Pediatric Stroke Belt
Geographic Variation in Stroke Mortality in US Children
Heather J. Fullerton, MD; Jacob S. Elkins, MD; S. Claiborne Johnston, MD, PhD

Background and Purpose—Numerous studies have demonstrated higher stroke mortality rates in adults residing in the Southeastern United States (the “Stroke Belt”). If the Stroke Belt is solely caused by regional differences in atherosclerotic stroke risk factors, it should not apply to children.

Methods—For the years 1979 to 1998, we determined rates of death from stroke in children <20 years of age based on death certificates, and compared age-adjusted stroke mortality rates in 11 Stroke Belt states versus other US states. For comparison, the same methods were applied to adults.

Results—Children in Stroke Belt states have an increased risk of death from stroke compared with children in other states (relative risk [RR], 1.21; 95% CI, 1.12 to 1.29). The greater risk in Stroke Belt states was apparent for ischemic and hemorrhagic stroke, for all age groups and both sexes, and persisted after adjustment for ethnicity. The geographic disparity in children was similar in magnitude to that in adults.

Conclusions—Similar to adults, children in Stroke Belt states have a higher risk of death from stroke than children in other US states. Stroke risk factors that are applicable to both children and adults should be considered in attempts to explain this geographic variation. (Stroke. 2004;35:1570-1573.)

Key Words: child ■ mortality ■ stroke ■ Southeastern United States

Geographic variation in stroke mortality rates in US adults was first appreciated in the 1960s with a report of higher stroke mortality rates in a cluster of Southeastern states.1 The existence of the so-called Stroke Belt has been confirmed by other investigators, and explanations for this geographic variation have been extensively sought.2–8 Many reports have suggested that the Stroke Belt is caused by geographic differences in atherosclerotic stroke risk factors, such as hypertension, diabetes, obesity, and smoking.6,7,9 Hypertension has been particularly implicated, with several studies demonstrating higher rates of hypertension in the Southern US.6,10–12

Recognized atherosclerotic stroke risk factors appear to be unimportant in the pathophysiology of childhood stroke.13–16 Known risk factors for stroke in children are many and varied, including hematological disorders such as sickle cell disease, congenital heart disease, hereditary prothrombotic states, central nervous system infections, and chicken pox, among others.13–18 However, even in recent series, up to 60% of strokes in children are idiopathic,16 suggesting that our understanding of risk factors for stroke in children remains limited.

Although atherosclerotic stroke risk factors are commonly implicated in attempts to explain the Stroke Belt, some investigators have argued that these factors explain only part of the geographic variation, and that other factors (socioeconomic status, environmental toxicity, genetic variation, delivery of healthcare) may contribute.6,8,19 An analysis of geographic variation in childhood stroke mortality could shed light on this issue. If the Stroke Belt observed in adults is solely caused by differences in atherosclerotic stroke risk factors, one would expect to find no parallel geographic variation in childhood stroke mortality rates. Conversely, the existence of a “Pediatric Stroke Belt” would suggest that alternative explanations, applicable to children and adults, should be sought.

Methods

After obtaining approval from the University of California, San Francisco Institutional Review Board, we analyzed US death certificate data from the National Center for Health Statistics (NCHS)20 to determine rates of death from childhood stroke from 1979 to 1998 in Stroke Belt states versus other US states. These publicly available mortality databases contain information on primary cause of death as listed on death certificates. Deaths due to stroke were identified using the following International Classification of Disease, 9th revision (ICD-9) codes, which have been associated with a high sensitivity for stroke when used as discharge codes:11,22: for hemorrhagic stroke, 431 (intracerebral hemorrhage) and 430 (subarachnoid hemorrhage); for ischemic stroke, 433 (occlusion and stenosis of precerebral arteries), 434 (occlusion of cerebral arteries), 436 (acute,
but ill-defined, cerebrovascular disease), and 437.6 (nonpyogenic thrombosis of intracranial venous sinus).

We used a previously published definition for the geographic boundaries of the Stroke Belt, which includes 11 Southeastern states (Alabama, Arkansas, Georgia, Indiana, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee, and Virginia). Residents of Washington, DC, were included among the "other US states." Childhood was defined as <20 years of age and included the neonatal period (the first month of life). The ethnicity classification system of the NCHS from 1977 is used for this database; individuals were classified into 1 of 3 groups: black, white, or "other" (includes American Indian or Alaska Native and Asian or Pacific Islander). People of Hispanic origin are considered to be "of any race" by this classification system; white Hispanics are classified as "white" and black Hispanics are classified as "black." Mortality rates for infants (<1 year of age) were calculated as the number of deaths per 100 000 live births. Mortality rates for all other ages were calculated as the number of deaths per 100 000 people in that population. Age-, race-, gender-, and state-specific population data were obtained from the US Census Bureau. Person-years were defined as the average number of persons in a category, multiplied by the number of years of study. All mortality rates were age-adjusted to the 2000 US population by direct method of standardization. For comparison, stroke mortality in adults (>25 years) in Stroke Belt states versus other US states was analyzed using the same methodology.

### Results

The Stroke Belt states accounted for 21% of the person-years included in the study (302 590 882 person-years in Stroke Belt states versus 1 459 529 242 in other US states). Black children constituted a higher percentage of the Stroke Belt population compared with other US states, although gender and age distributions were similar (Table 1). In the study period, a total of 4569 childhood deaths were attributed to stroke in the US; 24% occurred in Stroke Belt states. Age-adjusted childhood stroke mortality rates stratified by geographic region, stroke subtype, ethnicity, and gender are shown in Table 2. Overall, children in Stroke Belt states had a 21% increased risk of death from stroke compared with children residing in other US states; a similar relative risk was found in adults. This geographic disparity was observed for both hemorrhagic and ischemic stroke subtypes, and for both sexes. It was also observed for all age groups (Figure).

### Table 1. Demographics of US Children in Stroke-Belt States Versus Other States 1979–1998

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Stroke Belt States</th>
<th>Other States</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Person-Years %</td>
<td>Person-Years %</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>80 216 983 27</td>
<td>142 005 464 12</td>
</tr>
<tr>
<td>White</td>
<td>217 846 948 72</td>
<td>958 825 160 83</td>
</tr>
<tr>
<td>Female</td>
<td>147 917 781 49</td>
<td>564 751 880 49</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–4</td>
<td>74 049 470 24</td>
<td>295 569 080 26</td>
</tr>
<tr>
<td>5–9</td>
<td>73 061 406 24</td>
<td>281 782 080 24</td>
</tr>
<tr>
<td>10–14</td>
<td>75 120 551 25</td>
<td>282 745 000 24</td>
</tr>
<tr>
<td>15–19</td>
<td>80 359 455 27</td>
<td>296 842 200 26</td>
</tr>
</tbody>
</table>

### Table 2. Childhood Stroke Mortality Rates* in Stroke-Belt States Compared to Other US States Stratified By Ethnicity, Gender, and Stroke Subtype

<table>
<thead>
<tr>
<th></th>
<th>Children</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mortality Rates</td>
<td>RR</td>
</tr>
<tr>
<td>Overall</td>
<td>0.354 0.294</td>
<td>1.21</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>0.296 0.269</td>
<td>1.10</td>
</tr>
<tr>
<td>Black</td>
<td>0.526 0.470</td>
<td>1.12</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>0.373 0.319</td>
<td>1.16</td>
</tr>
<tr>
<td>Girls</td>
<td>0.335 0.267</td>
<td>1.25</td>
</tr>
<tr>
<td>Stroke subtype</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>0.100 0.079</td>
<td>1.27</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>0.253 0.214</td>
<td>1.18</td>
</tr>
</tbody>
</table>

*Deaths per 100 000 person-years; age adjusted to 2000 US population. RR indicates relative risk (stroke belt vs other states); values for adults shown for comparison.
After adjustment for ethnicity, the overall RR for stroke death in children in Stroke Belt states versus other US states declined, but remained significant: 1.10 (95% CI, 1.03 to 1.18, \( P = 0.005 \); data not shown), compared with the preadjustment RR of 1.21 (95% CI, 1.12 to 1.29, \( P < 0.0001 \); Table 2). After stratification by ethnicity, white children in Stroke Belt states had a significantly higher stroke mortality rate than those in other states (\( P = 0.03 \); Table 2); a similar trend was seen in black children, but did not reach significance (\( P = 0.07 \)).

Discussion

Although the Stroke Belt has been recognized since the 1960s, and has persisted since then, the geographic distribution of childhood stroke mortality has not been studied. The results of our investigation suggest that the Stroke Belt is not exclusive to adults—mortality rates from stroke are also higher in children residing in the Southeastern US compared with those in other US states. These findings suggest that potential explanations for the Stroke Belt, the source of which has remained elusive, should be reconsidered in light of this similar geographic disparity in children. Of note, in considering potential sources of the Stroke Belt, one should also keep in mind that (1) the Stroke Belt refers to excess mortality from both ischemic and hemorrhagic stroke, so factors contributing to both stroke subtypes should be considered, and (2) geographic differences in stroke mortality could reflect either geographic differences in stroke incidence or case fatality.

One possible explanation for the Stroke Belt is geographic variation in ethnicity. The Southeastern US has a higher proportion of blacks, and an association between black ethnicity and an increased risk for hemorrhagic and ischemic stroke incidence and mortality has been documented, in both adults and children.\(^{28-33}\) However, studies in adults have demonstrated that the geographic variation in stroke mortality rates persists after stratification by ethnicity.\(^2,7\) We found that the ethnicity-adjusted overall RR for Stroke Belt states versus other US states (1.10) was lower than the unadjusted RR (1.20), suggesting that ethnicity was contributing to the presence of the Stroke Belt in children. However, the ethnicity-adjusted RR was still significant (\( P = 0.005 \)) and, after stratification by ethnicity, a significant geographic disparity persisted among white children with a similar trend among black children. Thus, ethnicity alone does not fully explain the geographic variation in risk that we observed.

Another commonly proposed explanation for the Stroke Belt is geographic variation in atherosclerotic stroke risk factors, such as hypertension, diabetes, and smoking.\(^6\) Factors applicable to both hemorrhagic and ischemic stroke (such as hypertension and smoking) are particularly pertinent. Studies of regional disparities in hypertension have suggested that the prevalence of hypertension is higher in the Southern US.\(^{10-12}\)

In addition, this geographic variation in hypertension has been inferred from the pattern of other hypertension-related conditions, such as end-staged renal disease and congestive heart failure.\(^34\) Our results, however, suggest that the Stroke Belt cannot be explained solely by geographic variation in atherosclerotic stroke risk factors. Although risk factors for childhood stroke are not well understood, atherosclerotic stroke risk factors, including hypertension, do not appear to play a significant role in the pathophysiology of stroke in children.\(^15\) Therefore, geographic variations in such risk factors would not explain the “Pediatric Stroke Belt” that we observed.

Additional evidence suggests that the excess risk for stroke mortality in residents of the Southeastern US precedes exposure to atherosclerotic stroke risk factors. A recent study demonstrated the importance of nativity on Stroke Belt mortality.\(^35\) Regardless of race, gender, or socioeconomic status, residents of South Carolina that were born in South Carolina had higher proportions of stroke deaths than residents of South Carolina born outside of the Southeast. Furthermore, the geographic distribution of stroke mortality is different for immigrants to the US, with highest rates in the West among white immigrants, and in the Northeast among black immigrants.\(^36\)

Other potential explanations for the Stroke Belt include differences in environmental properties of the Southeast, such as softness of the water and toxins in the soil, including lead and cadmium.\(^6,19\) Although there is no evidence that such factors are associated with an increased risk for childhood stroke, it is conceivable that environmental exposures could lead to geographic variation in stroke risk in children and adults. However, evidence that the Stroke Belt is “shifting” westward has led some authors to suggest that such physical factors are an unlikely explanation for the Stroke Belt.\(^19\)

Socioeconomic status and its corollary, access to preventative and therapeutic health care, could also contribute to geographic variations in stroke mortality in adults and children, and would be applicable to excess mortality from both ischemic and hemorrhagic stroke. Low socioeconomic status is associated with increased risk for stroke mortality in adults.\(^6,37\) Although a study of childhood stroke failed to find a similar association,\(^33\) socioeconomic status remains a potential explanation for the Stroke Belt. Finally, it is possible that regional differences in genetic susceptibility to stroke, unrelated to hypertension or other atherosclerotic stroke risk factors, may contribute to the geographic variation in stroke mortality. However, a recent study in the US found no evidence that geography had a significant impact on genetic variation within several different ethnic groups.\(^38\) Geographic differences in cultural or environmental factors may therefore be of greater importance to the observed regional disparities in disease susceptibility. Our study is limited by its use of data derived from death certificates. Criteria for death certificate diagnoses are not clearly defined, and diagnosis may vary depending on the extent of work-up performed, the clinician completing the death certificate, and the administrator responsible for assigning an ICD-9 code to a diagnosis. However, when used as discharge codes, the primary ICD-9 codes used in our study (430, 431, 433, 434, 436) have been shown to have a true-positive rate for stroke of 83% in adults.\(^2\) In addition, death certificate diagnosis of stroke has been shown to have a specificity of 95% for hemorrhagic stroke and 98% for ischemic stroke.\(^19\) An additional limitation is that, because the
database includes only the primary cause of death, we could not analyze the specific etiologies of fatal stroke in children. Despite these limitations, our findings support the existence of a "Pediatric Stroke Belt," and suggest that attempts to explain the Stroke Belt should incorporate risk factors applicable to both children and adults.

Acknowledgments
This work was supported by the Neurological Sciences Academic Development Award from the the National Institute of Neurological Disorders and Stroke (NINDS) (K12 NS01692–05).

References

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Stroke. 2004;35:1570-1573; originally published online June 3, 2004;
doi: 10.1161/01.STR.0000130514.21773.95
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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World Wide Web at:
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