letters to the editor

Pharmacology of cranial dystonia

To the Editor: We read with interest the articles by Tolosa and Lai¹ and Casey,² who suggested that Meige's disease is due to "striatal dopaminergic preponderance," and the more recent papers by Micheli et al³ and Tanner et al⁴ on the pharmacology of this condition. The major difficulty with all these otherwise excellent and interesting reports is that they seek to establish a consistent pharmacology to this disorder on relatively small numbers of patients.

Tolosa and Lai reported inconsistent results in 5 patients, Casey described 2 patients, Micheli et al treated 2 individuals with the disease (and reported 2 others in an addendum), and Tanner et al studied 13 patients. Our own pharmacologic observations of 56 patients with cranial dystonia do not suggest that there is any uniform pharmacologic profile for this curious illness. All of the patients were treated with maximum tolerated doses of the drugs indicated in the table for periods of weeks to months. Slow titration of each drug also allowed evaluation of patient response to low doses, particularly in the case of lisuride, where a dosage of 1.2 to 3.0 mg was given for extended periods. Improvement refers to a degree of benefit sufficient to persuade the patient and the physician that it was worthwhile continuing the medication. It is also worth noting that, in our own double-blind studies of drug therapy for this condition, we have found that placebo treatment may cause an appreciable improvement of up to 20% in disability scores.

Tolosa and Lai observed a decrease in the intensity of cranial dystonia after apomorphine. They interpret this as indicating "striatal dopamine preponderance," because apomorphine, in the doses given, may reduce the chorea of Huntington's disease and the orofacial movements of tardive dyskinesia, perhaps by actions on presynaptic dopamine receptors. Micheli et al³ confirmed the effect of apomorphine in their two cases. However, other dopamine agonists, in general, have little or no effect on cranial dystonia. Tolosa and Lai were unable to demonstrate any

effect of levodopa in their small series of patients, and none of our 18 patients so treated improved; indeed, 2 got slightly worse. The other dopamine agonists shown in the table had no effect whatsoever, except lisuride, which improved one of our patients. Micheli et al³ reported improvement in four patients treated with lisuride (two of whom were mentioned in an addendum). This inconsistent response to lisuride may reflect variations in its absorption when given orally. However, even if lisuride does sometimes provide benefit, pharmacologic conclusions are difficult because it is a powerful serotonin agonist as well as a dopamine agonist. Furthermore, the effects of apomorphine may reflect its sedative properties rather than any selective presynaptic dopamine action.

Tolosa and Lai, and Casey, based their pharmacologic arguments on the effects of dopamine antagonists for haloperidol¹ and perphenazine² improved cranial dystonia in their patients. However, we have treated many patients with such drugs and with presynaptically acting dopamine antagonists such as tetrabenazine and alpha-methyl-paratyrosine (AMPT),⁵ but with no consistent effects (table). Indeed, we have seen the involuntary movements of various facial areas respond in opposing directions, as in one patient treated with AMPT in whom the jaw and tongue movements improved but blepharospasm increased.⁵ Less than 10% of patients treated with phenothiazines, haloperidol, pimozide, tetrabenazine, or AMPT gained useful benefit. Unwanted side effects of these drugs were common and disabling, particularly pseudoparkinsonism, akathisia, and depression.

Both Tolosa and Lai, and Casey, also used observations on the effects of anticholinergic and cholinergic drugs as subsidiary evidence to support their arguments for "striatal dopamine preponderance" in cranial dystonia. In fact, Tolosa and Lai found that physostigmine aggravated the condition in their patients, which is the reverse of what might be expected. They avoided this problem, however, by pointing out similar inconsistent responses to physostigmine in Huntington's disease. Casey described the opposite effect of deanol, a supposed cholinergic agent of dubious reputation which, in two of his patients, apparently improved matters; however, the anticholinergic drug benztropine had little effect. Tanner et al,⁴ in acute studies, found that intramuscular (IM) scopolamine improved their patients, an action that was reversed by subsequent IM physostigmine. In a subsequent chronic oral study using benztropine or trihexyphenidyl for some weeks or months, Tanner et al found that 12 of 13 patients improved. They conclude that "acetylcholine plays a role in the pathophysiology of Meige syndrome."

Our own experience with cholinergics (limited to choline chloride) and anticholinergic drugs has produced no consistent results (table). In a further study,⁶ we were unable to show any beneficial effect of intravenous atropine, benztropine, or chlorpheniramine when compared with placebo in six patients with cranial dystonia.

In summary, our own large experience of the treatment of cranial dystonia leads us to conclude that there is no consistent pharmacologic response to drugs manipulating either the dopamine or acetylcholine systems of the brain. This seems to be the case in all forms of torsion dystonia, including torticollis and writer's cramp. Unfortunately, the treatment of these distressing and disabling illnesses with

Table. Drugs used to treat cranial dystonia

Drug used	Number treated	Number improved
Anticholinergics	25	3
Cholinergics	5	0
Phenothiazines	17	0
Haloperidol	12	1
Pimozide	13	2
Tetrabenazine	20	1
AMPT	9	1
Levodopa	18	0
Amphetamine	5	0
Amantadine	5	0
Lisuride	7	1

Based on the experience of a personal series of 56 patients with blepharospasm and/or oromandibular dystonia. All drugs were used up to maximum tolerated dosage.

drugs remains unsatisfactory and empirical.

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To the Editor: The report of Tanner et al¹ on Meige's disease did not mention the drug dosage used in their successfully treated patients. This information would be helpful. The following case illustrates the long-term daily use of 10 mg benzotropine, a higher than usual dose. Starting at age 31, this woman successively noted a 4-inch amplitude flapping tremor of the right hand, tautness of shoulder muscles, flapping tremor of the left hand, blepharospasm, grimacing, facial spasms, tightness of throat and neck muscles, flexor spasms of the neck, and dysphonia. Benzotropine was prescribed in small doses but the patient, on her own initiative, increased the dose to 10 mg daily with "magical" 95% relief. She began to live normally, stopped visiting physicians, and did not report the beneficial effect. After 14 years, at age 51, she discontinued the benzotropine because of pupillary dilatation in her cataractous left eye.

Within 5 weeks all of the old complaints returned, but disappeared when medication was resumed. I first saw her at this time (1976), and the neurologic examination was normal. At her request, another trial without medication was undertaken, and in 5 days the eyes were again continuously closed and tremor reappeared. Resumption of benzotropine therapy brought relief, which has continued for another 6 years, some 20 years in all.

Because of this experience, we used benzotropine, 8 mg daily, in another woman, aged 75, who had been functionally blind and helpless because of blepharospasm for 4 years. Her eyes remained open, and she resumed walking outdoors. Patients with less severe, but disabling, blepharospasm have been relieved by 4 to 6 mg daily.

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1. Tanner CM, Glantz RH, and Klawans HL. Meige disease: acute and chronic cholinergic effects. *Neurology (NY)* 1982;32:783-5.

Reply from the Authors: "Improvement" as defined by Lang and Marsden fails to separate three distinct pharmacologic properties: effective dose, toxic dose, and therapeutic index. The failure of an agent with known effects on a specific neurotransmitter system to provide a "degree of benefit sufficient to persuade the patient and the physician that it was worthwhile continuing with the medication" does not negate the importance of the neurotransmitter to the pathophysiology of the disorder being treated. A drug may affect the appropriate neurotransmitter system, but its usefulness may be limited by its low therapeutic index.

Dose-limiting side effects are common when anticholinergic drugs are administered, especially in the older age group at risk for blepharospasm/oromandibular dystonia. In our chronically treated patients, side effects prompted dosage reduction in 50% of those whose movement disorder had improved with anticholinergic therapy. Despite the therapeutic difficulties posed by frequent side effects of anticholinergic therapy, the pharmacologic effect of this class of dystonic movements was beneficial.

Clinical studies aimed at defining the pharmacology of a disorder are frequently limited by unwanted side effects. Nevertheless, a distinct pharmacologic effect, if specially sought, may often be appreciated. We maintain from our data that the cholinergic system plays a role in the pathophysiology of blepharospasm/oromandibular dystonia.

We appreciate Dr. Fisher's addition of cases of blepharospasm responding to high dose benzotropine treatment. Of our nine patients with Meige's disease who sustained a clinical response to anticholinergics, five were taking benzotropine in daily doses of 2 mg to 8 mg (mean dose, 4.5 mg per day), and four were taking trihexyphenidyl in daily doses of 4 to 8 mg (mean dose, 6.5 mg) at 12 months follow-up. The one patient who responded to 8 mg per day benzotropine was similar to Dr. Fisher's patients. Further increase in anticholinergic dosage was limited by side effects (particularly, disabling memory loss and confusion) in these older patients. We have observed several young adults with partial dystonias who responded to benzotropine 10 mg per day to 16 mg per day. Marsden and Fahn¹ have reported dystonic children who responded well to 80 mg per day with few side effects.

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Russell H. Glantz, MD
Harold L. Klawans, MD

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Neurologists are like cops . . .

To the Editor: A physician friend once told me, on the day I agreed to see his ailing mother, "You neurologists are like cops . . . you're all over the place until you need one."

Much has been written recently about the optimal number of neurologists, based on demographic trends and projected health care needs for the nation.¹⁻⁶ The most recent survey by Dr. Menken projects a lugubrious future for our specialty and its related training programs.^{3,4} Specifically, he calls for closing neurologic residencies as a means of controlling numbers of neurologists, since oversupply leads to competition with primary care physicians, to the overuse of tests, and dilutes the impact and effectiveness of neurologic programs at academic centers.

His overview of the supply-side economics of neurology in the 80s is hardly a forecast—rather, a statement of the status quo in many localities. Neither does it go far enough in its implications for both neurologists and nonneurologists, because it examines the symptoms rather than the underlying disease.

But who needs neurologists, anyway? How do we account for this paradoxical scarcity of individuals in the midst of collective plenty?

Dr. Menken touches on the truth in his commentary. Clearly, the job description of the neurologist has changed and continues to evolve.

Marketing, in our present health care system, is based on the notion of "technofix." Health problems, like all problems, are a matter of technical troubleshooting until the source of the disease, pain, or discomfort is found, application of appropriate treatment is made and prompt subsequent relief of symptoms, reversal of disease, and quiescence of discomfort is obtained. While the paradigm apparently works for the worried well and minimally ill, neurologic diseases and symptoms rarely fit that model. Nonetheless, the public seems to have the "need to know" not only the source of every symptom, but the need to know today, what will become obvious tomorrow or the next day. Much of modern marketing of health care services is based on that need to know. As a consequence, the time-honored tradition of classical neurology—"Let the pathology mature; the diagnosis will declare itself"—is no longer permitted to us, at least not in America. The more time the physician has to make a diagnosis, the fewer the tests needed. On the other hand, the price of finding out the potential seriousness of any symptom or irritation on the day it occurs is astronomical indeed, and requires the use of every bit of technology available to the physician. Neurologists in many communities function precisely in the latter mode, using sophisticated technologic approaches to meet the demand for quick, accurate service by sophisticated consumers with high expectations. In the process, eclectic neurology has given way to electrical empiricism.

Of course, the consumers have plenty of help in the quest for medical technofix. They have emergency room physicians telling them they need to see a neurologist as

soon as possible for symptoms and complaints of brief duration. They have primary care doctors telling them that the routine tests done to evaluate their symptoms have failed to disclose their nature and now they must see a specialist. And there are those who have seen a series of specialists—otolaryngologists, cardiologists, and ophthalmologists—who have done numerous sensitive and expensive tests that establish the cause of symptoms to be definitely outside their field of expertise. To some, hysteria has been contagious; they caught it in their doctor's office. Still others have even seen one or more neurologists, have had all the neurotechnology, and have either a diagnosis or no diagnosis. Either way, they are bewildered and unhappy, because there is no quick fix; now they just need someone to talk to, to answer a few questions . . . about their future.

Academic neurologists are in a particularly uncomfortable crossfire. They are perceived by referring physicians, including other neurologists, as having plenty of time to engage patients, to discuss and analyze difficult diagnostic and therapeutic problems. Yet they are seen by their administrators as competitors of their own progeny in the private sector, who need to see patients in high volume to compensate for their poor income-generating capacity. Space-occupying lesions treated by neurosurgeons generate high professional fees and use multiple reimbursable hospital resources as well; in the neurology clinic, however, time-occupying lesions can be seen only in limited numbers, and often without third-party coverage.

One-on-one professional patient care is the most efficacious thing that doctors do. Unfortunately, in today's marketplace, it is least valuable as compared with the standard set by high-priced technology. Neurologic patients presenting to tertiary care centers have had all the technology done, all the routine therapies tried. When the more elaborate, expensive, and financially rewarding technologies are repeated, the economic benefits accrue to departments other than neurology. Tertiary care neurologists are asked to see ever-increasing numbers of patients, whether those patients have MS, intractable migraines, "low-pressure hydrocephalus," or proctalgia fugax. They are expected to do this at low cost and high volume, at overhead rates identical to those of other physicians, whose practices require high-cost milieus like radiology suites and operating rooms. Then, they are asked to either justify the continued existence of their cost-inefficient specialty or acquire some forms of technology to generate fees disproportionate to the time required to perform them.

Sooner or later, someone must play the traditional doctor's role without pretensions and merely minister to the sick. Technology was transferred to the point of ubiquity during the 70s; neurologists are among those to whom responsibility for technologies' failures will be transferred in the 80s.

Surely, there will be no dearth of referrals for neurologists' services. Despite packaging modern medicine as "health care" delivery, we in neurology know that eventually preventive medicine is bound to disappoint even its most staunch true believers. Even if all effective medications and surgeries do accomplish their goals as advertised, and prevent death from heart disease and even cancer, they are also deferring an increased load to the neurologist of the future, who must eventually deal with disease, complica-

tion, or side effects in the organ system that does not repair itself, is irreplaceable, and is not transplantable. Further, every therapeutic novelty (like hyperbaric oxygenation) and innovation (like chronic renal dialysis) seems to create a series of new neurologic syndromes or diseases.

Therefore, in contrast to Dr. Menken's hypothesis that there are too many, we will probably need more and more neurologists—or at least classical physicians who can function in a power failure, who can take a history and apply deductive and dialectical reasoning with the wisdom of talmudic scholars, yet who will serve as apologists, public relations men, even cheerleaders for the institutions they represent and for the physicians who refer patients to them. Someone has to maintain the cost efficiency of the more lucrative high-volume machines and services.

The problem is not one of need, the problem is one of value systems and how these neurologists will make a living! Their colleagues, their administrators, their patients, and "health" insurance carriers seem to have trouble establishing what they're worth.

Some aspects of medicine are simply and intrinsically not cost effective by modern standards. Traditional or classical neurology is one of them. The most cost-efficient method of dealing with the chronically ill and the symptomatically disabled is euthanasia. Since that is unlikely to become a socially or morally acceptable alternative for conscious patients, the future need for neurologists or their substitutes is guaranteed. What their services are worth, and to whom, has to be rethought!

Meanwhile, neurologists must respond to the demands of anxious patients and their equally anxious doctors. After all the tests, whatever the results, somebody has to sit down and engage the patient, to find out what's wrong with him, and, like a detective, to distinguish the natural history of the disease from its unnatural modifications by previous professionals . . . and to answer questions. That takes time.

Where are all the neurologists when you need one? They're doing "emergency" EMGs, trying to distinguish acute paresthesias due to hyperventilation from incipient Guillain-Barré syndrome—or they're seeing the doctor's mother.

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the 1980s: impressions based on data from three studies. *Neurology* (NY) 1982;32:651-6.

Reply from an Author: Professor Molinari's thoughtful and provocative letter addresses a keystone issue in manpower research: namely, the need to identify the role of each group of physicians in the provision of health care services. He asks: What is a neurologist?

I would suggest that, in our society, a neurologist is a medical specialist who has learned to approach disorders of the nervous system with the skills and attitudes of a clinical neuroscientist. He or she has acquired this approach in a neurology training program that teaches exclusively the biomedical science of neurologic care, and measures the quality of that care by the completeness of "work-ups." Accordingly, when practicing neurologists develop patient care protocols that make technology the master of medicine, and not its servant, it seems to me they are doing exactly what they have been trained to do.

Along with an overuse of technology, Professor Molinari has identified a serious shortfall of essential primary care services—such as counseling and the comprehensiveness and coordination of care. Could this shortage have emerged because the matrix and organization of care must now accommodate large numbers of neurologists to serve as principal care providers for large numbers of patients?

I question the general assumption among neurologists that those most knowledgeable about an organ system are, *inter alia*, most highly qualified to provide care for virtually all patients whose symptoms fall within their area of scientific expertise. We seem to have forgotten that most of the care required most of the time by the majority of patients with neurologic symptoms, signs, and diagnoses is primary care. (The same thing may be said of all organ systems and all medical specialties.) I would therefore suggest that many patients in need of neurologic care are best off when that care is provided by well-trained primary care physicians, who use the services of neurologists as needed to improve the quality, effectiveness, and economy of care.

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Cerebral embolism and anticoagulation

To the Editor: We read with interest the papers by Furlan et al¹ and Koller² dealing with cerebral embolism and anticoagulant therapy. They differ about the prognosis for recurrent emboli: fairly good in the Furlan et al report but a high mortality rate in Koller's report. Furlan et al¹ found only one case of hemorrhagic infarction in their CT series of 54 cases, but they did not specify whether the recurrent embolic events were studied by CT or not (maybe some of these cases could have been hemorrhagic infarctions). The low frequency of hemorrhagic infarction is not in accordance with the higher incidence of hemorrhagic infarction in other series of cerebral embolism³⁻⁵ or our own experience.

We have performed a retrospective survey on 32 cases of cerebral embolism secondary to rheumatic heart dis-

ease (without endocarditis). All of them were studied within 24 hours of the stroke, and at least one CT was performed in each case. Only the first week's outcome was noted. Seventeen patients were treated with IV heparin within 24 hours of admission. Fifteen patients did not receive anticoagulant therapy during the first week. There were no recurrent embolic events in any patient. CT showed hemorrhagic infarction in five patients. Four of these five patients followed a similar clinical and CT pattern: admission CT was normal or showed ischemic infarction (low-density lesion); and within 48 hours of the first stroke, a new stroke (or sudden worsening of the previous neurologic status) occurred. A new CT at this time showed a large hemorrhage on the same side as the first stroke. The first stroke had provoked a severe neurologic disability in two patients, moderate disability in one patient, and minimal disability in one patient. Two of the four patients who were on anticoagulant therapy died in the first days. The other two patients were left with severe and mild disability. In another patient, CT showed a hemorrhagic infarct with no clinical variation. Thus, a new stroke after a cerebral embolus can be due not only to a recurrent emboli, but also to a hemorrhage into the infarct. The global outcome of the 32 patients at the end of the first week was as follows: 4 were dead, 14 showed severe disability, 7 moderate disability, and 8 mild or no disability. We did not intend to compare the outcome of patients treated and those not treated with anticoagulants. The main conclusion from our series is that hemorrhagic infarction is not rare after an embolic stroke; it usually happens within the first 48 hours, and it carries a poor prognosis (probably worsened by anticoagulant therapy, as reported in experimental studies⁶). In deciding about anticoagulant therapy in embolic stroke, the danger of early hemorrhagic infarction should be weighted against the risk of recurrent embolus.

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cerebral infarction in experimental animals. *Arch Neurol* 1958;79:390-6.

To the Editor: The papers by Furlan et al¹ and Koller² on the risk of re-embolization after cerebral embolism of cardiac origin and the possible benefit of immediate anticoagulation are of great interest to us. Recently one of us (J.S.) reviewed the clinical records of 126 patients with embolic brain infarction admitted between January 1976 and July 1980.³ All patients had a definite cardiac source of emboli. Fifty-five patients (44%) had rheumatic heart disease (RHD) (Mitral 53, Aortic 2), 54 (43%) had nonrheumatic atrial fibrillation (NRAF) (chronic 50, paroxysmal 4), 11 (9%) had a prosthetic valve, and 6 (5%) a recent myocardial infarction (MI). Cerebral hemorrhage was ruled out by CT in 40 patients and angiography in 26. Lumbar puncture was not done routinely. At one time, our policy was to start anticoagulation 1 to 3 weeks after the cerebral embolism.

In patients with RHD, re-embolization in the first week occurred in six (11%) with nine events (six systemic). In patients with NRAF, re-embolization occurred in four (7%), all but one systemic. On the other hand, only one of the patients with a prosthetic valve and none with MI suffered early recurrence.

Re-embolization, especially in the first week, has hardly ever been considered in the literature; there is controversy about its real incidence and when it appears. Whisnant⁴ suggested that it was not necessary to start anticoagulation immediately to prevent re-embolization in the first week. However, the high incidence found in our study and those of Furlan et al¹ and Koller² suggests that immediate anticoagulation would be more beneficial than dangerous.

Early re-embolization was lower in patients with NRAF, but 11% of them had suffered a previous embolism in the year before admission. These results, although not described by Furlan et al¹ and Koller,² agree with Bharucha et al,⁵ who found recurrence of cerebral embolism in 10% of cases within 1 year. Later embolization in patients with NRAF adds more difficulties when one considers anticoagulant therapy. First, the incidence of hemorrhagic complications increases with time. Second, the possibility of re-embolization does not disappear completely; 20% of the patients of Furlan et al¹ had the first cerebral embolism while they were receiving adequate anticoagulation. Although immediate anticoagulation seems to prevent early re-embolization, further studies are needed to assess whether long-term anticoagulation can prevent late recurrence and if benefits outweigh the risks of hemorrhagic complications.

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Reply from the Authors: The data provided by Dr. Santamaria and her colleagues from Barcelona are most interesting and add to the mounting evidence that early recurrent embolization after nonseptic embolic brain infarction is not rare. We suspect that the relative risk of early recurrence parallels the relative risk of initial embolization for each cardiac condition. Although such a trend was not evident in our data, the small number of patients within each cardiac subgroup makes it difficult to draw firm conclusions. For example, there was only one early recurrence among the 14 patients with rheumatic valve disease, whereas there were 3 recurrences in the group with cardiomyopathy. However, many of the patients with rheumatic valve disease received immediate anticoagulation therapy. The only common risk factor appeared to be atrial fibrillation. Of the seven patients with early recurrence, six had atrial fibrillation, and in two the only cardiac problem was chronic atrial fibrillation. Examination of larger numbers of patients within each cardiac group will be necessary to clarify the relative risk of early recurrence.

As Doctor Santamaria points out, long-term anticoagulant therapy lowers, but does not eliminate, the risk of subsequent embolization. Such therapy carries definite risks of hemorrhage that are related to the duration of therapy, the patient's age, and several other variables. The efficacy of long-term anticoagulation is accepted for a number of cardiac conditions (mitral stenosis with atrial fibrillation), but is less clear for conditions such as chronic atrial fibrillation. Further studies are necessary to determine the long-term benefits and risks of anticoagulation therapy for patients with each of these different cardiac conditions. Nonetheless, once a patient with a persistent cardiac source of emboli is judged a candidate for long-term anticoagulant therapy, we recommend that it be instituted immediately after nonseptic embolic brain infarction if there is no evidence for brain hemorrhage.

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The letter from Dr. Santamaria and colleagues addresses a crucial issue in the long-term treatment of patients with a predisposition for cardiac embolization.

Easton and Sherman¹ reviewed the literature to address this issue. They stated that "in rheumatic heart disease the natural recurrence rate of approximately

50% is reduced to from 5 to 25%." Likewise, in patients with myocardial infarction, "the incidence of clinical cerebral embolism is diminished to approximately one-quarter of the natural incidence." While they were unable to cite specific figures concerning nonrheumatic atrial fibrillation, they suggest that here, too, recurrence rates are lowered by anticoagulation.

In regard to prosthetic valves, both Bonchek et al² and Kloster³ believe that the combination of cloth-covered valves and chronic anticoagulation has significantly reduced the risk of embolic events.

Wright et al,⁴ in a randomized prospective study, found that hemorrhagic complications occurred in approximately 6% of patients randomized to the dicumarol-treated group. Eaton et al cite complication rates of up to 20%, most of which were minor or transient.

In properly selected patients, it seems that long-term anticoagulation does reduce embolic events, and this benefit outweighs the risk of hemorrhagic complication.

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Since the publication of our report, we have been informed about patients who were taking heparin and suffered hemorrhage into an embolic infarct. We never implied that immediate anticoagulant therapy is without risk, but rather that the risk (ie, early recurrent emboli) of delaying therapy in carefully selected patients is far greater. Our subsequent experience and the data provided by Calandre et al do not change that opinion.

Pathologic evidence of microscopic hemorrhagic infarction should not be confused with macroscopic hemorrhagic infarction that is visible on CT. Furthermore, macroscopic hemorrhagic infarction without mass effect must be distinguished from frank intracerebral hemorrhage. CT evidence of hemorrhagic infarction following cerebral embolization is uncommon, occurring in about 2% of cases. In our extensive CT files we found that hemorrhagic infarction resulting from any cause was rather infrequent.

We do not treat all patients with nonhemorrhagic embolic infarction with anticoagulants. Based on the scant literature available and personal experience, we withhold anticoagulant therapy in patients with massive clinical or CT infarcts, extremely ill patients with multiple medical problems, patients over the age of 70, and patients with poorly controlled hypertension. We do not consider these patients good candidates for any anticoagulant therapy, either short or long-term. Inattention

to selection factors can be expected to result in a hemorrhagic catastrophe. However, in patients with non-hemorrhagic infarction who are candidates for long-term anticoagulant therapy, there seems to be little rationale for delaying treatment for an arbitrary number of days. There is considerable evidence that the risk of early recurrent embolization is between 10 and 15% in these patients. Careful monitoring of heparin dose, activated partial thromboplastin time, and blood pressure will minimize the risk of immediate heparin therapy.

All of the patients in our series with a recurrent event had repeat CT, and none of these episodes was hemorrhagic in nature.

More information is needed about the relative risks of hemorrhage and recurrent embolization for patient subgroups, and treatment must always be individualized. Until data are forthcoming, we intend to continue immediate anticoagulant therapy according to our stated guidelines.

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Global aphasia without hemiparesis

To the Editor: Although global aphasia without hemiparesis can be produced by two separate infarcts of Broca's and Wernicke's areas as reported by Van Horn and Hawes,¹ there are other anatomic possibilities.

Case reports. Patient 1. A 58-year-old, right-handed hypertensive man sustained a left middle cerebral artery (MCA) occlusion in January 1979 (figure). Right hemiparesis cleared quickly and he regained full use of his right hand. However, at 3 years after stroke, he remained a global aphasic. When tested with a standardized aphasia battery^{2,3} speech was nonfluent with occasional single word production, aural comprehension was disturbed (5 of 8 commands), as were visual naming (1 of

16) and word repetition (10/30). His Token Test (TT) performance was very poor (1/22).

Patient 2. A 61-year-old, right-handed man with atrial fibrillation presented in January 1980 with large left MCA and small right temporal infarcts (figure). He had a transient right hemiparesis but now he uses his preferred hand in everyday life. Despite good motor recovery his aphasia picture remained stable; 1 year after stroke he still presented a global aphasia. Speech was nonfluent with some single word production, naming and repetition were impossible, and comprehension disturbed (4/8). Performance on the TT was poor (5/22).

In both patients a single large infarct of both Broca's and Wernicke's area, partly sparing the posterior limb of the internal capsule and the corona radiata, caused by MCA occlusion without involvement of the lenticulostriate or the anterior choroidal arteries produced a stable global aphasia but only transient motor signs.

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Reply from the Authors: We appreciate Dr. Ferro's thoughtful letter and would like to hear from other physicians who have seen global aphasia without hemiparesis.

The original purpose in reporting our three patients was to point out a possible early sign of embolic cerebral infarcts. Our concluding statement could have read: It is suggested that global aphasia without hemiparesis, *appearing acutely*, is caused by two discrete lesions in the dominant hemisphere and is a sign of embolic encephalopathy. (Italics denote added phrase.)

Both of Dr. Ferro's patients had some degree of hemiparesis at the onset of their illnesses. Therefore, his patients were not strictly comparable to our three, each of whom had no hemiparesis at the onset. Neither the severity nor the duration of the associated hemiparesis was mentioned, but Dr. Ferro's experience appears to support our original conclusion.

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Transient global amnesia and migraine

To the Editor: Caplan et al (*Neurology* 31:1167-70) described 12 adults with transient global amnesia as-

Figure. CT of patient 1 (left) and 2 (right).

sociated with migraine. A syndrome similar to or identical with transient global amnesia in children with migraine has been called "acute confusional migraine"¹ or transient global amnesia in childhood.² Episodes are frequently but not always precipitated by trivial head injury, as in the following case.

Case report. A 14-year-old boy was playing football and sustained a mild blow to the head. He thought he was struck by the knee of an opponent but he was not unconscious. A few minutes later he had bifrontal pounding headache that was accompanied by 5 minutes of tingling in the right face, arm, and leg. He walked home, where his parents found that he was confused. He was disoriented for time and gave incorrect responses to questions; for example, "When do you get out of school?"—"When I am tired." Changing out of his football clothes, he tried to put a shirt on his legs. (For the past 4 years he had had pounding headaches about once a month, unilateral or bilateral, lasting up to several hours. Several times, there had been accompanying numbness on the right side. A maternal aunt had migraine; the mother and a brother had osteogenesis imperfecta.)

Because of persistent disorientation, confusion, and memory defect he was admitted to the hospital. Neurologic examination was otherwise normal and the headache was subsiding. By the next morning, when I saw him, his mental state was normal although he was partially amnesic for events of the previous evening.

Croft et al³ described a patient who from age 14, had amnesic episodes and migraine that were precipitated by playing football, "and especially after heading the ball"; episodes recurred for several years.

It is tempting to invoke benign vascular spasm as the explanation of the isolated transient global amnesia in older adults. However, Mazzucchi et al⁴ found deficits in verbal longterm memory and verbal IQ in 16 patients, who had had one episode of transient global amnesia; this suggests a less benign pathogenesis.

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Reply from the Author: Close interaction between adult and child neurologists has undoubtedly proven mutually helpful. An example is the recognition of neurobehavioral syndromes such as transient global amnesia (TGA) in children. Once a disorder of higher cortical

function is well characterized in adults, the distinctive features can be later dissected out in children in whom cognitive testing is more difficult. Gascon and Barlow¹ first called the attention of the pediatric community to acute confusional migraine in children, some of whom had definite amnesia. As Hahn indicates, the phenomenon is probably more common in childhood than is currently recognized.

TGA remains a disorder of uncertain cause. I would classify our brief article on this subject as hypothetical speculation. Until the cause is clarified, I would argue for two general precautions.

(1) Phenomenologic; let's reserve the term TGA for pure amnesic attacks of an acute nature uncontaminated by other neurologic symptoms or signs and without fixed deficits. Hahn's case had associated tingling and Mathews and Meyer's² cases had multiple associated symptoms and some patients had fixed deficits, that is, amnesic strokes.

(2) Etiologic; trauma needs to be considered separately. It has long been recognized that temporary amnesia frequently results from head injury and in fact temporary retrograde or anterograde amnesia is one of the criteria for the diagnosis of concussion.

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Correction

In "Classical 'parietal' neglect syndrome after subcortical right frontal lobe infarction" by Stein and Volpe, June 1983, page 798, figure 2 has been placed upside down. The correct position is shown here.

Figure 2. Noncontrast CT of patient 2, showing a subcortical infarct of the right frontal lobe involving the basal ganglia.

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Classical 'parietal' neglect syndrome after subcortical right frontal lobe infarction

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