

hinder implementation of these recommendations. Recognising the condition and the impact it can have on the lives of patients and their families is therefore a necessary preliminary to improving care.

- People with severe CFS/ME who are housebound or need prolonged bed rest require specialised care, but evidence is lacking about which treatments are most effective to reduce their symptoms.
- Little research exists on CFS/ME generally, and specifically on its causes and diagnosis.
- The guideline development group recognised the need for wider research on aetiology and pathogenesis, as a basis for developing new treatments.
- For all people with CFS/ME the guidelines recommend an integrated, multidisciplinary approach, incorporating health and social care, with support for education and work when and if the patient is ready. This comprehensive approach can be difficult to achieve unless one named professional has responsibility for coordinating the patient's care.

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A PATIENT'S JOURNEY

Ehlers-Danlos syndrome

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These three case histories illustrate the many problems facing patients with Ehlers-Danlos syndrome in its various forms

Patient 1: Jacqueline Mould

At birth my daughter, Jacqueline, had very visible veins on her head and body. She bruised badly when she fell. The doctors said it was nothing—just thin skin. Then, when she was 12 years old she developed an unusual localised rash on her knees. A dermatologist said she had perforating elastoma. She was an “interesting case,” but he did not know the cause. At age 23 Jacqueline developed pain in her legs. The doctor said it was just varicose veins—there was nothing to be done except to avoid standing and to wear support stockings. The pain got worse and Jacqueline went for a hospital consultation. At the clinic blood was taken and she bled for 13 minutes. She was sent to a joint consultation with a haematologist and a dermatologist, who said she should see a specialist interested in the genetics of Ehlers-Danlos syndrome. Still we had no idea of what was going on.

We waited two years to see the geneticist. He commented on her facial features and tested her joints, which were not hypermobile. He told us that Jacqueline had the vascular type of the syndrome. No one in the family was like her—her condition was caused by a mutation. She was told that she should not have children, must not take part in contact sport, and must avoid physical

stress. We were invited to ask questions, but it was all too much of a shock. We went home in silence. Jacqueline was particularly distressed about not being able to have children.

When I read the literature of the Ehlers-Danlos Syndrome Support Group I realised the full horror of probable sudden death. I felt numb. Jacqueline was a fit young woman in full time employment who was enjoying her life. I left the literature for her to read if she wished. She decided not to tell her friends about her illness. She had episodes of depression, but together we decided to carry on as normal.

Two years later, at work, Jacqueline's legs suddenly went numb. She was taken to the local hospital. The doctors didn't know about Ehlers-Danlos syndrome. They found nothing wrong and said she could go home. At this point Jacqueline collapsed. After resuscitation it was realised that she was bleeding internally. A renal artery had ruptured and despite surgery Jacqueline died on the operating table.

Today I work with the Ehlers-Danlos Syndrome Support Group to improve awareness of this rare condition and to help support those who have to face its problems.

Patient 2: Amanda Sperritt

I am 36 years old and have hypermobile Ehlers-Danlos syndrome. As a child I was “double jointed”—able to do party tricks that made people say “yuk.” When I was 15

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my hips began to slip spontaneously. My general practitioner said that it was my imagination. Later, at college, I could only shuffle, hips slipping out with every step. I was referred to hospital. The consultants were mystified. They insisted I would grow out of it.

Later, I was admitted to hospital and told that I had Ehlers-Danlos syndrome. The consultant stayed for only 10 minutes and spent most of this time telling me off for smoking, leaving me to find out the implications of the diagnosis for myself. I was devastated. Since then the symptoms have progressed. I have persistent pains in my shoulders, hips, neck, back, and hands. I have difficulty in standing and walking. I use a stick and occasionally a wheelchair. My grip is poor. I can't write or even type easily. I have stretchy, fragile skin that doesn't heal well. I have trouble speaking and swallowing. I get palpitations and night sweats.

Visiting hospital consultants has been unhelpful. They have so little time. Often I am just shown to medical students as an interesting case. Physiotherapists are much better. They allow me to play an active part in my treatment and have taught me to use my muscles to protect my joints.

Cannabis was also helpful. I learnt to grow my own and it reduced my dependence on pills. I slept better and I could do more physiotherapy and even a part time job. I told my doctors; none objected but my secret got out. The police came and took my plants away. A judge regarded my action as wrong doing and left me with a criminal record. How can that be right?

I have tried alternative medicine but always make sure that the practitioners know about the syndrome. The Alexander technique is good for relaxation and posture awareness. A short course of acupuncture also had a positive effect. My present philosophy is, "get all the information and advice you can and use what works for you."

An unconventional body doesn't suit a conventional lifestyle. I haven't slept all night for 17 years. I often wake up after a couple of hours, drenched in sweat. I arrange my life so that I can sleep when I need to and have devised ways of getting back into activities such as art, music, and cookery. I help my sister with charity work for severely disabled children. Once more I feel that I am making a contribution to society.

The most helpful professionals treat me as a partner in the management of my condition. They listen to the information I discover and support me in my struggle to get the equipment, services, and financial help that I need to make life that bit easier.

Patient 3: Fiona Neale

I am now 33 years old and like many people with Ehlers-Danlos syndrome I was in my late teens before being diagnosed. This delay had a big effect on how I was treated by doctors and how I coped with my condition. All the clues were there—hernia repair aged 4, flexible joints, easy bruising, and flat feet with unstable ankles, but for many years no one put it all together to make a diagnosis. My symptoms were regarded as unimportant, and with my flexible joints at least I was good at sports like acrobatics.

When I was about 11, joint pains became a problem. An injury to my elbow took a year to resolve; the symptoms from a badly sprained ankle persisted and the joint subluxed. Without a linking diagnosis I was regarded as "neurotic" and possibly "attention seeking." My feet became very painful and I couldn't walk any distance or stand for a long time. I took painkillers and had to use crutches. I was told never to consider using a wheelchair. Yet a lightweight wheelchair, that I could use as required, would have increased my mobility and the quality of my life. By the time I was 15 I was in daily pain, I could no longer do sport, and I wished I was dead. I was bullied at school for being different, and many of my physical problems were thought to be in my head. I hoped that this was true because if the pains were not real then all I had to do was get my head right and I would be "normal" again.

At university, after minimal trauma, I dislocated my shoulder and was sent to hospital. I was referred to a genetic counsellor who told me that I had Ehlers-Danlos syndrome. He put me in touch with the support group. Reading their literature I soon realised that I was not alone and that all the many problems were due to Ehlers-Danlos syndrome. Over the years I have dislocated and semidislocated many joints including my shoulders, wrists, ankles, knees, right hip, and fingers. A car accident when I was 20 left me having to use a wheelchair. This increased my mobility and decreased the pain in my legs (before this I had been struggling with crutches and callipers). When I was about 24 I developed a progressive kyphoscoliosis. I accepted the risks of surgical correction, which left me with a T6/7 incomplete paraplegia. After the surgery I developed encephalitis, which damaged my pituitary gland—I became dependent on cortisol and developed a condition called postencephalitic hypersomnolence.

For much of my life living with the syndrome has been a battle—me against "it." I feel that if I give in to my disability it has won. I can be very stubborn and Ehlers-Danlos syndrome can be very unforgiving—not a good combination! But life is a balance. To minimise the risk of injury I have adapted my life as much as possible and I ask for help when I need it. The "Access to work" programme has been brilliant in providing equipment and helping adapt my workplace.

I am determined to live as full and as active a life as possible and am helped by my general practitioner, physiotherapist, friends, and family. The problems associated with the syndrome are a daily challenge, but they have not stopped me from getting on with life, gaining

ADDITIONAL INFORMATION FOR PATIENTS

- Association Francaise des Syndromes d'Ehlers-Danlos (www.afsed.com)—French patient support group
- Ehlers-Danlos Foundation of New Zealand (www.edfnz.org.nz)—New Zealand patient support group
- Asociación Síndromes de Ehlers-Danlos e Hiperlaxitud (www.asedh.org)—Spanish patient support group
- Ehlers-Danlos Support Group (www.ehlers-danlos.org)—UK patient support group
- Ehlers-Danlos National Foundation (www.ednf.org)—US patient support group

DOCTORS' PERSPECTIVE

Each of these moving case histories illustrates the many problems that beset patients with Ehlers-Danlos syndrome in its various forms. What pervades all three accounts is an almost universal lack of understanding and awareness of the syndrome in medical circles at all levels.

The first patient died in her prime, an active young woman. Her story is a succession of missed opportunities to diagnose the vascular form of the disease. Originally classified "type IV," it is a rare but lethal autosomal dominant form of the disease. The correct diagnosis was made only in her mid-20s, yet the signs were present at birth. This form of the syndrome results from mutations in the gene for type III procollagen (COL3A1). Affected patients are at risk for arterial, bowel, and uterine rupture, events that occur mostly between the ages 20 and 40. In one study median survival was 48 years. Most deaths result from arterial rupture. The apparent lack of knowledge about the syndrome shown by most of the doctors this patient saw, the delay in seeing a suitably trained specialist, and the absence of laboratory corroboration of the diagnosis all led to the tragic outcome. Genetic testing for Ehlers-Danlos syndrome has always been difficult to obtain in the United Kingdom, and in the past specimens have been sent abroad. However, gene sequencing for this form of the disease is now offered by the North Trent Molecular Genetics Service in Sheffield.

The second patient gives a classic description of the common form of the syndrome, both in terms of her lifelong symptoms and the reactions of her medical advisors—typically bemusement, mystification, and disbelief—a familiar blend of emotional responses to clinical encounters with this

condition. She has the hypermobility form of the syndrome, previously known as type III and synonymous with benign joint hypermobility syndrome. Her brush with the law is certain to raise eyebrows. Her case illustrates the perennial problem of chronic pain, a common complication in this form of the syndrome, yet little is known in medical circles about the syndrome, despite a burgeoning literature. The pain responds poorly, if at all, to the most potent conventional analgesics. Is it surprising that patients seek relief from unconventional sources? Patients with this syndrome often have to rely on their own resources, yet physical rehabilitation and pain management can play a valuable part in management.

The third patient's sequence of symptoms was misunderstood, misinterpreted, and mishandled, and her condition remained undiagnosed throughout her childhood and adolescence. The hypermobility form of Ehlers-Danlos syndrome has had a major impact on her life, but she too has shown great resourcefulness and strength, which has enabled her to battle on in the face of increasing disability, not least the unfortunate postoperative paraplegia after surgery for scoliosis.

The ramifications of Ehlers-Danlos syndrome are wide and various, and the effects may be disabling and even life threatening. Emerging data suggest that while the vascular form is fortunately rare, the hypermobility form is common but continues to go undetected, or worse still, ignored.

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a degree, winning a silver medal for swimming at the Sydney 2000 Paralympic Games, teaching in a primary school, and working as a sports development officer.

When I see a doctor it helps to be told the treatment options and their likely outcomes, to have full answers to my questions, and to be involved in making decisions about my treatment. It is vital that doctors are aware of the implications of Ehlers-Danlos syndrome and adjust treatments and surgical techniques accord-

ingly. Without this the long term outcome of procedures may be poor.

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Remember the null hypothesis

My curiosity turned to excitement: I imagined my name in lights or, even more prestigious, the *BMJ*.

My eagerness concerned the case of a 65 year old man with alcohol dependency and comorbid depression. He had resumed drinking 12 months after having stopped because of an aortic dissection. The trigger for his relapse was his arrest for shoplifting.

His account of his crime was somewhat confused. On entering a large department store, he had bought some small items before noticing some expensive cameras. He explained that he had believed absolutely that the staff in the store were his friends and that, by demonstrating the ease with which goods could be stolen, he was being helpful. He placed a camera in his bag and proceeded to the exit. En route, he realised that being caught was a prerequisite for warning the staff about their vulnerability to theft. He became a prisoner of ambivalence, loitering just inside the store entrance unable to carry on.

Of course, the sharp eyed staff apprehended him the instant he stepped outside, when he suddenly grasped the bizarreness of his former belief that he was doing them a favour. He also then admitted stealing from the same store the previous week, when his theft of a clock

radio had gone unnoticed. What was interesting was that he said he had received a corticosteroid injection into his left shoulder the day before each shoplifting incident.

We all know corticosteroids can cause psychosis. I wondered if intra-articular steroid injections had been similarly implicated, as the link seemed logical. An extensive literature search located but one case report. Before writing my case up, however, I needed more details. At this point things began to unravel: yes, my patient had received injections of methylprednisolone, but in April and May, not in June, when he committed the thefts. A later injection in August was not associated with criminal activity, and further inquiry revealed a previous caution for shoplifting in 2001.

I was reminded of the value of a key statistical assumption: there is no association until proved otherwise. My dreams of fame and fortune temporarily shattered, I fell to earth, brought down by the null hypothesis.

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