
Cerebral Vascular Diseases

Cerebral Vascular Diseases

Transactions of the Fourth Conference Held under the Auspices of

THE AMERICAN NEUROLOGICAL ASSOCIATION

and

THE AMERICAN HEART ASSOCIATION

Princeton, New Jersey; January 8-10, 1964

Conference Supported by a Grant from

NATIONAL INSTITUTE OF NEUROLOGICAL

DISEASES AND BLINDNESS

CLARK H. MILLIKAN, Chairman

ROBERT G. SIEKERT and JACK P. WHISNANT,

Editors



Published for The American Neurological Association

and

The American Heart Association by

GRUNE & STRATTON

NEW YORK and LONDON

1965

Library of Congress Catalog Card Number 55-7790

Copyright © 1965
Grune & Stratton, Inc.
381 Park Avenue South
New York, N. Y. 10016

Printed and bound in U.S.A. (G-B)

Preface

INTEREST IN CEREBRAL VASCULAR DISEASE has continued at an increasing rate. This book contains the edited transcript of the Fourth Conference on Cerebral Vascular Disease which was held at the Nassau Inn, Princeton, New Jersey, on January, 8, 9, and 10, 1964. Review of these discussions will indicate that the base of interest in cerebral vascular disease has broadened, and it was deemed necessary, soon after the Third Princeton Conference in 1961, to consider organizing another conference. This was done under the chairmanship of Dr. Clark H. Millikan and the sponsorship of The American Neurological Association and The American Heart Association.

As will be noted, considerable attention has been placed on basic research having to do with the various facets of occlusive cerebral vascular disease. Included are reports of research on methods of study of cerebral blood flow, the toxicity of contrast agents, the effects of these agents on blood clotting, the effects of increased atmospheric pressure, and the physics of blood flow. In addition, further discussions—clinically oriented—are included. These discussions concern various new methods of arteriography, further experience with reversed blood flow in the vertebral artery (first described at this Conference in 1961), patterns of atherosclerosis, and review of various therapeutic measures, including a report by the cooperative study on the surgical treatment of occlusive cerebral vascular disease.

The format of the conference remained the same as the preceding ones. The participants had many opportunities to discuss informally many aspects of cerebral vascular disease. Changes in the transactions have been primarily editorial in order to preserve the feeling of spontaneity which was evident throughout the discussions.

The chairman and the editors are very appreciative of the help contributed by many people, in particular the sponsoring organizations and the National Institute of Neurological Diseases and Blindness which provided financial support. The editors acknowledge and greatly appreciate the secretarial assistance of Mrs. Marilyn Klomps and Miss Barbara Wenig, and the aid of Mr. John Carney, stenotypist.

ROBERT G. SIEKERT
JACK P. WHISNANT, *Editors*

Participants

- AMBRUS, JULIAN L.: *Principal Cancer Research Scientist, State of New York, Department of Health; Associate Professor of Pharmacology and Associate in Medicine, State University of New York; Roswell Park Memorial Institute, Buffalo, New York.*
- BAKER, A. B.: *Professor and Director, Division of Neurology, University of Minnesota Medical School, Minneapolis, Minnesota.*
- BAKER, H. L., JR.: *Assistant Professor of Radiology, Mayo Foundation, Rochester, Minnesota.*
- BANG, NILS U.: *Assistant Professor of Medicine, 2nd (Cornell) Medical Division, Bellevue Hospital, New York, New York.*
- BARNETT, G. OCTO: *Established Investigator, American Heart Association; Peter Bent Brigham Hospital, Boston, Massachusetts.*
- BERING, EDGAR A., JR.: *Intramural Program, National Institute of Neurological Diseases and Blindness, Bethesda, Maryland.*
- BOUCEK, ROBERT J.: *Senior Investigator, Howard Hughes Medical Institute; Professor of Medicine and Chairman, Section of Cardiology, University of Miami, Miami, Florida.*
- CANELIS, MICHAEL: *Chief, Stroke Section, Heart Diseases Control Program, Division of Chronic Diseases, Bureau of State Services, Washington, D.C.*
- DEBAKEY, MICHAEL E.: *Professor and Chairman of the Cora and Webb Mading Department of Surgery, Baylor University College of Medicine, Houston, Texas.*
- FIELDS, WILLIAM S.: *Professor and Chairman, Department of Neurology, Baylor University College of Medicine, Houston, Texas.*
- FISHER, C. MILLER: *Assistant Clinical Professor, Harvard Medical School; Neurologist, Department of Neurology, Massachusetts General Hospital, Boston, Massachusetts.*
- FLETCHER, ANTHONY P.: *Associate Professor of Medicine, Washington University School of Medicine, St. Louis, Missouri.*
- FOLEY, WILLIAM T.: *Associate Professor of Clinical Medicine, Cornell University Medical College, New York.*
- FOX, IRWIN J.: *Assistant Professor of Physiology, Department of Physiology, University of Minnesota Medical School, Minneapolis, Minnesota.*
- GOLDSTEIN, MURRAY: *Associate Director for Extramural Programs, National Institute of Neurological Diseases and Blindness, National Institute of Health, Bethesda, Maryland.*
- GURDJIAN, E. S.: *Professor and Chairman, Department of Neurosurgery, Wayne State University College of Medicine, Detroit, Michigan.*
- HALL, PETER: *Research Fellow, Department of Pharmacology, School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania.*
- HEDLUND, SVEN: *Associate Professor, Radioisotope Research Laboratory, Department of Cardiovascular Diseases, Södersjukhuset, Stockholm, Sweden.*
- HEYMAN, ALBERT: *Professor of Neurology, Duke University Medical Center, Durham, North Carolina.*

- HUBER, WARREN V.: *Chief, Neurology, Psychiatry and Psychology Division, Veterans Administration, Department of Medicine and Surgery, Washington, D.C.*
- JACKSON, WILLIAM D.: *Associate Professor, Department of Electrical Engineering, Laboratory of Electronics and Research, Massachusetts Institute of Technology, Cambridge, Massachusetts.*
- KETY, SEYMOUR: *National Institute of Mental Health, Bethesda, Maryland.*
- KNUTTI, RALPH E.: *Director, National Heart Institute, Bethesda, Maryland.*
- LASKER, MARY: *National Health Education Committee, Inc., New York, New York.*
- LASSEN, NIELS A.: *Chief, Department of Clinical Physiology, Bispebjerg Hospital, Copenhagen, Denmark.*
- LYONS, CHAMP: *Professor of Surgery, Medical College of Alabama, Birmingham, Alabama.*
- MCDEVITT, ELLEN: *Associate Professor of Medicine, Cornell University Medical College, New York, New York.*
- MCDOWELL, FLETCHER HUGHES: *Associate Professor of Medicine (Neurology), Cornell University Medical College, New York, New York.*
- MCSEWENEY, MRS. EDWARD: *National Health Education Committee, Inc., New York, New York.*
- MARGOLIS, GEORGE: *Professor of Pathology, Dartmouth Medical School, Hanover, New Hampshire.*
- MARKOVICH, SIMON E.: *Assistant Professor of Neurology, Director EEG Division, University of Miami School of Medicine, Jackson Memorial Hospital, Miami, Florida.*
- MARMORSTON, JESSIE: *Clinical Professor of Medicine, University of Southern California School of Medicine, Los Angeles, California.*
- MARSHALL, JOHN: *Reader in Neurology, University of London; Institute of Neurology, Queen Square, London, England.*
- MARSHALL, ROBERT J.: *Professor of Medicine and Head, Division of Cardiology; Director, Cardiovascular Laboratories, West Virginia University School of Medicine, Morgantown, West Virginia.*
- MASLAND, RICHARD L.: *Director, National Institute of Neurological Diseases and Blindness, Bethesda, Maryland.*
- MEYER, JOHN STERLING: *Professor and Chairman, Department of Neurology, Wayne State University College of Medicine, Detroit, Michigan.*
- MILLIKAN, C. H.: *Professor of Neurology, Mayo Foundation, Graduate School, University of Minnesota; Consultant in Neurology, Mayo Clinic, Rochester, Minnesota.*
- MOOSSY, JOHN: *Professor of Pathology and Neurology, Louisiana State University School of Medicine, New Orleans, Louisiana.*
- MURPHEY, FRANCIS: *Professor of Neurosurgery, University of Tennessee College of Medicine, Memphis, Tennessee.*
- MURPHY, EDMOND A.: *Instructor in Medicine, Johns Hopkins University, Baltimore, Maryland.*
- NAMON, RICHARD: *University of Miami School of Medicine, Miami, Florida.*
- OLDENDORF, W. H.: *Associate Chief, Neurology Section, Veterans Administration Center; Assistant Clinical Professor of Medicine (Neurology), Department of Medicine, University of California, Los Angeles, California.*

- O'LEARY, JAMES L.: *Professor of Neurology, Washington University School of Medicine, St. Louis, Missouri.*
- PLUM, FRED: *Professor of Neurology, Cornell University Medical College, New York, New York.*
- RADVAN-ZIEMNOWICZ, S. A.: *Attending in Neurology, Veterans Administration, Mount Alto Hospital, Washington, D.C.; Assistant Professor of Neurology and Director of Neurological Research, Georgetown University Medical Center, Washington, D.C.*
- REINMUTH, OSCAR M.: *Associate Professor of Neurology, University of Miami School of Medicine, Miami, Florida.*
- RICHTER, RICHARD B.: *Professor of Neurology, University of Chicago, Chicago, Illinois.*
- ROB, CHARLES: *Professor of Surgery and Chairman of the Department, University of Rochester Medical Center, Rochester, New York.*
- ROBERTSON, ABEL LAZZARINI, JR.: *Staff Member, Cleveland Clinic, Cleveland, Ohio.*
- SALTZMAN, HERBERT A.: *Assistant Professor of Medicine and Assistant Director of Hyperbaric Unit, Duke University Medical Center, Durham, North Carolina.*
- SCHEINBERG, PERITZ: *Professor of Neurology and Chairman of the Department, University of Miami School of Medicine, Miami, Florida.*
- SIEKERT, ROBERT: *Associate Professor of Neurology, Mayo Foundation, Graduate School, University of Minnesota; Consultant in Neurology, Mayo Clinic, Rochester, Minnesota.*
- SIMMONS, EARL: *Chief, Peripheral Vascular Section, Public Health Service, Bureau of State Services, Washington, D.C.*
- SMITH, GEORGE: *Regius Professor of Surgery, University Department of Surgery, University of Aberdeen, Scotland.*
- STENGLE, JAMES M.: *National Heart Institute, Bethesda, Maryland.*
- TAVERAS, JUAN M.: *Professor of Radiology, Columbia University College of Physicians and Surgeons, New York, New York.*
- THOMPSON, J. H., JR.: *Assistant Professor of Parasitology, Mayo Foundation, Graduate School, University of Minnesota; Consultant in Clinical Pathology, Mayo Clinic, Rochester, Minnesota.*
- TOOLE, JAMES F.: *Professor of Neurology, Bowman Gray School of Medicine, Winston-Salem, North Carolina.*
- WALKER, A. EARL: *Professor of Neurological Surgery, The Johns Hopkins University, Baltimore, Maryland.*
- WALTZ, ARTHUR G.: *Instructor in Neurology, Mayo Foundation, Graduate School, University of Minnesota; Consultant in Neurology, Mayo Clinic, Rochester, Minnesota.*
- WARD, ARTHUR A., JR.: *Professor and Head, Division of Neurosurgery, University of Washington School of Medicine, Seattle, Washington.*
- WHISNANT, JACK P.: *Associate Professor of Neurology, Mayo Foundation, Graduate School, University of Minnesota; Consultant in Neurology, Mayo Clinic, Rochester, Minnesota.*
- WOLF, STEWART: *Professor and Head, Department of Medicine, The University of Oklahoma Medical Center, Oklahoma City, Oklahoma.*
- WRIGHT, IRVING S.: *Professor of Clinical Medicine, Cornell University Medical College, New York, New York.*
- YAHN, MELVIN D.: *Professor of Neurology, Columbia University College of Physicians and Surgeons, New York, New York.*
- YEAGER, FRANKLIN: *Associate Director, National Heart Institute, Bethesda, Maryland.*

Contents

PREFACE	vii
PARTICIPANTS	ix
INTRODUCTORY REMARKS	1
ANGIOGRAPHY:	
ASSESSMENT OF CINEFLUOROGRAPHIC TECHNIQS IN THE STUDY OF EXTRACRANIAL CEREBRAL CIRCULATION	3
AN ASSESSMENT OF THE SUBTRACTION TECHNIC	7
THE EFFECT OF VARIOUS AGENTS ON THE TOXIC ACTION OF CONTRAST MEDIA	12
COMPLICATIONS OF ANGIOGRAPHY	18
PRACTICAL ASPECTS OF COMPLICATIONS OF ANGIOGRAPHY	27
CEREBRAL BLOOD FLOW:	
FACTORS INFLUENCING PULSATILE FLOW IN INDIVIDUAL VESSELS	32
MEASUREMENT OF PULSATILE FLOW IN INDIVIDUAL VESSELS	37
THEORETICAL AND PRACTICAL DIFFERENCES BETWEEN DIFFUSIBLE AND NONDIFFUSIBLE INDICATORS	47
VARIOUS DEFINITIONS OF CEREBRAL BLOOD FLOW	56
THEORETICAL AND PRACTICAL DIFFERENCES BETWEEN DIFFUSIBLE AND NONDIFFUSIBLE INDICATORS	62
THEORY AND FACTS CONCERNING RHEOENCEPHALOGRAPHY	68
SPECULATION CONCERNING THE VALUE OF VARIOUS METHODS FOR STUDYING CEREBRAL BLOOD FLOW	87
SUBCLAVIAN OCCLUSIVE DISEASE AND REVERSAL OF FLOW IN THE VERTEBRAL ARTERY:	
ARTERIOGRAPHY	102
EFFECT OF LIMB EXERCISE AND HYPERTENSION ON REVERSED VERTEBRAL ARTERY FLOW (SUBCLAVIAN STEAL SYNDROME)	105
SUBCLAVIAN ARTERY OCCLUSIVE DISEASE AND REVERSAL OF VERTEBRAL FLOW: CLINICAL PICTURE	113
SIGNIFICANCE OF REVERSAL OF BLOOD FLOW IN THE VERTEBRAL ARTERY..	117
SUBCLAVIAN OCCLUSIVE DISEASE AND REVERSAL OF FLOW IN THE IPSI LATERAL VERTEBRAL ARTERY: TREATMENT	122
HYPERBARIC OXYGENATION:	
TISSUE OXYGENATION WITH HYPERBARIC OXYGEN	128
LIMITATIONS OF HYPERBARIC OXYGENATION	138
EXPERIMENTAL AND CLINICAL RESULTS IN THE TREATMENT OF CEREBRAL HYPOXIA BY HYPERBARIC OXYGENATION	141

ATHEROSCLEROSIS:

STUDIES ON THE EFFECTS OF LOCAL FACTORS IN THE DEVELOPMENT OF SPONTANEOUS AND EXPERIMENTAL ATHEROSCLEROSIS	153
MECHANICAL FORCES IN THE ARTERIAL WALLS; BASIS FOR SITES OF ATHEROSCLEROSIS	159
CEREBRAL INFARCTS AND COMPLICATED LESIONS OF INTRACRANIAL AND EXTRACRANIAL ATHEROSCLEROSIS	162
AN APPROACH TO THE ETIOLOGIC MECHANISMS IN CEREBRAL ATHEROSCLEROSIS	168
CERVICAL AND CEREBRAL ATHEROSCLEROSIS	174

THERAPEUTIC AGENTS—CURRENT STATUS:

ANTICOAGULANT THERAPY IN CEREBROVASCULAR DISEASE	181
TREATMENT OF THE COMPLETED STROKE WITH LONG-TERM ANTICOAGULANT: SIX AND ONE-HALF YEARS EXPERIENCE	185
THERAPEUTIC THROMBOLYSIS IN CEREBRAL THROMBOEMBOLISM: RANDOMIZED EVALUATION OF INTRAVENOUS STREPTOKINASE	200
EFFECT OF ESTROGEN TREATMENT IN CEREBROVASCULAR DISEASE	214
PROGRESS REPORT OF THE JOINT STUDY OF EXTRACRANIAL ARTERIAL OCCLUSION	221

THROMBOSIS AND CLOTTING-LYSIS MECHANISM:

INTERRELATIONSHIPS BETWEEN BLOOD CONSTITUENTS, ATHEROSCLEROSIS, AND THROMBOSIS	240
CURRENT STATUS OF LABORATORY CONTROL OF THE ADMINISTRATION OF THROMBOLYTIC AGENT:	254
THE LABORATORY SEARCH FOR FACTORS WHICH SUGGEST THAT SIGNIFICANT THROMBOSIS IS IMMINENT	262

INDEX	272
-------------	-----

Introductory Remarks

Clark H. Millikan

*Mayo Clinic
Rochester, Minnesota*

WELCOME TO THE Fourth Princeton Conference!

As you know, this conference is sponsored by the American Heart Association and the American Neurological Association, and it is supported by a grant from the National Institute of Neurological Diseases and Blindness.

The general format of this program is the result of the work of the program planning committee, Dr. Rob, Dr. Paul, Dr. Scheinberg, Dr. Wright, and Dr. Plum. As in the past, it is presumed that formal introductions are not necessary. You have already had an opportunity to meet one another and to begin the exchange of a variety of ideas. The word "idea" can be defined in any way that you wish to define it.

We will have some people representing special areas of interest, including Dr. Knutti, Dr. Masland, Dr. Goldstein, Dr. Stengle, Dr. Huber, Mrs. Mary McSweeney, Mrs. Lasker, Dr. Walker, and Dr. Ward. Most of you know each other with the exception, possibly, of some folks who have come from a considerable distance; perhaps they would stand: Dr. Smith from Aberdeen, Scotland; Dr. Hedlund from Stockholm; Dr. Lassen from Copenhagen; and Dr. John Marshall from London.

The purposes of the conference are similar to those of the three preceding Princeton Conferences: to exchange ideas concerning various facets of cerebrovascular disease, to stimulate and promote further investigation and training of investigators in cerebrovascular disease, and, ultimately, to produce a publication which will act as a

cohesive volume bringing up to date those things which are new in clinical and, to some degree, in theoretical aspects of cerebrovascular disease. Many of you have been to the preceding conferences and know the format. The format is simple and it is designed to try to be as informal as possible. That is one of the reasons that we are starting the session without the aid of mechanical amplification. If it is needed, we can have it later in the conference.

The item of time is of vital importance to the conduct of any such conference. It is the prerogative of the individual in the chair—whoever he may be—to ring a gong at the appointed time. Those of you who have basic presentations or are opening discussions have been informed in your letters of invitation of the maximum time allocations. Those maximum time allocations must be adhered to in order to protect one of the primary purposes of such a conference as this: to have spontaneous, extemporaneous questions, answers, and general discussion from all of the conference participants. Therefore, there will be a vigorous approach as far as this matter of time is concerned. Speaking of time, I want to say that tomorrow morning's session will begin at 9 o'clock instead of 9:15. In case you are not familiar with the arrangements of the past Princeton Conferences, you will get well acquainted with this room in the next couple of days, because this is where we plan to be practically all of the time.

As you are aware, there will be a publication. Mr. Carney, our stenotypist, will do his job by a variety of technics. He will accept

manuscripts when there are formal manuscripts, notes when there are notes, and use his recording apparatus and stenotyping machine also. It is imperative that he hear you. When he does not, he will raise his hand and we will stop and get the whole thing clear and straight. The matter of names is important to him and to you; therefore, we request that the seating arrangement be continued during the remainder of the conference, unless there is some special reason to change it. This is particularly for Mr. Carney's benefit. The material will be transcribed, sent to you in legible form with notations concerning the pages of your participation, and you will have the opportunity and also the responsibility of editing the material and returning it to Dr. Siekert. Doctors Siekert and Whisnant have once again accepted the rather thankless task of editing the transactions of this conference.

It must be noted that certain prints, as arteriograms, and other kinds of illustrative material will not be included in the printed transactions; therefore, comments in the verbal and, later, written portion of the conference must be clear in order to explain the meaning of what has actually been shown on a slide.

The matter of discussion has come up as to how long should an individual discussion be. Free discussion must be limited to 5 minutes unless something very unusual happens to this program as we go along; and it may be, because of limitations of time, that it will have to be even shorter in order to get a variety of discussion into the record.

With these introductory remarks, let us then get on to the program of this evening, which, as you are aware, focuses on angiography. The first item: "Assessment of Ciné Technics." Dr. Heyman, will you start off?

Angiography:

Assessment of Cinefluorographic Technics in the Study of Extracranial Cerebral Circulation

Albert Heyman

*Duke University Medical Center
Durham, North Carolina*

PATIENTS WITH CEREBRAL ISCHEMIA caused by occlusive disease of the major arteries arising from the aortic arch can often be successfully treated by surgical methods. It is now well recognized that adequate preoperative evaluation of these patients requires visualization of the origins and of the branches of the innominate, subclavian, carotid, and vertebral arteries in the thoracic and cervical segments, as well as their intracranial portions.

The motion picture to be presented shows a method of selective catheterization and cinefluorographic visualization of each of the major cervical vessels supplying the brain. This procedure not only demonstrates the site of occlusive lesions in the extracranial cerebral circulation, but also frequently provides information in regard to dynamic changes in blood flow produced by head and neck movements, as well as by coughing, swallowing, and other physiologic maneuvers.

All of the studies were carried out with an 8-inch image intensifier coupled to an orthicon TV circuit and a 35 mm. camera which exposed the film at 60 frames per second. The position of the catheter is constantly visualized on the TV monitor, and its relationship to various vascular structures was frequently

confirmed by injection of 2 or 3 cc. of contrast medium. Arterial blood pressure was monitored through the catheter itself; the pressure tracing and the electrocardiogram were recorded either simultaneously on the cinefluorographic film or on a separate polygraph record. In most of these studies, 60 per cent Conray solution was injected by hand, the majority of patients receiving a total amount of 125 cc. of this contrast material. Cinefluorographic studies can be taken in various positions of the head and neck to obtain multiple views of the vascular lesions. The entire procedure usually requires less than an hour.

A specially designed S-shaped catheter is introduced percutaneously into the femoral artery by means of the Seldinger technic. The configuration of the catheter conforms with the anatomic structure of the aortic arch. The catheter is passed to the area proximal to the origin of the innominate artery and is then slowly withdrawn, allowing the tip to enter, successively, the origins of the innominate, left carotid, and left subclavian arteries.

The film of the first patient demonstrates occlusion of the right subclavian artery with retrograde vertebral blood flow. The site of

the occlusion is indicated in the model of the aortic arch vessels. Some of the arteriographic sequences you will see are repeated in order to emphasize certain interesting phenomena. Also, stop-frames are sometimes used to outline certain lesions.

The catheter is in the innominate artery, but no contrast material is seen directly entering the subclavian artery. Within a few moments one sees retrograde blood flow in the ipsilateral vertebral artery.

The catheter is now in the left subclavian artery and a large amount of contrast material is seen passing up the left vertebral and down the right. The catheter in this patient is somewhat close to the origin of the vertebral artery, but this is avoided when possible.

Three phenomena are shown in this film: (1) tracings of the blood pressure and of the ECG; (2) the movement of the carotid artery during swallowing; and (3) the retrograde blood flow following injection of the contrast medium into the carotid artery. A marked serpentine movement of the carotid artery appears during swallowing. There is moderate stenosis of the internal carotid artery distal to the bifurcation of the common carotid.

The next patient had surgery for stenosis of the right subclavian artery. The patient had recurring numbness of the right face and syncopal episodes. The blood pressure was decreased in the right arm. One year after surgery, the patient, who was a doctor's secretary, has remained asymptomatic, having had at least five episodes of transient cerebral ischemia preoperatively. The arteriogram preoperatively shows a definite stenosis of the right subclavian artery. At surgery a vein patchgraft was placed at the site of the arteriotomy, and the vascular lumen became fully patent.

The next patient is an elderly man with innominate and right subclavian arterial stenosis. He was asymptomatic, except for the complaint of a loud, swishing bruit with exercise. The stenosis involves the innominate and the right subclavian arteries. The

vertebral artery is quite large but cannot be seen in this view since it is lodged behind the carotid artery.

The next patient is a 48-year-old woman who had occlusion of the internal carotid artery several centimeters above the bifurcation of the common carotid. She had a previous transient hemiparesis, and then developed occlusion of the retinal artery and optic atrophy. In this patient, the catheter was placed high into the common carotid artery near the bifurcation. Injection of contrast medium showed a total block of the internal carotid artery. The dye can be seen to remain in the vessel for a moderately long period.

BLOOD PRESSURE STUDIES

This series of cinefluorograms shows the tracings of the blood pressure and electrocardiogram photographed directly and placed simultaneously on the film. This arteriogram shows the contrast medium in both carotid arteries, which have a moderate degree of stenosis in their proximal portions.

As the catheter is introduced into the stenotic area, a fall in blood pressure is noted in this region. The contrast material in the distal portion of the vessel remains stationary.

In the next films the catheter is passed through the subclavian stenosis, and the gradient across the lesion is determined by means of the indwelling catheter. The lesion in the subclavian artery is of moderate degree, but the patient had rather vague symptoms, probably unrelated to the stenosis. The catheter is inserted distal to the lesion, the blood pressure is taken, and dye is injected to be certain of the location. The catheter is withdrawn, the blood pressure is again taken, and the location is again confirmed by a small amount of contrast material. The polygraph record of the blood pressures taken in this patient show the pressure distal to the lesion to be 100/50, whereas that proximal to the lesion is 150/80.

The next patient also has stenosis of the left subclavian artery but, in addition, the film demonstrates retrograde vertebral blood flow with injection of contrast material into the ipsilateral subclavian artery. The patient had had several recurrent transient ischemic attacks. After surgery of the lesions of the subclavian and of the carotid arteries, he has remained asymptomatic for 9 months.

In this case, contrast material injected into the subclavian artery shows a very marked stenosis of this vessel. The contrast material fills only the proximal portion of the vertebral artery, which in this film sequence appears to be obstructed. However, no obstruction was seen on retrograde brachial arteriography. The following cinefluorographic studies show the contrast material to be flowing in a retrograde manner down the vertebral artery into the subclavian artery. Thus in this patient with marked stenosis of the subclavian artery, very little, if any, blood enters the ipsilateral vertebral artery. That which does enter this vessel is quickly washed down into the subclavian by the retrograde vertebral blood flow.

COMPARISON OF ROUTINE AORTOGRAMS WITH SELECTIVE CATHETERIZATION

A comparison is made between the routine aortogram and the films taken with selective aortic catheterization. This roentgenogram shows the appearance of the aorta following the mechanical injection of a large bolus of contrast material into a catheter in the aortic arch. Filling of both carotid arteries is observed, but as one focuses down on the aortic area, there is no arteriographic evidence of a left subclavian artery. Selective catheterization in this area, however, demonstrates a small remaining segment of the subclavian artery. A complete block of the vessel is noted several centimeters above its origin. In the oblique view, one sees much of the contrast material back-wash during ventricular diastole. It is surprising to see how much of the blood in the descending aorta

flows backwards toward the heart during this phase of the cardiac cycle. This patient had a successful endarterectomy producing a patent subclavian artery. There is, however, a moderate degree of stenosis of the vertebral artery just above its origin from the subclavian.

COMPLICATIONS

Three major complications have been noted: (1) the formation of a hematoma at the site of the arterial puncture; (2) intramural injection of the contrast medium into the vessel wall; and (3) embolic phenomena.

In this patient a small amount of contrast medium is injected to determine the location of the catheter. The fact that the contrast medium was injected into the vessel wall was not fully appreciated on the TV monitor, and 5 cc. of the contrast medium was subsequently injected. Here one sees the spread of the material within the wall of the aorta. The patient had a considerable amount of pain but recovered without residual manifestations.

The new technical developments with the use of video tape are helpful in preventing this particular complication. Whenever there is any doubt as to the nature of the arteriographic visualization or the site of the catheter following injection of the dye, the video tape of the particular sequence on the TV monitor can be immediately played back and reviewed. This does not require any photographic developing but is simply a matter of playing back a tape recording very much as one does on an ordinary dictaphone.

In several patients there was a loss of pulse in the dorsalis pedis artery following removal of the femoral catheter. On one other occasion, the patient had the sudden appearance of a pale, cold finger following the study, presumably the result of dislodging embolic material from atheromatous plaques during the passage of the catheter through the aortic arch. None of these patients, however, had permanent sequelae.

These catheterizations are similar in many respects to direct percutaneous punctures of the vessels supplying the brain.

At the present time the cinefluorographic technic does not give the fine details that are available with single or serial film roentgenographic technics. We have not been able thus far to obtain good visualization of the small intracranial vessels, but a combination of cinegraphic and serial roentgenograms is now possible with newer x-ray equipment. The resolving power of the cinefluorographic instrumentation may ultimately permit adequate visualization of intracranial circulation.

Despite these disadvantages, the cinefluorographic technic with its rapid speeds of 60 frames per second promises to provide a better understanding of the dynamic nature of

the extracranial cerebral circulation. It can demonstrate alterations in position of the vessels and changes in the vascular lumen during such physiologic maneuvers as swallowing and coughing. Careful analysis of the individual frames of the motion picture often shows turbulent blood flow in and around stenotic lesions, and such studies may be useful in understanding some of the hemodynamic factors in the formation of bruits or thrombi. It is believed that as radiographic technics improve, cinefluorography will provide valuable diagnostic information and prove to be a useful investigative tool.

CHAIRMAN MILLIKAN: Dr. Baker, will you continue with the "Assessment of Subtraction Technic"?

An Assessment of the Subtraction Technic

Hillier L. Baker, Jr.

*Mayo Clinic
Rochester, Minnesota*

SUBTRACTION IS essentially a method of enhancing the radiographic visualization of contrast medium. It was first described by Ziedses des Plantes,^{1,2} in 1935, as a photographic method in which a roentgenographic negative could be reversed or changed to a positive, after which superimposition of the positive and negative films resulted in the canceling out of identical images on each film. If one of these films contained added contrast medium, the composite showed only this added material as the prominent feature.

For 25 years the technic attracted some attention, but it remained virtually unused because the photographic manipulations necessary to produce reversed films with the proper density were complex and time-consuming, and because radiologists as well as radiographic examinations were somewhat unsophisticated. This combination of factors led to the belief that the value of the additional information to be gained through the use of subtraction would not outweigh the difficulties involved.

In the past two decades, as radiologic practice has matured, contrast examinations have been employed with increasing frequency. During much of this period the major effort was directed toward the development of surgical technics by which contrast material could be delivered to various vessels and organs with safety, and many advances were made. In recent years significant progress in this area has come more slowly, and thought-

ful investigators everywhere have turned their attention to the task of extracting more information from the studies performed with known surgical technics. Novel radiographic methods such as tomography and cineradiography have been applied, and a renewed interest in subtraction has evolved.

The greatest deterrent to the more widespread use of subtraction has been the difficulty of the photographic process. Recently, Hanafée and Stout,³ Levick and Mitchell,⁴ and Rockoff and Camp⁵ have reported simplified methods that can be easily applied and that will greatly expedite the procedure. The most outstanding breakthrough in this field, however, has been made by Holman and Bullard.⁶ They have achieved subtraction by electronic means through an adaptation of closed-circuit television. Their apparatus permits immediate viewing of the roentgenograms as the examination is in progress. Contrast and brightness can be varied at will, and the opaque medium may be viewed either as "white on black" or as "black on white." The way is now open for unlimited employment of the subtraction technic.

EVALUATION OF THE METHOD

For the past year we have used "electronic subtraction" in every angiographic study undertaken in our department, and as a result of this experience we have come to know its advantages as well as some of its limitations.

Limitations. Most of the limitations would seem to be relative rather than absolute, once we realize that structures that are not opacified in the original roentgenogram will not magically appear in the course of subtraction and that vessels less than 1 mm. in diameter will seldom be seen in the electronic process or those smaller than 0.5 mm. in the photographic process.

Radiographic technic often needs to be altered in order to produce films with maximal penetration of bone so that contrast-filled vessels which lie beneath will cast a shadow. This problem—as well as other purely technical details such as positioning, amount of medium injected, and so on—can be easily and rapidly solved.

At present, our greatest difficulties arise from our lack of familiarity with normal “subtraction anatomy.” The early arterial and late venous phases of the cerebral angiogram present no real problem. The marked blush of the contrast-filled brain in the capillary phase of circulation can be very confusing, however. Certain portions of the vascular bed empty more slowly than others, and the prolonged opacification can mimic the appearance of a tumor stain. To resolve this confusion, we are actively studying both the normal and the pathologic “subtraction anatomy” of the brain.

Advantages. The advantages of employing the subtraction technic in cerebral vascular studies far outweigh the limitations encountered. Certain regions cannot be evaluated in any other manner, and the depiction of many lesions which are, at present, best displayed by the angiographic technic is often enhanced.

Any arteries or veins in or adjacent to the base of the skull, vessels which formerly could not be visualized at all, are now subject to the closest analysis. The orbital and facial vasculature can now be seen easily. Vessels in the posterior fossa, cervical region, upper mediastinum, and, possibly, even the spinal cord will be visualized as never before. Certain radiographic projections formerly

thought to be of limited or no value in angiography can now be used, and they may yield more information than those in common use today. All this can be accomplished without the necessity of increasing the volume or concentration of the medium injected, so that the risks of angiography are not increased and, indeed, may eventually be reduced.

Even more dramatic advances in the field of radiology will undoubtedly evolve as techniques for subtraction are investigated more extensively and improvements are made.

AREAS OF FURTHER INVESTIGATION

At present, we are not only attempting to investigate all fields in which subtraction might be of some value, but we are also striving to improve the electronic technic and to incorporate newer devices in the system in order to extend its usefulness.

We are planning to alter our present television system from a 535-line to a 1000-line scan system in order to enhance resolution. We expect that this change will enable us to visualize vessels as small as any that can be reproduced with the best photographic subtraction methods.

More intriguing, perhaps, is our effort to combine cineradiography and subtraction. This can be approached in several ways. In one method, two synchronized motion picture projectors present cineangiograms to the television system; in another system, the combination of a positive signal from a video tape recorder or image-storing tube with a negative signal from an image amplifier tube results in a subtracted kinescopic image. Of the two systems, the former appears to be more practical at this time, and we are, therefore, investigating its possibilities initially.

CONCLUSION

The subtraction technic, which has been used only sparingly in the past, is a valuable addition to the radiologist's armamentarium. Newer developments should eliminate most