The introduction to the Conference by Dr. K. J. Zülich, Professor, Max-Planck-Institut für Hirnforschung, Köln-Merheim, West Germany, emphasized that the Salzburg Conference on Cerebral Vascular Disease is different from any other international conference on related subjects in that (1) we are primarily concerned with the clinical aspects of cerebrovascular disease. We look at the problem from the bedside. (2) We are an international group which is more representational than a regional group. (3) The whole design of the Salzburg Conference traditionally has been one that provided adequate time for discussion and intellectual interchange between the participants.

The opening session on biostatistics, natural history and risk factors in stroke was initiated by Dr. Zülich and associates, who gave some interesting statistics of ischemic cerebrovascular disease in 612 patients studied in Köln, West Germany. They found that about 65% or two-thirds of their patients had disease in the distribution of the carotid artery, that approximately one-third or 27% had disease in the vertebral artery system, and that in 8% these systems were combined, with disease in both. They showed a 3:2 ratio of male to female incidence, similar to that found elsewhere. The average age of maximum incidence was 65 years, which again is approximately equal to studies reported from other countries, particularly the United States; although in India, as we will see later, the average age of maximum incidence is lower. Carotid symptoms tend to appear in a younger group of patients than disease in the vertebrobasilar artery system, but there was no specific time of year or day of the week they could identify in relation to a higher risk incidence. They did point out, however, that between 4 and 8 A.M. there was a higher incidence of stroke when blood pressure was low, and also between 8 A.M. and 1 P.M. when orthostatic hypotension was likely to occur. Risk factors identified were hypertension, cardiac disease, obesity, previous symptoms of cerebrovascular insufficiency, peripheral vascular disease, diabetes and smoking. Emphasis in their patients was placed on the importance of hypotension, labile hypertension, myocardial infarction and cardiac dysrhythmia as hemodynamic factors. It is interesting that they reported a low incidence of emboli (being about 4%), although it is possible there was at least another 8% of strokes that could have been embolic in nature.

Dr. F. Pratesi, Chairman, Centro di Angiologia dell’Università di Firenze, Florence, Italy, reported
data about risk factors in 3,000 cases of stroke, which were in good agreement with those reported by Dr. Zülch. He found essentially the same risk factors for infarction of the brain as occurred in ischemia of the limbs, with some important exceptions. For example, hypertension as a risk factor was more related to cerebral infarction, whereas hypercholesterolemia, hyperbetalipoproteinemia, and hypertriglyceridemia were risk factors for both atherosclerosis of the extremities and the brain. He found that both systolic and diastolic blood pressure elevations were risk factors, and in accordance with reports recently made in an issue of this Journal, erythrocythemia was a risk factor in patients with cerebrovascular symptoms but not in patients with ischemia of the limbs.

Dr. J. Abraham, Professor, Department of Neurological Sciences, Christian Medical College and Hospital, Vellore, South India, presented us with a review of certain epidemiological differences in cerebrovascular disease in southern India. He made a prospective study of cerebrovascular disease in this community and found a very high incidence of strokes in the young. No less than 45% of his patients were 40 years of age or younger, and of these, 75% showed occlusion of the carotid artery. In southern India, occlusion of the carotid artery appears predominantly in young males. Hypertension, diabetes and syphilis were studied carefully, were found to present rarely, and were not identifiable as important risk factors. He found a sudden cone-shaped narrowing in carotid arteriograms of these cases occurring 1 to 1.5 cm above the bifurcation of the carotid artery. He made light and electron microscopic studies of the internal carotid artery wall and found both internal and external elastic membranes to be present (both not usually present in the internal carotid artery) and abnormal with increased collagen, narrowing of the artery and degeneration of the media. He concluded that this stroke population was suffering from a form of hypoplasia of the internal carotid artery which appears to be an extremely common genetic factor in this population, and that this was an important risk factor in the Vellore area. Consanguinity occurs in 30% to 40% of their population, so that genetic risk factors may reasonably be expected.

Dr. A. Agnoli, Professor, First Clinic for Mental and Nervous Disease, University of Rome, Rome, Italy, discussed the prognosis of transient ischemic attacks (TIA) in a retrospective study and found that this group of patients had three times the risk of stroke in the carotid territory. Eighty percent of his patients with TIA in the carotid territory were hypertensive, and 25% developed stroke in six months, 50% in one year, 75% in three to four years, and 100% in ten years. However, this was a retrospective study and this may have influenced the statistics. He found similar risk factors already identified by previous speakers.

Dr. C. Loeb, Chairman, Clinic of Nervous and Mental Disease, University of Genoa, Genoa, Italy, discussed the syndrome of “stroke with full recovery” and pointed out that many did not fall into the usual criteria of transient ischemic attacks—the symptoms lasted considerably longer than 24 hours and yet full recovery did occur. There were other names for this syndrome including “stroke with full recovery,” “reversible ischemic neurological deficits,” and so forth. All of these cases were examples of focal neurological deficits. The incidence was rare, occurring in 4.2% of his patient population. He felt it was probably higher than this if a true incidence per total population were given because he believed that many were treated by other physicians, such as internists, and were not referred to neurologists or neurological centers because of their recovery. He managed to obtain pathological studies in many cases and found that there was white softening in 28%, red softening in 18%, and hemorrhagic infarction or hemorrhage in 11%. The age span was from 56 to 65 years. The anatomical distribution consisted of 33 cases in the carotid system and nine cases in the vertebrobasilar system. The duration of neurological deficit was from four to 60 days with the majority being around 30 days or three weeks. The follow-up indicated that 16.7% were dead in four years, the majority from myocardial and cerebral infarction; 9.5% had other strokes in this follow-up period. He felt from angiographical studies that the most common cause was embolic occlusion.

Dr. D. N. Djibladse, Akademie der Med. Wiss. d. U.S.S.R., Institute für Neurologie, Moscow, USSR, reported on the incidence and clinical manifestations of carotid and vertebral insufficiency in his country, which were similar to those reported in Europe and the United States with ulcerated plaques in the neck as one common cause of emboli and vertebrobasilar insufficiency with hemodynamic crisis as another cause. He felt that TIA was a definite warning of impending stroke and pointed out that vertebrobasilar insufficiency affects the memory; he has seen a number of cases in which the patients became demented.

Dr. Zülch reviewed the anatomical distribution of the carotid syndromes. He emphasized mainly that they are in the distribution of the middle cerebral artery, and the incidence in the left cerebral hemisphere is greater than in the right.

Dr. H. Lechner, Vorstand der Psychiatrisch-Neurologischen Klinik der Universität Graz, and his group from Graz, Austria, pointed out that in studies using lipoprotein electrophoresis in 80 cases with
stroke, hypertriglyceridemia was significantly higher in this group than in the controls; an excess of 15% of his patients had pathological lipid values.

In the papers concerned with diagnostic procedures, Dr. M. D. O'Brien, Research Fellow, Department of Neurology, University of Minnesota, Minneapolis, Minnesota, reported on studies with Dr. A. G. Waltz, Professor of Neurology, University of Minnesota, Minneapolis, Minnesota, on experimental infarction in which they used intravenous injection of radioactive technetium, albumin and sodium to study the pathological changes going on in the infarcted area at different time intervals and compared these findings with the control hemisphere. He found that about 40 hours after the ischemic insult technetium uptake increased threefold, and this increase correlated better with radioactive sodium uptake than with the uptake of radioactive albumin which is much slower, suggesting that the movement of water and edema formation was more important than damage to the blood-brain barrier in the uptake of technetium.

Dr. G. Geraud, Professor, Neurology Service, Hôpital Purpan, Toulouse, France, studied platelet aggregation in patients with transient ischemic attack and found that the aggregation of platelets was increased and that acetylsalicylic acid blocks this for 48 hours.

Dr. E. Ott, Psychiatrisch-Neurologische Klinik der Universität Graz, Graz, Austria, showed that carotid compression plus cerebral impedance measurements through the intact skull can be used to evaluate the carotid collateral circulation, and that if this demonstrates good collateral circulation it further implies good prognosis.

Dr. H. R. Müller, Bürgerhospital Basel, Basel, Switzerland, reported on the diagnosis of carotid stenosis and occlusion using the ultrasonic directional flowmeter applied to that branch of the external carotid artery that passes from the orbit upward over the forehead.

Dr. H. Tschabitscher, Neurologisches Krankenhaus der Stadt Wien-Rosenhügel, Vienna, Austria, reported his experience with the EEG versus circulation times, technetium brain scans, and arteriograms in the diagnosis of cerebrovascular disease and concluded that arteriograms are necessary in order to make a definitive diagnosis, although the other tests have positive screening value.

The papers concerned with clinical findings and regional cerebral blood flow (rCBF) can be summarized as follows.

Dr. G. R. Pistolese, Professor, Second Surgical Clinic, University of Rome, Rome, Italy, studied 23 patients with TIA undergoing carotid endarterectomy and five patients with completed stroke. He found that the cerebral blood flow was lowered in the patients with completed stroke but less identifiably so in the patients with TIA. During carotid clamping the CBF was reduced more in patients with smooth plaques than in ulcerated plaques, which he offered as evidence that the ulcerated plaque caused embolic symptoms while hemodynamic crises were responsible for the remainder. He gave his estimation that 50% were embolic and 50% were hemodynamic.

Dr. J. Marshall, Professor, Institute of Neurology, National Hospital for Nervous Diseases, Queen Square, London, England, found good agreement between regional cerebral blood flow localization and clinical manifestation of TIAs and completed stroke; TIAs gave a correlational relationship in about 70% and completed stroke in 80%. My impression was that Dr. Marshall showed regional cerebral blood flow was of diagnostic value in cases of cerebrovascular disease not clearly identified as such, for example, cases of apparent dementia which would show focal reductions of CBF and cases of stroke with normal angiograms. He also emphasized that rational treatment can be based on results of measurements of rCBF before and after some drug or some surgical therapy had been administered.

Dr. M. Reivich, Professor of Neurology, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, described his studies of a model of acute stroke in the baboon by occluding the middle cerebral artery. He studied the EEG, rCBF and metabolism from arteriovenous differences, and in these measurements showed that cerebral blood flow fell 30% for 75 minutes and thereafter returned to normal. He pointed out that the determination of the AV oxygen difference measurement for estimating cerebral metabolism multiplied by rCBF measurements using radioactive isotopes was probably underestimating the disturbance in flow and in metabolism, since the flow probes record flow not only from the ischemic area but from the bordering zones also.

Dr. I. I. V. Gannushkina, Akademie der Med. Wiss. d. U.S.S.R., Institute für Neurologie, Moscow, USSR, reported experiments in rabbits with the Goldblatt type of experimental hypertension in which she showed edema of the cerebral vessel walls which resulted from hypertension; later there was also edema of the brain producing paradoxical responses of cerebral blood flow change in response to alteration of perfusion pressure (autoregulation) and CO₂ testing (chemical regulation).

Dr. W. D. Heiss, Professor of Neurology, University of Vienna School of Medicine, Vienna, Austria, studied the rCBF compared to sequential scintiphotography and static brain scan in cases of stroke, and showed that all three combined with
arteriograms gave an extremely detailed analysis of patients with stroke.

In a series of papers concerned with prognosis in stroke, Dr. Agnoli and Dr. C. Fazio, Director, First Clinic for Mental and Nervous Disease, University of Rome, Rome, Italy, pointed out that those patients with multiple risk factors had a poor prognosis compared to those with only one risk factor.

Dr. L. W. Popova, Institute of Neurology, Moscow, USSR, reported her observations on acute respiratory problems in a series of stroke patients. These occur primarily in patients with vertebrobasilar disease most commonly due to glossopharyngeal-palate paralysis and sometimes due to central disturbances of respiratory control and, of course, secondary to pulmonary pathology. She pointed out that prompt treatment of these improves survival.

Dr. J. H. A. van der Drift, Neuroradiologische en Neurochirurgische Kliniek St. Ursula, Wassenaar, The Netherlands, pointed out that bilateral EEG abnormalities had poor implications for prognosis.

In a series of papers concerned with morphology and pathology of the cerebral vasculature, Dr. H. van der Eecken, Professor of Psychology, University of Ghent, Belgium, and Dr. J. De Reuck, Kliniek voor Neurologie, Akad. Ziekenhuis Adelfing, Ghent, Belgium, described for the first time the anatomy of the ventriculopetal blood supply which might explain certain vascular disturbances causing problems particularly in cerebral palsy and mental retardation in the young.

Dr. R. Manelf, Neuroradiologist, Department of Radiology, University of Toulouse, Hospital Purpan, Toulouse, France, and Dr. G. Salamon, Hôpital de la Timone, Marseille, France, showed the feasibility of extremely detailed analysis of occlusion of the middle cerebral artery branches and resulting syndromes diagnosed by arteriography using a grid system.

Drs. C. Plets and R. van den Bergh, Universiteitshôpital pour Neurologie en Neurochirurgie, Louvain, Belgium, showed changes in the vasculature after experimental production of hydrocephalus, and the implication that the distortion of the diencephalic and telencephalic vessels recognized by arteriography might be of diagnostic value in this situation.

Dr. H. J. Goldberg, Director of Neuroradiology, Stroke Research Center, Philadelphia General Hospital, Philadelphia, Pennsylvania, showed the importance of the use of angiotomography and magnification methods, particularly for identifying disease of the lenticulostriate arteries. Examples of Charcot-Bouchard aneurysms, large hemorrhages in the basal ganglia, and small hemorrhages and infarction in the subcortical white matter were demonstrated in the living patient by these methods.

Dr. S. Wende, Neuroradiologische Abteilung der Neurochirurgischen Univ.-Klinik, Mainz, West Germany, had similar experiences as Dr. Goldberg using magnification angiography.

Dr. V. Hossmann, Max-Planck-Institut für Hirnforschung, Köln, West Germany, discussed the regulation of cerebral blood flow after experimental ischemia in cats, and pointed out that he was able to find no evidence of the "no-reflow" phenomena after prolonged ischemia for 60 minutes after total ischemia of 30 to 60 minutes he did obtain cerebral vasoparalysis to change in CO₂, but autoregulation was preserved. This provoked lively discussion, since this pattern of dysautoregulation was held to be extremely rare by other discussants.

Dr. N. T. Mathew, Assistant Professor of Neurology, Baylor College of Medicine, Houston, Texas, and associates showed the diagnostic usefulness of rCBF measurements in patients with subarachnoid hemorrhage and severe neurological deficits. These patients showed reduced CBF which (1) increased after intracarotid injection of phenytoin sodium if spasm was present in cerebral vessels (confirmed by arteriography), (2) increased after intravenous injection of 10% glycerol if cerebral edema was present, and (3) increased after lumbar puncture and removal of 25 ml of CSF if acute hydrocephalus or chronic (low pressure) hydrocephalus was present. He also showed how intracerebral hematoma could be diagnosed by rCBF measurements using CO₂ inhalation of hyperventilation to demonstrate regional intracerebral "squeeze" (paradoxical responses) around the hematoma.

Dr. K. Held, I. Med. Univ.-Klinik, Kiel, West Germany, described occlusive disease of the subclavian artery and aortic arch syndromes in which he had made measurements of limb blood flow for the first time. He showed that such patients were capable of increasing arm blood flow during exercise but that the reactive hyperemia persists for longer than in normals and was greater in degree in these patients. He considered this finding important when considering the pathogenesis of cerebrovascular symptoms due to the subclavian steal.

Dr. van der Drift and Dr. N. K. D. Kok, Wassenaar, Netherlands, gave some prospective studies of TIA with some data concerning their pathogenesis; some were embolic, some were hemodynamic.

Dr. W. S. Fields, Division of Continuing Education, Office for Neurological Programs, University of Texas School of Medicine, St. Anthony Center, Houston, Texas, discussed arteriosclerosis as a "noncause" of dementia. This term he felt was often a "wastebasket" diagnosis for many causes of
dementia, and he pleaded for adequate epidemiological and clinical studies. This produced a lively discussion in which we all apparently shared the opinion that there was a great deal of research to be done in the field of arteriosclerotic dementia and that this should be a topic for the next conference in 1974.

Dr. F. Hoff, Department of Neurology, Baylor College of Medicine, Houston, Texas, reported histochemical and electron microscopy studies of the pathogenesis of plaque formation in cerebral arteriosclerosis in man. His evidence was that imbibition of lipids contributes to plaque formation. At first there is an increase and later a decrease in the enzymes in the vessel walls where the plaque formed.

Dr. S. Hoyer, Pathologisches Institut der Universität Heidelberg, Heidelberg, West Germany, studied cases of early cerebral arteriosclerosis with dementia and found that there were some striking disorders of cerebral metabolism which were more evident in such patients than disorders of cerebral blood flow. There were several patterns of disturbed metabolism including reduction of glucose consumption greater than oxygen consumption, increase of lactate production, and a decreased respiratory quotient, indicating that other substrates are being utilized by the brain. Patterns of disturbance of amino acid and free fatty acid metabolism were demonstrated also. In many cases fatty acids and amino acids were being consumed by the brain; in other cases free fatty acids were released by the brain.

Dr. J. Quandt, Director, Bezirkskrankenhauses für Psychiatrie und Neurologie, Bernburg-Saale, East Germany, related observations on the pathogenesis of atherosclerosis from a histological point of view which demonstrated some interesting differences to those pointed out by Dr. Hoff; namely, that in his cases fibroblasts appeared to participate in the early plaque formation rather than smooth muscle cells.

Dr. L. Symon, Institute of Neurology, National Hospital for Nervous Diseases, Queen Square, London, England, gave a paper on the differential diagnosis of surgical remediable lesions causing dementia including tumors of the third ventricle and the pathways of the cerebrospinal fluid and so-called "normal pressure hydrocephalus." He listed other causes of hydrocephalus, particularly communicating or normal pressure hydrocephalus, and in the discussion by all participants, seven methods were suggested for achieving diagnosis of communicating and low-pressure hydrocephalus as a cause of dementia and cerebral ischemia.

1. Intracranial pressure monitoring for several days either from the intradural space with the pressure transducer, or
2. From the lumbar subarachnoid space with a catheter. Recording by methods (1) and (2) will show normal pressure most of the time with periodic increases in intracranial pressure, particularly at night.
3. The infusion of saline at 1.5 ml/min with recording of the pressure by a threeway system. If the pressure increases, it implies impaired absorption of cerebrospinal fluid.
4. Radioisotope cisternography.
5. Pneumoencephalography showing dilated ventricles and little or no air over the subarachnoid space.
6. tCBF before and after spinal tap with removal of 25 ml cerebrospinal fluid. As reported by Dr. Mathew et al. during the Conference, tCBF increases if communicating hydrocephalus is present.
7. Blood RISA activity after lumbar puncture injecting a standard dosage of RISA. Impaired absorption is indicated if this is still present in 24 to 48 hours.

During the discussion the following possible causes of low-pressure hydrocephalus and consequent reduction of CBF were listed:
1. Obstruction of the arachnoidal villi.
2. Capillary venous obstruction with chronic passive hyperemia.
3. Adhesive arachnoiditis with regional CSF pressure changes.
4. Impairment of cellular transport mechanisms, particularly after viral and inflammatory effects.
5. Disturbance of the Munro-Kelly "doctrine" with changes in intracranial blood-CSF-brain tissue volume relationships.
6. Consideration of Pascal's Law regarding ventricular size and its effects on the pressure required to enlarge the cerebral ventricles.

Dr. F. Torres, Division of Neurology, Director, EEG-Lab., University of Minnesota Medical School, Minneapolis, Minnesota, measured voltage distribution of an electrical signal applied to the human head which he believed can be used for localizing cerebral abnormalities including occlusion of the middle cerebral artery with infarction of the brain.

Dr. P. Fiorani, Second Surgical Clinic of the University of Rome, Rome, Italy, has continued his studies during carotid artery surgery showing that as the cerebral blood flow decreased below 30% so vasomotor responsiveness to both CO2 (chemical...
regulation) and alteration of blood pressure (autoregulation) is reduced.

Finally, there were three papers presented at the close of the meeting concerned essentially with the factors influencing the duration of ischemia that can be tolerated by the brain.

Usually we have been taught that the brain can tolerate four to eight minutes of ischemia, but the studies of E. Farkas and M. L. Arsenio-Nunes of Paris, France, suggest that periods for as long as 30 minutes under certain circumstances can be tolerated with recovery.

Dr. V. Hossmann and Dr. K. A. Hossmann, Max-Planck-Institut für Hirnforschung, Köln, West Germany, studied recovery of cerebral function in the cat after 30 minutes of cardiac arrest by ventricular fibrillation. After revival the cortex appeared "normal" by light microscopy.

Lastly, Dr. Held measured cerebral glucose and energy metabolism in experimental brain infarction produced by emboli in dogs. The regional metabolic changes were measured in and around the infarcted zone after freezing the head in liquid nitrogen. Evans blue intravenous injection prior to sacrifice showed that the blood-brain barrier was damaged in the infarcted zone. After infarction for 24 hours, creatine phosphate was reduced; ATP, glycogen and glucose were reduced, and lactate was increased. Water content of the brain was increased in both infarcted and bordering zones. Despite the hemiplegia manifested by these animals during life, residual oxidative metabolism was present in the infarcted zone, which led Dr. Held to conclude that irreversible damage in the brain resulting from cerebral infarction may be due to cerebral edema. Since cerebral edema is a therapeutically remediable condition, this gave the participants reason for consideration of further studies in animals and therapeutic trials in patients.
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