Current Indications for the Use of Anticoagulant Drugs in Cerebrovascular Disease

By Robert G. Siekert, M.D., Clark H. Millikan, M.D., and Richard M. Shick, M.D.

Considerable variation exists in the interplay of the factors influencing the occurrence of strokes and their final outcome. A final statement about the usefulness of anticoagulant drugs in the treatment of cerebrovascular disease must await further study. The current indications for their use include: (1) intermittent insufficiency of the basilar arterial system, (2) intermittent insufficiency of the internal carotid system, (3) thrombosis within the basilar arterial system, (4) recurrent cerebral emboli associated with a likely cardiac source and (5) possibly, recurrent cerebral thromboses.

Physicians concerned with diseases of the vascular system in general are well acquainted with the commonness of cerebrovascular disease, the problems it presents, and the therapeutic difficulties involved. General care and rehabilitation of patients with strokes have been greatly expanded in recent years, and these contributions cannot be minimized. Yet, satisfactory treatment also implies prevention and, in the present context, avoidance of cerebral damage. Thus, we have been concerned with the concepts of early diagnosis and early treatment.

Anticoagulants as therapeutic drugs in cerebrovascular disease were suggested by Allen and Barker1 more than 10 years ago. Although administered since then for recurrent cerebral emboli, anticoagulant drugs have been little used in the common variety of stroke. The lurking fears of intracerebral hemorrhage, and the causation of gross bleeding into an infarct by such treatment, have been the basis for much wariness. These fears are still present today and suggest caution in the use of anticoagulant therapy. This treatment is not to be recommended at this time as a “routine” for all strokes; it must be sharply limited to certain categories.

Originally it was recalled that a thrombus closing the basilar artery frequently had a laminated appearance. But of more importance were the facts that neurologic abnormalities often progress in steplike fashion when this artery becomes occluded and that transient episodes of neurologic dysfunction are common antecedent occurrences in such patients.2 These observations suggested the usefulness of anticoagulant therapy in preventing the devastating and often fatal result of thrombosis of the basilar artery. Occlusive disease of the basilar arterial system appeared to have a course that might be interrupted by appropriate treatment. The concept of preventing any cerebral damage or more cerebral damage became apparent. In a similar way, episodic symptoms due to insufficiency of the carotid arterial system were looked on also as precursors of occlusion of the internal carotid artery.

Indications

The current indications for anticoagulant therapy in cerebrovascular disease are limited sharply to certain categories. They include the following: (1) the syndrome of intermittent insufficiency of the basilar arterial system, (2) the syndrome of intermittent insufficiency of the carotid arterial system, (3) thrombosis within the basilar arterial system, (4) recur-

From the Section of Neurology, Mayo Clinic, Rochester, Minn.
Read by title at the meeting of the American Heart Association, New Orleans, October, 1955.
An abstract of this paper appeared in Circulation 12: 775, 1955.
rent cerebral emboli, and (5) possibly, multiple strokes. Each of these categories is discussed separately.

The Syndrome of Intermittent Insufficiency of the Basilar Arterial System. This syndrome consists of transient episodes of neurologic abnormalities, such as weakness of the limbs, dimness of vision, diplopia, dysphagia, dysarthria, vertigo, numbness, and confusion, in various combinations. When weakness on opposite sides of the body in separate attacks, poor vision, diplopia, vertigo, and pseudobulbar and bulbar phenomena are present, the diagnosis of intermittent insufficiency of the basilar arterial system would appear to be in order. Report of a typical case follows.

Case 1. A 64 year old man complained of “blind staggers” and “locking of the arms and legs.” Save for a heart attack 15 months before his admission, he was well until 3 weeks prior to registration at the Mayo Clinic. At that time episodes began, characterized by decreased vision, unsteady gait, vertigo, and dysarthria. They lasted about 2 to 5 minutes and varied in severity. He averaged one of these spells per day. In addition, he had spells of hemiparesis, numbness, and paresthesia of the right or left limbs. With each spell, regardless of the side involved, he noted numbness of the lips and perioral region. He had had about a dozen attacks involving each side. He was free of any spell for only a few days during this 3-week period; often the attacks occurred up to 5 times a day. Rest in a hospital for a week and administration of aminophyllin and nicotine acid were without apparent influence on the frequency of these spells.

The results of general and neurologic examinations were normal. He was normotensive. During an attack speech was weak and dysarthric (without evidence of aphasia), the left corner of the mouth drooped, and the tongue, pharynx, and palate moved poorly. Three minutes later the episode was over and examination did not show any abnormalities. Heparin, tromexan, and dicumarol were administered. He had one brief attack just prior to the fifth injection of heparin and none since.

The Syndrome of Intermittent Insufficiency of the Carotid Arterial System. This syndrome consists of transient episodes of unilateral impairment of motor or sensory function, or both, associated often with involvement of vision homolateral to the affected artery and a disorder of speech, frequently aphasia, if the dominant hemisphere is involved. Decrease in the retinal arterial blood pressure and in the pulsation of the common or internal carotid artery may be present.

Case 2. A 77 year old man was seen in July 1955, because during the preceding 6 weeks he had episodes of poor use of the left hand. The first episode occurred while he was driving his car; he suddenly noted that his left hand felt heavy and useless. It was awkward, felt numb and he could barely move it. Within 20 minutes the spell disappeared and he felt normal. He had similar attacks daily that lasted from 20 to 30 minutes. The attacks became severer, so that the arm also was involved. However, he had not had headaches or difficulty with vision or speech in association with these episodes. On the day before admission, and on the day of admission to the clinic, he had 2 or 3 episodes. Recovery from the recent spells was not quite complete.

Examination disclosed slight hyperactivity of the left biceps jerk and a -1 to -2 decrease in alternate-motion rate of the left hand. The pulsations of the right carotid artery were slightly diminished. Ophthalmodynamometer reading for the right eye was 38 mm. of mercury and that for the left, 60 mm., consistent with an occlusive process in the right internal carotid artery. Roentgenograms of the skull showed no evidence of abnormality. An electroencephalogram showed minimal dysrhythmia in the right hemisphere. An electrocardiogram showed ventricular premature contractions and evidence of left bundle branch block. Anticoagulant therapy was begun with dicumarol and tromexan. After effective anticoagulant action was obtained, he had no further spells.

Comment. Anticoagulant drugs have been administered to 33 patients with the two syndromes of insufficiency mentioned above; in 22 the basilar system was implicated and in 11 the internal carotid artery was involved. The attacks promptly abated after effective anticoagulant levels were obtained, and it is believed that these drugs are a prime factor in stopping these episodes. Since the periodic attacks often precede thrombosis of the main arteries and progression appears to be thwarted by anticoagulant drugs, one might infer that cerebral damage has been prevented.

It is too early to compare a “control” series, for the length of time patients have suffered from these episodes has varied a great deal. Some patients have had such spells for several years without apparent progression in their
disease and others have died after only a few attacks.

It is only too obvious that these two syndromes could encompass all episodes of cerebrovascular insufficiency. Among other things, however, careful delineation of the condition is an important means of avoiding pitfalls in diagnosis and, since our knowledge is incomplete, of limiting the use of these drugs to well-defined syndromes.

Thrombosis within the Basilar Arterial System. About two thirds of the patients who sustain occlusion of the basilar artery itself have histories of antecedent episodes of insufficiency to this system. When permanent damage has occurred, examination must indicate the lesion to be in the region supplied by the basilar arterial system. Neurologic abnormalities will include hemiparesis or quadriplegia, dysarthria, dysphagia, oculorotatory and pupillary abnormalities, superficial sensory loss, often bilateral or crossed face and body, and bilateral homonymous field defects. These neurologic abnormalities tend to advance and interruption of their progression is the goal of treatment.

Case 3. A 72 year old man registered at the clinic and was admitted to the hospital on August 8, 1955, because of difficulty in speaking and weakness of the left limbs.

During the preceding 2 months he had a number of episodes of dragging of the right foot, drooping of the right corner of the mouth, and slurred speech. Additionally, he had a number of attacks of dizziness and on one occasion, after a severe spell, he was somnolent for 6 hours. He was known to have been hypertensive for 10 years.

Early on the day of admission he suddenly fell and was “stiff” for a brief period. His blood pressure was said to have been 210 mm. of mercury systolic and 150 mm. diastolic and he was noted to be anarhxic. Throughout that day he had periods during which he could talk well; at other times he had slurred speech or anarhxia.

Examination some 12 hours after the ictus disclosed a blood pressure of 140 mm. systolic and 90 mm. diastolic, right-sided Horner’s syndrome, left lower facial palsy, dysarthria, labored swallowing, weak palatal elevation, weakness of the left side of the tongue, left hemiparesis with ankle clonus, and Babinski’s sign. During the examination it was noted that his condition fluctuated, at times being hemiplegic, although he never became normal. On several occasions Chaddock’s sign was noted on the right side. The administration of heparin, dicumarol, and tromexan was begun immediately. His condition stabilized and his abnormalities lessened. At the time of his dismissal 2 weeks later, he had only minimal slowness in alternate-motion rate of the left limbs and slightly hyperactive reflexes on the left.

Comment. About 50 patients with this lesion have been treated to date with anticoagulant drugs. There have been a striking decrease in mortality (as compared with a contrast group) and surprising improvement in the neurologic abnormalities. Data on the original group showed that 14 per cent of patients receiving anticoagulant therapy died, while 43 per cent of a contrast group (not receiving such therapy) died.

Recurrent Cerebral Emboli. These emboli may be associated with atrial fibrillation, rheumatic heart disease and myocardial infarction and they provide another indication for anticoagulant therapy. Wright and McDevitt have clearly pointed out the tremendous value of anticoagulants in the preventive treatment of such phenomena.

Multiple Strokes. Some patients who appear subject to recurrent cerebral thromboses, presumably supratentorial and often bilateral, also may benefit from anticoagulant therapy in the sense of prevention. Since only a few patients have been treated in this indeterminate group, this condition is a questionable indication at this time.

Comment

In any discussion of strokes, it must be remembered that considerable variation exists in the interplay of the factors influencing their occurrence and their final outcome. Assessment of any therapy is extremely difficult. Further study must be applied to the treatment with anticoagulant drugs before a final statement can be made about their usefulness in the treatment of cerebrovascular disease. On the basis of present knowledge, however, this treatment appears to be of definite value in the first four conditions discussed.

Careful diagnosis of the particular type of cerebrovascular involvement is essential. This
applies particularly to those instances of episodic symptoms, where the examination reveals normal findings unless an attack is observed. There is no diagnostic test, although appropriate laboratory studies are important aids in excluding other likely disorders. A single survey is not enough. Continued assessment of each patient is needed, for other lesions may be mimicking cerebrovascular disease and the course of the illness will aid in their differentiation.

In each case the general contraindications to anticoagulant therapy, both absolute and relative, must be considered. Many are relative, for we have not hesitated to use anticoagulant therapy in the treatment of certain patients with histories of duodenal ulcer who have early and advancing thrombosis of the basilar artery. On the other hand, the outlook for a patient with occlusion of the posterior inferior cerebellar artery is, in general, good, so that anticoagulants would be withheld in the presence of such a contraindication.

In those instances in which rapid action is required, heparin has been employed early. Otherwise, tromexan and dicumarol have been used, the latter for long-term management. Usually we have suggested use of the anticoagulants for an indefinite period, but in two instances of intermittent basilar insufficiency they were discontinued after three months and the patients have not had a recurrence of the episodes. On the other hand, discontinuance of anticoagulants in patients with thrombosis of the basilar artery itself has been associated in several cases with rapid progression of the illness.

Since it appears that anticoagulant drugs eliminate the transitory episodes, some action they possess must be included in a consideration of the pathogenesis of these states of insufficiency, although it is probable that a number of factors are involved.6

**Summary**

The current indications for anticoagulant therapy in cerebrovascular disease include:

1. intermittent insufficiency of the basilar arterial system,
2. intermittent insufficiency of the internal carotid system,
3. thrombosis within the basilar arterial system,
4. recurrent cerebral emboli associated with a likely cardiac source and
5. possibly, recurrent cerebral thromboses.

**Summario in Interlingua**

Sub le conditiones curentes, le indicationes pro le uso de drogas anticoagulante in le terapia de morbos cerebro-vascular includen:

1. intermittente insufficiencia del sistema de arteria basilar,
2. intermittente insufficiencia del sistema de carotide interne,
3. thrombosis intra le sistema de arteria basilar,
4. recurrente embolos cerebral associate con un probable origen cardiac, e
5. possiblemente, recurrente thromboses cerebral.

**References**

Current Indications for the Use of Anticoagulant Drugs in Cerebrovascular Disease

ROBERT G. SIEKERT, CLARK H. MILLIKAN and RICHARD M. SHICK

*Circulation.* 1956;13:725-728
doi: 10.1161/01.CIR.13.5.725
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1956 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/13/5/725

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/