

HOSPITAL PHYSICIAN®

PSYCHIATRY BOARD REVIEW MANUAL

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The *Hospital Physician Psychiatry Board Review Manual* is a study guide for residents and practicing physicians preparing for board examinations in psychiatry. Each manual reviews a topic essential to the current practice of psychiatry.

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Treatment-Resistant Depression

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Treatment-Resistant Depression

Rafay Atiq, MD

INTRODUCTION

Refractory depression, also called treatment-resistant depression, is commonly encountered by mental health professionals, even in the context of treatment with appropriate antidepressants. Approximately half of depressed patients have an inadequate response to monotherapy,¹⁻⁴ and as many as 20% have chronic depression despite multiple interventions.^{5,6}

Treatment-resistant depression can be broadly defined as a failure to respond completely to a treatment known to be effective for major depression. However, in clinical practice, treatment-resistant depression is best defined as occurring along a continuum ranging from partial response to complete refractoriness, in which the degree of treatment resistance is ascertained by taking into account such factors as total number of antidepressant trials and their outcome, the number of failed treatments, and the degree of lack of response.^{3,7} Proposed operational definitions for treatment-resistant depression terminology are shown in **Table 1**.

Treatment-resistant depression may contribute to the overwhelming morbidity and mortality rates associated with affective illness^{8,9} and account for a disproportionate amount of physician treatment time. This manual reviews the approach to evaluation and treatment of the patient with treatment-resistant depression.

CASE STUDY

INITIAL PRESENTATION

A 65-year-old woman with a history of chronic back pain presents to the clinic for treatment of recurrent and severe major depressive disorder.

HISTORY

The patient reports a 2-month history of worsening depression, initial insomnia and early morning awakening, anergia, seclusion, hopelessness and helplessness, decreased appetite, and a weight loss of 10 lb. She

has also stopped engaging in her hobbies of painting and playing music.

The patient was diagnosed with major depressive disorder 25 years earlier and had been treated ever since with adequate courses of various tricyclic antidepressant (TCA) and selective serotonin reuptake inhibitor (SSRI) monotherapies, nefazodone, and a combination of citalopram and bupropion. Her previous psychiatrists had also tried augmentation with lithium and triiodothyronine (T₃) but saw only partial improvement. She is currently being treated with a combination of escitalopram 20 mg/day and mirtazapine 30 mg once daily at night. The patient remains chronically depressed with a regular score of 15 or higher on the 21-item Hamilton Depression Rating Scale.

PHYSICAL EXAMINATION

The patient is a thin, frail, elderly woman who looks older than her stated age. Her speech is slow and impoverished, but she is oriented to place and person. She describes her mood as sad, and her affect is restricted and dysphoric. Her thought process is goal-directed and thought content is without any apparent delusions or preoccupations. She denies any suicidal ideations. No evidence of perceptual abnormality is found. No deficits are noted in her attention and concentration, and she has a good insight into her illness.

- **What is the approach to evaluation of the patient with treatment-resistant depression?**

In evaluating a patient with treatment-resistant depression, a careful history of all previous treatments must be elicited. Thase and Rush¹⁰ provide a practical system for staging treatment-resistant depression based on previous courses of treatment (**Table 2**). This system can be used as a guide for applying treatment strategies.

It is important to differentiate between true treatment resistance and pseudoresistance. Failure to provide adequate treatment, ie, prescribing inadequate doses of medication or treating for too short a duration, is a major cause of pseudoresistance. Patient factors that may contribute to pseudoresistance include premature discontinuation of medications due to intolerable side effects or