Twelve cases of fatal cerebral infarction due to arterial occlusion in the absence of atheromatous stenosis or embolism

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There has in recent years been an ever increasing tendency to emphasize the importance of atheromatous stenosis of the intracranial and extracranial cerebral arteries in the pathogenesis of cerebral infarction (Yates and Hutchinson, 1961; Fisher, Gore, Okabe, and White, 1965; Moossy, 1966a and b). Berlin, Tumarkin, and Martin (1955) believe that even in patients under the age of 40, cerebrovascular degeneration is responsible for cerebral thrombosis. The importance of atheromatous stenosis, particularly of the neck arteries, may, however, have been overstated (Schwartz and Mitchell, 1961), and Adams, Brierley, Connor, and Treip (1966) have shown that severe ischaemic brain damage, including frank infarction, may occur as a sequel to a profound reduction in cerebral blood flow in the absence of atheroma.

Many factors clearly influence the occurrence of thrombosis in major intracranial and extracranial cerebral arteries (Humphrey and Newton, 1960; Wisoff and Rothballer, 1961; Baker, Dahl, and Sandler, 1963) and of more recent concern is the possibly increased incidence of non-haemorrhagic strokes in young women taking oral contraceptives (Zilkha, 1964 and 1965; Baines, 1965; Illis, Kocen, McDonald, and Mondkar, 1965; Nevin, Elmes, and Weaver, 1965; Shafey and Scheinberg, 1966; Bickerstaff and Holmes, 1967). Nevertheless it is generally believed that thrombus usually forms on an atheromatous plaque although this is not always confirmed by histological examination. We do not wish to suggest that atheromatous stenosis is not of considerable importance in the pathogenesis of cerebral infarction but, in an attempt to emphasize that there are many other factors that may lead to occlusion of a major cerebral artery by thrombus, we wish to describe 12 cases of fatal cerebral infarction where post-mortem examination disclosed occlusion of a carotid artery or one of its main branches in the absence of embolism or a pre-existing stenosis.

Although it has been established that a large cerebral infarct may swell to the extent of simulating an acute expanding lesion (Clarke and Harris, 1958; Shaw, Alvord, and Berry, 1959; Adams, 1966; Trottenburg and Vinken, 1966), this is not yet sufficiently widely recognized. In every one of the 12 cases in this series the neuropathological features of an expanding intracranial lesion were present.

MATERIALS AND METHODS

The 12 cases (Table I) were encountered between 1961 and 1966 in either the Western Infirmary, Glasgow, or in the Institute of Neurological Sciences, Glasgow. Eleven were women between the ages of 25 and 52 and one was a man aged 37. Carotid angiography was undertaken in eight cases. To be included in the series, every case had to fulfil certain criteria: these were occlusion of a major intracranial and/or extracranial cerebral artery by thrombus, the absence of atheromatous stenosis in the major intracranial or extracranial cerebral arteries, the absence of a source of embolus, and an accurate knowledge of the duration of survival from the time of onset of the stroke until death.

A comprehensive necropsy was undertaken in every case. This included examination of the full length of the common and internal carotid arteries and inspection of the upper and lower ends of the vertebral arteries. In many cases the arch of the aorta and the neck arteries were removed in one block and dissected after fixation. The brains were suspended in 10% formol saline for at least three weeks before dissection. The fixed brain was first assessed for evidence of raised intracranial pressure. The midbrain was then transected and the cerebral hemispheres cut in the coronal plane into slices 1 cm. thick. The distribution and appearance of the infarct and any neuropathological features of raised intracranial pressure were recorded. In addition the width of any tentorial herniae and the maximum displacement of the interventricular septum or third ventricle from the midline were measured.

Representative blocks of brain were examined microscopically to confirm the presence of infarction. Multiple serial blocks of all occluded and many apparently normal intracranial and extracranial cerebral arteries were
prepared by the method of Beesley and Daniel (1956) and stained with haemalum and eosin and by Weigert's method for elastica.

CASE REPORTS

The cases will be presented in three groups: group I (cases 1-4) composed of four cases where a cause for the arterial thrombosis was determined; group II (cases 5-8) composed of four cases where some predisposing or contributing factor was present; group III (cases 9-12) composed of four cases where no cause for the thrombosis or predisposing factor was found.

The principal clinical, radiological and pathological findings are given in Tables I and II.

GROUP I: CASE 1

This 43-year-old woman (N, 17658, K 58/62) was admitted to the Institute for the investigation of one episode of transient loss of consciousness seven weeks previously, and diplopia, nausea, bilateral tinnitus, and unsteadiness of gait of more recent onset. Routine clinical and laboratory investigations were negative. Blood pressure was 110/60 mm. Hg. Three weeks after admission bilateral carotid angiography and ventriculography were undertaken without demonstrating any abnormalities. She did not recover from these procedures and remained unconscious with a right hemiplegia until death 32 hours later.

At necropsy the left common carotid artery was occluded by thrombus that had propagated into the internal and external carotid arteries and into the anterior and middle cerebral arteries. The principal acute neuropathological findings are given below but examination of the brain in this case showed in addition the features of multiple sclerosis. The only other abnormal findings were bilateral basal pulmonary congestion and focal chronic thyroiditis.

GROUP I: CASE 2

This 37-year-old man (283570, NP 63033) was struck on the right side of his neck by a lead pipe and sustained a fracture of the ramus of the mandible. This was reduced under general anaesthesia. Eighteen hours later he developed a left hemiplegia. A carotid angiogram showed complete occlusion of the right internal carotid artery. Blood pressure was 110/60 mm. Hg. Immediate disobliteration of the occluded artery was undertaken but despite a transient improvement of the hemiparesis, he deteriorated and died in coma, 38 hours after the onset of hemiplegia.

At necropsy the right internal carotid artery was occluded by thrombus. The only other abnormality outside the brain was bilateral pulmonary oedema.

GROUP I: CASE 3

This 39-year-old woman (60260, NP 64087) was admitted to the Western Infirmary with a right hemiplegia of recent onset. Blood pressure was 120/80 mm. Hg. Carotid angiography was not carried out. Her conscious level deteriorated rapidly and she died in coma two days after the onset of the stroke.

In the course of the previous year she had developed bilateral deep femoral vein thrombosis, occlusion of the left subclavian artery that had necessitated amputation of several fingers, and a facial rash of 'butterfly' distribution. Her E.S.R. had been persistently above 70 mm./hour Westergren despite synthetic steroid therapy. A biopsy from the face showed the features of chronic discoid lupus erythematosus.

At necropsy the left internal carotid artery was occluded by thrombus that had propagated into the anterior and middle cerebral arteries. The renal, splenic, and iliac arteries and the deep veins of the legs were also occluded by thrombus. The heart was normal, there being no source of emboli. Histological examination showed a generalized panarteritis and haematoxyphil bodies in the spleen and kidney of the type associated with systemic lupus erythematosus.

GROUP I: CASE 4

This 33-year-old woman (N, 21243, K 148/64) was admitted to another hospital with a three-week history of severe and recurrent frontal headaches associated with some visual disturbance. While in hospital
Fatal cerebral infarction due to arterial occlusion in the absence of atheromatous stenosis

she quite rapidly became unconscious and was found to have a left hemiparesis. On transfer to the Institute that day she was deeply unconscious and had bilateral extensor plantar responses. Blood pressure was 150/80 mm Hg. A ventriculogram next day demonstrated an expanding lesion in the right cerebral hemisphere and a biopsy showed features suggestive of recent cerebral infarction. Carotid angiography was not performed. She remained unconscious and died six days after the onset of hemiplegia.

At necropsy the right anterior and middle cerebral arteries were occluded by thrombus. There were no other abnormalities outside the brain.

GROUP II: CASE 5 This 25-year-old woman (N, 22986, K 107/65) underwent elective Caesarean section because of severe pre-eclamptic toxemia (blood pressure 190/125 mm Hg) for the delivery of her fifth child at the 28th week of pregnancy. The immediate postoperative course was uneventful, but seven days after delivery she developed a left hemiparesis associated with some sensory disturbance. Her conscious level deteriorated rapidly and she died in coma on admission to the Institute 36 hours after the onset of the hemiparesis.

At necropsy the right common carotid artery was occluded by thrombus that had propagated into the internal carotid artery and into the anterior and middle cerebral arteries. There was no thrombosis of cortical veins. The only other abnormality outside the brain was bilateral pulmonary oedema.

GROUP II: CASE 6 This 30-year-old woman (N, 19518, K 119/63) gave birth to her third child after an uneventful pregnancy and a normal delivery. The initial puerperium was uneventful but 14 days after delivery she developed headache, dysphasia, and a right hemiparesis. Blood pressure was 150/80 mm Hg. She was transferred to the Institute two days later where a carotid angiogram demonstrated occlusion of the left middle cerebral artery and a shift of the midline structures to the right. Thereafter her condition deteriorated rapidly and she died in coma three days after the onset of the stroke.

At necropsy the left middle cerebral artery was occluded by thrombus. The only other abnormality outside the brain was a small recent infarct in the anterior lobe of the pituitary. There was no thrombosis of cortical veins.

GROUP II: CASE 7 This 35-year-old woman (N, 21618, K 9/65) gave birth to a child after an uneventful pregnancy and a normal delivery. The initial puerperium was uneventful but 12 days after delivery she was found unconscious at home. On transfer to the Institute two days later she was aphasic and had a right hemianopia, facial weakness, and a right hemiparesis. Blood pressure was 160/90 mm Hg. A left carotid angiogram next day demonstrated occlusion of the upper end of the left internal carotid artery. Her conscious level progressively deteriorated and she died in coma five days after the onset of the stroke.

At necropsy the left internal carotid artery was occluded by thrombus that had propagated into the anterior and middle cerebral arteries. There was no thrombosis of cortical veins, and no other abnormalities outside the brain.

GROUP II: CASE 8 This 39-year-old woman (N, 23064, K 48/66) underwent a laparotomy for the investigation of pain in the right iliac fossa. Blood pressure before operation was 160/90 mm Hg. Tuberculous peritonitis was found and the course of the operation was uneventful. Some hours later she was found to be confused and dysphasic and to have a right hemiparesis. She was transferred to the Institute two days after the laparotomy by which time she had a right hemiplegia and fixed dilated pupils. An immediate left carotid angiogram showed poor filling of the left middle cerebral artery and an expanding lesion in the left cerebral hemisphere. A biopsy showed the features of recent cerebral infarction. She died in coma four days after the laparotomy.

At necropsy the left middle cerebral artery was completely occluded by thrombus. The only other abnormality outside the brain was tuberculosis of the pelvic organs.

GROUP III: CASE 9 This 52-year-old woman (N, 20195, K 30/64) was admitted to another hospital with a right hemiparesis, right homonymous hemianopia, and facial weakness of rapid onset. Blood pressure was 110/70 mm Hg. Seven days later she was transferred to the Institute where a carotid angiogram showed occlusion of the left middle cerebral artery and an expanding lesion in the left cerebral hemisphere. She died in coma next day, eight days after the onset of hemiparesis.

At necropsy the left middle cerebral artery was occluded by thrombus. The only other abnormality outside the brain was hypertrophy of the muscle of the left ventricle.

GROUP III: CASE 10 This 42-year-old woman (N, 14827, NP 60017) was referred to the Institute with a left hemiparesis of rapid onset where she was found to be drowsy but able to respond to commands. Blood pressure was 160/90 mm Hg. Bilateral carotid angiography demonstrated occlusion of the right anterior and middle cerebral arteries distal to the carotid bifurcation and a shift of the midline structures to the left. Her general condition progressively deteriorated and she died in coma three days after the onset of hemiplegia.

At necropsy the right anterior and middle cerebral arteries were occluded by thrombus. The only other abnormality was an acute purulent bronchiolitis.

GROUP III: CASE 11 This 47-year-old woman (79874, NP 65018) suddenly collapsed with loss of consciousness at home. On admission to the Western Infirmary she had a left hemiplegia and hemianesthesia, and weakness of the left side of the face. Blood pressure was 160/110 mm Hg. Carotid angiography was not undertaken. Coma deepened and she died three days after the onset of hemiplegia.

At necropsy the right internal carotid artery was occluded by thrombus that had propagated into the middle cerebral artery. There was early broncho-pneumonia.
GROUP III: CASE 12  This 46-year-old woman (N, 16929, K 116/61) was admitted to another hospital because of the rapid onset of confusion, clouding of consciousness, and weakness of the left arm and leg. Examination showed a left hemiparesis, weakness of the left side of the face, and a left homonymous hemianopia. Blood pressure was 160/80 mm. Hg. Three days later she rapidly lapsed into deep coma and the right pupil became dilated and fixed. After transfer to the Institute the right cerebral hemisphere was explored through a burr-hole but a haematoma was not found. Next day bilateral carotid angiography demonstrated occlusion of the right middle cerebral artery and a shift of the midline structures to the left. She died five days after the onset of the stroke without regaining consciousness.

At necropsy the right middle cerebral artery was occluded by thrombus. The only other abnormality was early bronchopneumonia.

PATHOLOGICAL FINDINGS

INTRACRANIAL AND EXTRACRANIAL CEREBRAL ARTERIES

The arteries found to be occluded at necropsy are listed in Table II. The apparent site of primary occlusion was the common carotid artery in two (cases 1 and 5), the internal carotid artery in four (cases 2, 3, 7, and 11), the middle cerebral artery alone in four (cases 6, 8, 9, and 12), and both the middle and anterior cerebral arteries in two (cases 4 and 10). In five there was propagation of thrombus from the extracranial to the intracranial arteries; in four of these the thrombus had extended into the middle and anterior cerebral arteries (cases 1, 3, 5, and 7) and in one into the middle cerebral artery only (case 11). In none of the cases were there any atheromatous plaques visible to the naked eye in

<table>
<thead>
<tr>
<th>Group</th>
<th>Case</th>
<th>Duration of Survival</th>
<th>Primary Site of Thrombus Formation</th>
<th>Other Arteries Occluded at Necropsy</th>
<th>Distribution of Infarct</th>
<th>Appearance of Infarct</th>
<th>Tight Conduction Lesions</th>
<th>Width of Tentorial Hernia (mm.)</th>
<th>Ton-torial Hernia</th>
<th>Ventricles</th>
<th>Maximal Midline Shift (mm.)</th>
<th>Supra-callosal Infarction</th>
<th>Calcarine Brainstem</th>
<th>Haemorrhage</th>
<th>Flattening of Oculomotor Nerve</th>
<th>B. Wei (g.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>38 hr. R.I.C.A.</td>
<td>-</td>
<td>R.M.C.A.</td>
<td>-</td>
<td>Pale + + 10 +</td>
<td>+ + 3</td>
<td>Small R &lt; L</td>
<td>10 - -</td>
<td>+</td>
<td>-</td>
<td>1,3</td>
<td>1.7</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2 days L.I.C.A.</td>
<td>L.R.C.A. and M.C.A.</td>
<td>L.M.C.A. and A.C.A.</td>
<td>Pale with punctate haemorrhages²</td>
<td>+ - + 6 +</td>
<td>+ + 1</td>
<td>Small R = L</td>
<td>- - -</td>
<td>+</td>
<td>-</td>
<td>1,45</td>
<td>1,330</td>
<td>+</td>
<td>+</td>
<td>1,3</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>6 days R.M.C.A. and A.C.A.</td>
<td>-</td>
<td>R.M.C.A.</td>
<td>Pale with punctate haemorrhages²</td>
<td>+ - + 6 +</td>
<td>+ + 1</td>
<td>Small R = L</td>
<td>- - -</td>
<td>+</td>
<td>-</td>
<td>1,45</td>
<td>1,330</td>
<td>+</td>
<td>+</td>
<td>1,3</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>5</td>
<td>36 hr. R.C.C.A.</td>
<td>R.I.C.A., E.C.A., A.C.A., and M.C.A.</td>
<td>R.M.C.A. and A.C.A.</td>
<td>Pale with punctate haemorrhages²</td>
<td>+ + 9 +</td>
<td>Small R &lt; L</td>
<td>4 - -</td>
<td>-</td>
<td>+</td>
<td>1,2</td>
<td>1,41‡</td>
<td>+</td>
<td>+</td>
<td>1,41</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>3 days L.M.C.A.</td>
<td>-</td>
<td>L.M.C.A.</td>
<td>Pale - - + 15 -</td>
<td>+</td>
<td>Very small R = L</td>
<td>Small R &lt; L</td>
<td>12 - -</td>
<td>+</td>
<td>-</td>
<td>1,3‡</td>
<td>1.330</td>
<td>+</td>
<td>+</td>
<td>1,3‡</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>4 days L.M.C.A.</td>
<td>-</td>
<td>L.M.C.A.</td>
<td>Pale with punctate haemorrhages²</td>
<td>+ + 10 +</td>
<td>+ + 1</td>
<td>Small L &lt; R</td>
<td>12 + -</td>
<td>+</td>
<td>-</td>
<td>1,330</td>
<td>1,330</td>
<td>+</td>
<td>+</td>
<td>1,330</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>9</td>
<td>8 days L.M.C.A.</td>
<td>-</td>
<td>L.M.C.A.</td>
<td>Pale with punctate haemorrhages²</td>
<td>+ - - +</td>
<td>Small L &lt; R</td>
<td>3 - -</td>
<td>-</td>
<td>+</td>
<td>1,41‡</td>
<td>1,41‡</td>
<td>+</td>
<td>+</td>
<td>1,41‡</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>3 days R.M.C.A. and A.C.A.</td>
<td>-</td>
<td>R.M.C.A. and A.C.A.</td>
<td>Pale + + 10 -</td>
<td>+ + 1</td>
<td>Small L &lt; R</td>
<td>9 + -</td>
<td>+</td>
<td>-</td>
<td>1,380</td>
<td>1,330</td>
<td>+</td>
<td>+</td>
<td>1,330</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>3 days R.I.C.A.</td>
<td>R.M.C.A.</td>
<td>R.M.C.A.</td>
<td>Pale + + 12 +</td>
<td>+ + 1</td>
<td>Small L &lt; R</td>
<td>11 + -</td>
<td>+</td>
<td>-</td>
<td>1,380</td>
<td>1,330</td>
<td>+</td>
<td>+</td>
<td>1,330</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>5 days R.M.C.A.</td>
<td>-</td>
<td>R.M.C.A.</td>
<td>Pale + + 5 -</td>
<td>+ + 1</td>
<td>Small L &lt; R</td>
<td>10 + -</td>
<td>+</td>
<td>-</td>
<td>1,220</td>
<td>1,800</td>
<td>+</td>
<td>+</td>
<td>1,800</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1The punctate haemorrhages were seen most often in the basal nuclei and in the cortex in the depths of sulci. They did not occur consistently in any particular part of an arterial territory or in the boundary zone between the anterior and middle cerebral arteries.
The distribution of the cerebral infarcts is given in Table II. The middle cerebral artery territory, including the basal nuclei and the internal capsule, was involved in every case, and in five the anterior cerebral artery territory also. The infarct was invariably soft and swollen. In six there were small foci of punctate haemorrhage, randomly distributed in the cortex in the depths of sulci or in the basal nuclei, but in none was there either an intensely haemorrhagic area or a haematoma.

In every case the swelling of the infarct had produced the neuropathological features of an acute expanding lesion with increased intracranial pressure (Table II). The dura was tight in eight, and there was flattening of the cerebral convolutions in eight, a tentorial hernia in 10, a tonsillar hernia in seven, and flattening of the ipsilateral oculomotor nerve in all 12 cases. In three there was in addition focal haemorrhage into the oculomotor nerve where it crossed the posterior cerebral artery (Fig. 5).

In coronal slices there was in every case a shift of the midline structures and a small ipsilateral lateral ventricle (Fig. 6). A supracallosal hernia was present in six, secondary calcarine infarction in two, and secondary brainstem haemorrhage in two cases.

As the degree of midline shift is probably the most accurate method of determining the amount of swelling in a cerebral hemisphere, this shift is correlated with the length of survival and the distribution of the infarct in Table III. From this it is seen that a shift of 9 mm. can be attained in as little as 32 hours after the onset of a large cerebral infarct but that in general the maximum shift occurs between the second and fifth days. An infarct involving the middle cerebral artery territory alone (cases 6, 11, and 12) may produce as great a shift as one involving both the anterior and middle cerebral artery territories (cases 1, 3, 7, and 10).

### Table III

<table>
<thead>
<tr>
<th>Case</th>
<th>Duration of Survival after Onset of Stroke</th>
<th>Distribution of Infarct</th>
<th>Maximum Midline Shift (mm.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>32 hr.</td>
<td>L. M.C.A. and A.C.A.</td>
<td>9</td>
</tr>
<tr>
<td>5</td>
<td>36 hr.</td>
<td>R. M.C.A. and A.C.A.</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>38 hr.</td>
<td>R. M.C.A.</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>2 days</td>
<td>L. M.C.A. and A.C.A.</td>
<td>10</td>
</tr>
<tr>
<td>10</td>
<td>3 days</td>
<td>R. M.C.A. and A.C.A.</td>
<td>9</td>
</tr>
<tr>
<td>11</td>
<td>3 days</td>
<td>R. M.C.A.</td>
<td>11</td>
</tr>
<tr>
<td>6</td>
<td>3 days</td>
<td>L. M.C.A.</td>
<td>12</td>
</tr>
<tr>
<td>8</td>
<td>4 days</td>
<td>L. M.C.A.</td>
<td>12</td>
</tr>
<tr>
<td>7</td>
<td>5 days</td>
<td>L. M.C.A. and A.C.A.</td>
<td>10</td>
</tr>
<tr>
<td>12</td>
<td>5 days</td>
<td>R. M.C.A.</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>6 days</td>
<td>R. M.C.A.</td>
<td>5</td>
</tr>
<tr>
<td>9</td>
<td>8 days</td>
<td>L. M.C.A.</td>
<td>3</td>
</tr>
</tbody>
</table>

R. = right M.C.A. = middle cerebral artery
L. = left A.C.A. = anterior cerebral artery
FIG. 1. Case 1. Internal carotid artery. There is an intramural haematoma between the adventitial and medial coats and the lumen is occluded by thrombus. Haemalum and eosin x 3.

FIG. 2. Case 4. Middle cerebral artery. There are numerous inflammatory cells and multinucleate giant cells in the intima. Haemalum and eosin x 125.

FIG. 3. Case 4. Same artery as in Figure 2. There is fragmentation of the internal elastic lamina. Weigert's elastica x 125.

DISCUSSION

These cases of fatal cerebral infarction are highly selected as nine of the 12 had been referred to the Institute's Neurosurgical Unit and because every case had to fulfil certain clearly defined criteria before being included in the series. No case fulfilling these criteria that has come to necropsy between 1961 and 1966 has, however, been omitted from the series. They are recorded for two principal reasons: to emphasize that occlusion of a carotid artery or one of its main branches by thrombus has many causes other than atheromatous stenosis or embolism and to stress that a large recent infarct may swell to the extent of producing the clinical, radiological, and neuropathological features of an acute expanding lesion in a cerebral hemisphere.

In all four cases in group I a specific aetiological factor for thrombosis was identified at necropsy. Occlusion of a carotid artery, as in case 1, is a known complication of percutaneous carotid angiography (Abbott, Gay, and Goodall, 1952; Baker, 1960; Lindner, Hardy, Thomas, and Gurdjian, 1962) but is in our experience a very rare occurrence. Traumatic occlusion of the internal carotid artery (case 2) is also well documented (Clarke, Dickson, and Smith, 1955; Murray, 1957; Gurdjian, Hardy, Lindner, and Thomas, 1963; Houck, Jackson, Odom, and Young, 1964; Toakley and McCaffrey, 1965) but of particular interest in the present case was the finding on histological examination of a haematoma between the medial and adventitial coats of the artery. Case 3 suffered from systemic lupus erythematosus, another known cause of arterial thrombosis (Dubois, Commons, Starr, Stein, and Morrison, 1952; Murphy, 1954). Although the histological features in case 4 are rather atypical in that the giant cells and the inflammatory reaction were mainly in the intima, the appearances were clearly those of a giant cell arteritis (Andrews, 1966). The patient, however, was considerably younger than most of the previously reported cases.

The four cases in group II, however, are more complex as the cause of thrombosis is not known although in each case there was a known predisposing or associated factor. Three (cases 5, 6, and 7) were strokes occurring in the puerperium. In none of these was cerebral venous thrombosis found and our experience leads us to endorse the opinion of Jennett and Cross (1967) that venous thrombosis is not the usual cause of non-haemorrhagic hemiplegia occurring in the puerperium. It is, however, now clear from their survey that strokes due to non-embolic arterial occlusion in young women are particularly liable to occur in the course of pregnancy and in the puerperium although the basic pathogenic

FIG. 5. Case 7. Occlusion of internal carotid artery with propagation of thrombus into anterior and middle cerebral arteries. Note occlusion of upper end of left internal carotid artery, focal haemorrhage in left oculomotor nerve, tentorial hernia, and haemorrhage into the displaced mid-brain. Survival five days. × 1.

FIG. 6. Case 8. Occlusion of left middle cerebral artery. Coronal section of brain to show swelling of the affected hemisphere, a well-defined supracallosal hernia, and shift of the midline structures. The infarct is essentially pale but there are a few punctate haemorrhages lateral to the thalamus. Survival four days. × 0·7.
mechanism remains unknown. It is possible that an alteration in platelet adhesiveness (Wright, 1942) or in blood coagulability may play a part, even though the reduced fibrinolytic activity of the third trimester of pregnancy and the first and second stages of labour returns rapidly to normal after delivery of the placenta (Bieznski and Moore, 1958; Shaper, MacIntosh, and Kyobe, 1966). It is possible therefore that the small focus of intimal haemorrhage seen in case 5 in relation to the very early atheromatous plaque at the apparent site of primary thrombus formation may be of significance as the thrombus appeared to be laminated. Rupture of the plaque as described by Constantinides (1966) in the coronary arteries was not seen, but if the small haemorrhage had precipitated the formation of a layer of thrombus on the intima, reduced fibrinolytic activity might have allowed subsequent deposition of thrombus proceeding to complete occlusion. This patient had also suffered from hypertension (range of diastolic blood pressure 95-125 mm. Hg) and this may have been a further contributing factor (Baker and Iannone, 1961). In case 8 occlusion of the middle cerebral artery occurred within a few hours of laparotomy for no apparent reason.

In the four cases in group III, the cause of thrombosis remains unknown. Although there was some hypertrophy of the left ventricle in case 9, the blood pressure was recorded as normal on several occasions before the onset of the stroke. Although the patients in this group were older than those in groups I and II, there was again no evidence of atheromatous stenosis in the intracranial or extracranial cerebral arteries.

Since the introduction of oral contraceptives in 1961, there has been an increasing awareness of an apparent rise in thrombo-embolic strokes in young women that may be associated with their use (Zilkha, 1964 and 1965; Baines, 1965; Shafey and Scheinberg, 1966). On the other hand Jennett and Cross (1967) have argued that this is not so, although Bickerstaff and Holmes (1967) believe that the apparent association between the use of oral contraceptives and the increased number of episodes of cerebral arterial insufficiency cannot be disregarded. The recent preliminary report from the M.R.C. (1967) suggests that there is possibly a relationship between cerebral thrombosis and the use of oral contraceptives. It was thought unlikely that oral contraceptives could be considered as a possible aetiological factor in cases 1-7 and in case 10, who died in 1960. Of the four remaining patients, it is known that three were not taking oral contraceptives.

The affected cerebral hemisphere in every case (Tables II and III) was found at necropsy to be enlarged and distorted, the major part of the swelling occurring in the infarcted tissue. There may have been some oedema in the immediate neighbourhood of the infarct but in no case did intense vascular congestion or frank haemorrhage contribute to the swelling. Similar observations have been made in animals where it has been shown that both swelling and an increased water content occur in experimentally induced infarcts (Plum, Posner, and Alvord, 1963; Sundt, Waltz, and Sayre, 1967).

It is clear therefore that a large recent infarct may act as an acute expanding lesion thus causing distortion and displacement of the brain and the typical neuropathological features of raised intracranial pressure. Similar observations have been made by Clarke and Harris (1958), Shaw et al. (1959) and, more recently, by Trotsenburg and Vinken (1966). Case 1 is of particular interest as a midline shift of 9 mm. was found only 32 hours after the onset of the stroke but, in general, our observations are similar to those of Shaw et al. (1959) who found that swelling of an infarct in the brain may be manifest within 24 hours and continues to develop over a period of three to five days.

Although the present cases are highly selected, it is our experience that a recent cerebral infarct, whatever its cause, is always soft and swollen when the brain is examined post mortem after proper fixation. The degree of expansion depends almost solely on the size of the infarct: if it is large, as in the present series and in the cases already briefly described by one of us (Adams, 1966), a significant midline shift and other features of raised intracranial pressure are the rule; if it is small, particularly in an elderly patient who already has some diffuse cerebral atrophy, the expansion may effect only a slight reduction in the size of the ipsilateral lateral ventricle. In patients dying with large recent cerebral infarcts we believe that swelling of the necrotic tissue contributes materially to their death and this is in keeping with the observation of Lascelles and Burrows (1965) that the prognosis in patients with occlusion of a middle cerebral artery is particularly bad when there is radiological evidence of midline displacement. In all of the present cases, death followed a period of progressively deepening coma.

It should, on the other hand, be recalled that Achar, Coe, and Marshall (1966) found a midline shift of 3 mm. or more in only two of 53 patients with non-embolic cerebral infarction in an echoencephalographic study. They therefore concluded that ultrasonic examination was a useful tool in distinguishing between cerebral infarction and cerebral haemorrhage, for a shift was observed in 10 of 13 patients with cerebral haemorrhage. As ultrasonograms were carried out on each patient shortly after admission and then daily for several
days and as 19 of the 53 patients died, it is very difficult to reconcile their findings with the typical swollen appearance of a recent fatal cerebral infarct at necropsy and with the angiographic observations of Lascelles and Burrows (1965). The infarcts in the cases described by Achar et al. (1966) may, however, have been small despite the mortality rate of 36% and, as most of their patients were over the age of 50, the cranial cavity may have been able to accommodate the swollen infarct without producing a midline shift, but their paper does not include pathological details of the fatal cases found to have non-embolic cerebral infarction at necropsy.

SUMMARY AND CONCLUSIONS

Twelve cases of fatal cerebral infarction due to thrombotic occlusion of a carotid artery or one of its main branches in the absence of atheromatous stenosis or embolism are described. As a cause for thrombosis was established after death in only four cases, many factors other than atheromatous stenosis must contribute to thrombotic occlusion of intracranial or extracranial cerebral arteries, particularly in the younger age group. In every case the large infarct had acted as an acute expanding lesion in the cerebral hemisphere with subsequent distortion of the brain and increased intracranial pressure. It is concluded that such secondary factors contributed significantly to the fatal outcome in each case.

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Twelve cases of fatal cerebral infarction due to arterial occlusion in the absence of atheromatous stenosis or embolism.

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