

DEPRESSIVE ILLNESS AND NEUROLOGICAL DISEASES

- AN OVERVIEW

- Dr. Dinshaw R Doongaji

Introduction

All human beings have experienced the feeling of depression at one time or another. However, a normal depressive state is not the same thing as a pathological depressive illness.

A pathological depression is a profound all pervasive disturbance in the feeling state or mood which can secondarily effect the individual's thinking and behaviour. In contrast to feelings, a mood state is prolonged over a period of time. It may or may not be triggered off by a set of circumstances. It is severe in intensity and it seldom remits without treatment.

Depression is recognised by a triad of classical symptoms or signs. The first symptom is depression of the mood. In pathological depression the mood is miserable, sad, sorry, suicidal and all pervasive. The patient cannot snap out of it. The second symptom is poverty of ideas. The patient complains that he cannot think, that he forgets easily. He has no self- confidence. He has gloomy pre-occupations. He visualises failure at work, in finances, in family life and in social life. The third symptom in psychomotor retardation. The patient walks and talks slowly. Everyday activities require a great deal of effort. He puts off doing things which he would otherwise do willingly and effortlessly.

Biological symptoms like a characteristic depressive insomnia during the later part of the night may also be present. The circadian rhythm may be disturbed. The patient feels worse during the early part of the day and then progressively better as the day advances. Autonomic symptoms like loss of weight, loss of appetite, loss of libido, constipation and a mildly elevated blood pressure can be present. The patient may complain of somatic symptoms e.g. vague pain for which there is no medical explanation. Some expressed patients develop psychotic symptoms like auditory hallucinations in the form of voices which condemn them or order them. There may be delusions of guilt or worthlessness or somatic delusions about body parts or their functions.

The documented association between neurological illness and depression is not of recent origin. Seventy years ago, Emil Krapelin recorded the co-existence of both elation and depression in the same patient and called it manic depressive psychosis. He observed that depression is often complicated by atherosclerotic brain disease. In 1922, Babinski noted that specific emotional states may be associated with a specific brain injury e.g. injury to the right hemisphere and the emergence of euphoria.

Depressive mood disorder and neurological disease interface in three ways: First, depression can precede a neurological disease as in dementia. Secondly, depression may accompany a neurological disease as in Parkinson's disease. Lastly, depression can follow a neurological disease as in post-stroke depression.

Over the years, depressive illnesses have been classified in various ways. A simple clinical way is to recognise two kinds of depression. One which is reactive to the disability and one which is not necessarily or exclusively reactive in origin. Many neurological disorders are associated with depression. The list includes dementia, epilepsy, Parkinson's disease, multiple sclerosis, neoplasms, cerebrovascular disorders, Huntington's chorea, Wilson's disease, brain trauma, progressive supranuclear palsy, magraine, hydrocephalus and brain infections.

Some drugs have also been reported to cause depression as a side effect. These include opiate analgesics, barbiturates, NSAIDs and anti-hypertensive drugs like reserpine, alpha methyl-dopa etc.

Depression and Dementia

Depression and anxiety are early features of Alzheimer's dementia. Although depression can be an early sign of dementia, it is not significantly more common in dementia than in age matched controls.

Several studies have also shown that a true progressive dementia later develops in a high percentage of these patients who have depression as their first symptom.

Symptoms develop slowly in the demented patient. Depressive mood is not the presenting symptom. The emotions tend to be labile and superficial. The demented patient is disinterested more than dejected. Autonomic symptoms of depression like loss of appetite, loss of weight, constipation and dryness of mouth may be quite prominent. Early morning insomnia and diurnal mood swings are frequent. The demented depressive patient is very likely to demonstrate delusions of guilt, phobias or somatic and nihilistic delusions. There is a tendency to be critical and irritable. Behaviour is characterised by incapability and social withdrawal. Failure of attention, concentration, memory and drive are prominent. A varying amount of impairment of cognitive and intellectual abilities can be seen. These symptoms are variable and the patient can be persuaded to concentrate for short periods of time.

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The Dementia of Depression (Pseudodementia)

Some depressed patients complain bitterly of profound memory loss and other cognitive symptoms. As these are secondary to the emotional disorders, they constitute a pseudodementia and not a true dementia.

Both depression and dementia share many common symptoms such as forgetfulness, poor concentration, lack of motivation and loss of interest.

Several factors may explain why some depressive patients show cognitive abnormalities. These can be due to personal predisposition, activation of hysterical mechanisms, cerebral metabolic abnormalities, changes in level of arousal and as a part of the general of psychomotor retardation.

The ageing process affecting the brain such as the neuronal loss may combine with the neurochemical changes in depression and lead to cognitive failure. It is these chemical and physiological alternations which are responsible for both depression and the cognitive changes. Therefore, this syndrome should be considered to be organic in origin and should be labeled as dementia of depression rather than pseudodementia.

Table No. 1 shows the differences between true dementia and the dementia of depression (Pseudodementia).

Between Pseudodementia and Dementia*

Table No 1		
	PSEUDODEMENTIA	DEMENTIA
Clinical course and history	<ol style="list-style-type: none">1. Onset fairly well demarcated2. History short3. Rapidly progressive4. History of previous difficulty or recent life crisis.	<ol style="list-style-type: none">1. Onset indistinct2. History quite long before consultation3. Early deficits often go unnoticed4. Previous psychiatric problems or emotional crisis uncommon
Clinical behaviour	<ol style="list-style-type: none">1. Detailed elaborate complaints of cognitive dysfunction2. Little effort expended on examination items3. Affective change often present4. Behavior does not reflect cognitive loss5. Rarely has exacerbation at night	<ol style="list-style-type: none">1. Little complaint of cognitive loss2. Struggle with cognitive task3. Usually apathetic with shallow emotions4. Behavior compatible with cognitive loss5. Nocturnal accentuation of dysfunction common
Examination findings	<ol style="list-style-type: none">1. Frequently answers "I don't know" before even trying2. Inconsistent memory Loss of both recent & remote items3. May have particular memory gaps	<ol style="list-style-type: none">1. Usually will try on items2. Memory loss for recent events worse than remote3. No specific memory gaps.4. Rather consistently

	4. In general performance is inconsistent	impaired performance.
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Treatment

Anxiety and depression can adversely affect intellectual and adapting functions of the patient with dementia. It is important to treat these problems. The anxiety and confusion are especially more obvious at night. The insomnia and restlessness may also be produced by aches and pains and simple analgesics may be preferable to hypnotics.

Barbiturates should be avoided as they can cause confusion and depression. Chloral hydrate 500 mg, diphenhydramine 25 mg and promethazine 10 to 25 mg are useful hypnotics in demented depressives.

Short acting benzodiazepines like lorazepam 0.5 to 2 mg or alprazolam 0.25 to 1.5 mg are better than long acting drugs like diazepam as there is less risk of accumulation. For motor agitation, small doses of neuroleptics like haloperidol 0.25 mg or thioridazine 10 to 25 mg can be used. Haloperidol has the least action on autonomic lability. Used antidepressants are trazadone, nortriptyline, dothiepin, etc. It must be remembered that the geriatric doses of most psychotropic drugs are close to the paediatric doses and it is advisable to start treatment with the lowest possible dose.

Most neuroleptics and antidepressants have anticholinergic side-effects. There is an acetylcholine deficiency in Alzheimer's dementia and drugs with high anticholinergic side-effects can be detrimental. In patients with prostatic enlargement or glaucoma, these side-effects can cause urinary retention or increase in the intraocular tension.

Dothiepin is an effective antidepressant with anxiolytic action and has lesser anticholinergic side-effects. An added advantage of dothiepin is that it also has sedative action which helps when sleep disturbances occur in depression.

Hypnotics and tranquilizers can be used on an SOS basis, but antidepressants should be administered daily for several weeks or months. As there is a degeneration of the nerve cells in dementia, drugs which increase cerebral blood flow like cyclospasmol, pyritinol or piracetam are not useful. Most recently, drugs which alter acetylcholine transmission are undergoing trials. To date their usefulness is not convincingly established.

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Parkinson's Disease and Depression

Parkinsonism is a relatively common neurological disease. Mild depression can be a prodromal feature in a small proportion cases. More commonly it occurs some time later in the course of the disease in 30 to 45% of cases. Like many other types of depression this is also common in females than in males. It is equally common in post-encephalitis, arteriosclerotic or idiopathic cases of Parkinson's disease.

An association between depression and Parkinson's disease is well established. Parkinsonian patients have a much higher incidence of depression than other patients of the same age who have physical disabilities. It is also more frequent in those patients who have accompanying dementia.

The depression can be reactive. It sets in as soon as the patient is informed about the nature of the disease, or later as a result of limitations due to the disability. This may lead to a reluctance to co-operate. About 25 to 50% of patients with Parkinsonism develop intellectual deterioration as the disease progresses. The severity of dementia correlates with the severity of Parkinsonian features especially the bradykinesia.

As opposed to bradykinesia, there is a bradyphrenia or subcortical dementia in Parkinson's disease. This is recognised by an undue delay in the production of appropriate verbal responses in a co-operative patient who has no communication difficulties. It is due to slowing of the mental processes and not of the motor processes. The psychological difficulties observed are changing mental concepts, defective attention and motivation.

Psychological defects similar to bradyphrenia are also seen in depression. This relationship between affect or mood and speed of cognition is closely linked, and there may be an overlap between depression and Parkinsonism.

The mesocortico-limbic system may be impaired in both conditions. Reduced turnover of dopamine, serotonin and nonadrenaline has been reported in retarded depression.

In some cases, the degree of depression is disproportionate to the degree of disability. The depression may respond to antidepressants or electroconvulsive treatment (ECT) while the disability may not.

Parkinsonian patients with depression exhibit hopelessness, pessimism, decreased motivation, increased pre-occupation with health and emotional lability. Impaired short term memory which is a feature of primary endogenous depression is absent. There is less self blame, guilt, worthlessness and self destructive feelings or behaviour compared to primary endogenous depression.

Treatment

The effect of L-dopa on mood is variable. Most patients experience an improvement in the mood. However, depression and suicide have also been reported, especially if the depression was present prior to starting L-dopa treatment. Antidepressants and electroconvulsive treatment effectively relieve the depressive symptoms and are not contraindicated. As a matter of fact, improvement in the Parkinsonian symptoms is seen sometimes during a course of ECT.

Changes in mood after stereotaxic surgery are also variable. Depression often improves after ventrolateral thalamic nuclei surgery. However, a high incidence of anxiety and depression in the first nine months after surgery has also been reported. The varying results may be explained by the pre-morbid psychiatric status of the patient, the precise site of the lesion and the effects of surgery.

Epilepsy and Depression

Epilepsy and depression are both common conditions and depression is a frequent complication of epilepsy. This has been observed since antiquity even as far back as in the time of Hippocrates.

The depression can be related ictally or post ictally.

Ictal depression occurs with temporal lobe seizures, during status epilepticus, petit mal status and partial seizure status. Fears and depression are the commonest ictal experiences.

Interictal depressions are common in patients with late onset epilepsy, in children, and in complex partial seizures. There is a relationship between declining fits and emerging depression. The longer the duration of epilepsy the more severe the depression. There is no relationship between depression and the age of onset of epilepsy, or frequency of epilepsy. Depression is more closely related to temporal lobe epilepsy than to other types of epilepsy. The depression can last for months. Laterality of lesion responsible for depression reported is controversial as both dominant hemispheric as well as non-dominant hemispheric lesions have been involved.

60% of epileptic patients with depression have interictal dysthymia or reactive depression. Endogenous depression can also occur. It is more common than mania.

The neurotic or reactive depression is accompanied by fluctuating anxiety and dysphoria in the form of sporadic irritability and aggressiveness.

The onset and subsidence of depression tends to be sudden and the mood disorder fluctuates markedly. Paranoid features frequently accompany the depression as well as depersonalisation, anxiety and hostility. There may be family history of depression in more than 50% of cases.

The suicidal rate is higher among epileptics than in the general population. The mortality is higher among mentally abnormal epileptics. Temporal lobe epileptics carry the greatest risk. Suicidal attempts are more common than successful suicides and multiple attempts are seen in 50% of cases, The ratio is twice as greater in men than in women. Most of them use their current antiepileptic medication for suicidal purposes.

Patients receiving carbamazepine are the least depressed while patients receiving phenobarbitone are the most depressed. The level of psychopathology correlates positively with phenobarbitone and negatively with carbamazepine.

Low foliate levels in serum, RBCs and CSF have been demonstrated in epileptics with mental symptoms including depression. Folic acid supplements do not influence the onset or prognosis of the depressive state. However S-adenosylmethionine which is involved in folate metabolism seems to have antidepressant properties. The folic acid metabolism is least affected by carbamazepine and sodium valproate.

Treatment

Epileptic patients need a higher dose of antidepressants. All non-MAOI and some MAOI antidepressants lower the sedation threshold and can potentially aggravate clinical seizures. Therapeutic doses of antidepressants can do this in predisposed individuals who have a family history of epilepsy, existing brain damage or previous history of electroconvulsive therapy. Patients receiving anticonvulsants demonstrate lower antidepressant level than patients who are not receiving anticonvulsants. Tricyclic antidepressants when given in high doses to patients receiving anticonvulsants may precipitate seizures, hence adjustment of dose of anticonvulsants may be required.

Electroconvulsive therapy is not contraindicated in epilepsy and can be life-saving in suicidal epileptics. Some epileptic patients may have a higher seizure threshold for ECT.

Reduction in polypharmacy may improve the medical state in some patients and so also can switching

over to carbamazepine treatment.

In conclusion, the common psycho-social variables in epilepsy with depression are the chronicity of the disability, repeated unconsciousness leading to morbidity, uncertainty, loss of self esteem, social stigmatisation, difficulty in finding a job and loss of dignity. The implicated biochemical abnormalities are, disorders of noradrenaline, dopamine, serotonin, and gamma-aminobutyric acid metabolism and malfunctioning of the hypothalamic, pituitary axis and disturbances in folic acid metabolism.

Post Stroke Depression

Depression is the commonest emotional disorder to follow a stroke. Anxiety reactions occur in 14 to 27% of patients following a stroke, while 30 to 50% of patients develop depression within 6 months of 2 years after a stroke.

There is some acceptance of the idea that mood disturbances represent a psychological response of the individual to severe stress. Patients with a self sufficient pre-morbid personality react more adversely than those with dependency needs. Those who have previously experienced anxiety and depression and those with unsatisfactory family relationships also react adversely.

Among the incriminating factors are included physical handicap, uncertainty about the future, enforced dependency, imposition of an invalid role, loss of job, loss of status, financial problems and a sense of uselessness.

Physical handicap however does not cause depression. But once it occurs it remains thereby creating a vicious circle.

It is common in patients with nonfluent aphasia than in those with global aphasia. But this aphasia does not produce the depression nor can it be accounted for by age or impaired social functioning.

Both the size and site of the lesion correlate independently with the degree of intellectual impairment.

Increased ventricle brain ratio reflection subcortical atrophy existing before the stroke may be an important predisposing factor.

The depression can be either major or minor. Major depression is associated with frontal or basal ganglia injury and may produce depressive pseudodementia. Minor depression is not associated with cognitive disturbances. Major depression after stroke may remit in a year's time, while the minor depression may linger on.

In 54% of the cases the lesion is in the region of the middle cerebral artery, while 245 are associated with lesions in the brain stem or cerebellum.

Left hemispheric lesions have been consistently shown to give a much higher incidence of both catastrophic anxiety reactions and depression . These lesions produce depression with cognitive impairment especially when anteriorly placed.

Right hemispheric lesions are not usually associated with cognitive impairment. If the right hemispheric lesion is anteriorly placed, it can be associated with cheerfulness or euphoria rather than depression.

Major depression following right hemispheric lesion may have a different aetiology than major depression following left hemispheric lesion. A significantly higher frequency of family history of depression has been observed in these patients.

Anterior left sided lesions produce depression by disrupting biogenic amine pathways. The noradrenergic and serotonergic pathways around the brain stem, hypothalamus and basal ganglia and the frontal cortex are involved. Significant depletion of brain serotonin and noradrenaline have been demonstrated in these cases which may be casual.

Right hemispheric lesions may produce depression as the expression and organisation of emotion are located in the right hemisphere.

Treatment

Nortriptyline is the drug which has been most frequently reported to be useful in post-stroke depression. The dose ranges from 25 mg to 150 mg per day.

Cerebral Tumors and Depression

Depressive changes rarely occur by themselves in tumors. They often accompany other mental manifestations. Irritability in the early stages is later succeeded by anxiety and depression. Impulsive suicidal attempts may be made during paroxysms of headache.

Frontal and temporal locations of tumour are associated with the greatest frequency of both depression and personality disturbances. The frontal location is characterized by irritability, depression or euphoria, and apathy. Irritability is a frequent presenting symptom.

Euphoria is as common in temporal lobe tumours as in frontal lobe tumours. It can be associated with intellectual impairment, anxiety, anger, hypomania. Manic symptoms have also been reported. The mental changes are commonly seen with dominant hemisphere lesion associated with dysphasia.

Parietal lobe tumours are less likely to produce mental changes than frontal or temporal lobe lesions. Parietal lobe lesions produce early neurological signs and are less likely to be missed or mistaken for a psychiatric disorder. Depression may occur. This may be associated with cognitive disturbances like dysphasia and apraxia acalcutia (gerstman's syndrome finger agnosia, dyscalculia, dysgraphia, right/left disorientation) when the dominant lobe is affected: Tumours of the non dominant lobe are often associated with visuospatial difficulties, typographical disorientation, dressing apraxia or body image disturbances.

Headtrauma and Depression

Major depression can also occur after minimal trauma both in the presence or in the absence of object signs of brain injury.

Depression is the most common emotional reaction to head injury.

Depression occurring after head injury may be related to the patient's insight to the cognitive and physical disability due to the trauma, the pre-morbid personality, and the family and social support systems during recovery.

The features may be those of a "reactive" depression. Anorexia and insomnia may be present. The depression responds to changes in activity and environment. The patient complains of difficulty with concentration and minor defects of forgetfulness and irritability. There are paranoid and hypochondriacal symptoms, a fluctuating headache, marked anxiety and depression and neurasthenic symptoms, the patient constantly complains of excessive mental and physical fatigue. The symptoms may last for many months after the injury.

Rapid cycling bipolar illness where alternate elation and depression lasting only for a few hours a day has been reported after closed head injury. No definite relationship can be demonstrated between the severity and site of trauma and the psychological symptoms.

Chances of death by suicide is considerably increased after head injury, accounting for 14% of all deaths. The factor responsible for suicide include financial difficulties, family quarrels due to disability, marital problems, difficulties in adjustment, difficulties in interpersonal relationships, excessive drinking etc. Significantly, a change in the character of the person, after the injury has been observed in 40% of patients who committed suicide.

Huntington's Chorea and Depression

Psychiatric changes may be present for some time before the onset of involuntary movements or intellectual impairment

There is a change in personality. The patient becomes morose, slow, apathetic, quarrelsome, neglectful and paranoid.

The anxiety and depression may be apparent right at the outset and may be ascribed to some depression event.

The depression can be severe in the early stages when the patient still retains insight. Later on the mood becomes apathetic, self neglect and euphoria replace the depression.

The incidence of affective disorders has been reported to be as high as 41%, the depression predating the chorea by 2 to 20 years in 66% of the cases.

Depression can be severe and suicide is a definite risk. In some reported series of 102 patients, 10 attempted suicide while 13% self mutilated.

The depression responds to antidepressant drugs and electroconvulsive therapy.

Systemic Lupus Erythematosus and Depression

The functional psychoses in SLE can be depressive, schizophrenia like, or rarely, manic.

Chronic psychotic depression is commoner than schizophrenia like states.

Neurotic reactions in the form of anxiety and depression can also occur. The depressive reaction starts gradually, lasts several weeks or months and resolves slowly.

The cause of the functional symptoms is obscure, their reversibility and recurrence suggests that they may be related to the disease process. On the other hand they may be in response to the psychosocial stress due to the illness. The vasculities and ischaemia can result in symptoms of confusion or dementia.

Steroids which are the mainstay of treatment in SLE can precipitate or aggravate the mental symptoms. These may respond to a reduction in dose of the steroids.

A patient in remission who is on steroid medication may develop depressive psychosis. The steroid could be gradually withdrawn, monitoring DNA antibodies at the same time. The titre falls if the disease is suppressed. A high titre or rising titre when the patient is on steroids will help to differentiate whether the psychosis is due to the disease itself or due to the steroids.

Immunosuppressive drugs like cyclophosphamide and azathioprine can be tried instead of steroids. Antidepressants and E.C.T. can be used for treating the depression.

Multiple Sclerosis and Depression

Though rare in India, multiple sclerosis is the commonest demyelinating disorder. Depression is as common as euphoria in multiple sclerosis.

The depression is seen in the earlier stages while euphoria is more typical of the later stages. The frequency of depression is from 6 to 27%.

In majority of instances the depression is reactive due to the psychosocial stress as a result of disability Sphincter disturbances, impotency, ataxia, impotency, ataxia, visual disturbances and increasingly dependency are the most distressing reasons.

The depression can be severe and suicide is 14 times commoner than in the general population.

Inspite of cheerful outward appearances many euphoric patients report feeling miserable and depressed.

Some amount of emotional liability and rapid changes of mood are often present. Intellectual impairment often accompanies these changes.

Recommended Reading

1. Dementia, A Clinical approach J M S Pearce 1984. Blackwell Scientific Publication, Oxford.
2. Neurobehavioral Disorders. Richard L Strub and F, William Black, 1988. (F.A.Davis & Co) Jaypee Bros. New Delhi.
3. Organic Psychiatry. Wiliam Alwyn Lish man 1987. Oxford Univ. Press Delhi.
4. Synopsis of Psychiatry Harold Kaplan and Benjamin Sadock 1988. William & Wilkins Baltimore MD
5. Psychopharmacology of Epilepsy, 1985, (Ed.) Michael Trimble, John Wiley and Sons, Chichester
6. Clinical use of anticonvulsants in Psychiatric disorders,1989. Robert Post, Michael Trimble, C E Peppinger, Demos Publications, New York.
7. Mood changes after right-hemisphere lesions, Sergio Starkstein, et al., Brit. J. of Psychiatry. 1989; 115: 77-85.
8. Lateralization of Depression in stroke patients Karen Bolla Wils et al Amer J of Psychiatry 1989; 154 : 170-187.
9. Neuroanatomical studies of major affective disorders. Dilip V Jeste et al Brit J of Psychiatry 1988; 153 444-459.
10. Affective Disorders and Cerebral Vascular Disease Sergio Starkstein and Robert G Robinson Brit J of Psychiatry 1989;154, 170-187.
11. Overview of Depression and Psychosis in Alzhemier's Disease, Robin E Wragg and Dilip V Jest Amer, J of Psychiatry 1989; 146, 577- 587.
12. Dementia and Parkinson's Disease W R G Gibb, 1989 Brit J of Psychiatry 1989 154; 598-614.