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Solving the mystery of emergency medicine: medically unexplained syndromes

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Medically unexplained symptoms (MUS) represent a complex challenge within emergency department (ED) settings, characterized by their high prevalence and significant economic and social burden. Despite extensive diagnostic efforts, patients often experience dissatisfaction, leading to unnecessary investigations and increased healthcare costs. This paper argues for a paradigm shift from a purely biomedical approach to a comprehensive biopsychosocial framework for managing MUS in emergency care. To improve diagnostic accuracy beyond mere exclusion, we propose integrating psychometric evaluations into standard emergency clinical assessments. We highlight the importance of validating symptoms and empathetically reattributing them within the context of the intricate relationship between mind and body. This approach fosters greater trust and facilitates more effective intervention strategies. A stepped-care approach encompassing education, self-care advice, evidence-based psychotherapies [e.g., Cognitive Behavioral Therapy (CBT), Intensive Short-Term Dynamic Psychotherapy (ISTDP)], pharmacotherapy, and integrated follow-up are recommended and can be facilitated by the ED to ensure continuity of care and prevent recurrent visits. Addressing the persistent challenges of stigma, insufficient professional training, and the limitations of a reductionist biomedical model is crucial. Ultimately, by embracing this holistic perspective, healthcare systems can alleviate significant burdens and provide more compassionate and effective care to patients presenting with MUS.

KEYWORDS

medically unexplained symptoms, somatic symptom disorder, emergency department, biopsychosocial model, somatoform disorders (MeSH)

Introduction

The emergency department (ED) is the frontline of healthcare, where decisive action and clear diagnoses are paramount. However, a significant portion of the daily workload is consumed by cases that defy easy categorization, such as patients presenting with real and debilitating symptoms for which extensive diagnostic workups yield no definitive organic cause. These are the "unsolved mysteries" of medically unexplained symptoms (MUS).

These medically unexplained physical symptoms represent a considerable challenge, consume substantial medical resources, and often lead to patient dissatisfaction (1–3). The lack of awareness and understanding of MUS and appropriate tools exacerbates the difficulties in addressing these complex cases (4).

Medically unexplained symptoms are traditionally defined as persistent somatic symptoms for which no sufficient organic pathology can be identified to fully account for

their nature or severity (3). These symptoms, whether single or multiple, typically result in considerable distress or impairment in the patient's social, occupational, or other functional areas of life. The nomenclature surrounding these conditions is complex, with terms such as functional symptoms, somatisation, and psychosomatic disorders often used (5).

While the terminology is evolving, with "Somatic Symptom Disorder" and "Bodily Distress Disorder" being introduced in the DSM-5 and ICD-11, respectively, the core concept remains the same: physical symptoms that cause significant distress and functional impairment without a sufficient organic explanation (6–8).

Prevalence and characteristics of MUS in the emergency department

Although the lack of consistent diagnostic criteria makes the prevalence of this "disease" difficult to estimate, there is evidence suggesting that MUS are highly prevalent in primary care and emergency settings. Some studies have shown that in primary care, the prevalence ranges from 20 to 25% but can be as high as up to 45% (9), while in certain specialized medical care settings, MUS may account for up to 76% of the cases (10, 11). These patients frequently seek care in the ED, and their presentations can range from chest, abdominal, or back pain to shortness of breath, headache, and tiredness (3, 12, 13).

The incidence of MUS in the emergency department is remarkably high. While studies report that it affects approximately 13%—18.5% of all non-traumatic emergency department visits based on strict diagnostic criteria, the actual rate of somatisation is likely considerably higher (2). The reported figure rises dramatically among frequent re-attenders, where MUS can be identified in up to 72% of cases (14). Specific presentations are particularly illustrative of this phenomenon. For instance, nearly half (46%) of patients presenting with chest pain and approximately one-third of adults and almost half of children with abdominal pain will have no identifiable organic pathology (15, 16).

The spectrum of symptoms is broad and includes common ED complaints such as abdominal pain, chest pain, palpitations, back pain, fatigue, dizziness, headaches, syncope, and even presentations mimicking seizures or stroke. Many patients already have a diagnosis of fibromyalgia, IBS, chronic fatigue syndrome, or other similar functional somatic syndromes (17). These symptoms often overlap and fluctuate, further complicating diagnosis and management (18).

Research has identified several demographic and clinical characteristics associated with MUS. Patients are often younger and female, but somatisation is common in any age group, from children to the elderly, and across all genders. They are more likely to self-refer and frequently use healthcare services. A significant observation is the increased occurrence of co-existing mental health conditions, notably anxiety and depression; nonetheless, the ongoing stress often remains unacknowledged and appears as physical symptoms rather than recognized mental health problems (2). Some studies have also suggested a link with lower levels of education and socioeconomic status.

The economic and social burden of MUS

The impact of MUS extends far beyond the individual patient, placing significant strain on healthcare resources and the wider economy. In the United Kingdom, the annual cost associated with MUS was estimated to be as high as £12.7 billion over a decade ago. In the European Union, the yearly cost was estimated at €74 billion, whereas in the United States, it reached a staggering $256 billion (19). These are direct healthcare costs related to investigations and treatments, as well as indirect costs related to work absenteeism, and make up to 10% of the total healthcare expenditure (20). The costs of disability claims and long-term social benefits are not included in this estimation.

However, the true burden of MUS cannot be measured in financial terms alone. For the individual, these conditions lead to a significantly reduced quality of life, often resulting in social and professional decline. At the societal level, the impact is felt through diminished productivity, increased work absenteeism, and higher rates of disability. The chronic suffering of these patients profoundly affects their families.

The extensive utilization of healthcare resources driven by MUS through repeated investigations and ineffective treatments redirects capacity from other patient groups, potentially compromising outcomes in areas such as cancer mortality, trauma survival, and organic diseases (21).

Challenges and stigma in clinical practice

One of the most significant barriers to effective care for patients with MUS is the stigma they often face from society, including healthcare professionals (22, 23). Pejorative labels such as "malingerer," "attention seeker," and "time waster" have historically been, and sometimes still are, applied to these individuals (24). This stigma is often perpetuated by senior clinicians who serve as role models, creating a challenging environment for junior doctors and trainees to develop a more compassionate approach toward patients (25). This attitude can lead to delayed or inadequate treatment, further exacerbating the patient's distress and perpetuating a cycle of healthcare-seeking and dissatisfaction (26, 27).

This negative perception is compounded by a lack of specific training in psychosomatic medicine, an overreliance on a purely biomedical model, and the absence of standardized diagnostic tools and protocols for MUS in the ED (4, 28, 29). Furthermore, the understandable fear of missing an underlying organic pathology can lead to medico-legal anxiety and defensive medicine, characterized by excessive and often unnecessary investigations (30). When clinicians are unable to determine an organic basis for a patient's symptoms, they may understandably express concern about the possibility of overlooking a diagnosis, potentially leading to further investigations or the acceptance of weakly supported diagnoses to initiate treatment. The apparent effectiveness of such treatments (due to their placebo effect) can create a false sense of security for the healthcare team, while simultaneously reinforcing the patient's conviction that an underlying organic pathology exists

(31). However, when the placebo effect diminishes and symptoms return, the initial belief in an organic cause is often reaffirmed (32). The recurrence of abdominal pain within 3–6 months following a seemingly successful surgical intervention to address its perceived causes presents a common diagnostic challenge for clinicians.

This approach not only increases healthcare costs but also exposes patients to potentially harmful procedures and radiation, aggravates their health anxiety, and ultimately worsens their symptoms.

Pathophysiology of MUS

It is crucial to recognize that the symptoms of MUS are real and have an increasingly well-understood biological basis. Emerging evidence points to a complex interplay between biological, psychological, and social factors (33).

The mind and body are in constant bidirectional communication, which is mediated by intricate immune-brain pathways. This interactive model, in which neural, immune, endocrine, and psychological processes are intertwined, provides a framework for understanding how emotional distress can manifest as physical symptoms.

Persistent stress (allostatic load) and unresolved emotional trauma, childhood experiences and even social factors can cause biological and neurohumoral changes across the body, affecting the autonomic nervous, endocrine, and immune systems (34–37).

These changes manifest as various physical symptoms, including pain, fatigue, and gastrointestinal distress (38, 39).

Key biological mechanisms include

- Neuroplasticity: neuroplastic changes in pain perception and processing lead to amplified pain signals and decreased pain thresholds (40–43).
- Dysregulation of the autonomic nervous system results in increased sympathetic activity and reduced parasympathetic tone. In response to mentally distressing tasks, it does not decrease physiological activity as it would in healthy individuals, suggesting a link between psychosocial stress and MUS (42).
- Altered brain activity, particularly in regions involved in emotional regulation and interoception, as observed in functional neuroimaging studies (44–48).
- Altered and dysfunctional serotonergic and noradrenergic neurotransmission may result in changes in signal processing and number or function of brain receptors (49).
- Dysregulation of the hypothalamic-pituitary-adrenal axis leads to chronic stress and inflammation (33, 50, 51).
- Central sensitisation: a state of persistent hyperexcitability of the central nervous system, causing the same symptom to be interpreted as gradually worsening (52).

From a psychological perspective, "somatosensory amplification"—the tendency to focus on and misinterpret benign bodily sensations as signs of serious illness—plays a significant role (33). Emotional processing of symptoms is also associated with symptom severity (53, 54). Additionally, abnormal proprioception, in which patients exhibit heightened sensitivity to minimal changes in muscle tension, can lead to benign physiological sensations being misinterpreted as signs of physical disease (42). This can lead to a vicious cycle of symptom amplification and distress in patients.

Abbas has summarized how different anxiety forms, causing striated or smooth muscle tensions, cognitive-perceptual disruption or neurological dysfunction (conversion), are related to commonly observed clinical symptoms and presentations in the Emergency Departments (55).

For instance, anxiety can lead to striated muscle tension, resulting in headaches and chest pain, or it can cause smooth muscle spasms, leading to symptoms such as abdominal pain or irritable bowel syndrome. Anxiety, which affects the cognitive-perceptual fields, can lead to dizziness, pseudoseizures, visual blurring, or fainting (55).

Autonomic stress responses can also result in feelings of warmth and coldness, palpitations, nausea, diarrhea, and constipation (56).

It is crucial to recognize that the symptoms reported by patients are genuine experiences and not merely figments of their imagination. These symptoms stem from complex interactions between the mind and body, reflecting physiological responses similar to those triggered by external or internal factors, such as infections or inflammation.

Clinical diagnosis of MUS in the emergency department

A structured and compassionate approach to MUS in the ED is essential for effective management. The primary and non-negotiable first step is the exclusion of any life-threatening emergencies. Following this, a comprehensive biopsychosocial assessment should be undertaken. This involves a detailed history, including a review of previous attendances, a thorough physical examination, and appropriate investigations to rule out organic causes (57, 58).

The assessment should include an exploration of psychosocial factors, such as stress, anxiety, depression, and past trauma, as these can significantly contribute to the presentation of physical symptoms (3, 59).

Several validated screening tools are available to aid in identifying somatic symptom patterns, including the PHQ-15, SSS-8, and SSD-12. These self-administered tests are feasible in the busy ED environment and demonstrate moderate-to-high sensitivity and specificity (60, 61). However, they are not used to diagnose somatisation as the cause of the current presentation; rather, a higher score on these psychometric tests indicates a higher likelihood and tendency toward it, highlighting the importance of considering psychological factors in patients presenting with physical complaints (3). Patients can fill out these questionnaires while waiting for assessment in the waiting room, and their scores can be added to the other diagnostic workup for clinical consideration.

Unfortunately, there is no straightforward diagnostic approach to easily identify somatisation. Biomarkers (like respiratory sinus arrhythmia, skin conductance, and finger temperature) combined

by machine learning were investigated but found not yet superior than the usual medical examinations and questionnaires (62).

While these tools can be valuable in identifying potential MUS, it is critical to use them judiciously and not solely rely on them for diagnosis, as MUS diagnosis requires careful clinical judgment and exclusion of organic pathology (17).

Pitfalls in the emergency department

While adopting a biopsychosocial approach shows promise and has already demonstrated success in certain areas (1, 63, 64), there remains significant and, in many respects, understandable resistance, particularly in emergency departments. Here, the pressures of time, limited resources, and overcrowding threaten operational safety.

The concern about missing a diagnosis is not without merit. Research indicates that the likelihood of overlooking an organic diagnosis in patients initially identified as having MUS is between 1 and 8%, which is not insignificant (65, 66). This risk increases with symptoms that are atypical, severe, or evolving. To minimize diagnostic errors, it is recommended to provide appropriate training, seek second opinions, employ structured teamwork, and use standardized clinical pathways, along with actively involving and engaging the patient (67, 68).

Management of MUS in the emergency department

Medically unexplained symptoms often arise from allostatic load, representing a sustained stress response that may be triggered by various underlying factors. Identifying the specific root cause during an Emergency Department visit is usually not possible. However, a judicious approach can facilitate problem identification, prevent iatrogenic harm through over-medicalisation, and guide the patient toward appropriate care (1, 69).

Symptom relief is essential, and if that requires medication (analgesia, antiemetic, etc.), then that should be provided. In addition to recognizing a psychosomatic component, it is also crucial not to miss organic diseases that should be treated with targeted therapeutic interventions (70).

Effective communication is the cornerstone of management. Patients with MUS may have had negative experiences in healthcare settings and may feel frustrated or misunderstood, making communication even more challenging (71). It is vital to **validate** the patient's symptoms and acknowledge the reality of their suffering (72). Based on the pediatric ED literature, it is inferred that explaining the condition as a specific disorder (for example, Somatic Symptom Disorder) rather than a lack of findings is a beneficial strategy for all age groups (73). Building trust and rapport through empathy can alleviate anxiety and facilitate more productive discussions about potential underlying psychological factors (74).

The next step is to gently reattribute the symptoms. Once the likely organic causes were ruled out, it is essential to explain the connection between psychological stress and physical sensations. This involves providing a clear and simple explanation of how stress, anxiety, or other emotional factors can manifest as physical symptoms without dismissing the patient's experience (73, 75). This explanation should be tailored to the patient's level of understanding and cultural background.

A stepped-care approach is recommended for ongoing management and should be initiated in the ED: (3, 50, 76, 77).

- Education: providing information on the mind-body connection, lifestyle modifications, physical activity, breathing exercises, sleep hygiene, diet, and mindfulness techniques. These self-management strategies hold considerable value when integrated with an understanding of the fundamental principles governing mind-body interactions, a perspective that emergency department clinicians can offer during the patient's visit (45, 72, 75, 78, 79).
- Psychotherapy: some cases may require more complex treatment. Referral to evidence-based therapies, such as Cognitive Behavioral Therapy (CBT) or Intensive Short-Term Dynamic Psychotherapy (ISTDP), may be indicated; however, such interventions are not typically initiated within the emergency department setting (55, 80–82).
- Pharmacotherapy: in some cases, antidepressant medications may be beneficial. New-generation antidepressants (such as SSRIs and SNRIs) were found to be moderately effective in reducing the severity of physical symptoms, anxiety, and depression compared with placebo. However, a major 2014 Cochrane review graded the quality of this evidence as "very low" due to a high risk of bias in the underlying studies, significant heterogeneity in the data, and small sample sizes (83). Similarly, low-level evidence suggests the beneficial effects of natural herbal products (specifically St. John's wort: "Hypericum perforatum") compared to placebo (84). Combination therapy with antidepressants and antipsychotic medications can also be considered (83).
- Integrated care: establishing a clear follow-up plan with a general practitioner to ensure continuity of care and prevent recurrent ED visits (3, 69, 77).

Limitations

This narrative review is subject to certain limitations that warrant consideration. The analysis is based on existing literature rather than original empirical research, which restricts the capacity to derive groundbreaking conclusions. Variations in the definitions and diagnostic criteria for MUS across different studies pose challenges in comparing findings and establishing consistent prevalence rates. Furthermore, recent changes in diagnostic classifications may not be fully represented in the older studies cited, potentially impacting the relevance of certain findings.

While this study aims to address MUS in emergency care, the literature review encompasses papers from primary care and other medical settings as well. Although this broader perspective enhances comprehension, it correspondingly limits the generalizability of findings to emergency departments.

We acknowledge the potential difficulties and limitations to implementing the biopsychosocial approach in the ED, such as time constraints, overcrowding, and training requirements; however,

these were outside the review's scope. Furthermore, due to the acute nature of ED care, the long term prognosis of MUS and the long term effectiveness of the proposed management strategies were not explored. While literature exists regarding prognosis and follow-up results, the focus remained on acute presentations.

Furthermore, the narrative structure of this review may introduce bias in the selection and interpretation of cited studies. Acknowledging these limitations, this review offers a valuable summary of current strategies and possible actions for MUS in the ED. It highlights chances for improvement and future progress, aiming to encourage more research in this area.

Conclusion: solving the mystery through a new lens

Medically unexplained symptoms are not a mystery to be solved with more tests or more powerful imaging. They are complex and deeply human experiences that demand a shift in our clinical perspective. The high prevalence of MUS in our emergency departments, coupled with its immense economic and social costs, necessitates a more enlightened and effective approach.

The challenges of stigma, lack of training, and constraints of a purely biomedical model are significant but not insurmountable. By embracing a biopsychosocial framework, we can move beyond the frustration of "unexplained" symptoms toward a more holistic understanding of our patients. By validating their suffering, reattributing their symptoms within a mind-body context, and initiating a structured stepped-care approach, we can provide more compassionate and effective care and alleviate a significant burden on our healthcare system. The mystery of MUS is not the absence of an explanation but our willingness to look for it in the right place: at the complex and fascinating intersection of the mind and body.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

CD: Conceptualization, Writing – review & editing, Writing – original draft. CP: Resources, Writing – review & editing, Project administration, Methodology.

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The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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