THE LATE SEQUELÆ OF ENCEPHALITIS LETHARGICA AND OF INFLUENZA

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WITH the passing years the disastrous consequences of* encephalitis lethargica have become only more apparent. For we have here no acute disease like poliomyelitis, which rapidly runs its course, with complete or, more often, slow and partial recovery from the attack; rather, the virus (still unidentified) of encephalitis lethargica, like that of syphilis, may remain active for years within the nervous system, causing by recurring outbursts, by slow inflammatory lesion, or by gradual disappearance of the nerve cells in the basal ganglia, increasing disability to the patient. It would thus be more logical to speak of chronic encephalitis lethargica than of the sequelæ of encephalitis lethargica.

As a general rule, those who have suffered severely in the initial stages are more prone to develop serious after-effects, but many cases are seen with marked Parkinsonian stiffness who have never had a frank attack of encephalitis. Most of these patients, however, give on close questioning a history of preceding illness (which may have passed for influenza), but which was associated with passing double vision, intractable pains of unusual distribution, or marked drowsiness; some, as Economo maintains, may have had merely a slight febrile attack with pharyngitis, or even no symptoms at all.

Parsons, in the British Ministry of Health Report, estimates that for every 100 cases of encephalitis lethargica notified, there are about 50 to 75 which are not notified, and of these a varying proportion escape discovery altogether owing to the mildness of the attack and the absence of serious sequelæ. On the other hand, in 15,935 *notified* cases, from 1919 to 1927, in England, there was a mortality of 47.8 per cent, the great majority of deaths occurring within three weeks of onset; Economo found a mortality of 40 per cent in the acute, fully developed cases, but reckoned that when all the mild ambulatory forms are included, the death rate would sink to 15 per cent, a figure corresponding to the estimate of the American Association for Research in Nervous and Mental Disease.

It appears from the figures of the British Ministry of Health that about 25 per cent recover from the acute attack sufficiently to pursue their usual occupations, though some of these still show clinical evidence of the infection overcome, while 50 per cent of all attacked suffer from sequelæ, of whom a half develop the Parkinsonian syndrome. The figures of Economo for all clinically well developed cases are: 40 per cent mortality; 14 per cent, complete recovery; 26 per cent recovery with some defect but sufficiently to continue work; and 20 per cent, chronic invalidism.

In every country, it is noted that, in some instances, the acute phase of the disease passes gradually into a chronic state, while in others, serious sequelæ appear at varying intervals (from months to several years) after apparent recovery from the primary attack of encephalitis.

CLINICAL FEATURES

The most common sequela is the development of the Parkinsonian syndrome. Though emerging sometimes from the acute phase of encephalitis, the symptoms more frequently develop after a latent period of some months, or even of four or five years. The patient complains of being tired mentally and physically. One arm may cease to swing automatically in walking and is held by the side flexed at the elbow; some stiffness of the neck muscles appears; possibly a little rhythmical tremor is seen in the upper extremity, though tremor is much less common in the Parkinsonian syndrome than in paralysis agitans, which it so closely resembles. The facial muscles lose their mobility and the expression becomes fixed, with widely open and seldom winking eyes; the speech is monotonous; the neck is bent forward, the spine held stiffly, the gait shuffling. The face often has a peculiarly greasy appearance from abnormal sebaceous secretion. The heightened tone of the muscles is more marked around the shoulder and hip than in the hand, in

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contrast with the condition seen in ordinary hemiplegia. Once present, the Parkinsonian syndrome persists. It may remain stationary for a long period, with occasionally slight improvement, but in the majority of cases, the patient gradually or by slight exacerbations becomes more helpless and is finally confined to the house and, later, to bed. Mental impairment accompanies the physical slowness though its degree varies; while many patients remain calm and apathetic, some are acutely aware of their unfortunate condition and are greatly depressed. An added tragedy is the comparative youth of most of the sufferers. Thus of 36 Parkinsonian patients in Birmingham, 30 were under 40 years, an important point in the differential diagnosis from paralysis agitans.

Second only in importance to the Parkinsonian syndrome are the *mental changes* which follow encephalitis lethargica. Particularly tragic is the fate of many children and young adults; bright, well balanced children become irritable, unable to concentrate, often drowsy by day, and extraordinarily wakeful and restless, even maniacal, by night. Marked changes in character and conduct occur. Excitable and impulsive, disobedient and untruthful, they often become mischievous, violent and criminal; asocial and uncontrollable at home, they are dangerous at school, appear often in the juvenile court, and sometimes have to be committed to an institution. Of 1,136 English school children attacked in 1924 by encephalitis lethargica, 300, or 26.4 per cent exhibited some degree of mental change, and in more than half this number, this change was severe. And Economo states that, of those children so attacked, two-thirds do not improve, while the English reports seem at least equally discouraging. One must remember that many of the young people exhibiting changes in character and conduct show also physical disabilities, sometimes of the Parkinsonian syndrome, sometimes one of the numerous sequelæ of encephalitis.

Ocular defects are common—paresis of accommodation, squint, diplopia, ptosis, nystagmus. Residual paralysis of the face muscles or of the extremities is, however, quite rare. The obscure pains of neuritic, sometimes of central, origin which may occur at the onset, associated often with myoclonic jerkings, rarely persist. Obesity and polyuria occasionally develop, and interesting respiratory sequelæ (of which paroxysmal or continuous attacks of rapid breathing are the most important) may occur.

In many cases, the patients are simply weak, depressed, and apathetic for a long time, while the *inverted sleep rhythm*, with extreme restlessness at night, combined with drowsiness by day, may long baffle therapeutic measures.

PATHOLOGY

The naked eye appearances of the brain show little abnormal, possibly a little congestion, a stray, minute hæmorrhage in the gray matter of the mid-brain. Microscopically, as Economo insists, the degenerative changes and disappearances of ganglion cells form the primary picture. The cells affected are those of the substantia nigra (especially prominent in the Parkinsonian syndrome) of the corpus striatum and optic thalamus, around the third ventricle and, to a less extent, of the cerebral cortex and pons. Associated with, and secondary to, these changes in the ganglion cells are inflammatory changes, indicating even in long standing cases the activity of the virus. These inflammatory changes consist of perivascular "sleeves" of lymphocytes and plasma cells around the veins and collections of glia cells, ultimately forming small scars mainly in the gray matter of the upper part of the mid-brain.

TREATMENT

The treatment of chronic encephalitis lethargica has been recently summarized by the Matheson Commission in most discouraging terms, and Professor Hall's verdict is endorsed:—"Any reliable therapeusis, either for the disease itself or for its many after results, does not exist." It is true, however, that Economo urges, even in chronic cases, the use of iodine in the form of Pregl's solution, or of 10 per cent sodium iodide solution (100 c.c. intravenously once a week for 10 to 15 weeks). Other remedies endorsed by individual physicians are acriflavine, and also 30 to 50 c.c. of a 2½ per cent solution of sodium salicylate in normal saline, intravenously twice a day for 7 to 10 days.

In the Parkinsonian state, there is no question of the value of hyoscine in relieving the stiffness and tremor, and in making the patient more comfortable. The drug can be used for years with safety and does not seem to lose its effect. One may begin with 1/150 grain twice a day and gradually increase to two, or three times this dose, reducing the amount if dryness of the mouth or difficulty in reading develops. Hyoscine relieves also the excess of saliva so often com-

plained of, and even other complications, such as abnormal sexual craving which is exceptionally met with.

The general regulation of the patient's life in food, sleep, work, etc., is most important. Intractable insomnia is sometimes helped by the intramuscular injection of 2 c.c. of milk; sun baths, light baths and massage have their place in particular cases. The problem of the management and disposal of young adults with varying mental change and with marked alteration of character and conduct is peculiarly difficult, even impossible, to solve satisfactorily.

THE SEQUELÆ OF INFLUENZA

The relation of influenza to encephalitis lethargica has been much discussed, some causal connection between the two diseases being assumed by many physicians, owing to their coincident prevalence. But the very different infectivity, clinical course, pathological findings and sequelæ in the two diseases, make it very unlikely that there is a common infecting agent, though in neither disease has the virus been unequivocally isolated.

The respiratory tract bears the brunt of the acute disease and is the site of the leading sequelæ of influenza. Acute infection of the nasal sinuses is extremely common during the influenzal attack, and often persists indefinitely, with the Pfeiffer's bacillus as the infecting organism. Chronic otitis media is similarly common. Following bronchitis and peribronchitis in the acute attack, the bronchial wall may become softened and readily distended so that dilatation gradually develops with in after years, the characteristic evidence of bronchiectasis; from the sputum in these cases, Pfeiffer's bacillus is sometimes isolated. Pleural effusions, generally purulent, were common following the broncho-pneumonias so generally present in severe attacks of influenza. These empyemata were the most frequent cause of continuing temperature with pulmonary involvement, and were not infrequently interlobar or "pocketed". Bronchial breathing and bronchophony often persist over these empyemata, a finding not sufficiently recognized by the profession. Displacement of the apex of the heart if present is significant, while the repeated use of the exploring needle and of the x-rays is essential in all doubtful cases, and is often resorted to, far too late.

Tuberculosis and influenza.—Cases of chronic tuberculosis are sometimes aggravated and incipient cases activated by influenza, but there is no statistical evidence that the number of cases of tuberculosis has shown any noteworthy increase since 1918, contrary to the prevalent notion that influenza predisposes to tuberculous infection. It must be remembered that following influenza, for many months, cough and physical signs suggestive of tuberculosis may persist, due to a slowly resolving influenzal pneumonia. Repeated examination of the sputum is advisable if the signs are at the apices and a guarded opinion may be advisable temporarily.

Occasionally tachycardia, palpitation, and precordial pain may occur for months after influenza, but it is remarkable how little the heart is permanently damaged by the disease—a fact which has been stressed by authorities like MacKenzie and Christian. Thrombosis of arteries is extremely rare; thrombosis of veins is more frequently seen, sometimes with resulting embolism.

Nervous disturbances.—Convalescence is often very slow. The patient is very weak, tires easily mentally and physically, and may be despondent. These neurasthenic symptoms pass off only gradually in the course of months.

Peripheral neuritis of varying types is not uncommon. Post-influenzal psychoses, particularly dementia precox, occur occasionally.

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PANTOCAINE.—Pantocaine is a new compound intended for local anæsthesia. According to a report of Dr. Kiess its advantage compared with novocain is that the duration of anæsthesia is much longer, up to five hours, even in a weaker than the usual novocain solution. For anæsthesia by infiltration a 0.5 per cent solution was used and also in lumbar, sacral, and splanchnic anæsthesia. For anæsthesia by loss of nerve conduction a higher concentration, up to 5 per cent, was necessary. Sometimes headache and vomiting developed but without any serious consequences. Dr. Wiedehopf, of the Marburg University Clinic, points out too that pantocaine is longer efficacious and less toxic than novocain, that it has no irritating effect and that it has proved valuable in infiltration and lumbar anæsthesia. It is moreover less expensive than novocain.