 45 | | 22 | | 8 | |
| Kincaid-Smith et al. (54, 66) | 1958-9 | M & F | 109 | R | 82 | Drug | 10 | 52 | 6 | 35 | 1 | 22 |
| Simpson & Gilchrist (61) | 1958 | F | 30 | F | | | 20 | | 3 | | 0 | |
| " | 1958 | M | 40 | F | | | 5 | | 0 | | 0 | |
| Peet & Isberg (58) | 1946 | M & F | | | 112 | Surgery | | | | | | 19 |
| Thorpe et al.(59) | 1950 | M & F | | | 54 | Surgery | | | | c.50 | | |
| Newborg & Kempner (60) | 1955 | M & F | 18 | R | 153 | Rice diet | 20 | 50 | | | | |
| Bjork et al.(62) | 1960 | M & F | 87 | R | 22 | Surgery | 20 | 45 | 10 | 32 | | 15 |
| " | 1960 | M & F | 87 | R | 93 | Drugs | | 76 | | 62 | | 50 |
| Dustan et al.(63) | 1958 | M & F | | | 84 | Drugs | | 70** | | 60 | | 35 |
| Perry & Schroeder (64)* | 1958 | M & F | | | 82 | Drugs | | | | 50 (4 yr) | | |
| Mohler & Freis (65)* | 1960 | M & F | | | 64 | Drugs | | 75 | | 35 | | 20 |
| Farmer et al. (67) | 1963 | M & F | | | 64 | Drugs | | 63 | | 45 | | 29 |

* - 15-30% Negro patients; all other series are largely white patients.
** - Eliminated all patients who died within three months (35% in series of Keith et al.).

F - Group followed prospectively
R - Group taken retrospectively from records

Table 3
RELATIONSHIP BETWEEN PROGNOSTIC CRITERIA AND MORTALITY
IN PATIENTS WITH NON-MALIGNANT HYPERTENSION*

| Males | Females | Mean Survival Percent 1 yr | 5 yrs | 10 yrs |
|---|---|---|---|---|
| Normals | Normals | 99 | 95 | 88 |
| Grade O-I eyegrounds (55,56)<br>Diast. BP in hospital < 100 (61) | Grade I eyegrounds (55,56,61)<br>Initial BP < 200/110 (56)<br>Diastolic BP 120-129 (73)<br>Initial diastolic BP < 110 (61)<br>Diast.BP in hospital < 110 (61)<br>Heart enlarged 0-10% (56)<br>ECG normal or high voltage only (56) | 94 | 79 | 51 |
| Grade I-II eyegrounds (55,56,61)<br>Diastolic BP 120-129 (73)<br>Initial diast.BP 100-129 (61)<br>Diast.BP in hospital < 110 (61) | Grade II eyegrounds (55,56,61)<br>Initial BP 200/110-250/130 (56)<br>Diastolic BP 130-149 (73)<br>Initial diast.BP 110-149 (61)<br>Diast.BP in hospital 120-139 (61)<br>Heart enlarged 11-20% (56)<br>ECG-High voltage plus low T (56) | 85 | 55 | 18 |
| Grade III eyegrounds (55, 56)<br>Diastolic BP 130-149 (73)<br>Initial diast.BP 130-149 (61)<br>Diast.BP in hospital 110-139 (61)<br>Heart enlarged 21-30% (56)<br>ECG - LVH and strain (56) | Grade III eyegrounds (55,56,61)<br>Initial BP > 250/130 (56)<br>Diastolic BP > 150 (73)<br>Initial diast.BP > 150 (61)<br>Diast. BP in hospital > 140 (61)<br>Heart enlarged 21-30% (56)<br>ECG - LVH and strain (56) | 60 | 26 | 10 |
| Grade III eyegrounds (61)<br>Diastolic BP > 150 (61,73)<br>Diast.BP in hospital > 140 (61)<br>Heart enlarged > 30% (56) | | 32 | 6 | |

*Table shows mean survival data for patients grouped on the basis of any one of the criteria in the class. An individual meeting several criteria in a class would be expected to have a less favorable outlook than is shown.

| Series Reviewed | Number of patients untreated<br>Males | Females | Males & Females Considered Together |
|---|---|---|---|
| Keith et al. (55) | | | 73 (59% M) |
| Sokolow & Perloff (56) | | | 439 (68% F) |
| Simpson & Gilchrist (61) | 87 | 142 | |
| Leishman (73) | 36 | 68 | |

Table 4
CAUSES OF DEATH IN HYPERTENSIVE PATIENTS (Ref. 78)

| | Percent of cases in each grade | | | | |
|---|---|---|---|---|---|
| No. of cases | Grade I 100 | Grade II 100 | Grade III 76 | Grade IV 100 | All Grades 376 |
| Heart failure | 21 | 26 | 40 | 21 | 26 |
| Coronary disease | 7 | 20 | 12 | 1 | 10 |
| CVA | 9 | 17 | 18 | 16 | 15 |
| Uremia | 3 | 2 | 16 | 59 | 20 |
| Other | 60 | 35 | 14 | 3 | 29 |
| Total | 100 | 100 | 100 | 100 | 100 |

Table 5
RESULTS OF TREATMENT IN HYPERTENSIVE PATIENTS (Ref. 73)

| | Initial Diastolic Pressure | | | | | |
|---|---|---|---|---|---|---|
| | 120-129 | | 130-149 | | > 150 | |
| Males: | C | T | C | T | C | T |
| Number | 15 | 12 | 13 | 48 | 8 | 29 |
| Per cent survivors: | | | | | | |
| 1 year | 94 | 100 | 60 | 95 | 13 | 95 |
| 3 years | 68 | 100 | 31 | 88 | 13 | 78 |
| 5 years | 48 | | 18 | 88 | 13 | 78 |
| K-W | II → 0 | | III → 0-I | | III-IV → I | |
| Females: | | | | | | |
| Number | 30 | 14 | 25 | 51 | 13 | 29 |
| Percent survivors: | | | | | | |
| 1 year | 92 | 100 | 73 | 94 | 55 | 95 |
| 3 years | 89 | 100 | 62 | 87 | 46 | 90 |
| 5 years | 73 | | 50 | 85 | 32 | 90 |
| K-W | I → 0 | | II → 0-I | | III → 0-I | |

Table 6

CAUSES OF DEATH IN TREATED AND UNTREATED HYPERTENSIVE PATIENTS (Ref. 90)

| | Percent of deaths | |
|---|---|---|
| | Untreated Series to 1958 | Treated Series 1959 - 61 |
| Heart failure | 23 | 4.3 |
| Myocardial infarction | 17 | 49 |
| Cerebral vascular accident | 40 | 23 |
| Uremia | 12 | 10 |
| Other | 8 | 14 |
| No. of patients | 82 | 82 |