

Laboratory diagnosis of factitious disorder: a systematic review of tools useful in the diagnosis of Munchausen's syndrome

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Abstract

Aims To assist clinicians in the diagnosis of factitious disorder.

Methods This is a systematic review of the role of laboratory, radiologic, procedural, and pathological modalities to assist in the diagnosis of factitious disorder (Munchausen's syndrome). The review evaluated 3104 article titles and abstracts that were identified from MEDLINE as of January 2010.

Results We found 190 articles that demonstrated techniques that will assist clinicians in recognizing fabricated manifestations of disease. The results are divided into 13 areas of clinical medicine for easy reference. They are further sub-divided by the diseases or conditions that patients have been reported to simulate and the diagnostic techniques suggested by the literature in each case.

Conclusions Factitious disorder is difficult to diagnose and may present as a wide array of fabricated conditions, but there are a range of laboratory and technical means available to assist clinicians in the 21st Century.

Patients with factitious disorder seek to be cared for despite the lack of an underlying illness. To obtain "the sick role" they fake symptoms, fabricate history and manipulate their bodies and medical investigations to simulate a condition that will require medical or surgical care. Unlike patients who are seeking a reward—e.g. workman's compensation, or narcotics, their goal is solely to receive emotional support and medical attention.

Despite the passage of 60 years since Asher first described factitious behaviour and labelled it Munchausen's syndrome, the accurate diagnosis of factitious disorder is still as challenging for clinicians today as it was in 1951.¹ As a psychiatric condition that is usually seen by non-psychiatrists, it is under-recognized and under-appreciated in terms of its contribution to unnecessary morbidity and mortality as well as the cost to healthcare systems.

Factitious disorder is usually first suspected when inexplicable laboratory results are noted in the course of a prolonged clinical investigation.² Therefore, it is essential that clinicians be aware of the state-of-the-art techniques available to diagnose illness fabrication in the context of factitious disorder.

Figure 1. Diagnostic criteria

DSM-IV Diagnostic criteria for factitious disorder

- A. Intentional production or feigning of physical or psychological signs or symptoms.
- B. The motivation for the behaviour is to assume the sick role.
- C. External incentives for the behaviour (such as economic gain, avoiding legal responsibility, or improving physical well-being, as in Malingering) are absent.

Surveys demonstrate that physicians across medical specialties are uncomfortable with diagnosing factitious disorder.³ Estimates of the incidence of factitious disorder among general hospital admissions range from 0.6% to 1.3%.^{3–5} Another report indicated that 3% of non-psychiatric hospital admissions over an 8-year period were by patients who had no known organic basis for their complaint.⁶

Other studies looking at specific problems such as fever of unknown origin have found a factitious basis for 3.5%–9.3% of cases.^{7,8} These numbers presumably represent a fraction of the cases that actually occur, since they do not include those who are not suspected or never detected.

Factitious disorder not only impacts the doctor-patient relationship, it also results in a financial burden on the healthcare system. From case reports, we know patients with factitious disorder often undergo lengthy hospital stays and numerous tests and procedures before their activities are recognised. With advances in technology, there is both an increase in our diagnostic armamentarium as well as a greater expectation that we will obtain a diagnosis in a rapid fashion.

Because factitious presentations will not make sense in a traditional medical context—wounds that do not heal, diarrhoea without an apparent cause, blood sugars that continue to be low despite treatment—most clinicians will assume that they are missing the diagnosis and pursue increasingly obscure (and often expensive or invasive) workups.

Methods

Definitions

Eligibility criteria for inclusion in the systematic review: Studies of patients who fabricated illness, where their fabrication was detected by the use of laboratory or technical means.

Technical means—This included any laboratory or procedural test that could be ordered from a hospital laboratory or a reference laboratory, or a reproducible test that involved technology or equipment that should be available at an academic medical centre through medical, neurological, surgical or pathology specialty and sub-specialty services in the first world.

Factitious disorder—For the purposes of this review, a patient with factitious disorder is defined as a person who intentionally feigns or manufactures symptoms or signs of disease for the purposes of obtaining medical care and without other external motives for their behaviour.

We intentionally exclude other conditions such as malingering, conversion disorder, hypochondriasis, noncompliance, suicidal acts, admitted self-harm behaviours, iatrogenic misadventures, and errors by laboratories or mistakes of interpretation by clinicians.

The authors performed a systemic review of the literature to evaluate laboratory and technical methods that can assist diagnosticians in recognizing factitious disorder. We evaluated a possible 3104 citations to develop a state of the art guide for clinicians to use in diagnosing factitious disorder.

The focus of our review was solely on the use of laboratory and technical methods (including the use of radiology, endoscopy, neurodiagnostic tools, and histology, among other modalities) to recognize when patients may have manipulated their clinical presentation to assume the sick role.

Primary search string—((Factitious – (as MeSH term and Keyword)) OR (Munchhausen) OR (Munchausen—(as MeSH term and Keyword)) OR (fantastica) OR (dermatitis artefacta)). The search was current through January 2010.

Note that adding the MeSH term or keyword of “somatoform” increases the yield to 9763 articles but did not appear to offer any advantage when this search was further developed or subcategories were added. “Psychogenic” was an exception to search terms as it did bring additional cases and reports to light, but only in the field of neurology where it is applied to non-epileptic seizures and to movement disorders without an identified organic basis.

Additional searches were performed using variants of: autodestructive, somatic, somatisation, hypochondr*, faking, fabricated, faked, fictitious, artefacta, pseudologia, Asher, Ganser’s, “by proxy.” However none of these search strings as keywords (or MESH terms) resulted in additional relevant articles. Three articles were found in the cited bibliographies of papers on factitious disorder that were not found in literature searches.

Databases reviewed—This search string in Medline (PubMed) resulted in 3104 articles. 1088 involved primary reports of factitious manifestations of specific disorders. 190 of these articles offered unique and applicable information. An additional search in PsyINFO did not offer any articles that addressed novel issues of clinical diagnostic methodology. We also consulted with multiple specialists from each medical and surgical specialty – at several major medical centres in the United States and New Zealand - for additional examples of useful tests not covered in the literature, but none were suggested.

The European literature database EMBASE was also reviewed but not systematically. No additional articles were found using checks of above terminology. Articles without English abstracts were not investigated if their title did not appear to be directly relevant.

A conscious decision was made not to survey the forensic pathology or biochemistry literature for discussions of techniques not previously applied to factitious disorder. This was done to limit the review to articles of significance to practicing clinicians, most of whom will not have access to specialized laboratories services.

In general, the tests discussed should be available at an academic medical centre, reference laboratory or through normal consultation with medical and surgical specialists and clinical pathologists.

Results

The table below represents the information gained from the 190 articles that offered methods for the diagnosis of factitious disorder.

Table 1. Tools for diagnosing factitious disorder by speciality and condition

| SYMPTOM | LABORATORY TEST | COMMENTS |
|--|---|--|
| Cardiovascular | | |
| Angina | Definitive test: coronary angiography. Also consider: stress test, ECG, Echocardiogram for wall motion abnormalities. ¹⁴ | History of prior myocardial infarction or cardiac bypass does NOT exclude factitious presentation– may represent the patient fabricating prior symptoms. |
| Arrhythmia | Consider indirect dysrhythmia though manipulated electrolytes (Mg, K). ¹⁵ Supervise telemetry lead placement to avoid manipulation. ^{16,17} Digitalis, beta-blockers and calcium channel blockers can be measured in serum. ¹⁸ | Arrhythmias have also been reported in patients with surreptitious laxative or thyroxine abuse (see below). |
| Aortic dissection | In patients reportedly unable to receive CT aortogram with contrast or MRI, consider transthoracic echocardiogram. ^{19,20} | Patient's goal may be thoracotomy. Patients have reported an allergy to radiography contrast prohibiting CT imaging. Also allergy to gadolinium or shrapnel residue in their body prohibiting MRI. |
| Hypotension | Serum assays for beta-blockers and calcium channel blockers. Electrochemiluminescence assays detect atenolol and metoprolol in urine samples. ^{21,22} | Capillary electrophoresis with electrochemiluminescence detection – assays developed to detect doping in sports. |
| Hypertension | Serum or urine assay for pseudoephedrine. ^{23,24} pheochromocytoma can also be simulated. ^{25,26} | Valsalva manoeuvre may be used by the patient during BP measurement to produce transient HTN. |
| Dermatologic | | |
| Chelitis granulomatosa | Liver and lymph node biopsies may show histiocytes that contain Polyvinylpyrrolidone (PVP) suggesting self-inoculation. | PVP, a polymer, is used in hair sprays, skin care products, fruit juices, |
| Dermatitis artefacta, chelitis, Subcutaneous emphysema | Punch biopsy with histopathology– may reveal evidence of mechanical trauma with areas of necrosis and extravasation of RBCs. ²⁷ Imaging or skin exam can note needle tracks for subcutaneous air. ²⁸ | |
| Erythematous lesion, pemphigus | Apply alcohol to lesion. ^{29,30} Direct immunofluorescence. ²⁹ | |
| Herpes Zoster | Negative viral PCR. ³¹ | |

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| Onychodystrophy | Microscopy. ³² | Nail file to replicate symptoms. |
| Scabies | Scabies PCR, microscopy. ³³ | |
| Endocrine | | |
| Cushing's syndrome | High-pressure liquid chromatography (HPLC) used to distinguish exogenous vs. endogenous glucocorticoids. ³⁴ Cortisol and corticosterone are co-secreted, so both should be checked since corticosterone will not be elevated if cortisol is surreptitiously added to urine samples. ³⁵ | Surreptitious addition of hydrocortisone requires measurement of upstream metabolites to check for evidence of suppressed pituitary secretion of ACTH. |
| Hyperaldosteronism | Glycyrrhizic acid can be detected in serum. ³⁶ | The ingestion of black liquorice has gained particular notoriety on the internet. The sweetener used to make licorice, glycyrrhizic acid can lead to treatment-resistant hypokalemia, metabolic alkalosis and hypernatremia. |
| Hyperthyroidism | TSH, T3, free T4, thyroglobulin, and thyroid autoantibody. Some recommend 24h radioiodine uptake testing. ³⁷ During thyroid storm factitious hyperthyroidism is the only aetiology in which TSH will be low. ³⁸ | Some herbal medications contain thyroid hormones. Serum thyroglobulin may less useful as 10-20% of people have anti-thyroglobulin antibodies that may affect thyroglobulin measurement. |
| Hypoglycaemia | Serum insulin, C-peptide, and proinsulin levels, assays for metformin, meglitinides, sulfonylureas. ³⁹ Novel incretin analogue exenatide and amylin analogue pramlintide not routinely included in hypoglycaemic drug screens. ⁴⁰ Also consider manipulation of testing strips. ⁴¹ | Urine can be more sensitive than serum and may remain positive for a longer period. ^{42,43} Anti-insulin antibodies no longer useful as more human recombinant insulin is used. Also C-peptide is cleared renally and will be elevated in renal failure. |
| Pheochromocytoma | Serum chromogranin A useful to identify true pheochromocytoma. 44 Meta-iodobenzylguanidine (nuclear scan is probably the gold standard. ⁴⁵ Vanillylmandelic acid (VMA) should not be used for suspected factitious pheochromocytoma because vanilla extract or foods high in vanillin can elevate VMA. ⁴⁶ | Agents to mimic pheochromocytoma symptoms include self-administration of epinephrine, metaraminol, and isoproterenol. ^{47,48} patients can use the Valsalva manoeuvre to produce a symptom pattern suggestive of pheochromocytoma. ^{25,26} |
| Gastrointestinal | | |
| Diarrhoea | Surreptitious addition of water to stools detected by measuring faecal fluid osmolality – if less than 290 mosm/kg, water or hypotonic solution may have been added to stool. ⁴⁹ Consider 3-day stool collection for 200g/day volume check. ^{50,51} Urine screen for phenolphthaleins, anthraquinones, and bisacodyl plus stool screen for magnesium and phosphate. ⁵² | Urine and stool “laxative abuse” screens often need to be performed multiple times due to intermittent laxative use by patients and low sensitivity of the tests. |
| Gastrointestinal (GI) bleeding | Factitious bleeding suggested when nasogastric tube shows blood but no cause found on oesophagogastroduodeno-scopy. ⁵³ Colonoscopy is less sensitive to elucidate lower GI bleeding. ⁵⁴ The “single-stripe” sign on colonoscopy may indicate non-steroidal anti-inflammatory abuse, which can be detected on high performance liquid chromatography (HPLC). ⁵⁵ | Ingestion of salicylates can also cause factitious lower GI bleeds. ⁵⁶ Radiolabelling only useful in a patient injecting themselves with blood they had obtained from transfusions in-hospital; discovered when rectal blood was found not to be radiolabelled after a radio-isotope injection. ⁵⁷ |

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| Nausea/vomiting | When produced by ipecac consumption, measure serum or urine emetine levels (detectable by HPLC). ⁵⁸ Elevated creatine kinase, leukocytosis, and transaminitis also associated with ipecac toxicity. ⁵⁹ After vomiting episodes, clinicians should see low serum potassium, low chloride after acute vomiting or prolonged episodes of vomiting. | Excess ipecac induces myopathic toxicity including skeletal muscle weakness and hypotonia and cardiomyopathy with dysrhythmias, T-wave abnormalities, and prolonged QT interval. ⁶⁰⁻⁶² |
| Pseudo-obstruction | Detect loperamide or another motility slowing agent by HPLC of blood or stool. ⁶³ | |
| Gynaecology and Obstetrics | | |
| False Ectopic Pregnancy | Self-injection of human chorionic gonadotropin (hCG) has been reported. This led to a negative urine beta-hCG and negative ultrasound. Also subsequent serum beta-hCG levels were widely varying. ⁶⁴ | |
| Vaginal Discharge | Typically the fluids have an inconsistent pH or the vaginal wall shows evidence of trauma/abrasion in patients denying intercourse or instrumentation. | |
| Hematologic | | |
| Anaemia/Bleeding | Examination may show evidence of venipuncture or instrumentation, particularly of orifices or the genital-urinary tract or gastrointestinal tract on endoscopy. ¹ | |
| Anticoagulation | For patients not known to be on warfarin, administer vitamin K, and then re-check PT/INR. Warfarin can be assayed directly but warfarin derivatives such as the rodenticide brodifacoum require use of HPLC. ^{65,66} For patients on warfarin, there can be “false-resistance” to warfarin that requires extensive clinical input and attention. This must be cautiously approached as genetics can play a large role. If vitamin K and plasma Warfarin levels are irregular, consider genetic testing if there is no indication of factitious behaviour. ⁶⁷ Prolonged PTT but normal reptilase time suggest presence of heparin. Another test is to add protamine sulphate or an ion-exchange resin to the blood sample which will indicate the presence of exogenous heparin. ⁶⁸ | The most common hematologic factitious disorder is surreptitious anticoagulation abuse. |
| Aplastic Anaemia | This has been provoked by the ingestion of alkylating agents such as busulfan or other chemotherapy agents. ^{69,70} | |
| Sickle Cell Disease | Confirmation with haemoglobin electrophoresis. ^{71,72} | Important for patients not known to local clinicians. |
| Thrombocytopenia/ITP (also see Rheumatologic-Purpura) | Purpura and ITP Feigned by quinidine ingestion—check serum quinidine level. ⁷³ Isolated thrombocytopenia has been caused by quinine ingestion. ⁷⁴ | |

| Infectious diseases | | |
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| Bacteraemia | Polymicrobial bacteraemia or unusual organisms in blood cultures should raise suspicion. ^{75,76} | Case reports note stool flora, pet flora as most common exogenous material. |
| Fever | Directly observed temperature measurement using electronic thermometer. | Ensure no recent ingestion of hot beverages, warm wax or wet cotton in ears. In 1979, 9% of patients presenting to an NIH study on fever of unknown origin were found to be suffering from factitious disorder. ⁷ |
| HIV/AIDS | Repeat HIV ELISA and Western blot, check viral load for acute HIV. ⁷⁷ | Patient with normal CD4 count and undetectable viral load can claim suppression with anti-retrovirals. But antibody should still be positive. |
| Wounds | Apply fluorescein or tetracycline to wound, then examine hands/nails for fluorescence. | Non-healing wounds will heal when casted- but this can be circumvented by patients. Substances introduced into wounds include: human/animal faeces, household toxins, aquarium water, foreign bodies, milk and others. ^{78,79} |
| Neurologic | | |
| Movement disorders | EMG and EEG reveal inconsistent amplitude patterns in factitious tremors and myoclonus. ⁸⁰ | Dopaminergic drugs including antipsychotics may be taken to induce Parkinsonian symptoms. |
| Multiple sclerosis | MRI brain demonstrating at least 2 different regions of white matter change CSF with mild lymphocytosis, oligoclonal bands in IgG region. | CSF protein electrophoresis is 90% sensitive in pts with active MS symptoms. |
| Non-epileptiform seizures | Serum prolactin level at baseline (near onset of epileptiform activity) then 20 minutes later. ⁸¹ However this can be normal in partial-seizures and elevated in epilepsy. ⁸¹ Video EEG useful but this can miss frontal lobe seizures which have movements that can suggest factitious behaviour such as pelvic thrusting and cycling movements. ^{82,83} | One estimate suggests that 15-30% of the patients presenting to epilepsy clinics with refractory epilepsy are psychogenic in nature. ⁸⁴ Most of these patients are unlikely to have factitious disorder. |
| Nephrologic/Urologic | | |
| Diuretic Abuse/Bartter syndrome | Urine assays can detect furosemide, torsemide, and hydrochlorothiazide. HPLC can detect Furosemide and other diuretics. ^{85,86} | Bartter syndrome is a rare inherited defect in the ascending loop of Henle, there are at least 6 reports of factitious presentations of this condition. ⁸⁷ |
| Goodpastures Syndrome | See haematuria and haemoptysis sections. | One patient appeared in 3 different peer reviewed articles. ⁸⁸⁻⁹⁰ |
| Haematuria | Direct observation of urine collection to ensure blood or iodine not added to sample. Three tube test to rule out urethral trauma—first tube should have most RBCs if self-inflicted urethral trauma is the source of blood. ^{91,92} Haematuria can be simulated by introducing foreign bodies such as paper clips or safety pins. This can be detected on X-ray or with direct cystoscopy. ⁹³ Air in the bladder on imaging is also indicative of self-manipulation. ⁹⁴ | Reports suggests that 0.6-3% of patients presenting with Haematuria have tampered with urine samples to produce false positive tests. ⁹⁵ |

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| Nephrolithiasis | Microscopic exam, infrared spectrophotometry, crystallography, X-ray diffraction to characterize crystals suspected to be non-physiologic. ⁹⁶ | 3.5% of stones submitted by patients were found to be artefacts (not all were factitious). One case report of subcutaneously implanted metal in abdomen at level of ureter mimicking stone on plain film in patient who claimed IV contrast allergy. ⁹⁷ |
| Proteinuria | Surreptitious protein addition to urine or bladder detectable by urine protein electrophoresis revealing abnormal alpha and beta globulin fractions. Egg albumin antibody can be used if this is suspected. ⁹⁸ | Normal serum protein, albumin, creatinine, and BUN levels should raise suspicion in a patient with proteinuria. ⁹⁹ |
| Oncology | | |
| Cancer | Manipulation of records. Multiple case reports of patients claiming to bring records of disease and diagnosis at remote or foreign institutions requiring treatment. Contact the document's authors/institution. If they are not available, police can be asked to assist verification. At least one report of a patient obtaining sample medical reports off of the internet. ^{100,101} | Multiple cases of prophylactic mastectomy for falsely claiming a strong family history of breast cancer. ¹⁰²⁻¹⁰⁵ |
| Ophthalmology | | |
| Mydriasis | Homatropine drops detected by identification of homatropine in tears. ¹⁰⁶ | |
| Other presentations | Successful techniques for investigating these injuries include pH testing to detect acidic and alkali chemicals and imaging and skin exam to look for evidence of traumatic puncture to introduce air or foreign body materials. ¹⁰⁷ | Other ophthalmic presentations include the insertion of foreign body crystals, ¹⁰⁸ fungal endophthalmitis, ¹⁰⁹ self-induced anterior scleritis, ^{110,111} and reports of factitious conjunctivitis, primarily by inserting dental plaque as an irritant. ¹¹²⁻¹¹⁴ |
| Otolaryngology | | |
| Airway and Swallowing difficulties | Videoflourscopy can be useful as well as surface EMG techniques. ¹¹⁵ | |
| Pulmonary | | |
| Asthma | Lung biopsy specimen analysed by x-ray energy-dispersive spectroscopy showed talc crystals.116 Chronic ingestion of aspirin in patients with known salicylate sensitivities. ^{117,118} | Clear tape has been used to fool pulse oximeters. |
| Cystic Fibrosis | Sweat chloride test, but exam should show digital clubbing and abnormal X-rays. ¹¹⁹ In one case the sweat-chloride test was manipulated and the patient discovered by evaluation of the sweat potassium. ¹²⁰ | |
| Haemoptysis | Fiberoptic bronchoscopies that don't show even a minute trace of blood in the oral cavity, glottic area or tracheobronchial tree during a presentation of "active haemoptysis" should elicit a possibility of factitious haemoptysis. In that case examine the nares, palate and posterior tongue for evidence of self-induced trauma. ^{121,122} Also consider ingestion of anti-clotting agents and cough abrasion of the lung. ⁵⁰ | A patient received 25+ admissions to more than 14 hospitals and at least 16 bronchoscopy investigations, all of which were negative. ¹²³ |

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| Respiratory Failure | Arterial Blood Gas measurements should demonstrate incongruities. | At least 10 reported cases of factitious patients receiving intubation for respiratory failure. ¹²⁴⁻¹²⁶ |
| Rheumatologic | | |
| Arthritis | Insertion of metal fragments into joint detected by diffraction radiology or microscopic analysis of synovial aspirate. ¹²⁷ | |
| Lupus | Feigned usually by symptomatic history +/- borderline elevation in ANA; repeat serum ANA, anti-dsDNA, anti-Smith antibodies. Seronegative lupus can occur however. Note that in an active flair complement CH50, C3 and C4 levels should be low. ^{128,129} | |
| Vasculitis (also see Hematologic – Thrombocytopenia, and Nephrologic-Goodpastures) | Tissue biopsy of lesions may reveal foreign material (saliva, talcum powder) injected to create purpuric lesions. ¹³⁰ | |

Discussion

This review attempts to comprehensively examine the limited information available on adjunctive methods to diagnose or suggest the diagnosis of factitious disorder. To make it more useful to the practicing clinician, we have attempted to list the methods available for each specialty by diagnostic category. When multiple authors described similar diagnostic techniques, we selected a representative reference from the group.

Potential limitations include search string errors, reviewer biases, and the lack of the systematic inclusion of the EMBASE database (although we felt the additional journals of that database were more oriented to biomedical rather than clinical literature). We also may have missed discussions in non-English literature as we only had articles translated if their titles or abstracts were available in English and appeared to be relevant.

Although this study was performed as a systematic review of the literature, we were unable to comment on the quality or characteristics of the tests used in most circumstances. The large majority of the reports were from case reports and did not provide sufficient data for critical analysis of test characteristics. Many of these tests have distinct limitations that are discussed in the pathology and toxicology literature.

In the age of enormous volumes of medical information on the Internet, there are specific sites for how to fake illnesses, as well as easy accessibility to terminology and copies of documents such as sample pathology reports.⁹⁻¹² Patients no longer need medical training or experience to engage in high-level factitious behaviour.¹⁰ While there may be some concern that we are providing a “how-to” guide for illness fabrication, we feel that it is more important for clinicians to have an easily accessible source of information for detecting factitious illness.

All the information in this article has been presented before in the medical literature and is available in piecemeal form. As patients with factitious disorder are generally found to have at least a high school education or higher, clinicians need to be prepared

to maintain a balanced index of suspicion when the history, clinical exam, and laboratory data do not make sense.¹³

Conclusion

Factitious Disorder will always be a challenging diagnosis for clinicians. In the modern hospital environment where the length of stay is short, it can easily be missed. This can result in multiple admissions for patients where batteries of increasingly obscure tests are undertaken to diagnose patients with inexplicable symptoms. This review is an attempt to provide a comprehensive reference of useful laboratory techniques for clinicians who suspect that a patient's illness may be due to factitious behaviour.

It still requires the clinician to maintain an index of suspicion and to include factitious disorder in the differential diagnosis. Every test can present with false positives or false negatives due to test limitations or laboratory error; this guide is not an end in the diagnosis of factitious disorder, but a beginning for clinicians who have developed a clinical concern that a patient may be fabricating illness. Repeat and or confirmatory testing should be encouraged as well as Liaison Psychiatry input and perhaps most importantly, collateral information from other caregivers. While laboratory testing may be invaluable for the diagnosis of factitious disorder in some cases, it needs to be interpreted within the context of the patient's complete history and physical findings.

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