CHIEF EDITOR DR. SYED MUBIN AKHTAR

KARACHI PSYCHIATRIC HOSPITAL

BULLETIN (Psychiatric Research Articles) DECEMBER 2013

Regd. No. SS-237

Karachi Psychiatric Hospital Nazimabad # 3, Karachi (Front View)

Medical Store Open Day and Night

Medicines used in psychiatric patients are available around the clock as well as Sundays and Holidays in all our branches.
Medicines can also be sent to addresses in Karachi or outside if payment is made in advance.

HOSPITALISATION SQUAD

SOMETIMES A PSYCHIATRIC PATIENT DOESN'T TAKE TREATMENT AT HOME, NOR DOES HE COME TO THE HOSPITAL. IN THAT CASE WE HAVE SET UP A TEAM OF DOCTORS AND ASSISTANTS WHO VISIT HIM/HER AT HOME, ADMINISTER THE NEEDED TRANQULISATION AND TRANSPORT THE PATIENT TO THE HOSPITAL.

Phone or visit any branch for this facility

KARACHI PSYCHIATRIC HOSPITAL

Head Office	Quaidabad Branch	Karachi Addiction Hospital	Hyderabad Branch
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	(021) 36013633, 36016632, 36070426	(021) 32726414, 32721504, 36166639	(022) 111-769-769, 3813020, 3813015, 4140610

KARACHI PSYCHIATRIC HOSPITAL

Vol.36 Issue No. XII DECEMBER - 2013 Regd. No. SS -237

MONTHLY BULLETIN

(Psychiatric Research Articles)

قائداعظم نے فرمایا

"قرآن مجید مسلمانوں کا شاہ حیات ہے۔ اس میں مذہبی، مجلسی، دیوانی، فوج داری، عسکری، تعزیری، معاشی اور عرفی یہ کہ تمام شعبوں کے احکام موجود ہیں۔ مذہبی رسوم سے لے کر روزانہ کے امور حیات تک، روح کی نجات سے لے کر جسم کی صحت تک، اخلاق سے لے کر انسداد جرم تک، زندگی میں جزا اور سزا سے لے کر عقبیٰ کی جزا تک .... یہ قول و فعل اور حرکت کے احکامات کا مجموعہ ہے۔"

(گورنمنٹ کالج لاہور 25 دسمبر کے خطاب سے ایک اقتباس)

Readers are requested to send their articles, comments & suggestions.
Doctors who desire to get the bulletin should send their address, contact number and email to:

Address: B-1/14, Nazimabad # 3, Karachi-74600
Phone:111-760-760
Fax: 36681610
Email: editor@kph.org.pk
Email: support@kph.org.pk

CONTENTS

(Special Issue on Depression)

DEPRESSION

TREATMENT AND MANAGEMENT

National Institute for Health and Clinical Excellence

Summary and Comments

By

Dr. Syed Mubin Akhtar

Diplomate American Board of Psychiatry and Neurology (USA)

Introduction

Depression is a broad and heterogeneous diagnosis. Central to it is depressed mood and/or lossof pleasure in most activities. Severity of the disorder is determined by both the number and severity of symptoms, as well as the degree of functional impairment. A formal diagnosis using the ICD-10 classification system requires at least four out of ten depressive symptoms. Symptoms should be present for at least 2 weeks and each symptom should be present at sufficient severity for most of every day. At least two (ICD10) key symptoms (low mood,loss of interest and pleasureor loss of energy) to be present.

Increasingly, it is recognised that depressive symptoms below the ICD10 threshold criteria can be distressing and disabling if persistent. Therefore this updated guideline covers 'subthreshold depressive symptoms', which fall below the criteria for major depression, and are defined as at least one key symptom of depression but with insufficient other symptoms and/or functional impairment to meet the criteria for full diagnosis. Symptoms are considered persistent if they continue despite active monitoring and/or low-intensity intervention, or have been present for a considerable time, typically several months. (For a diagnosis of dysthymia, symptoms should be present for at least 2 years.)

A wide range of biological, psychological and social factors, which are not captured well by current diagnostic systems, have a significant impact on the course of depression and the response to treatment. Therefore it is also important to consider both personal past history andfamily history of depression when undertaking a diagnostic assessment.

Depression often has a remitting and relapsing course, and symptoms may

persist between episodes. Where possible, the key goal of an intervention should be complete relief of symptoms (remission), which is associated with better functioning and a lower likelihood of relapse.

Person-centred care

This guideline offers best practice advice on the care of adults with depression.

Treatment and care should take into account patients' needs and preferences. People with depression should have the opportunity to make informed decisions about their care and treatment, in partnership with their practitioners.

Good communication between practitioners and patients is essential. It should be supported by evidence-based written information tailored to the patient's needs. Treatment and care, and the information patients are given about it, should be culturally appropriate.

If the patient agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

Families and carers should also be given the information and support they need.

Key priorities for implementation

Principles for assessment

When assessing a person who may have depression, conduct a comprehensive assessment that does not rely simply on a symptom count. Take into account both the degree offunctional impairment and/or disability associated with the possible depression and theduration of the episode.

Case identification and recognition

- Be alert to possible depression (particularly in people with a past history of depression or a chronic physical health problem with associated functional impairment) and consider asking people who may have depression two questions, specifically:
  - During the last month, have you often been bothered by feeling down, depressed or hopeless?
  - During the last month, have you often been bothered by having little interest orpleasure in doing things?

Treatment for moderate or severe depression

For people with moderate or severe depression, provide a combination of antidepressant medication and a high-intensity psychological intervention (CBT or IPT).

Continuation and relapse prevention

- Support and encourage a person who has benefited from taking an antidepressant to continue medication for at least 6 months after remission of an episode of

depression.Discuss with the person that:

- this greatly reduces the risk of relapse
- antidepressants are not associated with addiction.

Psychological interventions for relapse prevention

People with depression who are considered to be at significant risk of relapse (including those who have relapsed despite antidepressant treatment or who are unable or choose not to continue antidepressant treatment) or who have residual symptoms, should be offered one of the following psychological interventions: individual CBT for people who have relapsed despite antidepressant medication and for people with a significant history of depression and residual symptoms despite treatment mindfulness-based cognitive therapy for people who are currently well but have experienced three or more previous episodes of depression.

1 Guidance

The following guidance is based on the best available evidence.

Box 1 Depression definitions (taken from DSM-IV)

Subthreshold depressive symptoms: Fewer than 5 symptoms of depression.

Mild depression:

Few, if any, symptoms in excess of the 5 required to make the diagnosis, and symptoms result in only minor functional impairment.

Moderate depression:

Symptoms or functional impairment are between 'mild' and 'severe'.

Severe depression:

Most symptoms, and the symptoms markedly interfere with functioning. Can occur with or without psychotic symptoms.

Note that a comprehensive assessment of depression should not rely simply on a symptom count, but should take into account the degree of functional impairment and/or disability.

1.1 Care of all people with depression

1.1.1 Providing information and support, and obtaining informed consent

1.1.1.1 When working with people with depression and their families or carers:

- **o** build a trusting relationship and work in an open, engaging and nonjudgemental
- **o** manner explore treatment options in an atmosphere of hope and optimism, explaining the different courses of depression and that recovery is possible
- **o** be aware that stigma and

discrimination can be associated with a diagnosis of depression
- ensure that discussions take place in settings in which confidentiality, privacy anddignity are respected.

1.1.1.2 When working with people with depression and their families or carers:

provide information appropriate to their level of understanding about the nature of depression and the range of treatments available avoid clinical language without adequate explanation ensure that comprehensive written information is available in the appropriate language and in audio format if possible provide and work proficiently with independent interpreters (that is, someone who is not known to the person with depression) if needed.

1.1.3 Supporting families and carers

1.1.3.1 When families or carers are involved in supporting a person with severe or chronicdepression, consider:
- providing written and verbal information on depression and its management,including how families or carers can support the person
- offering a carer's assessment of their caring, physical and mental health needs if necessary

1.1.4 Principles for assessment, coordination of care and choosing treatments

1.1.4.1 When assessing a person who may have depression, conduct a comprehensive assessment that does not rely simply on a symptom count. Take into account both the degree of functional impairment and/or disability associated with the possible depression and the duration of the episode.

1.1.4.2 In addition to assessing symptoms and associated functional impairment,

consider how the following factors may have affected the development, course and severity of a person's depression:
- any history of depression and comorbid mental health or physical disorders
- any past history of mood elevation (to determine if the depression may be part of bipolar disorder)
- any past experience of, and response to, treatments
- the quality of interpersonal relationships
- living conditions and social isolation.

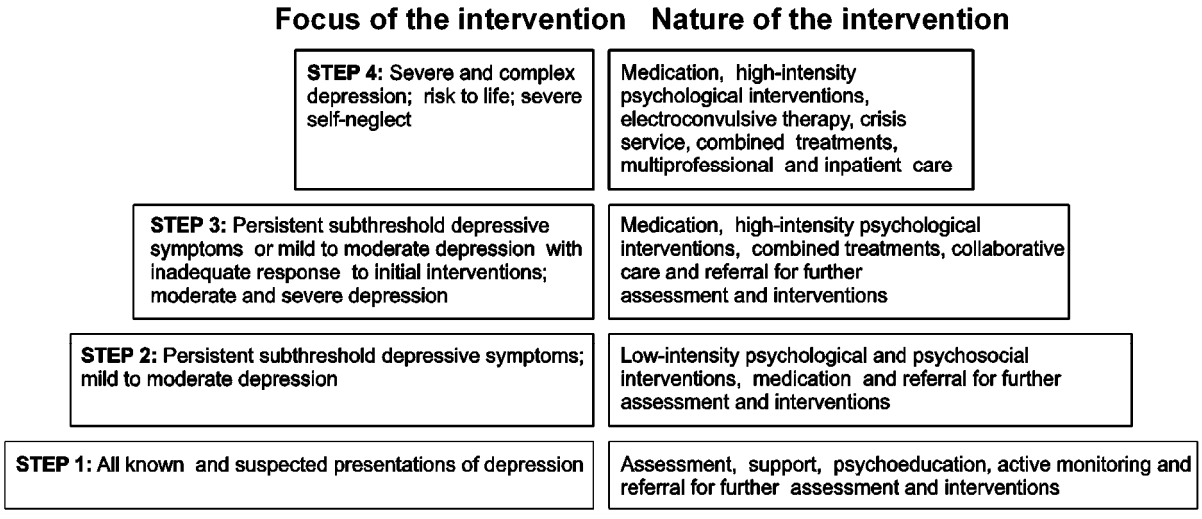
1.1.4.3 Be respectful of, and sensitive to, diverse cultural, ethnic and religious backgrounds when working with people with depression, and be aware of the possible variations in the presentation of depression.

1.1.4.6 Always ask people with depression directly about suicidal ideation and intent. Ifthere is a risk of self-harm or suicide:

1.2 Stepped care

The stepped-care model provides a

Fig 1. The Stepped- care model



framework in which to organise the provision of services, and supports patients, carers and practitioners in identifying and accessing the most effective interventions (see figure 1). In stepped care the least intrusive, most effective intervention isprovided first; if a person does not benefit from the intervention initially offered, or declines anintervention, they should be offered an appropriate intervention from the next step.

1.3 Step 1: recognition, assessment and initial management

1.3.1 Case identification and recognition

1.3.1.1 Be alert to possible depression (particularly in people with a past history of depression or a chronic physical health problem with associated functional impairment) and consider asking people who may have depression two questions, specifically:

- During the last month, have you often been bothered by feeling down, depressed or hopeless?
- During the last month, have you often been bothered by having little interest orpleasure in doing things?

1.3.1.3 If a person answers 'yes' to either of the depression identification questions (see 1.3.1.1), a practitioner who is competent to perform a mental health assessment should review the person's mental state and associated functional, interpersonal and social difficulties.

1.3.1.4 When assessing a person with suspected depression, consider using a validated measure (for example, for symptoms, functions and/or disability) to inform and evaluate treatment.

1.3.1.5 For people with significant language or communication difficulties, for examplepeople with sensory impairments or a learning disability, consider using the Distress Thermometer*and/or asking a family member or carer about the person's symptoms to identify possible depression. If a significant level of distress is identified, investigate further. (*the Distress Thermometer is a single item question screen that will identify distress coming from any source. The person places a mark on the scale answering: "How distressed have you been during the past week on a scale of 0 to 10?. Scores of 4 or more indicate a significant level)

1.3.2 Risk assessment and monitoring

1.3.2.2 Advise people with depression of the potential for increased agitation, anxiety and suicidal ideation in the initial stages of treatment; actively seek out these symptoms and:

- ensure that the person knows how to seek help promptly
- review the person's treatment if they develop marked and/or prolonged agitation.

1.3.2.3 Advise a person with depression and their family or carer to be vigilant for mood changes, negativity and hopelessness, and suicidal ideation, and to contact their practitioner if concerned. This is particularly important during highrisk periods, such as starting or changing treatment and at times of increased personal stress.

1.3.2.4 If a person with depression is assessed to be at risk of suicide:

- take into account toxicity in overdose if an antidepressant is prescribed or theperson is taking other medication; if necessary, limit the amount of drug(s) available
- consider increasing the level of support, such as more frequent direct or telephone contacts

1.4 Step 2: recognised depression - persistent subthreshold depressive symptoms or mild to moderate depression

1.4.1 General measures

Depression with anxiety

1.4.1.1 When depression is accompanied by symptoms of anxiety, the first priorityshould usually be to treat the depression. When the person has an anxietydisorder and comorbid depression or depressive symptoms, consider treatingthe anxiety disorder first (since effective treatment of the anxiety disorder willoften improve the depression or the depressive symptoms).

Sleep hygiene

1.4.1.2 Offer people with depression advice on sleep hygiene if needed, including:

- o establishing regular sleep and wake times
- o avoiding excess eating, smoking or drinking alcohol before sleep
- o creating a proper environment for sleep
- o taking regular physical exercise.

1.4.2 Low-intensity psychosocial interventions

1.4.2.1 For people with persistent subthreshold depressive symptoms or mild to moderate depression, consider offering one or more of the following interventions, guided by the person's preference:

- o individual guided self-help based on the principles of cognitive behavioural therapy(CBT)
- o a structured group physical activity programme.

Delivery of low-intensity psychosocial interventions

1.4.2.2 Individual guided self-help programmes based on the principles of CBT (andincluding behavioural activation and problem-solving techniques) for people with persistent subthreshold depressive symptoms or mild to moderate depression should:

- o include the provision of written materials of an appropriate reading age (or alternative media to support access)
- o consist of up to six to eight sessions (face-to-face and via telephone) normallytaking place over 9 to 12 weeks, including follow-up.

1.4.2.3 CCBT for people with persistent subthreshold depressive symptoms or mild to moderate depression should:

- o include an explanation of the CBT model, encourage tasks between sessions, anduse thought-challenging and active monitoring of behaviour, thought patterns and outcomes
- o facilitation ofthe programme and reviews progress and outcome
- o typically take place over 9 to 12 weeks, including follow-up.

1.4.2.4 Physical activity programmes for people with persistent subthreshold depressive symptoms or mild to moderate depression should:

- o be delivered in groups
- o consist typically of three sessions per week of moderate duration (45 minutes to1 hour) over 10 to 14 weeks (average 12 weeks).

1.4.3 Group cognitive behavioural therapy

1.4.3.1 Consider group-based CBT for people with persistent subthreshold depressivesymptoms or mild to moderate depression who decline lowintensity psychosocial interventions.

1.4.3.2 Group-based CBT for people with persistent subthreshold depressive symptoms or mild to moderate

depression should:

- consist of 10 to 12 meetings of eight to ten participants
- normally take place over 12 to 16 weeks, including follow-up.

1.4.4 Drug treatment

1.4.4.1 Do not use antidepressants routinely to treat persistent subthreshold depressive symptoms or mild depression because the risk-benefit ratio is poor,

but consider them for people with:

- a past history of moderate or severe depression or
- initial presentation of subthreshold depressive symptoms that have been present fora long period (typically at least 2 years) or
- subthreshold depressive symptoms or mild depression that persist(s) after otherinterventions.

1.5 Step 3: persistent subthreshold depressive symptoms or mild to moderate depression with inadequate response to initial interventions, and moderate and severe depression

1.5.1 Treatment option

1.5.1.1 For people with persistent subthreshold depressive symptoms or mild to

moderate depression who have not benefited from a low-intensity psychosocial intervention, discuss the relative merits of different interventions with the

person and provide:

- an antidepressant (normally a selective serotonin reuptake inhibitor [SSRI]) or
- a high-intensity psychological intervention, normally one of the following options:
  - CBT interpersonal therapy (IPT)
  - behavioural activation (but note that the evidence is less robust than for CBTor IPT)
  - behavioural couples therapy for people who have a regular partner and where the relationship may contribute to the development or maintenance of depression, or where involving the partner is considered to be of potential therapeutic benefit.

1.5.1.2 For people with moderate or severe depression, provide a combination of antidepressant medication and a high-intensity psychological intervention (CBT or IPT).

1.5.1.3 For people with depression who decline an antidepressant, CBT, IPT, behavioural activation and behavioural couples therapy, consider:

- counselling for people with persistent subthreshold depressive symptoms or mild to moderate depression
- short-term psychodynamic psychotherapy for people with mild to moderate depression.

Discuss with the person the uncertainty of the effectiveness of counselling and psychodynamic psychotherapy in

treating depression.

1.5.2 Antidepressant drugs

Choice of antidepressant

1.5.2.2 When an antidepressant is to be prescribed, it should normally be an SSRI in a generic form because SSRIs are equally effective as other antidepressants and have a favourable risk-benefit ratio.

(At Karachi Psychiatric Hospital we recommend starting with Tricyclics, especially if insominia is present and there is no contra indication. If side effects develop then treatment can shift to SSRIs)

- SSRIs are associated with an increased risk of bleeding, especially in older peopleor in people taking other drugs that have the potential to damage thegastrointestinal mucosa or interfere with clotting. In particular, consider prescribing agastroprotective drug in older people who are taking non-steroidal anti-inflammatorydrugs (NSAIDs) or aspirin.

Fluoxetine, fluvoxamine and paroxetine are associated with a higher propensity for drug interactions than other SSRIs.

Paroxetine is associated with a higher incidence of discontinuation symptoms than other SSRIs.

1.5.2.4 When prescribing drugs other than SSRIs, take the following into account:

- The increased likelihood of the person stopping treatment because of side effects(and the consequent need to increase the dose gradually) with venlafaxine,duloxetine and TCAs.
- The specific cautions, contraindications and monitoring requirements for somedrugs. For example:
  - the potential for higher doses of venlafaxine to exacerbate cardiac arrhythmias and the need to monitor the person's blood pressure
  - the possible exacerbation of hypertension with venlafaxine and duloxetine
  - the potential for postural hypotension and arrhythmias with TCAs
  - the need for haematological monitoring with mianserin in elderly people.

Starting and initial phase of treatment

1.5.2.3 When prescribing antidepressants, explore any concerns the person with depression has about taking medication, explain fully the reasons for prescribing, and provide information about taking antidepressants, including:

- the gradual development of the full antidepressant effect
- the importance of taking medication as prescribed and the need to continuetreatment after remission

- the potential for interactions with other medications
- the risk and nature of discontinuation symptoms with all antidepressants, particularlywith drugs with a shorter half-life (such as paroxetine and venlafaxine), and howthese symptoms can be minimized
- the fact that addiction does not occur with antidepressants.

Offer written information appropriate to the person's needs.

1.5.2.4 For people started on antidepressants who are not considered to be at increased risk of suicide, normally see them after 2 weeks. See them regularly thereafter, for example at intervals of 2 to 4 weeks in the first 3 months, and then at longer intervals if response is good.*

(At Karachi Psychiatric Hospital we advise seeing the patient every week, in the second, and as needed thereafter in order to provide counseling and track side effects if any.)

1.5.2.5 If a person with depression develops side effects early in antidepressant treatment, provide appropriate information and consider one of the following strategies:

- monitor symptoms closely where side effects are mild and acceptable to the personor
- stop the antidepressant or change to a different antidepressant if the person prefersor
- in discussion with the person, consider short-term concomitant treatment with abenzodiazepine if anxiety, agitation and/or insomnia are problematic (except inpeople with chronic symptoms of anxiety); this should usually be for no longer than2 weeks in order to prevent the development of dependence.

1.5.2.6 People who start on low-dose TCAs and who have a clear clinical response can be maintained on that dose with careful monitoring.

1.5.2.7 If the person's depression shows no improvement after 2 to 4 weeks with the first antidepressant, check that the drug has been taken regularly and in the prescribed dose.

1.5.2.8 If response is absent or minimal after 3 to 4 weeks of treatment with a therapeutic dose of an antidepressant, increase the level of support (for example, by weekly face-to-face or telephone contact) and consider:

- increasing the dose in line with the SPC if there are no significant side effects or
- switching to another antidepressant if there are sideeffects or if the person prefers.

1.5.2.12 If the person's depression shows some improvement by 4 weeks, continue treatment for another 2 to 4 weeks. Consider switching to another antidepressant if:

- response is still not adequate or
- there are side effects

Medication for chronic physical health problem	Recommended antidepressant(s)
Non-steroidal anti-inflammatory (NSAIDs)	• Do not normally offer SSRIs - but if no suitable alternatives can be identified, offer gastroprotective medicines (for example, proton pump inhibitors) together with the SSRI • Consider mianserin, mirtazapine, moclobemide, reboxetine or trazodone
Warfarin and heparin	• Do not normally offer SSRIs • Consider mirtazapine (note that when taken with warfarin, the international normalised ratio [INR] may increase slightly)
Aspirin	• Use SSRIs with caution - if no suitable alternatives can be identified, offer gastroprotective medicines together with the SSRI • When aspirin is used as a single agent, consider trazodone, mianserin or reboxetine • Consider mirtazapine
'Triptan' drugs for migraine	• Do not offer SSRIs • Offer mirtazapine, trazodone, mianserin or reboxetine
MAO-B inhibitors (for example, selegiline and rasagiline)	• Do not normally offer SSRIs • Offer mirtazapine, trazodone, mianserin or reboxetine
Theophylline, clozapine,	• Do not normally offer fluvoxamine • Offer sertraline or citalopram
Flecainide or propafenone	• Offer sertraline as the preferred antidepressant • Mirtazapine and moclobemide may also be used
Atomoxetine	• Do not offer fluoxetine or paroxetine • Offer a different SSRI

1.5.3: Psychological interventions

Delivering high-intensity psychological interventions

For all high-intensity psychological interventions, the duration of treatment should normally be within the limits indicated in this guideline. As the aim of treatment is to obtain significant improvement or remission the duration of treatment may be:

- reduced if remission has been achieved
- increased if progress is being made, and there is agreement between the practitioner and the person with depression that further sessions would be beneficial (for example, if there is a comorbid personality disorder or significant psychosocial factors that impact on the person's ability to benefit from treatment).

1.5.3.2 For all people with depression having individual CBT, the duration of treatment should typically be in the range of 16 to 20 sessions over 3 to 4 months. Also consider providing:

- two sessions per week for the first 2 to 3 weeks of treatment for people withmoderate or severe depression
- follow-up sessions typically consisting of three to four sessions over the following 3to 6 months for

all people with depression.

1.5.3.3 For all people with depression having IPT, the duration of treatment should typically be in the range of 16 to 20 sessions over 3 to 4 months. For people with severe depression, consider providing two sessions per week for the first 2 to 3 weeks of treatment.

1.5.3.4 For all people with depression having behavioural activation, the duration of treatment should typically be in the range of 16 to 20 sessions over 3 to 4 months. Also consider providing:

- o two sessions per week for the first 3 to 4 weeks of treatment for people withmoderate or severe depression
- o follow-up sessions typically consisting of three to four sessions over the following 3 to 6 months for all people with depression.

1.5.3.5 Behavioural couples therapy for depression should normally be based on behavioural principles, and an adequate course of therapy should be 15 to 20 sessions over 5 to 6 months.

Delivering counselling

1.5.3.6 For all people with persistent subthreshold depressive symptoms or mild to moderate depression having counselling, the duration of treatment should typically be in the range of six to ten sessions over 8 to 12 weeks.

Delivering short-term psychodynamic psychotherapy

1.5.3.7 For all people with mild to moderate depression having short-term psychodynamic psychotherapy, the duration of treatment should typically be in the range of 16 to 20 sessions over 4 to 6 months.

1.6 Treatment choice based on depression subtypes and personal characteristics

There is little evidence to guide prescribing in relation to depression subtypes or personal characteristics. The main issue concerns the impact of other physical disorders on the treatment of depression.

1.6.1.1 When prescribing antidepressants for older people:

- o prescribe at an age-appropriate dose taking into account the effect of general physical health and concomitant medication on pharmacokinetics and pharmacodynamics
- o carefully monitor for side effects.

1.6.1.2 For people with long-standing moderate or severe depression who would benefit from additional social or vocational support, consider:

- o befriending as an adjunct to pharmacological or psychological treatments; befriending should be by trained volunteers providing, typically, at least weekly contact for between 2 and 6 months
- o a rehabilitation programme if a person's depression has resulted in loss of work ordisengagement from

other social activities over a longer term.

1.7 Enhanced care for depression

1.7.1.1 Medication management as a separate intervention for people with depression should not be provided routinely by services. It is likely to be effective only when provided as part of a more complex intervention.

1.8 Sequencing treatments after initial inadequate response

Some people have depression that does not respond well to initial treatment. This section describes strategies to adopt if this occurs.

1.8.1 Drug treatments

1.8.1.1 When reviewing drug treatment for a person with depression whose symptoms have not adequately responded to initial pharmacological interventions:

- check adherence to, and side effects from, initial treatment
- increase the frequency of appointments using outcome monitoring with a validatedoutcome measure
- be aware that using a single antidepressant rather than combination medication oraugmentation is usually associated with a lower side-effect burden
- consider reintroducing previous treatments that have been inadequately deliveredor adhered to, including increasing the dose
- consider switching to an alternative antidepressant.

Switching antidepressants

1.8.1.2 When switching to another antidepressant, be aware that the evidence for the relative advantage of switching either within or between classes is weak.

Consider switching to:

- initially a different SSRI or a better tolerated newer-generation antidepressant
- subsequently an antidepressant of a different pharmacological class that may beless well tolerated, for example venlafaxine, or a TCA.

1.8.1.3 When switching to another antidepressant, which can normally be achieved within 1 week when switching from drugs with a short halflife, consider the potential for interactions in determining the choice of new drug and the nature and duration of the transition. Exercise particular caution when switching:

- from fluoxetine to other antidepressants, because fluoxetine has a long half-life(approximately 1 week)
- from fluoxetine or paroxetine to a TCA, because both of these drugs inhibit themetabolism of TCAs; a

lower starting dose of the TCA will be required, particularly ifswitching from fluoxetine because of its long half-life
- to a new serotonergic antidepressant, because of the risk of serotonin syndrome

Combining and augmenting medications

'Augmentation' is when an antidepressant is used with a non-antidepressant drug and 'combination' is when two antidepressants are used together.

1.8.1.4 When using combinations of medications :
- select medications that are known to be safe when used together
- be aware of the increased side-effect burden this usually causes
- discuss the rationale for any combination with the person with depression.

1.8.1.5 If a person with depression is informed about, and prepared to tolerate, the increased side-effect burden, consider combining or augmenting an antidepressant with:
- lithium or
- an antipsychotic such as aripiprazole*, olanzapine*, quetiapine* or risperidone* or
- another antidepressant such as mirtazapine or mianserin.

1.8.1.6 When prescribing lithium:
- monitor renal and thyroid function before treatment and every 6 months duringtreatment (more often if there is evidence of renal impairment)
- consider ECG monitoring in people with depression who are at high risk of cardiovascular disease
- monitor serum lithium levels 1 week after initiation and each dose change untilstable, and every 3 months thereafter.

1.8.1.7 When prescribing an antipsychotic, monitor weight, lipid and glucose levels, and side effects (for example, extrapyramidal side effects and prolactin-related side effects with risperidone).

1.8.1.8 The following strategies should not be used routinely:
- augmentation of an antidepressant with a benzodiazepine for more than 2 weeks asthere is a risk of dependence
- augmentation of an antidepressant with buspirone*, carbamazepine, lamotrigineor valproate as there is insufficient evidence for their use

Combined psychological and drug treatment

1.8.1.9 For a person whose depression has not responded to either pharmacological or psychological interventions, consider combining antidepressant medication with CBT.

1.9 Continuation and relapse prevention

1.9.1.1 Support and encourage a person who has benefited from taking

an antidepressant to continue medication for at least 6 months after remission of an episode of depression. Discuss with the person that:

- this greatly reduces the risk of relapse
- antidepressants are not associated with addiction.

1.9.1.2 Review with the person with depression the need for continued antidepressant treatment beyond 6 months after remission, taking into account:

- the number of previous episodes of depression
- the presence of residual symptoms
- concurrent physical health problems and psychosocial difficulties.

1.9.1.3 For people with depression who are at significant risk of relapse or have a history of recurrent depression, discuss with the person treatments to reduce the risk of recurrence, including continuing medication, augmentation of medication or psychological treatment (CBT). Treatment choice should be influenced by:

- previous treatment history, including the consequences of a relapse, residualsymptoms, response to previous treatment and any discontinuation symptoms

Using medication for relapse prevention

1.9.1.4 Advise people with depression to continue antidepressants for at least 2 years if they are at risk of relapse. Maintain the level of medication at which acute treatment was effective (unless there is good reason to reduce the dose, suchas unacceptable adverse effects) if:

- they have had two or more episodes of depression in the recent past, during whichthey experienced significant functional impairment
- they have other risk factors for relapse such as residual symptoms, multipleprevious episodes, or a history of severe or prolonged episodes or of inadequateresponse
- the consequences of relapse are likely to be severe (for example, suicide attempts,loss of functioning, severe life disruption, and inability to work).

1.9.1.5 When deciding whether to continue maintenance treatment beyond 2 years, re-evaluate with the person with depression, taking into account age, comorbid conditions and other risk factors.

1.9.1.6 People with depression on long-term maintenance treatment should be regularly re-evaluated, with frequency of contact determined by:

- comorbid conditions
- risk factors for relapse
- severity and frequency of episodes of depression.

1.9.1.7 People who have had multiple episodes of depression, and who have had agood response to treatment with an antidepressant and an augmenting agent, should remain on this

combination after remission if they find the side effects tolerable and acceptable. If one medication is stopped, it should usually be the augmenting agent. Lithium should not be used as a sole agent to prevent recurrence.

Psychological interventions for relapse prevention

1.9.1.8 People with depression who are considered to be at significant risk of relapse (including those who have relapsed despite antidepressant treatment or who are unable or choose not to continue antidepressant treatment) or who have residual symptoms, should be offered one of the following psychological interventions:

- individual CBT for people who have relapsed despite antidepressant medicationand for people with a significant history of depression and residual symptomsdespite treatment
- mindfulness-based cognitive therapy for people who are currently well but haveexperienced three or more previous episodes of depression.

Delivering psychological interventions for relapse prevention

1.9.1.9 For all people with depression who are having individual CBT for relapse prevention, the duration of treatment should typically be in the range of 16 to 20 sessions over 3 to 4 months. If the duration of treatment needs to be extended to achieve remission it should:

- consist of two sessions per week for the first 2 to 3 weeks of treatment
- include additional follow-up sessions, typically consisting of four to six sessions overthe following 6 months.

1.9.1.10 Mindfulness-based cognitive therapy should normally be delivered in groups of8 to 15 participants and consist of weekly 2-hour meetings over 8 weeks and four follow-up sessions in the 12 months after the end of treatment.

1.9.2 Stopping or reducing antidepressants

1.9.2.1 Advise people with depression who are taking antidepressants that discontinuation symptoms * may occur on stopping, missing doses or, occasionally, on reducing the dose of the drug. Explain that symptoms are usually mild and self-limiting over about 1 week, but can be severe, particularly if the drug is stopped abruptly.
(*Discontinuation symptoms include increased mood change, restlessness, difficulty sleeping, unsteadiness, sweating, abdominal symptoms and altered sensatios.)

1.9.2.2 When stopping an antidepressant, gradually reduce the dose, normally over a 4-week period, although some people may require longer periods, particularly with drugs

with a shorter half-life (such as paroxetine and venlafaxine). This is not required with fluoxetine because of its long half-life.

1.9.2.3 Inform the person that they should seek advice if they experience significant discontinuation symptoms. If discontinuation symptoms occur:

- monitor symptoms and reassure the person if symptoms are mild
- consider reintroducing the original antidepressant at the dose that was effective (oranother antidepressant with a longer half-life from the same class) if symptoms aresevere, and reduce the dose gradually while monitoring symptoms.

1.10 Step 4:complex and severe depression

1.10.1.1 The assessment of a person with complex and severe depression should include:

- their symptom profile, suicide risk and, where appropriate, previous treatmenthistory
- associated psychosocial stressors, personality factors and significant relationshipdifficulties, particularly where the depression is chronic or recurrent
- associated comorbidities including alcohol and substance misuse, and personalitydisorders.

1.10.1.2 After thoroughly reviewing previous treatments for depression, consider reintroducing previous treatments that have been inadequately delivered or adhered to.

1.10.1.3 Use crisis resolution and home treatment teams to manage crises for people with severe depression who present significant risk, and to deliver high-quality acute care. The teams should monitor risk as a high-priority routine activity in a way that allows people to continue their lives without disruption.

1.10.1.4 Teams working with people with complex and severe depression should

develop comprehensive multidisciplinary care plans in collaboration with the

person with depression (and their family or carer, if agreed with the person).

The care plan should:

- identify clearly the roles and responsibilities of all health and social care professionals involved
- develop a crisis plan that identifies potential triggers that could lead to a crisis andstrategies to manage such triggers
- be shared with the person with depression and other relevant peopleinvolved in the person's care.

1.10.2 Inpatient care, and crisis resolution and home treatment teams

1.10.2.1 Consider inpatient treatment for people with depression who are at significant risk of suicide, self-harm or self-neglect.

1.10.2.2 The full range of high-intensity psychological interventions should normally be offered in inpatient settings. However, consider increasing the intensity and duration of the interventions and ensure that they can be provided effectively and efficiently on discharge.

1.10.3 Pharmacological management of depression with psychotic symptoms

1.10.3.1 For people who have depression with psychotic symptoms, consider augmenting the current treatment plan with antipsychotic medication (although the optimum dose and duration of treatment are unknown).

1.10.4 Electroconvulsive therapy (ECT)

1.10.4.1 Consider ECT for acute treatment of severe depression that is life threatening and when a rapid response is required, or when other treatments have failed.

1.10.4.2 Do not use ECT routinely for people with moderate depression but consider it if their depression has not responded to multiple drug treatments and psychological treatment.

1.10.4.3 For people whose depression has not responded well to a previous course of ECT, consider a repeat trial of ECT only after:

- reviewing the adequacy of the previous treatment course and
- considering all other options and
- discussing the risks and benefits with the person and/or, where appropriate, theiradvocate or carer.

1.10.4.4 When considering ECT as a treatment choice, ensure that the person with depression is fully informed of the risks associated with ECT, and with the risks and benefits specific to them. Document the assessment and consider:

- the risks associated with a general anaesthetic **(At Karachi Psychiatric Hospital we provide ECT without anaesthesia to those can't the extra cost)**
- current medical comorbidities
- potential adverse events, notably cognitive impairment
- the risks associated with not receiving ECT.

The risks associated with ECT may be greater in older people; exercise particular caution when considering ECT treatment in this group.

1.10.4.5 A decision to use ECT should be made jointly with the person with depression as far as possible. Also be aware that:

- valid informed consent should be obtained (if the person has the capacity to grant orrefuse consent) without the pressure or coercion that might occur as a result of thecircumstances and clinical setting
- if informed consent is not possible,

ECT should only be given after the person's advocate or careris consulted.

1.10.4.6 The choice of electrode placement and stimulus dose related to seizure threshold should balance efficacy against the risk of cognitive impairment.

Take into account that:

- **o** bilateral ECT is more effective than unilateral ECT but may cause more cognitiveimpairment
- **o** with unilateral ECT, a higher stimulus dose is associated with greater efficacy, butalso increased cognitive impairment compared with a lower stimulus dose.

1.10.4.7 Assess clinical status after each ECT treatment using a formal valid outcome measure, and stop treatment when remission has been achieved, or sooner if side effects outweigh the potential benefits.

(We advise a course of the ten treatments because there is evidence that treatments are discontinued as soon there is more incidence of relapse.)

1.10.4.8 Assess cognitive function before the first ECT treatment and monitor at least every three to four treatments, and at the end of a course of treatment.

1.10.4.9 Assessment of cognitive function should include:

- **o** orientation and time to reorientation after each treatment
- **o** measures of new learning, retrograde amnesia and subjective memory impairmentcarried out at least 24 hours after a treatment.

If there is evidence of significant cognitive impairment at any stage consider, in discussion with the person with depression, changing from bilateral to unilateral electrode placement, reducing the stimulus dose or stopping treatment depending on the balance of risks and benefits.

1.10.4.10 If a person's depression has responded to a course of ECT, antidepressant medication should be continued to prevent relapse. Consider lithium augmentation of antidepressants.

Assessing depression and its severity

As set out in the introduction to this guideline, the assessment of depression is based on the criteria in DSM-IV. Assessment should include the number and severity of symptoms, duration of the current episode, and course of illness.

Key symptoms:

- **o** persistent sadness or low mood; and/or
- **o** marked loss of interests or pleasure.

At least one of these, most days, most of the time for at least 2 weeks.

If any of above present, ask about

associated symptoms:

- o disturbed sleep (decreased or increased compared to usual)
- o decreased or increased appetite and/or weight
- o fatigue or loss of energy
- o agitation or slowing of movements
- o poor concentration or indecisiveness
- o feelings of worthlessness or excessive or inappropriate guilt
- o suicidal thoughts or acts.

Then ask about duration and associated disability, past and family history of mood disorders, and availability of social support

1. Factors that favour general advice and active monitoring:

- o four or fewer of the above symptoms with little associated disability
- o symptoms intermittent, or less than 2 weeks' duration
- o recent onset with identified stressor
- o no past or family history of depression
- o social support available
- o lack of suicidal thoughts.

2. Factors that favour more active treatment:

- o five or more symptoms with associated disability
- o persistent or long-standing symptoms
- o personal or family history of depression
- o low social support
- o occasional suicidal thoughts.

3. Factors that favourintensive treatment:

- o inadequate or incomplete response to two or more interventions
- o recurrent episode within 1 year of last one
- o history suggestive of bipolar disorder
- o the person with depression or relatives request referral
- o more persistent suicidal thoughts
- o self-neglect.
- o actively suicidal ideas or plans
- o psychotic symptoms
- o severe agitation accompanying severe symptoms
- o severe self-neglect.

Depression definitions

Subthreshold depressive symptoms: Fewer than 5 symptoms of depression.

Mild depression: Few, if any, symptoms in excess of the 5 required to make the diagnosis, and symptoms result in only minor functional impairment.

Moderate depression: Symptoms or functional impairment are between 'mild' and 'severe'.

Severe depression: Most symptoms, and the symptoms markedly interfere with functioning. Can occur with or without psychotic symptoms.

ATYPICAL DEPRESSION IN THE 21ST CENTURY: DIAGNOSTIC AND TREATMENT ISSUES

By Mario A. Cristancho, MD, John P. O'reardon, MD, and Michael E. Thase, MD

The existence of different subtypes of depressive episodes (ie, endogenous and nonendogenous) was initially postulated at least 80 years ago. In the early formulations, the term "endogenous depression" was used to describe a more severe biologically mediated illness, whereas "nonendogenous depression" or "exogenous depression" referred to a less severe and environmentally mediated condition characterized by mood reactivity. It was not until the introduction of the first monoamine oxidase inhibitor (MAOI)-iproniazid-that the term "atypical depression" began to emerge to describe a particular variant of nonendogenous depression.

Originally, endogenous, or melancholic, depression was thought to be the prototypical form of depression. Endogenous depression manifested with neurovegetative symptoms and nonreactive mood and regularly responded to the tricyclic antidepressant (TCA) imipramine and/or electroconvulsive therapy (ECT). A different subgroup of patients was found to be responsive to iproniazid (the first commercially available MAOI, but currently off the market because of significant toxicity) and nonresponsive to well-established treatments for depression (ie, imipramine and ECT). Furthermore, those patients presented an unusual constellation of symptoms characterized by the absence of endogenous-type neurovegetative symptoms and the presence of emotional reactivity.

On the basis of these early observations, the existence of a unique subtype of nonendogenous depressive episodes characterized by mood reactivity with reversed neurovegetative symptoms (ie, hypersomnia and hyperphagia) and a predictable response to certain antidepressants was proposed and termed "atypical depression." The hypothesis that such depressions were relatively nonresponsive to TCAs and more responsive to MAOIs was further supported by studies in the 1970s and 1980s. Atypical depression was formally recognized in 1994, when it was included as an "episode specifier" in DSM-IV.

DIAGNOSIS

The DSM-IV specifier "with atypical features" can be used to characterize the current or most recent depressive episode in patients with either unipolar

or bipolar type mood disorder and in patients with dysthymic disorder. As described in the Table, the DSM-IV specifier requires the presence of mood reactivity (criterion A) and at least 2 of 4 criterion B features (significant weight gain or hyperphagia, hypersomnia, leaden paralysis, and interpersonal rejection sensitivity resulting in social or occupational impairment). If the patient meets criteria for either melancholic or catatonic features during the same major depressive episode, a diagnosis of atypical depression cannot be made (criterion C). To avoid overdiagnosis or underdiagnosis, bear in mind definitional aspects of the clinical features that constitute the criteria for atypical depression. Mood reactivity means that clinically depressed patients have the capacity to feel at least 50% better and even become transiently euthymic when exposed to positive events (eg, a compliment). Although never studied in a rigorous prospective manner, it has been reported that patients with atypical depression can remain euthymic for extended periods if the external circumstances remain positive. With respect to hyperphagia, a clear and sustained increase in appetite or a 5-lb weight gain during the depressive episode would satisfy criterion B1 (see Table).

Table **DSM-IV criteria for atypical depression features specifier**

A. Mood reactivity (ie, mood brightens in response to actual or potential positive events)

B. Two or more of the following features:

1. Significant weight gain or increase in appetite
2. Hypersomnia
3. Leaden paralysis (ie, heavy, leaden feeling in arms or legs)
4. Long-standing pattern of interpersonal rejection sensitivity (not limited to episodes of mood disturbance) that results in significant social or occupational impairment

C. Criteria are not met for "with melancholic features" or "with catatonic features" during the same episode

Note: The "with atypical features" specifier can be applied when these features predominate during the most recent 2 weeks of a current major depressive episode in major depressive disorder or in bipolar I or bipolar II disorder when a current major depressive episode is the most recent type of mood episode, or when these features predominate during the most recent 2 years of dysthymic disorder. If the major depressive episode is not current, it applies if the feature predominates during any 2-week period.

Adapted from American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. 1994.[18]

DSM-IV criteria for atypical depression features specifier Hypersomnia refers to either a total of at least 10 hours of sleep per day, including nighttime sleep and daytime naps, or at least 2 hours more than when not depressed. Leaden paralysis is defined as a sensation of heaviness in the arms or legs as if they were made of lead; it is generally present for at least an hour a day but can last for many hours at a time.

Interpersonal rejection sensitivity in the context of atypical depression implies a lifelong trait (during both periods of depression and periods of euthymia) that is typically exacerbated during depressive episodes. It is characterized by an excessive or pathological sensitivity to rejection and/or criticism leading to functional impairment (eg, stormy relationships, inability to sustain long-term relationships, problems at work, avoidance of relationships because of fear of rejection, avoidance and fear of embarrassment) or maladaptive behavioral responses such as substance abuse. Rejection sensitivity seems to be the most common clinical feature in atypical depression, as demonstrated by a study of 332 patients, of whom 71% reported rejection sensitivity, 47% hyperphagia, 47% leaden paralysis, and 35% oversleeping.

PREVALENCE, COURSE, AND COMORBIDITY

Although the term "atypical" implies an unusual or uncommon condition, depression with atypical features is in fact a common clinical presentation and is one of the most common forms of depression in outpatient settings. Estimates in both community and clinical settings suggest that 15.7% to 36.6% of patients with depression present with atypical features. This estimate is in harmony with the 18% prevalence of atypical depression detected in the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study series and with the 42% prevalence in a sample of 396 patients with depression. The presence of atypical features is even higher (up to 50%) in patients with bipolar II disorder and dysthymic disorder.

Studies have suggested that patients with atypical depression tend to have an earlier onset of symptoms and a more chronic course than their melancholic counterparts. Atypical depression is more common in younger women. Also, rates of comorbid conditions, such as anxiety, cluster B and C personality disorders, substance abuse, and somatization disorder, seem to be higher in patients with atypical depression than in those with other forms of depression.

Validity of atypical depression and its DSM-IV criteria

Although atypical depression appears to be clinically and diagnostically well

characterized, the DSM-IV criteria for diagnosing atypical depression and its validity as a subtype of depression have been questioned recently.3,4 Pertinent sources of controversy include the following.

- The inconsistency between reactive mood and the presence or absence of criterion B features
- Both the sex bias and the definition of rejection sensitivity
- The exclusion of state-dependent anxiety

Reactive mood

The validity of mood reactivity as a mandatory feature for diagnosing atypical depression has been challenged. Findings from 4 studies showed that mood reactivity does not significantly correlate with the presence of criterion B features, which suggests that mood reactivity should not be considered an obligatory feature for the diagnosis of atypical depression. Furthermore, regarding melancholia (which requires the loss of mood reactivity) as exclusionary of the diagnosis of atypical depression subtype makes the presence of reactive mood largely redundant. The inclusion of mood reactivity as an essential feature also neglects the fact that some depressive episodes, when quite severe, manifest with a nonreactive mood, even in the presence of reversed neurovegetative symptoms. The term "anergic depression" is sometimes used to describe depressive episodes that take this form.

One established characteristic of atypical depression is its differential response to MAOIs. The correlation between the presence or absence of reactive mood and a differential response to either TCAs or MAOIs has been challenged by a number of pharmacological studies. Findings from those studies suggest that the effectiveness of MAOIs in depression is not necessarily associated with mood reactivity, implying that the presence of this specific feature may not be essential for diagnosing this syndrome.

The hypothesis that reactive mood as a mandatory criterion is not indispensable for the diagnosis of atypical depression was supported by the community study by Angst and colleagues. Although mood reactivity was the most common symptom reported by their sample of patients with atypical depression (89% to 90%), other symptoms (ie, rejection sensitivity, leaden paralysis, and hypersomnia) were also quite commonly present (78% to 89%). This suggests that atypical depression could also be effectively diagnosed when mood reactivity is not considered a mandatory criterion. In a more recent analysis, Angst and colleagues reported that diagnosis of atypical depression could be made with equal validity if 3 of 5 criteria (including mood reactivity) or 2 of 4 criteria (excluding mood reactivity) were used.

Clearly, the inclusion of mood reactivity as a mandatory or hierarchical criterion for the diagnosis of atypical depression should be reassessed. This could be done using the available literature or, ideally, through more specific studies (ie, compare subjects with 2 or more criterion B symptoms and reactive mood with subjects with 2 or more criterion B symptoms without reactive mood).

Biological features of atypical depression

Evidence for the validity of atypical depression as a distinct subtype of depression includes distinct biological correlates, such as the following:

- Abnormalities of hypothalamic-pituitary-adrenal (HPA) axis activity
- Polysomnographic findings
- Asymmetry of hemispheric processing on psychophysiological testing
- Distinct regional cerebral blood flow patterns on single photon emission CT (SPECT)

The characteristic biological profile of atypical depression includes either normal or abnormally decreased HPA axis function; a relatively normal polysomnographic sleep profile; increased frontal, temporal, and parietal perfusion; and abnormally increased right hemispheric processing when performing psychophysiological tasks. Thus, the neurobiological profile of patients with atypical depression is both distinct from melancholia and, on select measures, abnormal compared with that of healthy controls. Interestingly, the most abnormal profiles appear to be evident in patients whose atypical depression has an early onset and a chronic course.

A SPECT brain perfusion study in patients with atypical depression showed increased frontal, temporal, and parietal perfusion coupled with decreased occipital perfusion relative to that seen in patients with melancholic and undifferentiated depression (ie, neither atypical nor melancholic). A SPECT study also showed increased right frontal perfusion relative to that seen in individuals in the control group. These specific biological characteristics imply that atypical depression is in fact a distinct entity and, as such, requires a distinct treatment approach.

TREATMENT

Differential response to standard treatments is historically the strongest determinant of atypical depression as a distinct subtype; patients with atypical depression have a preferential response to MAOIs compared with TCAs and less robust therapeutic responses to ECT. Although some studies have failed to demonstrate the relationship between atypical features and preferential response to certain

medications, the therapeutic benefit of MAOIs in atypical depression is widely accepted in practice guidelines and has been confirmed by meta-analyses.

MAOIs

The first reports of preferential response to MAOIs were based on uncontrolled case series; early attempts to replicate these findings in larger-scale randomized controlled trials (RCTs) met with only limited success (see Thase and colleagues for detailed review). Subsequent prospective trials using specific diagnostic criteria for atypical depression have generally supported the superiority of MAOIs-particularly phenelzine-over TCAs. For example, Liebowitz and colleagues randomized 119 patients with atypical depression to phenelzine, imipramine, or placebo. Improvement in both active groups was significantly superior to that in the placebo group; response rates were 71%, 50%, and 28% for phenelzine, imipramine, and placebo, respectively. Although the 21% difference in response rate between the phenelzine and imipramine groups was not statistically significant, the overall trend favored the MAOI.

Similar findings were obtained by Quitkin and colleagues in an RCT of 90 outpatients with atypical depression. They observed response rates of 83%, 50%, and 19% for phenelzine, imipramine, and placebo, respectively. In this study, the difference in response rate between phenelzine and imipramine was both clinically and statistically significant (P = .005).

The utility of phenelzine was also supported in a 2-stage, double-blind study of patients with atypical depression. During the first stage, response rates were significantly higher for phenelzine at both 6- and 12-week assessments (63% at 6 weeks and 51% at 12 weeks) than for imipramine (35% at 6 weeks and 24% at 12 weeks).56 During the second phase, nonresponders to imipramine were switched to phenelzine; a response rate of 67% was observed. Only 41% of the phenelzinenonresponders responded to imipramine.

Interestingly, another placebo-controlled RCT conducted by the same group of investigators compared phenelzine and imipramine in outpatients with a depressive episode characterized by reactive mood but none of the other criteria for atypical depression. In this trial, response rates to the MAOI and to the TCA were essentially identical (75% for phenelzine and 74% for imipramine); both drugs were superior to placebo. When taken together, these findings suggest that mood reactivity per se is not related to drug response, but rather it is the presence of criterion B features that predicts response to MAOIs.

It is also worth noting that results of a re-analysis suggest that the overall

advantage of the MAOI over the TCA in the aforementioned studies may well be the result of the relative inferiority of imipramine in patients with early onset of illness (ie, before age 21 years) and chronic atypical depression (ie, duration of at least 2 years with well periods of no longer than 2 months). In fact, among the patients with a later illness onset and a less chronic course, the imipramine response rate was about 65% (approximating that with phenelzine). Although 4 different MAOIs are licensed by the FDA for the treatment of major depression (ie, tranylcypromine, phenelzine, isocarboxazid, and selegiline transdermal delivery system), only the label for phenelzine includes a clear indication for atypical features.

SSRIs

Although MAOIs are clearly effective in patients with atypical depression, they are not considered first-line choices because of the required dietary restrictions and potential adverse effects. In light of this, researchers have switched their focus to the potential role of non-MAOI/non-TCA medications in the treatment of atypical depression.

In the first study to directly compare an SSRI with an MAOI, Pande and colleagues randomized 40 patients with atypical depression to a 6-week course of either fluoxetine (20 to 60 mg/d) or phenelzine (15 to 90 mg/d). Response rates (defined as a decrease of 50% or more in Hamilton Rating Scale for Depression-17 [HAMD-17] or a Clinical Global Impressions Improvement [CGI-I] score of 1 or 2) for fluoxetine and phenelzine were reported as 80% to 85% and 85%, respectively. Remission rates (HAMD-17 less than 5 and a CGI-I score of 1 or 2) were 80% for fluoxetine and 70% for phenelzine. No statistically significant differences were found between the groups, but the frequency of adverse effects was lower with fluoxetine. This study suggests that fluoxetine may be as effective as phenelzine in the treatment of atypical depression, with the SSRI having a better tolerability profile.

Further attempts to establish the utility of SSRIs in the treatment of atypical depression include trials of SSRIs (fluoxetine and sertraline) versus the reversible MAOI drug moclobemide. In the first trial, moclobemide (an investigational drug that is not commercially available in the United States) at a median dose of 379 mg displayed superiority as evidenced by response rates ranging from 71% to 91% (HAMD and CGI-I) over the 60% to 65% for fluoxetine at a median dose of 27 mg in the sample of 40 patients with atypical depression. In the second trial, there was a trend toward superiority for sertraline at 50 to 100 mg/d over moclobemide at 300 to 450 mg/d, as reflected by remission rates (CGI-I = 1)

of 77.5% and 67.5% for sertraline and moclobemide, respectively, after 12 weeks of treatment (P > .05; n = 172).

Interpretation of these studies is limited by the absence of a placebo arm and also by concerns about the limited clinical efficacy of moclobemide at the dosages studied (see, for example, Lotufo-Neto and colleagues). This work, nevertheless, provides some further support for the clinical impression that the SSRIs are more useful for treatment of patients with atypical depression than the TCAs.

The efficacy of fluoxetine was also demonstrated by McGrath and colleagues in their 20-week, double-blind, placebo-controlled study of atypical depression (N = 154), which used imipramine and placebo control groups. A significant advantage for both active groups compared with the placebo group was reported; however, no significant difference was found between the SSRI and TCA groups. Both active groups achieved comparable response rates (ie, 51% for fluoxetine and 53% for imipramine); fluoxetine had a better tolerability profile. Although both response rates are lower than the ones that have been reported for studies conducted by this group with phenelzine, they are still clinically significant and support the usefulness of SSRIs in the treatment of atypical depression.

Other treatment options

The irreversible MAOI selegiline, which is selective for monoamine oxidase B at low oral doses, and cognitive-behavioral therapy (CBT) both appear to be promising treatment options for patients with atypical depression. Initial studies of selegiline in atypical depression date back to 1984 and suggested a beneficial role with response rates of 59% at doses greater than 20 mg/d and up to 40 mg/d. Later, a placebo-controlled trial of selegiline (N = 98) also showed positive results, as evidenced by a response rate of 50% in the selegiline arm compared with 28% in the placebo arm. It is noteworthy that the doses of selegiline used in these studies were high enough to inhibit monoamine oxidase A. However, to date, no studies of atypical depression have been completed using the transdermal formulation of selegiline.

A 10-week, double-blind, placebo-controlled study found efficacy for CBT in the acute-phase treatment of atypical depression. A total of 108 subjects were randomly assigned to twice-weekly CBT, phenelzine, or placebo. A significant reduction in HAMD scores was reported with both active interventions. Response rates were 58% for both active modalities compared with 28% for placebo. There was no statistically significant difference between the active groups. CBT also

fared relatively well in the subset of patients with atypical depression in secondary analyses of the NIMH Treatment of Depression Collaborative Research Program, which also studied interpersonal psychotherapy and clinical management with double-blind placebo or imipramine.

CONCLUSIONS

Identification of atypical features is important in the treatment of depression for both treatment selection and prognosis, especially when initial measures prove ineffective. The concept of atypical depression has evolved over many years, and now it appears timely for a further revision. Our review of the current literature suggests a need for optimizing the precision and reliability of the current DSM criteria for atypical features. This could be achieved by the elimination of reactive mood as mandatory for diagnosis, by a more specific definition of criterion B features, and by the inclusion of chronicity and early age at onset as criteria.

Findings from the literature on the treatment of atypical depression show that phenelzine, and by implication the MAOIs as an antidepressant class, is the most effective pharmacological agent for atypical depression. Imipramine, and by implication the TCAs, is not as effective but still represents a treatment option for patients with atypical depression, particularly those with later onset of illness and less chronic courses. Given that neither MAOIs nor TCAs are widely prescribed now, other important treatment options include the SSRIs, notably fluoxetine and sertraline. Unfortunately, other antidepressants that may be useful in atypical depression, including bupropion and venlafaxine, have not been systematically studied. One form of depression-specific psychotherapy, CBT, has also been found to be efficacious and should be included in the treatment plan for atypical depression.

There is still a clear need for medication trials to better characterize the initial steps (before consideration of MAOIs or TCAs) in the treatment algorithm for atypical depression. Although historically ECT has been thought to be ineffective for atypical depression, recent reports suggest that it, too, may be effective in well-selected cases. The role of newer neuromodulation techniques, such as transcranial magnetic stimulation and, for patients with more advanced degrees of treatment resistance, vagus nerve stimulation and deep brain stimulation, still needs to be explored.

---

http://www.psychiatrictimes.com/login?referrer=http%3A//www.psychiatrictimes.com%2Fatypical-depression

POSTPARTUM DEPRESSION

Defazio G et al. Neurology

Postpartum depression (PPD) is a complex mix of physical, emotional, and behavioral changes that happen in a woman after giving birth. According to the DSM IV, a manual used to diagnose mental disorders, PPD is a form of major depression that has its onset within four weeks after delivery. The diagnosis of postpartum depression is based not only on the length of time between delivery and onset, but also on the severity of the depression

What Is Postpartum Depression?

Postpartum depression is linked to chemical, social, and psychological changes associated with having a baby. The term describes a range of physical and emotional changes that many new mothers experience. The good news is postpartum depression can be treated with medication and counseling.

The chemical changes involve a rapid drop in hormones after delivery. The actual link between this drop and depression is still not clear. But what is known is that the levels of estrogen and progesterone, the female reproductive hormones increase, tenfold during pregnancy. Then, they drop sharply after delivery. By three days after a woman gives birth, the levels of these hormones drop back to what they were before she got pregnant.

In addition to these chemical changes, social and psychological changes associated with having a baby create an increased risk of depression.

What Are the Symptoms of Postpartum Depression?

Symptoms of postpartum depression are similar to what happens normally following childbirth. They include lack of sleep, appetite changes, excessive fatigue, decreased libido, and frequent mood changes. However, these are also accompanied by other symptoms of major depression, which may include depressed mood; loss of pleasure; feelings of worthlessness, hopelessness, and helplessness; and thoughts of death or suicide.

What Are the Risk Factors for Getting Postpartum Depression?

A number of factors can increase the risk of postpartum depression, including:

- a history of depression during pregnancy
- age at time of pregnancy -- the younger you are, the higher the risk
- ambivalence about the pregnancy
- children -- the more you have, the more likely you are to be depressed in a subsequent pregnancy
- having a history of depression or

premenstrual dysphoric disorder (PMDD)
- o limited social support
- o living alone
- o marital conflict

Who Is at Risk for Postpartum Depression?

Most new mothers experience the "baby blues" after delivery. About one out of every 10 of these women will develop a more severe and longer-lasting depression after delivery. About one in 1,000 women develops a more serious condition called postpartum psychosis.

Are There Different Types of Postpartum Depression?

There are three types of mood changes women can have after giving birth:

- o The "baby blues," which occur in most women in the days right after childbirth, are considered normal. A new mother has sudden mood swings, such as feeling very happy and then feeling very sad. She may cry for no reason and can feel impatient, irritable, restless, anxious, lonely, and sad. The baby blues may last only a few hours or as long as one to two weeks after delivery. The baby blues do not usually require treatment from a health care provider. Often, joining a support group of new moms or talking with other moms helps.
- o Postpartum depression (PPD) can happen a few days or even months after childbirth. PPD can happen after the birth of any child, not just the first child. A woman can have feelings similar to the baby blues -- sadness, despair, anxiety, irritability -- but she feels them much more strongly than she would with the baby blues. PPD often keeps a woman from doing the things she needs to do every day. When a woman's ability to function is affected, she needs to see her health care provider. If a woman does not get treatment for PPD, symptoms can get worse. While PPD is a serious condition, it can be treated with medication and counseling.
- o Postpartum psychosis is a very serious mental illness that can affect new mothers. This illness can happen quickly, often within the first three months after childbirth. Women can lose touch with reality, having auditory hallucinations (hearing things that aren't actually happening, like a person talking) and delusions (strongly believing things that are clearly irrational). Visual hallucinations (seeing things that aren't there) are less common. Other symptoms include insomnia (not being able to sleep), feeling agitated (unsettled) and angry, and strange feelings and behaviors. Women who have postpartum psychosis need treatment right away and almost always need medication. Sometimes

women are put into the hospital because they are at risk for hurting themselves or someone else.

Do Anxiety Disorders Increase With Postpartum Depression?

Symptoms of obsessive-compulsive disorder may appear or worsen in the postpartum period. The obsessions are usually related to concerns about the baby or harming the baby. Panic disorder may also occur. Both conditions often coexist with depression.

Tips for Coping After Childbirth

Here are some tips that can help you cope with bringing home a newborn:

- Ask for help -- let others know how they can help you.
- Be realistic about your expectations for yourself and baby.
- Exercise; take a walk and get out of the house for a break.
- Expect some good days and some bad days.
- Follow a sensible diet; avoid alcohol and caffeine.
- Foster the relationship with your partner -- make time for each other.
- Keep in touch with family and friends -- do not isolate yourself.
- Limit visitors when you first go home.
- Screen phone calls.
- Sleep or rest when your baby sleeps!

How Is Postpartum Depression Treated?

Postpartum depression is treated differently depending on the type and severity of a woman's symptoms. Treatment options include anti-anxiety or antidepressant medications, psychotherapy, and participation in a support group for emotional support and education.

In the case of postpartum psychosis, drugs used to treat psychosis are usually added. Hospital admission is also often necessary.

If you are breastfeeding, don't assume that you can't take medication for depression, anxiety, or even psychosis. Talk to your doctor. Under a doctor's supervision, many women take medication while breastfeeding. This is a decision to be made between you and your doctor.

When Should a New Mom Seek Professional Treatment?

Untreated postpartum depression can be dangerous for new moms and their children. A new mom should seek professional help when:

- symptoms persist beyond two weeks.
- she is unable to function normally.
- she can't cope with everyday situations.
- she has thoughts of harming herself or her baby.
- she is feeling extremely anxious, scared, and panicked most of the day.

---

www.medicinenet.com/script/main/art.asp

WANTED

Full Time
&
Part Time

PSYCHIATRIST

Diplomate of the
American Board of Psychiatry

Send CV to:
Dr. Syed Mubin Akhtar
M.D. Karachi Psychiatric Hospital
Email: mubin@kph.org.pk
Nazimabad # 3, Karachi.
Phone: 111-760-760

"According to the computer, I need to back up your kidneys, defragment your liver and reboot your heart."

ATTENTION PSYCHIATRISTS, PG TRAINEES & OTHER DOCTORS INTERESTED IN RESEARCH ARTICLES

All Psychiatrists, PGs, Trainees & other Doctors who are interested in psychiatric research articles are requested to send their name, address & phone numbers to the Karachi Psychiatric Hospital Bulletin which will be send to them free of cost.

Karachi Psychiatric Hospital
Nazimabad # 3, Karachi.

Phone : 111-760-760
E.Mail : support@kph.org.pk
WebSite : www.kph.org.pk.

KARACHI PSYCHIATRIC HOSPITAL BULLETIN

SUBJECT INDEX-2013 (Psychiatric Issues)

(Feb, April, June, Dec.)

- WHY PANIC ATTACKS ARE NEARLY ALWAYS PATHOLOGICAL PANIC ON THE PRECIPICE (PART 1): DOES "CONTEXT" DETERMINE DISORDER IN PSYCHIATRY? (June Page 95)

BIPOLAR AFFECTIVE DISORDER

- I WANT IT NOW! NEURAL CORRELATES OF HYPERSENSITIVITY TO IMMEDIATE REWARD IN HYPOMANIA (Feb. Page 34)
- PERINATAL EPISODES ACROSS THE MOOD DISORDER SPECTRUM (June Page 111)
- THE ANXIOUS BIPOLAR PATIENT-STRATEGIES FOR TREATMENT (April Page 65)

CHILDREN

- DIFFERENTIAL GLUCOCORTICOID RECEPTOR EXON 1B, 1C, AND 1H EXPRESSION AND METHYLATION IN SUICIDE COMPLETERS WITH A HISTORY OF CHILDHOOD ABUSE (Feb. Page 30)
- TESTS OF A DIRECT EFFECT OF CHILDHOOD ABUSE ON ADULT BORDERLINE PERSONALITY DISORDER TRAITS (Feb. Page 36)
- WHITE MATTER DISRUPTIONS IN ADOLESCENTS EXPOSED TO CHILDHOOD MALTREATMENT AND VULNERABILITY TO PSYCHOPATHOLOGY (Feb. Page 31)

COGNITIVE THERAPY

- ASSOCIATION BETWEEN MATERNAL DEPRESSOGENIC COGNITIVE STYLE DURING PREGNANCY AND OFFSPRING COGNITIVE STYLE 18 YEARS LATER (April Page 69)
- COMPARING EFFICACY OF ECT WITH AND WITHOUT CONCURRENT SODIUM VALPROATE THERAPY IN MANIC PATIENTS (Feb. Page 35)
- COMPUTER-ASSISTED PSYCHOTHERAPY HUMAN THERAPISTS STILL NEEDED (April Page 38)
- EFFECTIVENESS OF INTERNET-BASED COGNITIVE BEHAVIOUR THERAPY FOR PANIC DISORDER IN ROUTINE PSYCHIATRIC CARE (June Page 110)

DEPRESSION

ELECTROCONVULSIVE THERAPY

MISCELLANEOUS

PSYCHOLOGY

PSYCHOSIS

SEIZURES

ooo