The COSMOS and CHAT, prompting blood pressure and heart rate monitoring for Dérer's week

Halberg F, Cornelissen G, Siegelova J, Fiser B, Dusek J, Otsuka K, Delyukov AA, Gorgo Y, Gubin DG, Gubin GD, Schwartzkopff O

COSMOS a CHAT. Monitorovanie krvného tlaku a pulzu počas Dérerovho týždňa

Abstract

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***Background*: The effects of natural environmental factors upon health, documented in Minnesota, support the proposition of Bratislava's champions of the cosmos and of the biological week, gauged via circaseptan rhythms by the late Ladislav Dérer, whose "macro-rhythm" lasted "most frequently about 6 days".**
***Main purpose*: To introduce 7-day monitoring of blood pressure and heart rate into routine practice.**
***Starting points and methods*: Cosinor analysis on 7-day series determines (conventionally ignored) consistent blood pressure overswinging, i.e., circadian hyper-amplitude-tension (CHAT), a disease risk syndrome, whether it is associated with a normal average blood pressure or a high blood pressure.**
***Results*: Summary of information understandable by the general population on the dynamics of blood pressure.**
C*onclusions and meaning for practice and theory*: Space weather reports may prompt preventive measures. Caution dictates in any event monitoring blood pressure and heart rate for 7 days to attempt to prevent strokes, rather than to ignore the greatest yet detectable risk of catastrophic vascular disease, CHAT, a risk greater than old age or high blood pressure. *(Tab. 1, Fig. 3, Ref. 31.)*
Key words: COSMOS, CHAT, blood pressure, heart rate monitoring, Dérer's week.

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Abstrakt

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Pozadie problému: Vplyv prirodzených faktorov prostredia na zdravie zdokumentovaný v Minnesote je v súlade s propozíciami bratislavských adeptov na kozmické lety a biologického týždňa merania cirkaseptánnych rytmov Ladislava Dérera, ktorého makrorytmus trval najčastejšie približne 6 týždňov.
Cieľ: Zaviesť 7-dňové monitorovanie krvného tlaku a frekvencie akcie srdca do rutinnej praxe. Cosinorova analýza v 7-dňových intervaloch (konvenčne ignorovaná) determinuje konzistentné zvyšovanie krvného tlaku, t.j. CHAT (circadian hyper-amplitude-tension), syndróm rizikového ochorenia nezávisle od toho, či je spojený s vysokým alebo nízkym tlakom.
Výsledky: Súhrn informácií o dynamike krvného tlaku je zrozumiteľný pre bežných obyvateľov.
Záver a význam pre prax: Predpovede počasia pomocou vesmírnych družíc môžu byť návodom na preventívne opatrenia. 7-dňové monitorovanie krvného tlaku a pulzu je potrebné z hľadiska prevencie mozgovej ischémie. Bolo by nerozumné ignorovať CHAT — najväčšie, no detegovateľné riziko cievnych ochorení, ktoré svojím rozsahom presahuje riziko vysokého veku a vysokého tlaku. *(Tab. 1, Fig. 3, Ref. 31.)*
Key words: COSMOS, CHAT, prompting blood pressure, heart rate monitoring, Dérer's week.

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Prologue: The week, the cosinor, and galacto-helio-geophysical effects

Bratislava is known for Jan Comenius in education, for Ladislav Dérer in clinical science (1, 2), and now for Miroslav Mikulecky's search for the effects of the moon, sun and stars (3—5). The latter endeavor is basic biomedical science; it will be a health care concern once a space weather report becomes routine, prompting countermeasures as yet to be developed. Against this background, the authors gladly accepted the invitation to remember Ladislav Dérer, who like one of us (6) recognized rhythms, i.a., in leukocytes and blood pressure. We write this homage also to Broader-than-Bratislavan Medicine, led by Dérer's intuition to the clinical importance of the "macrorhythm" with "periods lasting most frequently about 6 days" (1)[1], which in turn led to the discovery of a 6.74-day (circaseptan) component in a rhythm spectrum of geomagnetic disturbance (9—11). This periodicity was missed by a most prominent physicist, who focused rigorously, yet only on the anthropogenous precise 7-day periodicity in magnetic disturbances (12).

Honoring his mentor Dérer, Mikulecky, a generation later, himself deserves recognition as the first department head in internal medicine known to us to himself write a book on statistics for his medical students. He set an example for generations to come, namely to rely on numerical and inferential approximations of the evidence he assembles. We provide this paper to acknowledge a spontaneous laudatio by the late Gunther Hildebrandt of Marburg, Germany, also a scholar of circaseptans, who described Ladislav Dérer and Miroslav Mikulecký as champions of the biological week. Now that both Dérer and Hildebrandt have passed away, with his colleagues from Brno (15), Miroslav is a foremost proponent in Europe, on the frontiers of changing the current taking of *the* single blood pressure measurement into a minimum of a week's serial measurements. Thereby, one glances at the biological week, as a dividend from a more reliable assessment of the biological day[2]. Table 1 is intended for physicians who share Dérer's basic orientation. Indeed, we are under the effect of the cosmos, as recognized in Dérer's area by Jarmila Siegelova, Jiri Dusek and Bohumil Fiser (15; cf. 8, 16), who documented the greater-than-circadian prominence of the weekly component in the neonatal blood pressure and heart rate, and by Strestik and Prigancova (17, 18), who examined sudden cardiac mortality and traffic accidents in relation to space weather, whereas we found effects on both myocardial infarctions and heart rate variability in association with stormy weather in space (19).

On the applied side, 7-day blood pressure and heart rate monitoring is a start, but not always enough (14), as demonstrated on themselves and on one of their colleagues by the Mikuleckys, father and son (20). In keeping with them (cf. also 8, 21), we suggest that this 24-hour/7-day monitoring is important, not only for research but in particular for actual health care, guided by the medical practitioner. In this case, the following text could also be a handout to patients, possibly for use in physicians' offices. We add a memorandum for research in practice by institutions or individuals who wish to avail themselves of the opportunity to have relatively inexpensive monitoring instruments and/or analyses[3].

What everyone can learn about blood pressure

The usual way of the technically best measurement of blood pressure and its current interpretation can be substantially improved. "Casual" blood pressure readings taken in a health care office can be misleading. Measurements taken occasionally can be unusually high or low; false positive and false negative diagnoses can occur (14, 21). That means some individuals who receive unneeded treatment may suffer unnecessary concern, expense and side effects from medications. People who actually do need treatment can be lulled into a false sense of well-being by occasional "good" blood pressure readings. Moreover, the technically best single measurements will miss an altered variability. The change in extent of variation tells us about the greatest risk of stroke, even when each value appears to be "good", insofar as it is neither too high nor too low.

The use of fully automatic ambulatory blood pressure monitors—programmed to take measurements at preset intervals for at least one week, or longer, when analyzed by the science of time structures in variability, called chronobiology, can help to make a more reliable diagnosis. These blood pressure readings (with added heart rate measurements) are directly transferred into a computer and sent via e-mail for comparison with reference values.

[1]Of historical interest are Dérer's 6-day rhythms that may have resulted from analyses according to Fourier rather than Gauss, and hence from the length of the time series he happened to have analyzed, some of which were of 24-day length. Thus, Dérer's statistical colleague tested the 24-day period (i.e., 24/1=24 days) and its harmonics, 24/2=12, 24/3=8 and 24/4=6. By this procedure, he did not test for (and hence necessarily missed) a 7-day component, yet Dérer's intuition led him very near the about 7-day week (1). Had Dérer used the cosinor method as Mikulecky does, he would have found the 7-day component. This point could have been emphasized by Miroslav (7), i.e., as the positive feature of the method that had already proved useful in 1801, when Ceres was rediscovered by the least squares method of the young Gauss. In the case of Ceres, there was Kepler's ellipse, and in the case of circaseptans, there was Hippocrates' and Galen's observation of the seventh critical day of crisis or lysis (8). Mikulecky the critical scientist (7) did not dwell on the main issue of the usefulness of the cosinor method when there is prior evidence to guide it (8). Instead, Mikulecky's "defense" was an attack on those who misuse the method and by implication, he, perhaps unintentionally, condoned an attack on the method and on the person who developed it (7). Thid author takes his "friends" as they are, the more critical the better.

[2]Sir Humphry Davy (1778—1829) was Britain's most eminent chemist and physicist of the 18th and early 19th century. Among many other accomplishments, he established the elementary nature of chlorine, and isolated potassium, sodium, calcium, barium, boron, magnesium and strontium. Those who asked him to identify his major contribution to science expected him to cite one of his own accomplishments. Instead, he named his pupil Michael Faraday. If Ladislav Dérer, should he still be with us, were to be asked the same question, even though he had seen Miroslav only as a young fellow, he would pick the name of Miroslav Mikulecky. Who else, in this age of mainly molecular spotcheck medicine eager to learn everything about nothing (9), would turn to archival stastistics and seek the effect of the moon, the sun and the cosmos on disease? Miroslav does this (3—5) and much more (7, 13, 14).

[3]Analyses of properly formatted data in the light of an accumulating international data base and instruments at a highly reduced cost, after prior arrangements, are available from the Halberg Chronobiology Center at the University of Minnesota (contact Dr. Germaine Cornélissen, corne001@tc.umn.edu). Cf. memorandum.

Table 1: Inferential statistical biomedicine, non-photic and photic solar activity and terrestrial magnetism¶

Study (reference) Design Variable(s)***	*Location (latitude [geographic/ geomagnetic])*	*Population Sample Size Age (years)*	*Sampling* span	interval	Spectral components	*Results** Cross-spectral coherence (frequency) [period]
I. DATA LONGITUDINALLY COVERING UP TO 10 SCHWABE (ABOUT 10.5-YEAR) CYCLES ON HEIGHT AND OTHER MORPHOLOGY¶¶						
1. Nikityuk (1, 2; u.p.†) T i. BH; BW; HC ii. CC; AC	Moscow, Russia (55.45°N/50.76)	Russian babies 25-150/year Birth	i. 112 years ii. 41 years	yearly	About 10.5- and/or 21-year cycles	BH with Kp: 0.819 (0.143 $year^{-1}$) [6.99 years] BW with Kp: 0.867 (0.143 $year^{-1}$) [6.99 years] (using 10 degrees of freedom)
2. Nikityuk (1, 2; u.p.†) T BH; BW; HC; CC; AC	Alma-Ata, Kazakstan (43.19°N/33.67)	Russian and Kazak babies 25-150/year Birth	40 years	yearly	About 10.5- and 21-year cycles with common characteristics for different endpoints	
3. Cornélissen (1, 2; u.p.†) T BW	Minnesota (45.00°N/55.00)	Newborns 2,150,122 Birth	33 years	yearly	About 21-year cycle	
4. Weber et al. (3) T BH	Austria (49.02°N/48.57 [northernmost]-46.27°N/46.08 [southernmost])	Male recruits 507,125 18	10 years	monthly	After detrending (linearly): about 10-yearly component modulating circannual variation	With Kp: 0.813 (2.20 $year^{-1}$) [5.45 months] With sunshine: 0.545 (1.90 $year^{-1}$) [6.32 months] 0.963 (0.90 $year^{-1}$) [13.33 months] (using 22 degrees of freedom)
5. Weber et al. (4) T BH	Austria (49.02°N/48.57 [northernmost]-46.27°N/46.08 [southernmost])	Male recruits 713,162 18	14 years	yearly	After detrending (linearly): common about 9.25-year component consistent among recruits from 8 separate socio-economic strata	
6. Otto et al. (5) T BH; BW	Germany: Berlin (52.31°N/52.06) & Leipzig (51.20°N/51.19)	Newborns 574,600 Birth	1959; 1961; 1963; 1964	monthly	About-yearly and half-yearly changes	
7. Henneberg and Louw (6) T BH; BW (z-score)	South Africa (33.56°S/-32.70)	Impoverished rural schoolchildren 1,522 6-18	1 year	monthly	About-yearly change in BW and half-yearly variation in BH	
8. Garcia et al. (7, 8) H BH; BW	La Coruña, Spain (43.22°N/47.40)	Newborns 674 Birth	0-16 months	about-monthly	About-yearly and half-yearly components, more prominent by reference to the time of birth, i.e., as a partly endogenous function of age, than by reference to a fixed calendar date, i.e., as a function of exogenous factors such as sunlight, temperature and nutrition	
II. SUPPORTIVE EVIDENCE ON HUMAN PATHOLOGY						
9. Cornélissen et al. (9) T incidence	Worldwide	Morbidity 6,304,025 (largest only) Various ages	meta-analysis of 47 studies		About-weekly and half-weekly patterns of incidence of cardiovascular morbid events	
10. Halberg et al. (10) T incidence	Moscow, Russia (55.45°N/50.76)	Morbidity 6,304,025 Various ages	3 years	daily	About-yearly incidence of cardiovascular morbid events and half-yearly pattern of incidence of epileptic attacks	MI with Kp: 0.51 (0.315 day^{-1}) [3.17 days] MI with Bz: 0.58 (0.315 day^{-1}) [3.17 days] (using 25 degrees of freedom)

Study (reference) Design Variable(s)***	*Location (latitude [geographic/ geomagnetic])*	*Population Sample Size Age (years)*	*Sampling* span	interval	*Results** Spectral components	Cross-spectral coherence (frequency) [period]
11. Düll and Düll (11) T morbid events	Copenhagen, Denmark (55.43°N/55.19)	Adults 36,000 Various ages	5 years	daily	Maximal cross-correlation between magnetic storms and mortality at 1-day lag on data summarized by superimposed epochs in relation to peaks in geomagnetic disturbance ("electron invasion")	
12. Faraone et al. (12) T sectoring in colonies of microorganisms	Milan & Rome, Italy (45.28°N/46.31 & 41.53°N/41.89)	Colonies of air bacteria and *Staphylococcus aureus* 200-250/day	12.5 (air) and 7 (staph) years	daily	Prominent components resembling time structure of Kp and WN, notably with periods of about 5 and 0.5 years	Air bacteria with Dst: 0.647 (0.054 day^{-1} [18.6 days]) Staph with Kp: 0.700 (2.262 year^{-1} [0.442 year]) and 0.660 (0.303 day^{-1} [3.3 days], using 20 degrees of freedom)
III. SUPPORTIVE EVIDENCE ON HUMAN PHYSIOLOGY						
13. Portela et al. (13) L BP	USA (45.00°N/55.00; 45.33°N/51.42; 42.19°N/53.20)	Adult males 3 20; 65; 71	14; 15; 26 years	5-6/day; 2/day; about-weekly	About 11-year cycles paralleling solar activity	
14. Cornélissen et al. (14) H HR	USA (45.00°N/55.00 [2]; 41.18°N/52.19; 34.00°N/41.01; 47.17°N; 47.53)	Adults 5 28-81	5 selected spans between Aug 1967 and Apr 1975	1-6/day (N: 382-2840)	About 11.6-year cycle; remove-and-replace approach showing resonance of about 7-day component with corresponding variation in solar activity. When the sun "removes" an about 7-day component from the spectrum of its velocity changes, the circaseptan HR amplitude is smaller.	
15. Baevsky et al. (15) H HR	Space (Soyuz spacecraft)	Russian cosmonauts 49 25-50	2-15 min	beat-to-beat	About 30% reduction in HR variability (gauged by standard deviation of R-R intervals) during magnetic storms vs. quiet days in extraterrestrial space	
16. Syutkina et al. (16) H BP; HR	Moscow, Russia (55.45°N/50.76)	Newborns 32 First month of life	up to 20 days	15 min	Correlation between nonlinearly-determined period of about 7-day component of BP and HR vs. local magnetic disturbance (K)	With K: ≥0.70 (around 0.3 day^{-1} and around 0.14 hour^{-1}) [3.33 days and 8.77 hours] (using 10 degrees of freedom)
17. Halberg et al. (10) L BP; HR; blood pH	Minneapolis, Minnesota, USA (44.59°N/54.60)	Premature baby 1 Birth	up to 26 months	up to 1-5/day; denser at outset	Near-match of some spectral peaks of BP and HR vs. Kp	DBP with Bz: 0.74 (2.0 week^{-1}) [3.5 days] (using 14 degrees of freedom)
18. Halberg et al. (17; u.p.†) L BP; HR	Ancona, Italy (43.37°N/43.48)	Adult woman 1 28	1 year (267 days in isolation from society)	15-30 min	Closeness of nonlinearly-determined period of about-half-weekly component of HR vs. Kp during isolation	HR: -with Kp: 0.558 (0.045 hour^{-1}) [22.22 hours] -with CR: 0.524 (0.138 hour^{-1}) [7.25 hours] -with 3hCR-SD: 0.546 (0.153 hour^{-1}) [6.54 hours] (using 22 degrees of freedom)
19. Watanabe et al. (18) L BP; HR	Tokyo, Japan (35.42°N/25.75)	Adult man 1 35 (at start)	3 years	15-30 min		With Kp: ≥0.5 (0.036 day^{-1}) [27.8 days] (using 26 degrees of freedom)
20. Watanabe (3, 19; u.p.†) L BP; HR	Tokyo, Japan (35.42°N/25.75)	Adult man 1 35 (at start)	11 years	15-30min monthly summary	About 10.5-year component in mean and SD of HR and in SD of SBP	HR with WN: 0.664 (1.636 year^{-1}) [7.33 months] (using 14 degrees of freedom)
21. Halberg et al. (10) L BP; HR	Minneapolis, Minnesota, USA (44.59°N/54.60)	Adult man 1 68 (at start)	4 years (with interruptions)	15-30 min	About 5% increase in HR during magnetic storm and in BP on day preceding a magnetic storm on earth	

Study (reference) Design Variable(s)***	*Location (latitude [geographic/ geomagnetic])*	*Population Sample Size Age (years)*	*Sampling* span	interval	Spectral components	*Results** Cross-spectral coherence (frequency) [period]
22. Sothern (RBS) (3, 20, 21; u.p.†) L BW; SBP; DBP; HR; RR; PEF; TE; EH; mood; vigor	St. Paul, Minnesota, USA (45.00°N/55.00)	Minnesotan clinically healthy man 1 20.5 (at start)	30.8 years	1-6/day (N > 50,000/ variable; total N»5 million values)	About 10.5- and 21-year as well as yearly (P<0.001) cycles	With Kp: 0.740 (2.03 year^{-1}) [5.91 months] (using 22 degrees of freedom) [Cross-correlation with Kp of BP and HR maximal near lag 0]
23. Halberg et al. (22; unpublished) L Urine volume; urinary 17-ketosteroid excretion	Copenhagen, Denmark (55.43°N/55.19)	Clinically healthy man 1 44-59 years	15 years	daily	About 9.28 y (17-KS) or 4.18 y (UV), 1.0 y, 7 d and 3.5 d components, the latter two free-running from social schedule for 17-KS during last 3 y when subject self-administered testosterone	17-KS with Kp: 0.588 (11.98 year^{-1} [4.36 weeks] using 20 degrees of freedom)
IV. MODULATING ROLE OF MELATONIN ?						
24. Tarquini et al. (23) H melatonin (MEL)	Florence, Italy (43.78°N/44.26)	Adults 172 20-90	3 years	4-hourly for 24 hours	About-yearly variation in MEL during daytime but half-yearly changes during nighttime at latitude of 43.47°N; half-yearly variation at 65.00°N around noon	
25. Maggioni et al. (24) H Melatonin	Milan, Italy (45.28°N/46.31)	Women in 3rd trimester of pregnancy (14 healthy and 11 IUGR)	1 year	4-hourly for 24 hours	About half-yearly variation found only in IUGR group, with 1.0 y A and 0.5 y (A,ϕ) difference between the two groups	
V. THEORETICAL COMPUTATIONS						
26. Ulmer et al. (25)	For a field of about 1 nT typical of a magnetic field associated with the human circulatory system and with the interplanetary magnetic field, the oscillating period of some ions found in cells (Na^+, K^+, Ca^{++}, Mg^{++}) is about one week and that of some proteins (albumin, hemoglobin) is about 1 month, both periods corresponding to prominent components in the time structure of human physiology (computations based on Earth's magnetic field of 0.5 x 10^{-4} T typically found at mid latitudes for ions or molecules in a vacuum)					

¶Some analyses or meta-analyses in the Chronobiology Laboratories of the University of Minnesota in Minneapolis, Minnesota; a review of the vast literature is beyond the scope of this table.

¶¶In dealing with biomedical equivalents of the about 21-year Hale cycle (and there are components with even lower frequencies and even larger amplitudes in our anthropometric data), one cannot collect too many cycles over a single lifetime and turns for replications to populations; in the case of each of the population rhythms, one deals with findings on many individuals' cycles, as in the case of findings covering 112 years of population anthropometry; in each of the two studies by Weber et al.[1,2], over half a million individuals must be sufficiently concordant to allow a demonstration of the 10-year population rhythm. The 30.8 years of self-measurements of over 10 variables around the clock for a total of over half a million values provide a longitudinal validation check, supporting other evidence collected transversely, by virtue of (bio)ergodicity properties (that is the consistency of findings made transversely on populations and longitudinally on individuals, notably in relation to temporal characteristics of a process, assumed to be [bio]stationary in the sense of reproducibility of some of its characteristics).

*Strengthening and broadening the scope as to mechanisms of the propositions of Weber et al.[1] by cross-spectral coherence, superimposed epochs, and remove-and-replace approach, among other analyses on even larger and more diverse data sets. Results thus obtained reveal not only about-yearly rhythms but also other components with periods ranging from half a week to about 21 years that are not shared with sunshine. Overall, the evidence points to mechanisms complementing sunshine effects, including geomagnetic disturbance effects that may be mediated via intermodulations involving melatonin produced by the pineal gland.

Cross-spectral coherence coefficients have in common with correlation coefficients that they describe the relation between two variables. Cross-spectral coherence coefficients are less unspecific in that they describe the relationship at a specific frequency. In order to avoid listing spurious associations, only cross-spectral coherence coefficients away from spectral peaks are listed herein.

L = longitudinal; T = transverse; H = hybrid (linked cross-sectional).
BH = body height; BW = body weight; HC = head circumference; CC = chest circumference; AC = abdomen circumference; BP = blood pressure (S=systolic; D=diastolic); HR = heart rate; RR = respiratory rate; PEF = peak expiratory flow; TE = 1-minute time estimation; EH = eye-hand coordination; MI = myocardial infarctions; MEL = circulating melatonin; Kp = geomagnetic disturbance index; WN = Wolf number of solar activity; Bz = vertical component of interplanetary magnetic field; CR = cosmic ray intensity; 3hCR-SD = 3-hour standard deviation of CR; SD=standard deviation.
†u.p. = unpublished

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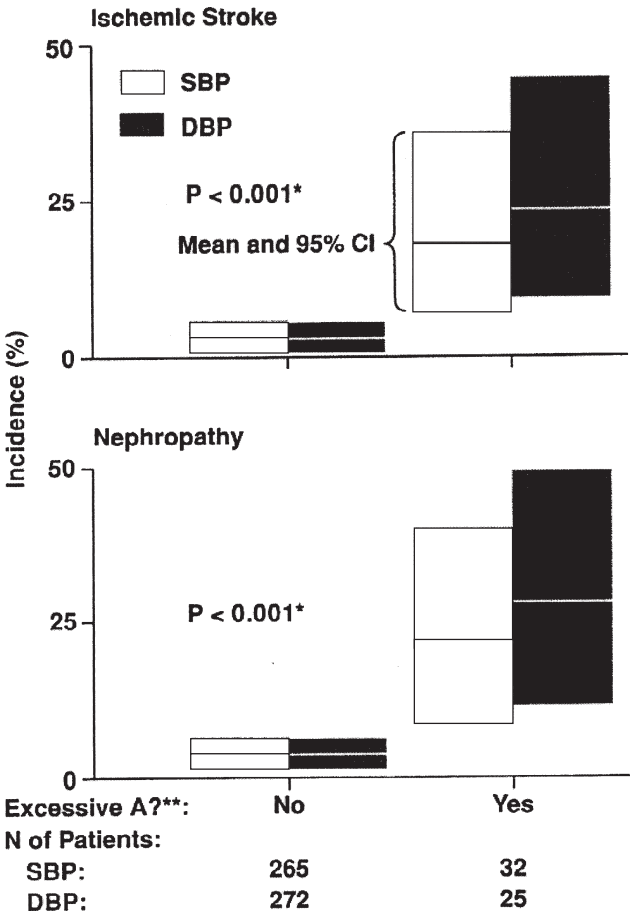

Fig. 1. In a 6-year prospective study, 297 patients provided a 48-hour blood pressure and heart rate profile with measurements taken at 15-min intervals with an ambulatory monitor. They were classified as having an acceptable or excessive circadian blood pressure amplitude. The classification was made in relation to either systolic or diastolic blood pressure. For 6 years, they were followed-up to record the incidence of cerebral ischemic events, coronary artery disease, kidney disease and retinopathy. Among patients with an acceptable circadian blood presure amplitude, only 2—3 % developed kidney disease or had a cerebral ischemic event, but about 25 % of patients with an excessive circadian blood pressure amplitude had untoward events. c Halberg.
Obr. 1. V šesťročnej prospektívnej štúdii bolo 297 pacientov podrobených 48-hodinovému monitorovaniu krvného tlaku a pulzu s meraniami v 15-minútových intervaloch pomocou ambulančného monitoru. U týchto pacientov boli tlakové amplitúdy klasifikované ako prijateľné alebo presahujúce cirkadiánnu tlakovú amplitúdu. Klasifikácia bola vykonaná buď vo vzťahu k systolickým, buď diastolickým tlakom. Pacienti boli vyšetrovaní počas 6 rokov na výskyt mozgových ischemických príhod, ochorenie koronárnych ciev, obličkové ochorenia a retinopatiu. Spomedzi pacientov s prijateľnou cirkadiánnou tlakovou amplitúdou len u 2—3 % sa vyvinulo obličkové ochorenie, alebo mozgová ischemická príhoda, ale približne 25 % pacientov s nadmernou cirkadiánnou tlakovou amplitúdou malo náhlu príhodu.

Variability as benefit

We're all born with natural variations in our circulation. Variations can also occur when we exercise physically and undergo excitement, anxiety or "stress". At the same time, we further respond to subtle factors in our environment, including the effect of storms in space (such as those causing the aurora in its oval) that can trickle down to middle and low latitudes on earth, Table 1. The development of "borderline" (and eventually of high) blood pressure is usually gradual and may not be accompanied by symptoms. The development of altered variability, even without any elevation in overall pressure, is also asymptomatic. Undesirable early changes in blood pressure variability are difficult or impossible to discover and to reliably ascertain without the collection of around-the-clock blood pressure measurements for at least 7 days.

Even when blood pressure is very high on average, it can be a "silent disease". There may not be any symptoms until complications become apparent. These complications can include a stroke, heart attack, kidney disease and blindness. It seems more reasonable to prevent blood pressure from becoming elevated or otherwise outside norms than it is to treat conditions resulting from an abnormal blood pressure pattern. Once high or otherwise abnormal blood pressure has damaged the heart, brain, kidney, eyes or other organs, major handicapping and fatal diseases are more likely to occur, Figure 1.

In the doctor's office, there's no way to obtain measurements around the clock. Yet modern instruments are available that collect readings while you sleep. And then they're analyzed by computer programs based on the principles of chronobiology. The new hardware/software/data base provides new opportunities to treat a faulty blood pressure pattern (without or with medication) and thus prevent serious illnesses.

Results of 24-hour/7-day blood pressure monitoring are interpreted by using special computer methods, applied to international data bases[3]. Changes in blood pressure patterns can be detected as indicators of an elevated health risk, not all apparent by using conventional methods, recommended by the World Health Organization (22–24), among others (25–27; cf. 8, 28, 29).

Why monitoring?

The extent of suffering is enormous and the healthcare costs related to high blood pressure are staggering – $30 billion in 1998 in the U.S. The ability to identify both those at risk and those with an already-elevated blood pressure reduces suffering and expense. It makes it possible to provide treatment early enough to prevent the actual development of blood pressure disorders as well as to lower a blood pressure that is already high or correct a blood pressure that is otherwise abnormal.

Your 24/7 blood pressure monitoring

Dan Wall, an attorney and emeritus mayor of the City of Roseville, Minnesota, a suburb of 35,000 of Minneapolis/St. Paul (as also intended by the incumbent mayor, who is currently monitoring himself), planned to offer blood pressure monitoring 24 hours a day at 30-minute intervals, 7 days a week, to all interested residents, from teenagers to seniors. The authors will gladly extend this offer to all those wishing to participate elsewhere, given some minimal investments are made by prospective participants. Provided proper arrangements for instrumentation mainly and for data formatting can be made, participants will wear an only slightly

obtrusive, fully automatic, ambulatory blood pressure monitor for a week (or longer if need be).

Why take blood pressure readings 24 hours a day?

Because in some people—possibly including you—high blood pressures occur at night rather than during the day. This may happen spontaneously or because of long-acting blood pressure-lowering medications that cease acting sooner than anticipated (14). These high blood pressures will not be recognized in measurements taken only during the day, Figure 2.

Why take blood pressure readings 7 days a week?

Because abnormality can be there on some days but not on others. Fewer than 7 days of monitoring mean a greater chance of a false diagnosis (14).

Two features of the chronobiologic approach to blood pressure monitoring make it highly effective.

First, blood pressure can be automatically monitored without interrupting everyday life. Nothing special need be done (except that the participant must stand still briefly while the cuff on the arm inflates) and the participant will hardly be aware that the process is going on, notably after the first day or two, when both transient elevations and overswinging are particularly likely to occur. This type of monitoring greatly reduces the likelihood of false diagnoses and unnecessary treatment.

Second, the 24/7 blood pressure data can be analyzed by special computer methods in the light of an extensive data base. (Longer series of readings are possible, as well, and more monitoring may be needed if 7 days were not enough.) This allows an evaluation of high-risk patterns of blood pressure and heart rate. For example, there could be an unacceptable degree of change within a day, as well as unusual times each day when blood pressures are high and/or low. A larger-than-usual change in blood pressure, overswinging or CHAT (circadian hyper-amplitude-tension), usually precedes an overall elevation in blood pressure and is an indication or predictor of a great risk of disease, Figure 3.

Among other abnormalities, a blood pressure pattern peaking at odd hours also warrants further examination. The detection of unusual patterns in blood pressure change during a day or week can prompt a quicker follow-up and earlier preventive treatment, when needed.

Moreover, a blood pressure increase is more reliably evaluated with regard to when it occurs. And it can be more meaningfully treated in the light of information provided by expert analyses.

Rationale for offering of chronobiologic blood pressure and heart rate monitoring and analysis to interested individuals

Benefits to participants

Blood pressure monitoring on a 24/7 basis — according to chronobiology — can provide a number of benefits that a traditional blood pressure reading cannot:

— It gives early warning signs of a heightened cardiovascular disease risk, which can prompt preventive action.
— It improves on the traditional diagnosis of acceptable vs. abnormal blood pressure.

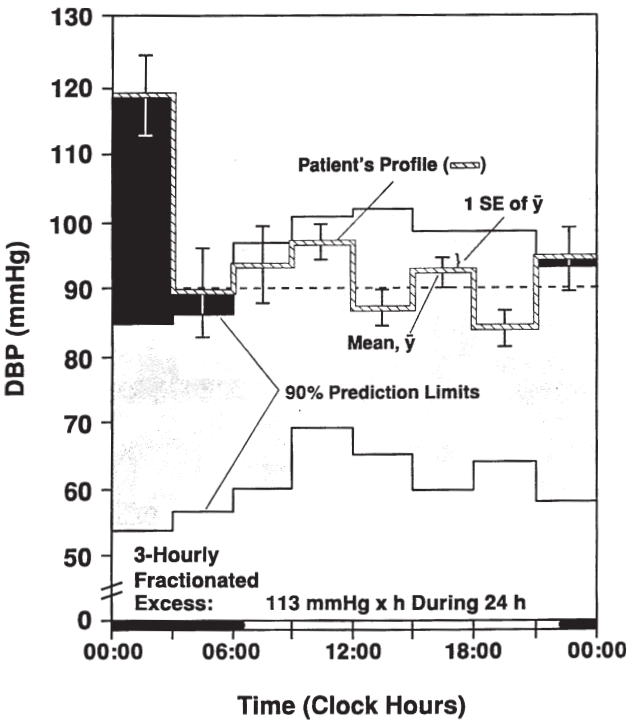

Fig. 2. Because high blood pressures can occur by night, reliance on office measurements between 8 a.m. and 5 p.m. can be grossly misleading, as in a case with diastolic blood pressures averaging over 115 mmHg during the span from midnight to 3 a.m. (shown in black). c Halberg.
Obr. 2. V dôsledku skutočnosti, že vysoký tlak sa vyskytuje v noci, spoľahlivosť meraní medzi 8. a 13. dennou hodinou môže byť výrazne zavádzajúca. Podobne to bolo v prípade s diastolickým tlakom, ktorý priemerne presahoval 115 mmHg stĺpca v intervale medzi 24. a 3. hodinou rannou (označené čiernou farbou).

— It helps the patient and physician make the decision to address blood pressure problems.
— It can help in the selection of the most appropriate treatment and dosages, if drug therapy is recommended.
— It provides better assessment and validation of treatment, particularly when it results in an increase of the extent of daily changes in blood pressure.

When an erroneous diagnosis is made as a result of the traditional method, negative consequences can occur:

— If one is incorrectly diagnosed with high blood pressure, one may experience occupational discrimination or difficulty in obtaining health insurance. Treatment with drugs may be accompanied by side effects, such as impotence, cardiac arrhythmia and gout. Drug therapy may put a strain on finances.
— If one is incorrectly diagnosed as having normal blood pressure — when, in fact, blood pressure is high or otherwise abnormal — the risk of heart disease increases, and with it the probability of organ damage. Minor symptoms such as easy fatigue and headache can gradually appear that may unnoticeably impair performance. Worst of all, painful and costly debilitating illness or death may occur.

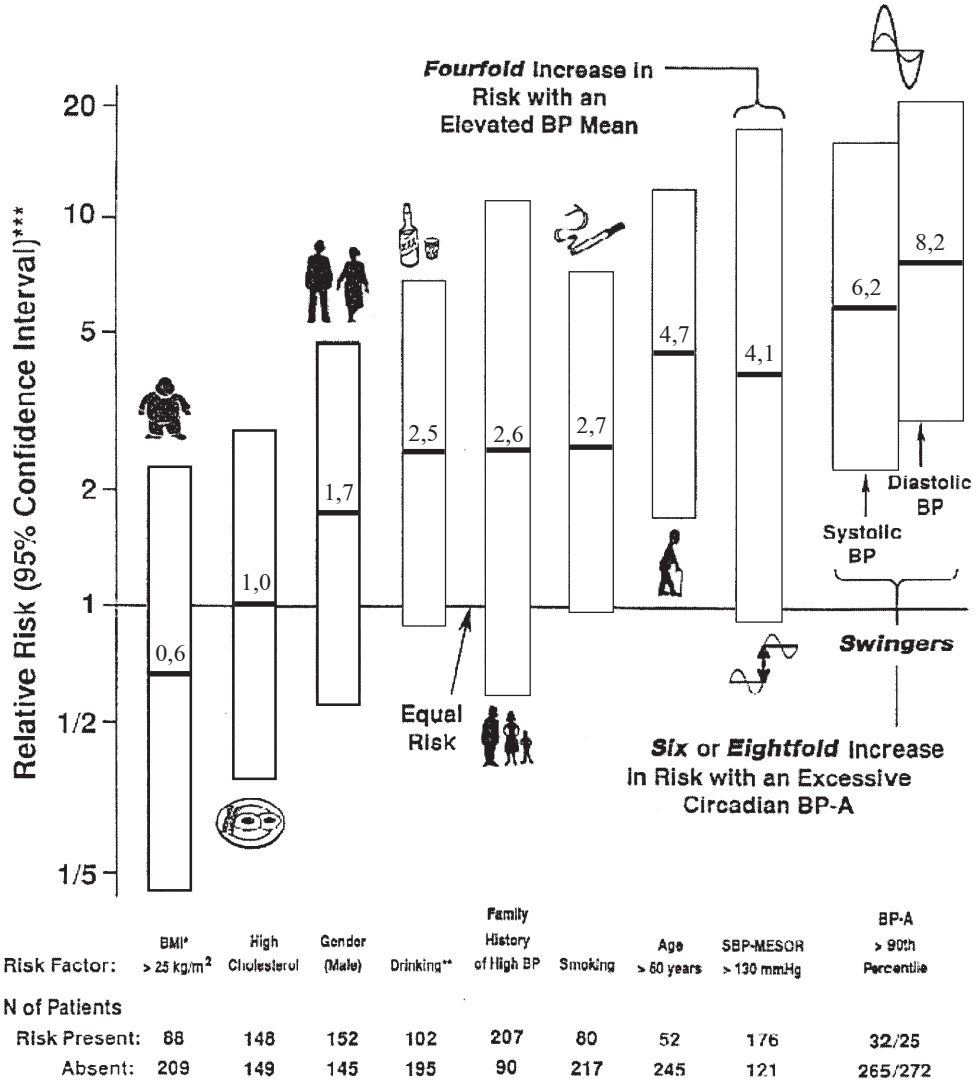

Fig. 3. In a population of 297 patients who provided a 48-hour ambulatory blood pressure profile, the incidence of cerebral ischemic events (and other adverse vascular events) was recorded for the next 6 years at 6-month intervals. The length of the vertical bars represents the 95 % confidence interval for the relative risk. Equal risk is indicated by the horizontal line at 1. The relative risk associated with an excessive circadian amplitude is the greatest of all conditions tested. c Halberg.
Obr. 3. Spomedzi 297 pacientov, u ktorých sa meral krvný tlak počas ambulantných hodín, sa incidencia mozgových ischemických príhod (a iných cievnych príhod) zaznamenávala počas ďalších 6 rokov v 6-mesačných intervaloch. Dĺžka vertikálnych stĺpcov je 95 % konfidenčný interval na relatívne riziko. Rovnaké riziko sa označuje horizontálnou čiarou 1. Relatívne riziko spojené s nadmernou cirkadiánnou amplitúdou je najvyššie zo všetkých testovaných podmienok.

Why chronobiologic monitoring and analysis?

Chronobiologic monitoring and analysis can identify, under routine conditions, persons at risk of developing a high blood pressure or heart disease by assessing the daily pattern of change in blood pressure and heart rate.

— Chronobiologic monitoring provides a more refined diagnosis of abnormal blood pressure by focusing not only on changes in the average, but also on altered daily patterns of blood-pressure change. This approach may mostly benefit persons with borderline or unstable hypertension, assumed to represent a large majority of the population with abnormal blood pressure.
— It reduces the number of misfortunes associated with false positives and false negatives.
— It provides improved reference limits specified in time and derived from extensive data on healthy individuals.
— It allows physicians to determine the duration, extent and timing of elevation in blood pressure or heart rate to gauge potential organ damage.
— It helps physicians decide whether to recommend drug or non-drug therapy (such as changing consumption of salt and calo-

ric intake or exercise). And it helps to determine the timing of treatment.
— After treatment has been initiated, this diagnostic technique helps to establish an individual's response to treatment.
— And it can continue to monitor the success of therapy. If needed, prompt action can be taken when problems arise.

Recommendation for the diagnosis of abnormal blood pressure

The chronobiologic method of blood pressure diagnosis — which consists of systematic 7-day (and, if need be, longer) monitoring of every individual's blood pressure — works best when an ambulatory monitor that is programmed to automatically inflate the cuff at intervals is used, such as the monitor the memorandum places at the disposal of patients. Moreover, the diagnosis by chronobiologic analyses — based upon the comparison of a given individual's data at a given time, with data obtained earlier on the same individual and/or with a large store of reference data from healthy peers — is very reliable and can pick up abnormality not otherwise detectable. When such abnormalities are found, there is a greater likelihood of effective therapy (14).

Conclusion

Michael Fossel, editor of the Journal of Anti-Aging Medicine, has written (21):

Talking about "blood pressure" as a single figure is similar to knowing the average height of a mountain range: an interesting statistic, but completely useless to a pilot trying to make it through a mountain pass alive. Realistically, we need to consider not merely the mean [average] stress on an aging vascular endothelial cell, but the "peaks" that it has to "fly over" as well. Aging vessels are — to an extent — the end result of such stresses. Halberg et al. suggest that many patients may be apparently normotensive (with normal blood pressure), yet (because of circadian peaks in blood pressure) have the catastrophic risks of any other severely hypertensive patient. They recommend that [medical practitioners] avoid "flying blind" and begin to measure peak pressures more accurately if we are to avoid disaster.

In the home town of Dérer and Mikulecky, a citywide blood pressure monitoring project can be a first step toward flying through the mountain range of physiological variation with open eyes.

Memorandum on stroke prevention

Offer of analyses and, when desired, also of an opportunity to cheaply purchase automatic monitors

Under conditions agreed upon beforehand, including a format previously agreed upon for self- or ambulatory automatic measurements, data sets, whether they are 3-hourly self-measurements during waking with one measurement during mid-sleep for 7 days or automatically monitored data at 1-hour or preferably 30-minute or shorter intervals, sent by e-mail to the Halberg Chronobiology Center at the University of Minnesota (HCC/UoM), will be summarized as a minimum by parametric and nonparametric procedures involving comparisons within an accumulating data base as described elsewhere (14, 21). Individuals or groups interested in cooperative research on the chronobiology of blood pressure and thus in acquiring automatic blood pressure and heart rate monitors at a price reduced by nearly 90 % may contact the HCC/UoM. Participants agree to fill out questionnaires and provide a short note in early January of each year concerning their address and their state of health, thus assuring follow-up. In exchange, they will receive analyses focusing upon the extent of about-daily or circadian and about-weekly or circaseptan variation, assessed by the amplitude on the one hand, and also providing any non-parametric deviations from the acceptable pressure behavior on the other hand, all assessed on the basis of gender-, age- and, when possible, ethnicity-specified norms.

Deviations will be differentiated into an elevation of the overall blood pressure mean (MESOR-hypertension) and/or the overswinging of blood pressure (**c**ircadian **h**yper-**a**mplitude-**t**ension, CHAT), without or with **w**eekly **h**yper-**a**mplitude-**t**ension (WHAT). The diagnosis will be specified as 1. MESOR- and amplitude-normotension; 2. high blood pressure (MESOR-hypertension), 3. overswinging (CHAT and/or WHAT), 4. a coexistence of MESOR-hypertension and CHAT and/or WHAT or 5. other deviations including altered timing. Groups 2-5 will each be randomized into two subgroups, one treated conventionally, the other chronobiologically. This approach will aim at a comparison of treatment when needed, according to a (mutually agreed-upon) chronodiagnosis-based chronotherapy on the one hand, or with a conventional diagnosis and therapy on the other hand. Under the conventional approach, we include a so-called "chronotherapy" concerned about a chronodiagnosis, consisting of no more than the administration of a long-acting preparation (whether or not it is designed to cover primarily the morning rise in blood pressure). This core approach will aim at stroke and catastrophic disease reduction.

II. Ancillary projects, preferably in The Biosphere and the Cosmos (BIOCOS) project (30)

To enlarge the data base, the automatic instrumentation will be made available at a reduced price via the HCC/UoM, also for ancillary projects that do not directly relate to stroke and heart attack prevention, but strengthen the data base accumulating on healthy subjects as well as on individuals with diagnosed health concerns.

Responsibilities of recipients

Prior to the receipt of the instruments, the undersigned will discuss their protocols with HCC/UoM staff members, will follow these or other protocols agreed upon and will discuss any modifications of the protocols with one or both of these HCC/UoM staff members. They will not implement a change in protocol unless it is agreed upon with the HCC/UoM. The participants agree further to provide a copy of all data obtained with the instrumentation to the HCC/UoM with a daily activity diary as agreed upon beforehand. Unless other prior agreements are made, the instruments are the property of the HCC/UoM, assigned, however, on an unlimited lease to the recipient for monitoring within the context of BIOCOS. The minimal purchase price is the equivalent of a one-time rental fee for as long as monitoring proceeds and/or the instrument functions. For any repairs, the instruments are to be returned to the manufacturer, who will solely decide on whether to replace the instrument and, if so, at what cost, if any. The HCC/UoM assumes no responsibility for their repair.

Responsibility of the HCC/UoM

Under conditions and in a form agreed upon beforehand, upon receipt of data by e-mail or otherwise, the HCC/UoM in turn will provide a blood pressure profile summary in time (sphygmochron) (28, 29; cf. 21) and will carry out other necessary inferential statistical tests within a reasonable time span, usually within a week or more promptly, when agreed upon beforehand.

Analyses and reporting of results

Added analyses on the data may also be carried out at intervals in the context of the Biosphere and the Cosmos (BIOCOS) project (30). In that context, the results will serve for updating a data base on blood pressure and heart rate behavior. This data base, in turn, will also explore influences by ethnicity, local socio-ecological and further helio- and geomagnetic and other solar and possibly extrasolar factors. Thereby, reference values will be improved for the principal applied aim of objectively comparing outcomes from a chronodiagnosis-based treatment with those from a conventional treatment in terms of the incidence of catastrophic disease such as stroke and myocardial infarction and possibly in terms of substitute outcome measures such as the left ventricular mass index.

The HCC/UoM reserves the right to use the data as a feature of their overall data base upon their receipt. If the data set from one source constitutes the sole or major aspect of a publication, the recipient is encouraged to publish jointly with the HCC/UoM, but may prefer to do so separately as long as the recipient does not publish analyses from the HCC/UoM. In the HCC/UoM publications, again as mutually agreed upon beforehand, depending on the extent of the contribution by the recipient(s) of the instrumentation, the recipient(s) will be first authors, co-authors or (notably after a first publication with the recipient), will receive an acknowledgement insofar as the given journal accepting a paper permits. At one year after their receipt, irrespective of whether or not they have been published earlier, the data become the property of the HCC/UoM as well as of the recipient with either party free to publish independently or jointly.

Significance

The demonstration of a reduction in the incidence of strokes and myocardial infarctions, even by a small percentage, and even if one takes into account expenses for education and instrumentation for monitoring and analysis, will imply a very large reduction in the cost of health care since strokes and myocardial infarctions constitute the major expense in health care, apart from constituting most crippling conditions. Such positive results, notably if the approach here already applied to vascular diseases can be extended to the prevention of other diseases by marker rhythm monitoring, such as cancer, emotional and cognitive disease (31), could make chronomedicine a medical specialty, chronobiology its underlying basic science. The accumulating archives of the HCC/UoM constitute a resource both for applied health care and for basic chronoastrobiology.

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RECENZIA

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Vo vydavateľstve Vojenská letecká akadémia v Košiciach pod vedením troch hlavných autorov prof. MUDr. Z. Tomoriho, DrSc., prof. MUDr. R. Redhammera, DrSc., a MUDr. V. Donica, CSc., a deväťástich spoluautorov vychádza kniha *Základy spánkovej medicíny.*

Knihu charakterizuje už jej podnadpis Poruchy spánku, poruchy životných funkcií spánku. Dielo nie je len teoretickou prezentáciou v literatúre nájdených najnovších poznatkov o danej problematike, ale má podklad v patofyziologicko-klinickej praxi autorov. Roku 1994 založili prof. Tomori a MUDr. Donic prvé spánkové laboratórium s centrom na LF UPJŠ v Košiciach, ktoré boli predvojom vzniku podobných centier v Bratislave a v Martine. Vznik týchto centier zaoberajúcich sa tou oblasťou medicíny, ktorej sa v našom aj celosvetovom meradle venuje neadekvátne málo pozornosti, súvisel s mnohoročnými skúsenosťami autorov z odboru patofyziológie a kliniky ochorení dýchacieho systému. Práve v spánku totiž dochádza k závažným respiračným poruchám, ktoré môžu viesť k celkovým poruchám zdravia. Pretože spánok je obdobie tvoriace až tretinu ľudského života, výskytu respiračných ochorení, ale aj porúch iných orgánov a systémov vzniknutých v súvislosti so spánkom sa venuje v týchto novozaložených centrách ústredná pozornosť z hľadiska diagnostiky aj liečby. Na to, aby si medicínska verejnosť uvedomila, aký je význam spánku a jeho porúch vo vzťahu k vzniku ochorení rôznych systémov, a naopak, ako somatické a psychické ochorenia môžu ovplyvniť kvalitu spánku, je napísanie a vydanie tejto publikácie jedinečným počinom.

Kniha má 368 strán, je rozdelená do 30 kapitol. V úvodných kapitolách sú prezentované údaje o súčasnom stave a perspektívach spánkovej medicíny na Slovensku, mechanizmy spánku z hľadiska neurofyziológie, psychiatrie a poruchy spánku. Súčasťou tejto časti knihy je aj zjednodušená, ale pritom veľmi inštruktívna a pre prax vhodná klasifikácia porúch spánku.

V ďalších kapitolách sa autori zamerali na opis a charakteristiku narušenia fyziologických činností niektorých systémov, predovšetkým so zameraním na poruchy dýchania počas spánku. Ide o poruchy regulácie dýchania, poruchy priechodnosti dýchacích ciest, mechanizmy chrápania, spánkového apnoe. V priamej alebo nepriamej súvislosti spánkových respiračných porúch rozličného charakteru dochádza k poruchám kardiovaskulárneho systému, endokrinných funkcií, neuropsychickým alteráciám, asfyxii plodu a novorodencov, k zvýšenému riziku anestézie, apnoickým stavom detí. Ďalej autori prezentujú diagnostiku a skríning týchto spánkových a s nimi súvisiacich respiračných porúch iných systémov.

Pre praktickú medicínu je najdôležitejším dôsledkom charakterizovania a diagnostiky týchto spánkových porúch ich liečba. V knihe je prezentovaná liečba medikamentózna a chirurgická, ale aj metódy ventilačné a využitie protéz. Vyčíslené sú aj sociálnoekonomické následky spánkových porúch a možnosti ich prevencie.

V závere knihy je stručný súhrn každej kapitoly v anglickom jazyku, čo umožňuje rýchlu orientáciu a výber tej kapitoly, o ktorú má momentálne čitateľ záujem.

Predslov knihy napísal odborný redaktor prof. MUDr. R. Korec, DrSc. Kniha je napísaná napriek podielu mnohých autorov na jej vzniku jednotiacim, veľmi zreteľným a zrozumiteľným vedeckým literárnym štýlom. Svojím obsahom vytvára taký ucelený pohľad na problematiku porúch spánku, ich patofyziológie, diagnostiky, liečby a prevencie, že dokáže aj medicínskeho laika upútať k prečítaniu celej knihy a kvalifikovaného čitateľa oboznámiť s tým, čomu sa v súčasnosti v tejto problematike venuje výnimočná pozornosť. Kniha patrí podľa nášho názoru k najlepším medicínskym publikáciám, ktoré u nás v posledných rokoch vznikli.

F. Šimko