DECEMBER 1976

The American Journal of Medicine

VOLUME 61

NUMBER 6

EDITORIAL

Labile Hypertension

Precursor of Sustained Essential Hypertension?

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Arterial blood pressure sometimes below and sometimes above 140/90 mm Hg is "labile hypertension" (stage I WHO classification) [1]. This fluctuation of blood pressure implies no hypertensive damage to organs. Identifying people as having labile hypertension is not easy because so little is known about the spontaneous variation of blood pressure in the labile hypertensive state in contrast to that in normal persons or in those with sustained hypertension [2,3]. The small number of patients evaluated and the lack of uniform assessment of blood pressure within each investigation have precluded isolation of these three groups. Despite the use of an intermittent increase in blood pressure above 140/90 mm Hg as the bottom marker for establishing hypertensive hemodynamic and hormonal characteristics [4–7], a very wide fluctuation in blood pressure has not been proved unequivocally in the labile hypertensive state. It is often called "borderline hypertension," "transient hypertension" or "prehypertension" [8,9]. The prevalence of labile hypertension exceeds 10 per cent and the estimated new case rate is 1 per cent per year [8]. The blood pressure survey of 12,371 persons aged 15 years or older in Charlottesville, Virginia (Figure 1) showed an 11 per cent prevalence of the labile hypertensive state after correlation with subsequent blood pressure measurements [10]. This high frequency of labile hypertension cannot be dismissed by statistical regression toward the mean. Since sequential blood pressure measurement in these people disclosed an increasing frequency of diastolic blood pressure above 90 mm Hg, justification appears to classify them as having labile hypertension.

The Charlottesville blood pressure survey, which showed a high prevalence of labile hypertension in the young which decreased with advancing age (Figure 2), contrasts with the belief that the prevalence of labile hypertension increases with age [8].

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The most complete examination of the relation between blood pressure and age which showed "transient hypertension" with increasing age is limited to a retrospective analysis of male U.S. Army officers [11]. The Charlottesville study showed a high prevalence of labile hypertension in white men which conforms to the greater prevalence of labile hypertension in men [8].

Retrospective analyses indicate that in 10 to 25 per cent of these patients the labile hypertension may progress to sustained hypertension [8]. Other investigations which suggest a much higher percentage are not limited to labile hypertension and include patients with mild sustained hypertension with subsequent progressive increases in blood pressure [12,13]. In 12 per cent of young airmen with labile hypertension, sustained hypertension developed over the subsequent 20 years whereas in only 2 per cent of those who were initially normotensive did sustained hypertension develop [14]. During the past year in the Charlottesville survey, 169 patients with labile hypertension, aged 15 to 55 years, were reassessed at six month intervals

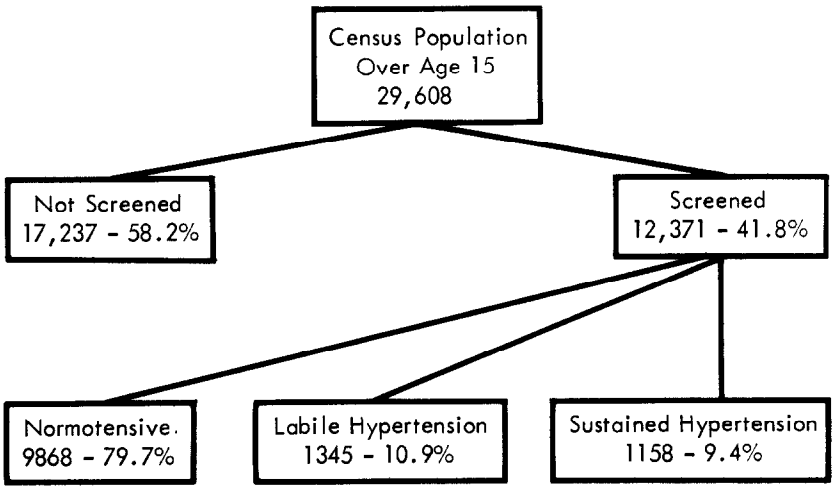

Figure 1. *Prevalence of labile and sustained hypertension in the population of Charlottesville, Virginia, after initial home screening, repeat blood pressure measurements of persons initially hypertensive and confirmation of hypertension in treated patients by chart review. (Criteria for hypertension: diastolic blood pressure ≥ 90 mm Hg < age 55; ≥ 100 mm Hg ≥ age 55.)*

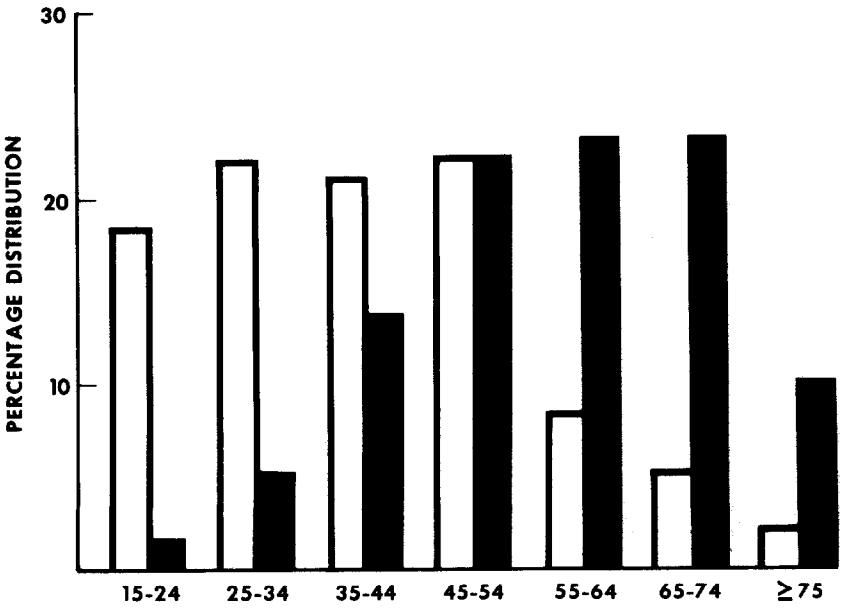

Figure 2. *Distribution of labile hypertension (open bars) and sustained hypertension (closed bars) in Charlottesville, Virginia, by age.*

[15]. During the first six months, sustained essential hypertension developed in nine patients (5.3 per cent), and 20 patients (12 per cent) became hypertensive within the year.

Most longitudinal studies of labile hypertensive patients suggest that they have increased risk of subsequent cardiovascular morbidity and mortality when compared to control subjects [9,16,17], and the risk in all age groups appears twice that of the normotensive population [18]. Retrospective assessment suggests that the risk of cardiovascular mortality and morbidity is probably increased only when labile hypertension progresses to sustained essential hypertension. The natural history of labile hypertension has not been prospectively examined, and the number of people with labile hypertension who acquire sustained hypertension remains unknown.

Many investigators have hypothesized that a number of patients with essential hypertension once had labile hypertension before their elevated diastolic blood pressure level became fixed [2,3,19]. In the hyperkinetic circulatory state of increased cardiac output, heart rate, systolic pressure, left ventricular ejection rate and ejection fraction, the peripheral vascular resistance is normal, but it may be inappropriately high relative to the cardiac output. This state resembles the "hyperdynamic beta-adrenergic circulatory state" with its increased sensitivity of the cardiovascular system to catecholamines during upright tilting, exercise or infusion of isoproterenol [20,21]. The hyperkinetic state mimics cardiovascular changes of emotional stress and of the defense response of animals during vagal inhibition [22,23]; it may be associated with decreased parasympathetic and increased sympathetic tone [6].

Half of the patients in the first report of the hyperkinetic heart syndrome had labile hypertension [24]; later workers suggested that the hyperkinetic circulatory state and labile hypertension represented an early stage in the development of fixed hypertension [5]. In these patients with labile hypertension the resting cardiac outputs and ventricular ejection rates are high when compared to those in normal subjects and in patients with fixed essential hypertension [4]. Total peripheral resistance appeared normal in labile hypertension, but increased progressively in mild, moderate and severe essential hypertension. Plasma renin activity was increased in labile hypertension. The decrease in blood pressure during treatment with the beta-adrenergic antagonist, propranolol, was directly related to the decrease in cardiac output. Although the hemodynamic abnormalities of labile hypertension are known, the relationship of the catecholamine and renin-angiotensin hormonal systems to the development and maintenance of the hyperkinetic circulatory state is unknown. Since most studies of labile hypertension are retrospective, its natural history and the evolution of hemodynamic and hormonal influences are not clearly defined.

Now, well-performed prospective study of a large population of patients can be accomplished by employing noninvasive technics, including echocardiography and vectorcardiography, for quantification of cardiovascular structure and function. Blood pressure, cardiac output, peripheral vascular resistance, left ventricular wall thickness, systolic time intervals, left ventricular circumferential fiber shortening rate and mean normalized posterior ventricular wall velocity can be measured at periodic intervals. Thus, a dynamic profile of cardiovascular physiology during the generation of the hypertensive process is now feasible.

Since we now have precise methods for measuring basal hormone levels in outpatients, the contribution of vasoactive compounds to the evolution of labile to fixed hypertension can be accessed concomitantly.

The hypothesis that labile hypertension progresses in severity with concomitant hormonal and hemodynamic changes to fixed essential hypertension needs testing urgently. Elucidation of the pathophysiology and natural history of labile hypertension will provide the basis for rational, specific therapeutic and preventive interventions in the future.

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