

# Inspiration-Induced Vascular Responses in Finger Dorsum Skin

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A rapid and deep inspiration triggers a sympathetically mediated transient vasoconstriction of skin arterioles (inspiratory gasp vascular response, IGVR). Because the IGVR has been most often measured and studied in skin that is rich in arteriovenous anastomoses (AVAs), such as the palmar aspect of the distal phalanx or plantar aspect of the toes, there is little information on its features in skin areas not dominated by thermoregulatory AVAs. Thus, the dependence of the magnitude of the IGVR on AVAs is unclear. We reasoned that if responses in a region of low AVA density, such as the finger dorsum distal phalanx, were comparable to those in AVA-rich skin, this would clarify the issue. Further, it might then be possible to use such areas to provide a useful complementary target for future study of sympathetically induced vasoconstriction. To test this, we determined the features of the finger dorsum IGVR in 28 healthy volunteers (age 19–57 years, 14 males) in whom distal phalanx skin blood perfusion (SBF) was monitored by laser-Doppler during 21 sequential IGVRs, each separated by 2 min. IGVR was quantified as the minimum SBF during each IGVR, expressed as a percentage of each immediately preceding 2-min SBF average. Results (mean  $\pm$  SD) revealed an overall IGVR of  $72.2 \pm 16.7\%$ , which is very near that reported from studies on the AVA-rich palmar finger pad. We therefore conclude that the IGVR does not depend on the presence of AVAs and that the dorsal distal phalanx is a viable alternative for the study of sympathetically related neurovascular responses. © 2002 Elsevier Science (USA)

**Key Words:** human microcirculation; skin blood flow; skin microcirculation; laser-Doppler; inspiratory gasp; vasoconstriction.

## INTRODUCTION

A vasomotor reflex triggered by a rapid and deep inspiration causes arteriolar vasoconstriction and a transient decrease in skin blood flow in most people.

This phenomenon was first reported in detail by Bolton *et al.* (1936), who also showed that it depends on an intact peripheral sympathetic system, since the vasoconstrictor response was absent in the digits of limbs that were either denervated or sympathectomized. The vasoconstrictor response was present with a complete occlusion of the arm circulation, indicating no major role of local circulation in the reflex. These early workers concluded that the afferent stimulus was due to chest wall expansion during the deep inspiration. However, others who were able to induce the reflex with either deep inspiration or negative pressure breathing, without chest wall expansion, argued for an increase in stretch of intrathoracic veins as the primary initiating factor (De Lalla, 1948). Gilliatt *et al.* (1948), having observed a vasoconstrictor reflex in paraplegic patients with a full break in functional continuity of the spinal cord above the level of sympathetic outflow to the hands, concluded that the re-

flex was not due to inspiratory induced hypotension with an associated carotid sinus reflex (Gilliatt, 1948). However, many details of the afferent and efferent pathways still are not fully clarified. That the reflex causes a significant reduction in blood flow was clearly demonstrated by plethysmography, which showed hand blood flow to be reduced by 83% during deep inspiration, and by nailfold capillaroscopy, which showed a rapid and complete cessation of capillary flow during a deep inspiration in most subjects (Mulinos and Shulman, 1939). Interestingly, when capillary flow was stopped by suprasystolic arm occlusion, a subsequent deep inspiration caused a transient forward capillary flow, presumably due to the expulsion of blood by the constriction of proximal arterioles.

The inspiratory gasp vascular response (IGVR) has most often been measured on the skin of the plantar aspect of the toes or the palmar surface of the fingers using laser-Doppler perfusion monitoring (Khan *et al.*, 1991; Netten *et al.*, 1996). These skin regions, which are rich in arteriovenous anastomoses, were used to study neurovascular function in patients with diabetes (Wilson *et al.*, 1992; Abbot *et al.*, 1993), Raynaud's phenomenon (Wollersheim *et al.*, 1991), erythromelalgia (Littleford *et al.*, 1999), and leprosy (Abbot *et al.*, 1993). However, an issue that has received little attention or systematic study is the characterization of IGVR features of a digit in a region that is not dominated by thermoregulatory arteriovenous anastomoses. We reasoned that if the normal pattern of responses in such a region (finger dorsum) were sufficiently large and uniform, then it would provide a useful complementary target for future study of sympathetically induced vasoconstrictor features in an array of conditions. Thus, our objective was to characterize the normal IGVR features of finger dorsum skin at the distal phalanx with emphasis on its magnitude, short-term variability, and gender differences.

## METHODS

### Subjects

Twenty-eight volunteers participated in this study after signing an institutional review board-approved

**TABLE 1**  
Summary of Subject Data

	Male (N = 14)	Female (N = 14)	Total group (N = 28)
Age (years)	32.3 ± 7.8	34.1 ± 13.3	33.1 ± 10.7
Height (cm)*	177 ± 6.3	167 ± 5.8	172 ± 8.0
Weight (kg)*	82.4 ± 11.0	62.2 ± 9.0	72.3 ± 14.3
Pressures (mm Hg)			
Systolic	130 ± 19	118 ± 12	123 ± 17
Diastolic*	89 ± 13	79 ± 9	85 ± 12

*Note.* Values are means ± SD.

\* Parameter values significantly greater for males ( $P < 0.01$ ).

informed consent form. Subjects were equally divided by gender and were drawn from the university medical student population and staff. No subject had a history of cardiovascular or respiratory abnormality, hypertension, or diabetes. Although it was not a requirement for entry into this study, all subjects were right-handed. Pertinent summary data are shown in Table 1.

### Initial Preparations

Subjects were seated in a comfortable, height-adjustable armchair with their hands placed palm down on a soft support surface across the arms of the chair. The surface is flat and minimizes pressure concentration effects. A laser-Doppler probe (Vasamedics P-440 Soflex, Vasamedics Inc., St Paul, MN) was placed on the dorsum of the index finger at the distal phalanx of the right hand, with its sensing area approximately 4 mm proximal to the nailfold. This probe has the fiber optic bundles embedded in a thin flexible silicone elastomer that conforms to the skin surface. The probe was connected to a standard laser-Doppler monitor (Vasamedic Model 403a) with an output proportional to the product of moving red cell volume concentration and red cell speed within the tissue sample region to a depth of about 1–2 mm (Mayrovitz, 1998). This perfusion output was recorded by a laptop computer for subsequent analyses. A small thermocouple was placed under the probe near the site of measurement and the combination of probe and thermocouple wire was secured by gentle wrapping with an elastic cohesive bandaging material (Coban 3M company). In ad-

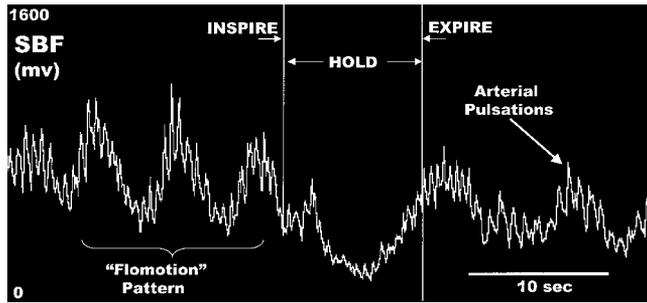


FIG. 1. Skin blood perfusion (SBF) before, during, and after a single inspiration. Subjects were instructed to take a deep and rapid inspiration starting at the end of a normal quiet expiration and hold it for 10 s. In some subjects a rhythmical flowmotion pattern was present. Time constant for laser-Doppler recording was 0.1 s, which allowed detection of arterial pulsations.

dition to providing support, the wrapping served to insulate the finger and render it relatively insensitive to drafts or direct effects of ambient temperature changes. The hand was then covered with a towel to further insulate the test area and to provide for a more stable local skin temperature. This procedure allowed the subject's skin temperature at the site of measurement to reach its normal steady state. Skin temperature was continuously monitored and testing did not begin until it had reached a steady state level; typically this took 15–20 min. During this interval the subject was instructed as to the breathing maneuver that was

required and was given multiple chances to practice it. The instruction was to take a deep and rapid inspiration, starting at the end of a normal quiet expiration, and to hold it for 10 s (Fig. 1). Subjects were instructed to first sense their breathing pattern so that they could feel comfortable in identifying the end-expiratory point and then to take the gasp when comfortable. During testing, the experimenter quietly informed the subject that their next gasp was in 20 s and, when the time arrived, they were instructed to “gasp when ready.” Following this last instruction, subjects usually initiated the gasp within 10 s.

**Test Procedures and Perfusion Parameters**

The test protocol consisted of a series of 21 sequential inspiratory gasps taken at uniform intervals of 2 min between adjacent gasps. The average finger skin blood perfusion (SBF) during the 2-min interval immediately preceding each successive gasp was used as the reference for the following IGVR. The IGVR was determined from the minimum perfusion during the gasp ( $SBF_{min}$ ) and its reference perfusion ( $SBF_0$ ) according to the relationship  $IGVR = 100\% \times (SBF_0 - SBF_{min})/SBF_0$  (Fig. 2). Accordingly the maximum range of IGVR was 0 to 100%. Skin and room temperatures were continuously monitored and recorded ev-

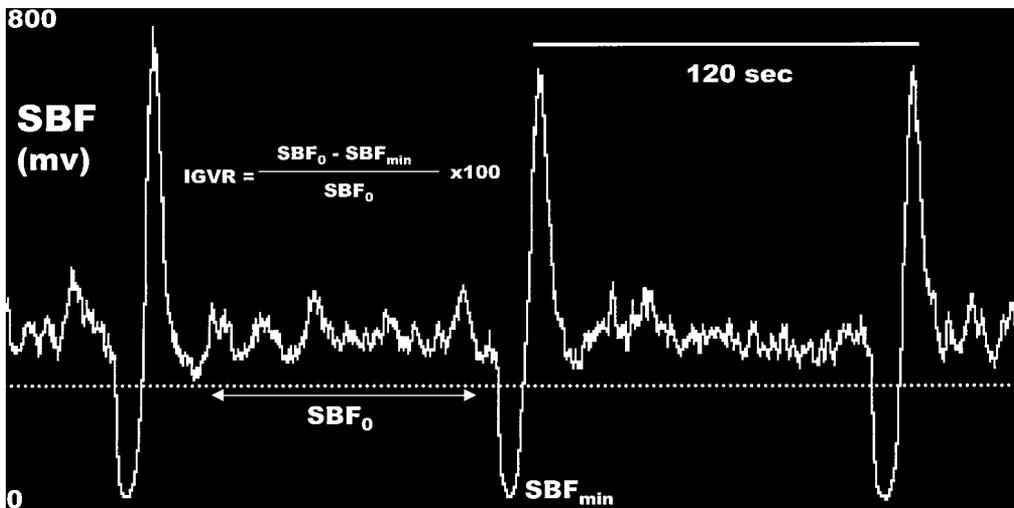


FIG. 2. Determination of inspiratory gasp vascular response (IGVR). In this subject the gasp-induced vasoconstriction was followed by a large transient hyperemic peak in SBF.

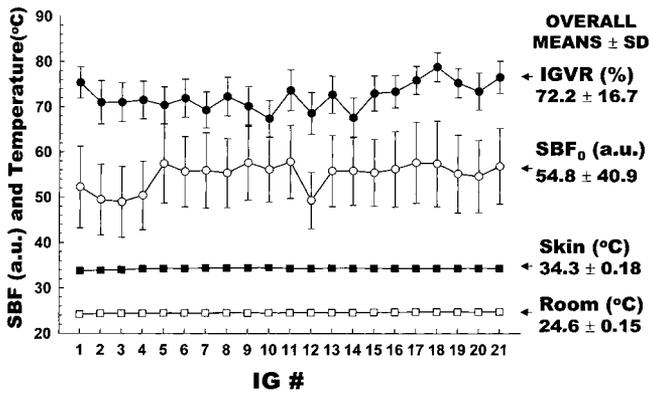


FIG. 3. Overall sequential parameter values. Each point is the mean of 28 subjects and bars are SEM at each IGVR. There were no significant trends in any parameter over the experimental sequence.

ery 2 min, corresponding to each of the inspiratory gasps. At the end of the procedure, blood pressure was measured in the right arm and a suprasystolic occlusion (200 mm Hg) of the brachial artery for 3 min was used to determine the laser-Doppler biological zero at the finger site. This value was subtracted from all raw SBF data prior to analyses.

All data reduction was done from the computer-acquired and -stored perfusion signals. The total data set consisted of 21 IGVRs for each of the 28 subjects, representing a total of 588 data points. To determine the effect of using smaller size sample-sets (which would be more practical for routine application), a comparison was made between the average IGVR of all 21 sequential samples and the IGVR associated with truncated sequences, starting from the first IGVR and having sample-set sizes of 2, 3, 4, 5, and 7. To determine overall short-term variability, mean responses of the first three IGVRs were compared with those obtained starting 30 min later (IGVRs 18, 19, and 20).

## RESULTS

### Overall and Sequential Parameter Features

Overall IGVR was  $72.2 \pm 16.7\%$  (mean  $\pm$  SD), (Fig. 3). There was no significant trend in sequential IGVR (Pearson  $r = 0.059$ ) but, as expected, there was a

significant positive autocorrelation among sequential IGVRs (Durbin-Watson,  $P < 0.01$ ). During the 42-min experimental interval, the average of the 21 reference SBF values (SBF<sub>0</sub>) across IG samples was  $54.8 \pm 42.4$  arbitrary units (au) with a considerable variation among subjects (range 130–2042 au). There was no significant trend in SBF<sub>0</sub> within subjects nor were there significant variations in skin temperatures ( $34.3 \pm 0.18^\circ\text{C}$ ) or room temperature ( $24.6 \pm 0.15^\circ\text{C}$ ).

### Gender and Age Comparisons

Mean IGVR of females tended to be less than that for males ( $67.1 \pm 14.3$  vs  $77.3 \pm 18.3$ ), but the difference did not reach statistical significance ( $P = 0.062$ , Mann-Whitney). Sequential features of the IGVR were similar for male and female subgroups. For the age range of the population studied (19–57 years), there was a slight but nonsignificant correlation between mean IGVR and subject age (Pearson  $r = -0.243$ ,  $P = 0.212$ ).

### Subsampling Comparisons

Truncating the sample-set size had little effect on the estimated overall mean response but increased the overall standard deviation by an amount that increased as the subsample size decreased (Table 2). Associated coefficients of variation ranged from 23.1% for the complete 21 IGVR sample set to 28.3% for a sample-set size of 2. Comparisons between the initial three IGVRs and 30-min displaced triplicate samples showed that a good correlation remained for these time-separated sample-sets ( $r = 0.710$ ,  $P < 0.001$ ) with the overall means estimated by each sample-set

TABLE 2  
Effect of Subsample Sizes

IG Sample set size	IGVR (%)	
	Mean	SD
21	72.2	16.7
7	72.3	17.4
5	72.8	18.3
3	73.2	19.6
2	73.1	20.7

being insignificantly different from one another and from the mean estimated by all 21 samples.

## DISCUSSION

The overall dorsum IGVR determined in the present study was 72%. This value is near the value of 77% obtained on finger pulp in a group of 20 young healthy people ( $26 \pm 4.7$  years) and essentially identical to the mean value of 71% obtained for a group of 10 middle-aged persons, 25–67 years (Khan *et al.*, 1991), and to the mean value of 71.4% obtained in a group of 10 young ( $21.8 \pm 0.9$  years) male subjects (Lau *et al.*, 1995). The fact that these workers used the fingertip pulp, whereas the finger dorsum was used here, suggests that despite a much lower density of arteriovenous shunts in finger dorsum, the net vasoconstrictor activity induced by the inspiratory gasp sympathetic reflex is similar. We believe that the present report is the first to describe the IGVR using finger dorsum skin.

It is noteworthy that finger pulp findings (Khan *et al.*, 1991) and the present finger dorsum findings were obtained at skin temperatures close to 34°C although Khan and co-workers achieved this via contralateral arm water-bath heating, whereas we used simple covering of the finger and hand. Skin temperature is of importance because of its effect on the magnitude of the IVGR, as has been previously described (du Buf-Vereijken *et al.*, 1997).

Although mean responses were similar, the IGVR variability of the finger pulp, as reported by Khan *et al.* (1991), was less than what we found for the dorsum. Thus, for their group of 20 young subjects, the between-subject and within-subject standard deviations were reported as both equal to 7%. Larger standard deviations (10.8–11.3%) were present for a different group of 20 young subjects (Lau *et al.*, 1995). Corresponding between- and within-standard deviations of the dorsum skin determined here were 16.7 and 8%, respectively. The higher between-subject variability that we found may be due to several factors. First, the mean age, and the age range, of our group was considerably greater. Although we found no significant

correlation between age and IGVR, the observed tendency for IGVR to slightly diminish with age would likely increase between-subject variability. In this regard it is noteworthy that although no significant difference in IGVR was detected on the finger pulp between a young normal group and 10 subjects with a mean age of 51 years (Khan *et al.*, 1991), the mean IGVR of the older group was lower (71%). Additionally, in a follow-up study (Khan *et al.*, 1992), an age-related reduction in IGVR and a significantly larger between-subject variance were in fact detected when triplicate IGVRs were used to compare 28 elderly subjects (mean age 68 years) with the younger group.

An additional factor that may have contributed to the greater between-subject variability of finger dorsum skin is the fact that the mean IGVR measured on the dorsum was somewhat less than that measured on the pulp. Thus, the maximal potential difference among subjects would be expected to be greater.

Another factor that has been suggested to affect the IGVR is vital capacity, since a significant positive correlation was found between vital capacity and the magnitude of the IGVR (Lau *et al.*, 1995). However, even after normalizing each subject's IGVR by their individual vital capacity, significant variability and differences in mean responses between genders remained.

Most previous studies that have used the inspiratory gasp vascular response to assess aspects of sympathetic vascular function have relied on single, duplicate, or at most triplicate sequential samples to estimate the mean response of a subject or patient. The use of 21 samples/subject in the present exploratory study was selected to provide a sufficiently large sample-set size consistent with a reasonable sequential time frame, to allow inferences regarding overall response patterns and variabilities in finger dorsum. However, from a practical point of view, it is desirable to use a smaller sample-set size. The results from the subsampling analyses suggest that, for the present subject group, sample-set sizes as small as 2 adequately estimated the overall mean response. The primary consideration therefore as to the sample-set size to be chosen for any particular study application depends mainly on the response variability, which increases with decreasing sample-set size.

In conclusion, the present results suggest that the finger dorsum vascular response to inspiratory gasps is similar in magnitude to those obtained in the finger pulp, an area with a high density of sympathetically innervated arteriovenous anastomoses. As a consequence, the finger dorsum is a viable alternative for the study of sympathetically mediated neurovascular responses.

## REFERENCES

- Abbot, N. C., Beck, J. S., Wilson, S. B., and Khan, F. (1993). Vasomotor reflexes in the fingertip skin of patients with type 1 diabetes and leprosy. *Clin. Auton. Res.* **3**, 189–193.
- Bolton, B., Carmichael, E. A., and Sturup, G. (1936). Vasoconstriction following deep inspiration. *J. Physiol.* **86**, 83–94.
- du Buf-Vereijken, P. W. G., Netten, P. M., Wollersheim, H., Festen, J., and Thien, T. (1997). Skin vasomotor reflexes during inspiratory gasp: Standardization by spirometric control does not improve reproducibility. *Int. J. Microcirc. Clin. Exp.* **17**, 86–92.
- De Lalla, V. (1948). Causes of skin cooling in pressure breathing, deep inspiration and deep expiration. *Am. J. Physiol.* **152**, 122–130.
- Gilliatt, R. W. (1948). Vaso-constriction in the finger after deep inspiration. *J. Physiol.* **107**, 76–88.
- Gilliatt, R. W., Guttmann, L., and Whitteridge, D. (1948). Inspiratory vaso-constriction in patients after spinal injuries. *J. Physiol.* **107**, 67–75.
- Khan, F., Spence, V. A., Wilson, S. B., and Abbot, N. C. (1991). Quantification of sympathetic vascular responses in skin by laser Doppler flowmetry. *Int. J. Microcirc. Clin. Exp.* **10**, 145–153.
- Khan, F., Spence, V. A., and Belch, J. J. F. (1992). Cutaneous vascular responses and thermoregulation in relation to age. *Clin. Sci.* **82**, 521–528.
- Lau, Y. T., Liu, C. F., and Tsai, C. C. (1995). Cutaneous vasoconstrictor response induced by inspiratory gasp in relation to sex and age. *Clin. Sci.* **89**, 233–237.
- Littleford, R. C., Khan, F., and Belch, J. J. F. (1999). Impaired skin vasomotor reflexes in patients with erythromelalgia. *Clin. Sci.* **96**, 507–512.
- Mayrovitz, H. N. (1998). Assessment of human microvascular function. In “Analysis of Cardiovascular Function” (G. Drzewiecki and J. Li, Eds.), Chap. 16, pp. 248–273. Springer Verlag, New York.
- Mulinos, M. G., and Shulman, I. (1939). Vasoconstriction in the hand from a deep inspiration. *Am. J. Physiol.* **125**, 310–322.
- Netten, P. M., Wollersheim, H., van den Broek, P., van der Heijden, H. F. M., and Thien, T. (1996). Evaluation of two sympathetic cutaneous vasomotor reflexes using laser Doppler fluxmetry. *Int. J. Microcirc. Clin. Exp.* **16**, 124–128.
- Wilson, S. B., Jennings, P. E., and Belch, J. J. F. (1992). Detection of microvascular impairment in type I diabetics by laser Doppler flowmetry. *Clin. Physiol.* **12**, 195–208.
- Wollersheim, H., Droste, H., Reyenga, J., and Thien, T. H. (1991). Laser Doppler evaluation of skin vasomotor reflexes during sympathetic stimulation in normals and in patients with primary Raynaud’s phenomenon. *Int. J. Microcirc.* **10**, 33–42.