6th Asian and Oceanian Congress of Neurology

Abstracts

November 13-17, 1983
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Panel discussion on the management of cerebrovascular disease

Monday, November 14, 1983
9.00, Room A

S1. General management of stroke patients

Y. TAZAKI and F. SAKAI, *Department of Medicine, Kitasato University, Sagamihara, Kanagawa, Japan*

With the increasing number of intensive care units in general hospitals in Japan during the past few years, physicians have been encouraged to transfer patients with stroke to hospitals for intensive medical treatment. As a consequence, our knowledge of the pathophysiological basis for emergency management of stroke has been improved, and recent statistics show a significant decline in the death rate for cerebrovascular disease. After several years' experience of active emergency treatment of patients at our and other acute care hospitals, several conclusions regarding general management of patients with stroke have been drawn, at least tentatively, as follows: (1) The immediate diagnostic evaluation using CT scan and other methods is of critical importance since 15% of patients who were initially diagnosed as having stroke and transferred to the intensive care unit were subsequently diagnosed as being in coma or having neurological deficits with other causes. (2) While the main cause of death was cerebral herniation, the direct cause of death in 33% of patients with stroke was not the cerebral insult itself but the ensuing complications during the later hospital course. The data on blood gases and electrolytes suggest that patients' mortality largely depends on the careful monitoring and control of ventilation, acid-base and fluid balances. (3) Since the main reason for the clinical deterioration is cerebral edema following either cerebral bleeding or infarction, consideration must be given to extensive medical treatment using antiedema agents. (4) It became possible to utilize computer assisted multivariate analysis for early indication of prognosis for patients with stroke, which should help clinicians to an appropriate decision regarding management, including the choice of surgical treatment. The present state of the art and limitations of medical treatment of stroke are reviewed and discussed.

S2. Management of intracerebral hemorrhage

S. SUKONDHABHANT, *Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Intracerebral hemorrhage is one of the deadliest conditions among neurological patients. Its incidence, approximately 0.35% of all admissions to Siriraj Hospital,

and its mortality of around 80% make the management of this condition important. The remedies consist of BP regulation, use of anticerebral edema agents, supportive treatments and surgical removal of the blood clot. Anticerebral edema agents are the most valuable at the early stage, while surgical intervention must be considered according to location, size, nature and the patient's condition.

In Thailand, an unusual cause of intracerebral hemorrhage, migrating larva of *Gnathostoma spinigerum,* is occasionally encountered.

S3. Stroke prevention and noninvasive diagnosis

W.S. FIELDS, *University of Texas Medical School at Houston, Houston, Texas, U.S.A.*

Prevention is the goal of all physicians and surgeons dealing with patients considered to be at high risk for stroke. It becomes imperative, therefore, to identify risk factors, particularly those which can be controlled with a reasonable degree of certainty and to obtain the compliance of the patient in the prescribed mode of management. Clearly, the most readily identifiable risk factor is systemic hypertension. Detection and control of hypertension in North America is considered by many to be the most likely explanation for the steady reduction in the incidence of stroke there over the past two decades.

A second important risk factor is the occurrence of one or more transient ischemic attacks, which must be considered as warnings of threatened cerebral infarction. Therefore, the identification and characterization of lesions in the circulation, which may be responsible for such attacks, become imperative. It is in this latter category of risk factors that noninvasive diagnosis becomes such an important tool. Localization of both extra- and intracranial lesions by noninvasive techniques has improved considerably over the past few years and hopefully will soon eliminate the need for conducting diagnostic procedures involving considerably greater risk. Directional Doppler, phonoangiography and oculoplethysmography, as well as direct techniques for arterial imaging, have all become important adjuncts to our diagnostic armamentarium. Computed tomography (CT) scanning has made it possible to differentiate readily between hemorrhagic and nonhemorrhagic stroke. Moreover, small infarcts and ischemic areas can be detected early by using a double dose of intravenous contrast and delayed scanning after one hour. Until recently, however, arteriography using intra-arterial catheter methods has been the only way in which the location, extent and pathological characteristics of lesions could be satisfactorily accomplished. New technical advances, particularly digital subtraction angiography, provide methods for screening large populations without the necessity for employing general anesthesia or arranging for hospital admission of persons who are undergoing diagnostic evaluation. Although this method is not completely noninvasive, the risk of intravenous angiography is considerably less than by the intra-arterial route which is conventionally employed. However, one can also produce intra-arterial digital subtraction images while using small catheters and a minimal amount of contrast material. A complete study can be done with 15 ml of contrast or less. Satisfactory radiographs can be obtained of both the intracranial vasculature

and the larger extracranial vessels. The quality of the films obtained has improved as the technology has advanced during the past two years, and it is anticipated that even better resolution may be possible. Films obtained by these and other techniques will be presented. The use of aspirin or antiplatelet agents during the period of diagnostic evaluation will also be discussed.

S4. Treatment of stroke in young patients

K. JAGANNATHAN, G. KUMARESAN and M. DHANARAJ, *Institute of Neurology, Government General Hospital, Madras, India*

Cerebrovascular accidents presenting as 'acute stroke' constituted approximately 1.2% of all admissions to the hospitals attached to the Madras Medical College. 'Young stroke' patients were defined as those between childhood and 40 years of age, and formed about 16% of all 'stroke' patients admitted to the hospitals. They also formed a heterogeneous aetiopathogenetic group. In the paediatric age group (up to 13 years) 56% of cases were due to infections of all kinds but in 26% the aetiology remained undetermined. In the age-group 14-40 years, arteritis (both specific and non-specific) was a major factor, occurring in 33%. The rest of the patients presenting with thrombotic or thromboembolic strokes did not show a definite aetiology and the pathology, though presumed to be atherosclerotic, remained unverified.

The management of these patients presented a problem in view of the varied aetiopathogenesis of these 'strokes'. Patients were classified as 'haemorrhagic' or 'ischaemic' with the help of the CT scan. Haemorrhagic strokes were managed conservatively and the need for surgical intervention was limited. Hypertension was among the commonest cause for haemorrhagic stroke. The more common ischaemic strokes, on recognition wherever possible of the specific cause, such as tuberculosis, were managed with a specific treatment schedule appropriate to the cause, in addition to the general management with anti-oedema agents, anticoagulants and antiplatelet adhesive factors, in varying combinations depending on the circumstances. The need for surgical management, such as STA-MCA anastomosis, was considered wherever possible.

The 'young stroke' patient carried better prognosis in terms of return to the activities of daily living; however, the rehabilitation of these patients poses a problem in a country like India. The experience at Madras and other centres in the country relating to these aspects are presented.

S5. Incidence and clinicopathological features of cerebrovascular lesions from 1,470 serial autopsies of patients aged 60 years or more at time of death

M. KAMEYAMA, H. SHIO and I. AKIGUCHI, *Department of Neurology, Kyoto University School of Medicine, Kyoto, Japan*

Among 1,470 autopsies, no cerebrovascular lesions were found in 334 cases (23%).

Fatal cerebral hemorrhage was seen in 94 (6%), and nonfatal in 200 cases (14%). Among cerebral infarcts, there were 94 fatal cases (6%), 569 nonfatal cases (38%), and multiple infarcts in 632 (43%). The frequency of fatal cerebral hemorrhage was almost equal to that of fatal cerebral infarction, but cases with nonfatal or multiple cerebral infarction were much more frequent than with hemorrhage.

The incidence of severe atherosclerosis, angionecrosis of the brain arteries and hypertension, among various pathological conditions, was studied in comparison to that in the total number of cases examined. In myocardial infarction and diabetes mellitus, the incidence of severe atherosclerosis in the cerebral arteries was significantly higher; on the contrary, in pulmonary emphysema, malignant neoplasm and liver cirrhosis, the incidence of severe cerebral atherosclerosis was significantly less than in the total cases. Angionecrosis, which is regarded as an important vascular lesion relating to cerebral hemorrhage, was significantly more frequent only in hypertension, while significantly less common in malignant neoplasm. Hypertension is rare in liver cirrhosis, or malignant neoplasm.

The incidence of cerebrovascular lesions in various conditions was compared to that in the total number of cases. Cerebral vascular lesions were significantly more frequent in myocardial infarction, atrial fibrillation, and less frequent in malignant neoplasm and liver cirrhosis. Cerebral infarction was significantly more frequent in myocardial infarction and atrial fibrillation, less frequent in malignancy. In hypertensives and diabetics, nonfatal or multiple infarction was significantly more common.

S6. Biochemical aspects of stroke treatment

F.M. YATSU, *Department of Neurology, University of Texas Health Science Center at Houston, Houston, Texas, U.S.A.*

The critical factors for stroke therapy are: (1) the microcirculation; (2) the brain parenchyma (edema and its exquisite vulnerability to ischemia); and (3) the blood elements (platelet aggregation and coagulation). Biochemical insights into these areas offer rational clues for prevention and therapy.

The so-called 'penumbra' represents tissue adjacent to an infarct compromised by reduced cerebral blood flow due to impairment of the microcirculation. With elucidation of prostacyclin, a vasodilatory prostaglandin, a potentially practical means of improving the 'penumbra' is available.

Brain edema complicates strokes by aggravating impaired cerebral blood flow and causing fatal brain herniation. Of potential therapeutic significance is the prevention and reversal of free radical-induced edema with free radical scavengers, such as superoxide dismutase. At present, dehydrating agents such as mannitol provide only temporary therapy for edema. The value of steroids is unproven. The vulnerability of brain to ischemia relates to its high obligate requirement for oxygen and glucose, and attempts to provide 'pharmacologic protection' or 'brain resuscitation' have been made with barbiturates, i.e. the induction of 'barbiturate coma'. Pharmacologic protection has been utilized for strokes, head trauma, cardiopulmo-

nary arrest, and metabolic encephalopathies, but its value is thus far unproven.

A great deal of information is available regarding the complexities of platelet aggregation and coagulation, but these data do not support either a hyperaggregable or hypercoagulable state for most thromboembolic strokes. Despite this, their secondary activation with the release of aggregants and coagulation factors can aggravate the initial thromboembolic stroke. Prostacyclin, the identification of which led to the 1982 Nobel Prize for Drs Vane, Samuelson, and Bergstrom, is a highly potent compound for vasodilation, platelet disaggregation and platelet anti-aggregation. Our studies on prostacyclin infusion in strokes demonstrate that the presence of increased platelet aggregation, presumably triggered by an offending atheromatous lesion, is normalized. Whether this form of therapy will result in neurological improvement and reversal of deficits will await prospective, double-blind study. Hypercoagulability is presumed to occur in the so-called 'progressing stroke' or 'stroke in evolution' and heparin is indicated to halt the progression of the coagulation process. Similarly, anticoagulation is indicated for embolic strokes of cardiac origin since this therapy will reduce re-embolization.

S7. Management of complications in the acute stage of stroke

T.K. LEE, *Department of Internal Medicine, National Taiwan University Hospital, Taipei, R.O.C.*

Various complications of cerebrovascular disease (CVD) may interfere with recovery and may even cause death. Appropriate management of these complications is therefore a matter of great importance.

Serum sodium concentration is the major determinant of the osmotic force in the extracellular fluid. In our study, 21.1% of inpatients with stroke were complicated by hypo-osmolality developing either early or late in the course. In order to prevent damage to the brain tissue, periodic determination of serum sodium and osmolality is advisable.

Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) has been seldom reported in patients with stroke; nevertheless, it was found in 15.1% of our stroke patients. Our study in these cases revealed a significantly higher plasma arginine vasopressin (AVP) level, lower serum osmolality and higher urinary prostaglandin E (PGE) excretion, and a significant positive correlation ($r = 0.72$, $P < 0.05$) between PGE excretion and plasma AVP. Since renal PGE has been reported to act as a modulator of ADH activity in SIADH, those agents capable of inhibiting prostaglandin synthesis should be used with caution in these patients.

An impaired state of consciousness and the use of various instruments for the management of CVD may increase the risk of infection. In addition, a considerable number of hospital-acquired infections are mixed in type and caused by organisms resistant to many antibiotics. In our patients, nosocomial urinary tract and respiratory tract infection occurred in 16.8% and 12.9%, respectively. The main causative organisms were *Escherichia coli, Citrobacter, Klebsiella pneumoniae* and *Pseudomonas aeruginosa.*

Bleeding from stress ulcers is potentially very dangerous in critically ill patients. Antacids were not found effective in prevention of upper gastrointestinal bleeding in this study.

S8. The surgical management of stroke

S.N. CHOU, *Department of Neurosurgery, University of Minnesota, Minneapolis, Minnesota, U.S.A.*

There are two major groups of surgical procedures for the treatment of a variety of strokes. One group deals with the extracranial vessels, the carotid and the vertebral arteries. The other is an attempt to deliver more blood from the extracranial into the intracranial circulation, bypassing the occlusive vascular site.

The extracranial vascular procedures are devised to eliminate the source of emboli from, and to relieve occlusion by, the atheromatous plaque that is generally located at the carotid bifurcation in the neck and at the take-off of the vertebral from the subclavian artery. Occasionally, such procedures may increase blood supply to the brain by removing external compression on a major artery in the neck, such as osteoarthritic spurs in the foramen transversarium which surrounds the vertebral artery. Carotid endarterectomy is the most well-known procedure. It can be carried out with either general or local anesthesia. The aim is to remove as cleanly and as completely as possible the occlusive plaque via an arteriotomy with temporary occlusions of the proximal parent artery and the distal branches. In certain conditions, an internal shunt may need to be used to maintain blood flow into the brain during the procedure. Intraoperative monitoring, using scalp electroencephalography or other means, may improve the safety of this procedure. Additionally, patching or grafting techniques may be used in addition to or in lieu of removing the plaque. Vertebral endarterectomy is less frequently done. An option for bypassing the diseased site, the vertebral subclavian junction, is an end-to-side anastomosis of the vertebral with the common carotid artery. Technical options that should be considered and used to perform these procedures will be discussed.

Extracranial-intracranial anastomosis procedures are designed to bypass occlusive sites which are technically difficult to expose or to re-open. The most well-known of such procedures is the anastomosis of the superficial temporal artery and a branch of the middle cerebral artery. Occipital artery to posterior inferior cerebellar artery, to posterior cerebral artery and to superior cerebellar artery can now also be performed for certain vertebral basilar insufficiencies. The rationale for and the technical aspects of these procedures will be discussed. Finally, such bypass procedures may be used prophylactically as a first-stage treatment to excise or to trap intracranial aneurysms that cannot, at the present, be surgically occluded. Examples of such cases will be presented.

Epidemiology of cerebrovascular disease in Asia

Monday, November 14, 1983
14.00, Room A

S9. Cerebrovascular disease in the young in Hong Kong

C.Y. HUANG, *Department of Medicine, University of Hong Kong, Queen Mary Hospital, Hong Kong*

Experience with young stroke patients (aged under 45 years) in Hong Kong is reviewed. The incidence of stroke mortality in this age group has steadily declined over the last two decades, compared with the older population where there has been a steady increase. Mortality per 100,000 was 3.61 in 1955, 3.38 in 1960, 3.64 in 1965, 2.85 in 1970, 2.16 in 1975 and 2.18 in 1980. The importance of controlling infectious disease in the prevention of cerebrovascular disease in the young is highlighted by data on rheumatic valvular disease, Moya Moya disease, and tuberculous arteritis.

S10. Strokes (CVD) in India

P.M. DALAI, *Stroke Research Units, Sir H.N. Hospital, and National Centre for Neuroscience Research, T.N. Medical College, Bombay, India*

There is no reliable information, as yet, on 'strokes in India'. However, use of hospital-based material on epidemiology, despite its limitations, has some potential applications. Analysis of such data from major urban university hospitals suggests that nearly 2% of all hospital cases (4.5% of medical and 20% of neurological admissions) are results of 'strokes'.

From a random survey, the prevalence rate for 'strokes' in South India was reported as 56.9/100,000. Such data would suggest a low incidence compared to the prevalence of 150 to 186/100,000 for the U.S.A. and Europe. Here, it is noteworthy that the age distribution pattern of Indians, with a life expectancy of only 52 years and where 50% are under the age of 20, is markedly different and not comparable to European populations. Therefore, the high incidence (25%) of 'strokes in the young' may be related to age sample bias. With longevity rising to the peak years at which strokes occur, the incidence of 'strokes' in Indians will rise and pose a major health problem. On the relative frequency of cerebrovascular disease (CVD) and other data, the predefined prospective Bombay Stroke Study, where the autopsy confirmation rate was high (86.5%) revealed the following:

'Though the Indian patients studied had altogether different social customs, living standards, and dietary habits from Western people, the relative incidence of various cerebral vascular lesions did not differ significantly. Irrespective of the poor

nutritional status of the patients, thrombosis with atherosclerosis was chiefly responsible for a non-embolic cerebral infarction. Atherothrombosis in the young normotensive persons not showing any evidence of arteritis, diabetes mellitus or hypercholesterolemia was also identified. As to prognosis, the nutritional status, the type and territory of an ictal lesion, and the blood levels of sugar and cholesterol had no significant influence on the immediate survival after a non-embolic cerebral infarction. However, a significantly greater number of deaths were encountered in the hypertensive patients. Female patients and patients with large cerebral infarction had poor prognosis."

Cerebral embolism from cardiac source ranks high in the young, whereas inflammatory CVD (giant cell 'aorto-arteritis', tuberculous, syphilitic etc.) and thrombotic venous CVD constitute only a small percentage of the entire 'stroke' material for any large general hospital. Furthermore, a recent WHO defined Community Survey on Casual Hypertension (160/95 mmHg) in Bombay has now shown that its prevalence in the rich and in the poor groups is not significantly different. Similarly, an International Collaborative Cerebral Athero Study on routine and accidental deaths showed that the 'atherosclerosis index' was nearly the same as was seen in U.S.A. and Japan; it increased with advancing age and in the presence of hypertension. Thus, a hypertension-stroke control programme will prove far more rewarding for India.

S11. Trends in cerebrovascular diseases and changes of dietary habits in Japan

M. IIDA, Y. KOMACHI, T. SHIMAMOTO, M. DOI, H. ISO and K. YASUI, *Institute of Community Medicine, University of Tsukuba, Ibaraki, Japan*

Stroke has been the most prevalent cerebrovascular disease in Japan, though, since 1971, its death rate has decreased. The primary risk factor of stroke is hypertension; hypercholesterolemia is the negative risk factor of cerebral hemorrhage. Farmers in Japan tend to take much salt (20-30 g/day) and less animal fat (10-20 g/day) and they are involved in hard manual work. These dietary habits and their work leads to the development of hypertension without obesity and keeps their serum cholesterol level low (140-160 mg/dl). As a result, a great number of cerebral hemorrhages occur among the middle-aged. It should be emphasized that the pathological finding of cerebral hemorrhage among the middle-aged is not atherosclerosis but angionecrosis in small brain arteries. However, cerebral hemorrhage has decreased because of recent changes in dietary habits (decrease in salt intake and increase in fat intake), the lessening of manual work with farming mechanization, and the treatment of hypertension. There have been several successful community intervention trials which markedly reduced the incidence of stroke by modifications in dietary habits and the treatment of hypertension. The government has taken steps to generalize these trials by means of the new act concerning the medical and health service for cardiovascular diseases. On the other hand, the Westernization of dietary habits and the increase of obesity threaten to increase CHD (coronary heart disease) in urbanized populations. No community survey, however,

has revealed the increase in CHD incidence. Finally, the result of the recent national cardiovascular survey will be shown.

S12. A clinical study of cerebrovascular accident

M.H. KIM, M. YANG and J.S. SONG, *Ham-Yang Medical School, Seoul, South Korea*

Four hundred and fifty cerebrovascular accident patients who underwent computerized tomographic (CT) scanning during the 45 months January 1978 to October 1981 were studied and the following results were obtained.

1. In Korea, intracerebral hematoma (48.2%) is commoner than cerebral infarction (26.7%).
2. Of intracerebral hemorrhages, 87.3% were confirmed while 61.5% of cerebral infarctions were identified by brain CT.
3. Cerebrovascular accidents are most common in the sixth decade (40.5%) and the male is more often affected.
4. Hypertension is the most common underlying disease: in 72.3% of cerebral hemorrhages, 52.4% of cerebral infarctions.
5. Hematoma occurs most frequently in the basal ganglia (40.6%) and cerebral infarction occurs most frequently in the global area (48.4%).
6. Changes of consciousness level were observed in 54.2% of cases of mild degree hematoma and 88.2% of cases of severe degree hematoma.
7. In 26.2% of cerebral hematomas, initial CSF findings were normal in spite of the evidence of cerebral hematoma confirmed by CT scanning.

S13. Epidemiology of stroke in Taiwan, R.O.C.

F.L. CHU, Z.A. WU, C. LU, S.J. CHIANG and H.H. HU, *Department of Neurology, Veterans General Hospital, Taipei, R.O.C.*

A household survey on stroke and hypertension with face-to-face interviews was carried out in 1979; 11,177 people in different parts of Taiwan were registered. The annual incidence of stroke was 2.37 per 1,000 and prevalence 9.30 per 1,000. The age-specific incidence and prevalence rose with age, highest in the 65-74 age group. Another study, from the stroke registry in the Yen-Ping precinct of Taipei City (population 50,160), conducted by Dr. W.P. Tseng of the National Taiwan University Hospital in 1975, showed an annual incidence of 3.54 per 1,000 and prevalence of 7.91 per 1,000 (age-adjusted to the population of our study by a direct method). This disclosed a marked decline (33.05%) in stroke incidence in Taiwan over a four-year period. As the methodology of these two studies was different, this comparison is not fair, but does give a general idea.

According to the available national mortality statistics of many other countries, there has been a definite decline in the stroke death rate over the past 2-4 decades. In Taiwan, the same is true for the past 10 years. The annual reports of vital statis-

tics from 1971 to 1980 showed a 17.4% decline in the age-adjusted death rate from stroke, though the crude death rate appears to be increasing (8.1% increase). This may be related to the increased life-span of people in Taiwan.

Data from the collaborative study of stroke in three major teaching hospitals in Taipei city revealed as causes cerebral hemorrhage 37.04%, cerebral infarction 46.99%, SAH 6.41% and unclassified 9.55%. Diagnosis with and without CT, risk factors, and outcome for each type of stroke will be discussed.

S14. The epidemiology of cerebrovascular disease in Thailand

A. VIRIYAVEJAKUL, S. VANNASAENG and N. POUNGVARIN, *Department of Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand*

In Thailand, it is generally agreed that cerebrovascular disease cases are the most common of all neurological disease cases admitted to medium-size/large general hospitals. According to the Thai Government Public Health Statistics, the death rate from cerebrovascular disease ranges from 6.8-8.7 per 100,000 population. No properly designed epidemiological study on stroke prevalence and incidence had ever been carried out in Thailand. However, a number of studies on various known risk factors of stroke, including diabetes mellitus and hypertension, have been published. Thus, it was found that the prevalence of hypertension ranged from 1.36% to 8.86%, depending on the criteria used. Estimating from this figure, the minimum hypertensive population in Thailand would be 400,000. In contrast, the prevalence of diabetes mellitus in Thailand was estimated at 2.5%, placing the number of diabetics in the country approximately in the region of 542,000. It is also known that there is a high association between both hypertension and diabetes mellitus, and cerebrovascular disease. The largest reported series in Thailand found the association between nonembolic cerebral infarction and hypertension and diabetes mellitus to be 48% for hypertension and 28.5% for diabetes mellitus.

A recent epidemiological study on stroke, diabetes and hypertension was carried out by the authors, which covered a medium-size community in Bangkok metropolis of 8,166 people (1,361 families). Of a randomly selected sample population of 1,317, 88% of the subjects responded. Each subject was given a physical examination by the authors, paying particular attention to blood pressure, carotid bruit, and neurological deficits. In addition, fasting venous glocuse and cholesterol were also analyzed. The preliminary results of this study revealed the prevalence of stroke in this community to be approximately 6.9 per 1,000. Using the WHO criteria for hypertension, namely diastolic blood pressure of or over 95 Torr, the prevalence of hypertension in this community would be around 76.86 per 1,000. As for diabetes mellitus, the number of subjects having fasting venous sugar level of or more than 121 mg/100 ml was 42, placing the prevalence of diabetes mellitus in this community at 35.95 per 1,000. Details of other aspects of the study, including the prevalence of carotid bruit, abnormal serum cholesterol, etc. will be presented at the symposium.

Neurotransmitters and neuropeptides

Tuesday, November 15, 1983
9.00, Room A

S15. The organization of neuronal systems in basal ganglia and their involvement in extrapyramidal disease

P. JENNER and C.D. MARSDEN, *Department of Neurology, Institute of Psychiatry and King's College Hospital Medical School, Denmark Hill, London, U.K.*

Altered neuronal function in basal ganglia is thought to be responsible for the occurrence of a variety of hypokinetic (e.g. Parkinson's disease) and hyperkinetic (e.g. dystonia, Huntington's chorea and tardive dyskinesia) movement disorders in man. In many cases alterations in dopamine neuronal function have been implicated although this may not represent the primary pathological change and other neuronal systems may be involved.

Dopamine-containing fibres arising from cell bodies in substantia nigra, zona compacta and the ventral tegmental area give rise to the mesostriatal, mesolimbic and mesocortical dopamine pathways. Within the striatal complex dopaminergic neurones synapse with cholinergic interneurones and with GABA-containing pathways. These latter systems form the major motor output pathways from striatum to the pallidal complex and to substantia nigra. Within substantia nigra GABAergic neurones alter the activity of dopamine cell bodies in zona compacta and GABA neurones arising from zona reticulata form motor outflow pathways to other brain stem areas. Dopamine is released from dendrites in substantia nigra and this too would appear an important controlling mechanism in motor behaviours. The striatum and substantia nigra receive numerous other neuronal inputs including noradrenaline- and 5HT-containing fibres from the locus coeruleus and raphe systems respectively. More recently many peptide-containing systems have been discovered within basal ganglia. In particular, substance P, met-encephalin, neurotensin and cholecystokinin containing pathways may be important in controlling motor events.

Parkinson's disease is characterized by a profound loss of dopamine-containing neurones throughout the brain. Noradrenaline and 5HT levels also are decreased. Alterations in the peptide content of the striatum and substantia nigra recently have been discovered. Huntington's chorea is characterized by a loss of GABA- and acetylcholine-containing neurones in basal ganglia but dopamine-containing neurones are spared. The concentration of substance P and some other peptides are decreased but somatostatin levels are unchanged. The biochemical and pathological changes underlying dystonia and tardive dyskinesia remain unknown. Experimental evidence suggests that in each case over-activity of brain dopamine function may be responsible.