

The diagnosis of psychosis: a review and clinical guide to the diagnosis of conditions causing psychotic symptoms

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Abstract

In a review [1], we first sought to describe all known causes of psychosis, including primary psychiatric diseases and psychosis secondary to other conditions. We gave disease characteristics, the frequency of psychosis in patients with that disease where this is known, and key investigations or diagnostic criteria. Next, we attempted to address the difficult question of how to approach the diagnosis of a patient with psychosis, covering clues from the history, physical and mental state examination, plus initial and specialist investigations. The work is intended for psychiatrists in training and as a reference for those with responsibility for patients with psychotic symptoms.

Introduction

Psychosis originally meant any kind of disordered mental state, and subsequently a severe mental disorder involving loss of contact with reality. Nowadays it may be defined (1) narrowly as the presence of delusions and/or hallucinations without insight, or (2) more broadly to include delusions and/or hallucinations with insight into their hallucinatory nature, or (3) more broadly still to include disordered thought or speech, or (4) yet more broadly to include severe behavioural abnormalities including behavioural disorganization, gross excitement and overactivity, or psychomotor retardation and catatonia [see 1].

Psychiatrists frequently meet patients exhibiting psychotic symptoms and signs. Major classificatory systems within psychiatry (e.g. ICD-10, DSM-IV) lay heavy emphasis on primary psychiatric disease, acknowledging that psychosis can be the result of other conditions but giving little guidance on what those conditions are, or how to diagnose them. We found no reference work explicitly and comprehensively addressing the differential diagnosis of psychosis.

Methods

The breadth of information covered did not allow for a systematic review of all possible primary sources (a PubMed search for 'psychosis OR delusion OR hallucination OR "thought disorder" OR schizophrenia' alone yielded in excess of 122,000 articles in December 2008). To obtain a list of known causes of psychosis, we conducted systematic reviews of the following: ICD-10, DSM-IV-TR and the proposals for DSM-V; textbooks and reference works of medicine, neurology, psychiatry, and therapeutics [see 1 for list]; reviews of physical illness in psychotic disorders and of causes of secondary psychosis [see 1 for list]; the Online Mendelian Inheritance in Man database; the US Agency for Toxic Substances and Disease Registry; and the RxList drug information database. We also searched the PubMed and Google databases nonsystematically. We then hand-reviewed each condition obtained, adding to the list of causes iteratively, and included all conditions where clear case reports or better evidence supported an association with psychosis. These methods have the potential for two kinds of error: the omission of psychotogenic conditions, and the inclusion of conditions whose causal role in producing psychosis is not established beyond all doubt (including the confounding of association with causation).

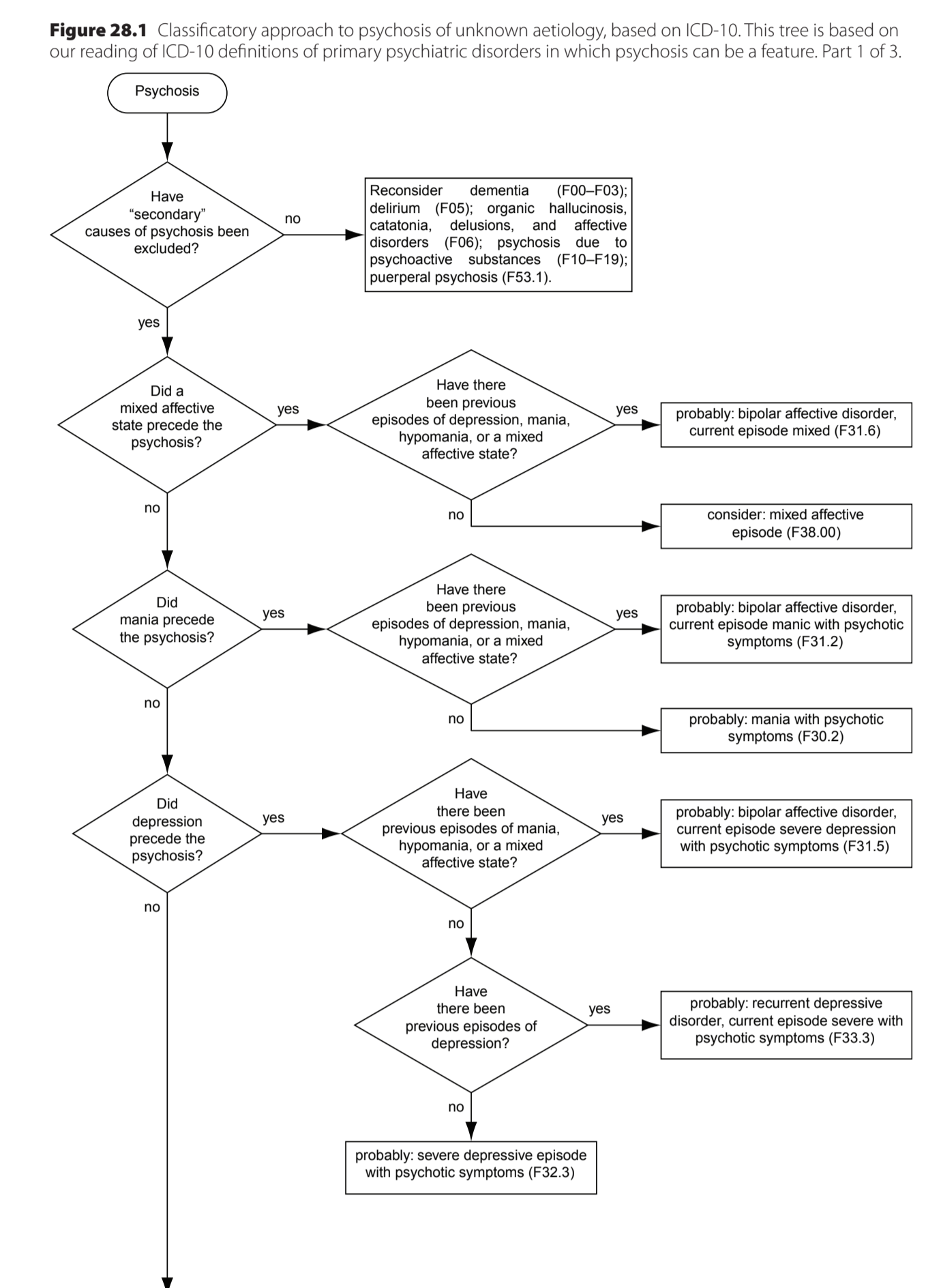
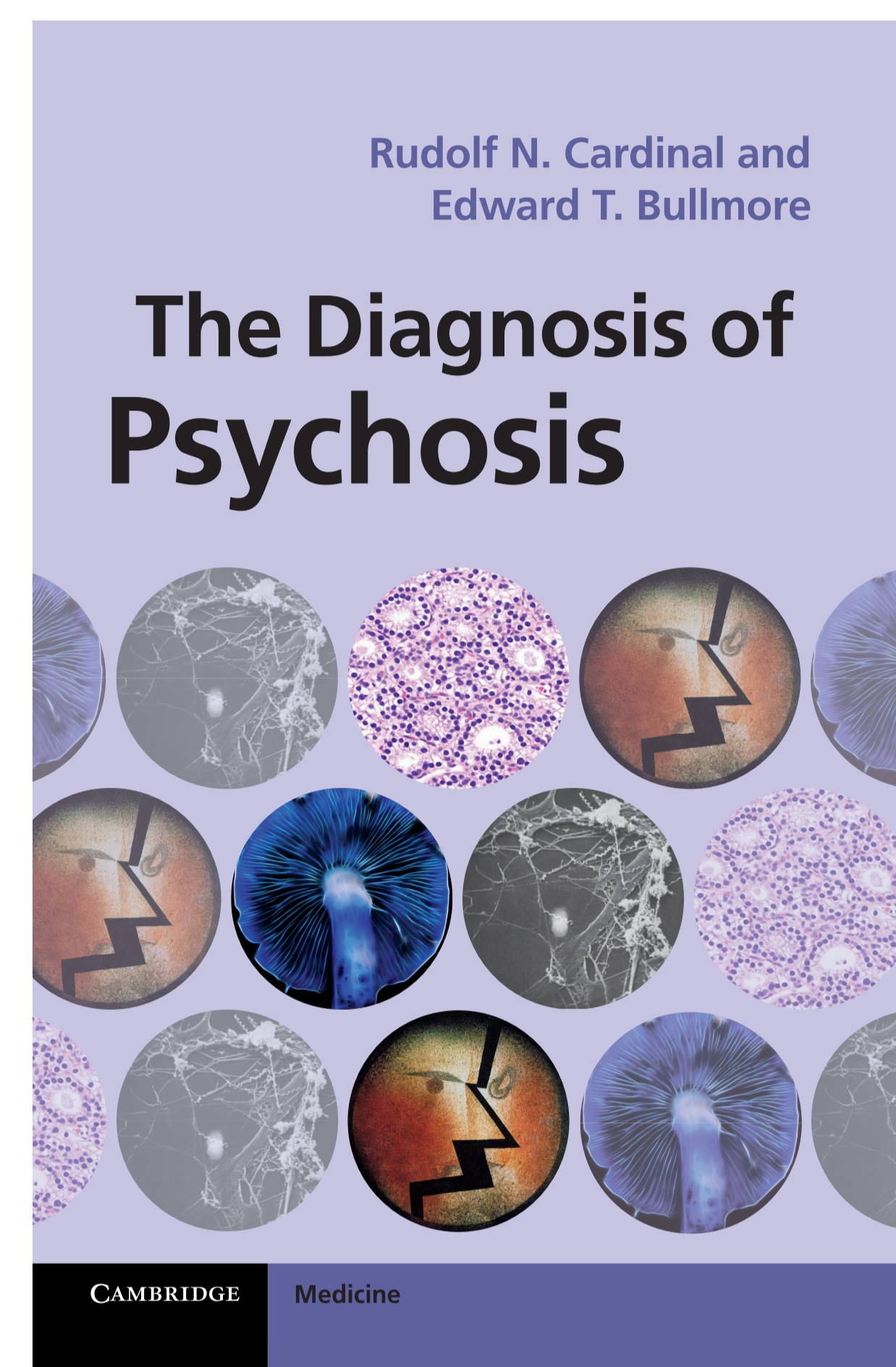
For the primary psychiatric psychoses, we described the disease characteristics and psychiatric diagnostic criteria. All are diagnoses of exclusion. For secondary psychoses, we described the causative condition. We emphasized the non-psychiatric phenotype for secondary psychoses, since there is no evidence that reliable exclusion of most such conditions can be made based on mental state [see 1]. We also sought to describe a practical approach to diagnosis.

Results

We found >220 conditions that can produce psychotic symptoms, in addition to a large number of therapeutic and recreational drugs and other toxins. We categorized the causes as follows: neurodevelopmental disorders and chromosomal abnormalities; neurodegenerative disorders; focal neurological disease; malignancy; delirium (as an intermediate mechanism); infectious and postinfectious syndromes; endocrine disease; inborn errors of metabolism; nutritional deficiency; other acquired metabolic disorders; autoimmune rheumatic disorders and vasculitides; other autoimmune encephalopathies; poisoning; sleep disorders; sensory deprivation and impairment; catatonic disorders; primary psychiatric disease; normal experiences; and factitious disorder and malingering. We listed also conditions that we considered, but for which we found no good evidence of psychotogenicity.

Space prohibits a full presentation here, but if one takes a common disease to be one with a lifetime prevalence of >1:1,000, and a common symptom to be one affecting >1:10 sufferers of the disease, then some examples are illustrative:

Top left: cover art. Top right: excerpt of flowchart for classification of primary psychiatric causes of psychosis via ICD-10. Bottom left: excerpt of checklist for symptom/sign categories seen in some secondary causes of psychosis. Bottom right: key to checklist.



| ENDOCRINE DISEASE | Cog | Pyr | IG | Sen | HF | MR | PN | Aut | CV | Resp | GI | Ren | SK | MSK | Hae | Inf | Dev | Key points |
|---------------------|-----|-----|----|-----|----|----|----|-----|----|------|----|-----|----|-----|-----|-----|-----|--|
| Hypothyroidism | Cog | | | | | | | | | | | | | | | | | fatigue, cold intolerance, dry skin, hair, weight gain, constipation, eyelid lag, menstrual disturbances, bradycardia, diastolic hypertension, hoarseness, gynaecomastia and peripheral oedema, hypothermia, depression or mania, cognitive impairment |
| Hypertension | Cog | | | | | | | | | | | | | | | | | hypertensive encephalopathy, heart failure, stroke, aortic aneurysm, renal impairment, weight loss, diabetes, anaemia, low serum albumin, anaemia, low serum albumin, peripheral neuropathy, hyperreflexia, low vision |
| Cushing's syndrome | Cog | | | | | | | | | | | | | | | | | moon face, weight gain, depression, obesity, diabetes, insulin resistance, hypertension, diabetes, infections, bruising, gynaecomastia |
| Adrenal failure | Cog | | | | | | | | | | | | | | | | | hypotension, hypotension, weakness, fatigue, weight loss, nausea, vomiting, abdominal pain, diarrhoea, constipation, muscle cramps, hypotension, low blood pressure |
| Hyperparathyroidism | Cog | | | | | | | | | | | | | | | | | multiple fractures, depression, weight loss, anorexia, constipation, polyuria, polydipsia, hypercalcaemia, renal stones |

| Key | Key points |
|------------|--|
| Cog | cognitive dysfunction |
| Pyr | pyramidal motor dysfunction (upper motor neuron pattern weakness with hyperreflexia and increased tone in a spastic pattern - disproportionately increased force in upper limb/flexors and lower limb/extension) |
| IG | basal ganglia motor dysfunction (e.g. hypokinetic, bradykinesia, dystonia, dyskinesia, rigidity/immobility in equal or flexion and extension, akathisia, tremor, chorea, ataxia, ballismus) |
| Sen | sensory disturbance (beyond peripheral neuropathy) |
| HF | relatively non-focal non-psychiatric neurological disease, e.g. disturbance of consciousness, diffuse encephalopathy, seizures |
| MR | structural brain abnormalities detectable |
| PN | peripheral or cranial neuropathies, including lower motor neuron signs |
| Aut | autonomic dysfunction |
| CV | cardiovascular involvement |
| Resp | respiratory tract involvement |
| GI | liver involvement |
| GI | other gastrointestinal involvement (including nausea/vomiting) |
| SK | skin involvement |
| MSK | musculoskeletal (e.g. myalgia, myositis, myopathy, arthralgia, arthritis, skeletal deformity) |
| Hae | haematological disturbance |
| Inf | infectious aetiology |
| Inf | inflammation and related systemic symptoms (e.g. fever, acute phase response) |
| Dev | developmental abnormalities, including dysmorphism |
| Key points | important risk factors and clinical features |

- ▶ **Common disorders commonly associated with psychotic symptoms:** e.g. dementia (esp. Alzheimer's disease, vascular dementia, dementia with Lewy bodies); delirium (not a final diagnosis); epilepsy; substance-induced psychosis; schizophrenia; affective psychosis.
- ▶ **Common disorders rarely producing psychotic symptoms:** e.g. migraine, hypothyroidism, alcoholism.
- ▶ **Rare disorders commonly associated with psychotic symptoms:** e.g. velocardiofacial syndrome, Prader-Willi syndrome, viral encephalitis, Cushing's syndrome, systemic lupus erythematosus and other autoimmune encephalopathies.
- ▶ **Rare disorders rarely producing psychotic symptoms:** e.g. sarcoidosis, Wilson's disease, heavy metal poisoning.

Discussion and conclusions

Primary and secondary psychoses are common. One recent study suggested that the lifetime prevalence of psychotic disorders is 3.06%–3.48%. Of these, approximately 63% had a primary psychiatric diagnosis, 14% a poisoning syndrome (substance-induced psychotic disorder), 7% psychosis secondary to a general medical condition, and 16% a brief psychotic disorder or a psychotic disorder not otherwise specified [2]. Other studies have also emphasized that physical illness not uncommonly causes or contributes to psychosis [see 1]. Since primary psychoses are diagnoses of exclusion, there is always potential for the discovery of new causes of secondary psychosis, as has been observed recently in the field of autoimmune encephalopathy. The field is complex and interesting. Nonetheless, the problem of diagnosis of an individual patient with psychosis will persist and that differential diagnosis will remain large.

Acknowledgements and references

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[1] Cardinal & Bullmore (2011), *The Diagnosis of Psychosis*, Cambridge University Press.
[2] Perala et al. (2007), *Archives of General Psychiatry* 64: 19–28.