A MULTICENTER STUDY of Reversible Ischemic Attacks has been carried out in 8 Italian neurological and neurosurgical centers as part of the Italian National Research Council, Special Preventive Medicine Project for Atherosclerosis. Four hundred and sixty consecutive patients have been entered into the study. These were evaluated by standardized neurological, cardiological, laboratory and neurovascular procedures. All patients had cerebral angiography, with multiple vessel visualization through femoral catheterization.

Recruitment of patients took place between 1977 and 1978 and the 3 year follow up will end in 1981. The aim of the study is to determine the present status of the disease in Italy and its relation to the main risk factors, the type of clinical events, modification of cardiovascular state and evolution of the angiographic picture.

Data available to date were presented in Rome, Oct. 14-16, 1980, at a 3-day conference devoted to a review of atherosclerotic vascular disease. This conference covered reports of other aspects of the Special Preventive Medicine Project for Atherosclerosis, including multicenter studies on pathological aspects of atherosclerosis, coordinated by Prof. G. Baroldi; and on myocardial ischemia, by Prof. A. Maseri, professor of cardiology of the Postgraduate Medical School, Hammersmith Hospital, London.

The conference included lectures given by invited guests. Among them were “Clinical pathology and risk factors of TIAs,” A. Bes (Toulouse); “Tissue metabolism in TIAs and in ischemia,” J.M. Fein (New York); “Contribution of CBF studies to diagnosis and prevention of cerebral ischemia,” J.M. Orsogolo (Bordeaux); “Metabolic aspects of cerebrovascular disorders studied with positron tomography,” G.L. Lenzi, (Rome); “Natural history and causes of death in TIAs,” J.F. Toole (Winston-Salem, NC); “Cardiac dysfunction and brain ischemia,” S. Lavy (Jerusalem); “Contribution of angiography in preventive studies, risks and complications,” O.M. Reinmuth (Pittsburgh, PA); “Brain hemorrhage: present status of diagnosis, prevention and treatment,” J.T. Robertson (Memphis, TN); “Clinical management of TIA patients,” A. Heyman (Durham, NC); “Medical preventive trials in cerebral ischemia,” J.P. Whisnant (Rochester, MN); “Surgical preventive trials in cerebral ischemia,” P. Conforti (Naples).

The results of the Italian cooperative study on reversible ischemic attacks were presented by C. Fieschi (Rome) and others.

Dr. De Zanche (Padua) described the population analyses. The average age at time of entry was 49 with 51% of the cases below 55. The present study differs from others which included primarily older patients. Sixty-four percent had 2 or more ischemic attacks at the time of study. Fifty-six percent of the attacks lasted longer than 24 hours. Identification of the arterial territory involved was determined clinically by the participating authors: 60% were carotid attacks

A COMPANION STUDY comprising a survey of the frequency of TIAs in Italy and a prospective registry called the Italian Cooperative Study of Reversible Ischemic Attacks (ICST) was started in June 1977. To date, 2,200 cases of TIAs have been ascertained. Of these, 60% were carotid attacks, 14% were vertebral attacks, 14% were basilar attacks, and 12% were occlusions of the middle cerebral artery territory. The ICST is a multicenter cooperative project involving 59 centers in Italy.

The ICST will cooperate with the Italian Cooperative Study of Cerebral Ischemia (ICSCI) in the European Stroke Register (ESR), which is a prospective registry of 50 centers in 13 European countries.

Italian Study of Reversible Ischemic Attacks


C. FIESCHI, M.D., C. ARGENTINO, M.D. AND M. RASURA, M.D.
(34% left, 26% right ICA), 21% vertebrobasilar attacks and 15% were attacks in more than one arterial territory. The site of the attack was undefined in 4%.

Dr. De Zanche reported on the examination for cardiac disease. Cardiac arrhythmias (atrial fibrillation) were limited in number; only 128 (29%) had other significant cardiac disease, which was more frequent in patients with repeated episodes of cerebral ischemia. The sub-group with cardiac disease, which is associated with hemodynamic impairment, was more likely to have vertebrobasilar attacks.

Half the patients with significant cardiac disease did not have evidence of atherosclerosis on cerebral angiography. This emphasizes the need for accurate cardiological examination.

At the onset of the study, dynamic electrocardiography (Holter) and echocardiography were not available in all participating centers. These studies were limited to 100 patients and demonstrated "clinically unsuspected" cardiopathies in 6% and mitral valve prolapse in 20% of patients below 45 (Fieschi et al.).

Dr. Bozzao (Rome) reported on the angiographic analyses which revealed a complication rate of 5% (general or restricted to the nervous system). Only 57% of patients with TIA admitted to the study had significant lesions demonstrated by angiograms. Extracranial lesions were 4 times more frequent than stenosis or plaques at intracranial sites.

Angiographic abnormalities were more frequent in patients with carotid TIA than V-B TIA. Patients with clinically diagnosed V-B TIA had a high frequency of significant carotid lesions on angiograms.

Dr. Nardini (Siena) correlated the abnormalities on angiograms with age, sex, tobacco and alcohol consumption, work stress, high blood pressure and hyperlipidemia type II and type IV. The most relevant single correlation was with age. This indicated that a comparison of different population sub-groups in terms of degree of cerebral atherosclerosis as a function of any factor, whether it is clinical severity, plasma cholesterol, high blood pressure or any other, must be corrected for age.

Drs. G. Crepaldi, Professor of Gerontology and Metabolic Diseases (Padua), and G.L. Brambilla (Pavia), presented a detailed analysis of blood lipid findings. In our patients, triglycerides are higher than in controls while cholesterol levels are not. In patients with TIA and with atherosclerotic lesions, the mean cholesterol was higher than in patients with TIA, but without atherosclerotic lesions. The mean HDL-cholesterol values were significantly lower in males with carotid artery lesions than in females, or in males with V-B lesions.

Dr. Tomasello (Naples), reported on a clinical cross-validation of the 8 centers involving history-taking, neurovascular and neurological examination. This demonstrated that the reproducibility of clinical findings requires specific training. The subjectivity of both the patient and the examiner who describe a past event without objective findings to support a diagnosis, plays a major role in deciding the exact nature, duration and site of a supposedly focal transient neurological deficit. Once written or recorded on tape for a computer, the event becomes apparently true, when, in fact, other observers examining the same patient on a subsequent occasion, may describe and judge the information differently. Dr. Tomasello substantiated this with his "reliability study," and he said he hoped to interest others in carrying out similar studies.

Dr. Bono and others (Pavia) discussed CT findings in these patients. Thirty-five percent had a focal lesion on CT, thus indicating that the process was not "reversible or transient." Twenty-one percent of patients with a normal neurological examination and duration of symptoms of less than 24 hours had minimal focal lesions on CT, as did 40% of patients with symptoms of a duration of more than 24 hours. Positive CT scans were more frequent after repeated attacks, although all had been reported to be "clinically" reversible. This indicates that focal cerebral ischemia — no matter if clinically reversible — is seldom a harmless event for the brain. As a result, the concept of TIA's becomes more cloudy. Should it be diagnosed when the neurological event is subjectively reversible, or when newer diagnostic techniques are available? Does the event require an objective validation? Is the standard neurological examination sufficient or should it be accompanied by neuropsychological evaluation and a negative CT scan and, next, by a PET scan?

Dr. Nichelli (Modena) reviewed the neuropsychological studies of the patients in the project. He reported that patients with TIA may have minor permanent defects revealed by a simple but accurate neuropsychological battery of tests as compared to matched controls with transient cardiac events. The test battery proposed by Nichelli does not replace a complete neuropsychological examination, but is useful as a complement to the standard neurological examination of patients with TIA.

Dr. Candelise (Milan) and Dr. Inzitari (Florence) presented data on medical and surgical treatment and on follow up at one year. Twenty percent of patients had some form of surgical treatment, the remaining had platelet antiaggregant therapy; the type was left to the discretion of the physician. A total of 20 patients have been lost to follow up. Fifty-seven percent of the patients were symptom free at 1 year, 36 percent had experienced a new transient ischemic attack. Four percent had a stroke or myocardial infarction. Cerebrovascular accidents were slightly more common than cardiac events. In a previous series, the percent of cardiac deaths exceeded the percent of cerebrovascular deaths; it is likely that this may occur with further follow up of this study as indicated by a trend of increasing cardiac deaths in the second 6 months.

A correlation between the clinical (neurological, cardiological) studies and pathological studies represents one of the future goals of the Italian Project on Atherosclerosis.
ANNEX

Participants in the Italian Study of Reversible Ischemic Attack

D. Andreani (Rome), G. Baroldi (Pisa), coordinator of the atherosclerosis subproject; C. Bartorelli (Milan), A. Beretta Anguissola (Rome), A. Bes (Toulouse, France), H. Blieden (Tel Hashomer, Israel), L. Bonomo (Bari), coordinator of special project preventive medicine; L. Bergamini (Turin), P. Conforti (Naples), C. R. Conti (Gainesville, Texas), L. Cohen (New Haven, CT), H. Denolin (Brussels), L. Donato (Pisa), C. Fazio (Rome), J. Fein (New York, NY), V. Ferrans (Bethesda, MD), R. E. Jennings (Durham, S.A.), D. E. Gregg (Boston, MA), B. Guidetti (Rome), M. Goldstein (Bethesda, MD), S. Goldstein (Detroit, MI), A. Heyman (Durham, NC).

Also, P. Harris (London), W. D. Heiss (Cologne, West Germany), P. G. Hugenholtz (Rotterdam), G. A. Klassen (Halifax, Canada), S. Lavy (Jerusalem, Israel), G. L. Lenzi (Rome), F. H. McDowell (New York, NY), A. Maseri (London-Pisa), R. Navalesi (Pisa), G. G. Neri Serneri (Firenze), M. F. Oliver (Edinburgh, Scotland), J. M. Orgogozo (Bordeaux, France), R. Paoletti (Milano), P. Pinelli (Pavia), Q. M. Reinmuth (Pittsburgh, PA), W. C. Roberts (Bethesda, MD), J. T. Robertson (Memphis, TN), R. Ross (Seattle, WA), M. D. Silver (Toronto, Canada), B. E. Sobel (Saint Louis, MO), E. H. Sonnenblick (New York, NY), J. P. Strong (New Orleans, LA), J. Toole (Winston-Salem, NC), G. Weber (Stena), R. W. Wissler (Chicago, IL).

Special Project Preventive Medicine: Atherosclerosis

Project Coordinator: C. Fieschi (IIIa Cl. Neurologica — Roma).

Clinical Units


Biostatistics Unit

F. Mariani, D. Bardelli, F. Bianchi, R. Cristofani, M. Protti (Pisa).

Consultant Neuroradiologists

L. Bozzao (Roma), F. Galligioni (Padova).

Consultant Neuropsychologist

P. Nichelli (Modena).

Consultant Cardiologist

A. L. Abate (Pisa).

Chairmen

F. McDowell, R. Ross, M. Goldstein, L. Bergamini, C. Fazio, and C. Loeb
C Fieschi, C Argentino and M Rasura

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