Letters to the Editor

Arrogance Re-Revisited

To the Editor:

Dr. Robert G. Hart’s letter in response to our article on carotid endarterectomy requires further comment. Dr. Hart’s letter was published under the title of “Arrogance Revisited,” and takes us to task for criticizing the well-known, but controversial clinical trials in extracranial-intracranial (EC-IC) bypass. It is possible that Dr. Hart misinterpreted us.

We do not call for a retreat from scientific investigation or for a return to experimental anecdotalism in the pursuit of knowledge. We do not call for abandonment of the randomized clinical trial as a tool by which knowledge should be pursued. We do call for some caution in interpreting the results of some of these clinical trials, and we certainly do not agree that randomized clinical trials are the only way in which knowledge can be achieved.

Randomized clinical trials of surgical therapy are extremely difficult to design and interpret because of the inherent variability of the surgical procedure itself. Furthermore, randomized clinical trials have a propensity to produce a false negative result, which can lead to continuing confusion rather than to truth.

We believe that there is an important role for randomized clinical trials, but that the results of these trials should not be accepted blindly simply because the trial was randomized and controlled. We must beware of the illusion of infallibility that is attendant to the randomized clinical trial. The best way to avoid that trap is to maintain a healthy skepticism and to judge each trial on its own merits. We do not think that this is arrogance, but, rather, prudence.

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References


Cerebral Infarction in Hereditary Spherocytosis

To the Editor:

Abnormalities in the red blood cell membrane may occasionally cause stroke.1 In hereditary spherocytosis (HS), stroke has been reported only once.2 We conducted rheological investigations in two brothers with HS who suffered cerebral infarction. These studies were performed 2 and 3 years after the occurrence of stroke in Patient 1 and 1 month and 1 year after stroke in Patient 2. Viscosity of whole blood and plasma, red blood cell deformability, and red blood cell aggregation were determined as described previously.3–5

Patient 1, a 66-year-old man, was admitted because of progressive respiratory distress and a left-sided hemiplegia. Two weeks earlier, he had had a relapse of chronic bronchitis with progressive dyspnea. On admission he was unresponsive, with a pulse rate of 170, blood pressure of 90/70 mm Hg, and no carotid bruits. Severe respiratory and metabolic acidosis were present. Erythrocyte sedimentation rate was 121 mm, but other laboratory investigations were normal. Electrocardiography showed a grade 1 atrioventricular block, and X-ray of the chest showed enlargement of the heart. Computed tomography (CT) of the brain revealed right-sided capsular, temporal, parietal, and occipital infarcts. Doppler ultrasonography showed no flow in the right common carotid artery. Shortly after artificial ventilation, the patient regained consciousness and subsequently displayed anosognosia, a left hemineglect, hemiplegia, hypalgesia, and hypaesthesia.

Rheological investigation (Table 1) revealed blood viscosity to be significantly elevated at low and high shear rates on two occasions. Plasma viscosity was higher than in normal controls, but fibrinogen was normal. The extent of red cell aggregation, determined at t = 0, was higher than in normal controls. Red cell deformability was strongly reduced, as expected, especially at higher shear rates (Figure 1).

The 65-year-old brother of Patient 1 suddenly had difficulty using his right arm and leg. One year earlier, he had experienced transient aphasia, but echocardiography done at that time was normal. He smoked approximately 20 cigarettes daily for years. On admission, pulse rate was 80 and blood pressure 190/75 mm Hg, with no carotid bruits. Neurological examination revealed weakness of the right lower face and a right extensor planter response. Erythrocyte sedimentation rate was 30 mm, hematocrit 0.45, and white cell count 14.7 10^9/L. The lipid spectrum disclosed a Frederickson type 4 pattern. Further laboratory investigations, X-ray of the chest, and CT of the brain were normal. However, electrocardiography revealed transient supraventricular arrhythmias, and cerebral angiography demonstrated occlusion of the left anterior cerebral artery.

Rheological investigation of this patient showed a blood viscosity at low and middle shear rates in the high-normal range,
Table 1. Hemorheological Values in Two Patients With Hereditary Spherocytosis

<table>
<thead>
<tr>
<th>Value</th>
<th>Patient 1</th>
<th>Reference values</th>
<th>Patient 2</th>
<th>Reference values</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Test 1</td>
<td>Test 2</td>
<td>Test 1</td>
<td>Test 2</td>
</tr>
<tr>
<td>Blood viscosity (mPa/sec)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>at shear rate</td>
<td></td>
<td></td>
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<tr>
<td>0.04/sec</td>
<td>42.46</td>
<td>49.41</td>
<td>77.34</td>
<td>72.69</td>
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<tr>
<td>0.64/sec</td>
<td>13.33</td>
<td>14.97</td>
<td>27.49</td>
<td>25.09</td>
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<td>114.5/sec</td>
<td>3.8</td>
<td>3.84</td>
<td>5.36</td>
<td>5.34</td>
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<tr>
<td>Hematocrit</td>
<td>0.33</td>
<td>0.33</td>
<td>0.44</td>
<td>0.44</td>
</tr>
<tr>
<td>Plasma viscosity (mPa/sec)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.6</td>
<td>1.59</td>
<td>1.67</td>
<td>1.51</td>
</tr>
<tr>
<td>Fibrinogen (mg/dl)</td>
<td>NP</td>
<td>360</td>
<td>NP</td>
<td>300</td>
</tr>
<tr>
<td>Red cell aggregation (MAI) at shear rate 0/sec</td>
<td>NP</td>
<td>7.2</td>
<td>(3.3-6.1)</td>
<td>NP</td>
</tr>
</tbody>
</table>

Values determined on two separate occasions (Tests 1 and 2). NP, not performed; MAI, Myrenne Aggregation Index.

*Blood viscosity for hematocrit 0.33.
†Blood viscosity for hematocrit 0.44.

whereas blood viscosity at high shear rates was significantly elevated (Table 1). Fibrinogen was normal and red cell deformability was reduced. There was also increased red cell aggregation in this patient. In both patients, elevated red cell aggregation and reduced red cell deformability was found, with Patient 1 showing a greater abnormality in red cell deformability and Patient 2 in red cell aggregation. Plasma viscosity was consistently raised in both patients.

The question remains whether the rheological abnormalities contributed to the development of stroke. Based on our results, distal small-vessel disease (sludging syndrome) should have been more likely to develop, but both patients had clear evidence of large-vessel disease, which cannot be considered a peculiarity resulting from their age or the presence of cardiovascular risk factors. Furthermore, considering the high prevalence of HS, the lack of reports on its association with stroke should cast doubt on the possible role of rheological abnormalities in HS. On the other hand, decreased flow through nutrient vessels of the arterial wall, which is a postulated cause of large-vessel occlusion in sickle-cell disease, remains to be established in HS.

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