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Treating Medically Unexplained Symptoms Empirically: Ethical Implications for Concurrent Diagnosis

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In a nuanced analysis of the ethical importance of medically unexplained symptoms (MUS), O’Leary calls attention to one of the most significant issues affecting outpatient clinical practice: the difficulty of evaluating and transparently addressing MUS (O’Leary 2018). O’Leary highlights sources of conceptual ambiguity in the characterization of MUS that hinder clinical decision-making, ethical analysis and access to quality care. She criticizes the under-treatment of biological symptoms in patients with MUS in light of the current emphasis in research on potential harms of overtreatment. This discussion is enhanced by greater recognition of the ubiquitous medical practice of “treating empirically,” particularly when interventions present low risks. Further, instances in which psychogenic MUS accompany biological symptoms of medically-explained, “organic” disorders challenge binary notions in clinical and ethical discourse on MUS. In this commentary, we build on O’Leary’s framework for the analysis of MUS by considering the ethical implications of: (1) the blurred distinction between diagnosis and intervention, described in the tendency to “treat empirically” in the absence of a definitive diagnosis; and (2) the co-occurrence of both psychogenic symptoms and organic symptoms attributable to identifiable biological causes.

O’Leary posits that, under the current model of medical practice, clinicians proceed from diagnosis to treatment on the basis of the identification of definitive biological markers of an illness or disease. While O’Leary introduces diagnostic uncertainty into this model of medical practice, her analysis foundationally assumes a clear distinction can be made between diagnosis and therapy. In addition, she posits that clinicians have a tendency to withhold treatment in cases of diagnostic uncertainty. This characterization of clinical decision-making underestimates the predominance in most medical practice of “treating empirically.” Frequently, clinicians initiate therapeutic interventions in the absence of a definitive diagnosis of the biological mechanisms underlying symptom presentation. Antimicrobial therapy provides an illustrative example of this empiric approach: clinicians observing symptoms of an infection may prescribe broad-spectrum antibiotics before or without diagnostic testing to identify a specific pathogen. Many times, lab tests simply provide assurance antibiotic use should continue or suggest a need to change the antibiotic. In Dermatology, topical treatment may be prescribed as a first-line treatment. If topical treatment fails, this information aids in the differential diagnosis. However, if symptoms resolve after use of the topical treatment then the problem is solved for the patient and no further diagnostic inquiry may be necessary to confirm the physician judged correctly. The

patient's symptoms resolved either over time or due to the topical treatment, so the provider pragmatically moves on to the next patient whose symptoms need to be resolved. In making clinical judgments, healthcare providers weigh the diagnostic value of cost-intensive, burdensome and potentially inconclusive diagnostic testing against concerns about morbidity in delaying initiation of therapy, efficiency, and pragmatism. Even when empiric antimicrobial therapy achieves symptom reduction or resolution, pathogenesis and the therapeutic mechanism of action of a given intervention may remain unclear.

When therapy is recommended for both diagnostic and therapeutic purposes, a different set of ethical challenges arise in relation to setting expectations for therapeutic response and providing a diagnostic label to the illness. This can cause both patients and other clinicians to make assumptions about the diagnostic justification for treatment recommendations. Psychogenic Non-Epileptic Seizures (PNES) provide an important example. When a patient presents with symptoms that match those of epilepsy, a clinician may treat empirically by prescribing a first-line anti-epilepsy drug (AED). For many of these patients, their seizures remit for a period of time after taking the AED. The clinician wrongly assumes the chemical effect of the AED that caused the seizures to temporarily subside. When the patient's seizures return, they are "empirically" treated again with a different AED, since the first AED seemed to prove that the patient was responsive to medical therapy. This is one reason patients with PNES on average spend over seven years on AEDs before they are properly diagnosed (Reuber 2008). This provides a strong example of the current emphasis on overtreatment of MUS. Just like in epilepsy, most areas of medicine look to first apply their standard interventions to empirically treat, and then further explore when biological treatments fail. Although we appreciate O'Leary's point that it is important to ensure psychogenic diagnoses do not wrongly preclude access to needed treatment, we need to recognize the potential harms attributable to a culture of overtreatment in the face of uncertainty.

In describing a conceptual leap in clinical decision-making from MUS to psychogenic diagnosis, O'Leary overlooks an important source of complexity: the common co-occurrence of psychogenic symptoms and "organic" symptoms of medically-explained disease processes. For example, 5–60% of patients with PNES have comorbid epilepsy (Gordon 2014). That is to say, under video-electroencephalography (VEEG) observation, some patients experience both PNES and epileptic seizures. The detection of psychogenic symptoms may cause clinicians to question the validity of organic findings and misdiagnose organic symptoms as psychogenic. Although this uncertainty does not usually obstruct access to usual and customary treatment, this diagnostic error may disqualify patients from access to more intensive interventions such as brain resection or implanted electrical stimulators. This underscores the importance of raising awareness of the potential comorbidity of psychogenic and organic conditions. Rather than keeping patients from therapy, the identification of comorbid conditions should prompt offering both psychological treatment as well as biological treatments.

The difficulty of distinguishing between psychogenic and organic features on an ongoing basis adds to the challenges associated with delivering coherent diagnoses and focusing therapeutic efforts. This can make informed consent particularly difficult because it can be

unknown which of the two diagnoses contribute more to the patient's functional impairments. In a movement disorders clinic, a patient may present with an intractable hand tremor that is partially "distractable." This language suggests dual organic and psychogenic diagnoses. The clinician now must try to judge whether a procedure like Deep Brain Stimulation (DBS), for which outcomes and mechanisms of action are primarily understood in relation to organic rather than psychogenic movement disorders, will give the patient a chance of regaining the desired function in their life. Additional attention to psychogenic comorbidities in outcomes research is needed to enhance the movement disorder specialist's ability to provide evidence-based recommendations for therapies such as DBS to patients with both organic and psychogenic diagnoses.

Finally, O'Leary argues clinicians maintain "a duty to at least provide biological care to every patient who seeks it with a biological need" (O'Leary 2018). This statement is too broad and ambiguous to be helpful in clinical practice. It may be that O'Leary simply means each person deserves to be evaluated with an open mind regarding the root cause of their illness. Sorting out what a patient actually needs, as opposed to what a patient wants or mistakenly believes they need, is a deeply vague and contested notion. In the messy world of clinical medicine, it is the ethical obligation of the health care provider to efficiently begin to decipher the healthcare needs and desires of each patient in order to help them. Time and knowledge constraints mean that clinical judgment arises in each case as to whether the clinician would rather risk under- or over-treating a patient's symptoms. Given what we know about PNES, we rightfully should be worried that busy clinicians are inclined to assume the presence of biological need at the expense of ensuring patients access the emotional and psychological care they need for wellbeing.

O'Leary moves the conversation about MUS forward in important ways. She frames the dialogue so that we can develop meaningful work in this area. Characterizing the dichotomy between psychogenic and biological diagnoses helps to clarify important aspects to which we must attend. However, the co-presence of both psychogenic and biological symptoms needs to be recognized. When both of these components are substantially responsible for disease burden, the "empirical" treatment of symptoms needs to be carefully evaluated. Ethical analysis must account for a culture of "treating empirically" in the face of diagnostic uncertainty and a tendency to attribute symptoms to a single causal explanation. If clinicians too quickly attribute symptoms only to either psychogenic or to biological diagnoses, they will overlook important aspects of their duty to treat patients as a whole.

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