

Screening for secondary causes (and monitoring for side effects and cardiovascular risk)

1. History: Key for differential diagnosis, needs to be re-taken over time as symptoms stabilize, alliance improves, and collateral becomes available.

- Evaluating for TBIs: remember these are *rarely remembered by the patient*, get collateral
- Evaluating for seizure disorders: ask about episodic changes in mental status, get collateral
- Evaluating for substance use disorders: information quality often improves over time, as alliance improves
- Evaluating for rare etiologies: see General Principles below

2. Laboratory/Imaging (for both w/u and monitoring purposes): Review tests already done at ER/Hospital and add as necessary.

Physical exam with emphasis on neurological exam

Vital signs

Weight and height (BMI), waist circumference

ECG (if cardiac risk)

Laboratory tests

Broad screening and medical baseline:

CBC

Electrolytes including calcium

Renal function tests (BUN/creatinine)

Liver function tests

Erythrocyte sedimentation rate

Antinuclear antibody

Fasting glucose

Lipid profile

Consider prolactin level

Consider hepatitis C (if risk factors)

Pregnancy test (in women of child-bearing age)

Urine drug screen

Exclude specific treatable disorders:

TSH

FTA-ABS (fluorescent treponemal antibody absorbed)

HIV test

Ceruloplasmin

Vitamin B12

Neuroimaging

MRI (preferred over CT)

Ancillary tests

Expand aetiological search if indicated, taking into account epidemiology:

For example, CXR, EEG, lumbar puncture, karyotype, heavy metal testing

Expand medical monitoring if indicated:

For example, eye exam (if risk factors for cataracts)

BMI, body mass index; BUN, blood urea nitrogen; CBC, complete blood count; CT, computed tomography; CXR, chest X-ray; ECG, electrocardiogram; EEG, electroencephalogram; MRI, magnetic resonance imaging; TSH, thyroid-stimulating hormone.

Additional Notes:

- Waist circumference is optional, weight will do for most
- CMHC screening for syphilis is RPR, and FTA-ABS is automatically done if this is -ve
- Would replace fasting glucose with (non-fasting) HbA1c at first visit (and f/u with fasting if borderline or elevated)

TABLE 3. Indications for ordering an electroencephalogram for the work-up of first-episode psychosis

Any documented seizure history†

History suggestive of ictal events (e.g. episodic loss of consciousness, staring spells)†

Serious past head injury†

Uncooperative patient with confusion

Suspicion of narcolepsy (i.e. hallucinations occurring at sleep-wake cycle transitions)‡

†Sleep-deprived electroencephalogram preferred.

‡Requires Multiple Sleep Latency Test.

- Record smoking in ppd (also ask about e-cigarettes, pipes, other)
- Patients in fMRI studies at STEP will already have (lower quality) structural MRI available

(Tables from *Freudenreich, et al 2009*).

** Consider ECG on admission for all and monitoring annually and more often based on mild/moderate/high-effect classification of APDs (ref: Maudsley handbook)

** Consider PRL baseline or post-admission for all, especially females

** Consider serum HCG/pregnancy test for all females

General background and principles:

- Most common causes of diagnostic errors are related to cognitive biases in clinicians
- >100 possible 'secondary' causes of psychosis and impossible to screen for all
- The best protection against a 'missed' secondary cause for psychosis is longitudinal f/u by a clinician alert for atypical features in presentation, course or responsiveness to treatment (*what is between your ears may be more important than what is in front of your eyes*)
- Embrace Bayes: (i) Stay alert to rare diseases (on way is to read about them every time it comes up in a differential - you are more likely to 'see' what you are able to call to mind) so you can set prior expectations appropriately; and (ii) understand the performance of the test you order (i.e. how much does it increase or decrease your prior expectation of the disease being present?): a probabilistic, revisionist approach vs. quest for certainty.

Procedures (that follow from above):

- Careful, iterative History and targeted Examination and lab testing:
- Evaluate for common disorders and co-morbidities (e.g. substance use, mood disorders)
- Evaluate for rare but easily treatable disorders (e.g. B12 deficiency, syphilis, HIV)
- Revisit rare and especially secondary causes that would modify treatment approach: consider risks/costs of invasive testing but pursue strong suspicions!
 - Remember the aphorism: "If you go fishing and don't catch anything, you cannot conclude that there are no fish in the ocean" (George Murray) e.g. for a seizure disorder masquerading as primary psychosis, random EEGs ordered randomly are often uninformative: consider serial/sleep-deprived/provocative EEGs if you have a high index of suspicion.
- Continued education about etiologies you have not seen but you or others have worried raised in the differential (i.e. priming your Bayesian priors): 'if you think you see something, read something'.
- Continued education about best tests to order and their performance (e.g. sensitivity /specificity of urine tests for substances of abuse)
- Baseline measures and continued monitoring to assess for medication side effects (e.g. baseline weight, movement disorders, PRL, pregnancy) and especially monitoring for cardiovascular risk should be regularly audited.

Annotated Bibliography:

Freudenreich O, Schulz SC, Goff DC: Initial medical work-up of first-episode psychosis: A conceptual review. *Early Interv Psychiatry* 2009; 3:10-18. *An 'early psychosis' clinic, if its referral base is broad enough, can soon become the equivalent of a 'fever' clinic in terms of the heterogeneity of diagnoses that could masquerade as a primary (unknown etiology) psychotic disorder. Screening for all possibilities would be infeasible and also poor healthcare. On the other hand, missing a zebra can lead to a markedly poorer outcome for some. This paper offers the first and, so far, the best response to this Bayesian conundrum.*

Coleman M, Gillberg C: A biological approach to the schizophrenia spectrum disorders. *J Neuropsychiatry Clin Neurosci* 1997; 9:601-605 *A markedly different and more aggressive approach to the diagnostic conundrum described above. The authors have also written a book on the subject. We do not implement this approach in STEP, I suggest it as a counterpoint to the previous paper.*

Singh SP, Burns T, Amin S, Jones PB, Harrison G: Acute and transient psychotic disorders: Precursors, epidemiology, course and outcome. *Br J Psychiatry* 2004; 185:452-459. *It is important to recognize the variety of illness courses /prognoses subsumed under the category of primary psychosis. The ICD 'Acute and transient' psychosis category is a useful reminder that primary psychotic illnesses can also be phasic (not just mood disorders).*

Keshavan MS, Kaneko Y. (2013). Secondary psychoses: an update. *World Psychiatry* 4 ed. John Wiley & Sons, Ltd., 12(1), 4-15. *A useful summary of presenting features of various secondary psychoses.*

Lishman's Organic Psychiatry. *A classic that includes detailed descriptions of several neurological/medical disorders that can include psychiatric manifestations.*