

SCIENTIFIC DATA—REPRODUCTION OF ORIGINAL WORK: THOUGHTS FOR ACADEMICS AND OTHER SCRIVENERS

A small, but often galling nuisance for those who publish books, reviews and teaching material is the inability to freely re-use one's original illustrations from published investigations and clinical reports. Although some publishers want to know the precise details of where the material will appear, permission is nearly always granted. Yet, ideally, the rights to original illustrations and tables should belong to those who do the work, and it can be annoying to continually solicit permissions from journal editors and publishers.

Recently, specific assignments of copyright for every manuscript accepted—including even letters to the editor—is routinely obtained by editorial offices through a form for all authors to sign. That would seem to offer an ideal opportunity to simplify the question of future access to the fruits of one's own efforts. I propose that—subject to citation of the original source—publishers exchange for that transfer of copyright their blanket permission for reproduction of illustrations and tables.

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21 December 1984

ALL THAT STICKS IS NOT A BAND-AID

Several novel drug delivery systems of topical nitroglycerin, designed to deliver a constant dose over a 24-hour period, have recently become available. These products involve a delivery system not familiar to many patients and, therefore, are prone to accidental misuse. We encountered a patient who had been given Nitro-Dur[®], 10 cm² (Key Pharmaceuticals), for angina pectoris, with good relief. One day the patient injured her lower leg. This resulted in a small superficial laceration. Because she had no bandages available and the Nitro-Dur patch seemed appropriately shaped with a convenient surrounding adhesive strip, she applied it to her injured leg. This rapidly resulted in a headache, dizziness and weakness. On arrival in the emergency room, the patient was neither hypotensive nor orthostatic. However, her symptoms resolved rapidly when the Nitro-Dur patch was replaced with a more conventional dressing.

This patient was fortunate that her laceration was minor. Probably only a small

amount of nitroglycerin was absorbed from the patch into the bloodstream, causing these symptoms. If the wound had been larger, the patient could have experienced a greater degree of vasodilation and subsequent hypotension that occurs with the large systemic levels of nitroglycerin. A change in the character of the stratum corneum can influence the degree of nitroglycerin absorbed from topical preparations. Nitro-Dur has a matrix construction in which nitroglycerin diffusion is dependent on the stratum corneum as the absorption-rate-controlling step. It is worthwhile to question whether a product that incorporates a semipermeable membrane to control the release rate of nitroglycerin could reduce such exaggerated effects. Nevertheless, this case emphasizes the importance of explaining the use of these new medications to patients, as they can easily become confused about the use of this new therapeutic modality.

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18 September 1984

OCLUSION OF BJÖRK-SHILEY AORTIC VALVE PROSTHESIS BY HYPERTROPHIED VENTRICULAR SEPTUM

The report by Ross and Roberts (*Am J Cardiol* 1984;54:231-233) documents interference of function of the St. Jude Medical aortic valve prosthesis by hypertrophied ventricular septum. Such a phenomenon is not unique to this particular mechanical valve as a recent case illustrates.

A 70-year-old man had a history of severe systemic hypertension and anterior aortic dissection 13 years previously that was repaired primarily. One year later, aortic regurgitation necessitated aortic valve replacement, accomplished with a 25-cm Björk-Shiley prosthesis. He was subsequently followed up for progressive aneurysmal dilatation and pronounced rightward deviation of the ascending aorta; this segment was not involved in the current event.

He presented on this admission with acute posterior aortic dissection that did not respond to medical therapy. The dissection was repaired uneventfully through a posterolateral incision with graft interposition using femoral vein-femoral artery bypass. Wound closure was delayed by diffuse chest wall hemorrhage accounted for by preoperative anticoagulation with platelet inhibition, a regimen necessitated by intolerance to warfarin. He was nevertheless kept stable with steady colloidal volume replacement when sudden hypotension occurred. Prompt recovery resulted from intravenous phenylephrine and rapid volume infusion from the pump oxygenator. Precipitous, irreversible hypotension recurred a few minutes later. He

was totally refractory to additional volume, CaCl₂, dopamine, and open massage of the left side of the heart.

Autopsy revealed the cause of death to be fixation of the aortic prosthesis in the closed position. The lesser orifice of the valve had been oriented to the commissure between right and noncoronary sinuses, and the lesser orifice side of the disc was held firmly shut by the underlying bulge of an extraordinarily hypertrophied ventricular septum. The combination of hypovolemia and enhanced cardiac inotropy undoubtedly had contributed dynamically to this acute mechanical event.

Olin et al¹ recently showed that optimal hydraulic performance of the Björk-Shiley aortic valve is achieved with orientation of the greater orifice toward the noncoronary sinus, opposite and posterior to that found in our patient, and additionally, preventive of the complication we encountered. Ross and Roberts properly caution about appropriate orientation of the St. Jude Medical aortic valve prosthesis. This warning and the anatomic reason behind it should not be regarded as prosthesis-specific.

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19 September 1984

- Olin CL, Bomlin V, Halvazulu V, Holmgren AG, Lamke BJ. Optimal insertion technique for the Björk-Shiley valve in the narrow aortic ostium. *Ann Thorac Surg* 1983; 36:567-576.

RECORDING AND ANALYSIS OF CIRCADIAN BLOOD PRESSURE PATTERNS

We read the article by Weber et al¹ on circadian blood pressure (BP) patterns in ambulatory normal subjects. Some basic work on rhythmic BP changes² was not referred to by them. Halberg et al performed and compared self-measurements and automated recordings of 24-hour, 48-hour and 7-day long series. They also studied reproducibility after 1 year.³ The difficulties by Weber et al to reproduce circadian BP patterns might be partly explained by circannual variation, since there were rather long intervals of up to 8 weeks between recordings. We wonder whether the series with the longest intervals show the poorest reproducibility.

Weber et al proposed to define major types of BP abnormalities. This has been done on the basis of chronobiologic analysis.⁴ Mesor and amplitude hypertension have been defined.⁵ With their careful documentation of 24-hour BP variations in a larger number of subjects, the study by Weber et al is valuable and important. However, use of "cosinor analysis," first introduced by Halberg et al,⁶ might improve accuracy of analysis and reproducibility of the reported data. Cosinor analysis provides exact evaluation of rhythm parameters, such as mesor, amplitude and acrophase of circadian rhythmic changes.^{7,8}

* Letters (from the United States) concerning a particular article in the *Journal* must be received within 2 months of the article's publication, and should be limited (with rare exceptions) to 2 double-spaced typewritten pages. Two copies must be submitted.

It would be interesting to evaluate the data of Weber et al by cosinor analysis.

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20 September 1984

1. Weber MA, Drayer JIM, Nakamura DK, Wyle FA. The circadian blood pressure pattern in ambulatory normal subjects. *Am J Cardiol* 1984;54:115-119.
2. Halberg F. Quo vadis basis and clinical chronobiology: promise for health maintenance. *Am J Anat* 1983; 168:543-584.
3. Rabatin JS, Sothorn RD, Brunning RD, Goetz FC, Halberg F. Circadian rhythms in blood and self-measured variables of ten children, 9-14 years of age. *Proc XIII Intern. Conf. ISC*. Halberg F, Scheving LE, Powell EW, Hayes DK, eds. Il Ponte, Milan, 1981:373-385.
4. Halberg F, Caradente F, Cornelissen G, Katinas GS. Glossary of chronobiology 1977;4:suppl 1:130-132.
5. Halberg F, Barnes B, Tuna N. Amplitude (A)- and mesor (M)-hypertension gauged by tensopies on and off a cardioselective β -blocking drug. *Minn Acad Sci* 1983; 51:10.
6. Halberg F, Tong YL, Johnson EA. Circadian system phase—an aspect of temporal morphology: procedures and illustrative examples. In: v Mayersbach H, ed. *The Cellular Aspect of Biorhythms*. Berlin: Springer, 1987: 20-48.
7. Gerbes AL, Arbogast B. The influence of timeshift on circadian rhythm of sensitivity to x-irradiation in mice. *Chronobiologia* 1983;10:127-128.
8. Haen E, Halberg F, Cornelissen G. Cortisol marker rhythmometry in pediatrics and clinical pharmacology. *Ann Rev Chronopharm*. In: Reinberg A, Smolensky M, Labrecque G, eds. Oxford: Pergamon Press, 1984.

REPLY: Gerbes et al make the interesting point that the rhythmicity of the BP pattern in humans may be best studied during periods of 48 hours or even longer rather than the 24-hour studies that we reported. I agree with

this possibility, but the practicality of performing such long studies, even with noninvasive techniques, is limited clinically. Moreover, an important part of our intent in performing our study was to evaluate the reproducibility of the 24-hour BP pattern, because this is the likely basis for studies of the therapy of systemic hypertension. We also agree that the circannual variation in BP patterns might have helped explain the lack of reproducibility of BP in some patients, although in our relatively small patient numbers we did not see a clear difference in reproducibility between patients studied after shorter or longer time intervals.

We are well aware of the work of Halberg in this area, key parts of which have been published under our editorship.¹ The writers of the letter also may be interested to know that the data presented in our article (Ref. 1 above) is currently being analyzed in conjunction with Halberg so as to further answer some of the questions they raised.

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13 October 1984

1. Ambulatory Blood Pressure Monitoring. In: Weber MA, Drayer JIM, eds. Darmstadt: Springer Verlag, 1984.

PREMATURE ATRIAL STIMULATION DURING REGULAR ATRIAL PACING: A NEW APPROACH TO STUDY OF THE SINUS NODE

In the article by Kirkorian et al,¹ sinoatrial conduction time (SACT) was defined as the

difference between mean return cycle and postreturn cycle lengths. This equation was first suggested by Raviele et al² and by Griebenow et al³ as a modification of the method for determining indirect sinoatrial conduction time described by Narula et al.⁴ We demonstrated that continuous atrial stimulation led to a frequency-dependent depression of sinus node automaticity, which can be partially attributed to the baroreflex mechanism.⁵ The subsequent frequency-dependent increase of SACT values can be compensated for by calculating SACT from the difference between return cycle and postreturn cycle lengths. This equation, therefore, was justifiably used by Kirkorian et al,¹ since they performed premature atrial stimulation during continuous atrial pacing at different frequencies.

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9 October 1984

1. Kirkorian G, Touboul P, Atallah G, Moleur P, Zuloaga C de. Premature atrial stimulation during regular atrial pacing: a new approach to the study of the sinus node. *Am J Cardiol* 1984;54:109-114.
2. Raviele A, D'Este D, Sartori F, Delise P, Dainese F, Di Pede F, Callegari E, Piccolo E. Attendibilita' della tecnica di Narula per il calcolo del tempo di conduzione seno-atriale. *G Ital Cardiol* 1980;10:290-300.
3. Griebenow R, Hossmann V, Saborowski F. Bestimmung der sinoatrialen Leitungszeit mit einer modifizierten Methode nach Narula. *Z Kardiol* 1979;68:643.
4. Narula OS, Shantha N, Vasquez M, Towne WD, Linhart JW. A new method for measurement of sinoatrial conduction time. *Circulation* 1978;58:706-714.
5. Griebenow R, Hossmann V, Saborowski F. Determination of the sinoatrial conduction time by a modified continuous atrial pacing technique. In: Feruglio GA, ed. *Cardiac Pacing*. Padua: Piccin Medical Books, 1982; 65-68.