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PSYCHIATRIC MANIFESTATIONS OF ENDOCRINE DISORDERS: DIAGNOSTIC CHALLENGES IN CLINICAL PSYCHIATRY

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ABSTRACT

Endocrine disorders can present with depression, anxiety, cognitive impairment, behavioral change or psychosis, sometimes before their physical manifestations are recognized. For psychiatrists, the difficulty extends beyond identifying a possible medical mimic: endocrine disease, primary psychiatric illness, treatment effects and psychosocial distress may coexist. This narrative review examines these diagnostic challenges using a predefined collection of clinical studies, reviews, guidance and illustrative case reports. Particular attention is given to thyroid and adrenal disease, with complementary discussion of pituitary disorders, calcium disturbances, diabetes and reproductive or developmental factors. Psychiatric phenomenology rarely identifies a specific endocrine cause, while abnormal hormone concentrations may reflect established gland disease, medication exposure, acute illness or physiological adaptation. Observational associations therefore require careful separation from evidence of causation in an individual patient. Clinical assessment should integrate symptom chronology, collateral information, physical findings, medication history and appropriately interpreted laboratory results. Treatment resistance or an altered course should prompt diagnostic reconsideration when accompanied by relevant systemic features, but neither finding independently establishes an endocrine etiology. Improvement after endocrine treatment can strengthen causal attribution, although concurrent psychiatric interventions and incomplete recovery complicate interpretation. Persistent psychiatric symptoms after biochemical normalization require renewed assessment rather than automatic attribution to either unresolved endocrinopathy or an unrelated psychiatric disorder. The available literature supports coordinated psychiatric and endocrine care but provides limited evidence validating universal screening panels or diagnostic prediction rules. Prospective studies should evaluate diagnostic yield, time to recognition, patient functioning and psychiatric outcomes alongside biochemical measures.

Keywords: Endocrine disorders; Psychiatric manifestations; Differential diagnosis; Thyroid disease; Adrenal disorders; Consultation-liaison psychiatry Introduction

1 INTRODUCTION

An endocrine disorder may first become clinically visible through a change in mood, thought or behavior. Depression, anxiety, impaired concentration and psychosis occur across several endocrinopathies, yet these manifestations commonly resemble primary psychiatric disorders. The clinical task is consequently more demanding than recalling a list of medical mimics. A psychiatrist must determine whether an endocrine abnormality plausibly explains the presenting syndrome, contributes to an established disorder, reflects its treatment, or accompanies illness without accounting for the patient's principal difficulties. [1, 2, 3]

The breadth of psychiatric-medical comorbidity makes this distinction important. A Norwegian primary-care register study involving 2,203,553 people found widespread co-occurrence and temporal associations between mental disorders and physical disease categories, including endocrine conditions. Such findings support attention to physical health throughout psychiatric care, but they cannot identify the biological cause of symptoms in an individual patient. The endocrine category encompassed heterogeneous conditions, and recorded clinical contacts did not establish the true onset of either illness. [4]

This review considers how psychiatrists can recognize endocrine disease while avoiding premature causal attribution. It emphasizes the interpretation of overlapping symptoms, discordant laboratory findings and changes in illness course. Endocrine treatment is considered where it informs diagnostic reasoning or continuing psychiatric care; detailed endocrine prescribing and disorder-specific treatment protocols lie outside its scope.

1.1 Scope and approach

The review draws exclusively on a predefined collection of 39 supplied PDFs, comprising primary observational studies, clinical reviews, practice guidance, case reports, conceptual articles and an edited collection containing individual full-text papers. Duplicate versions and an editorial reproduced within the collection were reconciled. A conference abstract was distinguished from full-length evidence. Sources were examined for their relevance to clinical psychiatric diagnosis, study design, population, interpretation and limitations. No independent database search, pooled analysis or formal risk-of-bias scoring was undertaken. This is a critical narrative synthesis rather than a systematic review or a clinical guideline. Studies discussed within secondary sources were not treated as independently verified primary research unless their full texts were also available in the collection.

2 ENDOCRINE FINDINGS AND PSYCHIATRIC CAUSATION

Several relationships can produce the same clinical encounter. Hormone excess or deficiency may directly contribute to psychiatric symptoms; systemic metabolic changes may affect cognition or consciousness; chronic illness may generate distress; and a primary psychiatric disorder may coexist with endocrine disease. Medication exposure adds another pathway. These possibilities should remain separate in the diagnostic formulation because confirming an endocrinopathy does not establish that it explains every accompanying symptom. The diabetes literature explicitly describes independent comorbidity, reciprocal influences, overlapping presentations and treatment-related effects. [2, 5, 6]

Biological plausibility helps explain overlap but offers limited diagnostic specificity. Thyroid hormones influence cerebral function, while glucocorticoid signaling participates in stress responses and affects cognition and mood. Reviews also describe endocrine-axis abnormalities within psychiatric populations without established primary gland disease. These observations concern related biological systems, but an altered stress response in depression is not equivalent to a diagnosis of Cushing's syndrome. Likewise, a proposed change in local cerebral hormone availability cannot be inferred directly from a patient's nonspecific symptoms or a single peripheral measurement. [7, 8, 9]

Genetic evidence further complicates a purely hormonal explanation. Soheili-Nezhad and colleagues found shared genetic liability between autoimmune thyroid disease and depression or anxiety, whereas significant genetic correlations with thyrotropin or free thyroxine were not demonstrated in the examined datasets. This finding suggests that pathways associated with autoimmunity may contribute to comorbidity. It does not establish immune mediation in every patient or exclude clinically important effects of overt hormone deficiency. Population-level genetic correlations cannot substitute for assessment of the patient's endocrine state and psychiatric course. [10]

The diagnostic weight of a finding therefore depends on its context. A coherent combination of physical signs, biochemical abnormalities and temporal evolution is more informative than symptom resemblance alone. Conversely, modest laboratory changes during acute psychiatric illness may have uncertain clinical significance. The central interpretive question is whether the endocrine findings fit the syndrome under evaluation, while allowing that more than one process may be active. This approach follows the clinical reviews' emphasis on integrating history, examination and laboratory interpretation rather than using any single observation as an etiological verdict. [1, 3, 11]

3 THYROID DISEASE AND AMBIGUOUS LABORATORY FINDINGS

3.1 Hypothyroidism beyond depressive slowing

Hypothyroidism may produce fatigability, slowed thinking, reduced initiative, impaired attention and memory, and depressive symptoms. These features are easily absorbed into a diagnosis of depression, especially when onset is gradual. Cold intolerance, constipation, a change in voice, dry skin, bradycardia or delayed relaxation of tendon reflexes provide additional reasons to investigate. Their value lies in the combined clinical picture; the reviews do not establish a psychiatric symptom pattern that reliably distinguishes hypothyroidism from primary depression. [1, 3, 11]

Psychosis requires similar caution. In the case described by Heinrich and Grahm, a 73-year-old woman developed auditory and visual hallucinations in association with marked thyroid dysfunction and physical findings compatible with hypothyroidism. Symptoms resolved during treatment with thyroid replacement and low-dose risperidone. The report demonstrates a clinically plausible endocrine presentation but cannot separate the effects of the two interventions. Its accompanying review also documents that hypothyroid psychosis can occur without the impaired consciousness of delirium. Clear consciousness therefore does not exclude an endocrine contribution to psychosis. [11]

Laboratory interpretation should distinguish the level of dysfunction. Elevated thyrotropin with reduced free thyroxine supports primary hypothyroidism, whereas elevated thyrotropin with normal circulating free hormone concentrations indicates a subclinical pattern. Central hypothyroidism can instead involve low free thyroxine with a low, normal or only mildly elevated thyrotropin concentration. A reassuring thyrotropin result alone can therefore be misleading when pituitary disease is clinically plausible. The purpose of testing is to characterize the endocrine abnormality before deciding how much explanatory weight to assign it. [3, 11]

The distinction between overt and subclinical disease matters psychiatrically. Jurado-Flores and colleagues describe inconsistent associations and treatment findings in subclinical hypothyroidism, including trials in which levothyroxine did not improve depressive outcomes compared with placebo. These trial findings are available here through the review rather than independent assessment of the primary reports. They argue against assuming that a modest thyrotropin elevation explains depression or predicts its resolution with replacement. Endocrine indications for treatment and psychiatric expectations should be discussed separately. [7]

3.2 Hyperthyroidism without a uniformly activated presentation

Hyperthyroidism can resemble anxiety, agitation or a mood episode through nervousness, emotional lability, insomnia, distractibility and increased activity. Heat intolerance, sweating, tremor, persistent tachycardia and weight loss despite increased appetite may make an endocrine explanation more plausible. However, activation is not universal. Older patients may present with apathy, lethargy, depressive symptoms or mental slowing, a presentation described as apathetic hyperthyroidism. Reliance on a stereotyped anxious or overactive phenotype risks missing this alternative presentation. [1, 3, 7]

A prior psychiatric diagnosis can make recognition particularly difficult. New thyrotoxicosis may be interpreted as another episode of bipolar illness or an exacerbation of psychosis, especially when physical complaints are poorly communicated. The existence of recent stressors provides little reassurance: psychosocial stress and endocrine disease can occur together. Reviews of Graves' disease also show why stress should not be assigned a simple causal role, since retrospective recall and uncertainty about disease onset complicate the direction of reported associations. [1, 12]

Acute psychiatric illness can itself accompany transient thyroid-test abnormalities. Nonthyroidal illness and acute hyperthyroxinemia complicate the interpretation of results obtained during hospitalization. In a retrospective psychiatric inpatient study, thyroid data were available for 343 of 468 reviewed patients. Abnormal hormonal status was reported in 43 of 147 patients with schizophrenia-spectrum disorders and 43 of 185 with mood disorders. Most abnormalities were subclinical, and clinical signs, medication exposure and longitudinal outcomes were insufficiently characterized. These findings describe laboratory abnormalities in selected inpatients rather than the proportion whose psychiatric illness was caused by thyroid disease. [3, 13]

3.3 Thyroid antibodies and neurological assessment

The presence of thyroid antibodies introduces a different interpretive problem. Reviews describe encephalopathy associated with autoimmune thyroid disease presenting with cognitive change, psychosis, seizures, movement abnormalities or focal neurological features. Yet thyroid antibodies may be coincidental, and the syndrome remains a diagnosis of exclusion. Antibody positivity alone should not convert an otherwise unexplained psychiatric presentation into an autoimmune encephalopathy diagnosis. Neurological examination and specialist assessment are needed to interpret the broader syndrome and consider competing explanations. [7]

This caution preserves a wider differential. Psychiatric symptoms can precede recognizable manifestations of neurodegenerative or neuroinflammatory disease, as reviewed by Menculini and colleagues. An endocrine finding should therefore not end investigation when neurological features remain unexplained. The clinical importance of the finding depends on whether it accounts for the patient's actual pattern of impairment, including the course of cognitive decline, altered awareness or associated neurological signs. [7, 14]

4 ADRENAL DISORDERS AND APPARENT PSYCHIATRIC TREATMENT RESISTANCE

4.1 Cushing's syndrome and the problem of overlapping metabolic features

Depression, irritability, anxiety, disturbed sleep and cognitive difficulties are described in Cushing's syndrome; mania and psychosis may also occur. Psychiatric symptoms can precede recognition of the characteristic physical syndrome. Central weight gain, hypertension or dysglycemia may be attributed to lifestyle or psychotropic treatment, making them less conspicuous in psychiatric practice. Their combination with progressive proximal weakness, skin changes, easy bruising or abdominal striae should increase concern about an endocrine contribution. These are clinical prompts for investigation rather than a validated psychiatric screening rule. [1, 15, 16]

Ummar and colleagues reported a young man with recurrent mood episodes whose later presentation included resistant hypertension, dysglycemia, central obesity, severe acne and abdominal striae. Investigation identified Cushing's syndrome after several psychiatric treatment changes. The diagnostic lesson is the importance of reassessing an evolving systemic pattern during an apparently psychiatric illness. Improvement after diagnosis occurred alongside endocrine treatment and further psychotropic changes, so the report does not establish an isolated endocrine treatment effect or show that treatment resistance alone predicts Cushing's syndrome. [16]

Differentiation is also difficult because depression and other psychiatric conditions may accompany hypothalamic-pituitary-adrenal axis dysregulation. Cortisol varies with diurnal timing, stress and clinical context, and the updated cortisol review describes heterogeneous findings across diagnoses and populations. A high cortisol result obtained in a distressed patient cannot independently establish autonomous cortisol excess. When the clinical picture raises concern, endocrine assessment must distinguish established disease from psychiatric-associated physiological changes. Historical test recommendations in older clinical reviews should not be mistaken for a newly validated universal protocol. [1, 8, 9]

4.2 Adrenal insufficiency and misleading psychiatric labels

Adrenal insufficiency can present with fatigue, anorexia, weight loss, reduced initiative and depressed mood. These manifestations may initially suggest depression or an eating disorder. Hypotension, dehydration, gastrointestinal symptoms, pigmentation changes and biochemical disturbances provide additional diagnostic information. A psychiatric explanation becomes less satisfactory when these systemic features progress. Conversely, pigmentation is associated with primary adrenal failure and is not expected in the same way in secondary insufficiency, so its absence cannot exclude all forms of adrenal dysfunction. [1, 17]

The case reported by Momayez Sanat and Mohajeri-Tehrani illustrates delayed recognition. A 28-year-old woman received psychiatric treatment before progressive weight loss, gastrointestinal symptoms, hypotension and hyperpigmentation led to the diagnosis of Addison disease. Marked psychiatric improvement was reported within 72 hours of hydrocortisone and saline treatment, with sustained improvement during follow-up. The temporal response supports an endocrine contribution in this case, but concurrent correction of systemic abnormalities and the single-patient design prevent generalization about response rates or diagnostic accuracy. [18]

Weight loss should be interpreted through both physical and psychiatric assessment. Loss of appetite from adrenal insufficiency is different from a syndrome characterized by weight and shape concerns or fear of gaining weight, although medical and psychiatric disorders can coexist. The point is to investigate the reason for reduced intake rather than assigning an eating-disorder diagnosis from body weight alone. A review comparing constitutional thinness and restrictive anorexia nervosa similarly emphasizes clinical phenotype and nutritional adaptation, but its proposed biological distinctions do not constitute a universally validated exclusion test for an eating disorder. [17, 19]

4.3 Paroxysmal symptoms and catecholamine excess

Pheochromocytoma is another potential explanation for episodic anxiety-like symptoms. Headache, palpitations, sweating and sustained or intermittent hypertension may resemble panic attacks. Older clinical reviews suggest that prominent somatic episodes can differ from the anticipatory fear and avoidance associated with panic disorder, but these observations are insufficient for a categorical distinction. The appropriate implication is to reconsider an

endocrine cause when the systemic pattern warrants it, while avoiding the assumption that the subjective experience of panic either proves or excludes a medical explanation. [1, 6]

5 PITUITARY DISEASE AND CALCIUM DISTURBANCES

Pituitary disease can affect several hormonal axes and may also introduce neurological symptoms, treatment effects and changes in physical appearance. Its psychiatric manifestations therefore resist attribution to a single hormone. A Taiwanese claims cohort compared 1,194 patients with hypopituitarism with 4,776 controls. Adjusted hazard ratios were 2.98 for depression (95% confidence interval 1.81-4.91) and 1.67 for anxiety (1.17-2.37). These associations support psychiatric assessment in hypopituitarism but do not establish the mechanism of morbidity. [20]

The cohort was relatively young, with a mean age of approximately 22 years, and included children and adults. Endocrine severity, treatment adherence and replacement status were incompletely captured, and diagnoses were derived from routine records rather than uniform structured interviews. Estimates for schizophrenia, bipolar disorder and dementia were not statistically significant; this is not evidence that such presentations cannot occur. The study's results should therefore inform clinical awareness without being converted into a diagnostic prediction rule for all patients with pituitary disease. [20]

The interaction of biological and psychosocial factors is illustrated by a case of pituitary macroadenoma in an adolescent with altered physical appearance, persistent headache, depression and harmful opioid use. Psychiatric improvement followed a combination of medication, psychological work, structured activities and opioid withdrawal. The report supports a formulation that can accommodate endocrine and intracranial disease, distress about bodily changes and treatment-related behavior at the same time. It does not justify dismissing pain as psychogenic or explaining the entire presentation through hormonal dysfunction. [21]

Calcium disturbances deserve consideration when affective or cognitive symptoms accompany neuromuscular, gastrointestinal or renal complaints. Hypercalcemia associated with hyperparathyroidism can present with fatigue, apathy, depression or impaired concentration, and more severe disturbances may produce delirium. Hypocalcemia may involve anxiety, irritability, paresthesias, cramps or seizures. A history of neck surgery or lithium exposure can be relevant. These presentations support interpreting calcium measurements alongside the clinical picture and, where indicated, parathyroid assessment, rather than assuming that behavioral changes represent an uncomplicated psychiatric relapse. [1, 3]

The discovery of mild biochemical disease does not settle treatment expectations. The practice review describes uncertainty about the clinical significance of psychiatric improvement after surgery for mild primary hyperparathyroidism. Evidence from severe disease or selected case reports cannot establish that intervention will resolve nonspecific symptoms in milder cases. Psychiatric assessment should characterize the symptoms and their functional consequences while endocrine decisions consider the full disease context. [3]

6 GLUCOSE DISTURBANCES AND DEVELOPMENTAL CONTEXT

Acute glucose disturbances can change the immediate diagnostic priority. Hypoglycemia may produce autonomic anxiety, behavioral change and impaired cognition; metabolic decompensation in diabetes can produce delirium. Fluctuating awareness, disorientation or rapidly changing psychomotor activity should shift attention toward an acute medical syndrome. Balhara's review describes both hyperactive and hypoactive delirium, so a quiet or withdrawn patient may require the same diagnostic vigilance as an agitated patient. Treating behavioral disturbance alone would leave the underlying metabolic process unaddressed. [1, 5]

Chronic diabetes presents a different problem. Fatigue, appetite changes and difficulties with self-management overlap with depression, while disease burden, fear of complications and medication effects can contribute to distress. Assessment should examine mood, cognition, behavior and daily functioning rather than relying entirely on somatic symptoms. Insulin omission associated with weight concerns also requires a different formulation from general nonadherence or depressive loss of motivation. The clinical reviews support joint psychiatric and diabetes assessment because the reasons for impaired self-care alter the intervention required. [3, 5]

Developmental and reproductive contexts also influence interpretation. Hormonal transitions involve several simultaneous changes, and circulating concentrations do not directly describe hormone action within specific brain regions. Altemus emphasizes individual vulnerability and local metabolism when considering hormone-related psychiatric syndromes. This argues against assigning symptoms to a single reproductive hormone on the basis of timing alone. Menstrual history, pubertal development and reproductive transitions can inform assessment while psychiatric syndromes retain their own clinical significance. [17, 22]

Pediatric evidence requires separate treatment. A review of 14 studies concerning selected endocrine conditions in children and adolescents identified depressive and anxiety symptoms but also substantial variation in instruments, populations and findings. A large population-based thyroid study summarized in that review did not reproduce the same pattern as some selected clinical studies. Growth, body image, peer relationships and treatment demands can influence psychological outcomes alongside endocrine physiology. These observations support developmentally appropriate assessment without importing adult prevalence estimates or interpreting every behavioral difficulty as a direct hormonal effect. [23]

7 A DIAGNOSTIC APPROACH FOR PSYCHIATRIC PRACTICE

7.1 Reconstructing the course before interpreting the test

Assessment should begin by defining the psychiatric syndrome and its course. The chronology should relate changes in mood, thought, cognition and functioning to physical symptoms, medication exposure, endocrine diagnoses and treatment. Collateral accounts may be especially helpful when disorganization or cognitive impairment limits the patient's description. A previous psychiatric diagnosis does not explain every subsequent physical complaint, and an unusual description of a symptom does not make the underlying complaint medically insignificant. [1, 24]

Physical examination contributes information that psychiatric phenomenology cannot supply. The relevant findings depend on the suspected disorder: changes in pulse or blood pressure, skin and hair, weight trajectory, tremor, muscle strength, reflexes and hydration can help connect subjective symptoms with an endocrine hypothesis. A cluster of findings is more informative than an isolated nonspecific complaint. The clinical reviews consistently support examination and targeted history, although they do not provide contemporary estimates of the sensitivity or specificity of these combinations in psychiatric settings. [1, 3, 11]

Treatment resistance should prompt reconsideration of the formulation when the clinical course contains unexplained systemic changes. It should not, by itself, be treated as a biomarker of occult endocrinopathy. The Cushing case demonstrates the value of recognizing an accumulating physical pattern, while the thyroid literature shows why subtle abnormalities may coexist with difficult-to-treat mood disorders without explaining their whole course. Diagnostic reassessment should therefore evaluate what has changed and which observations the existing formulation leaves unexplained. [1, 7, 16]

Psychiatric characterization also needs to remain precise. A questionnaire indicating fatigue, poor sleep and low mood does not, by itself, resolve whether a patient has a depressive disorder, distress related to chronic illness or overlapping endocrine symptoms. The pediatric review illustrates how estimates differ across self-report scales, parent reports and diagnostic interviews. The psychosocial literature additionally describes demoralization and irritability that may be clinically important without fitting a major psychiatric syndrome. These distinctions matter when comparing studies and when judging whether endocrine treatment has improved the problem that originally brought the patient to psychiatric care. [5, 6, 23]

7.2 Accounting for medication and acute illness

Medication review is essential both before testing and when interpreting results. Lithium can affect thyroid function and calcium regulation; carbamazepine can lower free thyroxine without necessarily producing clinical hypothyroidism. Antipsychotic treatment can contribute to glucose and other metabolic abnormalities. Endocrine therapies can also affect mental state, including glucocorticoid exposure and overly rapid or excessive thyroid replacement. Temporal links to starting, stopping or adjusting treatment should be considered alongside the endocrine and psychiatric histories. [3, 11, 17]

An abnormal result must then be assessed for consistency with the suspected disorder, the patient's acute condition and other measured hormones. Discordant thyroid findings can reflect central disease, medication effects or nonthyroidal illness, each with different implications. Where the context is uncertain, confirmation and specialist interpretation are more defensible than immediate causal labeling. This is particularly relevant when the psychiatric presentation lacks the accompanying systemic features expected from the proposed endocrine explanation. [3, 11, 13]

The reviewed material supports clinical case finding, but it does not establish the diagnostic yield or patient benefit of an unrestricted endocrine panel for every psychiatric presentation. Recommendations vary in scope, and abnormality detection is frequently reported without evidence that testing changed diagnosis or improved outcomes. The synthesis therefore supports matching investigation to the presentation, treatment exposure and physical findings, with further assessment guided by the results. It should not be read as a prospectively validated sequence or a replacement for disorder-specific specialist judgment. [1, 3, 13]

Urgency depends on the whole presentation. In diabetes, confusion and fluctuating awareness may indicate an acute metabolic problem; in adrenal insufficiency, psychiatric symptoms can accompany hypotension and progressive systemic deterioration. Such presentations require medical assessment alongside psychiatric evaluation rather than completion of a prolonged psychiatric differential first. The contrast with stable, mild thyroid-test abnormalities is clinically important: the same level of urgency cannot be inferred from every abnormal endocrine measurement. The reviews and case reports support attention to severity and systemic instability, without supplying a single threshold applicable across these disorders. [3, 5, 18]

7.3 Updating causal attribution over time

Follow-up is part of diagnosis. Improvement after correction of established endocrine disease can strengthen attribution, especially when psychiatric and systemic changes evolve together. However, the case literature frequently includes concurrent psychiatric medication changes, supportive treatment or correction of several metabolic abnormalities. These interventions limit causal certainty. Equally, persistence of symptoms does not automatically refute an earlier endocrine contribution, since the reviews describe delayed or incomplete psychiatric recovery after biochemical improvement. [11, 15, 16, 18]

The formulation should distinguish what is established from what remains provisional. An endocrinopathy may be confirmed while its contribution to depression or psychosis remains uncertain. A shared formulation can describe the relevant chronology, competing explanations and expected course without requiring premature diagnostic closure. This is an interpretive application of the reviewed clinical literature, rather than a new set of diagnostic criteria. Its purpose is to make subsequent reassessment responsive to both psychiatric and endocrine outcomes. [1, 6, 24]

8 CONTINUING CARE AFTER ENDOCRINE TREATMENT

Investigation and psychiatric care should proceed together when symptoms are severe. Suicidal thinking, marked agitation or disabling psychosis require direct assessment and, when indicated, symptomatic treatment or hospitalization while the underlying endocrine disorder is addressed. The presence of a potentially reversible cause does not make these manifestations clinically negligible. Conversely, prescribing psychotropics without treating the endocrine disturbance may leave a major contributor unaddressed. The reviewed clinical guidance supports coordinated care with continuing attention to medical status and treatment tolerability. [3, 11, 24]

Biochemical normalization should not be the sole endpoint. The Cushing review describes persistent depression, anxiety and cognitive impairment after resolution of hypercortisolism, and the Graves review similarly notes ongoing symptoms after euthyroidism. These findings require careful interpretation: residual symptoms may relate to prior disease effects, continuing psychosocial difficulties, treatment or an accompanying psychiatric disorder. The available evidence does not permit a uniform explanation. Reassessment should therefore examine functioning and symptom course rather than treating a normal hormone result as proof of psychiatric recovery. [6, 12, 15]

The acromegaly literature provides a useful example. Geraedts and colleagues studied 80 patients at baseline, with 36 participating in follow-up. Depressive and anxiety symptoms were associated with poorer quality of life, while biochemical control was not significantly associated with quality of life in their models. Attrition and unavailable antidepressant-use data limit interpretation. The study identifies a reason to assess psychopathology directly; it does not prove that treating depression or anxiety improves endocrine outcomes or that biochemical control is unimportant. [25]

Treatment-related endocrine disease also does not automatically require abandonment of an effective psychiatric medication. The practice guidance describes thyroid replacement and monitoring in lithium-associated hypothyroidism, allowing psychiatric treatment to continue where appropriate. This example illustrates why identifying a drug contribution and choosing a medication change are separate decisions. The psychiatric benefit, the nature of the endocrine abnormality and the available treatment options all remain relevant. Joint assessment is particularly useful when symptoms could reflect psychiatric relapse, endocrine dysfunction or both, and when changing treatment would make subsequent interpretation more difficult. [3]

9 EVIDENCE LIMITATIONS AND RESEARCH PRIORITIES

The reference collection contains substantial clinical experience but comparatively little research validating diagnostic decisions in psychiatric practice. Narrative reviews, historical descriptions and case reports are prominent. Older prevalence estimates reflect different ascertainment methods and psychiatric classifications, while selected hospital populations cannot represent all psychiatric patients. Even large register studies characterize recorded associations more reliably than individual causation. This review is additionally limited by its predefined source set and lack of an independent systematic search. [1, 2, 4, 13]

Biomarker research should be interpreted at the same level of caution. Inflammatory and endocrine associations in schizophrenia or affective disorders may clarify mechanisms without discriminating primary psychiatric illness from an endocrine-induced syndrome. In the cross-sectional schizophrenia biomarker study, associations were influenced by gastrointestinal and metabolic comorbidity. Contemporary biomarker discussions likewise emphasize heterogeneity and incomplete clinical translation. None of these observations establishes a broadly validated endocrine biosignature for routine psychiatric differential diagnosis. [26, 27, 28]

Research should evaluate clinically defined diagnostic pathways prospectively, recording examination findings, medication exposure, testing indications and whether results changed care. Relevant outcomes include time to endocrine recognition, psychiatric symptoms, cognitive function, daily functioning and unnecessary investigation. Studies also need to distinguish symptom scores from psychiatric diagnoses and biochemical correction from meaningful recovery. Longitudinal endocrine and psychiatric assessment would better clarify which features predict improvement and which patients require continuing psychiatric treatment after endocrine control. [13, 15, 20, 23, 25]

10 CONCLUSION

Endocrine disease should remain an active consideration when psychiatric symptoms accompany unexplained physical findings or an altered clinical course. Psychiatric symptoms alone rarely identify the endocrine cause, and hormonal abnormalities do not independently establish psychiatric causation. Diagnosis requires integration of chronology, examination, medication history, laboratory context and follow-up. Coordinated care should address confirmed endocrine disease and active psychiatric morbidity, with continued assessment when biochemical recovery leaves symptoms or disability unresolved.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The authors declare no conflicts of interest regarding this manuscript.

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