The Syndrome of Latent Cerebral Venous Thrombosis: Its Frequency and Relation to Age and Congestive Heart Failure

BY ABRAHAM TOWBIN, M.D.

Abstract:
The present investigation indicates the high incidence of intracranial venous thrombosis in adults in the older age groups, especially in the female. Commonly overlooked clinically and pathologically, cerebral venous thrombosis is usually preceded by congestive circulatory failure and other related systemic disturbances. Most patients with venous thrombosis intracranially also develop thromboembolic complications at other sites in the body. Although often latent clinically, concurrent pulmonary embolism (as revealed in postmortem studies) occurs in a majority of patients with cerebral venous thrombosis. With clinical and pathological aspects of the process correlated, cerebral venous thrombosis in the aged presents a characteristic pattern. In some cases, in patients with enigmatic progressive coma and neurological deterioration, cerebral venous thrombosis occurs as the primary cause of death. In other instances, in patients with cardiac disease or other major systemic disorders, intracranial venous thrombosis develops as a terminal complication leading to death. Cerebral venous thrombosis is of increasing incidence. There is an expressed need that this form of stroke be more widely recognized clinically.

Additional Key Words: stroke, aging, thromboembolic disease

Cerebral venous thrombosis commonly escapes diagnosis clinically and pathologically. The frequency of venous infarction of the brain, especially in the aged, is generally not realized. The occurrence of other forms of thromboembolic disease has been broadly emphasized in recent decades. Increasing attention has been given to the high incidence of pulmonary embolism in the aged, the process stemming from circulatory stasis and latent thrombosis peripherally in the veins of the lower extremities. Significantly, stagnation of venous circulation also occurs, with similar effect, in other distal structures of the body, especially intracranially. In bedridden patients, stasis of intracranial circulation leads to thrombosis of dural sinuses and tributary veins, with cerebral infarction. At times cerebral venous thrombosis proves to be the primary mechanism of death. More often, as with femoral vein thrombosis and pulmonary embolism, in aged debilitated patients, the intracranial thrombotic process makes its appearance as a terminal complication leading to death.

Clinically, cerebral venous thrombosis is usually thought of as an infrequent condition, with two types generally recognized, the primary (aseptic, marantic) form, appearing in infants and children after prolonged debilitating illness, and the secondary (septic) type, occurring as thrombophlebitis consequent to mastoiditis or other local inflammatory process. It is increasingly evident, however, that this incidence pattern, as defined in the past, is obsolete. In the present day, cases of cerebral venous thrombosis due to childhood debilitating disease and local pathological processes are infrequently encountered. Likewise, other cases as described in past literature, occurring as a consequence of trauma and hematological disease, and in women after parturition, are rare.

Studies recently have identified broad areas of incidence not previously realized. Cerebral venous thrombosis appears mainly in two specific age groups, at the extremes of life, in the newborn and in the aged. In both groups, antecedent systemic circulatory failure contributes essentially to the development of the local intracranial thrombotic process.

Attention has been directed recently to the occurrence of cerebral venous thrombosis appearing as a tangential complication of medical treatment.

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TABLE 1
Correlation of Clinical-Pathological Factors in Cases of Cerebral Venous Thrombosis

<table>
<thead>
<tr>
<th>Case number</th>
<th>Age</th>
<th>Sex</th>
<th>Systemic, neurological symptoms</th>
<th>Cerebral venous thrombosis, distribution</th>
<th>Acute cerebral damage diffuse, focal*</th>
<th>Other sites of thrombosis and embolism in the body</th>
<th>Other significant autopsy findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>D 68-64</td>
<td>87 F</td>
<td>Lethargy and coma, 2 days; afebrile</td>
<td>Right lateral and sigmoid sinuses</td>
<td>Diffuse 2+</td>
<td>Pulmonary embolism</td>
<td>Multiple pulmonary infarcts; mitral stenosis; congestive heart failure</td>
</tr>
<tr>
<td>2</td>
<td>D 68-70</td>
<td>77 F</td>
<td>Increasing weakness, lethargy, 2 weeks; afebrile</td>
<td>Left lateral and sigmoid sinuses, with extension into internal jugular vein</td>
<td>Diffuse 2+</td>
<td>Coronary artery thrombosis; femoral vein thrombosis; pulmonary embolism</td>
<td>Pulmonary infarcts; old myocardial infarction; congestive heart failure</td>
</tr>
<tr>
<td>3</td>
<td>D 68-76</td>
<td>74 F</td>
<td>Lethargy, difficulty swallowing, progressive coma in terminal 4 days</td>
<td>Left lateral and sigmoid sinuses; extension of thrombus to internal jugular vein</td>
<td>Diffuse 2+</td>
<td>Focal 1+</td>
<td>Dehydration, emaciation</td>
</tr>
<tr>
<td>4</td>
<td>D 68-89</td>
<td>78 M</td>
<td>Increasing weakness, 1 month</td>
<td>Right lateral and sigmoid sinus and internal jugular vein; vein of Galen</td>
<td>Diffuse 3+</td>
<td>Focal 2+</td>
<td>Carcinoma of right parotid gland with compression of internal jugular vein; lobar pneumonia</td>
</tr>
<tr>
<td>5</td>
<td>D 68-91</td>
<td>78 F</td>
<td>Lethargy and coma, 2 days; afebrile</td>
<td>Superior sagittal sinus</td>
<td>Diffuse 2+</td>
<td>Focal 2+</td>
<td>Bronchopneumonia, emaciation</td>
</tr>
<tr>
<td>6</td>
<td>D 68-93</td>
<td>68 F</td>
<td>Coma, 2 days</td>
<td>Superior sagittal and right lateral sinuses</td>
<td>Diffuse 2+</td>
<td>Bronchopneumonia, dehydration</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>D 69-16</td>
<td>81 F</td>
<td>Increasing coma, 2 weeks</td>
<td>Left lateral sinus</td>
<td>Diffuse 2+</td>
<td>Pulmonary embolism</td>
<td>Dehydration; old myocardial infarct</td>
</tr>
<tr>
<td>8</td>
<td>D 69-36</td>
<td>62 M</td>
<td>Lethargy, difficulty swallowing, increasing coma, 3 weeks</td>
<td>Superior sagittal, right and left lateral and sigmoid sinuses</td>
<td>Diffuse 3+</td>
<td>Pulmonary embolism; femoral vein thrombosis; cerebral artery thrombosis</td>
<td>Emaciation mitral stenosis; congestive heart failure; pulmonary infarction</td>
</tr>
<tr>
<td>9</td>
<td>D 69-61</td>
<td>74 M</td>
<td>Lethargy and coma, 4 days</td>
<td>Right and left lateral and sigmoid sinuses</td>
<td>Diffuse 2+</td>
<td>Focal 1+</td>
<td>Old myocardial infarction; congestive heart failure; bronchopneumonia</td>
</tr>
<tr>
<td>10</td>
<td>D 69-65</td>
<td>78 F</td>
<td>Lethargy, difficulty swallowing, seizures, increasing coma, 3 weeks</td>
<td>Left lateral and sigmoid sinuses</td>
<td>Diffuse 2+</td>
<td>Bronchopneumonia; acute duodenal ulcers (Cushing type); bronchopneumonia; congestive heart failure</td>
<td>Emaciation; multiple system chronic tuberculosis</td>
</tr>
<tr>
<td>11</td>
<td>D 69-72</td>
<td>47 F</td>
<td>Increasing debility and lethargy, 2 weeks</td>
<td>Superior sagittal sinus, superficial cerebral veins</td>
<td>Diffuse 3+</td>
<td>Focal 2+</td>
<td>Gangrene of left foot</td>
</tr>
<tr>
<td>12</td>
<td>D 70-2</td>
<td>68 F</td>
<td>Left-sided paralysis and coma, 3 days</td>
<td>Superior sagittal sinus and superficial cerebral veins; right and left lateral and sigmoid sinuses</td>
<td>Diffuse 3+</td>
<td>Cerebral artery thrombosis; femoral vein thrombosis; pulmonary embolism</td>
<td></td>
</tr>
</tbody>
</table>

* Focal indicates a localized area of damage.
The literature contains a number of cases of dural venous thrombosis and cerebral infarction in women receiving oral contraceptive agents.1

In another group of cases, of increasing significance, cerebral venous thrombosis with infarction has been observed in patients treated for prolonged periods in the respirator.2, 3 This complication is associated clinically with the syndrome commonly known as "brain death."

Past studies of cerebral vascular disease in the adult have been dominated by a preoccupation with occlusion of arteries. Clinically the diagnosis of "cerebral thrombosis" usually conveys a single meaning, arterial thrombosis. The medical literature is richly imprinted with studies defining the occurrence and effects of thromboembolic occlusive disease of cerebral arteries.

In contrast, cerebral venous thrombosis has been the subject of relatively little direct investigation. Interest in this problem has been episodic, unsustained. Substantially it is said, the pathology of cerebral venous thrombosis has an "historie à eclipse."4

The recently published studies of cerebral venous thrombosis by Kalbag and Woolf,5 Hennex,6 and Hahn7 offer comprehensive case material data; however, in these works and in other recent studies, information indicating the incidence of cerebral venous thrombosis, its occurrence in the aged, has not been available. Most reports dealing with incidence patterns are of the remote past, based on data obtained indirectly; these past analyses are mainly retrospective, derived on the basis of cumulative autopsy records—case material in which the completeness and precision of the necropsy dissection are patently uncertain. Thus in a review of 30,000 autopsies at the Los Angeles General Hospital only 14 instances of primary thrombosis of intracranial channels were reported.8 At Toronto General Hospital 38 cases of noninfective intracranial venous thrombosis were reported at autopsy in the 20-year period to 1953.9 The occurrence of cerebral venous thrombosis in England, as reported in recent vital statistics, averages less than 22 cases per year in a population over 56 million.6 Most investigators concerned with the problem of cerebral venous thrombosis have expressed the opinion that the condition has been underestimated in the past, its rarity greatly exaggerated, and its presence grossly overlooked clinically and pathologically.5, 9, 10

**Methods**

The basic study presented here, analyzing the occurrence of cerebral venous thrombosis in aged adults, was carried out in the three-year period between July 1, 1968, and July 1, 1971, at Danvers State Hospital, Hathorne, Massachusetts. In the present report, reference also is made to laboratory data and case

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The text continues with further details and analysis regarding the incidence and implications of cerebral venous thrombosis, including a discussion on the methods used for the study and the findings from the investigation.
TABLE 2
Age Distribution of Cerebral Venous Thrombosis in Adults

<table>
<thead>
<tr>
<th>Age</th>
<th>Total no. of cases autopsied</th>
<th>Cases with cerebral venous thrombosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>30-39</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>40-49</td>
<td>5</td>
<td>1</td>
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<tr>
<td>50-59</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>60-69</td>
<td>34</td>
<td>4</td>
</tr>
<tr>
<td>70-79</td>
<td>66</td>
<td>8</td>
</tr>
<tr>
<td>80-89</td>
<td>43</td>
<td>4</td>
</tr>
<tr>
<td>90-99</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>182</td>
<td>17</td>
</tr>
</tbody>
</table>

TABLE 3
Incidence of Cerebral Venous Thrombosis in Adults

<table>
<thead>
<tr>
<th>Cases autopsied</th>
<th>Number</th>
<th>Age average</th>
<th>Cases with cerebral venous thrombosis</th>
<th>Number</th>
<th>Age average</th>
<th>Incidence, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>97</td>
<td>71.8</td>
<td>13</td>
<td>73.7</td>
<td>13.4</td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>85</td>
<td>69.0</td>
<td>4</td>
<td>71.7</td>
<td>4.7</td>
<td></td>
</tr>
<tr>
<td>All cases</td>
<td>182</td>
<td>70.5</td>
<td>17</td>
<td>73.2</td>
<td>9.3</td>
<td></td>
</tr>
</tbody>
</table>
duraion, and severity of the neurological manifesterations.

**PATHOLOGICALLY**, in the brain both diffuse and localized damage occurs in cases of cerebral venous thrombosis (table 1).

Diffuse parenchymal changes in the brain, varying in severity, result from stasis and thrombosis present in the dural sinuses and in tributary deep and superficial cerebral veins. The brain characteristically is heavy, swollen, edematous and flabby, and externally presents a mottled gray cyanotic discoloration. Microscopically, hypoxic tissue damage reflecting circulatory stasis is evident. Distinctive cerebral neuronal changes occur. The cortex becomes punctuated by shrunken, deeply staining neurons which appear singly or in clusters (fig. 1). Some of the affected nerve cells, more labile, are quickly wiped out by the oxygen deprivation; neighboring cells of similar caste and form, having a higher threshold and proving more durable, appear unchanged and survive. Scholz has emphasized that the diffusely distributed depletion of neuronal elements in the brain which occurs in conditions of circulatory failure with hypoxia, although appearing unimportant anatomically, is associated with significant functional disability.

Diffuse cerebral damage of more severe form is often evident microscopically, occurring in a patchy, confluent pattern widely distributed through the cortex (fig. 2). The damage tends to be laminar, the third and fifth layers of the cortex becoming depleted; in the devastated, pale cortical zones, the cellular structures, neurons as well as glia, are wiped out.

Localized damage in the brain, focal areas of hemorrhagic infarction which occur with intracranial venous thrombosis, is of two basic forms, cortical and deep, corresponding to the occlusion of the superficial or the deep venous drainage of the brain. In the aged, cortical damage is the more frequently observed form.

Cortical and subcortical infarction, illustrated in figures 3a and b, results from stasis-thrombosis of the superficial cerebral veins and associated peripheral dural sinuses. On the cerebral surface, groups of veins stand out as turgid snakelike cords. The affected venous channels contain firm, dark red, laminated thrombi. The damaged cerebral convolutions have a dusky mottled appearance and are broadened and flattened. In the more involved regions, areas of venous infarction are evident as islands of gray-red softening (fig. 3a). On section, the cerebral hemispheres are edematous and thickened; the cortex in areas of minimal involvement appears as a thick congested ribbon, often stippled with minute focal hemorrhages. Microscopically, hypoxic neuronal damage is evident, and, at times, laminar cortical necrosis also is evident. In the more severely infarcted regions of the brain, broad areas of hemorrhagic necrosis appear extending down from the occluded surface veins, through the cortex into the underlying subcortical white matter (fig. 3b).

Deep cerebral infarction (major damage at the core of the hemispheres) is caused by thrombosis of the confluent and straight sinuses with occlusion of the vein of Galen and its deep tributaries (figs. 4a and b). Often, both cortical and deep infarcts appear in the same case.

Infarction in the brain produced by venous
Cortical form of cerebral venous thrombosis and infarction. The cerebral veins, distended with thrombus material, appear as turgid dark cords branching over the cerebral surface. The arteries, contrastingly, are evident as white wire-like structures (arterial system injected postmortem with light-colored pigment). In the frontoparietal areas, especially on the right, swollen occluded veins surround large, mottled discolorated portions of infarcted convolutions. Patient was a 75-year-old woman with a history of two weeks of increasing weakness and coma (case no. D 67-52).

Thrombosis is distinctly different, pathologically and topographically, from that resulting from thrombosis of cerebral arteries.

Pathologically, infarcts due to venous occlusion in the brain, as in any organ, are characterized by their uneven, hemorrhagic, necrotic pattern, in contrast to lesions of arterial origin which are generally pale and more circumscribed.

With thrombosis of major cerebral arteries, the topography of the resulting infarcts and the syndromic focal functional disabilities are generally well known medically. Much less known clinically and pathologically are the specific patterns of infarction related to thrombosis of major intracranial venous channels. The pattern and location of cerebral infarcts due to occlusion of large cerebral venous elements are plainly different from the distribution of infarcts in the cerebrum caused by thrombosis of major cerebral arterial branches. Anatomical-pathological studies by Kalbag and Woolf, Hahn, and others have established the basic regional patterns of infarctions in the brain resulting from occlusion of specific intracranial venous channels. Thus, occlusion of the superior sagittal sinus leads to infarction of the mid-sagittal and adjacent regions of the outer hemispheric walls, as illustrated in the case in figures 3a and b. Occlusion of the lateral venous sinus and its tributaries leads to infarction of the posterior convexity and adjacent white matter. In the thalamus and neighboring white matter, an associated deep, periventricular area of infarction is present.

Cortical and subcortical cerebral venous infarction. Section taken in the plane indicated by arrows in figure 3a. The massive hemorrhagic infarcts lie subjacent to the distended, occluded surface veins of the cerebrum. In each infarct the central area of hemorrhagic necrosis is bordered by less severely infarcted tissue and by pale, petechia-stippled tissue. On the right, in the thalamus and neighboring white matter, an associated deep, periventricular area of infarction is present.

Thrombotic impaction of the confluent dural venous sinus. The thrombosis extended to the lateral sinus on each side, upward into the superior sagittal sinus, and into the straight sinus and vein of Galen, resulting in deep cerebral infarction. The patient was a 74-year-old man with a six-day history of progressive weakness, paralysis, and coma (case no. NW 70-3).
LATENT CEREBRAL VENOUS THROMBOSIS

Deep cerebral venous infarction. Frontal section of brain in case described in figure 4a. The structures at the core of the cerebral hemispheres are necrotic, shredded, and hemorrhagic, with resulting intraventricular hemorrhage.

FIGURE 4b

temporal and occipital regions. Occlusions of the deep cerebral veins, as noted, lead to periventricular infarction. The deep core of hemorrhagic infarction, present in the case in figure 4, is manifestly attributable to occlusion of the deep venous drainage system; patently, no form of major artery occlusion can be substantially related to this pattern of cerebral infarction.

In most instances in the present study, the pathogenesis of the infarcted lesions (the underlying causal mechanism—venous thrombosis) was clearly defined both grossly and microscopically. In the case presented in figure 3a, at autopsy the arterial system of the brain was injected with radiopaque yellow pigment. In the illustration the arteries stand out as white branching vessels on the cerebral surface. The right frontoparietal region shows a mottled hemorrhagic area of infarction closely related anatomically to occluded large superficial veins (veins of Trolard); the infarcted area is surrounded and covered by veins distended with thrombus material. The infarcted area lies anatomically unrelated to the (injected) arteries which by x-ray were demonstrated to be patent. The intimate anatomical relationship of thrombosis of veins and infarction of subjacent cerebral cortex likewise is evident grossly in figure 7c and correspondingly, microscopically, in figure 2.

Syndrome Pattern

Clinically, in reviewing the case material in the current investigation, it was evident that cerebral venous thrombosis in the aged evokes a familiar symptom pattern. The basic consistent features of this syndrome have been recognized by clinical observers in the past. In patients affected, the first related symptom usually noted is the gradual development of lethargy and unresponsiveness in patients previously in good contact. Difficulty in swallowing often appears as an early symptom. At times there are focal neurological signs and other specific central nervous system findings. However, usually at the bedside there is evident a diffuse, subtle loss of neurological function. Somnolence extends into a deepening coma lasting over a period of days. In this period, with the gradual ebbing of bodily functions, it is of note that the temperature generally remains normal or near normal. Respiratory difficulty often appears terminally; the respiratory symptoms many times prove at autopsy to be due to pulmonary embolism. This basic pattern of afebrile progressive coma and respiratory insufficiency was recorded in the patient's chart in most cases of cerebral venous thrombosis reviewed in the present study (table 1). In the present series, most cases occurred in bed patients, some with chronic cardiac, respiratory, or renal disorders, others suffering from apparent minor interval illnesses.

The clinical pattern observed in patients with cerebral venous thrombosis, marked by an afebrile course with gradual neurological and respiratory deterioration, stands in contrast to the picture evident in other aged patients who develop bronchopneumonia or other complicating infectious diseases, who although septic with a rising terminal temperature, usually remain responsive during their illness until near the end.

The following two cases demonstrate the basic clinical and pathological patterns which characterize the syndrome of cerebral venous thrombosis in the aged; the first case clinically was a chronically ill bedridden patient who, at autopsy, showed the common cortical form of cerebral venous infarction, the second case was an elderly male who clinically was relatively well prior to his terminal illness, who pathologically proved to have the deep, periventricular form of cerebral venous infarction.

The first case (D-67-52), a 75-year-old woman, had had a bleeding peptic ulcer which had been controlled with medical treatment. However, despite supportive care she became weakened. During the last two weeks she became confused, drowsy, then comatose. At autopsy, there was extensive intracranial venous thrombosis, as well as bilateral femoral vein thrombosis. The brain externally presented widespread thrombosis of the superficial cerebral veins (fig. 3a). Thrombosis present in the superior sagittal and right lateral dural sinuses and in the tributary veins was associated with extensive cerebral cortical and subcortical hemorrhagic infarctions (fig. 3b).

The second case (NW 70-3) was a 74-year-old man, previously ambulatory, who first complained of malaise and symptoms of a cold; he then became weakened and unable to walk. This was followed by a period of transient aphasia and unconsciousness. The history revealed that three years previously the patient had been treated for femoral vein thrombosis and pulmonary embolism. In his terminal hospital course, he steadily deteriorated, presenting increasingly diffuse
neurological signs, with loss of deep tendon reflexes, weakness, paralysis of the extremities, and steadily deepening coma. Death occurred six days after the onset of his acute neurological symptoms. At autopsy there was evidence of congestive heart failure with pulmonary edema and congestion of viscera. The heart showed severe coronary sclerosis. In the aorta there was a small flat mural thrombus above the celiac artery orifice. The brain was swollen and heavy, weighing 1,500 gm (average, 1,250 gm). The main arteries at the base of the brain were strikingly free of sclerosis; the carotid artery system in the neck was demonstrated to be patent. The cerebral convolutions showed conspicuous flattening. The medial surfaces of the hemispheres and the parasagittal frontal and parietal areas showed patchy hemorrhagic infarction. The superficial cerebral veins were engorged, especially the bridging veins. The dural venous sinuses contained bulging deposits of adherent thrombi. The confluence of the sinuses was impacted; the thrombosis extended continuously into the superior sagittal, straight, and lateral sinuses (fig. 4a). Sectioning the brain revealed massive deep infarction extending outward into the hemispheric walls, and inward, with the ventricles becoming distended with blood (fig. 4b). Scattered patchy cortical infarction, also present in this case, was attributable to the occlusion of the peripheral venous sinuses and tributary veins.

FACTORS INFLUENCING THE OCCURRENCE OF CEREBRAL VENOUS THROMBOSIS

Age Factor
A high incidence of latent, unrecognized cerebral venous thrombosis in aged adults has been postulated in the past. Gowers wrote of the common occurrence of the condition in the "very old." However, this observation did not gain lasting attention. There is a need in the present day for direct information based upon detailed autopsy studies to define the frequency of cerebral venous thrombosis in the aged.

In the present study, in the group of patients over the age of 60 years (comprising 147 patients), there were 16 cases (10.8%) with cerebral venous thrombosis (table 2). In contrast, in the 35 cases autopsied in the age group below 60 years at death, there was one case of cerebral venous thrombosis. Significantly, the high incidence of intracranial venous thrombosis in aged patients corresponds to the high incidence of pulmonary embolism and other forms of thromboembolic disease in the aged.

Sex Incidence
Female patients present an incidence of cerebral venous thrombosis over twice as great as males (table 3); in the present study, 13.4% of females had cerebral venous thrombosis compared to 4.7% in males. The greater incidence of thromboembolic disease in the female, particularly pulmonary embolism, has been evident in autopsy studies in the past.

Systemic Processes
Congestive heart failure, dehydration, and debility manifestly contribute to the occurrence of cerebral venous thrombosis.

Congestive heart failure. Congestive heart failure, leading to systemic venous congestion, ultimately with local visceral venous stasis-thrombosis and consequent hemorrhagic infarction, is an elementary clinical-pathological relationship. In adults with congestive failure, the development of phlebothrombosis in extremities is common, and the occurrence of renal and other visceral venous infarction is not rare. Particularly susceptible to this mechanism of damage is the brain. Gowers and other investigators related circulatory failure to the occurrence of cerebral venous thrombosis. This process, the occurrence of congestive heart failure with consequent cerebral venous thrombosis and infarction, as noted, makes its appearance frequently in the human fetus and newborn. In studies of adult cases, in a review of 39 patients with cerebral venous thrombosis, Barnett and Hyland reported that in ten cases there was heart disease, usually with right heart failure. Noetzel and Jerusalem indicated the occurrence of cardiovascular disease in 24 of 105 collected cases of cerebral venous thrombosis. This relationship of cardiac and cerebral disease has not been adequately explored in the past. As plainly stated by Kalbag and Woolf, "One can only conclude that the sinuses are far from being regularly examined in patients with cardiovascular disease."

In the present study, congestive heart failure was evident in six of 17 cases with cerebral venous thrombosis (table 1).

Dehydration, debility, and emaciation are factors which have long been associated with the occurrence of cerebral venous thrombosis, in children as well as in adults, especially in the aged. These bodily conditions were commonly evident in the cases reviewed in the present investigation (table 1).

In the debilitated, thromboembolic disease is often associated with circulatory failure and infectious disease, as in the following case (D 69-72).

This was a 47-year-old female, the youngest individual in the series with cerebral venous thrombosis, who had multiple-system chronic tuberculosis. The cranial examination revealed firm gray-tan-red adherent thrombi in the anterior portion of the superior sagittal sinus; the attached bridging veins were turgid, occluded by thrombi. The peripheral dural venous sinuses in other portions contained firm dark red clot material. The surface of the cerebrum showed areas of mottled gray-purple discoloration and softening, especially in the paracentral regions (fig. 5).

Coagulation defects of varied severity appear to manifest their effects often in the aged, especially in the female, contributing to the occurrence of
thrombotic processes. The investigation of this hematological factor, of broad significance, was not within the province of the present study.

Multiple Thrombotic Processes
Multiple thrombotic processes are often present in patients with cerebral venous thrombosis. In the current study, ten of the 17 patients with cerebral venous thrombosis had thrombotic lesions, venous and arterial, at other sites in the body.

In the following case (D 70-12), the patient, an 83-year-old female with moderate hypertension, initially had symptoms of an upper respiratory infection. In bed, she became weakened and listless, was unable to swallow, and developed tremors of the extremities. Increasing cyanosis of the legs appeared. Coma developed gradually. At autopsy there was pronounced cyanosis of the face and nailbeds. The neck veins were distended. The skin was dehydrated. The heart was dilated and flabby. There was prominent venous engorgement through the body. Venous thrombosis and infarction were present in the following sites: intracra-

![Figure 5](http://stroke.ahajournals.org/)

Cerebral venous thrombosis in a debilitated patient with chronic tuberculosis. Large cerebral veins in the frontoparietal regions occluded by firm, mottled thrombi which extend into the superior sagittal sinus (case no. D 69-72).
Discussion

The present study serves to emphasize that, as with most pathological phenomena, the process of cerebral venous thrombosis and infarction is not an all-or-none matter. In this investigation, in addition to the 17 cases of cerebral venous thrombosis defined, attention was drawn to the occurrence of 19 other cases of equivocal nature, with early brain infarction but without well-formed venous thromboses. Pathologically, in the brain as in other organs, with the occurrence of prolonged slowing of local venous blood flow, hypoxic tissue damage results, at times extensive, without the establishment of organized thromboses. The recognition of cases with cerebral damage of this nature is of basic importance pathologically and clinically.

In analyzing the clinical and pathological data in the current study, five basic concepts which emerge, bearing upon the underlying causes and
manifestations of cerebral venous thrombosis in the aged, merit emphasis:

(1) **Age incidence.** The occurrence of cerebral venous thrombosis increases with advancing age in adults.

(2) **Sex incidence.** Cerebral venous thrombosis is statistically of greater incidence in females.

(3) **Progressive lethargy and coma** in the period prior to death, often preceded by difficulty in swallowing, often with afebrile course, marks the syndrome of cerebral venous thrombosis in the aged.

(4) **Multiple sites of thrombotic disease** are often present in patients with cerebral venous thrombosis; concurrent pulmonary embolism is frequent.

(5) **Antecedent systemic disease**, especially congestive heart failure, contributes essentially to the local process of circulatory stasis, to the development of cerebral venous thrombosis.

The high incidence of cerebral venous thrombosis in the aged (and in the newborn) has been overlooked in the past largely because of technical faults at postmortem examination. The present study focuses attention on the need for a more vigilant, unhurried examination of the cranial cavity at autopsy. In the interpretation of nervous system disease stemming from circulatory and other systemic bodily dysfunction, there is need for a closer correlation of the clinical record and the general autopsy data with the findings in the brain.

Cerebral venous thrombosis has long posed a diagnostic challenge to the clinician, especially to the neurologist and radiologist. In the last few years,
however, significant advances have been made in developing more precise methods of clinical diagnosis. Electroencephalography and brain scan have been used increasingly. Arteriography, supplemented by retrograde venography, is reported effective in confirming the clinical diagnosis of cerebral venous thrombosis. In the past, the diagnosis of cerebral venous thrombosis clinically was associated with a very poor prognosis. As evidenced in the present study, however, the damage to the brain with intracranial venous thrombosis varies in a wide range. The condition need not be viewed as hopeless. In adult cases as well as in the newborn, there are well-documented reports of survival, often with minimal sequent disability.

It is imperative that the diagnosis be made early. In older adults as well as in younger patients, if the condition is anticipated and recognized, the diagnosis may be confirmed promptly by radiographical and other available means. As in other forms of thromboembolic disease, anticoagulation, in selected cases, remains the standard treatment. Recently developed thrombolytic agents have been added to therapy. In current reports, in cases diagnosed early and treated actively, resolution of the process with increasingly favorable results has been obtained. In the present day, as the extent of its incidence is revealed, cerebral venous thrombosis poses a problem of broad concern. With this process occurring predominantly in adults of advanced age, and with this age group making up an increasingly large proportion of the population, it can be anticipated that the incidence of cerebral venous thrombosis will correspondingly increase.

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