SUMMARY Regional cerebral blood flow (bicompartmental and stochastic method) was measured in a series of 20 patients with unilateral brain softening. Measurements were repeated during the administration of a vasodilator. A detrimental effect on the perfusion of the diseased area was observed in the majority of cases. It has been shown that the chances for a vasodilator to decrease the perfusion in the diseased area were greater when the angiogram showed obstruction of an intracranial artery.

**Method.** The bicompartmental method provided the values of the flows in the gray matter and white matter of 24 to 34 regions of interest. Their size was 22 x 22 mm. The details of this method were reported elsewhere. In the control measurement, the flows in the gray matter were classified into five groups in relation to the mean of the whole hemisphere: (1) more than 24% higher, (2) 12% to 24% higher, (3) between 12% higher and 12% lower, (4) 12% to 24% lower, and (5) more than 24% lower than the mean (fig. 1A). In the second measurement, made under the action of the vasodilator, the flow in a given area was considered as either "slightly" or "strongly" modified if its value differed by either two and four or by more than four times the standard deviation of the measurement made in the same area before the drug administration (figs. 1B and 2A).

The stochastic method was used for measuring the regional blood flows in every channel of the 64 x 64 matrix. The image of the explored hemisphere is thus divided into 600 to 800 individual areas, the size of which is 4.5 x 4.5 mm on the skull. This second method is less accurate but has the same resolution as a static gamma camera image. It is entirely automated as described previously.

**Pharmacological Tests.** The following drugs were investigated: in patient series F, halothane, 1% in O2-N2O gas mixture (Fluothane®, I.C.I.); in patient series P, papaverine chloride, 100 mg in i.v. drip; in patient series D, methoxy-6-quinolil-4-V-vinil-2 piperidyl-5-3-propanol-I-chlorhydrate, 80 mg in i.v. drip (Desclidium®, S.P.R.E.T.); and in patient series V, vincamine chloride, 40 mg in i.v. drip (Pervone®, Millot Laboratories, France). Each drug was administered for 30 minutes after the end of the first measurement and continued for the duration of the second measurement.

**Results.** The location of the brain softening, as determined from clinical data, was in the territory of the anterior cerebral artery in one patient (hemiparesis prominent in lower limb), in the territory of the middle cerebral artery in 17 patients (hemiplegia and/or hemianesthesia) and in the territory of the posterior cerebral artery in one patient (hemianopia).

In two patients (P4 and P6), the angiogram was normal. It showed stenosis of the internal carotid artery in two patients (P1 and P2), stenosis of the anterior cerebral artery in one (P4), displacement of some cerebral arteries (edema?)
FIGURE 1. Relative decrease in flow induced in the diseased area. Patient D1: 43-year-old woman with paresthesias in the right hand, right superior quadrantanopia, and thrombosis of the left rolandic artery. (A) Gray matter flow in 25 regions during control measurement. Flow increased (+) or decreased (−) by more than 24% (black) or by 12% to 23% (hatched) as compared to the mean of the whole hemisphere (Pco2: 39.1 ± 0.56, BP: 84). (B) Increase in flow during perfusion of Descludim® by more than 4 SD (black) or between 2 and 4 SD (hatched) (Pco2: 39.4 ± 0.79, BP: 83). (C) Regional CBF determined by the stochastic method during the control measurement (Pco2: 39.1 ± 0.56, BP: 84). (D) Differential printout of the increases in flow (stochastic method) under the action of Descludim® (Pco2: 39.4 ± 0.39, BP: 83).

in two (P5 and D2), thrombosis of the posterior cerebral artery in one (P3), and complete or partial thrombosis of the middle cerebral artery in all the other patients.

Values of Regional CBF

Individual values of the flows in the various regions of the explored hemisphere were used to establish the "mean" cerebral blood flow (table 1). With the bicompartimental method, the mean value was 44.14 ± 6.47 ml/100 gm per minute for the gray matter and 17.18 ± 2.48 ml/100 gm per minute for the white matter. With the stochastic method, the mean regional CBF was equal to 25.22 ± 5.81 ml/100 gm per minute.

CBF in the Diseased Areas

In the diseased area, the flow in the gray matter was found to be decreased in ten cases, increased in four and not significantly different from the whole of the hemisphere in four. In two cases an increased flow surrounded by ischemia was found in the diseased area. The duration of the disease was 14 ± 10 days in the series of patients with an increased flow and 37 ± 25 days in those with a decreased flow in the softened area.

Effect of the Vasodilators on CBF

The action of the various drugs on the mean blood flow of the hemisphere is shown in table 2.

In the diseased area itself, the CBF was either increased or decreased (fig. 2) or relatively decreased, i.e., unmodified as opposed to an increase in flow in the surrounding normal regions (figs. 1B and D).

As shown in table 2, the results obtained by both measurement procedures were similar except for patients F3 and D1. In Patient D1, a discrepancy was noted between the clinical
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data which suggested a temporal lesion (superior quadrant-
anopia) and the angiogram which demonstrated a throm-
bosis of the rolandic artery (fig. 1).

**Correlation With Angiographical Data**

Thrombosis of one of the cerebral arteries was demonstrated by angiography in 11 patients. In the majority of these (table 2), an unfavorable effect of the drug on the diseased area was shown by the bicompartmental method (eight decreases in flow versus one increase) as well as by the stochastic method (eight decreases in flow versus two increases). In eight patients with no demonstrable arterial thrombosis, opposite proportions were observed: two decreases in flow versus six increases (bicompartmental method) and one decrease in flow versus five increases (stochastic method).

**Discussion**

Recording the radioactivity of the skull with a gamma camera allows the brain surface to be subdivided at will. With the data being stored in a magnetic memory, this subdivision can be modified later; new regions of interest can be chosen according to the clinical data or the results of previous measurements.

When a high resolution is desired, a maximum number of channels (600 to 800) are used. The counting rate in each channel is equal to 60/10 seconds on an average, with a standard deviation of 15%. Of course, the size of the individual areas studied in this way is smaller than the minimum authorized by the resolution of the device, which is approximately 20 × 20 mm. The image of the flow distribution has the same resolution as a static brain scan obtained with the same gamma camera. Areas of similar perfusion thus delineated are made of a certain number of unitary areas which do not differ statistically from their neighbors (fig. 1).

In order to insure precise measurement as well as a maximum discrimination of regional differences in the flows, two methods of calculation were used simultaneously in this work. The results were actually similar in all cases except two (table 2).

The bicompartmental method, yielding specific information on the flow in the gray matter, is used for the determination of abnormal perfusions in the control measurement. Although the distribution of the gray matter flows is uneven in a normal brain, it is even more so for the flows determined by the stochastic method; indeed, they depend essentially on the relative volume of the highly perfused gray matter. A high flow area is normally observed along the upper border of the brain image (corresponding to a two-fold cortical layer) and in the insular region (corresponding to the folds of the insular cortex and the basal ganglia). Nevertheless, the stochastic method, by the differential printout of the two measurements (independent of the gray matter volume) gives valuable information about the redistribution of the flows caused by the vasodilator.

General anesthesia was used to maintain a steady position of the head and stable respiratory parameters with a constant arterial PCO₂. This insures a better reproducibility of the two measurements, as shown previously in a series of six patients. According to the method of Wilkinson et al., the average standard deviation of our two measurements in the

**Table 1 Individual Values of Regional CBF**

<table>
<thead>
<tr>
<th>Case</th>
<th>BPᵃ</th>
<th>FPᵃ</th>
<th>FPᵇ</th>
<th>IPᵃ</th>
<th>IFᵃ</th>
<th>AFᵇ</th>
<th>FWᵇ</th>
<th>∆FWᵇ</th>
<th>rCBFᵇ</th>
<th>∆rCBFᵇ</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>130</td>
<td>117</td>
<td>34.7 ± 0.1</td>
<td>35.6 ± 0.65</td>
<td>35.2</td>
<td>42.7</td>
<td>+21.3</td>
<td>14.0</td>
<td>13.4</td>
<td>-4.3</td>
</tr>
<tr>
<td>F2</td>
<td>68</td>
<td>66</td>
<td>38.1 ± 1.06</td>
<td>41.0 ± 5.65</td>
<td>54.6</td>
<td>56.1</td>
<td>+3.2</td>
<td>18.6</td>
<td>16.7</td>
<td>-10.0</td>
</tr>
<tr>
<td>F3</td>
<td>80</td>
<td>80</td>
<td>34.9 ± 0.14</td>
<td>34.7 ± 0.92</td>
<td>55.0</td>
<td>62.6</td>
<td>+13.8</td>
<td>19.6</td>
<td>18.8</td>
<td>-4.2</td>
</tr>
<tr>
<td>F4</td>
<td>83</td>
<td>42</td>
<td>39.4 ± 1.41</td>
<td>38.7 ± 1.63</td>
<td>43.0</td>
<td>39.0</td>
<td>-9.3</td>
<td>18.7</td>
<td>15.6</td>
<td>-26.7</td>
</tr>
<tr>
<td>F5</td>
<td>65</td>
<td>61</td>
<td>38.5 ± 1.63</td>
<td>37.5 ± 1.0</td>
<td>40.0</td>
<td>62.1</td>
<td>+55.2</td>
<td>15.6</td>
<td>16.0</td>
<td>+2.6</td>
</tr>
<tr>
<td>F6</td>
<td>93</td>
<td>70</td>
<td>38.0 ± 1.06</td>
<td>39.2 ± 0.6</td>
<td>43.0</td>
<td>59.3</td>
<td>+38.0</td>
<td>15.3</td>
<td>13.65</td>
<td>-10.8</td>
</tr>
<tr>
<td>P1</td>
<td>80</td>
<td>70</td>
<td>38.6 ± 0.36</td>
<td>41.8 ± 0.57</td>
<td>51.8</td>
<td>52.7</td>
<td>+2.0</td>
<td>18.8</td>
<td>20.0</td>
<td>+6.8</td>
</tr>
<tr>
<td>P2</td>
<td>75</td>
<td>80</td>
<td>39.8 ± 0.0</td>
<td>39.5 ± 0.48</td>
<td>47.5</td>
<td>47.0</td>
<td>-1.0</td>
<td>21.7</td>
<td>24.2</td>
<td>+1.14</td>
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<tr>
<td>P3</td>
<td>102</td>
<td>100</td>
<td>38.3 ± 0.32</td>
<td>39.9 ± 0.33</td>
<td>40.7</td>
<td>44.4</td>
<td>+9.0</td>
<td>13.6</td>
<td>20.6</td>
<td>+50.7</td>
</tr>
<tr>
<td>P4</td>
<td>77</td>
<td>71</td>
<td>40.2 ± 1.3</td>
<td>41.9 ± 1.0</td>
<td>43.5</td>
<td>56.3</td>
<td>+29.4</td>
<td>21.8</td>
<td>23.4</td>
<td>+7.0</td>
</tr>
<tr>
<td>P5</td>
<td>90</td>
<td>90</td>
<td>37.5 ± 0.1</td>
<td>38.07 ± 0.4</td>
<td>39.7</td>
<td>45.2</td>
<td>+13.7</td>
<td>16.4</td>
<td>16.7</td>
<td>+2.0</td>
</tr>
<tr>
<td>P6</td>
<td>81</td>
<td>77</td>
<td>40.05 ± 1.62</td>
<td>38.9 ± 0.14</td>
<td>43.3</td>
<td>53.4</td>
<td>+23.6</td>
<td>16.0</td>
<td>18.3</td>
<td>+14.4</td>
</tr>
<tr>
<td>D1</td>
<td>84</td>
<td>83</td>
<td>39.1 ± 0.56</td>
<td>39.4 ± 0.79</td>
<td>55.2</td>
<td>53.9</td>
<td>+2.2</td>
<td>18.3</td>
<td>18.6</td>
<td>+2.0</td>
</tr>
<tr>
<td>D2</td>
<td>90</td>
<td>110</td>
<td>37.5 ± 0.28</td>
<td>41.0 ± 0.85</td>
<td>34.9</td>
<td>37.2</td>
<td>+6.6</td>
<td>15.5</td>
<td>15.5</td>
<td>0</td>
</tr>
<tr>
<td>D3</td>
<td>76</td>
<td>82</td>
<td>39.0</td>
<td>38.5 ± 0.78</td>
<td>47.6</td>
<td>47.7</td>
<td>+0.2</td>
<td>16.6</td>
<td>16.8</td>
<td>+1.3</td>
</tr>
<tr>
<td>D5</td>
<td>90</td>
<td>90</td>
<td>40.55 ± 0.64</td>
<td>40.5 ± 0.14</td>
<td>42.1</td>
<td>44.9</td>
<td>+6.4</td>
<td>18.5</td>
<td>17.3</td>
<td>-0.5</td>
</tr>
<tr>
<td>D6</td>
<td>82</td>
<td>90</td>
<td>—</td>
<td>—</td>
<td>40.5</td>
<td>40.1</td>
<td>—</td>
<td>13.6</td>
<td>13.6</td>
<td>23</td>
</tr>
<tr>
<td>V1</td>
<td>82</td>
<td>90</td>
<td>38.25 ± 0.35</td>
<td>39.75 ± 1.77</td>
<td>37.2</td>
<td>43.6</td>
<td>+17.0</td>
<td>16.7</td>
<td>16.5</td>
<td>-1.0</td>
</tr>
<tr>
<td>V3</td>
<td>80</td>
<td>88</td>
<td>38.47 ± 0.35</td>
<td>38.89 ± 0.27</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>20</td>
</tr>
<tr>
<td>V4</td>
<td>75</td>
<td>87</td>
<td>38.7</td>
<td>35</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>20</td>
</tr>
</tbody>
</table>

Mean values: 44.14 ± 6.47, 17.18 ± 2.48, 25.22 ± 5.81

BP: mean arterial blood pressure, FP: average flow in gray matter, FW: average flow in white matter, rCBF: average flow determined by the stochastic method, ∆FG, ∆FW, ∆rCBF: variations in average flows (in percentage), 1st = first measurement, 2nd = second measurement.
same region was found to be 6.2\% for the flow in the gray matter and 7.7\% for the flow in the white matter. 7

The average values obtained for the regional cerebral blood flows (25.22 ml/100 gm per minute) are definitely lower than normal. This is not due to a reduction of brain metabolism under general anesthesia because the same method, applied under local anesthesia in a series of six patients (mean age 63 years) with a brain tumor, yielded similar values for regional CBF (28.31 ± 7.67 ml/100 gm per minute). 9 It is more likely due to a general reduction of the perfusion of the whole hemisphere, as usually noted in regional brain ischemia. 10

In addition, the values obtained for the flows are lower when the duration of the washout recording is longer. This duration was 15 to 17 minutes for the bicompartamental method instead of 10 minutes or less which is commonly used by others. In a series of ten patients, Charlet and Marc-Vergnes 11 obtained gray matter flows of either 66 ± 7.56 ml or 45.9 ± 2.42 ml according to a recording duration of either 10 or 15.5 minutes. Our investigation was devoted to the redistribution of the flows under the action of the vasodilators and not to the absolute determination of the flows.

We are aware that the method used for localizing the lesion being based on clinical data is open to criticism. Since none of our patients died during the period of observation, no correlation has been made between clinical and pathological data.

In the control measurement, the perfusion of the diseased area was found to be decreased in ten cases and increased in four. Increased perfusion was indeed observed in cases investigated earlier after the stroke (14 ± 10 days instead of 37 ± 25 days), but our difference in delay between the two groups is not as marked as in the data published by Paulson. 12

Halothane decreased the mean arterial blood pressure while the other drugs did not (table 1), but the four drugs had no significantly different effect on the redistribution of the flows. In the entire series of patients, the vasodilator action on the perfusion of the diseased areas was more often

TABLE 2 Effect of the Vasodilators on CBF in the Diseased Area

<table>
<thead>
<tr>
<th>Case</th>
<th>Angiography</th>
<th>F gray</th>
<th>Regional CBF</th>
<th>Case</th>
<th>Angiography</th>
<th>F gray</th>
<th>Regional CBF</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>?</td>
<td>Decrease</td>
<td>RD</td>
<td>F1</td>
<td>N</td>
<td>Increase</td>
<td>0</td>
</tr>
<tr>
<td>F2</td>
<td>Arterial thrombosis</td>
<td>Decrease</td>
<td>Decrease</td>
<td>F2</td>
<td>N</td>
<td>Decrease</td>
<td>0</td>
</tr>
<tr>
<td>F3</td>
<td>Arterial thrombosis</td>
<td>Decrease</td>
<td>Increase</td>
<td>F3</td>
<td>Arterial thrombosis</td>
<td>Decrease</td>
<td>RD?</td>
</tr>
<tr>
<td>F4</td>
<td>Arterial thrombosis</td>
<td>Decrease</td>
<td>Decrease</td>
<td>F4</td>
<td>N</td>
<td>Increase</td>
<td>Increase</td>
</tr>
<tr>
<td>F5</td>
<td>Arterial thrombosis</td>
<td>Decrease</td>
<td>Increase</td>
<td>F5</td>
<td>N</td>
<td>Increase</td>
<td>Increase</td>
</tr>
<tr>
<td>F6</td>
<td>Arterial thrombosis</td>
<td>Decrease</td>
<td>RD</td>
<td>F6</td>
<td>N</td>
<td>Increase</td>
<td>Increase</td>
</tr>
<tr>
<td>D1 N</td>
<td>Decrease</td>
<td>RD</td>
<td>V1 Arterial thrombosis</td>
<td>RD</td>
<td>RD?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D2 N</td>
<td>Decrease</td>
<td>RD 0</td>
<td>V3 Arterial thrombosis</td>
<td>—</td>
<td>RD?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D3 N</td>
<td>Arterial thrombosis</td>
<td>Decrease</td>
<td>Increase</td>
<td>V4 Arterial thrombosis</td>
<td>—</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>D5 N</td>
<td>Decrease</td>
<td>Increase</td>
<td>Decrease</td>
<td>D6 Arterial thrombosis</td>
<td>Decrease</td>
<td>Decrease</td>
<td></td>
</tr>
</tbody>
</table>

N = no arterial thrombosis, RD = relative decrease in flow, 0 = no significant change in flow.
granulomatous angiitis (61.1% to 62.5%) than beneficial (38.9% or 37.5%).

Correlations between the type of response (beneficial or detrimental) and various factors have been searched for in order to predict the type of response in other patients. Only angiographical findings gave a positive correlation. As shown in table 2, the probability for the occurrence of a decreased perfusion is higher when the arteriogram shows an intracranial thrombosis. It is indeed conceivable that a cerebral region deprived of its main arterial supply but with all its patent arteries already maximally dilated can by no means benefit by the action of a vasodilator.

References

Granulomatous Angiitis
An Unusual Etiology of Stroke

Peter C. Burger, M.D., J. Gordon Burch, M.D., and F. Stephen Vogel, M.D.

Summary
A 43-year-old man, who died five months after the onset of left-sided sensory deficit, had angiographical and pathological evidence of an angiitis confined largely to the distal cerebral arteries. Histological examination identified this process to be intracranial noninfectious granulomatous angiitis. Although certain clinical and pathological features of this disorder overlap with other vasculitides which affect the central nervous system, the disease nevertheless retains sufficient individuality to warrant status as an entity, and should be considered in the differential diagnosis in adults with lesions which produce focal neurological deficits and signs of increased intracranial pressure.

The definitive answer regarding an infectious etiology will come only from detailed culture studies of the affected vessels.

Introduction
Granulomatous angiitis is an inflammatory disorder of unknown etiology whose curious preference for vessels of the central nervous system may be expressed clinically as stroke. This report describes the clinical and pathological manifestations of this disorder and considers its nosological position among the other vasculitides which may affect the central nervous system.

Report of a Case
Clinical History
The patient was a 43-year-old black man who was first admitted to Duke University Medical Center on November 9, 1970, for evaluation of repetitive attacks of numbness of the left side of the body which had begun two months previously. The initial attack of 20 minutes' duration was characterized by numbness of the left foot, staggering gait, difficulty with speech, and decreased use of the left arm and leg. Within a week the numbness extended to the entire left side of the body, at which time there was urinary urgency with precipitate micturation, anorexia, and a six-pound weight loss. The patient denied seizure activity, headache, visual disturbance, or loss of consciousness. The past medical history contained no relevant illnesses. Specifically, there was no history of asthma, allergies, sinusitis, or lesions of the skin.

The patient was well developed and cooperative, and did not appear ill. The blood pressure was normal. Decreased cranial pressure. The definitive answer regarding an infectious etiology will come only from detailed culture studies of the affected vessels.

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Action of vasodilators on regional cerebral blood flow in subacute or chronic cerebral ischemia.
A Capon, M De Rood, A Verbist and J Fruhling

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