Recognizing mimics of depression:

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Dr. Rackley: How to spot conditions that may masquerade as depression

The '8 Ds'

This mnemonic helps recall conditions that may make medically ill patients appear depressed

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Many psychiatric and medical illnesses—as well as normal reactions to stressors—have symptoms that overlap with those of depressive disorders, including outwardly sad or dysphoric appearance, irritability, apathy or amotivation, fatigue, difficulty making decisions, social withdrawal, and sleep disturbances. This cluster of symptoms forms a readily observable behavioral phenotype that clinicians may label as depression before considering a broader differential diagnosis.

To better understand what other conditions belong in the differential diagnosis, we reviewed a sample of 100 consecutive medical/surgical inpatients referred to our consultation-liaison psychiatry practice for evaluation of "depression." Ultimately, only 29 of these patients received a depression diagnosis. Many of the other diagnoses given in our sample required attention during inpatient medical or surgical care because they were potentially life-threatening if left unaddressed—such as delirium—or they interfered with managing the primary medical or surgical condition for which the patient was hospitalized.

Hurried or uncertain primary care clinicians frequently use "depression" as a catch-all term when requesting psychiatric consultation for patients who seem depressed. A wide range of conditions can mimic depression, and the art of psychosomatic psychiatry includes considering protean possibilities when assessing a patient. We identified 7 diagnoses that mimic major depression and developed our "8 D" differential to help clinicians properly diagnose "depressed" patients who have something other than a depressive disorder. Although our sample consisted of hospitalized patients, these mimics of depression

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Mimics of depression

may be found among patients referred from other clinical settings for evaluation of possible depression.

The perils of misdiagnosis

Depression is common among patients hospitalized with medical or surgical conditions. DSM-IV-TR diagnostic criteria for a major depressive episode (MDE) include the presence of low mood and/or anhedonia, plus ≥4 other depressive symptoms for ≥2 weeks.[1] Growing evidence suggests that the relationship between depression and morbidity and mortality in medical illness is bidirectional, and nonpsychiatrists are becoming increasingly aware of major depression's serious impact on their patients' physical health.[2-5]

Although improving nonpsychiatrists' recognition of depression in medically ill patients is laudable, it comes with a high false-positive rate. In a study of primary care outpatients, Berardi et al found that 45% of patients labeled "depressed" did not meet ICD-10 criteria for major depression, but >25% of those patients were prescribed an antidepressant.[6] In a large retrospective study, Boland et al found that approximately 40% of patients referred to an inpatient psychiatric consultation service for depression did not meet criteria for a depressive illness, and primary medical services often confused organic syndromes such as delirium and dementia with depression.[7] Similarly, Clarke et al found that 26% of medical and surgical inpatients referred to psychiatry with "depression" had another diagnosis—commonly delirium—that better accounted for their symptoms.[8]

What is the harm in overdiagnosing depression? Missing a serious or life-threatening diagnosis is a primary concern. For example, unrecognized delirium, which frequently was misdiagnosed as depression in the Berardi,[6] Boland,[7] and Clarke[8] studies, is associated with myriad difficulties, including higher morbidity and mortality.[9] Substance use disorders, which also commonly masquerade as depression, frequently are comorbid with medical illness. Delays in appropriate treatment of withdrawal syndromes—particularly of alcohol and sedative/hypnotic medications—are risk factors for increased mortality in these illnesses.[10]

Inappropriate, potentially harmful interventions are another concern. Many patients diagnosed with depression are prescribed antidepressants, but this is not always a benign intervention. Smith et al found that >10% of adult medical inpatients referred to a psychiatry consultation service who were started on an antidepressant had an adverse drug reaction severe enough to warrant discontinuing the medication.[11] Antidepressant side effects relevant to medically ill patients include hyponatremia, serotonin syndrome, and exacerbation of delirium.[12]

Polypharmacy in medically ill patients increases the risk for serious drug-drug interactions. For example, serotonergic antidepressants can increase the risk for serotonin syndrome when combined with the analgesic tramadol, which has serotonergic activity,[13] or the antibiotic linezolid, which is a reversible monoamine oxidase inhibitor.[14] Many antidepressants—including paroxetine, fluoxetine, bupropion, sertraline, and duloxetine—are moderate to strong inhibitors of cytochrome P450 2D6 and therefore affect metabolism of many medications, including several beta blockers and antiarrhythmics, as well as the anti-estrogen tamoxifen. In the case of tamoxifen, which is a prodrug converted to active form by 2D6, concomitant use of a 2D6 inhibitor can substantially reduce the medication's in vivo efficacy and lead to higher morbidity and mortality in breast cancer patients.[15] As with any treatment, a decision to prescribe antidepressants needs to carefully be weighed in light of individual risks and benefits. This analysis starts by ensuring that an antidepressant is indicated.

Another concern is failing to recognize immediate human suffering for what it is. Hospitals and doctors' offices are places of pain and loss as patients encounter morbidity and mortality in themselves and their loved ones. Rushing to pathologize the psychological or social manifestations of this pain can be invalidating to patients and may impair the doctor-patient relationship.

Clinical Point

Studies have found that 26% to 45% of patients referred for 'depression' did not meet diagnostic criteria for a depressive illness

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Table 1

Psychological crises that may look like depression

Category	Percentage of our sample	Distinguishing features	Suggested interventions
"Depressed" patients met DSM-IV-TR criteria for a depressive disorder	29%	Emotional symptoms: Depressed mood, anhedonia Cognitive symptoms: concentration problems, indecisiveness, negative thoughts, irrational guilt Physical symptoms: changes in sleep, appetite, energy	Initiate psychotherapy with or without antidepressants
"Demoralized" patients had difficulty coping with a medical illness	23%	Close temporal association with illness. Few neurovegetative symptoms. Able to maintain future orientation/hope	Provide compassion, recognition, and normalization. Connect patients with illness-specific supports (groups, social work, chaplaincy). Implement interventions to improve functioning (eg, PT/OT). Encourage patients to engage in activities that have helped them cope in the past
"Disaffiliated" patients had dysphoria attributable to grief from losing a major relationship	3%	Few neurovegetative symptoms. Able to maintain future orientation/hope. Improvement typical as time since loss increases	Encourage patients to connect with other supportive relationships. Refer patients to grief resources (eg, hospice, spiritual supports)

OT: occupational therapy; PT: physical therapy

Clinical Point

Misdiagnosis of depression could lead to delays in treatment for other disorders or inappropriate, potentially harmful interventions

The 8 Ds

To determine what these "depression look-alike" syndromes could be, we identified 100 consecutive consultations to our adult inpatient psychiatry consultation-liaison team with a question of "depression." We reviewed each patient's chart, and recorded the diagnosis the psychiatrist gave to explain the patient's depressed appearance. Data were recorded without patient identifiers, and the Mayo Clinic institutional review board (IRB) determined this study was exempt from IRB review.

Our sample included 45 men and 55 women with an average age of 48 (range: 18 to 91). On evaluation, 3 patients were given no psychiatric diagnosis, 29 were categorized as depressed, and 68 fell into one of 7 other "D" categories we describe below.

Depressed. These patients met criteria for a MDE in the context of major depressive disorder (MDD) or bipolar disorder, dysthymic disorder, mood disorder due to a general medical condition, substance-induced mood disorder, or depressive disorder not otherwise specified.

Demoralized. Patients who had difficulty adjusting to or coping with illness, and received a DSM-IV-TR diagnosis of adjustment disorder with the illness as the inciting stressor were placed in this category. Consistent with adjustment disorder criteria, these patients did not have depressive symptoms of sufficient intensity or duration to meet criteria for MDD or another primary mood disorder.

Difficult. For these patients, the primary issue was a breakdown in the therapeutic alliance with their treatment team. They received DSM-IV-TR diagnoses of personality disorder, noncompliance with treatment, or adult antisocial behavior.

Drugged. Patients in this category appeared depressed as a result of illicit substance use or misuse of alcohol or pharmaceuticals. DSM-IV-TR diagnoses includ-

Mimics of depression

Clinical Point

In our sample, the most commonly misdiagnosed patients were those having difficulty adjusting to illness or other life events

Table 2

Differentiating patients with social challenges from those with depression

Category	Percentage of our sample	Distinguishing features	Suggested interventions
"Difficult" patients have a breakdown in the therapeutic alliance with their treatment team	15%	Mood changes often intense, immediate, and reactive to situation. Frequent breakdowns in communication with care team. Care team more distressed by patient's symptoms than the patient	Establish frequent communication among care team members. Use multidisciplinary care conferences to clarify salient issues for patients and their team. Provide patients with consistent information and expectations
"Delusional" patients had affective blunting as a result of a psychotic disorder	2%	Suspicious about care team/procedures. Seems frightened or scans the room. On antipsychotics at admission. Slowly developing symptoms over several days after home medications are held	Acquire collateral history (an assigned community case manager or social worker can be an important source). Establish a plan for administering psychotropics in chronically mentally ill patients; consider IM or orally disintegrating formulations
"Dulled" patients had irreversible cognitive deficits	2%	Baseline impairments in memory and/or independent functioning	Acquire collateral history. Perform a safety assessment of home environment with attention to need for additional supports

IM: intramuscular

ed substance intoxication or withdrawal and substance abuse or dependence.

Delirious. This group consisted of patients with acute disruption in attention and level of consciousness that met DSM-IV-TR criteria for delirium. Patients whose delirious appearance was the result of illicit substance use or pharmaceutical misuse were categorized as "Drugged" rather than "Delirious."

Disaffiliated. Patients in this category had dysphoria not commensurate with a full-blown mood disorder but attributable to grief from losing a major relationship to death, separation, or divorce. These patients received a DSM-IV-TR diagnosis of bereavement or a partner relational problem.

Delusional. These patients demonstrated amotivation and affective blunting as a result of a primary psychotic disorder such as schizophrenia. In preparation for emergent surgery, these patients had been prevented from taking anything orally, including antipsychotics, and their antipsychotics had not been restarted, which precipitated a gradual return of psychotic symptoms in the days after surgery.

Dulled. Two patients in our sample had irreversible cognitive deficits that explained their withdrawal and blunted affect; 1 had dementia and the other had mental retardation.

Managing the other Ds

In our sample, the most commonly misdiagnosed patients were those having difficulty adjusting to illness (Demoralized) or to other life events (Disaffiliated) (***Table 1, page 33***). In these cases, misdiagnosis has substantial treatment implications because these patients are better served by acute, illness-specific interventions that bolster coping skills, rather than pharmacotherapy or psychotherapy that targets entrenched depressive symptoms. For these patients,

Table 3

Substance abuse and delirium can mimic depression

Category	Percentage of our sample	Distinguishing features	Suggested interventions
"Drugged" patients appeared depressed as a result of substance use/ withdrawal	12%	Acute presentation closely mimicking mood, anxiety, or psychotic disorders. Emotional symptoms present when intoxicated or withdrawing and resolved during sobriety	Implement safety interventions to prevent self-harm or aggression during acute phase. Support and monitor withdrawal as indicated. Reassess mood state and symptoms once the patient is sober. Refer for chemical dependency evaluation
"Delirious" patients met DSM-IV-TR criteria for delirium	11%	Disoriented and inattentive. Onset over hours to days. Waxing and waning throughout the day. Possible hallucinations (often visual or tactile)	Identify and correct underlying medical cause(s). Restore the patient's sleep-wake cycle. Provide frequent reorientation and reassurance

psychiatrists may "prescribe" interventions such as visits with a chaplain or other spiritual advisor, telephone calls or visits from family, friends, and other social supports, participation in physical or occupational therapy to improve adaptive functioning, or connecting with other patients in similar situations. Often, the key with these patients is to identify ways they have managed previous stressors and creatively use those resources to adapt to their new situation.

A second large group in our sample consisted of patients actively or passively fighting with their treatment team—the Difficult (***Table 2***). The treatment team or the patient's caregivers and loved ones often are more distressed by the "difficult" patient's symptoms than the patient, who may instead focus on his or her disappointment with caregivers who are unable to meet the patient's unreasonable expectations. These challenges typically can be addressed by clarifying the salient issues for both the patient and team and establishing a liaison between patient and team to improve communication among all parties. Multidisciplinary care conferences can be an excellent way to ensure that the care team provides the patient with consistent communication and care.

A third group had potentially life-threatening conditions such as substance abuse/withdrawal or delirium as the cause of their "depressive" symptoms—the Drugged and the Delirious (***Table 3***). Recognizing an organic etiology of mood or behavioral symptoms is important because managing the underlying problem is the primary treatment strategy, not psychopharmacologic or psychotherapeutic intervention. Early identification and appropriate management of these patients could prevent further deterioration, improve medical outcomes, and shorten length of hospital stay.

A final group of patients was those whose chronic psychiatric and cognitive issues may go unrecognized or unappreciated until they interfere with the patient's medical care—the Delusional and the Dulled (***Table 2***). In these cases, the correct diagnosis often hinges on obtaining a thorough history through collateral sources. The consulting psychiatrist can be crucial in co-managing these patients by establishing a liaison with outpatient providers, suggesting in-hospital management strategies such as alternate routes of administration of antipsychotics for patients with psychotic disorders, and connecting patients with outpatient supports after hospitalization. Continuity between inpatient and outpatient management is necessary to ensure a successful medical and psychiatric outcome.

Our 8 Ds are limited to the subset of patients referred by their medical teams

Clinical Point

Some 'depressed' patients had mood symptoms as a result of a breakdown in the therapeutic alliance with their treatment team

Mimics of depression

Clinical Point

Recognizing an organic etiology of mood or behavioral symptoms will allow you to focus on managing the underlying problem

Related Resources

- Stern TA, Fricchione GL, Cassem NH, et al, eds. Massachusetts General Hospital handbook of general hospital psychiatry, 6th ed. Philadelphia, PA: Saunders Elsevier; 2010.
- Levenson JL, ed. The American Psychiatric Publishing textbook of psychosomatic medicine. 2nd ed. Arlington, VA: American Psychiatric Publishing, Inc.; 2011.
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Drug Brand Names

Bupropion • Wellbutrin, Zyban
Duloxetine • Cymbalta
Fluoxetine • Prozac
Linezolid • Zyvox
Paroxetine • Paxil
Sertraline • Zoloft
Tamoxifen • Nolvadex
Tramadol • Ultracet

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with a question of depression. These referrals may have been motivated by a variety of patient, family, and team factors above and beyond the categories discussed in this article, and therefore may not accurately represent all patients who present with depressive symptoms in an inpatient setting. However, we hope that providing a mnemonic that suggests an extensive differential for a depressed phenotype may improve identification and management of these issues.

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Bottom Line

Many conditions masquerade as depression, and the art of psychiatry includes considering protean possibilities when assessing a patient who appears depressed. Our '8 Ds' mnemonic is intended to remind clinicians that more than two-thirds of 'depressed' medically ill patients may have something other than a depressive disorder.