Cerebral Manifestations of Ergotism
Report of a Case and Review of the Literature

HOWARD J. SENTER, M.D.* ABRAHAM N. LIEBERMAN, M.D.,†
AND RICHARD PINTO, M.D.$

SUMMARY A patient with diffuse and focal cerebral dysfunction was found to have absent peripheral pulses. Cerebral angiography revealed evidence of an arteritis with bilateral high grade carotid stenosis. When there was no laboratory confirmation of the arteritis, an iatrogenic etiology (ergotism) was suspected. This was later confirmed by the patient. The pertinent literature on ergotism is reviewed, and it is emphasized that ergotism may develop in patients on therapeutic doses of the drug.

There was no history of congenital or rheumatic heart disease, local neck trauma or infection, hypertension, diabetes or hyperlipidemia. The patient was not taking oral contraceptives or any other medication. There was no family history of heart disease, stroke, hypertension, or diabetes.

On admission the temperature, pulse and respirations were normal. Blood pressure was 110 mm Hg by palpation on the right and unobtainable on the left. Examination of the lungs, heart and abdomen was normal. There were bilateral subclavian pulses but no axillary, brachial, or radial pulses. Carotid pulses were palpable and there were no bruits. There were weak femoral pulses but none below the groin. All extremities were pale and cold. Neurologically, the patient was lethargic but arousable; she was confused and disoriented to time and place with a short attention span and exhibited marked emotional lability; she was not aphasic. Examination of the fundi was unremarkable. There was a dense left homonymous hemianopia, a left hemisensory deficit, and a left hemiplegia (as marked in the arm as in the leg). There was a left Babinski sign without a reflex preponderance.

Hematocrit, hemoglobin, white blood cell count, differential and platelet count were all normal. Sedimentation rate was 12 mm per hour. Kaolin partial thromboplastin time was slightly shortened and there was mild elevation of factors II and V; otherwise, the coagulation profile was normal. Sodium, potassium, chloride, CO₂, calcium, phosphorus, total protein, albumin, direct and indirect bilirubin, alkaline phosphatase, lactic dehydrogenase, creatinine phosphokinase, uric acid, fasting blood sugar, two-hour postprandial sugar, cholesterol, triglycerides, VDRL, T3, T4, serum and immune electrophoresis, antinuclear antibody and lupus preparations were all normal. Urinalysis revealed no protein or red cells. Skull films, chest x-ray, and flat plate of the abdomen were normal. Electrocardiogram and echocardiogram were normal. Electroencephalogram (done one day after admission) revealed 1.5 to 4 cycles per second

THE TOXIC EFFECTS OF ERGOT on the peripheral vasculature are well recognized, but the toxic effects of ergot on the cerebral vasculature are less well known. This paper describes the neurological and angiographical manifestations of ergotism in a patient, and reviews the pertinent literature.

Case Report

A 36-year-old, right-handed white woman awoke confused on the morning of admission, and had a left hemiparesis. At age 17, the patient had migraine headaches characterized by a prodrome of scintillating scotomata followed by a right or left hemicanal headache terminated by nausea. For 20 years she had been taking ergotamine tartrate suppositories (Cafergot®) with good symptomatic relief. For the three weeks prior to admission she had been under unusual emotional stress and noted a sharp increase in the frequency of her headaches. However, she denied taking more than half a suppository (1 mg of ergotamine) a day. One week prior to admission she consulted a physician because of leg cramps. He found absent pulses below the groin and, unaware of the history of ergot usage, prescribed a vasodilating agent, nylidrin hydrochloride (Arlidin®), without symptomatic relief. Nylidrin was discontinued a few days later. On the day prior to admission, the patient was unusually drowsy and that night had difficulty climbing stairs and getting into bed. She awoke at 6 A.M. on the day of admission and was unable to move her left side.

irregular slow waves bilaterally. Lumbar puncture revealed normal opening and closing pressures, no cells, and normal protein, glucose and gamma globulin. Computerized tomography (CT scan), with and without contrast, revealed large bifrontal areas of decreased absorption. There was no ventricular dilation or shift of midline structures (fig. 1).

The patient underwent cerebral angiography with selective catheterization of both common carotids. Abrupt rat-tail tapering of the cervical portion of the right internal carotid artery (ICA) was demonstrated. The artery was maximally narrowed at the level of C2-3 (fig. 2a) with the narrowing extending to involve the petrous, precavernous and cavernous portions of the vessel. Intracranially, an enlarged ophthalmic artery filled in a retrograde fashion from the external carotid and opacified the middle and anterior cerebral arteries; it also filled the petrous, precavernous and cavernous portions of the internal carotid (fig. 2b). Cerebral circulation time was nine seconds. The left common carotid angiogram was a mirror image of the right (figs. 3a and b). Following the left common carotid injection, the patient had a transient right hemiparesis. Angiography was not continued.

Hospital Course

Upon admission neither the physicians nor the husband were aware of the patient's daily use of ergotamine. On the basis of the CT scan and the angiogram, a diagnosis of bifrontal infarctions secondary to an arteritis was made and the patient was begun on corticosteroids, methylprednisolone (Solumedrol®) 40 mg intravenously every six hours. The patient received a total of 160 mg of methylprednisolone during 24 hours. The patient was also anticoagulated with heparin. The normal sedimentation rate and negative ANA and LE preparations prompted several physicians to raise the possibility of an iatrogenic (drug-induced) arteritis. Upon further questioning of the husband, the possibility of ergotism was strongly suggested and steroids and heparin were discontinued. Thirty-six hours later peripheral pulses in all four extremities returned. The hemiplegia, hemisensory defect and hemianopia resolved completely in ten days. At that time, the patient exhibited inappropriate affect, short attention span and childlike un-
inhibited behavior. She complained of burning dysesthesias in both feet. Ten days after this, all signs and symptoms completely resolved.

Discussion
The ergot alkaloids have a number of effects on the vascular system, some mutually antagonistic. They are direct vasoconstrictors, alpha adrenergic blockers, and central sympatholytics. Their effectiveness as vasoconstrictors is the basis of their use in the treatment of migraine. Structural differences among the ergot alkaloids determine their relative strength as vasoconstrictors, alpha blockers or central sympatholytics. Additionally, their effects in man depend upon differences in individual sensitivities and in the sensitivity of the various vascular beds (cerebral, coronary, peripheral, renal, hepatic, mesenteric). Furthermore, the route of administration may influence their effectiveness: Orally, the ergot alkaloids are irregularly absorbed from the small intestine; rectally, they are absorbed faster and attain higher blood levels. Ergot toxicity may be aggravated and/or precipitated by sepsis, hepatic or renal disease, thyrotoxicosis or pregnancy. Specific drugs known to potentiate the effects of ergot are oral contraceptives and certain antibiotics.

The toxic effects of the ergot alkaloids have been known for a thousand years. Individuals who ingested rye contaminated with the fungus Claviceps purpurea had “epidemic ergotism” consisting of (1) gangrene of the extremities, or (2) seizures, coma and dementia, or (3) a combination of the two. The gangrene was thought to be a result of intense peripheral vasoconstriction while the seizures, coma and dementia were thought to result from either a direct toxic effect on the CNS or intense cerebral vasoconstriction with subsequent hypoxia and infarction.

The introduction of angiography enabled investigators to verify that the mechanism responsible for the toxic effects of
ergot was intense vasoconstriction with secondary occlusion and thrombosis of medium and small arteries.1, 6 Most reports have stressed the effects of ergot on the peripheral vasculature.1, 6 This effect is usually bilateral and symmetrical, but both asymmetrical and unilateral vasoconstriction has been described.6 Some reports have stressed the multiplicity of vascular beds affected10 including the mesenteric,11 renal,12 coronary,13 and ophthalmic.14 Thus, Merhoff and Porter2 described one patient with bilateral peroneal nerve palsies (thought to be secondary to constriction of the vasonervorum) and one patient with transient monocular blindness (thought to be secondary to vasoconstriction of the retinal arteries). Gupta and Strobos14 also reported a patient with bilateral amblyopia. They reviewed the literature on the ophthalmological complications of ergotism and concluded that ischemia occurred at a watershed zone between the peripheral and axial vasculature of the optic nerve. Most of these patients were not septic and did not have renal or hepatic dysfunction.

Cerebral manifestations of nonepidemic ergotism have been less frequently described and rarely has the underlying mechanism been documented. Thus, although Hudgson and Hart15 described a patient who, after taking 30 Cafergot tablets, went into coma without lateralizing findings and without pulses below the groin, the mechanism of the cerebral symptoms remains speculative because angiography had not been performed. The symptoms could represent a direct toxic effect of ergot on the brain or diffuse cerebral vasoconstriction. Adequate documentation of the mechanism responsible for some of the cerebral manifestations is found in the reports of Brohult, Forsberg and Hellstrom1 and of Richter and Banker.16 Brohult et al.1 described a patient who had signs of diffuse cerebral dysfunction (confusion) in addition to a left hemiparesis. Angiography revealed occlusion of the right internal carotid artery. Thus, while the mechanism underlying the right cerebral dysfunction is known, the mechanism underlying the diffuse dysfunction is not. Richter and Banker16 reported a patient with a minimal left facial palsy, hypesthesia of the left arm, and nystagmus on right lateral gaze. These findings were interpreted as being consistent with right cerebral dysfunction (omitting the nystagmus). Angiography revealed marked "rat-tail" narrowing of the distal right internal carotid artery at the base of the neck.

Our patient presented with signs of both diffuse and right cerebral dysfunction. The mechanism for both was revealed to be vasoconstriction with bifrontal infarction. Our failure to promptly recognize the cerebral symptoms as being due

![Figure 3B](http://stroke.ahajournals.org/)

**Figure 3B** Left common carotid angiogram: lateral projection, mid-arterial phase, "head series." The angiogram demonstrates retrograde filling of the ophthalmic artery which then opacifies the supraclinoid, intracavernous, and petrous portions of the ICA (arrows), and the middle cerebral complex. No opacification of the anterior cerebral artery is seen.
TABLE 1  Neurological Manifestations of Ergotism

<table>
<thead>
<tr>
<th>Neurological deficit</th>
<th>Site of vascular disease</th>
<th>Dose of ergotamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coma*</td>
<td>Diffuse cortical</td>
<td>30 mg, single dose</td>
</tr>
<tr>
<td>Uninhibited behavior</td>
<td>Bifrontal</td>
<td>1 mg/day, rectally</td>
</tr>
<tr>
<td>Hemiparesis/</td>
<td>Internal carotid</td>
<td>1 mg/day, rectally</td>
</tr>
<tr>
<td>hemianopia*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amaurosis*</td>
<td>Retinal artery</td>
<td>4-6 mg/day, rectally</td>
</tr>
<tr>
<td>Papillitis*</td>
<td>Optic nerve ischemia</td>
<td>6-8 mg/day, orally</td>
</tr>
<tr>
<td>Peroneal nerve palsy</td>
<td>Vasovascular</td>
<td>4 mg/day, rectally</td>
</tr>
</tbody>
</table>

*This patient.

to ergotism was related to the rarity of this presentation. In retrospect the occurrence of diffuse and focal (right) cerebral dysfunction associated with absent peripheral pulses in a young person with angiographical evidence of an arteritis but without laboratory confirmation should have raised the possibility of an iatrogenic etiology. If the patient's history was accurate, then the arteritis occurred with a dosage of ergot which is well below the maximum recommended dosage. The patient had been on no more than 1 mg per day (rectally) for three weeks, 7 mg per week. The maximum recommended dosage is 8 mg per week (rectally). Moreover, she had used the drug safely for 20 years. Either the patient’s symptoms were due to a cumulative effect of the drug or she took more of the drug than she remembers. Table 1 summarizes some of the recorded cases of neurological dysfunction occurring during ergot therapy and correlates them with the dosage at which they occurred.

Lastly, with regard to treatment, various procedures including sympathetic blockade, vasodilating agents, corticosteroids and anticoagulants have been employed without success. In our patient a vasodilating agent, corticosteroids, and anticoagulants did not alter the course of the dys-

function. As ergotism is self-limiting, the best treatment is prompt recognition and withdrawal of the drug.

Acknowledgment

The authors wish to thank Drs. Morton Leibowitz, Abraham Sunshine, Frank C. Spencer, Joseph Cunningham and Al Culliford for their invaluable help in diagnosis and treatment; Drs. Bennett Derby, William K. Haas and Clark T. Randt for reviewing the manuscript; and Ms. Kathleen Faridazar for typing the manuscript.

References

6. Yater WM, Cahill JA: Bilateral gangrene of feet due to ergotamine tartrate used for pruritus of jaundice. JAMA 106:1625-1631, 1936

H J Senter, A N Lieverman and R Pinto

Stroke. 1976;7:88-92
doi: 10.1161/01.STR.7.1.88

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1976 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/7/1/88