



This Week in the Journal

November 21, 2002

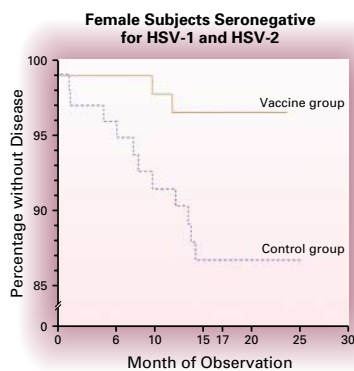
“All nine cases of HPV-16–related cervical intraepithelial neoplasia occurred among the placebo recipients.”

A Vaccine against Human Papillomavirus Type 16

Human papillomavirus type 16 (HPV-16) is sexually transmitted and is present in 50 percent of cervical cancers. This randomized, double-blind trial assessed the effectiveness of a vaccine that consists of HPV-16 L1 virus-like particles in women who were seronegative for HPV-16. The vaccine was highly effective in preventing HPV-16 infection.

This study may have important public health implications, since immunization of uninfected women against HPV-16 infection should reduce the incidence of cervical cancer. Of the women who received the vaccine, 99.7 percent had seroconversion and none became infected with HPV-16 after a median follow-up of 17.4 months.

see page 1645 (editorial, page 1703)



A Vaccine against Genital Herpes

Two double-blind, controlled trials assessed the efficacy of a glycoprotein-D–subunit vaccine to prevent genital herpes disease. The vaccine elicited humoral and cellular responses, but efficacy was found only in women who were seronegative for both herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 (HSV-2) (efficacy in the two studies was 73 and 74 percent). The vaccine was not efficacious in women who were seronegative for HSV-2 if they were seropositive for HSV-1, nor was it efficacious in men.

Genital herpes is epidemic, and a vaccine is needed that can prevent both symptomatic disease and transmission of the virus. These trials find some efficacy for this vaccine, but only in women who are seronegative for both HSV-1 and HSV-2. We do not yet know whether this vaccine can prevent asymptomatic infection and reduce the transmission of HSV.

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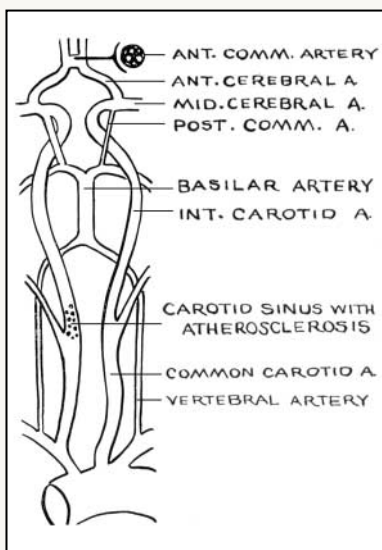
PERSPECTIVE

Transient Ischemic Attacks

The occurrence of fleeting episodes of numbness or paralysis was known to early physicians. One referred to them as “straws which show how the intracranial wind is blowing.” In 1950, a patient with a left-sided paralysis reported that before his stroke he had several brief spells of blindness in his right eye. “Isn’t it funny, it was in the wrong eye? I went blind in the right eye and got paralyzed on the left side.” The patient had metastatic colorectal cancer and died shortly afterward. Autopsy disclosed occlusion of the right internal carotid artery in the neck (see Figure). Transient blindness in one eye (transient monocular blindness) had identified the artery involved in the stroke but, more important, had provided a warning that a stroke was in the offing.

The period in which prodromal attacks occurred offered an opportunity to stave off the stroke. Anticoagulation and possibly arterial surgery were proposed. Warning spells, it was found, occurred in association with thrombosis at many arterial sites — internal carotid, middle cerebral, anterior cerebral, posterior cerebral, basilar, vertebral, and the many penetrating arterial branches running to the deeper parts of the brain, internal capsule, thalamus, and pons. Until that time, the possibility of doing something about strokes had not been considered.

The past 50 years have witnessed impressive advances in the prevention of fatal and paralyzing strokes. The landscape of stroke has greatly changed for the better. The most effective preventive measure, by far, is the treatment of high blood pressure. If blood pressure were kept at or below 130/80 mm Hg, 75 per-



Site of Carotid Occlusion in the 1950 Case.

Adapted from the *AMA Archives of Neurology and Psychiatry* (1951;65:347-52) with the permission of the publisher.

cent of strokes would be eliminated. A second crucial measure is the use of anticoagulation to prevent embolism from the left atrial appendage in atrial fibrillation and from left ventricular mural thrombus associated with myocardial infarction. Correction of blood lipid profiles provides a valuable assist.

A more immediate opportunity to prevent or attenuate the effects of a stroke arises when patients present with transient ischemic attacks — usually brief spells of numbness, weakness, or blindness, which are common harbingers of an imminent thrombotic stroke. The peri-

od in which such prodromal transient ischemic attacks occur gives physicians the time and opportunity to introduce measures aimed at staving off the stroke.

Transient ischemic attacks are a clinical entity. Although the standard current definition allows a 24-hour limit, as pointed out in two articles in this issue of the *Journal* (pages 1687–1692 and 1713–1716), symptoms and signs usually last less than an hour. Actually, in 90 percent of cases, the symptoms last less than 10 minutes. In a personal series of 50 cases, the longest duration of a basilar-artery transient ischemic attack was one hour. Because of their brief duration, transient ischemic attacks are rarely witnessed by a physician; the patient and his or her family usually provide the description.

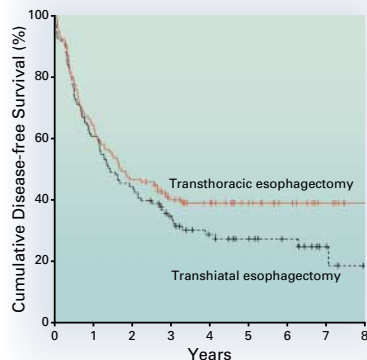
The clinical characteristics of transient ischemic attacks depend on the artery undergoing thrombosis. There are more than 17 possible arterial sites on each side of the brain, and transient ischemic attacks at each site have their own pattern of symptoms and signs. The number of possible clinical pictures is formidable — numbness, with or without weakness of the face, hand, or leg; paralysis; slurred speech; dizziness; double vision; hemianopia; transient monocular blindness; imbalance; aphasia; confusion; head pain; and even upside-down vision. The symptoms can occur in many different patterns.

Diagnosis may not be easy. In the interpretation of transient ischemic

Conditions That May Cause Symptoms or Signs Suggestive of Transient Ischemic Attack.

Migraine	Hypoglycemia
Inner-ear dizziness	Thrombocythemia
Arterial dissection	Polycythemia
Transient global amnesia	Severe postural hypotension
Subdural hematoma	Hyperviscosity
Anticardiolipin-antibody syndrome	Cervical disk disease
Akinetic seizure	Carpal tunnel syndrome
Parietal-lobe epilepsy	Cerebral venous thrombosis
Subacute bacterial endocarditis	Temporal arteritis

Transthoracic versus Transhiatal Esophagectomy for Adenocarcinoma



This study compared extended transthoracic resection with limited transhiatal resection for adenocarcinoma of the esophagus or gastric cardia. The five-year survival rates in the two groups were not significantly different, but a nonsignificant trend in overall survival favored transthoracic resection in later years.

Is a more extensive, more invasive operation for cancer better than a more limited, less invasive procedure? The choice between extended surgery with its associated morbidity and a more limited operation still depends on individual preference and on the presence or absence of coexisting conditions.

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attacks, an important distinction must be made. Has there been only one attack, or have there been multiple attacks with the same pattern? Multiple transient ischemic attacks usually indicate critical narrowing of the lumen of the involved artery by an atherosclerotic plaque with superimposed thrombus — a precarious situation calling for immediate intervention. If there has been only one transient ischemic attack when the patient presents, it may simply be the first of several that will follow; thus, a site of arterial stenosis consistent with the clinical picture must still be sought. Alternatively, a single attack may reflect a different cause — a small embolus that has entered the cerebral circulation and caused brief ischemia. This is a single event. There will be no additional transient ischemic attacks, since emboli do not cause repeated attacks of the same pattern. The source of an embolic transient ischemic attack must be sought in the heart, lungs, aortic arch, or large arteries of the neck. Emboli associated with atrial fibrillation are usually larger and more damaging and cause longer-lasting deficits, rather than transient ischemic attacks.

A good many conditions may be associated with brief spells suggesting transient ischemic attacks. Several of these are listed in the Table. Some 50 percent of cases of transient monocular blindness occur in

the absence of carotid vascular disease. A spell that is consistent with a transient ischemic attack is a medical emergency, and the patient should be evaluated immediately. The physical examination should include measurement of blood pressure, evaluation of cardiovascular status, and a neurologic examination. The blood pressure will usually be elevated and should not be lowered in the face of arterial narrowing. A carotid bruit may be a clue. Ultrasonography, magnetic resonance angiography, and computed tomographic angiography will detect severe stenosis and disturbed blood-flow patterns in the large arteries. The use of standard angiography has waned, although it remains the gold standard. Computed tomography may detect a subdural hematoma, tumor, or other unexpected condition. The penetrating arteries are too small to be assessed by the foregoing methods, and their involvement is inferred from the exclusion of other sites, backed by the clinical picture and possibly by evidence of abnormalities in the parenchyma on magnetic resonance imaging.

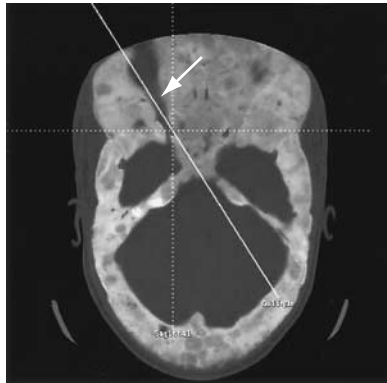
A bolus of heparin should be given intravenously in case the situation is critical. The patient may be a candidate for carotid endarterectomy, angioplasty, or stenting. The use of fibrinolysis at the transient-ischemic-attack stage of arterial stenosis has

not been reported. The use of angioplasty in the intracranial arteries is reported with increasing frequency. Otherwise, long-term therapy with warfarin or platelet antiaggregants should be begun, with the goal of preventing the formation of fresh thrombus and thus avoiding a stroke. But the risks of anticoagulation must also be recognized.

In this issue of the *Journal*, Johnston's Clinical Practice article (pages 1687–1692) discusses current recommendations for the evaluation and management of transient ischemic attacks and emphasizes that rapid diagnosis and intervention are essential. A Sounding Board article by Albers and colleagues (pages 1713–1716) recommends redefinition of a transient ischemic attack as lasting less than one hour, further qualified by whether imaging shows brain-tissue damage. Nosologic precision is improved by such a definition, but the question of whether minor ischemic brain damage has occurred should not distract the physician from the essential question of whether a cerebral artery is severely narrowed and a stroke threatening. Both articles highlight what was first recognized more than 50 years ago — that a transient ischemic attack sounds an alarm.

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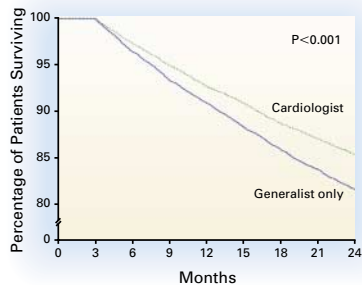
Narrowing of the Optic Canal in Fibrous Dysplasia

In patients with fibrous dysplasia, the optic canals may become encased by abnormal bone. Loss of vision is a complication, but there is controversy about whether prophylactic surgical decompression of the optic nerve can be helpful. Careful analysis of computed tomographic studies in 38 patients with polyostotic fibrous dysplasia or the McCune–Albright syndrome showed that most had complete encasement of the optic canal, but there was no clear relation between the size of the canals and visual function.

The data in this study are cross-sectional, and a longitudinal study is needed. But the findings indicate that narrowing of the optic canals does not in itself result in loss of vision. Therefore, prophylactic surgical decompression may not be indicated in patients with these abnormalities.

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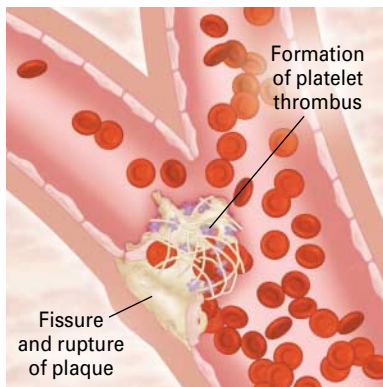
Special Article: Ambulatory Care and Mortality after Myocardial Infarction



The investigators used Medicare data to assess associations between the type of physician providing ambulatory care and mortality after myocardial infarction among 35,520 patients 65 years of age or older. After adjustment for multiple potential confounders, patients who saw a cardiologist in the three months after discharge from the hospital had lower mortality at two years than similar patients who saw only an internist or a family practitioner (14.6 percent vs. 18.3 percent, $P < 0.001$). Patients who saw both a cardiologist and an internist or a family practitioner had the lowest mortality rates.

Although the possibility of some residual confounding cannot be dismissed, these results suggest that survival after myocardial infarction is improved when a cardiologist is involved in ambulatory care, preferably together with an internist or a family practitioner.

see page 1678 (editorial, page 1709)



Clinical Practice: Transient Ischemic Attack

A 72-year-old woman telephones her physician immediately after recovering from a 30-minute episode of difficulty speaking and weakness of the right side of the face and right arm. Her medical history is unremarkable. How should she be treated?

see page 1687 (Perspective, page 1642)