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Prehypertensive and Other Variabilities Also Await Treatment

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To the Editor

A systolic blood pressure of 120 to 139 mm Hg and a diastolic blood pressure of 80 to 89 mm Hg, usually considered normal yet described as prehypertensive, are associated with an elevated risk of cardiovascular disease.¹ This result is based on conventional spot-checks of blood pressure after 5 minutes of rest on 4 occasions 3 years apart. A more demanding approach to prehypertension, visualized in 1904 and more practicable today,² that is, a half-hourly around-the-clock record of blood pressure and heart rate for 7 days, interpreted chronobiologically,² reveals a persistent increase in cardiovascular disease risk associated with an excessive extent of daily blood pressure swing assessed by the double amplitude of the best-fitting 24-hour cosine curve, in relation to gender- and age-specified standards: circadian hyper-amplitude-tension.² An increase in circadian blood pressure amplitude can precede an increase in 24-hour blood pressure midline estimating statistic of rhythm (MESOR, a circadian rhythm-adjusted mean) in spontaneously hypertensive stroke-prone rats³ and in humans,⁴ constituting a longitudinally detectable real prehypertension. Whatever the blood pressure MESOR may be, circadian hyper-amplitude-tension, with an overall circadian elevation of pulse pressure, and a decreased circadian heart rate variability (compared with an acceptable variability) can increase cardiovascular disease risk in the next 6 years from 4% to 100% (Figure 1). These silent risks and an odd timing of the circadian blood pressure, but not heart rate rhythms, are great, even in the absence of hypertension. They can often be reversed, notably the risk of circadian hyper-amplitude-tension, by a nondrug (relaxation) or drug (specified in timing and in kind and dose) approach, and the need for intervention can be found when it occurs.² Yet all this is impossible to find and implement during office visits or in a conventionally interpreted 24-hour record. Chronobiologically interpreted 24-hour blood pressure and heart rate monitoring, preferably but not necessarily for 7 days,² serves to treat circadian hyper-amplitude-tension when it constitutes variability-revealed prehypertension and to treat circadian hyper-amplitude-tension when it complicates untreated or treated MESOR hypertension. As shown in Figure 2, chronobiology helps for the following:

- Detection of nocturnal abnormality (black bar, top left) when medication may no longer be effective (or is too effective, inducing circadian hyper-amplitude-tension; not shown), neither seen during office visits by day.
- Detection of circadian hyper-amplitude-tension associated with a risk of stroke (top middle) and kidney disease (top right; last 2 bars for systolic and diastolic circadian hyper-amplitude-tension) greater than other risks (including “MESOR-hypertension”) assessed concomitantly.
- Detection of circadian hyper-amplitude-tension as high risk in normotensive persons who may need drug and nondrug treatment (first 2 columns, bottom left).
- Individualized inferential statistical testing to determine whether an intervention such as autogenic training (relaxation) is effective and for how long (bottom, second from left, showing initial success and later failure).

- Individualization of treatment timing optimized, as ascertained by sequential testing (bottom, last graph) and parameter tests (bottom, penultimate graph).

Chronobiologically assessing blood pressure and heart rate variability can prompt the institution of preventive measures to reduce the numbers of strokes or cardiac deaths, or false-positive and false-negative diagnoses of hypertension, and optimize the efficacy of timed treatment² when substitute approaches fail.⁵

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Decreased Heart Rate Variability (DHRV), Circadian Hyper-Amplitude-Tension (CHAT) and Elevated Pulse Pressure (EPP) are Separate Cardiovascular Disease Risks*

*Results from 6-year prospective study on 297 (adding all Ns) patients classified by 3 risks (8 circles), supported by findings on total of 2,807 subjects for total of over 160,769 sets of blood pressure and heart rate measurements. Data from K Otsuka.

Figure 1.

As compared to patients with an acceptable variability of blood pressure and heart rate (top left) who have <4% cardiovascular morbidity after 6 years, the presence of DHRV or EPP alone (top middle) greatly increases the risk, even more so when both conditions coexist (top right). In each case, the added diagnosis of circadian blood pressure overswing, CHAT (bottom) further increases risk.

Figure 2.
Merits of chronobiology for the early detection and timely as well as timed treatment of blood pressure disorders.