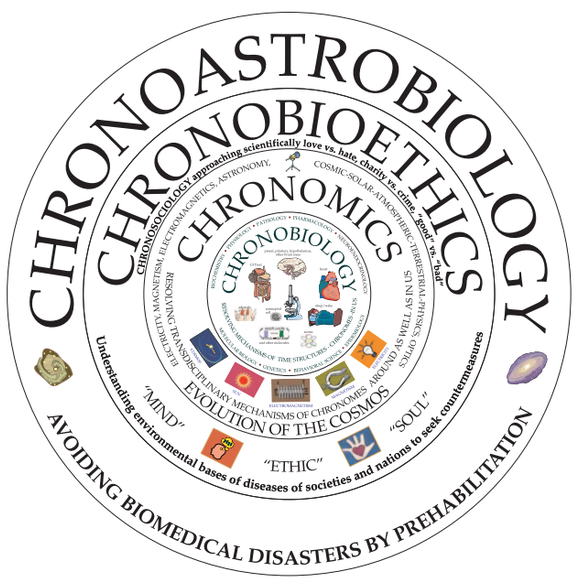
SAVING LIVES BY CHRONOBIOLOGICALLY INTERPRETED

24-hour or preferably longer (24-hour/7-day) blood pressure and heart rate monitoring assesses vascular disease risk through VARIABILITY*

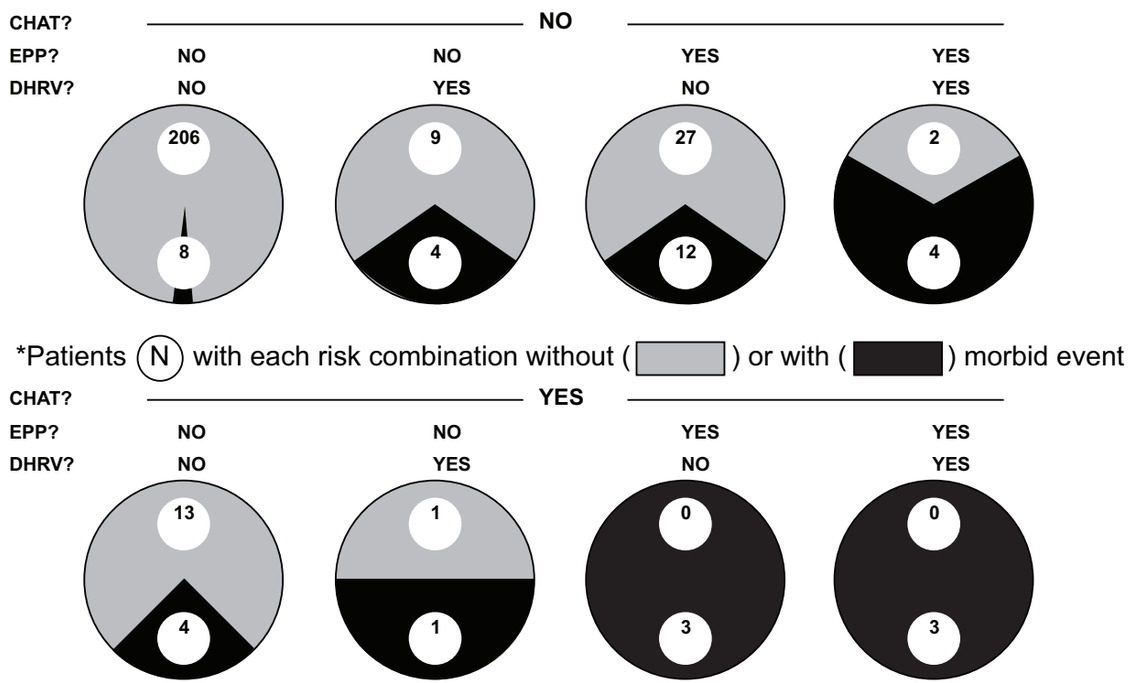


*No longer "flying blind" as spotcheck–"evidence"–based health care does most of the time.

- Abnormalities in the variability of blood pressure and heart rate, impossible to find during a conventional office visit (the latter aiming at the fiction of a "true" blood pressure), can raise cardiovascular disease risk in the next six years from 4% to 100% (graphs below and on back).
- As compared to an acceptable variability, the relative vascular disease risk associated with a decreased heart rate variability (DHRV), an elevated pulse pressure (EPP) and/or **c**ircadian **h**yper-**a**mplitude-**t**ension (CHAT) is greatly and statistically significantly increased (graph below).
- These silent risks are very great, even in the absence of hypertension; they can often be reversed, notably the risk of CHAT, by a non-drug (relaxation) or drug (specified in timing as well as in kind and dose) approach; and the need for intervention can be found when it occurs (graphs on back).

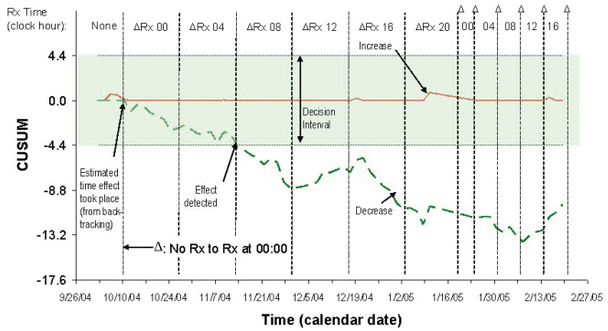
Odd timing of blood pressure but not of heart rate variation along the 24-hour scale also increases vascular disease risk (not here shown). These diagnoses are statistically significantly related to risk when classifications by dipping are not.

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

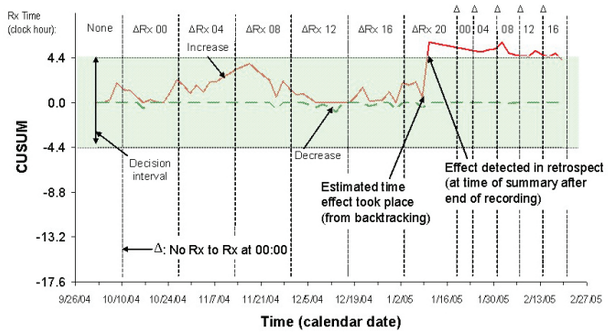


**Results from 6-year prospective study on 297 (adding all Ns) patients classified by 3 risks (8 circles), supported by findings on total of 2,807 subjects for total of over 160,769 sets of blood pressure and heart rate measurements (Biomedicine & Pharmacotherapy 2005; 59 [Suppl. 1]: S152-S157, and Biomedicine & Pharmacotherapy 2004; 58 [Suppl. 1]: S150-S187.)

Changing Timing of Medication (ΔRx) during Consecutive Spans Shows Macroscopically Varying Efficacy of Treatment***



And Risk of Iatrogenic CHAT at some Timing***

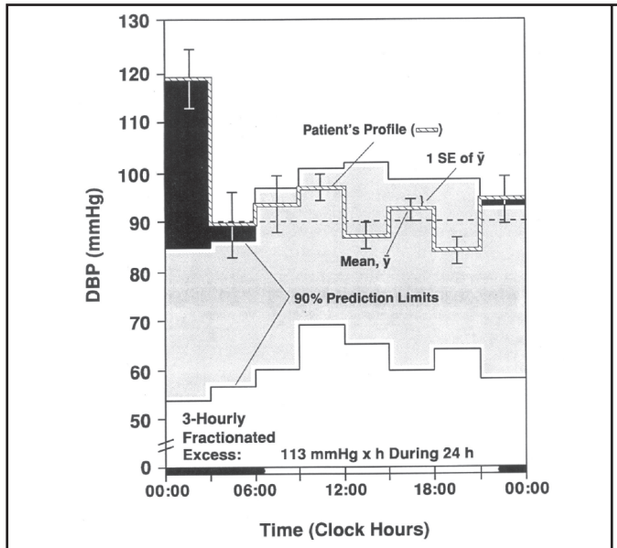


***Empirical chronotherapy: after diagnosis, one ascertains 1. Rx efficacy (top half), seemingly less at noon (12) on two occasions (11/29/04 & 2/7/05), and 2. that one does not induce circadian hyper-amplitude-tension (CHAT) by inappropriate timing of anti-hypertensive medication (bottom half). In this 24-year old man (TT) who advanced the time of treatment by 4 hours every 17 days initially and at shorter intervals thereafter, treatment in the evening was associated with iatrogenic circadian amplitude elevation (see upward breakout of positive CUSUM line in bottom graph), raising the question whether the risk of MESOR-hypertension may not have been traded for the even higher risk that CHAT represents if he had stayed on the 20 (8 pm) Rx.

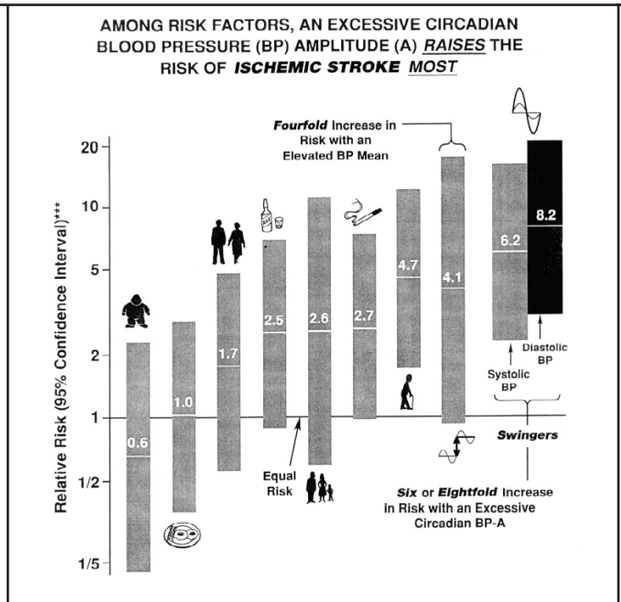
Variability Assessment (by Chronobiology) is Important for:

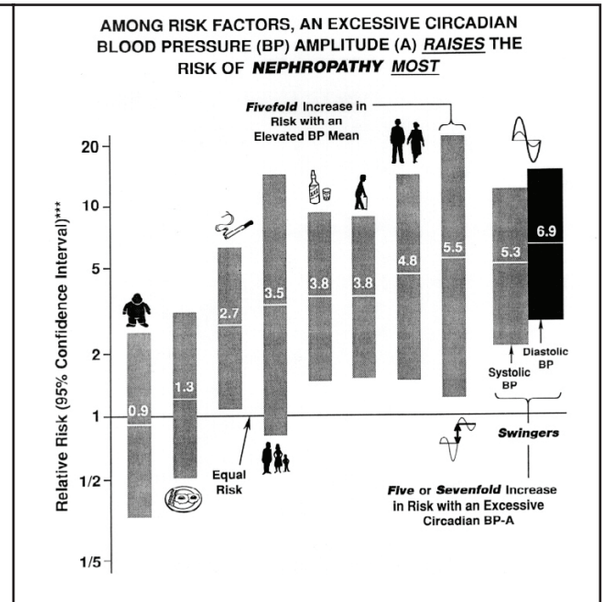
- Detection of nocturnal abnormality (black bar, top left) when medication may no longer be effective (or is too effective; not shown) neither seen during office visits by day;
- Detection of CHAT associated with a risk of brain attack (top middle) and kidney disease (top right; last gray and black bars for systolic and diastolic CHAT) greater than other risks (including “hypertension”, penultimate gray bar) assessed concomitantly;
- Detection of CHAT as high risk among normotensives who may not need anti-hypertensive medication (first two 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), that without chronobiology will not be detected;
- Individualization of treatment timing, since the same dose of the same medication can further lower the subject’s blood pressure average and circadian amplitude when the timing of daily administration is optimized, as ascertained by sequential testing (bottom, last graph) and parameter tests (bottom, penultimate graph).

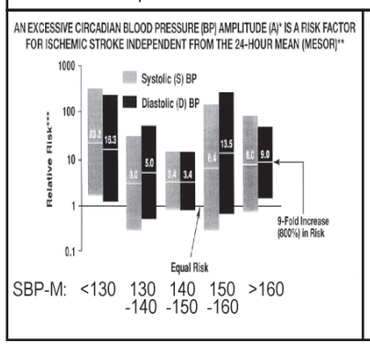
Chronomics Detects Nocturnal Escape from Treatment, Risk of Stroke and Nephropathy Greater than Hypertension, even in MESOR-Normotension and Monitors Transient and/or Lasting Success of Treatment*

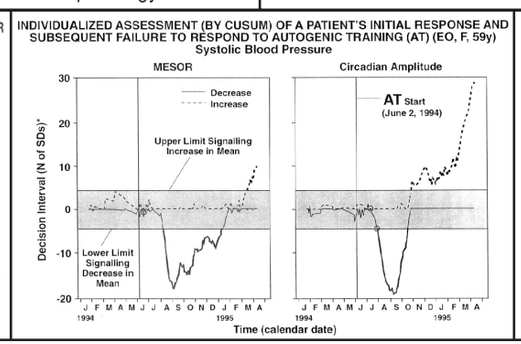


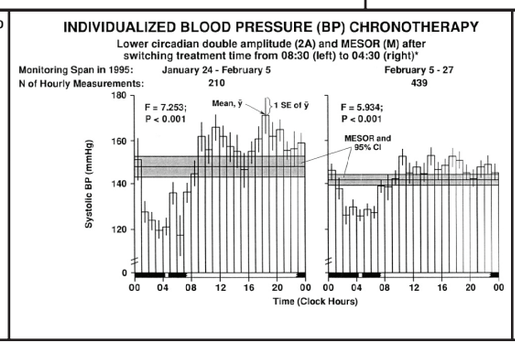
Stacked from 11 days of around-the-clock monitoring; Office spotchecks cannot detect nocturnal pathology.

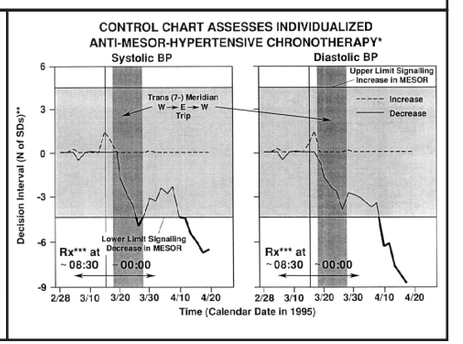












*During span examined, demonstrating the desirability of lifetime monitoring once abnormality in the normal range is detected.
See following text and International Resolution (http://www.msi.umn.edu/~halberg/) for details of above graphs.

Conclusion

Let us reduce the likelihood of stroke or cardiac death by chronobiologically assessing blood pressure and heart rate variability and by optimizing the efficacy of timed treatment rather than relying on an unacceptable and often inaccurate spotcheck and treating by convenience rather than pertinence.

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