Effect of Endogenous Estrogen on Blood Flow Through Carotid Arteries

Jaroslaw Krejza, MD, PhD; Zenon Mariak, MD, PhD; Magdalena Huba, MS, BS; Slawomir Wolczynski, MD, PhD; Janusz Lewko, MD, PhD

Background and Purpose—Recent evidence suggests that physiological changes in the concentration of endogenous estrogens may influence stroke outcome. The purpose of this study was to determine a menstrual cycle–related profile of blood flow through the carotid arteries and its correlation with estrogen concentration.

Methods—The flow velocity and cross-sectional area of the common carotid artery, internal carotid artery (ICA), and external carotid artery (ECA) were measured with duplex Doppler sonography throughout the menstrual cycle in 14 healthy women. Concentration of plasma 17β-estradiol, progesterone, hematocrit, hemoglobin, and blood pressure were also determined.

Results—In the follicular phase, the concentration of estrogen increased to reach a peak on day 14, whereas concentration of progesterone remained low. The mean and end-diastolic velocities in the ICA increased on average by 15% of their base values, along with increasing concentrations of estrogen (r=0.59 and 0.65, respectively). The profile of flow velocity changes in this artery corresponded to the profile of estrogen concentration. In contrast to the ICA, flow velocities in the ECA decreased from their base value, reaching their minimum in the luteal phase. The mean flow velocity in the common carotid artery increased on day 14 by just 2% of its base value. The lumen of the carotid arteries was stable throughout the cycle. Hematocrit, hemoglobin, and systolic blood pressure also remained unchanged.

Conclusions—Increased concentration of endogenous estrogen correlates with substantial augmentation of flow in the internal carotid artery. This promotion of flow is caused mainly by decreased cerebrovascular resistance with consequent “stealing” of blood from the ECA. (Stroke. 2001;32:30-36.)

Key Words: carotid arteries ■ cerebral blood flow ■ estrogen
We examined 14 healthy nulliparous women recruited from medical students (age range, 23 to 25) who met the strict entry criteria to the study. All had 6 self-reported regular consecutive menstrual cycles of \( \approx 28 \) days (range, 27 to 32 days) before investigation. None reported a history of any serious disease, particularly head trauma, diabetes, and/or psychiatric, cardiovascular, and gynecological disorders. Smokers and those who had ever used oral contraceptives or hormones or who had abused alcohol, drugs, or coffee were not included, nor were those taking any medication for at least 3 months before and during the month of the study.

Subjects were found to be strictly normal on clinical examination by a physician. Their body mass index was \(<30\). Blood cell count, liver function tests, and the concentrations of electrolyte, blood glucose, cholesterol, and triglyceride were within normal limits. MRI of the brain was also performed to rule out subjects with intracranial abnormalities. Out of 17 subjects who entered the program, 3 were excluded at the final stage of the study: one because of an unovulatory cycle, another because of the detection of an enlarged cerebral ventricular system, and a third because of an incident of fever.

**Study Design**

Every participant was evaluated at least 11 times: during menses (cycle day 3), during the follicular phase (cycle days 6, 10, 12, 13, and 14), and during the luteal phase (cycle days 15, 16, 17, 20, and 24). Two initial examinations, taken on days 1 and 2 of the cycle, were not included in analysis because they were designed to minimize the effects of anxiety in the subject.\(^6\) Ovulation was determined by direct sonographic follow-up of the follicle and with measurements of plasma \( \beta \)-estradiol and progesterone concentrations. The cycles were counted from the first day of menses and were standardized to a 28-day period. Ovulation was taken as occurring between days 14 and 15.

On the days of testing, subjects reported to the laboratory after having fasted for 12 hours and having abstained from vigorous exercise, alcohol intake, and caffeine-containing beverages for at least 24 hours before the study. All examinations were performed between 6 and 8 AM to minimize the effect of circadian rhythms on cerebral blood flow and metabolism.\(^4\) The study was carried out in a quiet room, with subjects lying in a supine position, after a 15-minute rest period. After all sonographic studies were complete, blood pressure and heart rate were measured and 10 mL of blood was sampled to determine hematocrit, hemoglobin, and plasma concentration of \( \beta \)-estradiol and progesterone. The concentration of these hormones was measured immediately by an automated chemiluminescence system (ACS 180PLUS Immunnoassay; Bayer). Precision of measurements, expressed as coefficient of variation, provided by the manufacturer for progesterone and \( \beta \)-estradiol was less than 12% and 9%, respectively.

**Duplex Sonography of Carotid Arteries**

We used a 7.5-MHz linear array transducer (Toshiba SSH 140, Toshiba Medical System Division), and our technique of examination was similar to that of Scheel et al.\(^5\) To avoid interobserver error, all examinations were performed by one investigator. The common carotid artery (CCA), internal carotid artery (ICA), and external carotid artery (ECA) were examined on both sides with a gray-scale, pulsed Doppler and color Doppler flow imaging. The sample volume, adjusted to the size of an insonated vessel, was placed within the ICA and ECA at 15 to 20 mm distal to the CCA bifurcation, respectively. To obtain waveforms from the CCA, the sample was placed at 10 to 20 mm below the bifurcation. The mean, peak systolic, and end-diastolic velocities were obtained by manually tracing the maximum frequency envelope of the Doppler waveform over completed cycles. Manual tracing was chosen deliberately to avoid possible errors associated with inadequate signal-to-noise ratio. The values of all Doppler parameters were standardized by relating them to the base value of average velocities from 2 initial examinations (days 3 and 6) and are given as percentages.

The cross-sectional areas of the arteries were measured on magnified, high-resolution gray-scale transverse images taken from the sites of velocity sampling. The measurement was obtained by manual tracing of the hypoechoic lumen, surrounded by the bright intimar layers. With the use of cine mode function, the lumen of a vessel was measured in systole and diastole.

**Statistical Analyses**

All data were analyzed on a personal computer with statistical software (SYSTAT for Windows [Microsoft]). Because distribution of both hormone concentrations and flow velocities was clearly skewed in some days of the cycle (Figure 1), we decided to use nonparametric tests for hypotheses testing and consistently median-based graphic presentation of the results. The Friedman 2-way repeated-measures ANOVA was used to test hypotheses regarding the homogeneity of blood flow Doppler parameters across the cycle. If significant differences were observed, a Wilcoxon signed rank test was performed. Levels of probability \(<0.05\) were considered statistically significant. Distributions of the cross-sectional areas of the vessels were symmetrical, so their comparisons were performed with the \( t \) test. To quantify the relation between estrogen concentration and flow velocities, the Spearman correlation coefficient and regression equation were calculated for the follicular phase because the distribution of the variables could only be approximated to a linear model over this period.

**Results**

Plasma levels of \( \beta \)-estradiol and progesterone appear in Figure 1. The concentration of estrogen was found to increase throughout the follicular phase of the cycle and to reach a peak of 150 to 300 pg/mL at approximately day 14. At the same time, the concentration of progesterone remained \(<1\) ng/mL. Increases in progesterone concentration above this level, together with a collapse of the dominant follicle and/or appearance of free fluid in the cul-de-sac, specified the day of ovulation. This usually occurred on the day after the estrogen concentration reached its peak. On the subsequent 3 days, the concentration of estrogen decreased abruptly to a level of 50 to 80 pg/mL and then rose again to a median value of 119 pg/mL at the mid-luteal phase of the cycle. The level of hematocrit, hemoglobin, and heart rate remained stable throughout the cycle (Table 1). There were no statistically significant changes in the systolic blood pressure in contrast to the diastolic pressure, which diminished by 5 to 7 mm Hg after days 14 and 15, that is, along the entire luteal phase. Descriptive characteristics of these variables during the follicular plateau of estrogen (day 3), periovulatory estrogen peak (day 14) during the luteal decline of estrogen (day 17), and during the mid-luteal plateau of this hormone (days 20 and 24) are given in Table 1.

Estimation of the cross-sectional area of the ECA was difficult in some subjects because of the anatomic tortuosity of this vessel and its early branching. The cross-sectional areas of the ICA and CCA, as determined at systolic and diastolic phases of the heart cycle, remained stable throughout the menstrual cycle. Therefore, the values of blood flow velocities within these vessels can be regarded as being proportional to blood flow rate. Nevertheless, the cross-sectional area of both of the vessels examined fluctuated significantly across the heart cycle. On the basis of 308 measurements, we have estimated this difference to be on average \( 22.8\pm10.4\% \) (30.7±5.1 mm\(^2\) in systole and 25±4.5 mm\(^2\) in diastole, \( t=14, P<0.01 \)) for the CCA and...
TABLE 1. Physiological Variables During Follicular Plateau of Estrogen (Day 3), During Periovulatory Estrogen Peak (Day 14), During Luteal Decline of Estrogen (Day 17), and During Mid-Luteal Plateau of This Hormone (Days 20 and 24) in 14 Young, Healthy Women

<table>
<thead>
<tr>
<th></th>
<th>Day 3</th>
<th>Day 14</th>
<th>Day 17</th>
<th>Day 20</th>
<th>Day 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, bpm</td>
<td>67±8</td>
<td>68±5</td>
<td>69±4</td>
<td>68±6</td>
<td>71±5</td>
</tr>
<tr>
<td>Systolic AP, mm Hg</td>
<td>113±9</td>
<td>113±8</td>
<td>109±9</td>
<td>109±10</td>
<td>112±10</td>
</tr>
<tr>
<td>Diastolic AP, mm Hg</td>
<td>75±8</td>
<td>72±4</td>
<td>72±7</td>
<td>69.6*</td>
<td>70.5*</td>
</tr>
<tr>
<td>Hgb, g/dL</td>
<td>12.5±1.3</td>
<td>12.5±0.8</td>
<td>12.4±1.6</td>
<td>12.1±0.9</td>
<td>12.6±0.9</td>
</tr>
<tr>
<td>Hct, %</td>
<td>37.6±3.6</td>
<td>37.8±2.3</td>
<td>37.4±3.5</td>
<td>37.3±3.4</td>
<td>38.2±2.9</td>
</tr>
<tr>
<td>17β-Estradiol, pg/mL</td>
<td>19±17</td>
<td>225±53*</td>
<td>69±20*</td>
<td>118±47*</td>
<td>122±64*</td>
</tr>
<tr>
<td>Progesterone, ng/mL</td>
<td>0.8±0.3</td>
<td>0.8±0.3</td>
<td>2.4±0.7*</td>
<td>8.4±3.6*</td>
<td>11.0±4.3*</td>
</tr>
</tbody>
</table>

AP indicates arterial pressure; Hgb, hemoglobin; and Hct, hematocrit.
Values are mean±SD.
*Values significantly different from day 3, P<0.05 (Wilcoxon test).

12.4±13.1% (14.5±3.4 mm² in systole and 12.9±2.9 mm² in diastole, t=6, P<0.01) for the ICA. Because the changes in vessel caliber throughout the heart cycle were substantial, we have refrained from transforming our velocity measurements into blood flow volume, according to the method of Scheel et al. These methodological shortcomings of Scheel’s method might be overcome with the use of an algorithm described recently by Ho and Metreweli and by Juul et al., but we do not have access to the technical options used by these authors.

As shown in Figures 1 and 2 and Table 2, blood flow velocities in the arteries examined display substantial fluctuations throughout the menstrual cycle. In the follicular phase, the end-diastolic velocity rose gradually in the ICA along with the concentration of estrogen. Both variables reached statistically significant differences in comparison to their base values after day 10 of the cycle with the exception of day 17, in which the flow velocity approached its base level. The variables reached their maximum on day 14 of the cycle and then abruptly declined after ovulation to rise again in the mid-luteal phase. As seen in Figure 1, the shape of the curve of standardized end-diastolic velocity in the ICA and that of estrogen concentration showed similar trends. The Spearman correlation coefficient of these variables, calculated for the follicular phase, amounted to 0.65. The linear regression equation for these variables was as follows: velocity (%) = 100.7 + 0.061 × estrogen concentration (P < 0.01). The course of the mean flow velocity in the ICA resembled that of the end-diastolic velocity, as the latter contributes mainly to the mean velocity (Figure 2). The correlation coefficient between estrogen concentration and standardized mean flow velocity in the ICA amounted to 0.59. The linear regression equation for these variables was as follows: velocity (%) = 100.6 + 0.056 × estrogen concentration (P<0.01). In contrast to the end-diastolic and mean velocities, the systolic blood flow velocity within the ICA fluctuated minimally throughout the menstrual cycle (Figure 2). The median value of this variable reached a statistically significant level of 7% increase from the base value on days 14 and 15. Its correlation with estrogen concentration in the follicular phase amounted only to 0.15.

The flow in the ECA showed a pattern different from that of the ICA. The end-diastolic velocity in this artery tended to decrease from its base value, and on days 20 to 24 this difference reached statistical significance (Figure 1 and Table 2). A small, nonsignificant peak of its periovulatory increase appeared on the same days as a peak of the maximal velocity in all the carotid arteries and was of similar magnitude (Figure 2 and Table 2). This supports a notion that its presence was related to increased cardiac output in these days. The mean velocity in the ECA showed a trend similar to the end-diastolic velocity (Figures 1 and 2). In general, both the end-diastolic and mean velocity appeared to show disparate trends in the ECA and ICA throughout the cycle, and the differences in their relative values were found to reach a level of statistical significance on days 10 to 14 and 20 to 24. To highlight these differences on the Figures, the courses of the velocities in the ICA have been superimposed on the plot of the velocities in the ECA as thin dotted lines. The peak systole velocity in the ECA decreased slightly along the follicular phase, and this trend reverted only as a result of the periovulatory increase in cardiac output.

Discussion

With the use of the duplex Doppler technique for the assessment of hemodynamics in the extracranial arteries, the spectrum of blood flow velocities within these arteries can be obtained. It has been shown that the volume of blood, flowing through the internal carotid artery to the brain, can be estimated reliably as a product of mean flow velocity and cross-sectional area of the artery. Therefore, the flow velocity obtained in our study is in proportion to cerebral blood flow within the territory supplied by the internal carotid artery, because we found that the systolic and diastolic caliber of the common and internal carotid arteries remained fairly stable during the entire menstrual cycle. This finding is in line with observations of Valdueza et al and Serrador et al, who found constant caliber of the middle cerebral artery throughout different phases of cerebral autoregulation. There is a consensus that the peak flow velocity, associated with systole, remains in direct proportion to the stroke volume of the left cardiac ventricle, whereas the end-diastolic velocity increases with decreasing resistance of the vasculature supplied by the examined artery. Thus, our results indicate that the blood velocities within the carotid arteries
and consequently the flow within their territories vary considerably throughout the menstrual cycle. These findings may contribute to the explanation of higher variability of blood flow velocities and flow volume in premenopausal women compared with age-matched men.1,4,26

Differences in cerebral blood flow velocities have been found in studies comparing the follicular and luteal phases of the cycle,27,28 but as far as we are aware no study has been published on cerebral hemodynamics across the entire cycle and particularly in relation to the hormonal status of women. “Blind” comparison of hormone-related events between the follicular and luteal phases may lead to confusion because not only the overall length of the luteal phase but also incidence and magnitude of the estrogen peak vary considerably, and in some of our subjects ovulation occurred as late as 7 days before menses. This may explain why some studies reported no differences in blood flow velocities in the ICA between the follicular and luteal phases of the cycle.27

Determination of potential differences in Doppler flow parameters in the carotid arteries across the menstrual cycle has proved not to be straightforward. The differences we observed appear quite substantial if expressed as a percentage of their base value. If taken as absolute figures, they were as small as 1 to 2 cm/s for the end-diastolic velocity (Table 2). Therefore, strict standardization of both technique and conditions of examination was crucial in this study, as stated in the section on Subjects and Methods.

The follicular phase of the cycle provides a convenient model for adequate separation of the possible effect of 17β-estradiol and progesterone on cerebral circulation. This is because the concentration of estrogen rises gradually in this phase to reach levels ≈20 times higher than during menses, whereas the concentration of progesterone remains low and stable.17 Therefore, the overall increase in mean flow velocity within the ICA and consequently the increase of blood flow volume can be related to the level of estrogen.

The average increase in flow during the follicular phase was 15% and sometimes as high as 25% in single subjects, whereas the correlation coefficient between mean flow velocity in the ICA and estrogen concentration was found to reach a figure of 0.59 for the standardized values. Assuming a linear model of regression, a 10-fold increase in concentration of 17β-estradiol is associated with an increase in flow velocity of ≈6%. An increase of similar magnitude for cerebral blood flow (15% to 20%) was found in ovariectomized rats after supplementation of the estrogen to levels seen normally during proestrus.29 In a recent study,30 17β-estradiol dilated rabbit pial vessels by ≈15%. Furthermore, the circulation level of nitric oxide (NO) metabolites in healthy fertile women examined throughout the menstrual cycle was found to increase by ≈20% in mid-cycle; NO is considered to be the agent by which estrogen dilates vessels, consequently promoting flow through the vascular tree.31,32

Because the peak systolic velocity in the ICA increased only minimally, the majority of the increment in blood flow volume appeared to be the result of a rise in the end-diastolic

Figure 1. Concentration of progesterone, 17β-estradiol, and end-diastolic velocity in ICA and ECA during menstrual cycle in 14 young, healthy women. Velocity values are expressed as percent of base value; latter calculated as average of 2 initial examinations (days 3 and 6). Course of velocity in ICA has been superimposed on plot of velocities in ECA as thin dotted line to better visualize difference in trends across cycle. Box-and-whisker graphs represent distribution of daily values. Edges of central box delimit quartiles; circle inside, median of batch. Outlying and far-outlying values are marked with asterisk and open circle, respectively.
velocity. Consequently, this finding convincingly supports the notion that the increased flow volume through the ICA, associated with high concentrations of plasma estrogen, is caused mainly by a decrease in peripheral vascular resistance.15,27,33,34 It could be argued, however, that the observed increase in blood flow velocity in the ICA is caused by decreased resistance of the artery itself. This argument is countered by our observations, which confirmed that the caliber of the carotid arteries remains stable throughout the menstrual cycle. The observed increase of flow velocity in the ICA could have been caused only by contraction of this vessel if the primary site of action of estrogen was the wall of the ICA. However, no vasocontractile properties of estrogen have been described, and this strengthens our premise that estrogen acts mainly on cerebrovascular smooth muscles. Generally, it is commonly accepted that arterioles and capillaries dissipate most of the pressure and therefore are responsible for most of the resistance to the flow of blood. Thus, regulatory mechanisms must be targeted to this segment of the vascular tree to be effective.

That the site of action of estrogen is within the brain rather than in the wall of the carotid artery is also supported by recent reports that estrogen increases the activity of the neuronal NO synthase rather than endothelial NO synthase.35,36 These studies suggest that many regions of the brain, such as the hippocampus and the striatum, are rich in neuronal NO synthase, whereas in peripheral arteries vasodilation most likely occurs through activation of the endothelial NO synthase.

Estrogen-related increases in flow through the ICA in the follicular phase were accompanied by barely traceable (1%) increases in flow volume within the CCA up to day 13. During the ovulatory maximum of estrogen, the peak systolic velocity increased slightly but noticeably in all the arteries examined, including the CCA. These findings indirectly support the argument that increased cardiac output contributed only minimally to the observed increase in flow volume in the ICA, and this slight influence was mainly limited to the phase of ovulation. Because the lumen of the CCA is approximately twice that of the ICA, the observed 2% of flow increase in the CCA on day 14 can cover at most only 25% to 50% of flow increase in the ICA (Table 2). The rest appears to be covered at the expense of flow in the external carotid artery. This result strengthens the notion that estrogen-related increases in carotid flow are caused mainly by a decrease in cerebral vascular resistance.

Some authors suggest that flow velocity may be related to changes in blood viscosity, hematocrit level, or both.10,37 In our subjects, the levels of hematocrit and hemoglobin remained fairly stable throughout the cycle, as did the systolic blood pressure. The diastolic blood pressure, which is related to peripheral vascular resistance,38 decreased in the luteal phase by 5 to 7 mm Hg ($P<0.05$). Thus, it appears that from among the factors we controlled in our setup, predominantly a decrease in systemic and cerebral vascular resistance was responsible for estrogen-associated augmentation of blood flow through the ICA. Any possible increases in stroke volume and/or reduced blood viscosity appear to be less important.

In parallel with the increase in flow in the ICA, the flow in the ECA actually decreased, and this trend was maintained throughout the luteal phase. This relative decrease in flow in the ECA, which prevailed throughout most of the cycle, was also noticed in the women studied by Scheel et al.5 This phenomenon is apparently caused by a redistribution of flow between the ICA and ECA. Relatively small increases in the flow in the CCA and the stable diameter of the carotid arteries, combined with decreased microvascular resistance in the territory supplied by the ICA, must inevitably produce a

### TABLE 2. Blood Flow Velocities in Carotid Arteries During Follicular Plateau of Estrogen (Day 3), During Periovulatory Estrogen Peak (Day 14), During Luteal Decline of Estrogen (Day 17), and During Mid-Luteal Plateau of This Hormone (Days 20 and 24) in 14 Young, Healthy Women

<table>
<thead>
<tr>
<th></th>
<th>Velocities</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 3</td>
<td>Day 14</td>
<td>Day 17</td>
<td>Day 20</td>
</tr>
<tr>
<td>ICA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-diastolic</td>
<td>28±3 (28)</td>
<td>33±3 (33)*</td>
<td>29±4 (30)</td>
<td>31±5 (32)*</td>
</tr>
<tr>
<td>Mean</td>
<td>42±5 (43)</td>
<td>48±5 (49)*</td>
<td>44±6 (44)</td>
<td>47±7 (49)*</td>
</tr>
<tr>
<td>Peak systolic</td>
<td>72±15 (75)</td>
<td>78±13 (80)</td>
<td>73±11 (67)</td>
<td>78±13 (77)</td>
</tr>
<tr>
<td>ECA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-diastolic</td>
<td>13±4 (13)</td>
<td>12±3 (13)</td>
<td>12±2 (12)</td>
<td>11±2 (11)*</td>
</tr>
<tr>
<td>Mean</td>
<td>28±5 (28)</td>
<td>28±5 (28)</td>
<td>26±3 (27)</td>
<td>26±3 (26)</td>
</tr>
<tr>
<td>Peak systolic</td>
<td>72±14 (68)</td>
<td>75±15 (76)</td>
<td>67±7 (67)</td>
<td>73±6 (75)</td>
</tr>
<tr>
<td>CCA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>42±4 (43)</td>
<td>43±5 (43)</td>
<td>43±5 (43)</td>
<td>43±3 (43)</td>
</tr>
<tr>
<td>Peak systolic</td>
<td>99±16 (95)</td>
<td>101±16 (104)</td>
<td>100±19 (101)</td>
<td>104±12 (105)</td>
</tr>
</tbody>
</table>

Values (in cm/s) are mean±SD (median).

*Values significantly different from day 3, $P<0.05$ (Wilcoxon signed rank sum test).
decrease in flow volume through the ECA—an effect that was actually found in our subjects.

Our results support the notion that the brain, in contrast to the structures supplied by the ECA, is a target organ for estrogen. Therefore, when exposed to a high concentration and/or abrupt fluctuations of estrogen, the brain is likely to undergo redistribution of blood flow similar to that occurring between the two branches of the CCA. In other words, regions rich in estrogen receptors may “steal” blood from regions poorly endowed with these receptors. This can play a role in the pathogenesis of menstrual cycle–related epilepsy and migraine, as it has been shown that these clinical events may be triggered by a slight reduction of flow within certain regions of the brain.

In summary, we have demonstrated that fluctuations of endogenous estrogen across the menstrual cycle are associated with substantial changes in blood flow volume in the ICA. Mainly decreased vascular resistance within the brain causes the estrogen-related promotion of flow. Along with high concentrations of plasma estrogen in the luteal phase, the flow in the ECA actually decreases, to supplement the volume of blood in the territory of the ICA.

Acknowledgments

This study was supported by Białystok Medical Academy grant No. 4-27989. The authors thank Dr Nabil Alkayed of Johns Hopkins Medical Institutions for his help in revision of the manuscript.

References


Figure 2. Peak systolic and mean velocity in ICA and ECA during menstrual cycle in 14 young, healthy women. Presentation of results are as in Figure 1.


Effect of Endogenous Estrogen on Blood Flow Through Carotid Arteries
Jaroslaw Krejza, Zenon Mariak, Magdalena Huba, Sławomir Wolczynski and Janusz Lewko

Stroke. 2001;32:30-36
doi: 10.1161/01.STR.32.1.30
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2001 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/32/1/30