Medical Evaluation of Psychosis

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The need for medical evaluation is described in the schizophrenia diagnostic criteria in the DSM-V

"The disturbance is not attributed to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition."

National Guidelines Summary: Lab Tests

	UK NICE, 2013	Australia and NZ RANZCP, 2005	Canada CPA, 2005	USA APA, 2004
CBC			X	X
Electrolyte panel			X	X
Renal fxn tests			X	X
Liver fxn tests			X	X
Thyroid fxn tests			X	X
Fasting glucose	X	X		
Hemoglobin A1c	X	X		
Lipid panel	X	X		
Prolactin level	X			
Toxicology screen		X	X	X
Syphilis			X	X
HIV			If indicated	If indicated
Hepatitis			If indicated	If indicated
Heavy metals				If indicated
Pregnancy				If childbearing potential

Partial list of diseases that can cause schizophrenia-like symptoms

Addison's disease	Adrenomyeloneuropathy	Celiac disease	Cerebral cysts and abscesses
Cerebral malaria	Cerebrovascular lesions	Chromosomal disorders	Cranial trauma
Cushing's disease	Encephalitis and its sequelae	Fabry's disease	Familial basal ganglia calcification
GM2 gangliosidosis	Hartnup disease	Hashimoto's encephalopathy	HIV
Homocystinuria (MTHFR reductase deficiency)	Huntington's disease	Hydrocephalus	Hyperparathyroidism
Hyperthyroidism	Hypoparathyroidism	Hypopituitarism	Hypothyroidism
Kartagener's syndrome	Klinefelter's syndrome	Metachromatic leukodystrophy	Narcolepsy
Neurosyphilis	NMDA receptor antibody encephalitis	Occult hydrocephalus	Oculocutaneous albinism
Pellagra	Pernicious anemia	Pick's disease	Porphyrias
Prenatal static encephalopathy	Rheumatic chorea	Schilder's cerebral sclerosis	Sheehan's syndrome
Subarachnoid hemorrhage	Systemic lupus erythematosus	Tourette syndrome	Toxicity (drugs, medications, heavy metals)
Tuberous sclerosis	Tumors of the brain	Velocardiofacial syndrome	Vitamin A deficiency
Vitamin B12 deficiency	Vitamin D deficiency	Wilson's disease	Zinc deficiency

Why do a complete medical evaluation?

- To discover treatable causes of psychosis
  - Patients have the right of accurate diagnosis
  - Assure that no reversible of treatable physical form of schizophrenia missed
  - To alleviate unnecessary suffering
  - To reduce costs/burdens of misdirected treatment
  - (Schizophrenia care in year 2000 was approx. $26,000 per year per patient McCombs et al., 2000)
    - 40 years of misdirected care = $1,000,000 of wasted healthcare spending

- To discover non-treatable causes of psychosis
  - Avoids exposure to unnecessary treatments and stigma
  - Access to more appropriate care/resources

- To establish baseline status

  Higher rates of movement disorders and of insulin resistance occur in schizophrenia, independent of antipsychotic medication treatment

- To screen for other significant illness or illness risk factors

  Preventable disease-related mortality contributes to the reduced life expectancy of those with schizophrenia versus the general population

Arguments against comprehensive medical work up

- Screening test for an ‘esoteric’ disease will usually be negative
- Should not order tests if not ‘clinically indicated’
- Not sure what to do if a result comes back positive
- Will increase cost of medical care

How often do psychiatrically-relevant physical conditions occur in schizophrenia?

- **12%** of 250 consecutive admissions to psychiatric inpatient service had physical disorders that were productive of their psychiatric symptoms and that caused their admission (Johnson, 1968)

  80% of those were missed in the initial assessment
- https://www.ncbi.nlm.nih.gov/pubmed/9447505

- **5.6%** of 268 *first episode* schizophrenia patients had organic disease of possible or probable relevance to etiology (Johnstone et al., 1987)

- 7.0% of 328 recently-admitted patients with psychosis had underlying organic illness (Johnstone et al., 1988)

- 6% to 10% of schizophrenia patients had clinically unsuspected brain lesions of etiological relevance (Falkai, 1996)

Physical exam and Neurological Exam

- Physical exam, including neurological exam
- Vital signs
- Weight, Height (→ body mass index)
- Waist circumference

Laboratory testing

Standard Blood Tests

- CBC with differential
- Erythrocyte sedimentation rate
- Electrolytes
- Renal function tests (BUN, creatinine)
- Glucose
- Liver function tests
- Calcium, phosphorous
- TSH; T3/T4, if abnormal

Laboratory testing

Tests of inflammation and immunity

- C-reactive protein
- Erythrocyte sedimentation rate
- Ferritin
- Anti-nuclear antibody
- Thyroid peroxidase antibody
- Mayo encephalopathy, autoimmune evaluation (serum)
- Tissue transglutaminase IgA antibody
- Globulin level; Albumin:Globulin ratio

Laboratory testing

Infections, intoxications, deficiencies

- Syphilis (FTA preferred over RPR)
- HIV
- Hepatitis
- Serum Vitamin A
- Serum Vitamin B3 (niacin)
- Serum Vitamin B12
- Serum Vitamin D (1,25 dihydroxy)
- Serum copper & Ceruloplasmin
- Serum Zinc
- Heavy metals

Laboratory testing

Urine

- Drug/Tox screen
- Urinalysis

Imaging

- Chest X-ray (sarcoidosis and bronchial tumor were found in the Johnstone first episode psychosis cohort)
- Brain imagining (MRI preferred)

- APA guidelines say imaging “if indicated”
- But mental status change **is** an imaging indication.

- Lesions most likely to cause psychosis symptoms occur in:
  - Frontal cortex
  - Temporal cortex
  - Limbic structures
  - Internal midline structures
- These regions are typically neurologically silent; lesions here do not produce defects of sensation, coordination, or motion

NMDA Receptor Encephalitis

- Involves autoantibodies against the glycine-binding NR1 subunit of the NMDA receptor → hypofunction of the NMDA receptor
- NMDA receptor antibodies present in 6.5% of first episode psychosis cases (Zandi et al., 2011), and immune therapies reduce psychotic symptoms in such cases. Outcomes are better with early detection.
- Antibody screening in young people presenting with psychosis, seizures and cognitive disturbance is now part of routine clinical practice in many neurological and intensive care settings.
- CSF antibody testing is 100% sensitive/specific. Serum antibody testing is 75% - 97% sensitive/specific

Hashimoto's encephalopathy

- Also known as SREAAT – steroid responsive encephalopathy associated with autoimmune thyroiditis
- No relationship with thyroid hormone levels
- Antibody titers are unrelated to clinical severity or treatment response
- Psychosis is present in > 25% of HE cases
- Anti-thyroid antibodies are present in > 10% of cases of schizophrenia (Radakrishnan et al., 2013)
- Anti-thyroid antibodies don't make the diagnosis, but should start the process of further workup

Radhakrishnan, R., Calvin, S., Singh, J.K., Thomas, B., and Srinivasan, K. (2013). Thyroid dysfunction in major psychiatric disorders in a hospital based sample. Indian J Med Res *138*, 888–893.

Summary

- Up to > 10% of schizophrenias will have a physical condition that either exacerbates, or directly causes the symptoms of schizophrenia.
- Comprehensive assessment should include: physical exam, neuro exam, brain imaging, and moderately expanded initial lab testing
- Psychosis **is** a sufficient clinical indication for imaging or other tests.
- Consider full evaluation for:
  - Every new case
  - Every treatment-resistant case
  - Atypical presentations
  - Significant change in clinical picture