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EDITORIAL

As clear as MUD

Somewhat contrary to popular perception, it is both very and increasingly common for people to have medically unexplainable symptoms; this is also referred to as 'medically unexplained disease' or MUD. The basis of MUD is 'symptoms' that cannot be fully explained by an 'organic' cause. Managing patients with such a condition is a challenge for physicians, as most people present with a high level of concern and worry about their symptoms and are difficult to reassure. Perhaps the most important role for physicians is to restrict the likelihood of harm caused by unnecessary investigations and treatment.

The subject of MUD is controversial and has been so both before and after a chronically fatigued Florence Nightingale took to her bed; the prevalence, outcome and cost of MUD is now such that it 'deserves' editorial attention.[1–4] Treating doctors often feel frustrated and inadequate, and sufferers frequently think they have been rejected; many receive little or no support, or meaningful care on the one hand, or 'consume' considerable and usually unhelpful healthcare on the other.

There are several reasons for this controversy.

First, MUD is frustratingly common and increasingly so.[1–3,5–8] In a range of primary care settings:

- Complaints of chest pain, fatigue, dizziness, headache, swelling, back pain, shortness of breath, insomnia, abdominal pain and numbness were responsible for as much as 40% of all visits, but only 26% were ever 'medically explained';
- More than 25% of all patients in studied English general practices had symptoms that were not medically explicable;
- Between 25% and 50% of patients had unexplainable symptoms in various cohorts, which made this problem the most common category of complaint in primary care patients;
- Medical explanations were found over a 3-year period in a North American general practice for only about 10% of those presenting with chest pain and headache, and in less than half of those whose primary initial complaint was fatigue, dizziness, oedema, numbness, back pain, dyspnoea, abdominal pain and insomnia, and in another similar study, more than half of patients presenting with a physical symptom had 'resolved' by 5 years while a third remain medically unexplained.

This level of MUD is also true but less well studied in developing communities. Predictably, given that a common reason for a referral from a primary to a secondary care physician is the former not being able to identify a medical explanation for a patient's symptoms, the rate of persistence is even greater in secondary care settings – the symptoms of 25% of patients with MUD managed by primary healthcare providers persisted for more than a year compared with 50% in secondary care.[9,10]

Second, the label of medically unexplained symptoms or disease is itself part of the problem. It is an unhelpful term for patients at a time when they are often seeking an explanation for their symptoms, as it promotes a mode of thinking about the issue that regards symptoms as either being 'organic' or 'psychological', and perhaps most importantly, the term characterises the patient's complaints by what they are not rather than what they are.[11] This frustration has led the working group revising somatoform disorders for the new version of the American Diagnostic and Statistical Manual of Mental Disorders to propose the term 'Complex Somatic Symptom Disorder'. Debate continues about the number of symptoms required to reach the threshold for this diagnosis, but it is clear that health-related anxiety will be part of the criteria.

Third, many patients who have unexplained symptoms often present with more than one symptom. Some symptom clusters are diagnosed as a functional somatic syndrome, such as chronic fatigue syndrome, fibromyalgia and irritable bowel syndrome. In fact, there is considerable overlap of symptoms between these and other functional somatic disorders.[12] The eventual diagnosis is largely determined by which medical specialty the patient is referred to rather than the set of symptom complaints because each medical specialty has at least one term for these patients.[13]

Fourth, mood and anxiety disorders may not be more common in people with MUD or associated with worse outcomes, but most patients with somatoform disorders have MUD and do not improve.[6] Three or more general physical symptoms or unexplainable symptoms are positively associated with depression, anxiety, substance abuse, and service use and psychological distress.[5] A significant mental health underpinning of any biopsychosocial concept of MUD is also supported by a number of other observations:[2,3,14,15]

- In developing countries, depression and anxiety commonly present with medically unexplainable symptoms;
- Cognitive behavioural therapy (CBT) is an effective treatment of MUD, especially for physical as compared with psychological symptoms; and
- Among people who have MUD, associated 'organic' pathology is rare and rarely missed, whereas psychiatric diagnoses are common and often missed.

It is still a sad truism that many consumers and conventional allopathic healthcare providers collude in a pejorative view of mental health. Insurance and actuarial exclusion of mental health is common. Doctors consequently 'advocate' for their patients by 'representing' unexplainable symptoms and/or mental health disease as 'explicable' medical problems. This advocacy often becomes fraudulent.[4] Other related issues here include limited access to appropriate mental health providers in most jurisdictions, a somatically focused health disease industry, and healthcare providers' concern about the risk of complaint if they miss a 'real' disease. Not surprisingly, MUD is a rich fodder for alternative or irregular health providers.

Avoidance of iatrogenic harm is essential and perhaps the most important role any doctor can play in the management of a patient who has unexplained symptoms.[2,3,16,17] These patients are of considerable risk of overinvestigation and overtreatment. Unfortunately, repeat and more intensive investigations 'encourage' patients to search for an 'organic' explanation for their symptoms and usually increase, rather than reduce, anxiety about their condition. The likelihood of a plausible medical explanation ever being found for someone who has a dozen or more unexplained symptoms approaches zero.[7] There is much art then in any referral or investigation, and in the treatment of people with MUD. This is a process of recruitment and not of confrontation, and the purpose of any referral should generally be for rehabilitative and 'functional' restoration. In this context, even as little as 1-day training for doctors in how to manage patients with MUD can lead to a significant reduction in healthcare utilisation.[18]

In the milieu of this controversy, we suggest a four-step process to the recognition and management of people who have MUD.

Step One: Use a reasonable diagnostic sieve to identify important and prevalent somatic disorders. Whereas as few as 4% of people with a conversion disorder develop an 'organic' illness that could explain their symptoms, as many as 45% of those with unexplained somatic symptoms may have an undetected psychiatric illness.[14,15] Once the exclusion of 'important organic disease' is undertaken, the objective is to withdraw unnecessary treatment and to dismantle disabling illness beliefs, and to avoid further investigations and referrals to other physicians and surgeons.

Step Two: Acknowledge the reality of the person's experience and reassure them about your insight and competence. The question the person may or may not address to you directly but the one you need to address explicitly is commonly cited as, 'Is this real doctor or is it in my head?' This 'mind-body dualism' is a commonplace, disabling and an extraordinarily persistent hangover of René Descartes' almost 400-year-old philosophy.[4]

Almost always, you will have to explain the 'biological and evolutionary nature' of somatisation if your patient is to be reassured and if their symptoms are to be 'validated'. It is not uncommon for people to get very angry during this type of discussion. Adequate information about normal tests has also been shown to reduce symptoms[19] in contrast with patients feeling rejected when told that the normal test indicates that 'nothing is wrong'.

Step Three: Ensure holistic and concurrent management of work-related, domestic, spiritual, and other contributory and confounding factors. This may include a selective serotonin reuptake inhibitor prescription to treat a depressed mood, haemoglobin A1c-based control of diabetes, and so on. It is important to 'look for' psychological concerns, relevant family and cultural issues, a history of a dysfunctional childhood, and symptoms of depression, anxiety and post-traumatic stress disorder – as already cited, three or more general physical symptoms or unexplained symptoms are positively associated with depression, anxiety, substance abuse and service use, and psychological distress.[5]

Step Four: Actively manage any somatoform disorders. Referral for CBT and other forms of psychological intervention is necessary, as these can be highly effective;[2,3,17] but again, this is where the art of the referral is most demanding. Antidepressants, CBT, hypnotherapy and reattribution approaches have all been shown to have value. Low-dose antidepressants are of benefit even if comorbid depression does not reach threshold for treatment; by contrast, benzodiazepines are of no proven benefit and have a high addictive risk.

Physicians frequently make disparaging remarks about patients with MUD, and/or avoid them, refer them to 'colleagues', or interrogate them with unnecessary and expensive tests prior to telling them that 'nothing is wrong'; these patients are unwell, distressed and disabled, and deserve better.

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References

1 Bermingham SL, Cohen A, Hague J, Parsonage M. The cost of somatisation among the working age population in England for the year 2008-2009. *Ment Health Fam Med* 2010; **7**: 71–84.
2 Edwards TM, Stern A, Clarke DD, Ivbijaro G, Kasney LM. The treatment of patients with medically unexplained symptoms in primary care: a review of the literature. *Ment Health Fam Med* 2010; **7**: 209–21.
3 Hatcher S, Arroll B. Assessment and management of medically unexplained symptoms. *BMJ* 2008; **336**: 1124–8.
4 Porter R. *The Greatest Benefit to Mankind: A Medical History of Humanity from Antiquity to the Present*. London: Harper Collins; 1997.
5 Escobar JI, Cook B, Chen C-N, Gara MA, Algeria M, Interian A *et al*. Whether medically unexplained or not, three or more concurrent somatic symptoms predict psychopathology and service use in community populations. *J Psychosom Res* 2010; **69**: 1–8.
6 Jackson JL, Passamonti M. The outcomes among patients presenting in primary care with a physical symptom at 5 years. *J Gen Intern Med* 2005; **20**: 1032–7.
7 Mayou R. Functional somatic symptoms and syndromes. *BMJ* 2002; **325**: 265–8.
8 van Ravenzwaaij J, olde Hartman TC, van Ravesteijn H, Eveleigh R, van Rijswijk E, Lucassen PLBJ. Explanatory models of medically unexplained symptoms: a qualitative analysis of the literature. *Ment Health Fam Med* 2010; **7**: 223–31.
9 Khan AA, Khan A, Hareziak J, Tu W, Kroenke K. Somatic symptoms in primary care: etiology and outcome. *Psychosomatics* 2003; **44**: 471–8.
10 Stone J, Sharpe M, Rothwell PM, Warlow CP. The 12 year prognosis of unilateral functional weakness and sensory disturbance. *J Neurol Neurosurg Psychiatry* 2003; **74**: 591–6.
11 Creed F, Guthrie E, Fink P, Henningsen P, Rief W, Sharpe M *et al*. Is there a better term than 'medically unexplained symptoms'? *J Psychosom Res* 2010; **68**: 5–8.
12 Aaron LA, Burke MM, Buchwald D. Overlapping conditions among patients with chronic fatigue syndrome, fibromyalgia, and temporomandibular disorder. *Arch Intern Med* 2000; **160**: 221–7.
13 Kanaan RAA, Lepine JP, Wessely S. The association or otherwise of the functional somatic syndromes. *Psychosom Med* 2007; **69**: 855–9.
14 Crimlisk HL, Bhatia K, Cope H, David A, Marsden CD, Ron MA. Slater revisited: six year follow up study of patients with medically unexplained motor symptoms. *BMJ* 1998; **316**: 582–6.
15 Stone J, Smyth R, Carson A, Lewis S, Prescott R, Warlow C *et al*. Systematic review of misdiagnosis of conversion syndrome and 'hysteria'. *BMJ* 2005; **331**: 989.
16 Illich I. *Medical Nemesis: The Expropriation of Health*. London: Bantam Books; 1977.
17 Rief W. Analyzing the problems in managing patients with medically unexplained symptoms. *J Gen Intern Med* 2007; **22**: 704–6.
18 Rief W, Martin A, Rauh E, Zech T, Bender A. Evaluation of general practitioners' training: how to manage patients with unexplained physical symptoms. *Psychosomatics* 2006; **47**: 304–11.
19 Petrie K, Muller JT, Schirmbeck F, Donkin L, Broadbent E, Ellis CJ *et al*. Effect of providing information about normal tests on patients' reassurance: randomised controlled trial. *BMJ* 2007; **334**: 352.

REVIEW

Stochastic processes in the aetiopathogenesis of scleroderma

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Abstract

We review the aetiology of scleroderma from an epidemiological perspective examining genetic, environmental and stochastic risk factors. The presence of familial clustering (but with low twin concordance) suggests a genetic contribution, and this has been confirmed with recent candidate gene and genome-wide association screening demonstrating both major histocompatibility complex and non-major histocompatibility complex genetic linkage. In contrast, environmental associations are weak or inconsistent. An examination of the age-adjusted incidence curve of scleroderma is consistent with a stochastic process involving five to eight random events. In pathogenesis, scleroderma is best considered as an autoimmune disorder where genetic and environmental factors are both important variables, but random events are also likely to play a pivotal role. We suggest that these random events might result in acquired somatic mutations or epigenetic alterations involving genes coding for immune receptors, tolerogenic gates or proteins involved in immune regulation, inflammation and/or repair that, over time, might summate to form a requisite cassette (of genetic changes), which allows the initiation and progression of the autoimmune process.