REFRESHER COURSE FOR GENERAL PRACTITIONERS**EARLY DEMENTIA**

BY

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As a social phenomenon premature or early dementia constitutes one of the major tragedies seen by medical men. It seems unbelievable that a man apparently in the prime of life should suddenly begin to fail to find the names of common objects or take to wandering aimlessly in the streets around his home, or that the housewife should become incapable of managing a familiar household or be unable to find her home on returning from shopping. Even worse is the failure of judgment in social, professional, or business matters so that the sufferer makes mistakes in habitual work which may involve a family in distress or ruin. This same failure of judgment resulting from intellectual decay is the cause of gross errors in living—the appearance of unwonted alcoholic habits, sexual follies, and extravagance.

Certain mental illnesses in young persons have been formerly labelled primary dementia. It is not proposed to include here what is now called schizophrenic illness among the early dementias.

What is dementia, and when is it early? The term "dementia" is restricted to mean a gross impairment of intellect in a hitherto normally developed individual. Dementia has to be distinguished from amentia, which indicates absence of intellect or mental deficiency. It is worth recalling the words of Esquirol: "The demented man is deprived of the good that he formerly enjoyed: he is a rich man become poor. The ament has always lived in misfortune and poverty." What is early dementia? It is a dementia appearing at any time before the senium, when the processes of old age inevitably cause some intellectual deterioration.

Dementia is a term we are apt to use loosely to cover many disturbances of conduct and habit due to a varied pathology not necessarily associated with intellectual decay. It is essential to keep clearly in mind the precise meaning of our terms in dealing with early dementia. It must be distinguished from physiological senescence, which is a natural process to which we are all subject sooner or later. Senescence comprises a narrowing of interests and a varying failure of intellect and memory. Other characteristics are a tendency to resist departure from routine and the adoption of conservative attitudes with an inability to compromise. All this is normal and without pathological significance, and is in sharp contrast to senile dementia and what are now to be briefly described as the *early dementias*.

Their causes may conveniently be divided into six main groups, as follows:

1. *Vascular Disorders of the Brain.*—(a) Arteriopathic dementia; (b) hypertensive encephalopathy.
2. *Inflammatory Conditions of the Brain.*—(a) Syphilis; (b) epidemic encephalitis.
3. *Degenerative Conditions of the Brain.*—(a) Huntington's chorea; (b) Pick's disease; (c) Alzheimer's disease.

4. *Deficiency Diseases.*—(a) Pellagra; (b) Korsakoff's psychosis; (c) Wernicke's encephalopathy.

5. *Neoplasms.*

6. *Trauma.*

Arteriopathic Dementia

Arteriopathic dementia results from arteriosclerosis of the cerebral vessels, which it is important to remember can be more advanced in the cerebral arteries than in the rest of the vascular system. Dementia can result either from ischaemic changes or from the results of multiple focal lesions which interfere with the functioning of the brain as a whole, so that advanced dementia can develop rapidly when thromboses are frequent.

Patients are about 50 years of age when symptoms first arise, and progress is so rapid that in five years the doctor may be dealing with a demented wreck.

Insomnia is a frequent initial symptom, often accompanied by somnolence by day. This disturbance of the sleep rhythm leads to confusion and motor restlessness at night, with anxiety and depression as prominent features. The patient often complains of severe headaches and giddiness. Memory loss is progressive. Superficially, the personality may be well preserved. In older patients a condition of "elated chattiness," in which memory losses are compensated for by extensive confabulations, constitutes the syndrome known as *presbypsophrenia*.

During the early phases of cerebral arteriopathy there are disturbances of the habitual pattern of conduct in which sexual misdemeanours are sometimes prominent. Progress is rapid, and death can result from vascular cerebral lesions at any time.

Hypertensive Encephalopathy

When hypertension is prominent in an arteriosclerotic, "crises" of severe headache, clouding of consciousness, and drowsiness or delirium with excitement may occur. When repeated, such crises lead to a condition of progressive dementia. Renal involvement resulting in uraemia is not infrequent.

Treatment

In general, the treatment of vascular conditions of the brain should be preventive. The earliest diagnosis of arteriosclerosis will enable some effective measures to be taken. The life of the patient must be closely examined and regulated to reduce physical and mental stress to a minimum. Regular periods of absolute rest in bed at week-ends, for example, may be necessary. Some sedation is wise in the case of arteriopathic patients, whose activities must be reduced without undue interference with their accustomed routine.

In hypertensive crises the immediate treatment must aim at the reduction of increased cerebrospinal pressure by lumbar puncture. Severe attacks, accompanied by grave neurological signs, such as transient weakness in the limbs, difficulty in speech, or epileptiform fits, should be treated by rest, strong sedatives, a sodium-free diet, and the administration of tetraethyl ammonium bromide or the methonium compounds (C5 or C6).

Syphilis

Syphilis of the central nervous system may lead to an early dementia which can progress rapidly and become profound.

General paralysis of the insane is a progressive parenchymatous degeneration of brain cells with secondary meningeal and glial reactions. A common fallacy persists about the symptomatology of this disease. Many doctors still expect grandiose ideas to be presenting symptoms of the disorder. In fact, such delusional symptoms are now uncommon. It is more usual to encounter a dementing patient with ideas of unworthiness and sin or with paranoid notions of persecution by others.

G.P.I. is less common than it was at the beginning of the century, and if diagnosed and treated early 35% of sufferers are able to return to their habitual work. The condition is roughly four times as common in men as in women, except in the juvenile form resulting from congenital syphilis, when the sexes are equally affected. The usual age of onset is from 35 to 50 years. An average of 12 to 15 years elapses from the date of the original infection with syphilis. Taboparesis combines the pathology of *tabes dorsalis* and paresis. The dementing process is perhaps rather less rapid than in an uncomplicated G.P.I. Some taboparetics show a very gradual onset and a tendency to spontaneous remission in which the disease dies out even without treatment.

Symptoms vary greatly. The patient will often attend his doctor for vague "neurotic" symptoms, or his relatives will complain that he is "changed" and has become irritable and forgetful, and careless of appearance and daily work. Then character changes will become pronounced: gluttony, alcoholic excesses, sexual follies, silly suicidal attempts, and senseless stealing may all appear suddenly and get the patient into trouble with police or other authorities. By this time an anxious family will be taking active steps to secure care and control for the patient. Often it will be found that there has been a period, even a year, during which subtle changes of character have been present and medical opinion may have been sought. In these early stages the patient has a capacity for covering up his indiscretions, and few neurological signs may be present. Yet early diagnosis is essential to success in treatment. Certain cases are sudden in onset and manifest themselves by acute depression or a sudden excitement. An occasional case starts with epileptiform attacks as either grand mal or petit mal. It is easy to overlook the signs of paresis in such cases. Untreated, the progress of the dementia can be desperately rapid.

The essential step in diagnosis is lumbar puncture. This will reveal a lymphocytosis in the fluid up to 200 cells (averaging 60–100), an increase of total protein and a positive globulin reaction, a strongly positive Wassermann reaction, and a paretic reading from the gold-sol test (Lange) tubes; for example, 5555432100 is a typical result for this test.

Treatment

The discovery of penicillin is likely to effect a great improvement in the treatment of parasyphilitic disease of the nervous system, and it is possible that it may supplant the malarial therapy of Wagner-Jauregg, introduced in 1917. At present it is better to give both penicillin and malaria. Immediately diagnosis is made penicillin can be begun and the patient infected with malaria. Give half a million units of penicillin intramuscularly daily for 24 days—a total of 12 million units. This will often result in considerable improvement, and most patients are then well able to put up with the undoubted strain of the malarial rigors, which should be continued unchecked to the number of at least 10. Very special nursing and medical supervision are essential during malarial therapy, and laboratory facilities for parasite counts are convenient. Having stopped the rigors with antimalarials (quinine, mepacrine, proguanil, etc.), the patient can be left to convalesce over a period of 6–12 weeks. Lumbar puncture must then be performed and the cytology and reactions of the C.S.F. checked. There should be material improvement—a fall in the cell count, weakening of the Wassermann reaction, a fall in globulin, and a change in the Lange reaction, which may be expected to continue to be abnormal for 12 months after treatment is ended. A persistent increase in the cell count in the C.S.F. for 12 weeks after the end of treatment indicates the need for a fresh course of penicillin.

It is worth while repeating that success in treatment depends on early diagnosis.

Epidemic Encephalitis

This chronic infection of the nervous system is mentioned on account of the sequelae which arise as the result of an acute encephalitis, possibly undiagnosed, and recognized only in retrospect as having occurred some years before.

There is neurological evidence of parkinsonism, with increasing rigidity of the limbs. Accompanying these signs of extrapyramidal involvement there occur apathy and depression, which in time may be succeeded by an insidious and progressive dementia—in contrast with the absence of dementia in paralysis agitans.

Treatment

Treatment consists in a cheerful supportive attitude towards the patient and encouragement to take up some occupation rather than sitting in chairs and staring into space. Drugs are useful in relaxing the rigidity: the following may be tried: Hyoscine by mouth up to 1/50 gr. (1.3 mg.) three or four times daily. Tincture of stramonium from 60 to 90 minims (3.6 to 5.4 ml.) three to four times daily. The antihistamine group of drugs is also sometimes useful, care being taken to avoid them if they induce prolonged drowsiness. One dose is best given at night and another in the morning.

Some of the antispasmodics have excellent effects—e.g., the preparation known as "artane" (trihexyphenidyl). This is given in doses of 2 mg. on the first day, increasing by 2 mg. a day until a total of 6 to 10 mg. daily is being taken with meals. Nausea accompanied by dimness of vision may occur, when the drug should be discontinued for a week and resumed at a lower dosage. Other useful antispasmodics are: "Lysivane" tablets (ethopropazine hydrochloride), starting with one or two 50-mg. tablets and increasing to a total of six or eight tablets (300–400 mg.), administered in

two daily doses. "Thephorin" (phenylmethyltetrahydroazofluorine), one tablet of 50 mg., can be tried, also increasing slowly up to six tablets. A preparation found useful by me is an elixir of "myanesin"; it is given in doses of two to four drachms (7 to 14 ml.) once to six times daily according to the severity of the condition. A combination of an antihistamine and an antispasmodic may be tried if both are well tolerated.

Degenerative Conditions of the Brain

Huntington's Chorea

This is a heredito-familial degeneration of the nervous system which manifests itself between the ages of 30 and 50 and is characterized by choreiform and athetotic movements and ultimately by a profound dementia. As the disease develops, the patient is tortured by an unending muscular writhing and jerking of the limbs. This is accompanied by a constant grinning and nodding of the head, which the patient attempts vainly to control.

Mental changes vary considerably. At first there is a diminution of higher control: delicately nurtured women will use obscene expressions in strangely coarse conversations. Patients sometimes get into serious trouble with their own families. Early mental and moral changes entirely foreign to the individual and his entourage may precede the diagnostic movements. Later, dementia becomes profound, though in some cases it is more apparent than real, and the personality can occasionally be remarkably well preserved. Memory loss is pronounced and increases throughout the illness. Progress is rapid, and ends in a wasted, restless body and a mind without memory, incapable even of recalling the names of common objects. Death occurs from an exhaustive state or intercurrent infection within 12 to 15 years of the diagnosis being made.

The disorder is unique in psychiatry in being inherited as a pure Mendelian characteristic. It behaves as a dominant, so that from one-quarter to one-half of the offspring of a sufferer is bound to develop the disease. It is transmitted through many generations, and Kennedy* quotes over 1,000 cases in the United States as having been traced to three individuals who emigrated from a Suffolk village in 1630.

Pick's Disease (1892)

There is increasing evidence that Pick's disease is also a familial disorder. It shows itself between the ages of 40 and 60, but may occur earlier or later. Characteristic of the disease is the prominence of localizing or focal neurological signs as opposed to the ill-defined signs present in Alzheimer's disease. Apraxias, agnosias, and other localized disturbances, accompanied by increasing apathy and withdrawal of interest from habitual affairs, contrast with the absence of localizing signs and the general motor restlessness of Alzheimer's dementia. The inexorable progress of Pick's disease is accompanied by increasing memory losses, intellectual deterioration, and moral impoverishment.

Alzheimer's Disease (1906)

There is no well-established genetic factor in the aetiology of this early dementia. It shows itself between

the ages of 40 and 60 and is more inclined to resemble a senile decay at an abnormally premature age. Early symptoms are memory losses, disorientation in space, and an increasing slovenliness in appearance. Slurred speech is an early sign. This condition progresses to a restless motor activity, a complete lack of memory and comprehension, and reiteration of stereotyped phrases in speech. Throughout the whole course of the illness epileptiform seizures may occur. The patient early becomes bed-ridden and incontinent from a rapid physical decline.

Pathology and Treatment

In all these degenerative conditions there is a generalized neuronal degeneration, with an overgrowth of glial tissue, so that the post-mortem appearance of the brain is one of shrinkage and flattening of the convolutions with widening of the sulci and dilatation of the ventricles. In particular, the degenerative process in Huntington's chorea is especially marked in the corpora striata; in Pick's disease the process tends to be localized in the frontal and temporal regions, often demonstrable in life by air encephalography. In Alzheimer's disease the degenerative process is widely diffused in the cerebral cortex, with a special concentration in the motor cortex.

No treatment has any effect on the course of these early dementias. Mental hospital care is usually the best means of ensuring the protection such unfortunates require.

Deficiency Diseases

Remarkable conditions of early dementia are met with as a result of deficiency diseases. The causes of some are:

Pellagrous Encephalopathy

The well-known skin lesions resemble sunburn, and occur on the backs of the hands, the face, the neck, elbows, and, in natives without shoes, on the feet. At first an erythema, the lesion becomes a dermatitis and finally an exfoliative thickening of the skin. The tongue shows a characteristic appearance of rawness and redness; this is associated with a generalized stomatitis which makes swallowing painful. Mental changes occur, often introduced by a phase of excited delirium. If the deficiency is not relieved the disease progresses to a state of dementia with marked apathy and intellectual decay.

The condition is due to a deficiency of nicotinic acid (pellagra-preventive factor) and is apt to appear when the diet lacks fresh milk, eggs, and lean meat. It occurs sporadically in the United Kingdom, and is sometimes seen in elderly people with inadequate means to ensure a well-balanced diet. It also occurs at times in institutions in which too little care is paid to variety in diet.

The condition responds readily to nicotinic acid, and as much as 100 mg. should be given daily for the first 10 days.

Korsakoff's Psychosis

This is usually seen in association with long-continued alcoholic habits, but is now known also to occur with poisoning by lead or arsenic, and in association with infections, of which the commonest is typhoid. It is also seen with head injuries and hyperemesis gravidarum.

The psychosis consists of profound memory disturbances with compensatory confabulation and romancing. There is loss of relation in time (disorientation), and vivid visual and auditory hallucinations occur in some

*Kennedy, A. (1949). In *Modern Practice in Psychological Medicine*, edited by J. R. Rees. Butterworth, London.

cases. Physically there is a polyneuritis with absent tendon reflexes and marked tenderness on pressure over nerve trunks. These conditions result from a thiamin (vitamin B₁) deficiency, which arises from diminished absorption of thiamin due to an alcoholic gastritis, loss of food as in vomiting, or from lack of vitamin B₁ in some invalid diets. It would seem that the cases of head injury in which the psychosis occurs often give a history of chronic alcoholic habits.

Treatment consists in the administration of thiamin in sufficient doses. It can be given as baker's yeast, half an ounce (15.5 g.) three times a day, or in tablets in synthetic form in doses up to 3,000 international units daily. Thiamin can also be given intravenously in acute conditions up to 32,000 international units at one injection.

If the psychosis is of considerable standing a residual dementia often remains after peripheral nerve lesions have been cleared.

Wernicke's Encephalopathy

This condition is mentioned, as it has been regarded as an effect of alcoholism. It can occur with any long-continued deficiency of thiamin in the diet, and should be thought of where there are gross psychological upsets in chronic diarrhoea, hyperemesis, or carcinoma of the stomach. Acute excitement suddenly occurring in a person of alcoholic habits with neuritis and ocular signs such as nystagmus is suggestive of this encephalopathy.

Treatment consists in giving thiamin at once in adequate doses.

Neoplasms

Space-filling lesions within the skull may give rise to symptoms of an early dementia. Intellectual deterioration, loss of memory, apathy, and disturbances of consciousness and sleep are frequent. In frontal tumours there can be antisocial conduct and an absence of wisdom and moral sense which leads to unfortunate behaviour characterized by lack of restraint and discrimination. In the case of frontal tumours such changes in personality and intellect are not necessarily accompanied by florid neurological signs and symptoms, such as headache, vomiting, and papilloedema. The practitioner is well advised, when confronted with symptoms suggesting an early dementia in persons between 30 and 55 years of age, to think of a possible neoplasm.

Treatment, of course, consists in accurate localization and surgical removal of the tumour when possible.

Trauma

Serious head injuries involving destruction of cerebral tissue can lead to a great reduction in intellectual efficiency. This deterioration may end in a progressive and early dementia, particularly in those cases complicated by post-traumatic epilepsy. It is important to have the degree of deterioration measured accurately by one of the recognized batteries of intelligence tests. Thus, in the treatment and rehabilitation of such patients the reduced capacity for intellectual work should be known to the patient and to the officers of the Ministry of Labour who have the task of finding suitable employment.

When early dementia appears as a late effect of a head injury common-sense measures are as effective as the more specialized approaches of psychiatry. Reassur-

ance, occupation within the limits of capacity, and instruction of the family of the patient in his management are the essentials which can be undertaken by the practitioner. Such patients require much tolerance on the part of others, and to keep them at their occupation may require indulgence on the part of doctor, employer, and relatives. Some cases are reduced to "pottering" about garden and house, carrying out simple menial tasks. Alcohol should be forbidden, sleep should be assisted if necessary, and careful use of anticonvulsants should be prescribed where epilepsy is an additional complication.

THE NUFFIELD ENDOWMENTS

The sixth report of the Nuffield Foundation¹—the largest endowed charity of its kind in Britain—contains a note of warning. A decrease in State spending upon some social and intellectual purposes may be inevitable in the years immediately ahead, and this will mean that bodies like the Foundation may be faced with difficult decisions between, on the one hand, sustaining even such minimum activities as may be endangered by enforced public retrenchment and, on the other, encouraging new proposals which must, in the sharpening competition for scarce support, find it even more difficult to command a hearing.

Meanwhile the report is a record of continuing benefactions, especially in support of biological and sociological research. In the medical field it has never been Nuffield policy to subsidize work on specific diseases, with the single exception of chronic rheumatism. On this rather unrewarding research it spent large sums at a time when the subject was as unscientific as it was unfashionable. With the advent of cortisone there has been no shortage of medical and other scientists to work upon the new clues, but at first there was a shortage of the expensive American products for test. Some months ago Merck and Company, Inc., made a gift of one kilogram of cortisone jointly to the Medical Research Council and to the Foundation for scientific purposes and trial in Great Britain, and a joint committee of the two bodies has been set up for the allocation of this gift. Grants have also been made during the past year for a survey of the incidence of rheumatism in East Anglia, for a study of tendons, cartilage, and tissue components and their structural organic chemistry, and for an attempt to synthesize cortisone from ergosterol. The Foundation has also financed an objective assessment by the British Orthopaedic Association of over 2,000 patients who have had surgical treatment for osteoarthritis, and grants to clinical units at London, Edinburgh, and Bath have been renewed for a second year.

Many fundamental biological and social studies have been assisted. Several years ago in the Department of Child Health at the University of Durham a study of infant mortality was undertaken, and afterwards this was extended to a study of morbidity as well. The investigation, which began with the study of a thousand Newcastle babies, has become the study of a thousand families, and the Foundation is further meeting the salary of an additional whole-time worker who will specialize in a combined epidemiological and bacteriological investigation. A grant of £1,000 a year for five years has been made to the Physiological Department of the University of Cambridge with a view to furthering certain advances in neurophysiology. Another has been made to the Department of Chemical Pathology at University College Hospital Medical School for the investigation of problems relating to the pyrrole pigments (including haemoglobin and porphyrin) in health and disease.

A new medical fellowships scheme, with preference for those wishing to train for teaching or research in child

¹The Nuffield Foundation. *Sixth Report*. 1951. Oxford University Press.

²Oxford University Gazette. Supplement to No. 2706. June 15, 1951. 6d.