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Not "all in the mind"

In the quest to find a cause for "medically unexplained symptoms" patients need supportive doctors who don't trivialise their problems, says Tessa Richards

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Patients with persistent, severe, but medically unexplained physical symptoms baffle and frustrate doctors. Without a diagnosis they can't be put on established disease pathways and it's hard to know how best to manage them. Patients struggle with "unvalidated" illness and seek views from many different practitioners. Recently, a multidisciplinary group of clinicians and patients with an interest in "medically unexplained symptoms" (MUS) got together in London to shed light on a problem which deserves more attention than it gets.

As I travelled to the meeting, I remembered a middle aged man we (junior doctors) repeatedly admitted to the medical wards complaining of excruciating pain for which no cause was ever found. Few of us believed his symptoms were genuine. Fortunately for him, the lead physician did, and ensured he was given strong analgesics. Over time, the consultant had become convinced he had a rare disorder called stiff person syndrome.[1]

Given the rate of medical advances, I wondered how many people, formerly labelled as having MUS, now get a diagnosis? And whether health professionals are better at managing these patients, estimated to account for one in five consultations in primary care and more in some secondary care clinics such as rheumatology.[2]

On the diagnostic front there is some encouragement. Around 1 in 17 people are estimated to have a rare disease of which there are over 7000. Genomic testing can help identify many, but blanket genomic testing for MUS is not appropriate, suggested Julian Barwell, a clinical geneticist from Leicester.

"It's not only your DNA that matters," he said, epigenetics matter too. Whole genome screening should be used selectively after accurate phenotyping and obtaining a good family history.[3] He also flagged how pharmacogenomics can help unpick MUS which are caused by medications.

New research suggests that many patients labelled as having MUS may have autonomic dysfunction, and mast cell activation abnormalities, said Sanjay Gupta, a cardiologist at York, with an interest in POTS (postural orthostatic tachycardia syndrome). This dysfunction may be triggered by a variety of factors including covid–19 infection, he said.[4]

Managing patients with MUS remains challenging

As a patient with progressive symptoms of brain fog and tiredness dismissed for over a year as "worry about your cancer" before a diagnosis of pernicious anaemia, a presentation from two lay members of a multidisciplinary charity called Forgotten Patients Overlooked Diseases, struck a chord with me.[5]

Both described protracted journey's involving multiple referrals before getting a diagnosis (in their case of Ehlers Danlos syndrome). Over this time, the hardest thing to cope with was not being "listened to, heard, and believed." They were also undermined by doctors' "disapproval" of their relentless pursuit of a diagnosis.

"Getting a diagnosis is important, even if there is limited or no effective treatment for the condition," they underlined. Its validation for yourself and others spurs creation of a coping strategy and opens the door to support from charitable organisations and financial help from the government.

Lack of time to listen to patients, and lack of continuity of care makes management of patients with MUS very challenging, said Jay Verma, a London based GP whose practice workload has tripled post covid. In an effort to do more to help his patients, he documents cases under the SNOMED code "uncertain diagnosis" and regularly reviews patients in this category with the practices multidisciplinary team.[6] "Members of my team often know better than I do what is going on in these patients' lives" he said, and we formulate a management plan together."

An indication of the prevalence and cost of dealing with patients with MUS in emergency care, was presented by Jon Matthews, an accident and emergency consultant at St Mary's Paddington.

"A minimum of 4.5% of attendees don't have a diagnosis when they leave the unit, but dealing with them takes up 10% of our budget. This is because they tend to present with a myriad of symptoms, complex psychosocial problems, and don't fit into one of our standard medical boxes. They therefore can't be speedily transferred on to medical, surgical, and community teams," he said.

He and colleagues have set up a working group to identify frequent attenders with MUS, explore their symptoms in more depth, and try to change the culture in A&E to avoid staff "trivialising" patients' symptoms.

Look for white ravens (rare but they do exist)

A key problem for patients is that there is no specialty that "owns MUS." In the past many were seen and were managed by rheumatologists, but this avenue is about to close, as their focus in the UK looks set to be exclusively on inflammatory joint disease.

So, should dedicated clinics be set up for patients with MUS? And how would they be financed and run?

A Dutch initiative called the Witte Raven "White Ravens" provides an example of one model.[7]

The group was set up in 2016 by doctors who had themselves experienced unexplained severe persistent medical symptoms. GPs (but not patients) refer patients to them via their website and are requested to send on all the information in the medical record.

The group collate the information and brainstorm unusual causes for the MUS using the VINDICATE sieve.[8] They then do a literature search of PubMed, Google (scholar), Find Zebra, and Chat GPT. A report is subsequently sent to the referring doctor with a list of differential diagnoses and advice about ongoing management.

Generative AI may help patients and patient organisations, as well as doctors in the search for a diagnosis. With increasing access to health information (personal and the medical literature) patients will be able to aggregate, analyse, and interrogate the data for themselves, said Keith Grimes, former GP turned digital health specialist from London.

But while a diagnosis is hugely helpful, it's not enough. Patient organisations often play a key role in supporting patients and their families, but professional support is needed too. Clinicians will do better by these patients if they are non judgemental, offer holistic care, and are transparent about the limits of modern medicine. A causation and cure for symptoms may be elusive, but humane care and compassion should not be.

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