# MCV/Q

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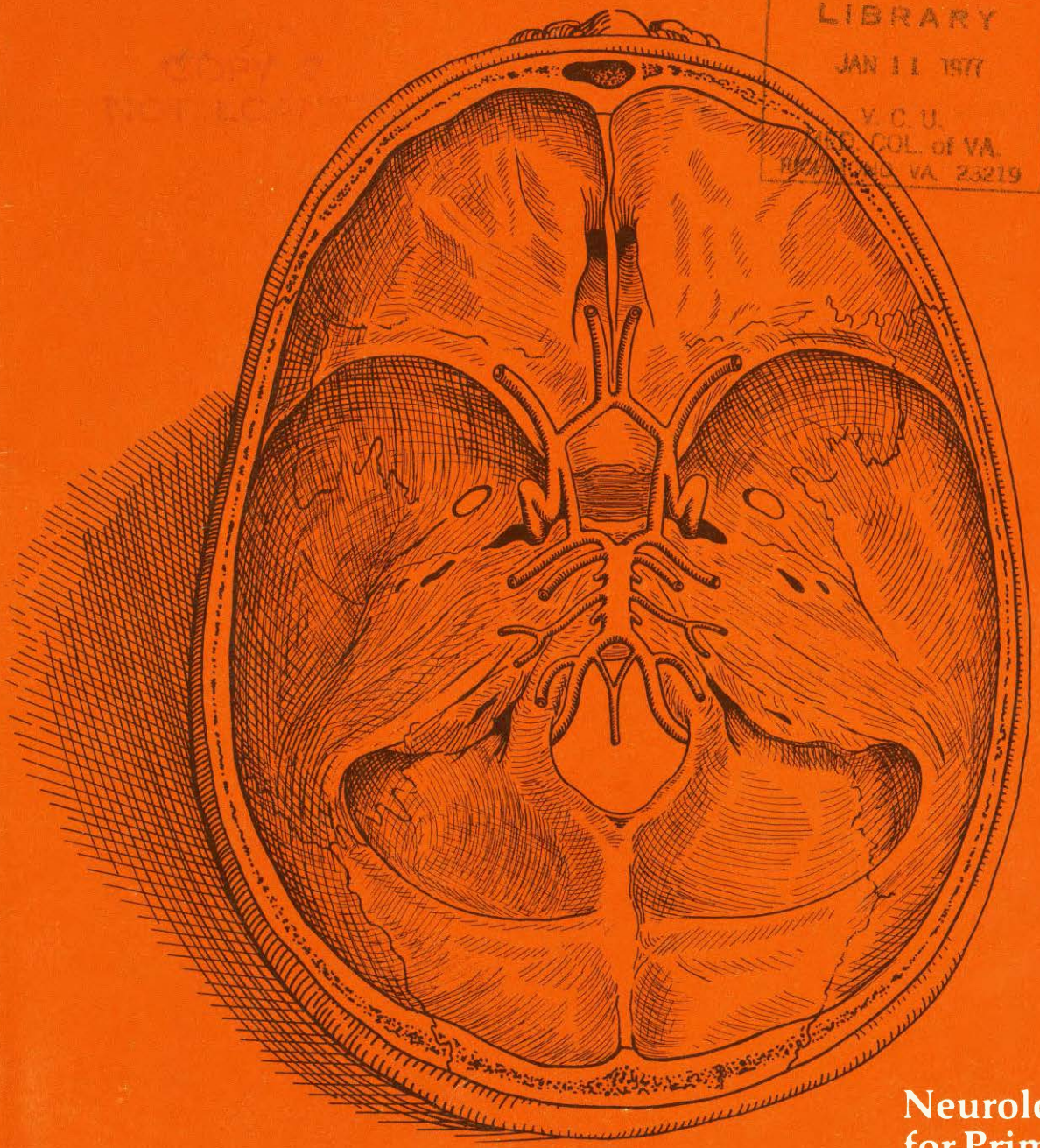

## Neurology for Primary Care Physicians

## PART II

# MCV/Q

MEDICAL COLLEGE OF VIRGINIA QUARTERLY

# A Message to Our Readers:

Two years ago the MCV/Q announced that due to increased production costs, gratis distribution would be limited to alumni, MCV faculty, and students of MCV/VCU. Because of a continuing rise in printing costs and in fairness to our non-alumni readers who have enthusiastically supported us since 1974, we have decided to ask that alumni also pay for their subscriptions. In this way much needed funds will be generated for a journal whose quality and value as a teaching tool are receiving wide recognition.

In 1977, we will change our format slightly to offer a wider range of articles and place a greater emphasis on reports of original research. Our rates are modest and we hope that you will fill out the enclosed subscription form and mail it to us soon.

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*Health Sciences Division of Virginia Commonwealth University*

**1976 • Volume Twelve • Number Four**


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*Neurology for Primary Care Physicians—Part II*

A postgraduate course in Neurology sponsored by the Department of Neurology and the Department of Continuing Education, Medical College of Virginia, Health Sciences Division of Virginia Commonwealth University.

JOHN R. TAYLOR, M.D., *Guest Editor*




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# INTRODUCTION

We conclude our two-part issue on Neurology for Primary Care Physicians with both the new and the old. Attempting to avoid repetition, our authors address themselves to the overlooked, under-emphasized, and sometimes new area of familiar subjects. Our guest speakers, Dr. Millikan and Dr. Horenstein discuss acute cerebral infarction and the perennial problem of dementia. Exciting new fronts are explored by Drs. Isaacs and Sakalas as they expand on their ideas on neuromuscular disease and surgical techniques for extra-intracranial oscular anastamoses, respectively. Dr. Selhorst contributes some interesting views on low back problems.

The 1976 Stoneburner Lecture Series has sought to bring to the primary care physician a potpourri of discussions of clinical problems in neurology—sometimes with solutions, often with only a better understanding. The success of this effort cannot be measured, but we invite your comments and opinions on the matter.

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# Management of the Demented Patient

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There are four essential points to the rational management of the demented patient which will be dealt with here. They are 1) the definition of the term dementia, facilitating the identification of a specific group of patients, 2) the sequence of diagnostic steps required to identify manageable and treatable features in demented patients, 3) the effective separation of dementia from depression, which is probably the most significant diagnostic point for primary care physicians, and 4) the description of a few clinical features encountered in demented patients which the physician can often modify by family education and training, by the manipulation of the patient's environment, and by medication needed to maintain the patient's general health.

Dementia is defined as a sustained decline in intellectual, behavioral, and cognitive function from a previously attained level, whatever the cause, and does not necessarily indicate an irreversible or untreatable state. Most demented patients retain large areas of neurological function and many may remain at home for the major part of their illness. As a symptom complex, dementia is a very important health problem and some estimates indicate that nearly one quarter of hospital patients in the United States are so afflicted. In the year 2025, an estimated 40% of the population of the United States will be over 65 with a comparable increase in the number of individuals defined as demented.

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This is an edited transcript of a lecture given by Dr. Horenstein at the 29th Annual Stoneburner Lecture Series, 25 March, 1976, at the Medical College of Virginia, Richmond, Virginia.

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Dementia should be differentiated from confusion, which is usually thought of as impaired ability to adapt to rapidly changing environmental stimuli, owing to a disorder of attentive mechanisms, but with little disturbance of intellect. Although demented patients may sometimes become confused, confusion per se may exist in the absence of dementia. The combined states may result in an apparent though reversible intensification of the preexisting dementia which is often called "decompensation." This may rapidly reverse itself as the cause of the superimposed confusion disappears.

When the ambulatory demented patient is brought to the primary care physician, the family is more apt to complain of the patient's behavior than his or her intellectual performance or capability. Few patients suffering dementia consult physicians on their own and many are unaware of their deficiencies. Ordinarily there are three conditions which may exist alone or in combination which disturb the families, causing them to consult the physician: 1) Progressive weight loss, most often in the individual who is trying to live alone, which usually means that he or she is not eating enough, 2) Mood disorder, often characterized by volatility which may express in a distorted way elements of the patient's prior personality, and 3) Abnormal neurological states such as defective memory, inability to dress, difficulty in maintaining personal cleanliness, and a disorder of gait which may be interpreted as Parkinsonism. Often these states appear to have been precipitated by fever, dehydration, or the inappropriate use of psychoactive drugs.

Other neurological behavioral abnormalities which the patient may exhibit include disturbance of learning, diminution of cognitive ability regarding his

or her surroundings, spatial disorientation owing to loss of capacity to discriminate the form, shape, and dimension of objects seen in context, perceptual dysfunction relating to the abstract meaning of events, words, or things, and impaired calculation, usually manifested early by simple arithmetical errors. There may also be a subtle degradation in the patient's use of language from a former expresssiveness to a progressively elementary and repetitive mode. Usually, language tends to disintegrate as the patient's condition worsens, and he or she may have difficulty remembering individual words, formulating intelligible complex sentences, and repeating ideas and words. Disorientation of time and space occurs early, with time being by far the most easily disrupted sense and thus the one more obviously disturbed.

Emotional control often becomes impaired early and is usually manifested by inappropriate expression of feelings; such individuals become increasingly unable to regulate their anger or rage or to interpret expressions of love and affection. Thus many of the older men who have fondled their granddaughters' breasts or exposed themselves to their nieces are in fact demented persons, who having been kissed as an act of filial devotion, have misinterpreted both meaning and intent. At the same time, ineffectively regulated defense reactions result in their excessive expression due in part once again to the patient's misinterpretation of the situation and his corresponding intolerance of frustration. This is frequently seen in the writings of a mildly demented and often elderly patient who has written over his errors, or crumpled, torn, or scratched through the page when simple erasure would have been adequate.

Difficulty in walking is among the most common motor manifestations which occur in demented patients. Many of these individuals suffer hip injuries from an inability to break a fall backwards when rising from a chair or the toilet. These gait disorders are characterized by walking on a narrow base, marked instability on starting or stopping, and the tendency to fall backwards upon rising from a sitting position. These disorders result in part from a marked tendency of the foot and toes to flex plantarward and inward on contact with a flat surface, followed by stiffening of the leg. Disturbances of tone can usually be seen upon passive manipulation of the patient's limbs, especially the legs, so that resistance to manipulation is felt and seems equal in force, and opposite in direction, to the movement which the examiner is attempting to impose. This may be followed by the patient's adopting the rhythm of the examiner's movement and resisting further change in its amplitude or rate. Heedless urinary incontinence often accompanies these gait disorders. Clumsiness (or apraxia), even for tasks as apparently simple as opening a can, dialing a telephone, or using a pair of scissors, may occur in these patients.

Compulsive acts such as touching, licking, or tasting objects, and a variety of automatic movements such as tapping, patting, grasping, or avoiding are common. Less often, patients develop a distal wrist and finger tremor at rest or on action, but this usually differs from Parkinsonian tremor which is maximal at rest; some tremors, however, very closely resemble those of Parkinsonism. Oculomotor manifestations, basically a disturbance of horizontal eye movements, alter facial expression as fixation becomes tonically maintained at the expense of gaze. The resulting staring expression is often followed by loss of ability to dissociate head from eye movements.

As indicated above, demented patients invariably develop some type of language disturbance. Since it evolves slowly and is rarely global in ambulatory patients, it may escape recognition. Two basic tendencies are common: one is relative mutism, the other is a disorder of syntax in which incorrect sentences are formed, accompanied by degrees of difficulty in choosing the correct word. In addition to, and often concomitant with, the disorder of language, there may be automatisms of chewing, sucking, or lip smacking which are provoked by perioral skin contact or movements in the visual periphery. These resemble the rooting and sucking responses which are seen normally in the nursing infant. While these are customary and adaptive in the first year of life, they should never be seen after weaning except in the presence of brain disorders usually involving the frontal or temporal lobes. Their appearance in the adult is invariably an indication of severe disintegration of forebrain function.

The facial expression becomes altered in nearly all demented individuals. This reflects in part the abnormalities of ocular movement mentioned above, accompanied by postures which maintain dystonically released fragments of sucking and rooting. Beyond that, however, two variations in facial expression are commonly encountered. The first is the bewildered appearance of the patient who fails to comprehend. The facial expression, while mobile, does not reflect the circumstance which evoked it and is thus recognized as abnormal. The other is perhaps

more common and is characterized by immobility of the face and eyes. Usually, marked tonic fixation of gaze accompanies ocular immobility, and change in fixation requires movement of the head. The palpebral fissures are widened due in part to persistent contraction of the frontalis muscles, resulting in a furrowed forehead. At the same time, overaction of the levator anguli oris deepens the nasolabial fold, while the mouth usually remains tonically agape. This attitude is characteristic of lesions about the lateral frontal regions or the white matter carrying motor fibers from them. Such facial dystonia is common in multi-infarct dementia which occurs in hypertension and following arterial border zone infarcts resulting from ischemic anoxia.

The grasp reflex, like the sucking response, is an automatism evoked by skin contact. Since they both bring the body part into closer contact with the stimulus, they are regarded as "positive" automatisms. In elicitation of the grasp reflex, the tendons must not be stretched, otherwise an entirely different kind of response will result. Usually, when the examiner's fingers are drawn lightly across the patient's palm the patient will grasp the fingers within a few moments. If the examiner then tries to pull his fingers away, the patient's grasp becomes even tighter in a response known as the trap reaction. Further, if the examiner moves his own hand after grasping has occurred, the patient's hand follows this movement as though attracted irresistibly; the so-called magnet reaction. Perioral and upper limb automatisms are very important features of the physical examination of the demented patient. Like abnormalities of gait, they help predict degrees of functional loss of skilled movements (limb-kinetic apraxia) which are common in such patients.

Demented individuals invariably lose reading and writing skills in a hierarchical fashion. The patient who has lost the ability to read sentences can often read words. When no longer capable of reading words, he or she can usually form letters. Alternatively, the patient who has lost the capacity to perform skilled movements usually becomes unable to form letters or numbers. Such individuals may write repetitiously, often tracing and retracing their own figures in whole or in part. When asked to copy simple geometric designs, the patient renders drawings that are often distorted in terms of space and form. Errors in spatial configuration usually correlate with impaired visual perception; those of form correlate with altered language function.

As the patient's dementia worsens, there is a tendency to develop a posture which in some ways resembles the flexed attitude of Parkinsonism. All four limbs and the spine become bent, with the head held thrust forward. Sometimes when the patient is lying flat the head will be held off the pillow, especially upon visual stimulation from the end of the bed. This appears to be a positive visual automatism as the posture is stimulus bound. It is an abnormal event and rarely seen except in the presence of severe forebrain disease. The degree to which such postures of flexion are present appears to reflect the severity of the underlying disease process. The ultimate manifestation of postural disintegration is an attitude of dystonic flexion at the pelvis and knees, often with severe adduction of the hips. Later similar attitudes affect the upper limbs and neck as the patient lapses into the terminal posture of his illness. As the flexed postures just described are assumed, there is invariably some disturbance of walking known as gait apraxia. In other cases patients stand with their limbs and spine overextended, tending to topple backwards. The response to foot contact in these individuals is exactly the opposite of the tonic foot response and is marked by extension at the toes and ankle and eversion at the latter. This phenomenon of "foot avoiding" underlies the overextension gait disorder as the tonic foot response underlies gait apraxia.

Just as the tonic foot response accompanies palmar grasping and sucking and belongs to the family of positive automatisms, the negative avoiding reaction of the foot accompanies a similar movement of the hand; this is characterized by dorsal flexion of the wrist and extension and abduction of the fingers upon tactile stimulation, especially along the ulnar margin. Head retraction on visual stimulation is the oculocephalic component of this system of negative automatisms, called thus because the response is one of withdrawal from stimulation.

The major diagnostic problems are to separate cases of dementia, regardless of etiology, from those of depression (Table 1), and to differentiate cases of treatable from untreatable dementia. The physician should be interested in making the first distinction because depression is a condition for which there is particular and effective treatment which often results in the rapid restoration of the patient to his customary pattern of living. The reason for making the second distinction is self-evident.

Many clinical features in addition to those previously examined will help separate depression

**TABLE 1**
**Differentiating Depression from Dementia**

| | Depression | Dementia |
|---|---|---|
| Mood | Altered-Sustained | Volatile-Unstable |
| Automatisms | None | Copious-Persistent |
| Perception | Preserved | Impaired |
| Comprehension | Acute | Dull |
| Language | Linguistically intact, reflects the mood | Many semantic and syntactic errors |
| Antidepressant Treatment | Effective | Useless |
| Neurological Signs | None | Many |
| CSF | Normal (except in diabetics) | Often abnormal |
| CT Scan | Normal | Often shows atrophy and large ventricles |
| EEG | Normal | May be abnormal |
| Neuropsychological Tests | Confirm mood depression | Loss of function invariably |
| Extraneurological Disease | Variable | Frequent |

from dementia. Mood is one of the most important; the depressed patient's mood is sustained whether he is agitated or depressed. In demented patients mood disturbances occur, but are usually unstable. Over the course of minutes there may be moments of depression, agitation, or euphoria; affect is usually extremely volatile and shifts rapidly from one phase to another. Moreover, the mood shifts are commonly either excessive in degree or inappropriate in nature. These features may be of importance in identifying dementing disorders caused by such chronic meningoencephalitides as general paresis or cryptococcosis in which patients may appear depressed, but the correct diagnosis is suggested by volatility and instability of mood.

The positive and negative automatisms of sucking, grasping, avoiding, tonic foot responses, the gait and posture disturbances, and the disorders of language so characteristic of dementia are totally absent in depressed patients, but most demented individuals exhibit one or more of these abnormalities.

Gross and readily detected disturbances of perception are ordinarily absent in depressed patients, though many older persons may suffer hearing or visual impairment. Depressed patients not only preserve their perception but frequently are acute and sensitive even to the point of being referential and paranoid in response to even the most trivial environmental event. The demented patient is just the opposite. The depressed patient retains perfect comprehension, although it may be distorted against the background of his mood disorder. Alternatively, the demented patient frequently understands only the most material and concrete things and is often unable to detect meaning or relationships.

The language of the depressed person reflects his mood. His word retrieval and syntax are normal. The demented patient makes many errors in sentence organization and often has marked difficulty retrieving correct words, frequently resorting to inadequate substitutes or clumsy phrases. Such awkwardness in phrasing is called periphrasis.

Patients with dementia do not respond to antidepressant treatment and indeed many of them become worse. Patients with depression generally respond well to one or more forms of antidepressant therapy.

A reasonable work-up for a demented patient, following exclusion of depression, is directed toward discovering treatable disease. Its most important single constituent is the spinal fluid examination. The physician should be attentive to such components of the spinal fluid as its appearance, pressure, protein, sugar and cellular constituents, and the results of an immunological test for syphilis. While syphilis remains relatively uncommon, fungus meningoencephalitis occurs with relative frequency and the diagnosis is most readily established by examination of some aspect of the spinal fluid. Budding yeasts may actually be found, but in many cases it is necessary to examine the fluid for cryptococcal antigen. For practical purposes this disease is the sole cause of mycotic meningoencephalitis in the United States except in southern California and southwestern Arizona where coccidioidomycosis is prevalent. Both of these diseases are treatable and hence whenever there are cells in the spinal fluid with mildly reduced sugar and raised protein in combination, these conditions should be considered. Similar changes in the spinal fluid may indicate some other chronic infection such as tuberculosis, but like this condition, neurosyphilis, has become exceedingly uncommon in the United States. Tumor cell meningeal infiltration with altered cerebral function is a more likely cause of dementia. Cytologic examination of the spinal fluid in tumor cell meningeal infiltration frequently, but not always, leads to a correct diagnosis. Measuring such lysosomal enzymes as $\beta$-glucuronidase and acid phosphatase may, however, disclose the nature of the process. Since these conditions, though relatively uncommon as causes of de-

mentia, are often largely treatable, the effort is worthwhile.

The electroencephalogram is usually normal in conditions such as Alzheimer's disease and senile dementia, but even so it is a very important part of the evaluation of demented patients as it may provide a clue to focal or lateralized disease. Further, the finding of diffuse slow activity in a patient whose dementia is of less than six months' duration usually indicates some treatable condition such as endocrinopathy. In recording the electroencephalogram it is helpful if the patient is free of sedative and tranquilizing medication, fed within four hours of the test, and kept awake throughout the recording period. Anticonvulsant drugs should be continued in those individuals already receiving them.

Skull x-rays are always made. They often disclose little, but the high value of the occasional finding of a displaced pineal gland, an erosive lesion of the skull, or an unsuspected intracranial calcification makes the procedure worthwhile.

At some point an attempt is made to identify the size and shape of the cerebral ventricles. In the past this has been done by means of pneumoencephalography which permits precise definition of the location of the ventricles and determination of the shape of their roof and the size of the subarachnoid air spaces. Flattening of the roof may indicate a wasting of the corpus callosum and hence loss of cortical nerve cells. This condition is ordinarily associated with enlargement of the cerebral sulci caused by attendant cortical nerve cell atrophy. The significance of these findings is widespread neuronal loss. Conversely, the pneumoencephalogram may show obliteration of the sulci and absence of air in the subarachnoid spaces on the brain surface; the ventricular roof may be saddle-shaped rather than flat. These features may help to identify hydrocephalic dementia secondary to obstruction of spinal fluid absorption, a condition which is often treatable. Although pneumoencephalography with modern radiological equipment discloses the ventricular configuration with precision, the test is cumbersome, costly, and usually causes moderate discomfort. It has lately been superseded by computerized axial tomography, a radiographic technique which, while incapable at present of resolution approaching the precision of air encephalography, is highly accurate, rapidly developing, and has the great advantage of comfort, convenience, and lower risk to the patient.

In the event that the ventriculographic studies suggest enlargement, particularly with collapse of the subarachnoid space and a saddle-shaped roof, it is very important to determine the direction in which the spinal fluid flows. This may be achieved by an isotope or radionuclide cisternogram which is performed by injecting a labeled substance, such as iodinated serum albumin, into the lumbar subarachnoid space and then recording the progressive flow of the isotope into the head. Normally the flow is over the surface of the brain toward the pacchionian granulations and the draining venous sinuses. In hydrocephalic dementia of the communicating type these surface channels are blocked for a variety of reasons and the spinal fluid is absorbed across the lining of the ventricle. This condition is detectable because the cisternogram will clearly disclose the presence of the indicator substance in the ventricles. While some amount may normally remain for as long as 48 hours, none should be seen at 72 hours. Thus, if nuclide is present in the ventricle at the end of the third day, it is likely that communicating hydrocephalus is present. If the clinical features include headache, torpor, incontinence, gait apraxia, impaired upward gaze, and dementia of less than six months' duration, ventricular shunting should lead to marked improvement.

Psychological tests are also used in assessing patients. The field of neuropsychological research is rapidly expanding and the implications of modern developments in anatomy, physiology, and psychology are being applied to the study of clinical cases. Neuropsychological testing in the demented patient may help approximate the prior level of the patient's intelligence, expose specific perceptual deficits which have been overlooked, help separate personality and behavioral responses, especially depression, and identify areas of preservation of function which may then be of importance in managing specific features of the illness.

No evaluation of a demented patient is complete without attempting to detect extra-neurological disease which may be causal or complicating. Among the most treatable of the causal diseases are drug intoxication with any of a variety of the substances commonly used independently by patients or in medical practice; the most common are bromides, barbiturates, anticholinergic agents, reserpine-containing compounds, and certain anticonvulsants. Their absolute serum drug levels are not necessarily correlated with their behavioral side effects because blood level does not always parallel the intracellular concentration of the substance, and older or de-

bilitated patients may become intoxicated at lower doses and serum concentrations.

Endocrinopathies, metabolic disorders, chronic hypoxia, or respiratory acidosis are among the medical illnesses which may manifest in part by a sustained decline in intellectual function. Ordinarily, correction of the causal illness is associated with improvement or recovery.

Relief of complicating factors such as malnutrition, dehydration, loss of sight or hearing, and congestive heart failure may also improve the behavior of the demented patient.

In the differentiation of dementia from depression, psychological testing, psychiatric interviewing, and various items of case study listed above often aid in resolving the problem. Occasional patients, however, have received (or administered to themselves) large amounts of medication and it may only be after a period of hospitalization without the use of drugs that the separation can clearly be made. Despite these measures there may still be a situation in which dementia cannot be distinguished from depression; this may indicate the limitations of our capacity to differentiate, but in fact some demented patients remain aware of their intellectual losses and react to them with depression. At present, many neurologists escape the dilemma by choosing antidepressant treatment empirically which may result in marked improvement.

Once the cause has been defined the management of the demented patient should lead either to a cure (as in the case of myxedema) or the arrest of the progress of the disease (as in the case of meningeal tuberculosis), thus permitting adaptation both by the patient and his family. Table 2 lists the treatable causes of dementia, but a few comments about them are worth noting. Neurosyphilis, while far less common than 35 or 40 years ago, still accounts for some treatable dementias. The diagnostic criteria of increased protein, up to 100 lymphocytes per cubic millimeter, and positive serology in the spinal fluid may require some alteration owing to the recent and current widespread use of drugs like penicillin, chloramphenicol, and erythromycin which are effective antiluetic agents. When administered in the treatment of some other illness, they may attenuate but not eliminate the syphilitic infection and thus alter the disease course. Chronic fungal infection, especially cryptococcosis, may also cause a reversible dementia. In contrast to neurosyphilis, however, both spontaneous remissions and post-treatment relapses are known. Cryptococcal meningitis, moreover, is very likely to occur concurrently with other disorders (tuberculosis, lymphoma, collagen disease) in which there has been disorder of immune mechanisms.

**TABLE 2**
**Treatable Causes of Dementia**

| | |
|---|---|
| Infection | Epilepsy |
| Inflammation | Endocrinopathy |
| Compression | Vascular |
| Obstruction | Hepatopathy |
| Intoxication | Pulmonary Disease |
| Metabolic Disorder | Perceptual Impairment |
| Malnutrition | |

Inflammatory conditions such as sarcoid or cellular meningeal infiltration resulting from neoplastic illnesses may be treatable, especially those resulting from lymphoma. These conditions may be identified cytologically or by measurement of spinal fluid lysosomal enzymes. Often they are associated with low spinal fluid sugar.

Compression of the nervous system by extra-axial tumors or fluid collections may give rise to dementia resulting from collapse of surface circulation over a broad area of brain even though there has been no displacement or herniation. Usually this state obtains in the older patient whose smaller brain permits the presence of relatively large compressing masses without edema or displacement of the underlying organ.

Communicating hydrocephalus with altered patterns of flow of spinal fluid and its absorption into the brain across the ependymal lining of the ventricle, intoxications, and metabolic disorders have been discussed above.

Malnutrition is currently a rare cause of dementia in the United States except in the alcoholic population. An occasional case of pellagra or $B_{12}$ deficiency with confusional dementia still occurs, but Korsakoff's disease is common in alcoholic patients who are thiamine deficient. In pellagra there is often a characteristic skin lesion and usually a history of alcoholism. In Korsakoff's disease there is ordinarily atactic paraparesis with extensive loss of position and vibration senses and typical hematologic findings including multilobulated polymorphonuclear cells. It is always worthwhile to treat these conditions vigorously as all of them, including Korsakoff's disease, are capable of substantial improvement.

While untreated frequent partial complex sei-

zures are rarely encountered as causes of dementia, drug treatment of epileptic disorders may cause significant impairment of visuomotor control, perceptual processes, and cognition. It is not always necessary that the patient develop ataxia, nystagmus, neuropathy, or other signs of intoxication to be demented, and blood levels may be "normal" according to published standards. This is more likely to occur in patients whose epilepsy is secondary to or associated with widespread brain disease and who are receiving barbiturates, carbamazepine, or succinic acid derivatives.

Among the endocrinopathies likely to cause dementia, thyroid deficiency or myxedema is by far the most common, especially in patients who have previously undergone thyroidectomy and are on replacement therapy which for some reason has been abandoned and forgotten. These persons will often have an old faded necklace scar which along with other features of myxedema may then be the clue both to diagnosis and cure. Failure of myxedema-related dementia to resolve with replacement therapy should raise the question of an alternative or additional diagnosis. Other endocrinopathies including both hypo- and hyperparathyroidism with abnormalities of calcium and phosporus, and hypo- and hyperadrenal states with abnormalities of mineral metabolism, may display profound but reversible dementia.

Vascular factors in dementia sometimes offer possibilities of relief. Obviously there is an opportunity for prevention by the early detection and sustained treatment of hypertension. However, in the face of established vascular disease, especially stenosis or occlusion of one or more of the extracranial cerebral vessels (carotid, vertebral), excessively vigorous treatment of hypertension may result in lowering the intracranial perfusion pressure below that needed for effective neuronal metabolism.

The important point here would seem to be that a major cause of dementia in the present era is the cerebral deficit which results from the accumulation of many small infarcts, no one of which is adequate to give rise to a clear local sign but which together produce a marked loss of intellectual function. This is a challenge to the contemporary physician and represents one area where the immediate application of knowledge (normalizing blood pressure in the early asymptomatic phase of hypertension) and effective modification of patient attitudes (compliance with treatment) offer the greatest hope for the future.

Chronic hepatic insufficiency may cause a mental disorder associated with choreoathetosis of the face and limbs. This condition is often manageable by restricting the amount of dietary nitrogen.

**TABLE 3**
**Specific Problems in Dementia for Which Management is Possible**

| |
|---|
| Decompensation |
| Apraxia |
| Gait |
| Limb-Kinetic |
| Language |
| Perception |
| Memory |
| Appetite |
| Seizures |
| Orientation |
| Emotional Control |
| Anxiety |
| Agitation |
| Sense Organ Deficit |
| General Medical Disease |

That chronic pulmonary disorders, especially hypercarbia, may cause dementia is relatively well known. It need only be pointed out that the pulmonary disease is usually gross and has been present for a long time prior to the development of neurological symptoms. In hypercarbia, furthermore, there are usually headache, raised intracranial pressure, respiratory acidosis, plethora, and bradypnea. Papilledema, while unusual, is not unknown.

Perceptual impairments resulting from hearing or visual loss may result in behavioral alterations in the elderly which resemble some features of dementia, but usually the patient calls attention to his losses, and otologic or ophthalmologic treatment may be restorative.

A variety of reversible brain disorders may produce dementia which will resolve over the course of time. Among these are head injury, hypoxia, sustained hypoglycemia, demyelination, and subarachnoid hemorrhages. Head injuries and subarachnoid hemorrhages may, however, cause communicating hydrocephalus with dementia.

Even in those instances in which the cause for the dementia is untreatable, there are frequently manageable elements (Table 3). Among the most important of these is behavioral decompensation (Table 4). This term refers to an abrupt reversible change in the behavior of the patient usually resulting from fever, dehydration, infection, intoxication, or perceptual impairment. Moreover, decompensation need not be

**TABLE 4**
**Reversible Behavioral Decompensation in Dementia**

| |
|---|
| Delirium, Disorientation, Hallucinosis, Stupor, Mutism Following: |
| Drugs |
| Toxins |
| Infections |
| Dehydration |
| Metabolic Disorders |
| Perceptual Isolation |
| Psychological Demands |
| Trauma |
| Compression of Brain |
| Hypoxia |
| Stress of Adaptation |

a sustained phenomenon. Thus, the mildly demented, presbyacusic or visually impaired older person may waken during the night unable to find the light switch, uncertain as to its location, and unable to understand why the sun is not shining. He may wander about or out of the house as he seeks orientation. The simple act of leaving a night light in his room or a radio playing softly may help avert such predicaments.

Gait apraxia has already been defined. It is one of the more difficult aspects of dementia to manage. By causing falls it is responsible for fractures, subdural hematomas, and painful injuries. Such injuries can usually be averted by equipping the patient's living quarters with handrails, bars in the bathroom and near the commode, by the removal of scatter rugs, and by refraining from waxing floors. If a walking frame is prescribed, it should be reversed so that the patient will not walk into it and tumble. Of equal importance in the management of such patients is the education of the family or nursing personnel as to the meaning of the gait disorder and the techniques for guiding the patient's walking, climbing stairs, or entering or leaving vehicles.

Limb-kinetic apraxia is an important deficit, as those who suffer from it become incompetent in the use of tools and implements. Thus, shaving, using a toothbrush, opening a can, and handling table utensils may be difficult or impossible. An electric razor or toothbrush may sometimes be substituted, but the patient often requires supervision. Food must often be cut so that it can be picked up easily on a spoon, or finger foods such as sandwiches substituted.

Semantic aphasic features may emerge with disordered language function, especially sentence formation and choosing words. Related words such as father, son, brother, husband, nephew, uncle as male relatives, may be used interchangeably. This is no more amenable to speech therapy than aphasia of any other cause. Management efforts should be directed toward the family as the nature of the errors and correct context are usually obvious and with correction and encouragement the patient may be able to express the burden of his thoughts.

Disorders of perception of cerebral origin such as loss of the capacity to recognize by sight alone or detect the nature of an object by feeling it, like language losses, are usually not accessible to therapy, but the family can often be taught to compensate by altering its expectations.

Memory loss may be more apparent or relative than absolute. Essential to the operation of memory are four processes; registration of information, its storage, recall to mind, and reproduction in a form nearly identical to that of the memorandum itself. In most demented patients memory processes become distorted. There may be major problems of initiating retrieval of the item or the sequence in which it is recalled. Rarely is memory totally abolished except when there is a problem of registration. Thus, with a knowledge of the context and some prompting, a sympathetic relative or attendant may enable the patient to use his memory with greater efficiency. Tables of memoranda may also be helpful. Since loss of memory and the frustration associated with it are often clearly recognized by the patient, relief of this point of stress often leads to a greater degree of comfort and hence more stable performance.

The compensation for sense organ defects and attention to treating disturbances of general health, especially pulmonary and cardiac conditions, are important control points which have been discussed above.

Most of the elderly demented and many others suffer some disorder of appetite. It is common for patients to be anorectic, and weight loss of considerable degree may occur. This reflects in part the limb-kinetic apraxia noted above making it difficult to cut food and use utensils, but it also reflects the fact that such persons are less likely to eat well when alone or left with the responsibility for preparing their own meals. Eating prepared food in the company of others often results in reversal of weight loss.

Seizures in demented patients may reflect a basic feature of the underlying disease and hence will respond to anticonvulsant drugs. If these agents are used, it is prudent to regulate them by blood level or a

dose determined by body weight as some, such as carbamazepine, may cause stupor in the elderly in "standard" oral doses and others such as phenytoin may cause ataxia. If the demented patient is elderly, the physician should remember that an important cause of seizures may be hypoxia secondary to altered cerebral perfusion, most often owing to cardiac arrhythmia.

In moderately demented patients who are still ambulatory, orientation for time, place, and space may be improved by the use of a technique called reality orientation popularized by James Folsom at the Tuscaloosa Veterans Administration Hospital. It consists of teaching patients about themselves and their environment, stressing one thing at a time at a rate concordant with the patient's capacity to learn. Name, place, date, day of week, room number, the location of the dining room and bathroom, the next holiday, and so forth can all be communicated with reinforcement of retention by placing a blackboard or bulletin board with essential information in the patient's room. Improvement in social behavior has been impressive in many patients.

Agitation, anxiety, and emotional volatility are common in dementing disorders, especially those involving the frontal and temporal lobes. The use of small and carefully controlled doses of diazepam and chlorpromazine may produce not only daytime stability but more natural sleep patterns. The emotional volatility is not usually responsive to reassurance.

# The Management of Acute Cerebral Infarction

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There is no evidence that we are able to reverse cerebral infarction once it gets underway. The day may come when some form of protection for neuronal activity is available to us, but at present there is no such treatment. Prevention is the most important concept; prevention of transient ischemic attack (TIA) or prevention of progression once the process has started. Progressing stroke is that all too common circumstance where focal ischemia is worsening and the process of infarction is beginning or extending. The patient may be seen in the office, emergency room, or in the hospital, and the patient's classification may be changed on successive examinations. There is nothing unusual about such reclassification. For instance, a patient may be admitted to an intensive cardiac care unit with a tentative diagnosis of myocardial infarction; the diagnosis will be changed if the findings change. Thus we look at a patient entering the hospital with a modest neurological defect in the right arm and reexamine the individual some time later. If the defect is worse, we say that the stroke is progressing; if the patient is the same, it appears that the process is completed; if the defect has disappeared, the diagnosis may be TIA.

It is important to differentiate between the carotid and vertebrobasilar systems. The neurological picture in progressing stroke in the carotid system may range from monoparesis to hemiplegia with or without a homonymous defect in vision, a variety of impairments of speech and language, and a range of partial to full sensory abnormalities on the opposite side of the body.

The combination of defects in vertebrobasilar occlusive events is often more complex. The most common defects include abnormalities of motor function; weakness, clumsiness, or paralysis of any combination of the limbs with appropriate pyramidal tract signs combined with unilateral or sometimes bilateral cranial nerve palsies, particularly oculomotor defects or signs of trigeminal or facial nerve involvement. A so-called "crossed" defect (motor or sensory on one side of the face and opposite side of the body) is evidence of a brain stem lesion until proven otherwise. Bilaterality of motor or sensory abnormalities, or both, coupled with cranial nerve palsies indicates brain stem involvement.

The work-up of a patient with acute progressing stroke, whether in the carotid or vertebrobasilar arterial systems must proceed immediately. Particular emphasis is placed on what we now call the neurovascular examination. Certain items have been grouped together under this term. These include:

1. Inspection of vessels
2. Palpation of vessels
3. Auscultation at cervical and cranial sites
4. Ophthalmoscopy (including inspection of the retinae for emboli, cotton-wool patches, vascular occlusions, hemorrhage, and ischemic retinopathy)
5. Ophthalmodynamometry

1. *Inspection of vessels.* Cranial arteritis is an unusual cause of stroke. However, accurate diagnosis is vital to correct treatment, and significant arterial

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change may be detected by viewing the superficial temporal arteries, coupled with palpation.

2. *Palpation* of the cervical cerebral vessels should be done gently. Minor differences in pulse between sides are difficult to interpret and it may be impossible to distinguish a pulse coming from the first portion of the internal carotid artery or from the external carotid artery. Patients suspected of having atherosclerosis of cervical vessels may have ulcerated plaques or early thrombus formation; both are situations where manipulation of the arteries could dislodge emboli.

3. *Auscultation* of the cervical vessels often provides important evidence of the pattern of blood flow. A bell-type stethoscope is most easily applied in the supraclavicular fossa and over the eyes, without using physical pressure which may produce artifactual noise. The bell of the stethoscope is first placed over the aortic valve and then moved (1 cm or less at a time) upwards. This movement of the stethoscope is necessary to distinguish transmitted cardiac sounds from sounds arising in the innominate, subclavian, common carotid, or internal carotid arteries. A neutral position (patient sitting or lying with face straightforward) is less likely to create sounds difficult to interpret than a variety of twisted neck positions. If respiratory (tracheal) sounds obscure auscultation, the patient is requested to "stop" breathing for a few seconds and then instructed to "start" breathing. Bruits should be graded for loudness, the scale being 1 (least) to 6 (loudest); for example 1/6 is barely audible, 6/6 is the loudest. The timing (systolic, diastolic, systolic-diastolic), duration (short, medium, long), and quality (rough, soft, smooth, and so forth) should be described. A bruit of 1/6 loudness is of little significance, while one of 2/6 to 3/6 loudness, long systolic-diastolic duration, and timing of fairly high pitch over the origin of the internal carotid artery means high-grade carotid stenosis until proven otherwise. A soft (1/6 to 2/6) diastolic sound, varying with slight change in neck position, is usually an unimportant venous hum. Soft, sometimes almost continuous, cervical bruits are fairly common in children and ordinarily do not indicate the presence of significant pathology. By carefully recording the description of bruits and correlating this with arteriographical and other findings, the examiner will quickly learn to interpret such sounds correctly.

If the patient's history suggests the presence of a neoplasm or arteriovenous malformation, auscultation over the cranial vault and orbits should be performed. When there is a complaint of a rhythmic head noise, particular attention is directed to auscultation of the site of the sound. It may be necessary to wet the patient's hair to eliminate artifactual noise. Auscultation of the orbit is performed by instructing the patient to close the eyes, placing the bell of the stethoscope over the eye, and having the patient open the eyes to eliminate artifactual muscle sounds. Soft bruits over the cranial vault of children are of little importance. Loud bruits may be caused by angiomas, an arteriovenous shunt, and, rarely, brain neoplasms. A continuous, almost machinery-like murmur or bruit over the orbit is most commonly caused by a carotid cavernous arteriovenous shunt. Noises heard over the orbit have been of little help in establishing the site and severity of lesions of the internal carotid artery.

4. *Ophthalmoscopy* provides an opportunity to inspect small blood vessels directly; these blood vessels are a direct continuation of the internal carotid arterial system. In office and hospital practice relatively little use is made of this simple, safe method of acquiring important data concerning the cervical-cerebral portion of the circulation. The retina should be inspected for arterial or venous occlusion, emboli (cholesterol, platelet-fibrin, calcific, mixed, foreign body), hemorrhages, cotton-wool patches, venous stasis, microaneurysms, changes associated with arterial hypertension, papilledema, and ischemic retinopathy.

In the last two decades the importance of detecting a retinal embolus, or emboli, with the ophthalmoscope has been demonstrated. The most common emboli are made up of cholesterol crystals. These appear as shiny orange-yellow plaques often situated at the bifurcation of retinal arterioles. The plaque may appear to be wider than the arteriole; one sees the outer dimension of the column of red blood cells rather than the wall of the arteriole. Pressure on the eye often changes the position of the embolus slightly; the material may appear to glint or change shade, a characteristic sometimes referred to as a heliographic reflection. The blood flow in the arteriole often seems to be unimpeded by these bright orange-yellow plaques. These emboli may move distally and often disappear in a few days. The presence of one or more cholesterol retinal emboli indicates that there is or has been an ulcerated atheromatous carotid (internal) lesion until proven otherwise.

Another important type of embolus in retinal

vessels consists of gray-white material, thought to consist of blood platelets and fibrin. These emboli may be long and seen to move through an arteriole but are commonly stationary; pressing on the eye does not move the embolus, and there is no heliographic reflection. Blood does not appear to flow past these emboli; there may be infarction of the retina. Special studies show that some of these emboli have a high lipid content. In many instances the source of these emboli is an atheromatous lesion at the origin of the internal carotid artery. Particles of calcium form another type of retinal embolus. These are white, generally short, and stationary. Calcium emboli commonly come from heart valve lesions.

Septic emboli, talc, cornstarch, and other less common emboli may also be seen in the retina.

5. *Ophthalmodynamometry* is a procedure for measuring arterial systolic and diastolic pressures in the main retinal branch or branches of the ophthalmic artery. The convex foot-plate of the instrument is applied to the conjunctiva over the insertion of the lateral rectus muscle in a horizontal manner so that the instrument points directly toward the opposite eye. When measurements are being made in the patient's right eye, the instrument is held in the observer's left hand and the ophthalmoscope is held in the right hand. To measure pressure in the left retinal artery, the observer holds the ophthalmodynamometer in the right hand and the ophthalmoscope in the left. When the instrument is in position, the observer must bring the central artery on the disc into focus through the ophthalmoscope. The instrument is then pressed gradually against the eye to raise the intraocular pressure sufficiently to exceed the diastolic level of the blood pressure in the retinal artery. The diastolic pressure is that level which produces the first collapsing pulsation of the artery. At this point, a finger is applied to the brake on the instrument and the reading is taken from the scale. The ophthalmodynamometer is reapplied and several more readings are taken to insure accuracy. The systolic pressure is obtained by increasing the force of application of the instrument still further. The visible arterial pulsation gradually diminishes as the pressure increases and when pulsation ceases, the reading on the instrument is the systolic blood pressure. Ophthalmodynamometry is usually useless unless the arterial pressures are measured in both eyes. It cannot be performed unless the patient is cooperative. It is helpful to instill a mydriatic, but this should not be done if there is glaucoma. The test should not be performed soon after cataract extraction or recent retinal detachment. The clinical significance of the retinal arterial pressure is dependent on comparing the values in the two eyes. A difference of 15% to 20% is almost always a sign of stenosis or occlusion of the internal carotid artery ipsilateral to the lower pressure. The arterial pressures may be equal or normal or both in the presence of unilateral carotid stenosis or occlusion because of the development of a collateral blood supply. Immediately following acute occlusion of an internal carotid artery, the ipsilateral retinal artery pressure drops. Return of the pressure to that of the contralateral eye depends on the speed with which the collateral circulation develops. A marked decrease in retinal arterial pressure (brachial arterial pressure remaining normal) when the patient moves from the supine position to the upright position (ocular orthostatism) is important evidence of carotid occlusive disease.

A number of laboratory tests should be performed. These include common items such as urinalysis, red blood count, white blood count, differential blood count, blood hemoglobin, sedimentation rate, fasting blood sugar, creatinine or urea, prothrombin time, cholesterol, triglycerides, and uric acid. It is important to make a diagnosis of such items as polycythemia; it has been known for decades that there is a high incidence of focal cerebrovascular disease in individuals who have this disorder. One may do a platelet count although it is extraordinarily unusual for thrombocythemia to be a cause of progressing stoke. When cranial arteritis is present, the sedimentation rate will be elevated; this diagnosis should be made quickly because of the risk of permanent impairment of vision. Diabetes is a part of the risk factor profile for stroke and the fasting blood sugar will assist in detecting individuals with this disorder. Renal function should be screened and the prothrombin time determined for baseline value. In acute progressing stroke, cholesterol and triglycerides are probably not of much significance unless they are excessively raised. The uric acid has been determined mainly as an item for study because of the association of hyperuricemia with atherosclerosis; the value is often elevated in patients with stroke.

It is common to do x-rays of the head although the number of instances where a significant abnormality is detected is small. X-rays of the chest are done and an electrocardiogram is performed. The possibility of a hidden myocardial infarction is always present; other evidence of cardiac abnormality

may also be of importance in the long-range management of the disorder.

Cerebrospinal fluid examination should be performed (when choke is absent due to papilledema) when the clinician has a serious problem in establishing the differential diagnosis of the intracranial pathology—bleeding, focal ischemia or inflammatory disease. The common problem for differential diagnosis in this setting is bleeding; only a small amount of fluid needs to be withdrawn to settle this question.

In the usual stroke patient (in a typical TIA, in most instances of progressing stroke, and in amost all cases of completed stroke) the electroencephalogram adds little significant information and is not necessary in the work-up of the patient. Commonly, in vertebrobasilar disease, the electroencephalogram shows no focal abnormality. It has been said that serial electroencephalograms may very well portray accurately the favorable or unfavorable progression of the brain lesion in stroke. However, the clinician can almost always get this information by spending three or four minutes with the patient one or more times a day. In selected instances, an electroencephalogram may reveal multiple focal abnormalities, thus giving potential evidence concerning the presence of multiple metastatic lesions. Particularly in medical centers where computerized axial tomography (EMI scanner, ACTA scanner, DELTA scanner, and others) is available, there is very little need for the electroencephalogram in the diagnosis of stroke patients. Doppler techniques, including the use of a Doppler flowmeter are under research and may be developed for clinical use. The static isotope brain scan has become an established procedure for the detection of intracranial neoplasms. However, where computerized axial tomography is available, there is now very little need for the static brain scan in the differential diagnosis of focal brain lesions. Likewise, dynamic rapid serial scintigraphy using a gamma camera, which gives a serial display to the images, provides much less precise information of clinical significance than computerized axial tomography or arteriography.

Indications for angiography are:

1. Differential diagnosis of the brain pathology (much less often used in institutions where computerized axial tomography is available).

2. Transient focal ischemic attacks—particularly the carotid system. In such instances, cervical-cerebral angiography should be performed if there is one, or more than one, of: amaurosis fugax, bruit over the beginning of the internal carotid artery, retinal emboli, unilateral decrease in retinal artery pressure, or ischemic retinopathy.

3. Selected instances of vertebrobasilar TIAs. In some instances, it may be difficult to make a clinical distinction between the carotid and the vertebrobasilar system. If the TIAs are characteristic of those coming from the vertebrobasilar system, there is little reason to do extensive angiography.

4. Very early progressing stroke or very frequent TIAs in the carotid system with, as part of the history, amaurosis, an appropriate bruit, retinal emboli, and so forth.

5. Many patients with subarachnoid hemorrhage and some patients with intracerebral hemorrhage.

6. A long systolic or systolic-diastolic carotid bruit, particularly with retinal emboli.

This completes the work-up of the patient.

As the patient with acute progressing stoke is worked up, the physician is interested in prognosis. Little has been written about this, if one starts with patients early in the course of their illness. It is important to understand that mortality statistics will vary, depending upon the type of hospital, nature of the population being hospitalized, availability of intensive care units, and other factors. Recently Jones and Millikan[1] studied the records of 179 consecutive patients with acute carotid system cerebral infarction to describe the clinical events during the first week of the illness. Only those patients admitted to the Cerebrovascular Hospital Service within 36 hours of the onset of the first symptom were included. The neurological status of 39% was stable (unchanged) at the end of seven days; 35% of the patients gradually improved. Nineteen percent had a progressing neurological deficit which stabilized within 48 hours of the onset. Six patients (3%) had a remitting-relapsing course during the first 36 hours and eight patients (4%) had a significant late worsening after 48 hours of stable or improving course. The mortality was 11% for the entire group. However, a "high risk of death" group was identified; the mortality was 41% for those patients who had any degree of decreased level of consciousness and hemiplegia at the time of admission. Of 67 patients having hemiplegia or some similar maximum neurological deficit with normal consciousness when admitted, only one died, a mortality of less than 2%. These percentage values have become a baseline for us to use in our institution in comparing possible new therapy with the results of earlier

treatment. In a hospital where there is a sizable population of patients with acute onset cerebral infarction, it probably would be wise to determine similar percentages; the data could then also be used as a baseline for that particular hospital.

**Therapy.** The primary objective of therapy in occlusive cerebrovascular disease is to maintain a normal or adequate metabolic substrate by maintaining the quality and quantity of blood delivered and removed from brain tissue. This primary goal may need to be attained by treatment of any mechanism which:

1. Interferes with the cardiac capacity to maintain adequate cerebral perfusion,
2. Alters any property of the blood which may maintain adequate neurometabolic substrate (including thrombus formation, anemia, and so forth),
3. Changes in the arterial wall leading to occlusion or thrombus formation (including atherosclerosis, arteritis, and so forth),
4. Affords transient protection of certain aspects of neuron metabolism (hypothermia, steroids, and so forth).

Treatment will be discussed under the following categories: 1) therapy related to the heart, 2) therapy related to alterations of the blood, 3) management of problems concerning the arterial wall, and 4) treatment concerning protection of brain parenchyma.

*1. Heart.* When there is any kind of causal relationship between cerebral infarction and a change in cardiac rhythm the cardiac dysrhythmia should be corrected. If there is impaired cardiac output, whether due to primary cardiac failure or to hypertension from some systemic abnormality, the cardiac output should be returned to normal. There is uncertainty about the percentage of occlusive disease strokes caused by embolism (mainly from the heart); it may well be higher than previously suspected. Cerebral embolism may occur at various times after myocardial infarction with mural thrombosis, but it most commonly comes within the first six weeks after the infarction. Anticoagulant therapy has been recommended. The principal reason for using an anticoagulant is to prevent the release of further emboli to the brain and other sites. The use of an anticoagulant continues to be a common recommendation in instances where prosthetic cardiac valves have been implanted. When the cause of cerebral infarction is related to subacute bacterial endocarditis, it continues to appear to be unwise to use anticoagulants.

Rather rarely, progressing stroke is a portion of the substructure of hypertensive encephalopathy. The use of the term "hypertensive encephalopathy" is specifically reserved for a syndrome in which there is a stereotyped sequence of events of serious import and dramatic development; in such instances, treatment consists of immediate control of the hypertension. In the usual progressing cerebral infarction, hypertension should be treated cautiously—the blood pressure not being decreased precipitously. If an anticoagulant is being used, the blood pressure should be brought under control, but this need not be done as emergency therapy.

*2. Blood constituents.* There are very few reports in the literature in which the term "progressing stroke" is used in relatively uniform fashion and comparison made between a group of patients treated with anticoagulant and a group not receiving such medication. The extraordinary variability in the natural history of acute progressing stroke makes it important that comparison be made of treated and untreated patients of similar type. Over two decades ago, I reported on the natural history of 204 consecutive patients with acute onset of progressing stroke in the carotid system. Fourteen days after the onset, 12% of the patients were normal, 5% (using motor phenomena as a basis for comparisons) had varying degrees of monoparesis, 69% had varying degrees of hemiparesis, and 14% were dead.

The Table summarizes those studies reported in the literature which are relatively comparable. A primary determination was made of the status of the patient at the time of the patient's admission to the study; progression of the neurological deficit had occurred in the preceding few minutes. There was frequent reevaluation of the neurological deficit, and subsequently comparison was made between the maximal deficit developed and the deficit present on entering the study. The percentage of patients showing progression of neurological deficit (after primary assessment) in the control and treated groups of each report is in the right-hand column of the Table. In every instance, the treated group fared better than those not receiving an anticoagulant; thus, in one study,[2] 20% of those treated showed evidence of neurological progression after entry into the study, whereas 52% of patients not receiving an anticoagulant showed progression after initial evaluation. Thus, in a few carefully performed investigations using an anticoagulant for acute progressing stroke, the evidence points to fewer patients having progression when receiving an anticoagulant contrasted to the

TABLE

| Study | Number of Patients | Follow-up (Mos.) | Cerebral Infarcts (Lethal) | Cerebral Hemorrhage (Lethal) | Progressive Infarcts | Total Percentage Progressive |
|---|---|---|---|---|---|---|
| Millikan[2] | | | | | | |
| Control | 60 | 12 | 25 (40%) | 0 | 8 (13%) | 52% |
| Treated | 181 | 12 | 12 (7%) | 0 | 25 (14%) | 20% |
| Carter[3] | | | | | | |
| Control | 38 | 6 | 7 (17%) | 0 | 12 (33%) | 50% |
| Treated | 38 | 6 | 3 (7%) | 0 | 9 (24%) | 32% |
| Cooperative Study[4] | | | | | | |
| Control | 67 | 15 | 10 (15%) | 0 | 21 (31%) | 46% |
| Treated | 61 | 12 | 5 (8%) | 1 (2%) | 8 (13%) | 23% |
| Fisher[5] | | | | | | |
| Control | 14 | ? | 0 | 0 | 9 | 64% |
| Treated | 14 | ? | 0 | 0 | 3 | 21% |
| Fisher (National Study)[6] | | | | | | |
| Control | 49 | 7.4 | 7 | | 14 (29%) | 20 (40%) |
| Treated | 51 | 5.7 | 4 | 1 | 7 (14%) | 7 (14%) |

number having progression and not getting such drugs.

If one considers the use of platelet antiagglutinating agents, there are no current data concerning the effectiveness of such drugs as dipyridamole, aspirin, or sulfinpyrazone in the treatment of acute progressing stroke. Gilroy et al[7] reported the treatment of acute stroke with low molecular weight dextran and were optimistic about the effect of the medication. Apparently, however, no widespread enthusiasm for this method of treatment has developed.

The notion that a fibrinolytic (thrombolytic) agent could lyse a clot obstructing arterial flow to the brain has always been an attractive one. Fletcher et al[8] have recently reported a study of the use of the thrombolytic agent, urokinase, in doses sufficient to produce a twenty- to fortyfold increase of plasma thrombolytic activity. However, hemorrhagic complications occurred in several patients and distinctly favorable therapeutic results were not observed.

No comparative studies have been done to guide treatment of polycythemia, anemia, and hypoglycemia in acute progressing stroke. It is presumed that as soon as feasible these phenomena should be corrected and normal values attained. In a usual acute progressing stroke, hyperlipidemia does not receive special therapeutic attention during the first days of hospital admission.

If hyponatremia, hypernatruria, and increased urine osmolality are present [evidence of inappropriate antidiurectic hormone (ADH) secretion], fluid intake should be restricted to approximately 1000 cc/day until the abnormality has disappeared.

*3. Arterial wall.* The idea of improving the status of a progressing cerebral infarct by some treatment causing vasodilatation took a practical form in 1938 when Mackey and Scott[9] described the treatment of apoplexy by infiltration of the stellate ganglion with novocaine and reported that marked benefit was produced. A variety of techniques for causing vasodilatation have been invoked including the inhalation of 5% carbon dioxide, and the administration of papaverine, isoxsuprine and acetazolamide. In summary, no general enthusiasm has developed for this type of treatment of progressing cerebral infarction.

The use of hypocarbia has also been studied by Paulson.[10] No therapeutic benefit was found, so there is no reason to pursue this method of therapy.

When cerebral infarction occurs secondary to arterial obstruction associated with any form of arteritis or meningitis, attention must be paid to treatment of the primary disease causing the lesion of the arterial wall. Panarteritis, lupus erythematosis, cranial arteritis, and so forth, ordinarily receive steroid therapy while meningitis is treated with antibiotic or other agents, depending upon the organism producing the inflammation.

There is a difference of opinion concerning emergency surgery for patients with rapidly changing flow in the cervical portion of the carotid artery. Blaisdell[11] believes that individuals with progressing stroke should probably not have arteriographic evaluation because of the high risk of surgery or the small possi-

bility of a favorable result. The Joint Study of Extracranial Arterial Occlusion[12] reported a mortality of 42% in 50 patients operated upon within two weeks following an acute stroke while the mortality was only 20% for patients in the same category not having surgery. Bruetman et al[13] and Wylie et al[14] have reported intracerebral hemorrhage as a complication of carotid surgery. Apparently, the opening of carotid occlusion, reestablishing a normal head of perfusion pressure into an area of acute softening, may be associated with the production of intracerebral bleeding. In contrast, Millikan[15] has reported a group of carefully selected individuals, in whom emergency anticoagulant therapy and surgery appeared to be beneficial. The indications for emergency treatment are: 1) clinical events such as a cluster of frequent severe carotid TIAs (a persisting mild neurological deficit accumulates as evidence of mild progressing stroke); 2) a recent mild cerebral infarction in the carotid system followed by a cluster of TIAs; 3) onset of a focal neurological deficit during or soon after arteriography; or 4) sometimes immediate postoperative thrombosis after carotid thromboendarterectomy, and physical signs such as a) retinal emboli, b) long systolic or systolic-diastolic bruit of grade 2 or 3 over the carotid bifurcation, or c) ipsilateral decrease in the retinal artery pressure. A changing carotid bruit suggesting a change in the morphology of the carotid lesion probably should be added to this list of physical signs—signs which coupled with the clinical profile suggest that emergency surgery should be instituted.

4. *Protection of brain parenchyma—anti-edema.*

A. *Steroids.* Dyken and White[16] found the incidence of death in patients with acute cerebral infarction to be the same whether they were treated with cortisone (300 mg/day) or a placebo. Rubinstein[17] noted that the immediate mortality may be reduced and the level of consciousness may be improved when large doses of dexamethasone are administered early in the course of massive cerebral infarction, but once the slightest degree of brain stem dysfunction has occurred, the use of steroids appears to be without benefit. Patten et al[18] reported some slight benefit from the use of dexamethasone in acute stroke in a double-blind study, but if cases of cerebral hemorrhage were excluded, the results were unconvincing. Bauer and Tellez[19] found no difference in morbidity or mortality in 54 patients with acute cerebral infarcts divided into steroid-treated and placebo groups. In a recent report, Norris[20] studied 53 patients with acute cerebral infarction using a double-blind method. One group was treated with dexamethasone and the other portion with placebo, and all observations began within 24 hours of onset of the cerebral infarction. Forty-one of the total number of patients survived longer than 28 days; the patients treated with steroid did slightly worse than those in the placebo group at the end of this time. Two of five individuals who died in the placebo group died of cerebral edema; compared with three of seven patients who died in the steroid group. Because of problems with infectious complications, gastrointestinal hemorrhage, and an occasional serious worsening of diabetes mellitus in the steroid group, Norris believed that there was an increasing body of evidence against the use of such medication in the treatment of acute cerebral infarction.

B. *Hyperosmolar therapy.* In certain instances, intravenous administration of hypertonic agents may reduce the fluid content of the brain. Mannitol, in concentrations of 10% to 25%, may be administered intravenously in a dose of 1 gm/kg of body weight. When it is effective, the maximal reduction of intracranial pressure is achieved within 30 to 60 minutes. However, intracranial pressure often returns quickly to normal. At least, from the lack of reports in the literature, this substance is not widely used in the treatment of acute progressing cerebral infarction.

Meyer et al[21] reported treatment of cerebral edema due to acute cerebral infarction with glycerol. The glycerol was given intravenously in doses of 1.2 gm/kg of body weight or, in other instances, orally in doses of 1.5 gm/kg of body weight. The authors believe that glycerol "given within five days of onset of severe, progressing or sustained neurological deficit, is beneficial in patients with acute cerebral infarction." Gilsanz et al[22] compared treatment with 10% glycerol given for six days to 30 patients with acute cerebral infarction to results obtained after treating 31 similar patients with dexamethasone. One patient treated with glycerol died of hemoglobinuria and acute renal failure while six patients treated with dexamethasone died. The authors concluded that improvement was significantly greater in the glycerol group after 8 and 15 days. The results of these observations appear to require further study.

Although hypothermia, anesthesia, hyperbaric oxygenation and normobaric oxygenation might theoretically provide a favorable metabolic substrate for focal areas of brain ischemia, none of these are therapeutically practical for progressing stroke.

When convulsions, either at the time of progressing stroke or subsequently, become a problem, it is prudent to administer an anticonvulsant. The drug most commonly used is diphenylhydantoin, now called phenytoin (Dilantin®).

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# Extracranial-Intracranial Vascular Shunt Procedures

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Cerebrovascular occlusive disease has been and continues to be a leading cause of death and disability throughout the world. In the United States there are about 400,000 new strokes each year.[1] Some 90% of strokes are a result of vascular occlusion of the extracranial circulation.[2] Surgical treatment of occlusive vascular diseases, principally carotid endarterectomy, has become an accepted method of treatment of a large number of patients. However, only about 70% of patients with cerebrovascular disease have surgically accessible lesions in the extracranial circulation. The remaining 30% are a result of intracranial occlusive disease which cannot at present be treated by carotid endarterectomy.

Endarterectomies or embolectomies or both have been attempted intracranially but have carried high morbidity and mortality rates. Middle cerebral artery embolectomy, for example, has been successfully performed technically, but the results have been poor. Presently, bypass procedures seem to carry a smaller mortality and morbidity rate and a better clinical result. Austin has estimated that there are about 12,000 patients with inoperable lesions by conventional vascular techniques who might be candidates for a bypass procedure of an obstructed or stenosed intracranial vessel.[3]

The first intracerebral bypass procedure was performed in 1944 by Henschen.[4] He transplanted a pedicle of temporalis muscle over the surface of the brain. The patient apparently improved, but this bypass procedure did not become popular. In 1967, following the development of the operating microscope and the reduction in size of suture material, a new microvascular bypass procedure was developed by Donaghy and Yasargil.[5,6] Blood was diverted from a scalp vessel, the superficial temporal artery, to a small middle cerebral artery branch on the surface of the brain to provide a blood supply distal to the site of the occluding lesion. This approach offered the possibility of surgical treatment for previously inoperable lesions in order to prevent, delay, or lessen the possibility of infarction.

The extracranial-intracranial anastomosis as described by Donaghy and Yasargil[5,7,8] is performed with minor modifications (Figure). A frontal temporal incision is made to include both branches of the superficial temporal artery. The branches of the artery are meticulously dissected, using the operating microscope. This is often the longest part of the procedure. The brain is exposed over the sylvian fissure through a craniectomy of about 3 to 4 cm in diameter. A cortical artery is selected on the basis of size, absence of penetrating branches, and location. The most commonly used branches have been the opercular, the angular, and the temporal. If the situation suggests that a particular area is at risk, and if a suitable cortical vessel can be identified as serving the area, this vessel is selected. Temporary clips are placed across the selected artery, an elliptical incision is made, and an internal silicone rubber stent is inserted to keep the edges apart. The superficial temporal artery is brought into the field and an end-to-side anastomosis is performed using a 10-0 suture. The stent and temporary clips are removed. Patency

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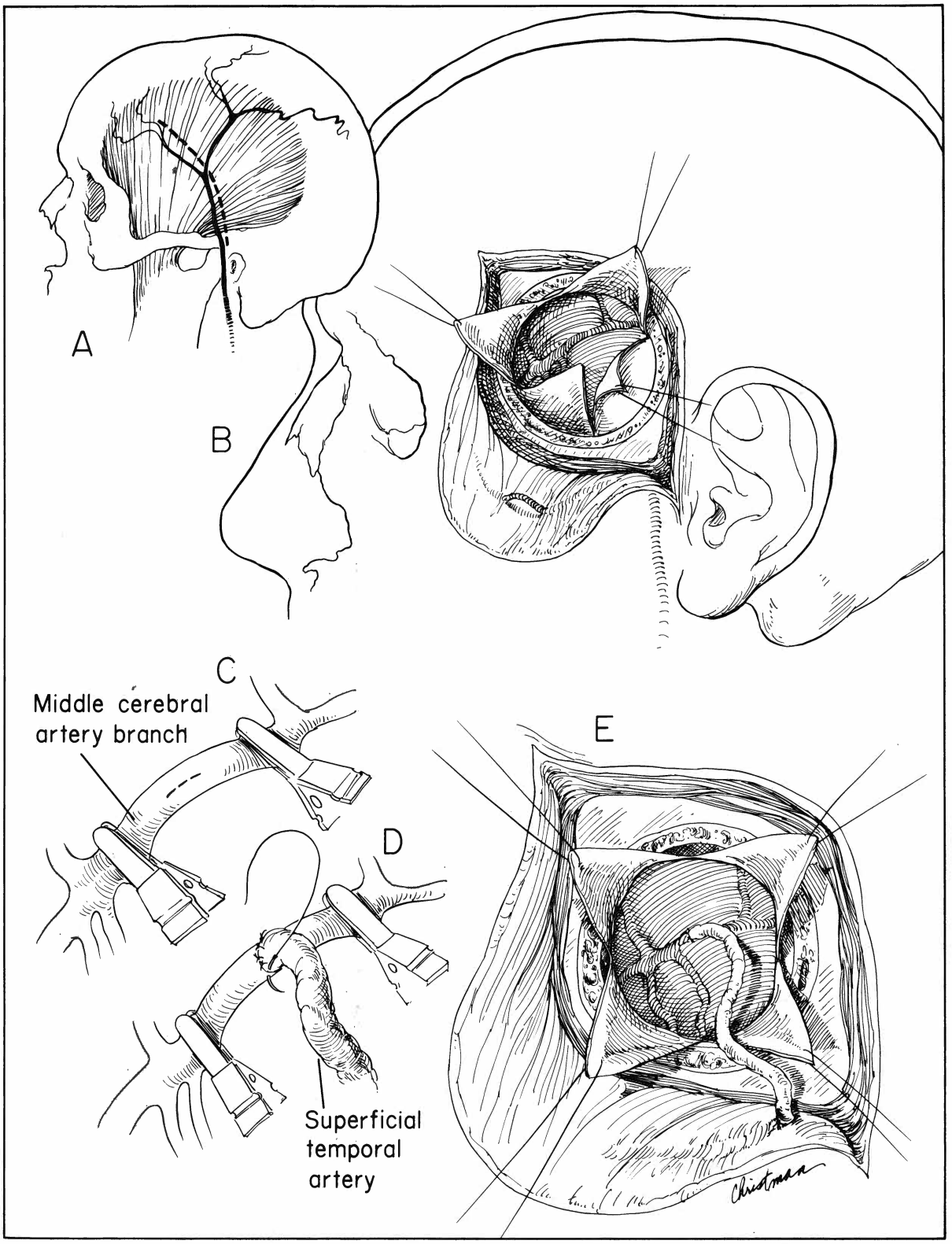


The Superficial Temporal Artery-Middle Cerebral Artery Branch Anastomosis (STA-MCAB). *A*. Placement of skin incision for exposure of STA. *B*. 4 cm craniotomy performed to expose the sylvian vessels. *C*. Isolation of MCAB. *D*. Microsuturing of STA-MCAB. *E*. STA-MCAB anastomosis.

can be observed by the pulsating vessels. Using electromagnetic flow meters, Crowell found that the anastomosis provided 20 to 40 cc/min of blood.[9]

Ideally, a large vessel should be used for establishing a bypass procedure. The superficial temporal artery to middle cerebral artery anastomosis has several disadvantages. The vessel diameters are small; about 1.5 mm ± .5 mm. With this small cross-sectional area, only a limited amount of blood is available (20 to 40 cc/min) which may not be sufficient to provide adequate flow. Middle cerebral artery flow is in the neighbornood of 120 cc/min. Therefore, flow through the anastomosis can account for only about 25% of the total arterial blood flow. It seems unlikely that superficial temporal artery-middle cerebral artery (STA-MCA) bypass flow of this magnitude will be able to sustain an entire human hemisphere, although it could provide functional improvement in cases of focal cerebral ischemia with focal deficits. It is conceivable, however, that with time the anastomosis could provide adequate flow, since flow is proportional to the fourth power of the radius, and increase in graft size with time has been observed. The limited size of the vessels poses a second problem. The chances for occlusion due to thrombus formation at the operative site are increased as the diameter of the vessels decreases. Meticulous surgery, however, can overcome this problem. Reichman has reported a 100% patency rate in 19 patients at the end of four years.[10]

Theoretically, the value of the STA-MCA anastomosis relates to the question of whether the pathogenesis of transient ischemic attack (TIA) and reversible ischemic neurologic deficit (RIND) is related to decreased total brain perfusion from inadequate collateral circulation in the presence of occluded or stenosed vessels, or secondary to emboli associated with ulcerated atheromatous plaques. Certainly there has been adequate documentation of the ulcerative, stenotic plaque at the carotid bifurcation discharging emboli during TIAs, that is, cholesterol emboli visualized in the fundus during an episode of amaurosis fugax. There are also some TIAs which result from transitory depression of cardiac output in patients who already have a significantly depressed cerebral blood flow (CBF) on the basis of a major vascular occlusion, cerebral small vessel disease, or a high stenosis. Evidence of this comes from Sengupta et al, studies in baboons following carotid ligation.[11,12] They showed that the cerebral vasculature cannot respond to stress (anoxia, $CO_2$ reactivity, and changes in BP) in a normal manner after ligation of a carotid artery. This suggests that when the blood flow is borderline, due to a basic lesion, further stress, such as a drop in pressure from decreased cardiac output may not be compensated for by the normal process of autoregulation and thereby provides the setting for the occurrence of TIA or stroke or both. A large group of workers have shown that a 25% to 40% reduction in gray matter blood flow is sufficient to produce the onset of symptoms.[13,14,15,16]

The volume of CBF cannot be accurately predicted on the basis of angiography alone; it must be measured directly. Patients with stenotic lesions often have both ipsilateral and contralateral decreased flow. Reichman studied 16 patients with carotid occlusion, and middle cerebral artery occlusion and stenosis, all of whom had globally reduced CBF.[17] Schmiedek and Gratzl have noted five different flow patterns in patients with severe cerebrovascular disease.[18,19,20] In these patterns regional CBF was:

1. severely reduced throughout (>50% reduction),
2. moderately reduced throughout,
3. generally reduced with an additional focus of relative ischemia,
4. normal in flow with focal areas of ischemia, and
5. generally normal.

Following STA-MCA anastomosis, Austin,[3] Reichman,[17] and Schmiedek[21,22] demonstrated a statistically significant increase in CBF both regionally and globally.

The world-wide clinical experience with STA-MCA bypass procedures has also been extremely encouraging in about 1,000 cases. Combining the overall results from several large reported series, about 85% of those operated upon for TIA or RIND or both were considered improved, while for strokes in progress or completed stroke, about 40% to 80% showed improvement.[3,23,17] There have been no reported deaths due to this procedure, although there has been a 3% to 5% mortality in this group of patients. The most common cause of death has been myocardial infarction. Some 6% of the patients were transiently worse following surgery, but only one case has been reported in which the increased neurologic deficit was permanent. This was probably due to the rupture of an aneurysm which was operated on at the same time. Scalp necrosis has occurred in about 3% of the cases.

The indications for microsurgical cerebral revascularization are quite specific. These procedures are to be considered *only* when conventional disobliterative vascular techniques are inappropriate, inadequate, or contraindicated in patients who are *symptomatic* from angiographically demonstrated lesions. Thus, the following are indications for STA-MCA anastomosis in *symptomatic* patients:

1. Complete long-standing obstruction of the internal carotid artery.
2. Fibromuscular hyperplasia where disease extends into the base of the skull.
3. Severe stenosis of the internal carotid artery at the base of the skull.
4. Lesions of the proximal middle cerebral artery.

Contraindications to the bypass procedures are similar to those for carotid endarterectomy.

1. Completed stroke with hemiplegia or aphasia or both.
2. Severe vascular disease of the external carotid artery.
3. Malignancy or any other process in which prognosis is extremely poor, that is:
   (a) Myocardial infarction within a six-month period of time.
   (b) Severe, unstable ischemia, or valvular heart disease.
   (c) Severe liver, pulmonary, or renal disease.

In summary, superficial temporal artery-middle cerebral artery anastomosis has been successfully performed in over 1,000 patients with a good patency rate and low morbidity. It appears to be successful in alleviating symptoms or improving neurologic function in a significant number of patients who have not responded to medical management and who are unsuitable for routine vascular surgery.

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# Uncommon Disorders of the Lower Spinal Region A Report on Eleven Patients*

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**Introduction.** Prompt diagnosis of lower spinal diseases is essential for successful treatment. Appropriate medical therapy or surgical decompression arrests progression and reverses existing neurologic deficit. Delayed or improper diagnosis seriously jeopardizes the patient's ultimate neurologic status. Too often early symptoms are disregarded or passed over as insignificant.

Diseases of the lower spinal region caused by congenital malformation, trauma, spondylosis, demyelination, and metastasis are readily recognized; however, there are a variety of additional disease processes which affect the lower spine and its contents. These processes are either rapid and devastating or elusive and slowly progressive. A keen sense of awareness on the part of the physician will aid the recognition of these disorders. In this regard eleven patients with uncommon disorders of the lower spinal region are presented. All had delayed or problematic diagnoses and were encountered directly or indirectly during the past seven years. Viewed collectively these infrequently occurring disorders of the lower spine appear with some regularity. This review shows that adherence to tenets of neurologic localization, deduction of pathologic processes, and use of available laboratory tests often lead to the correct diagnosis.

The disease states presented are divided into five categories: metabolic, vascular, tumorous, infectious, and those due to physical agents. Some, but not all, additional disorders within these categories are discussed.

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**Metabolic Disorders.**

*Patient 1.* A 53-year-old steel worker complained of stiffness in his right ankle and knee for three months. He was treated with heat and analgesics for arthritis. His leg became clumsy and his knee "buckled" on several occasions. Then his right foot began to "drag" and became swollen.

Examination showed that he walked slowly with short steps. There was increased tone in both legs. His only weakness was a minimal loss of power in both hamstring muscles. Deep tendon reflexes were all brisk except for the ankle jerks which were absent. Superficial abdominal reflexes were present. Vibratory sense was slightly reduced at the ankles. Position sense was impaired only in the toes. Romberg test was positive. Remaining sensory and neurologic examinations were normal. Atrophic papilla were seen along the lateral border of the tongue. The thyroid gland was mildly enlarged. Patches of vitiligo on his hands, forearms, chest, and face had appeared and gradually progressed over the previous 23 years.

Laboratory data included a hematocrit of 38.6%. Peripheral smear contained macrocytes and multisegmented, large polymorphonuclear cells. Mean corpuscular volume (MCV) was 111, mean corpuscular hemoglobin (MCH) was 35.6, and mean corpuscular hemoglobin concentration (MCHC) was 32. Two grams of valine taken orally caused methylmalonic acid to appear in the urine and indicated a deficiency of vitamin $B_{12}$ acting as a coenzyme for conversion of methylmalonic acid to succinic acid.[1] Aspiration of

sternal bone marrow revealed a megaloblastic erythropoiesis. Gastric analysis showed a 28 cc/hour basal acid secretion rate and an alkaline pH in response to histamine stimulation. Serum vitamin $B_{12}$ assay was 22 micrograms (<85 micrograms/ml occurs in pernicious anemia). Schilling test showed less than 5% excretion of radioactive tagged vitamin $B_{12}$.

The patient was treated daily with 100 $\mu$g vitamin $B_{12}$ intramuscularly. Within one week his gait was normal. All his neurologic signs disappeared except for his hyperactive deep tendon reflexes. In retrospect he acknowledged slow thinking and irritability for the previous 6 months.

**Discussion.** The typical presentation of subacute combined degeneration of the spinal cord or vitamin $B_{12}$ myelopathy is with weakness of the legs and paresthesias of all four limbs.[2] These neurologic findings are consistent with pathologic changes in dorsal and lateral columns. In these zones diffuse, asymmetric, spongy foci of degeneration occur in both axons and myelin sheaths. Impairment of vibratory sense often extends to the trunk while position sense is usually lost in the joints of the toes and feet. Pyramidal signs of weakness and spasticity are initially limited to the legs along with extensor plantar signs. Depressed deep tendon reflexes in the ankle and knee are thought to reflect involvement of peripheral nerves.

This patient presented with a subtle form of asymmetric spasticity. Attention to a slight reduction in the hematocrit prompted discovery of a macrocytic anemia and vitamin $B_{12}$ deficiency. Proper therapy was then initiated. Myelography was avoided, and prompt improvement in the neurologic condition resulted. Since 15% to 25% of patients with vitamin $B_{12}$ deficiency present with neurologic difficulties, subacute combined degeneration of the spinal cord must always be kept in mind for patients with signs and symptoms below the foramen magnum. The 23-year progression of vitiligo is of interest in respect to the autoimmune hypothesis of pernicious anemia.[3] Immunologic destruction of melanocytes is a proposed cause of vitiligo, and presumably a similar mechanism causes atrophy of the intrinsic factor secreting mucosa of the stomach.

There are other metabolic disorders which affect the spinal cord. Folic acid deficiency mimicking the neurologic and hematologic presentation of subacute combined degeneration has been reported.[4] Lateral column degeneration has followed portal-caval shunts or spontaneous portal systemic anastomoses in patients with severe cirrhosis of the liver.[5] In these patients spastic paraplegia is irreversible and accompanied by an encephalopathy. Pathology in this condition shows demyelination of the lateral columns which, unlike subacute combined degeneration, does not affect axons. The metabolic mechanism of the demyelination is not known.

**Vascular Disorders.**

*Patient 2.* A 10-year-old girl entered the Pediatric Clinic with a shuffling gait two months after repair of her aortic coarctation. Surgery went well, but atelectasis complicated the immediate postoperative period. Her chest x-ray cleared after one week and she was discharged. Upon arriving home her mother observed that her daughter walked slowly and was unable to climb stairs. Examination showed mild bilateral weakness in the iliopsoas and quadriceps muscles. Knee jerks and ankle jerks were hyperactive, and plantar responses were bilaterally extensor. There was a mild diminution to pain and temperature sensation in each leg, but position sense and vibratory discrimination were normal.

**Discussion.** The neurologic signs in this patient showed bilateral dysfunction of the pyramidal and spinothalamic tracts which, with normal dorsal column function, is indicative of the anterior spinal artery syndrome.[6] Intramedullary blood supply to spinal cord segments is similar throughout the length of the spinal cord. The radicular artery on the spinal nerve root gives a ventral branch to the single anterior spinal artery and a dorsal branch to paired posterior spinal arteries. A ring of superficially anastomosing vessels connects these two systems and supplies the underlying spinal cord surface. Reduction in blood flow to terminal sulcal and penetrating branches of the anterior spinal artery results in ischemic infarction of the clinically important pyramidal and spinothalamic tracts of the lateral columns. Occlusion of the anterior spinal artery results in infarction of the anterior columns, ventral horn, and central grey matter so that touch insensibility, segmental muscular atrophy, and incontinence of bowel and bladder occur. The dorsal columns and dorsal horns remain functional because of the separate blood supply of the paired and interconnecting posterior spinal arteries.

Current clinical and anatomic evidence indicate that circulation through the anterior spinal artery is

either interrupted or inadequate to allow for blood flow throughout the length of the spinal cord.[7] The nature and variability of radicular arteries further divide the spinal cord into vertical zones of blood supply.[8] Although each nerve trunk has a radicular artery, only seven or eight radicular arteries have sufficient size and flow to contribute to the anterior spinal artery circulation. The upper cord and its highest segments are supplied by the intracranial and transverse branches of the vertebral artery and in lower cervical and upper thoracic segments by deep cervical and ascending cervical branches of the subclavian artery. The lower cord is often supplied by a single large radicular artery between segments T-10 and L-2; the artery of Adamkiewicz. The middle spinal cord between segments T-4 and T-8 is supplied by a single radicular artery usually found at T-7. Thus the middle thoracic segment has little compensatory flow and is especially vulnerable to ischemic infarction.

Brewer reviewed 66 cases of bilateral lower limb weakness following repair of aortic coarctations.[9] Duration of aortic clamping and the number of intercostal arteries sacrificed were not related to the occurrence of spinal cord infarction. He proposes that anatomic variations in the anterior spinal artery and poor preoperative collateral circulation around the coarctation were the most important factors contributing to postoperative paraparesis. He points out that poor collateral flow to the cord contributes to the occasional spontaneous development of paraparesis in patients with aortic coarctation. Sacrifice of a low-lying artery of Adamkiewicz or of a second radicular artery in the lumbar region causes paraparesis during repair of abdominal aneurysms.[10] Occlusion of these arteries is proposed as a mechanism for paraparesis occurring with dissecting aortic aneurysms and saddle embolization of the lower aorta.[11]

Several other myelopathies occur due to alterations in spinal cord blood supply. Transient ischemic attacks and spinal cord infarction from arteriosclerotic radicular arteries are documented but are rare.[12] Spinal arteriovenous malformations occur. Their presentations are acute, intermittent, or progressive. Segmental cutaneous hemangiomas have been reported by Doppmann and associates to occur with underlying spinal arteriovenous malformation.[13] Recognition of these cutaneous angiomas is facilitated by a Valsalva maneuver and assists the angiographer in pinpointing the level of the major arterial blood supply to the malformation. Foix and Alajouanine described thrombosis in dilated, tortuous spinal arteries with thick walls as a unique cause of subacute necrotizing myelopathy. Clinically this disorder is characterized by a stuttering progression with leakage of red blood cells and protein into the spinal fluid. Later Alajouanine and others recognized these abnormal vessels as components of an arteriovenous malformation.[14] Thickened vascular walls found by pathologic examination differentiate this condition from the more rarely reported thrombosis of spinal veins.[15]

Claudication or exercise-induced limping occasionally results from spinal cord ischemia.[16] Paresthesias in lumbosacral dermatomes and cramping pain in the legs develop shortly after ambulation is begun or a posture involving extension of the lumbar spine is assumed. While at rest, the neurologic examination including the straight leg raising test is normal. Sensory loss and weakness develop with exercise rather than reduction of peripheral pulses. Myelography is required to confirm a congenitally narrowed lumbar spinal canal, further narrowed by minor disc protrusions that compromise blood supply and compress lumbosacral nerve roots. Epstein found a wide anatomic variation in this canal and concluded that sagittal narrowing of less than 13 mm often is associated with clinical evidence of root compression.[17]

**Tumorous Disorders.**

*Patient 3.* A 51-year-old woman complained of stiffness in her legs and burning in the soles of her feet six months before hospitalization. While toweling herself she discovered that she was numb in the lower back. Twice upon seeking consultation she was advised to lose weight. She came to the hospital when she began to drag her right leg while ascending stairs. Examination revealed mild weakness and spasticity in both legs with hyperactive deep tendon reflexes and extensor plantar responses. There was a positive Beevor's sign and a sensory level for pin prick to the umbilicus.

**Discussion.** This patient represents the frequency of spinal meningiomas occurring in middle-aged women. The thoracic area is by far the most common site for spinal meningiomas. Slow growth of these intradural tumors frequently contributes to their delay in diagnosis; hence insidious onset is typical. In this stage localized pain, determined by percussion of the spinous process of each vertebra, and early symptoms

of compression are vaguely defined and unaccompanied by frank neurologic signs. X-ray changes in thoracic vertebrae are often absent in contrast to the hyperostosis or bony erosion of the skull seen with intracranial meningiomas.

Mention should be made of the sign of segmental weakness of abdominal muscles which occurred in this patient. Beevor described migration of the umbilicus toward the functioning recti muscles of the abdomen and away from those weakened by interruption of their T-8 to T-12 thoracic root innervation. Usually upward movement of the umbilicus is recognized and occurs with lesions across the T-10 segment, but lateral migration of the umbilicus occurring with unilateral lower abdominal nerve paralysis is infrequently observed. Segmental loss of superficial abdominal reflexes ordinarily accompanies Beevor's sign.

*Patient 4.* A 32-year-old security agent had occasional pain in his right leg and foot for 14 years. He walked with a limp in his right leg. His condition was attributed to a congenital defect in association with spina bifida of his lumbar spine. For four years he had one to three band-like headaches per day lasting 25 to 30 minutes with occasional obscurations of vision lasting several seconds. He came to the hospital when he awoke momentarily blind for the second morning in three days. Examination showed papilledema, mild weakness in the flexors and extensors of the right foot, hypoactive knee jerks, and absent ankle jerks. Pain and temperature were slightly diminished in the left leg. Position and vibratory discrimination were bilaterally impaired in the toes.

**Discussion.** It is not surprising that the combination of papilledema and unilateral leg weakness led first to intracranial neuroradiologic studies in this patient with a lumbosacral ependymoma. The occurrence of papilledema with lower spinal tumors is recognized, but its mechanism is poorly understood.[18] Often cerebrospinal fluid (CSF) protein is elevated; it was 320 mg% in this patient. Curiously, nearly half of these patients have ependymomas. Despite the papilledema, ipsilateral weakness and crossed sensory loss to pain and temperature point directly to a spinal cord lesion. This is the Brown-Séquard syndrome and was undoubtedly demonstrated in the laboratory by Brown-Séquard himself when he taught at the Medical College of Virginia in 1855.

Since it was a source of confusion in this patient, a point should be made regarding the finding of congenital defects about the lower spine. In the presence of a neurologic deficit these anomalies should undergo a thorough evaluation. For example, spina bifida is sometimes associated with myelomeningoceles and intraspinal lipomas. Dermal sinuses are known to have fistulous connections to the subarachnoid space and serve as the source of recurrent meningitis.[19] A patch of hair, cutaneous nerves, or skin dimple in the lumbosacral region suggest the possibility of an underlying calcified septum and duplication of the cord which occurs in diastematomyelia.[20,21] All of these conditions have the potential for neurologic progression and are, once recognized, neurosurgically remediable.

*Patient 5.* For three years, a 48-year-old housewife complained of aching pain in the mid-thoracic region as she rose from a sitting or lying position. Occasionally pain became sharp and radiated down both thighs. A tight feeling developed in her right lower ribs as she stood up. For several years she received cortisone injections for "spinal arthritis." Six months prior to hospitalization, she often awoke with uncomfortable, tight, squeezing sensations in her legs. She began to have frequent falls. Examination showed a mild spastic paraparesis with a sensory level to segment T-8. Position and vibratory sense in the toes were absent. Myelography showed a ventral extradural block. At exploration, protrusion of a thoracic intervertebral disc was exposed.

**Discussion.** Changes in posture, as illustrated by this patient, affect both the blood supply and conduction capacity of a partially compressed spinal cord and its nerve roots. Increased intraspinal pressure caused by a cough or sneeze similarly produces intermittent symptoms. Thoracic pain occurring with a change in posture or coughing is a frequent symptom of patients with extrusion of a thoracic disc. In this disease unpleasant and segmental paresthesias were frequently found among 14 patients reported by Carson and associates.[22] He stated that recognition of this condition draws attention to the typical symptom complex, care in the myleographic diagnosis, and a wide lateral approach to the ventral disc at laminectomy.

**Infectious Disorders.**

*Patient 6.* A 25-year-old escapee from a Virginia prison developed low back pain which steadily intensified and spread down the back of each leg over five days. He entered a Washington hospital with bowel and bladder incontinence and limited movement of both legs. Due to the intense hyperesthetic pain, motor power and plantar responses could not be determined. Deep tendon reflexes were hyperac-

tive. Normal CSF pressures were found, and the CSF contained three red blood cells, protein of 150 mg%, and normal sugar. Myelography was normal. Over ten days he became paraplegic and anesthetic to the T-8 level. Deep tendon reflexes were now absent.

**Discussion.** Clinically this patient presents with the picture of acute transverse myelitis. Local or radicular pain often occur early, and loss of bowel and bladder function is common. Prognosis in acute transverse myelitis is frequently not as grave as the paraplegic state suggests. More than half the patients walk again and, if this is their first neurologic illness, they infrequently develop additional signs of multiple sclerosis.[23] Often a viral or vascular etiology is postulated, but at the turn of the century, in young men, syphilitic myelitis was the most common etiology. Syphilitic infection is considered the cause of this patient's myelitis because the pathology specimen obtained five years later shows a thickened arachnoid that is characteristic of syphilitic meningomyelitis. This thickening not only surrounded the entire cord in the lumbar region, but also extended along its length into the cervical region. Serum serology was positive, and he received more than adequate treatment for central nervous system (CNS) lues due to frequent urinary tract infections. Unfortunately, no CSF examination for syphilis is on record. This problem underlines the continued need to consider neurosyphilis in every instance of CNS disease and to obtain, as appropriate, both serum and CSF serology.

*Patient 7.* A 52-year-old diabetic was brought to the hospital in a delirious state. He complained of low back pain. There was costovertebral and mild, diffuse low back tenderness. He had no neurologic deficit. Temperature was 101.6 F. The urine contained white blood cells, bacteria, and acetone. Blood sugar was 380 mg% and electrolytes were normal. No acetone was found in the blood. He was treated for a urinary tract infection and dehydration. An attempt at lumbar puncture was aborted when it yielded only several drops of pus. A perinephric abscess was diagnosed and "drained." Three days later the patient became paraplegic.

It is unfortunate that the diagnosis of an epidural abscess was not made.

**Discussion.** Baker states that the typical course of epidural abscess is the progression from spinal ache to radicular pain, to weakness and then paraplegia.[24] Frequently these patients are delirious which obscures the clarity of this progression and probably explains the absence of the complaint of radicular pain in this patient. The combination of back pain, local tenderness, and fever should raise this possible diagnosis in every practitioner's mind since evolution to paraplegia may be quite rapid. Most patients initially have some neurologic deficit, but as in this patient, not all do. In some instances a site of infection such as a furuncle, dental abscess, or vertebral osteomyelitis is obviously apparent. With early surgical intervention neurologic recovery is expected and sometimes is complete.

*Patient 8.* A 48-year-old foundry worker had night sweats and cough with purulent sputum for three days. He was given tetracycline. Two days later he complained of diffuse back pain. The next day he became confused and was admitted to the hospital in a delirious state shouting and singing. He was afebrile, his neck was stiff, and ankle jerks were absent. There were no other abnormal neurologic findings. A lumbar puncture obtained yellowish fluid which was under normal pressure. CSF contained 480 white cells of which 90% were monocytes and 10% were polymorphonuclear cells. CSF sugar was 60 mg% and CSF protein was 4428 mg%. The next day the patient became febrile and paraplegic. Another lumbar puncture showed a similar spinal fluid formula. The patient died the following day.

**Discussion.** CSF protein that exceeds 0.5 gram is referred to as Froin's syndrome. This condition usually occurs with either complete spinal cord block or meningitis of a syphilitic or bacterial origin. If the spinal fluid has a high protein content and is allowed to sit, a pedicle of coagulated protein forms which should be stained for the tubercle bacillus. This patient had a rapidly progressive form of tuberculous meningitis for which he was treated on the basis of the elevated protein in the CSF. Wadia and Dastur, from their wide experience with tuberculosis meningitis in India, suggest that such a fulminant course results from a highly virulent organism or an unusual hypersensitive response to the tubercle bacillus.[25,26]

### Disorders Due to Physical Agents.

*Patient 9.* An 18-year-old primigravida was in good health during her pregnancy. She entered an obstetric ward late one evening and eight hours later gave birth with epidural and brief inhalation anesthesia. Repeated catheterization was needed for relief of bladder distension. On the second post partum day she found it difficult to walk or rise up from a sitting position. This difficulty was ostensibly attributed to perineal pain. She was discharged and carried out of the hospital on the third post partum day. Upon her

return to clinic six weeks after delivery she reported her difficulty walking. Examination showed mild weakness in thigh extensors and leg flexors. There was a mild diminution of sensation in the saddle region about the buttocks and posterior thighs. Ankle jerks and knee jerks were intact, but deep tendon responses of the hamstring muscles were diminished. Plantar signs were flexor. The rectal sphincter was hypotonic. There was no complaint of low back tenderness and the straight leg raising test was normal. She reported gradual improvement in her disability, and six months later there was nearly complete resolution of her neurologic deficits.

**Discussion.** The neurologic findings in this patient are indicative of the cauda equina syndrome. This structure consists of low lumbar and conus medullaris nerve roots. The conus is composed of sacral segments of the terminal spinal cord. Literally the cauda equina nerve roots grossly resemble a horse's tail as they drape off the conus medullaris. For patients with low back pain, examination of the neural function of these sacral roots should be emphasized. Inquiry into bowel, bladder, and sexual function should be made, and rectal sphincter tone assessed since these functions are subserved by S-2 to S-5 nerve roots. Muscle testing of gluteus maximus and hamstring muscles, best obtained with the patient in the prone position, is too often omitted once anterior leg muscles such as the iliopsoas, quadriceps femoris, and flexors of the foot are found to be strong. In patients complaining of low back pain, sensory testing too often does not include dorsal sacral dermatomes about the buttocks and posterior thighs, the so-called saddle region. In the cauda equina syndrome a normal knee and ankle reflex is misleading unless hamstring stretch reflexes of the lateral biceps femoris and medial semitendinosus and semimembranosus muscles are ascertained.

In the patient reported here a precise diagnosis was not determined because the successful clinical remission experienced by the patient negated need for further diagnostic evaluation. The history suggests that a caudal root neuropathy occurred as a consequence of an anesthetic accident following epidural or inadvertent intraspinal anesthesia. The mechanism is reportedly associated with a detergent or other contaminant of the anesthetic.[27] An epidural hematoma is a less likely explanation in the absence of back pain, anticoagulant treatment, or coagulopathy.

*Patient 10.* A 69-year-old heavy drinker was admitted to a medical ward following a generalized seizure. Examination showed flat buttocks and thin posterior thigh muscles. The overlying area was anesthetic. Hamstring deep tendon reflexes were absent. Anal sphincter tone was flaccid. Straight leg raising was unremarkable. As his sensorium cleared he stated that 24 years previously fecal incontinenece began. Loss of sacral sensation appeared over several more years. There had been little change in his condition in the ensuing 20-year period. He denied low back pain, although review of his medical records showed that 30 years earlier he complained of lower spinal discomfort for several years. X-rays revealed an increased density of the medial aspect of the iliac bones.

**Discussion.** Further review of the patient's medical records disclosed the probable cause of his neurologic deficit. During the two-year period of lower spinal pain, he received two myelograms which employed a colloidal solution of thorium dioxide or Thorotrast®. In certain centers this agent was widely used between 1938 and 1945. Its use was discontinued because of recognition that its low-penetrating alpha ray activity with a half life of 14 billion years has a deleterious effect on surrounding tissue and subjects the patient to a risk of subsequent neoplasia. This patient should be added to the reports of Maltby[28] and Tucker et al[29] of patients with a cauda equina syndrome beginning five to fifteen years after their exposure to thorium dioxide. The delayed effect of radiation upon the nervous system which occurred in these cases resembles a similar delayed onset in cases of radiation myelopathy.[30,31] This complication of irradiation therapy is infrequent. Its onset occurs about one year after irradiation is given to the cord or adjacent surrounding areas. Clinically the neurologic deficits are benign and remissive, or chronic and relentlessly progressive. Its etiology is related to the rapidity and total dose of radiation received as well as to individual variations in vascular supply to the portion of the cord which is exposed during therapy. Its diagnosis is problematic since consideration usually is given to a metastatic tumor of the cord.

*Patient 11.* A 34-year-old drug pusher was shot and fell to the ground. In the emergency room he moved all extremities in response to pain. A bullet entry wound was observed in the left lower abdominal quadrant, and its exit was found in the right posterior flank. At laparotomy several bleeding vessels were ligated. The pancreas was reported to be contused. The patient awoke in an intensive care

ward, complaining bitterly of pain in his legs. He cursed those attempting to examine the lower extremities and demanded that a tent of sheets be constructed over his legs so that nothing could possibly touch them. His stools soiled the bed sheets, and he was incontinent of urine. X-rays of the spine were normal. Lumbar puncture showed normal pressures, and his spinal fluid contained 75 red blood cells, 82 mg% sugar, and 70 mg% protein.

After one month his severe pain diminished. Bowel and bladder function returned. Examination showed moderate bilateral weakness of the glutei and hamstring muscles. He was unable to stand on the toes of his right foot. Hamstring and ankle jerks were absent. There was anesthesia of the buttock and posterior thigh. Mild tactile stimulation of the posterior legs or feet often provoked dysesthetic pain. The rectal sphincter was patulous. Over a two-year period his dysesthetic pain entirely disappeared.

**Discussion.** This patient presented a difficult situation in the intensive care unit since he would not allow a complete examination, and the true nature of his complaints were not understood. Further difficulty ensued with demands for narcotics to temper either his drug withdrawal or his poorly appreciated causalgic pains. Tomography of the lower spine was in this instance helpful in reaching a plausible explanation of his signs and symptoms. Tomograms of the lumbar spine showed a bullet hole through L-2, L-3 lumbar disc space. Evidently either the concussive shock of the bullet or extruded disc material contused the roots of his cauda equina. Use of the polytomogram is advised in unexplained cases of nerve root injury which occur in the region of the nerve's osseous compartments.

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# New Horizons in Muscle Disease

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As information concerning the interactions between nerve and muscle increases, the concepts which divide disorders of the motor unit into the two basic categories of neurogenic atrophy and myopathy become less accurate. While it is still true that these concepts provide the clinical basis for classifying such disorders,[1,2] they must be regarded as an oversimplification which establishes a point of reference for future understanding of these diseases. At present, attempts are made to isolate that portion of the motor unit, for example, anterior horn cell, axon (peripheral nerve), neuromuscular junction, and the muscle fibers innervated by that anterior horn cell, which can be primarily responsible for muscle weakness (Fig 1). To this end every patient so afflicted undergoes a series of evaluations which begins with a careful history and thorough examination.[3] As part of this examination, muscles which are particularly affected are noted and graded as to size and strength. Next, serum is analyzed for the presence of enzymes which may "leak out" from the muscle, such as creatine phosphokinase, aldolase, and lactose dehydrogenase. Nerve conduction times, high- and low-frequency stimulation tests, and needle electrode studies constitute the electromyographic investigations which individually test each portion of the motor unit. Finally, a muscle biopsy, carefully removed from a moderately involved muscle, is analyzed with routine staining as well as a battery of histochemical techniques and, in selected cases, electron microscopy. When all of these data are assimilated, an attempt is made to identify this disorder which is then classified basically as neurogenic or myopathic.[3] Yet, even after such a complete work-up, there are a number of ever-increasing cases where no categorization can be made and a noncommital term such as "neuromyopathy" is used.

The reason for growing uncertainty in this entire field is an appreciation of the profound influence of the trophic effects of nerve on muscle.[4] The most obvious of these is that there is a reduction in fiber diameter and collapse of the sarcolemmal membrane as denervated muscles atrophy (Figs 2, 3). Normally, the only area sensitive to acetylcholine resides in the junctional folds of the endplate region, but in denervated muscle, receptor sites can be identified over the entire sarcolemmal membrane. One can then infer that innervation is in some way responsible for the establishment and maintenance of fiber diameter as well as limiting the location of active acetylcholine receptor sites to the neuromuscular junction.[5]

Aside from trophic influences on the size of muscle fibers, innervation affects the basic metabolic and physiologic characteristics of muscle fibers.[6] Without offering unwarranted comparisons, it is known, either by taste or visual impression, that there is both light and dark meat on turkeys and other fowl. The light meat is found in the breasts and primarily functions to mobilize the wings; the dark meat is found in the legs and functions for support and posture. Lower mammals have been described in terms of red, slow or tonic muscle, and white, fast or phasic muscle. Physiologically, entire muscles seem to have one or the other characteristics. When stained histochemically for oxidative enzyme content, correlations were made for those muscles rich in oxidative enzymes with slow or "red" muscle, and those muscles which relied primarily on glycolytic pathways and were therefore low in oxidative enzymes, with fast or "white" muscle. By preparing human muscle

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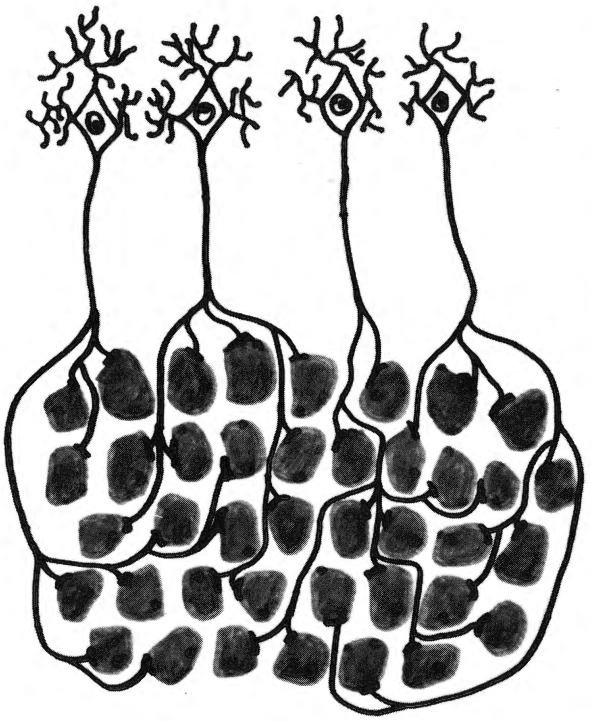


Fig 1—Diagram showing four motor units with components including anterior horn cell, peripheral nerve (axon), neuromuscular junctions, and innervated muscle fibers.

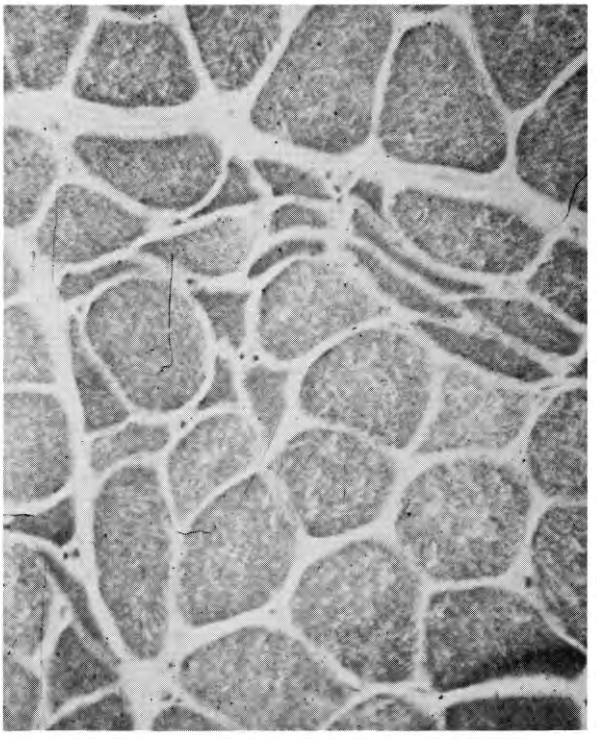


Fig 3—Photomicrograph showing focal atrophy.

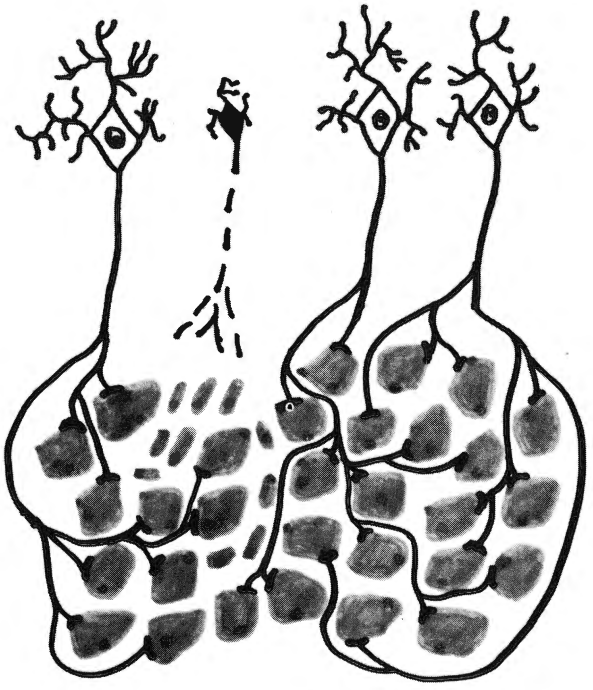


Fig 2—Diagram showing focal atrophy due to denervation.

Fig 4—Diagram showing four motor units stained histochemically. All of the fibers within the same motor unit are of the same type.

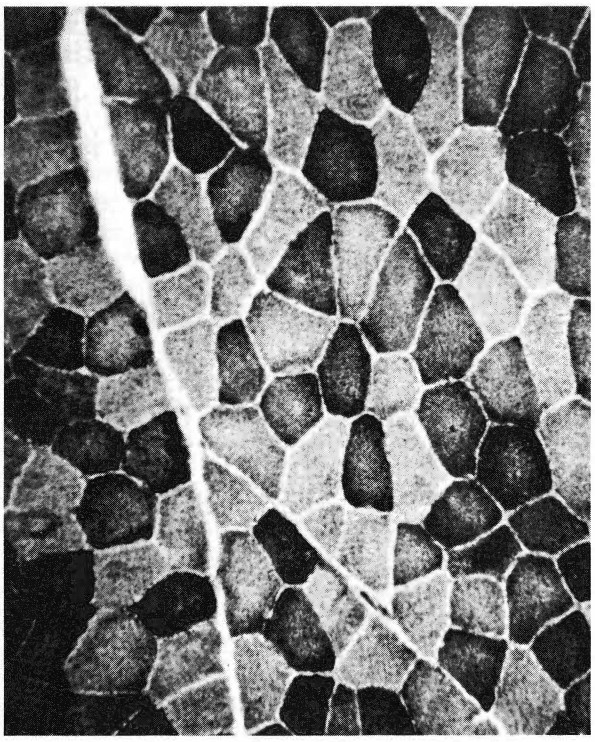


Fig 5—Photomicrograph of the normal muscle stained for NADH diaphorase. Type I fibers are dark; Type II fibers are light. This appears as a 'checkerboard' pattern of light and dark staining fibers.

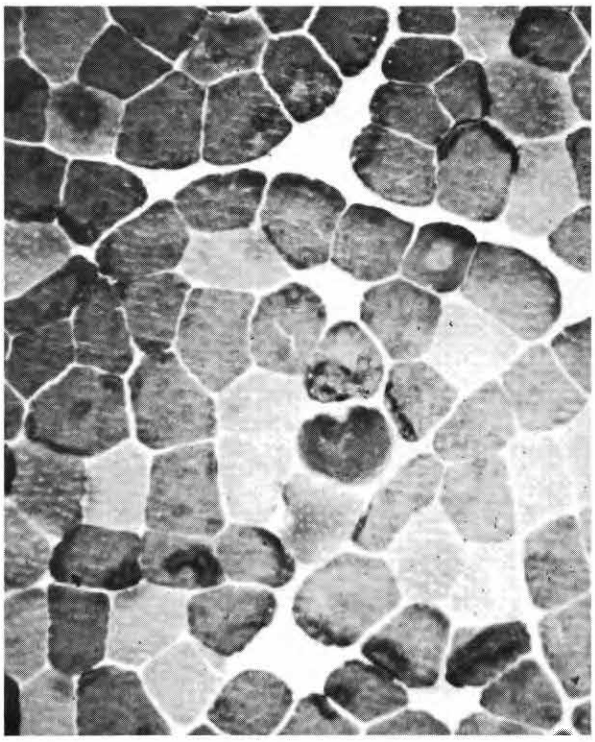


Fig 6—Photomicrograph of normal muscle stained for myofibrillar ATPase. Type I fibers are light; Type II fibers are dark.

samples in a similar (Fig 4) fashion,[2,6] it was seen that there are also two basic types of muscle fibers; Type I, rich in oxidative enzymes and staining darkly for mitochondrial nicotinamide-adenine dinucleotide (NADH) tetrazolium reductase (Fig 5) and Type II, low in oxidative enzymes but staining darkly for myofibrillar adenosinetriphosphatase (ATPase) (Fig 6).[4] Subtypes have been identified with a wider variety of histochemical techniques. Several features concerning fibers stained by these techniques include; 1) the fiber type remains the same along the length of the fiber, 2) all of the muscle fibers within a given motor unit are of the same histochemical type so that there are Type I and Type II motor units, 3) the fibers of a motor unit are distributed in a random fashion throughout the muscle, mixing with, and dispersed among, muscle fibers of other units and, 4) both Type I and Type II muscle fibers are found within the same muscle in humans so that, normally, the randomized distribution of muscle fibers[7] of the motor unit causes an alternating or "checkerboard" pattern of light and dark fibers when

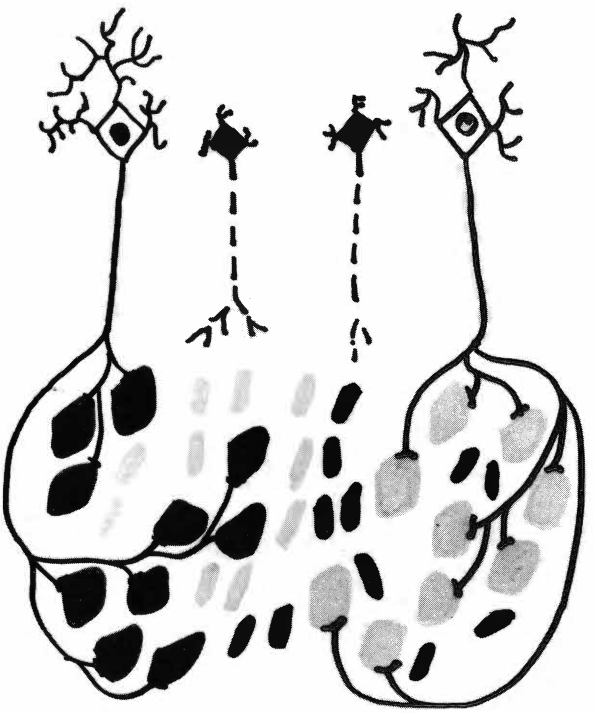


Fig 7—Diagram showing atrophy due to anterior horn cell disease. The muscle is stained by histochemical techniques.

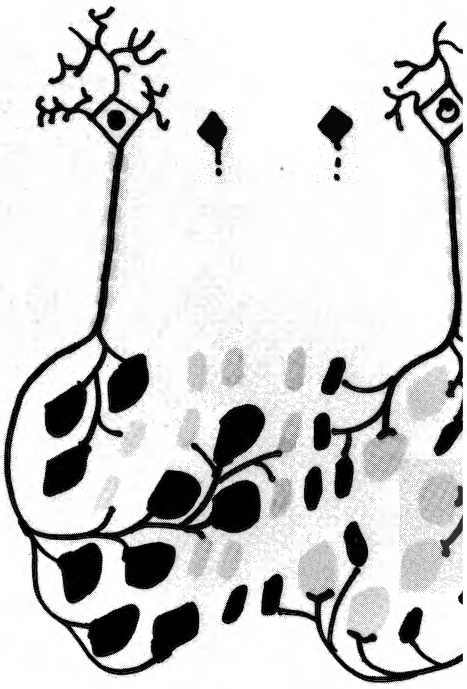


Fig 8—Diagram showing reinnervation collateral s
still intact motor units.

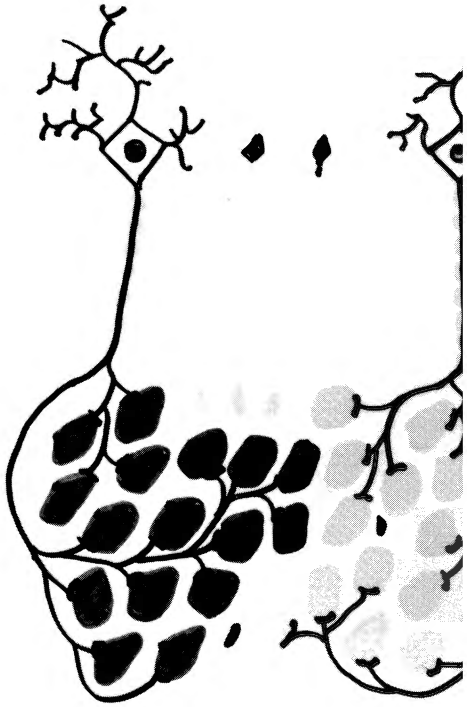
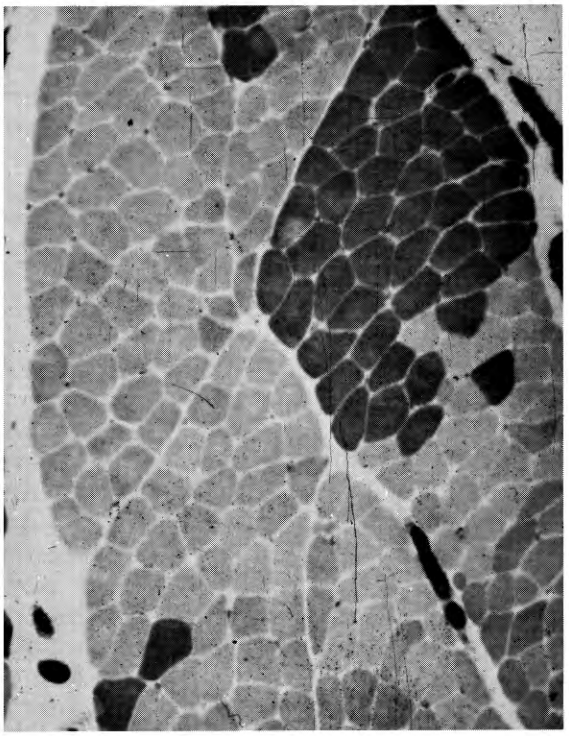


Fig 9—Diagram showing incorporation of reinne
fibers into still intact motor units and conversion o
that of innervating motor unit.



; 10—Photomicrograph showing a grouping of fiber types
ined for myofibrillar ATPase. This grouping and loss of the
eckerboard' pattern indicates denervation-reinnervation has oc-
red.

e muscle is stained by histochemical techniques.[2] In
ronic disease states, such as neurogenic atrophy
ıe either to anterior horn cell disease or peripheral
uropathy, there is both denervation and reinnerva-
ɔn by collateral sprouts of still intact axons (Figs 7,
.[4] If denervated muscle fibers are reinnervated by
llateral sprouts from axons of motor units which
e of a different type, the reinnervated fibers will
sume the histochemical type of that motor unit
ɔm which they are reinnervated. There is then a loss
the "checkerboard" appearance as a grouping of
ıers of the same type occurs (Figs 9, 10)[2,4] This
enomenon is also observed in animal experiments
which there is denervation and cross reinnervation
ɔm one muscle type to the other, and a subsequent
ɔrganization of fiber types when reinnervation is
mplete.[8] That the basic metabolic pathways of
ergy production in muscle are so drastically in-
enced by innervation must be considered when
yopathies are viewed as primary derangements of
uscle metabolism.

When the physiologic characteristics of the vari-

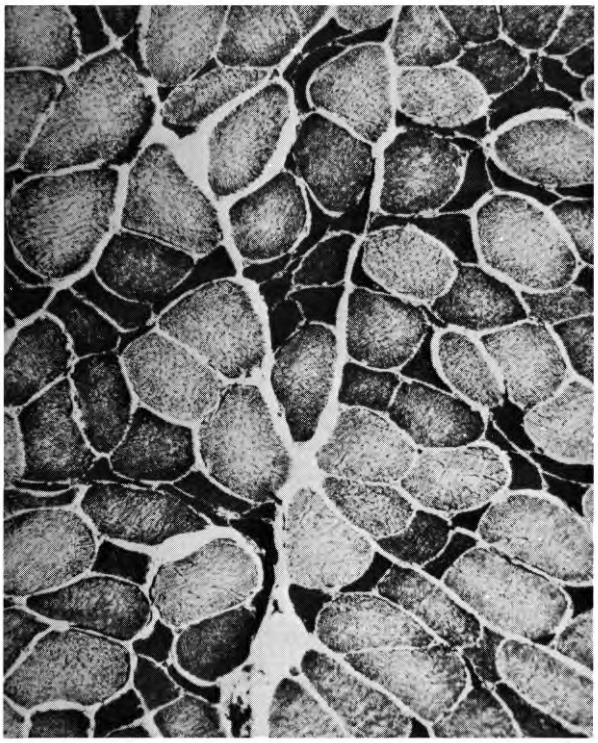


Fig 11—Photomicrograph showing selective atrophy of Type I fibers (dark) stained for NADH diaphorase.

ous types of motor units are studied, differences can be identified as to configuration of motor unit potentials, frequency of firing, duration of firing, and sequence of firing during voluntary contraction.[9,10] Attempts to correlate these characteristics with histochemical differentiation are now in progress.[12] Since there is no discernible difference between motoneurons which innervate different fiber types, it would seem that the influence may be purely physiological and depend upon firing rates as well as the frequency with which these neurons are called upon to perform.[13] In that sense, the fiber type of a particular unit may be ultimately dependent upon the central organization which programs and controls motor function.[14,15]

Many of these primary disorders of muscle, now subject to evaluation by histochemical techniques, are being either reinterpreted or at least held in their classification categories with less certainty. At present there is international debate regarding a primary neurogenic etiology for Duchenne's dystrophy.[16,17] Many cases of limb girdle dystrophy are reclassified as motoneuron disease or as "neuromyopathy." Furthermore, myotonic dystrophy may not be 'dystrophy' at all, since the most obvious pathological finding is a selective atrophy of Type I fibers (Fig 11).

Histochemical techniques have permitted the identification of these pathological changes, which in the past were considered to be denervation atrophy, as 'type atrophy.' Selective atrophy of Type II (Fig 12) fibers is seen in disuse atrophy, polymyalgia rheumatica, in steroid arthritis, oculopharyngeal dystrophy, and, as mentioned, myotonic dystrophy. In addition, there are a host of congenital myopathies in which specific histochemical changes are observed.

Currently, at the Medical College of Virginia, new techniques are being modified and applied in the evaluation of neuromuscular disorders. One of these is open biopsy electromyography, which permits a direct electrophysiological examination of a sample of muscle just prior to its removal. Information obtained in this way is being analyzed and correlated with the histochemical characteristics of the sampled muscle and has provided new as well as more precise interpretations.[18]

Sophisticated physiological and histochemical information is accumulating at a rate which at present is faster than the clinician can assimilate. The

Fig 12—Photomicrograph showing selective atrophy of Type II fibers (dark) stained for myofibrillar ATPase.

contributions made by electron microscopy further burden an overwhelming stockpile of data. In a true sense, many pieces to the puzzle have been found, and as these are cautiously put in place, a more complete understanding of muscle disease is foreseeable. One hopes that with better insight into the pathophysiology of muscle diseases, these new horizons will permit eventual treatment or cure for those suffering from these disorders.

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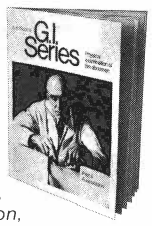
**A service to medical education from A. H. Robins:**

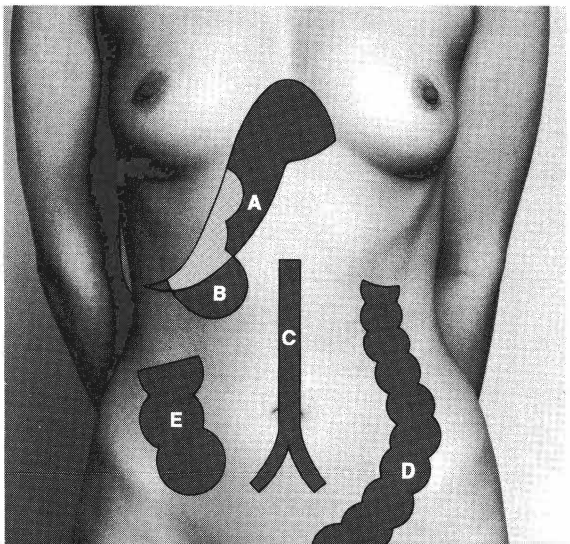
Excerpted from Volume 2 of the **G.I. Series** on physical examination of the abdomen:




The A. H. Robins G.I. Series consists of six booklets, designed to provide a quick, yet comprehensive review of basic procedures and practices in G.I. medicine—with particular emphasis on the physical examination as performed in the office or at bedside. If you have teaching responsibilities, limited quantities are available: Part 1—*Inspection*, Part 2—*Palpation*, Part 3—*Percussion*, Part 4—*Auscultation*, Part 5—*Abdominal Pain* and Part 6—*Differential Diagnosis of Abdominal Disorders*. Write to: The Medical Department, A. H. Robins Company, 1407 Cummings Drive, Richmond, Virginia 23220.

***Normally palpable organs:*** the edge of the liver descending, on inspiration, below the costal margin (A); the lower pole of the right kidney (B); the abdominal aorta (C); the descending colon and the sigmoid (D); the ascending colon (E); and occasionally the bladder (though rising of this organ beyond the pubis does not necessarily indicate disease).

Impossible to outline, unless diseased, distended or enlarged: the gallbladder, pancreas, stomach, small intestine, transverse colon and spleen.



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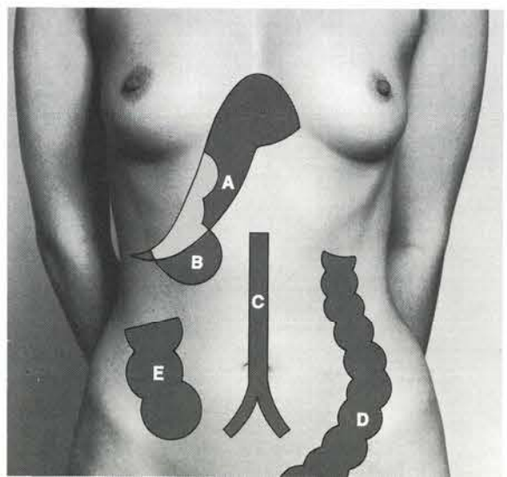


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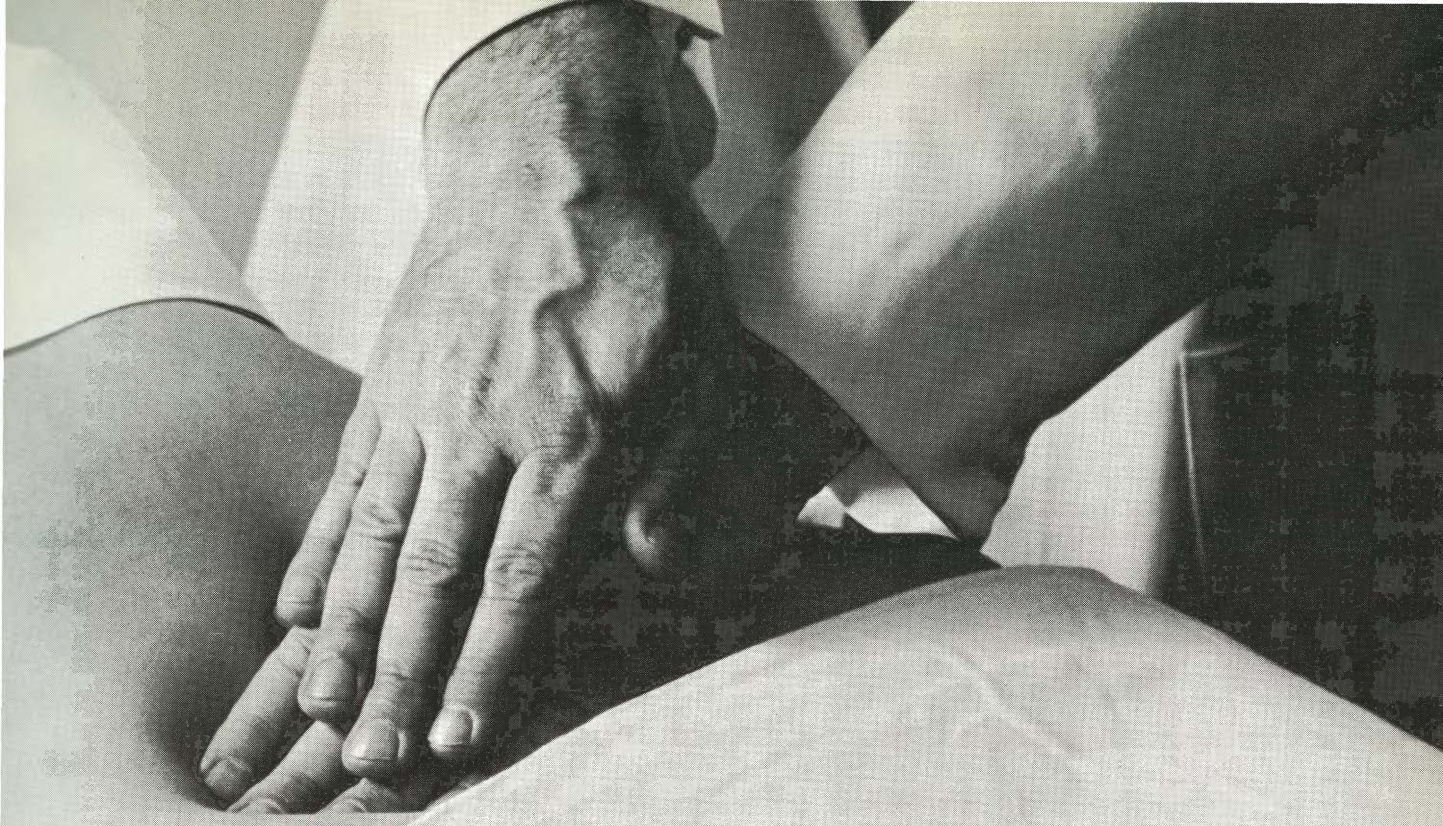

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