American Handbook of Psychiatry

POSTENCEPHALITIC STATES OR CONDITIONS

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Various acute encephalitic syndromes have long been recognized but postencephalitic states, as they are now understood, did not emerge as important until the 1916-1930 epidemic of encephalitis lethargica which showed that such a disease could do vast damage and that medicine was quite unprepared to cope with viral encephalitis. This experience had a profound impact on medical thinking and left great concern that this disease or even a more devastating one might break out again. This fear has now abated, but recent advances in general virology indicate that the concern was not without foundation. In an article entitled "Viruses may Surprise Us" Sabin is quoted as saying that new syndromes may be caused by familiar viruses, by new ones, or by new antigenic variants as in the case of influenza. He feels that more study needs to be directed toward pre- and postnatal viral infections in congenital defects. The potential scope of this problem is seen in his statement that "The viruses of the human heritage which maintain themselves in nature by passing from one human being to another, now number about 200—the vast majority identified during the last 10 years." He states, "In addition, studies mostly of recent years have revealed at least 200 distinct viruses in the arthropod-borne group."

It is clear that we live more intimately with the world of viruses than was previously realized and many of them are now known to attack the

central nervous system. The resulting syndromes are described as meningitis, meningo-encephalitis, and encephalomyelitis, according to the pathology which tends to predominate, but there is a continuum among these pathological forms and mixed states are common.

Most of these infections, such as herpes simplex, Japanese B encephalitis, and St. Louis encephalitis, do not become chronic, and they leave residual central nervous system damage in only a minority of cases. Such damage can be severe and may be focal and/or diffuse, but it is not progressive. The acute infection may be marked by a well-defined febrile episode associated with the usual cerebral signs such as stiff neck, stupor, coma, convulsions, and myoclonia, but at least in some postencephalitic states there may be no such history. One can only speculate what part such infections may play in the total psychiatric scene. So far we know only about cases where the damage is severe or the clinical syndrome is specific. It remains to be seen whether viral infections can also cause minor degrees of damage which lead to conduct disorders, hyperkinesis of children, and other syndromes now gathered under the controversial rubric of minimal brain dysfunction (MBD). For a time, the experience with Von Economo's encephalitis suggested that this was a distinct possibility, but most authorities now seem to reject this view.

To some extent, the question has been reopened by the discovery of

chronic virus infections of the central nervous system, especially that of Kuru and slow measles in man, as well as scrapie and visna in animals (see p. 163). In addition it has been shown that viruses may multiply within morphologically intact neurons and produce disease through dysfunction of these neurons. What may be the psychiatric significance of these data remains for future research to decide, but it is now certain that encephalitis lethargica is not the only chronic progressive viral infection of the brain.

Classification and Nomenclature

Terminology in this field makes use of anatomical, clinical, and etiological names but is actually controlled by usage. Thus the so called postencephalitic states following Von Economo's disease are, in fact, chronic encephalitic states, with pathological evidence of continued active inflammation alongside evidence of previous destruction. They were designated as postencephalitic because historically they were observed after acute infections and long before the chronic nature of the infection was fully understood; the term has now been established by usage. Usage has also decreed that the major postencephalitic and chronic encephalitic states, which were known before Von Economo's disease was discovered, should continue to be described separately under their old designations, and this includes such entities as rheumatic chorea, paresis, and rabies, as well as infantile cerebral palsy. On the other hand, the postencephalitic and chronic

encephalitic disorders which were recognized after Von Economo's encephalitis tend to be classed with the postencephalitic states.

This is true even though postencephalitic residuals were recognized well before Von Economo's time. Oppenheim, as quoted by Mayer, noted already in 1900 that such damage could be left after measles, scarlet fever, pneumonia, erysipelas, whooping cough, and mumps, and after the hemorrhagic encephalitis of influenza. These syndromes must, however, have been considered neurological rather than psychiatric because the prestigious Tuke's *Dictionary of Psychological Medicine* in 1892 does not even list a category of encephalitis. It describes "inflammation of the brain" but only under the heading of "delirium." The *Dictionary* even mentions mental disorders following influenza but does not appear to relate them to brain damage.

Advance has been spectacular since the days of Oppenheim and even Von Economo, but many uncertainties still remain, and we still have no fully established system of classification of the syndromes now recognized as encephalitic or postencephalitic.

Some of the disorders are classified by their vectors as in the case of arthopod-borne viruses (arbo viruses); others are classified on the basis of pathology (hemorrhagic encephalitis); some by the distribution of pathology

(leukoencephalitis), still others by geographical titles (Japanese B., Australian X, Russian summer encephalitis), and some by the host species (fox encephalitis, equine encephalitis). Finally, the classification by pathological syndrome is also of a multiple nature and may be based on the distribution of the reaction (leukoencephalitis), the location of the pathology as in encephalomyelitis, or the nature of response (inclusion body encephalitis).

As the etiological agents are identified, descriptive terms are becoming more specific, or are being displaced by terms derived from the etiological agent such as "encephalitis due to slow measles virus." Even an etiological classification must at this time, however, remain incomplete because the classification of the viruses themselves is still a matter of vigorous debate.

Distinctions among the various forms of encephalitis and postencephalitic states, other than the Von Economo type, still remain of limited clinical importance, and a simple account of the major forms seems adequate for most purposes since they represent essentially chronic, static, nonspecific organic brain syndromes. Nevertheless, the clinician cannot ignore even the acute reactions, if only because he must usually diagnose the postencephalitic states retrospectively and on the basis of clinical history and hospital records of the initial infection.

Encephalitis Lethargica (Von Economo's Disease)

History

In 1917 Von Economo described what seemed to be a new epidemic disease which he called encephalitis lethargica. During the next few years this disorder took on pandemic proportions and involved tens of thousands of victims leaving an estimated one third of them with permanent, progressive, bizarre neuropsychiatric residuals. Decades of research have failed to resolve the mystery of the origin of this disorder or its mode of transmission. The etiological agent is presumed to be a virus, but it has not been isolated nor have specific immune bodies been identified, even though a considerable number of cases still survive with what appears to be a chronic active encephalitic process.

The original outbreak overlapped the 1919 pandemic of influenza and for a long time these two disorders were confused with each other, but they are now considered to be entirely separate.

During the epidemic and for some time thereafter scientific interest was intense, and it was hoped that this strange new disease would be a sort of a medical Rosetta Stone which would provide neurophysiological equivalents of somatic events and vice versa. Many challenging questions were raised because of the close association of a well-defined neuropathology with classical functional disorders such as compulsive obsessive states, hysterical neuroses, and psychoses with severe conduct disorders, all of them

intertwined with neurological and neurovegetative changes. Contemporary observers were firmly convinced that they were observing not simple release phenomena but specific reactions to the damage caused by encephalitis. For a time the issues which had been raised seemed to have good hopes of resolution, but research results were minimal, and scientific interest finally faded. It was not until the development of the major tranquilizers and the subsequent introduction of L-Dopa that such hopes were revived.

Epidemiology

The epidemiology of encephalitis lethargica has now receded into medical history. The disease may have been endemic in Eastern Europe, and Neal quotes papers to that effect, but the first well-documented scientific report deals with the 1916-1917 epidemic which soon became pandemic and persisted for at least a dozen years as a disease of winter months. It involved persons of all ages, but mainly between ten and thirty. Direct transmission was not shown to be a factor, and the incubation period appeared to run from several days to two weeks. The total number of victims is unknown, although in Britain the peak of the outbreak was reached with 5036 cases reported in 1924. In New York 1247 cases were admitted to mental hospitals between 1919 and 1939. Wilson states that mental signs remained in over half the cases who had them during the acute phase and were seen in about a third of all survivors below the age of sixteen. Other authorities estimate that about a

third of all the victims died, while another third suffered the progressive disorder and only a third recovered. Many of those subsequently disabled could give no history of an acute attack.

The subsequent course of the epidemic was no less mysterious than its origin. By 1930 it had apparently run its course, although sporadic cases were reported for the next decade or more and some authors were still reporting occasional cases in the 1960s. The *Lancet* published such a paper and raised serious questions editorially as to the diagnosis, but still was moved to ask: "If the infection has not vanished, does it perhaps lurk under other guise . . . and is recrudescence still a possibility?" This unanswered question still haunts the subject.

Pathology

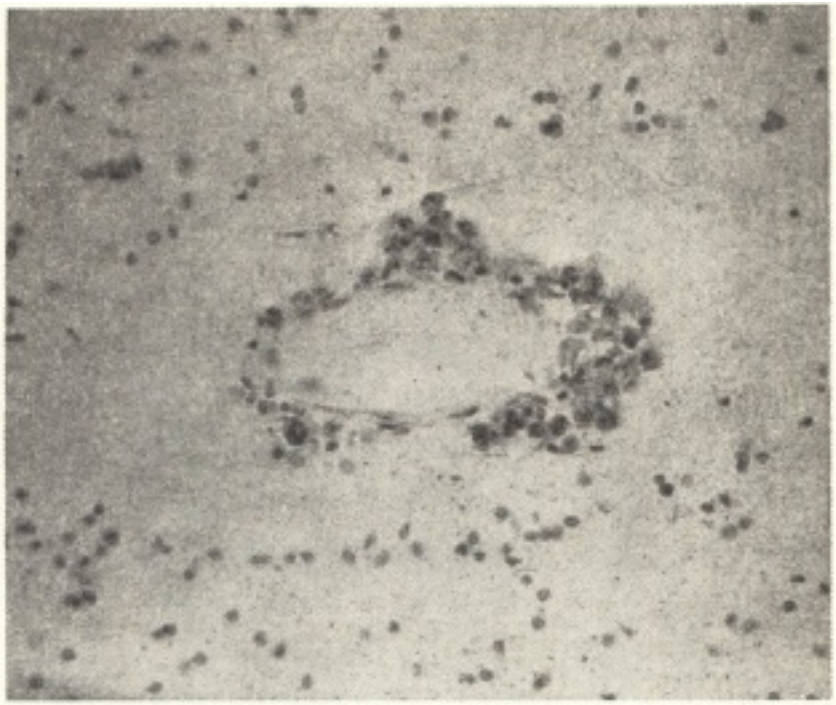
The acute lesion is nonpurulent and non-hemorrhagic, which distinguishes it from the bacterial infections and influenza, respectively. It is located in the gray matter of the brain and the cord, which separates it from various types of leukoencephalitis (measles, mumps, vaccina). Inflammatory perivascular reaction is usually severe, and microscopic foci are widely disseminated, particularly in the cortex (Figure 6-1), basal ganglia (Figure 6-2), hypothalamus, and periaqueductal gray matter of the brain stem. The substantia nigra is especially damaged (Figure 6-3), and this damage remains

a hallmark of the disease. In chronic cases the usual residuals of old inflammation are found, particularly in the basal ganglia and mesencephalon, but in addition, even after many years, new areas of active inflammation are to be seen in the same general distribution. The pathological findings are highly variable as to intensity and distribution, which is in striking contrast to the relative uniformity of the clinical typology.

Etiology and Pathogenesis

The etiology has always been assumed to be a filterable virus, even though no inclusion bodies have been described, no virus isolated, and no specific immune bodies identified.

Figure 6-1.

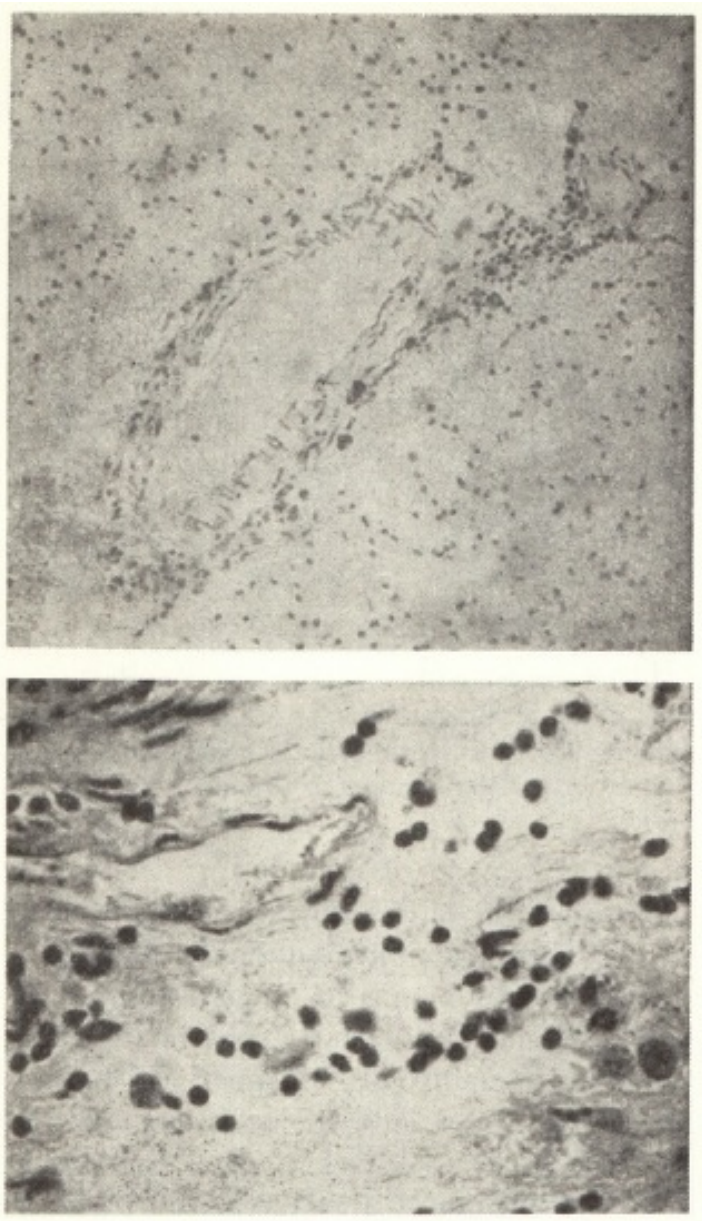


Cerebrum: White matter disclosing a blood vessel with enlarged perivascular space containing an inflammatory exudate (some macrophages are filled with yellowish or greenish pigmentation). Nissl stain; medium-power magnification.

Originally, theories as to pathogenesis revolved about the location of the neuropathology and the nature of the underlying psychopathology of the individual. It is perhaps a measure of the state of medical thinking at that time that social issues received no attention. The neuropathology did indeed indicate that the central gray was important for psychic functioning, and the damage to the basal ganglia and substantia nigra was correlated with the

Parkinsonian syndrome. Nevertheless, the available explanations were never adequate to account for the complex pattern of this disorder. Theories based on psychodynamics and personality studies were equally unsatisfying, and indeed most authors opposed the idea that this postencephalitic syndrome was simply a release phenomenon and an expression of underlying personality. As Rosner said, "The tragic feature is personality change, not personality exaggeration." A new chapter in the understanding of the pathogenesis of this disorder was opened in the early 1950s, and some of the mystery was dispelled when it was found that full doses of the tranquilizing agents of the phenothiazine and Rauwolfia series can reproduce many of the features of the chronic encephalitic syndrome in a quantitatively controllable, reversible, and nonprogressive form. Such symptoms include Parkinsonian rigidity, masked facies, tremor, salivation, and on occasion even oculogyric crises, dystonia, torsion spasm, and akathesia. Use of these tranquilizers may also precipitate emotional complications, especially depression, restlessness, and tension, all of which are seen in the postencephalitic syndrome. One can even see some parallel between the reusable stupor of acute encephalitis and that produced by heavy phenothiazine dosage.

Figure 6-2.

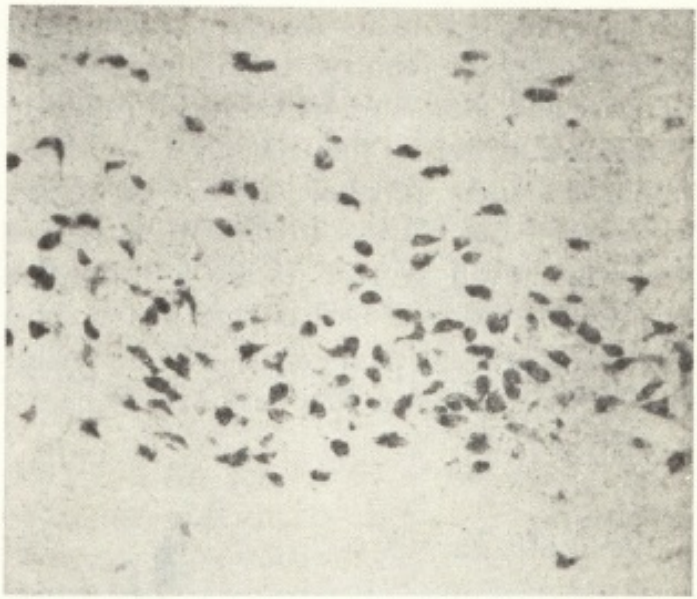


(top) An area in the globus pallidus revealing the presence of a perivascular inflammatory reaction. Nissl stain; low-power magnification.

(bottom) Perivascular inflammatory exudate showing predominance of lymphocytes. Nissl stain; medium-power magnification.

The significance of the curious parallelism between the tranquilizer-induced reactions and those resulting from lethargic encephalitis has since been further clarified by observations of the action of another drug, L-Dopa. This drug was originally developed on the basis of a hypothesis that the Parkinsonian symptoms were related to the observed depletion of brain dopamine, especially in the basal ganglia and

Figure 6-3.



(top) Substantia nigra of an adult (control case), (bottom) Depigmentation and pronounced loss of neurons in the substantia nigra in a postencephalitic Parkinsonian syndrome. Nissl stain; medium-power magnification.

substantia nigra. Dopamine itself proved ineffective, but L-Dopa, which is converted to dopamine in the brain, proved to be of value. It is thought to act as a neurotransmitter of inhibitory impulses, and counterbalances the central acetylcholine which is excitatory. A lack of dopamine appears to release an overaction of acetylcholine, and this imbalance is thought to be a fundamental cause of Parkinson's syndrome. It is of great theoretical interest that the new drug can itself initiate a wide variety of dose-dependent reversible psychiatric and neurological symptoms, because this gives further evidence that dopamine is indeed important in psychic as well as neurological functioning. All this has again directed major scientific attention to a study of the Parkinsonian syndrome, but this time it is at the level of molecular biology.

Psychiatric Symptoms

Perhaps the most difficult aspect of this singular disease to describe is the psychiatric symptomatology. To those who know the cases, chronic encephalitis has a high degree of specificity and a quality which can hardly be mistaken, but it is virtually impossible to identify and completely separate the components of the diagnosis. The physician's impression is constellative,

global, and composed of a blend of psychiatric, neurological, and vegetative symptoms and signs, no one of which is specific in isolation from the others. The psychiatric symptoms are not typically organic in nature, since memory and intellect are not impaired, and when they occur in the absence of other findings, there is nothing to distinguish this disorder from personality disorder, neurosis, hypochondriasis, or functional psychosis. Many postencephalitics were indeed treated under other diagnoses during their pre-Parkinsonian phase and correctly classified only as neurological symptoms emerged, often an event of chagrin and surprise for the psychiatrist.

Wilson comments that "despite variations the generic picture is curiously precise, but none the less cumbersome to define." This holds true of the psychiatric as well as the neurological aspects and, indeed, any separation between the two must be, to a large extent, artificial, since even the grossest postencephalitic Parkinsonian syndrome has functional components, while tics and characteristic compulsive and phobic symptoms are found so regularly associated with the disorder that it is hard to escape the conclusion that some organic factor underlies both. The view that symptoms are determined by both organic and dynamic factors as stated by Schilder seems entirely tenable. We will now consider some of the commoner postencephalitic subsyndromes.

Conduct Disorder

Especially in children, even before the onset of gross neurological symptoms, severe conduct disorder was a frequent sequel, beginning immediately after the acute infection or after a delay of months. Among the characteristics of the children, particularly the group aged three to ten years, were a marked destructiveness and impulsiveness, with a tendency to carry primitive impulses into headlong action. Children who had previously behaved normally, would he, steal, destroy property, set fire, and commit sexual offenses, without thought of punishment. The motivation was even less comprehensible and less subject to immediate control than in the so-called psychopathies, but the capacity for real remorse was strikingly well retained. A characteristic instability of emotion, coupled with disinhibition of action, led to serious aggressions, usually against others, but occasionally against the patient himself, resulting in gruesome self-mutilations. Institutionalization of these cases was imperative and led to the development of some of the early units for inpatient care of emotionally disturbed children, notably the one at Kings Park State Hospital in New York, in 1924.

In adults, conduct disorder was also a serious problem, although not to the same degree as in children. Yet the results were a serious problem, and a famous virologist whose father was a victim of this disease once commented to me that it had changed him from a well-known academician into “an

animal." Like the children, adults would express deep remorse and retained the capacity for self-criticism of their behavior, which seemed to have a compulsive quality. There was often a marked discrepancy between the good intellectual capacity and the primitive behavior. Such a patient was a "master of what he said" but, in his compulsive action, was a "slave of what he did." In the mental hospital these patients were known for their impulsive behavior and occasional aggressiveness, even though they usually made good emotional contact and could discuss things quite clearly. Lethargic encephalitis is described as being able to cause convulsive disorder in children; in very young patients mental deficiency is also a possible outcome.

Cases of conduct disorder due to Von Economo's disease are now no longer seen. They were usually at their worst before the onset of obvious neurological symptoms, and the behavior problems gradually disappeared as the neurological disability advanced. In addition, of course, childhood cases have long since ceased to appear.

Schizophrenic-like Reactions

Reactions similar to schizophrenia have been described, but true schizophrenia is quite unusual, and, on closer examination, these are seen to be pseudoschizophrenias. The emotional reaction is shallow and often dull and apathetic, but it is still postencephalitic and not schizophrenic. Delusions

of reference and hallucinations may occur, but they are superficial and lacking in schizophrenic symbolism. Certain of the motor rigidities of encephalitis lethargica sometimes bear a superficial resemblance to catatonia, and various paranoid reactions, especially of transitory nature, also occur. Paranoid hallucinatory and delusional syndromes are sometimes due to atropine-type medications but are usually a part of the postencephalitic picture. They are distinguished from schizophrenia by the absence of the usual schizophrenic disorders of emotion and thought and the lack of autism. Actually, the postencephalitic patient tends to manifest strong dependency needs, and this leads to a clinging relationship which is quite the opposite of schizophrenic withdrawal, and his ability to discuss and control his problems is also different in quality from that seen in schizophrenia. This aspect of the chronic encephalitic reaction is well described by Schilder.

Depression

A strong tendency to depression is reflected in the characteristic whining voice, clinging manner, and dependent and complaining attitude. Depression often centers about the physical symptoms, and is hard to distinguish from hypochondriasis. Self-accusations and delusions of guilt may take the form of a monotonous plaint whose pattern is perhaps so strongly colored by the facies, the voice, and the bradykinesis and bradyphrenia that it seems different from ordinary depressions. The pleading, demanding, and

impatient clinging resembles what one sometimes encounters in epileptics. The content tends to be of an organic depressive nature. Euphoria is described but is relatively unusual.

In a review of 201 cases of postencephalitic Parkinsonism, Neal found pathological depression listed nine times, psychotic depression eight times, and hypomania eight times, but depression of the pattern described above is far more frequent.

Hypochondriasis

Patients may complain of almost all forms of physical discomfort. These include pains, burning, tension, restless feelings, shooting sensations, and dead feelings, as well as hypochondriacal concern about heart, lungs, stomach, etc. Verbal productions are often marked by a compulsive quality and are full of expressions of frustration, impatience, and discomfort, but these are difficult to evaluate since the disease attacks neural elements throughout the central nervous system; often the patients leave the impression that they may be suffering from something akin to central pain.

The response to placebo is striking and could well shake the confidence of the strongest organicist; no patients are more suggestible or more readily pacified for a short time by a new therapy. Yet they are equally suggestible with respect to some of the gross neurological symptoms and can even be

brought to suppress the Parkinsonian tremors for brief periods of time. In this connection they seem to be manifesting an organically determined disorder of volition.

Eye Findings

Among the most common complaints are those centered about the eyes. The patients seem to be trying to verbalize some indescribable sense of discomfort, and indeed, their eyes often appear congested and uncomfortable. Some of this must be laid to loss of eye blink and the long periods of rigid stare with resultant fatigue and discomfort in the muscles and periocular tissues, but the oculogyric crisis as yet remains without full explanation of either functional or organic type. It is now reproduceable chemically with some of the phenothiazines and with L-Dopa. In postencephalitics it is strongly associated with other psychiatric symptoms such as forced thinking and stereotyped ideas or a compulsive preoccupation with the eyes of others. Attacks may be periodic and fairly regular but are usually irregular. They may be controlled for a time by an effort of will, but the patients do not consider the attacks as subject to volition since they complain, “My eyes turn up,” and not “I have to turn my eyes up.” The usual direction of gaze is upward, but variants include forced gaze in other directions and combinations with postural distortions. Attacks may last from minutes to hours and may be interrupted only by falling asleep.

Other ocular complaints include burning, blurred vision, photophobia, shooting pains, macropsia, micropsia, and visual distortion. Here too one can identify functional components, but disorder of the visual neurological apparatus is extensive, and these patients also suffer from various opthalmoplegias, often with diplopia, and show pupillary anomalies and accommodation difficulties. The staring, unblinking expression and masklike greasy facies may suggest the diagnosis at first glance.

Work Capacity

Loss of work capacity is sometimes given little emphasis in psychiatric descriptions, perhaps because it is not obvious in the examining room, and it often seems to be assumed that this impairment is, somehow, secondary to other factors. However, in a number of neuropsychiatric disorders and especially in the postencephalitic state, as well as in other conditions with brain damage, impairment of work capacity can be a leading symptom and a disability of its own, not strongly correlated with other signs or symptoms and highly resistant to therapy. As yet little studied, except in relation to vocational and other types of rehabilitation, this problem is prominent and persistent in postencephalitics, may antedate gross neuropsychiatric findings, and quite commonly continues after they are brought under control by medication; it may be related to the chronic sense of fatigue often described and to slowness of thinking or bradyphrenia.

Neurological and Vegetative Symptoms

Parkinsonism is by far the commonest finding. This is characterized by masking of the face, loss of blink, and in the extremities a characteristic rhythmical tremor, rigidity, and loss of associated reflexes. It is less frequent in children and has a marked tendency to progress. Onset is characteristically insidious, local and asymmetrical; it spreads gradually to other parts of the body, becoming more intense and more general, until the fully developed syndrome is present. The motor disability, even when severe, may be briefly reversible, sometimes in a spectacular manner. The author once saw a severely incapacitated former boxer, who had been annoyed for days by a fellow patient, suddenly recapture his motor capacity with great effect, and then lapse again into a full Parkinsonian state. On command, such patients can regularly suspend their tremor for a short time, and catch a ball or carry out some other brief coordinated task, but despite pride in their performance, they do not initiate it themselves. The moment they relax, the rigidity and rhythmical tremor take over again. Gait is characteristic and diagnostic. Associated movements of the arms and trunk are impaired or lost. The arms do not swing, and in the fully developed syndrome the body is carried "en bloc." In addition, there are almost always bizarre changes and motor distortions. The patient leans conspicuously, usually forward but sometimes backward or to the side; he sidles, or shuffles along with some typical oddity of movement; often it looks like a tic blended into the walk. Among the

variants are propulsive gait, a tendency to lean forward and walk always faster in a half run which may not stop till the patient reaches a point of support, or retropulsion—-a similar tendency to walk or run backward. The usual postencephalitic compulsive quality characterizes these symptoms too.

Rigidity is of cogwheel type and asymmetrical. Tics and mannerisms of many kinds are seen, among them torticollis, facial grimaces, and movements difficult to distinguish from torsion spasms. The tremor, which is a rhythmical rest tremor, ceases only during sleep; it is most often seen in the upper extremities but may involve other parts, especially the legs, jaw, and tongue, in various combinations. Among the rarer syndromes are cataplexies and myasthenoid disturbances as well as chorealike movements. All of these bear the stamp of the basic disease.

The speech of the well-developed case is highly characteristic, and the many varieties have a common denominator. The voice is monotonous, nasal and somewhat singsong, and often trails off into nothingness, as does the writing, because spasm increases as the activity progresses. Frequently observed is palilalia, a needless repetition of words or phrases. Sometimes dysarthria is prominent, and sometimes bradykinesis; often, refuge is taken in a few hastily spoken words, followed by staring silence.

Hypersalivation is the most prominent of the purely vegetative findings

and, combined with the masking and stiffness of the face and lips, often leads to drooling. Among the wide variety of other neurovegetative disturbances are seborrhea of the face, irregularity of respiration often of bizarre form, marked adiposity (sometimes with polydipsia and polyuria), disturbances of appetite and of sleep, lability of temperature control, excess perspiration, and pupillary irregularities.

Course

The chronic syndrome may follow the initial infection immediately or after a latent period which may last for many years. Once neurological symptoms have been established, the usual course is irregularly progressive although static cases have been described. Pregnancy, trauma, infection, or other stress can produce exacerbations. A majority of the cases now seen in ordinary clinic and hospital practice give no history of acute encephalitis, although sometimes a story of illness with diplopia or hypersomnia can be elicited. In this respect the sequence is analogous to that of paresis.

Differential Diagnosis

Diagnosis rests on the neurological and neurovegetative findings and the history of progression. This disorder is distinguished from Parkinsons disease by the asymmetry and irregularity of the symptoms and the bizarre additional elements. The postencephalitic form is also to be distinguished

from the many nonprogressive types of Parkinsonian syndrome. None of these has the vegetative findings or the typical encephalitic disturbances of gait, station, and behavior. Poisoning by carbon monoxide or manganese, cerebral trauma, and Wilson's disease may also produce basal ganglion symptoms, and these are similarly differentiated. Parkinsonism due to medication may combine with a neurological disability of other origin to produce puzzling syndromes, but the matter becomes clear when medication is withdrawn.

In the case of a child with pure behavior disorder, diagnosis poses a more difficult problem, and in the absence of at least minor specific progressive neurological findings, or of a known outbreak it would seem that the diagnosis of encephalitis lethargica should not be made.

Treatment

Treatment of the chronic encephalitic syndrome remains symptomatic. Medication, regimen, psychotherapy, and psychosurgery are all used, and effects in the psychic, somatic, and social spheres reinforce each other.

Medication

The pharmacological therapies are, in general, used according to schedules which call for titrating drugs against symptoms, the end point

being a satisfactory effect, or symptoms of toxic overdose, whichever comes first, and often the two are not far apart. The topic is so complex as to forbid a complete review of all drugs in this paper, but drug-induced Parkinsonism has made this type of treatment commonplace, and there are many excellent descriptions; one example is Chap. 72 in the 1971 *AMA Drug Evaluations.*

Three general classes of drugs are now available, the anticholinergic, the antihistamines, and the newer drugs levodopa and amantidine. The anticholinergic drugs tend to lose their effectiveness with continued administration, and for this reason a fairly complex pharmacy is necessary, but shifts from one to another medication should not be made abruptly. The anticholinergic group produces atropinelike side effects and one must watch for such complications as prostatism, glaucoma, and serious loss of accommodation for near vision. Temperature control may also be impaired, and this is doubly important because it appears that this function is already weakened by the encephailitis, and deaths from heat stroke can occur. Fortunately, the newer anticholinergics have far less peripheral effect than the original drugs which they have now virtually replaced. The older drugs include atropine itself, scopolamine, hyoscyamine, stramonium, and bellabulgara. In addition, the amphetamines once had considerable vogue.

The anticholinergic drugs in current use are synthetic and include trihexyphenedyl HCl (Artane, Pipanol, Tremin HCl), biperiden (Akineton),

cycrimine HCl (Pagitane) and procyclidine HCl (Kemadrin).

The antihistamine-type drugs are of weaker action, have fewer side effects and are used chiefly to potentiate the effects of the anticholinergics or for patients who cannot tolerate the more potent drugs. They include diphenhydramine HCl (Benadryl), chlor-phenoxamine HCl (Phenoxene), and orphen-adrine HCl (Disipal). Benztropine mesylate (Cogentin) is described as intermediate between the anticholinergics and the antihistaminics in therapeutic potency and side reactions.

Both L-Dopa and amantidine appear to be effective in postencephalitic Parkinsonism and seem to represent a distinct advance in practice as well as theory. L-Dopa (levodopa) influences all the symptoms, akinesia, ridigity, and tremor being benefited in that order. Toxic effects are frequent and include mental symptoms and various types of involuntary movement. It appears that in the present state of knowledge, L-Dopa is best reserved to treat the exacerbations of the postencephalitic state and to give relief in the intractable cases. Amantidine is also effective but far less dramatic. It has milder side effects, is additive to the anticholinergic drugs and does not appear to establish tolerance. Where, for any reason, the anticholinergic drugs are withdrawn, the process should be gradual to avoid serious aggravation of symptoms.

Regimen

All authors acknowledge that the general management of the patient is important. Adequate nutrition, regular exercise within the limits of the patient's capacity, maintenance of interest and activity, moderate recreational interests and hobbies, physiotherapy, vocational training, and rehabilitation where indicated, are all important elements. On the other hand, overstress is harmful, and excess fatigue is to be avoided. Alcohol is usually poorly tolerated and is not advised. Above all, an optimistic constructive attitude on the part of the physician is crucial.

Psychotherapy

Complex psychotherapeutic techniques have been described by various authors, but I am inclined to agree with Bosner quoted by Neal, that "effective psychotherapy in chronic encephalitis still demands a rather primitive dependence on rapport between patient and doctor." While there are limitations, the psychotherapeutic modalities which are available should be tried. Used in conjunction with the drug therapy and regimen, they can produce marked amelioration of an otherwise intolerable existence.

Neurosurgery

Neurosurgery has been reserved for far advanced intractable cases of

postencephalitic Parkinsonism. Destructive lesions of the globus pallidus, the thalamus, the subthalamic region, and even the internal capsule have all been reported as producing desirable results. When successful, these procedures improve both rigidity and tremor on the opposite side of the body, with corresponding general improvement of symptoms. Bilateral operations are common. Among the earlier operations were cortical excisions to control tremor and rigidity, and nerve sections for torticollis.

Other Postencephalitic States

The spectacular experience with encephalitis lethargica focused medical attention on encephalitis as a cause of neuropsychiatric disorders, and within a few years a number of new entities were identified. The first was St. Louis encephalitis described in 1933. Others include Japanese B encephalitis, Australian X disease, and Murray Valley encephalitis.

The late 1960s have seen spectacular advances in virology due to such technical improvements as new methods of virus culture, the use of the electron microscope for identification, and the development of new immunological techniques, such as immunofluorescent staining methods. As a result the number of identified viruses has greatly increased and various types of viral encephalitis are being diagnosed and reported routinely. They remain, however, more important from the point of view of public health than

from that of psychiatry, because in most types the acute attack generally ends in complete recovery, although death rates are sometimes high. When residuals do occur they are nonspecific and nonprogressive, and their treatment belongs to that of the organic syndromes. Certain rare types of chronic progressive encephalitis have, however, been identified and because of this fact and because the various forms of encephalitis do represent a variety of central nervous system pathology, these viral infections do have some psychiatric interest. A brief discussion of several of the more important types of viral encephalitis is presented here. For a more exhaustive account of the virology, the reader is referred to the comprehensive report by Whitty et al.

Encephalitis Due to Arbo Viruses (Arthropod-Borne)

These include St. Louis, Japanese B, equine, and California encephalitis, and Colorado tick fever, some sixty types in all. They vary widely as to morbidity and mortality; recovery with severe sequelae is not unusual. The residual defect is nonspecific and therapy is that of the focal and diffuse syndromes which follow. Many of these disorders occur in epidemic form.

Hemorrhagic Encephalitis

Hemorrhagic encephalitis has been known for at least 200 years. It may

complicate many types of infection but is most frequently associated with influenza. Recovery with serious damage is reported even in the older literature. The lesion is nonprogressive, nonspecific, focal and/or diffuse, and the treatment of these postencephalitic states is that of the chronic brain syndrome which follows.

Postinfectious Encephalitis (Leukoencephalitis)

Postinfectious encephalitis is a variety occasionally seen after many viral infections, especially the exanthems, and the statement is often made that within recent years such reactions have become more frequent.

After infection with such viruses as varicella, variola, measles, mumps, vaccina, or after rabies vaccination, acute demyelinating encephalomyelitis may develop very rapidly. This is primarily in the white matter and tends to center about the venous system. The nature of the reaction remains obscure; it is not considered to be due to a direct attack of the virus on the nervous tissue but probably represents an immunologic allergic mechanism similar to that of experimental allergic encephalomyelitis. The location of the offending virus, the site of autoimmune body formation, and the nature of the reaction remain to be explored. Thrombosis of small vessels and areas of necrosis and hemorrhage are found. When recovery occurs, it is usually complete, but there may be severe residuals with hemiplegia, convulsions, mental defect,

and behavior disorder. Such syndromes may be also due to vascular lesions of unknown mechanism which can complicate a wide variety of systemic infections in children.

Other Types

Among the types left to be discussed, the slow, latent, or chronic types are especially interesting. The demonstration of "slow" measles virus as an etiological agent in encephalitis of children is of great theoretical importance even though the condition is relatively rare. This virus attacks the parenchyma directly, invades the cells and replicates within them and is thus quite different in mechanism from the encephalitis which is generally caused by the exanthems. It is of insidious onset, and generally progresses with increasing cerebral symptoms such as mental deterioration and myoclonus to a fatal outcome within a year. Measles can also cause the usual leukoencephalitis like that following other exanthems.

Amantidine has been reported as checking the spread of slow measles encephalitis, which is now thought to include several disorders previously known under such names as subacute sclerosing panencephalitis (SSPE) (Pette Dohring), subacute sclerosing leukoencephalitis (Van Bogaert), and Dawson's inclusion body encephalitis. Another form of slow virus infection known as Kuru is found only in New Guinea among the Fore people where it

appears to be of relatively recent origin. It takes the course of a fatal degenerative cerebellar disease, but it has been shown to be transmittable to chimpanzees. Other forms of chronic virus encephalitis have been identified in humans and in animals (Cytomegalus virus, fetal rubella, visna and scrapie in sheep, mumps in hamsters, etc. So far as is known today, such disorders are rare in humans, but the potential implications of these discoveries is obvious.

Another important recently discovered viral encephalitis is that due to herpes simplex. Now considered to be the commonest cause of nonepidemic encephalitis, it often leaves severe neuropsychiatric residuals. It does not belong to the "slow virus" group.

Finally, one may note that virus infections of the central nervous system may be not only latent or chronic, but they may also not be demonstrable by ordinary neuropathological techniques. Such viruses may produce disease by causing dysfunction in morphologically intact but infected neurons.

What such findings may mean for neuropsychiatric practice remains to be seen. At the very least, the door has been opened to diagnosis, prevention, and even treatment of some relatively rare obscure diseases which till now were thought to be degenerative. The preponderance of evidence today seems to be against assigning a significant role to the virus infection with respect to major psychiatric problems such as the highly controversial MBD.

But virus infections have surprised us before, and as Sabin has pointed out, they may do so again. The scene for such a surprise may have been set by the laboratory demonstrations of chronic latent virus infection of the central nervous system. For this we find clinical support in the observation that clinical symptoms of viral encephalitis may break out when immunosuppressant drugs are used.

It is to be expected that we shall hear much more on these issues in the near future. It does not seem likely that interest in the viral forms of encephalitis will again be lost as happened after the 1916-1930 epidemic.

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