EASILY MISSED?

Joint hypermobility syndrome

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This is one of a series of occasional articles highlighting conditions that may be more common than many doctors realise or may be missed at first presentation. The series advisers are Anthony Harnden, university lecturer in general practice, Department of Primary Health Care, University of Oxford, and Richard Lehman, general practitioner, Banbury. To suggest a topic for this series, please email us at easilymissed@bmj.com.

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- Septic arthritis in children (*BMJ* 2010;341:c4407)
- Human brucellosis (*BMJ* 2010;341:c4545)

Joint hypermobility syndrome (JHS), previously known as benign joint hypermobility syndrome (BJHS), is a heritable disorder of connective tissue that comprises symptomatic hypermobility predisposing to arthralgia, soft tissue injury, and joint instability.[1] It is indistinguishable from the hypermobility type of Ehlers-Danlos syndrome.[2] Complications may include autonomic dysfunction, proprioceptive impairment, premature osteoarthritis, intestinal dysmotility, and laxity in other tissues causing hernias or uterine or rectal prolapse. Symptoms are often minimal or mild, but 168 out of 700 patients with joint hypermobility syndrome (24%) attending the UCH Hypermobility Clinic already had an established chronic pain syndrome at the time of their first outpatient attendance. These patients were experiencing serious pain, disability, and impairment of the quality of life, some patients becoming chairbound or even bedbound.[3]

Why is it missed?

In a recent survey among members of the Hypermobility Syndrome Association (a patient self help group), largely due to missed diagnosis, 52% of 251 patients waited over 10 years from the onset of symptoms to get a correct diagnosis.[11]

Doctors may be unaware of the prevalence of the condition, its effect on quality of life, or its multisystemic nature (box 2) and may not routinely look for hypermobility in the clinical examination, especially as the condition rarely forms part of the curriculum in medical schools or in postgraduate training programmes for general practitioners, specialists, or physiotherapists or occupational therapists.[12] The erroneous view that hypermobility is a variant of normality, rather than part of an inherited connective tissue disorder, is also still widely held. In a survey of 319 UK consultant rheumatologists, only 9% of respondents believed that joint hypermobil-

CASE SCENARIO

A 30 year old project manager, who is new to your general practice, presents with right anterior knee pain after slipping and landing on his knee three months ago. Imaging shows no abnormality, but he describes a long history of recurrent shoulder subluxation, and many soft tissue problems and joint pains, often after similarly trivial trauma, and he states that imaging and blood tests "for arthritis" have always been normal. You note that he has no signs of inflammation but that he is hypermobile according to the Beighton score (see box 1), and looking up the Brighton criteria, which includes and extends the older Beighton score (see box 2), you mention he fulfils the criteria for joint hypermobility syndrome, and he expresses relief there is an explanation for his symptoms.

Box 1 | Nine-point Beighton score for joint hypermobility syndrome[4]

One point is gained for each side of the body for the first four manoeuvres listed below, such that the hypermobility score is a maximum of 9 if all are positive.

Passive dorsiflexion of the fifth metacarpophalangeal joint to ≥90° (1 point for left; 1 point for right) (fig 1A)

Opposition of the thumb to the volar aspect of the ipsilateral forearm (1 point for left; 1 point for right) (fig 1B)

Hyperextension of the elbow to ≥10° (1 point for left; 1 point for right) (fig 1C)

Hyperextension of the knee to ≥10° (1 point for left; 1 point for right) (fig 1D)

Placing of hands flat on the floor without bending the knees (1 point) (fig 1E)

Box 2 | 1998 Brighton criteria for classification of joint hypermobility syndrome*[6]

Joint hypermobility syndrome is diagnosed in the presence of two major criteria; one major criterion plus two minor criteria; or four minor criteria. Two minor criteria will suffice where there is an unequivocally affected first degree relative.

The syndrome is excluded by the presence of Marfan's or Ehlers-Danlos syndromes (other than the hypermobility type of Ehlers-Danlos syndrome) as defined by the Ghent 1996[7] and Villefranche 1998[8] criteria respectively.

Major criteria

- Beighton score of ≥4 (either currently or previously)
- Arthralgia for longer than three months in four or more joints

Minor criteria

- Beighton score of 1, 2, or 3 (0, 1, 2, or 3 if aged >50 years)
- Arthralgia in one to three joints or back pain or spondylosis, spondylolysis and/or spondylolisthesis
- Dislocation in more than one joint or in one joint on more than one occasion
- Three or more soft tissue lesions (eg, epicondylitis, tenosynovitis, bursitis)
- Marfanoid habitus (tall, slim, ratio of span to height greater than 1.03 and/or ratio of upper segment to lower segment less than 0.89, arachnodactyly)
- Abnormal skin: striae, hyperextensibility, thin skin, papyraceous scarring
- Eye signs: drooping eyelids, myopia, or antimongoloid slant
- Varicose veins, hernia, or uterine or rectal prolapse

*Although originally designed for use as a research tool in defining a cohort of patients for recruitment into clinical studies, in practice the criteria have proved to be a useful diagnostic aid in the clinical setting.

Patients illustrate the application of the nine point Beighton hypermobility score.[5] Adapted with permission from Springer Science+Business Media

Box 3 | Common clues suggesting joint hypermobility syndrome (based on observations, expert opinion, and case series)

In children and adolescents

- Coincidental congenital dislocation of the hip[18]
- Late walking, with bottom shuffling instead of crawling[19]
- Recurrent ankle sprains[20]
- Poor ball catching and handwriting skills[21]
- Tiring easily compared with peers
- So called growing pains or chronic widespread pain[21]
- Joint dislocations[22]

In adults

- Non-inflammatory joint or spinal pain[23]
- Joint dislocations[22]
- Multiple soft tissue (including sporting) injuries[24]
- Increase in pain or progressive intensification of pain that is largely unresponsive to analgesics[5]
- Progressive loss of mobility owing to pain or kinesiophobia (pain avoidance through movement avoidance)[5]
- Premature osteoarthritis[25]
- Autonomic dysfunction, such as orthostatic intolerance (dizziness or faintness) or postural tachycardia syndrome (in this form of dysautonomia, in 60° upright tilt the blood pressure remains constant while the pulse rate rises by a minimum of 30 beats/min)
- Functional gastrointestinal disorders (sluggish bowel, bloating, rectal evacuatory dysfunction)[26]
- Laxity in other supporting tissues—for example, hernias, varicose veins, or uterine or rectal prolapse[27]

HOW COMMON IS IT?

Joint hypermobility is very common, occurring in 10-20% of populations of Western countries, and higher still in those in Indian, Chinese, and Middle Eastern groups. It is important to distinguish between joint hypermobility and joint hypermobility syndrome. People who are hypermobile without symptoms are merely people with hypermobility. Those with symptoms attributable to their hypermobility may have joint hypermobility syndrome if they conform to the Brighton criteria. The true prevalence of the syndrome is unknown. In surveys in London and in Santiago, Chile, routine searches in consecutive patients referred to general rheumatology clinics have found prevalences of joint hypermobility syndrome (as defined by the Brighton criteria) as high as 45%; the syndrome is higher in females and non-white people.[9 10] Therefore many patients presenting to their doctors with common, everyday, noninflammatory, painful, musculoskeletal conditions probably have unrecognised joint hypermobility syndrome.

ity syndrome and the hypermobility type of Ehlers-Danlos syndrome were the same condition. Furthermore, 46% of respondents were sceptical about a serious impact on people's lives and 72% about a serious contribution to the overall burden of rheumatic disease.[13]

Why does this matter?

If joint hypermobility syndrome is missed, the following problems may arise:

- Inappropriate and potentially harmful labelling or treatments may be applied on the basis of an erroneous diagnosis such as rheumatoid arthritis, hypochondriasis, or somatisation.
- Over zealous physical manipulation may cause avoidable damage, such as *(a)* precipitating subluxation or dislocation of intervertebral or peripheral joints, *(b)* inflicting rupture on ligaments, joint capsules, muscles, or tendons, or *(c)* precipitating pathological fractures in fragile bone. Exercise therapy may be either excessively forceful or ineffectual.[14]
- Anecdotal evidence exists that orthopaedic operations may be done without the surgeon knowing that the patient has an underlying connective tissue disorder, and this may lead to poorer outcomes.
- Chronic pain may sometimes lead to a potentially reversible downward spiral of immobility, deconditioning, dependency, and despair.[5] Out of 700 patients with joint hypermobility syndrome (24%) attending the UCH Hypermobility Clinic, 168 were experiencing serious pain, disability, and impairment of the quality of life, some patients becoming chairbound or even bedbound.[3]

How is it diagnosed?

Diagnosis is entirely clinical as currently no biological or imaging markers are available. The musculoskeletal symptoms mainly derive from a vulnerability to injury resulting from fragile collagenous tissues (tendon, ligament, muscle, bone, cartilage, and skin). In patients with arthralgia or post-injury musculoskeletal pain, screening blood tests and/or appropriate imaging are needed to exclude conditions such as inflammatory arthritis and fractures. Box 3 lists important common clues to joint hypermobility syndrome. The Beighton score (box 1) identifies joint hypermobility but is too insensitive an instrument for diagnosing joint hypermobility syndrome and is not intended for this purpose. Diagnosis requires the application of the 1998 Brighton criteria into which the Beighton score has been incorporated (box 2).[6]

The reproducibility and reliability of the Beighton score and the Brighton criteria have recently been scrutinised,[15-17] and an international panel is currently reviewing the Brighton criteria.[17]

How is it managed?

The key players are the family doctor and a suitably trained physiotherapist.

Doctor's role

- To establish an accurate diagnosis of joint hypermobility syndrome while being alert to the possibility of one of the rarer and more serious heritable disorders of connective tissue, such as Marfan's syndrome, or other forms of Ehlers-Danlos syndrome, such as vascular, or classical. A positive family history of sudden early death from aortic aneurysmal dissection and/or rupture should suggest the possibility of Marfan's syndrome, and a history of major spontaneous arterial rupture or uterine rupture in childbirth should raise suspicions of the vascular type of Ehlers-Danlos syndrome.
- To make a detailed assessment of the effects of the disorder on musculoskeletal function, systemic involvement (such as dysautonomia, gastrointestinal dysmotility), declining mobility, and quality of life.

Physiotherapist's role

- To adapt physiotherapy principles to the needs of patients with lax and fragile tissues. This involves:
  - -Core and joint stabilising and proprioception enhancing exercises
  - -General fitness training to offset or reverse the tendency for the body to lose condition
  - -The use of mobilising techniques to restore natural hypermobility to joints or spinal segments where these have been lost as a result of deconditioning and kinesiophobia.[28]

A before and after comparison study in 18 patients from Glasgow with joint hypermobility syndrome has shown that a home based programme of specific exercises may improve proprioception, symptoms, and quality of life.[29]

For patients with chronic pain for which analgesics are largely ineffective, a pain management programme based on cognitive behavioural techniques and delivered by a specially trained pain psychologist may reduce pain catastrophising, anxiety, and interference of pain with daily life.[30]

For patients with foot or hand problems, refer to a podiatrist for a mechanical foot assessment and tailor made orthotics[31] or to an occupational therapist for help with writing and other work related hand problems.

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A PATIENT'S JOURNEY

Joint hypermobility syndrome

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Chronic pain, frequent soft tissue trauma, and exhaustion compelled a keen recreational ballet dancer to give up classes and work

On reflection, I should have realised that I was either a little bit different or had some remarkable powers of flexibility. It is perhaps unusual to be able to put your legs behind your neck or to put both hands flat on the floor without warming up first. As a teenager I was told that I had "swayback knees," but I just got on with my life at the time, which was then (and remains) very ballet orientated. Not perhaps a wholly unexpected choice of activity for someone with an above average level of joint mobility; indeed, there is a high prevalence of hypermobility in the ballet world because of the desirable aesthetic qualities of hypermobile limbs. However, I had no idea that behind the beauty of my extensions lay immense pain and fatigue.

There is a difference between having hypermobile joints, which might be classified as generalised joint hypermobility and is asymptomatic, and the joint hypermobility syndrome, which has symptoms. My symptoms started when I was 17 years old (I am now 35), and I started to get pain in my lumbar spine. I had physiotherapy for an inflamed sacroiliac joint, but the pain became more established and painful over time. I had many years of back pain, which eventually became disruptive, and I gave up ballet classes in 1999 and even stopped work for six months in 2001 (aged 24). Magnetic resonance imaging showed a disc prolapse and degeneration at L4/5. Whenever I was referred to physiotherapists and osteopaths over those years, they used to ridicule my spine and say that it "looked" horrendous in terms of my range of movement and were often extremely unhelpful. Only one physiotherapist looked at giving me any core stability work to try to stabilise what is now described as a hinging at that level of the spine.

I attended a pain management course in a well known London hospital in the autumn of 2006, where they apparently knew I was hypermobile but did not look at all the symptoms that I was experiencing and piece things together. Unfortunately, joint hypermobility syndrome is a difficult condition to diagnose and only one in 20 people with the condition are given the correct diagnosis.

The clues to my diagnosis began two years ago. I had restarted ballet classes gradually in 2007 and by early 2008 was doing four classes a week; I was probably doing too much too soon, and not sensibly pacing my activity. As a result I partially tore my right calf. After some physiotherapy, I was discharged as soon as I was able to walk again. When I was dancing again I realised it was still not right, and decided to see a dance specialist physiotherapist at Laban Health in southeast London.

My physiotherapist initially gave me some rehabilitation exercises for the area of concern but soon realised that most of my problems were due to gross instability caused by my (many) hypermobile joints and that I was going to need extensive strengthening and core stability work. I am still nowhere near being "fixed," but I have come a considerable way since then (the journey can be seen in my blog, www.danceinjuryrecovery.blogspot.com). It has taken immense determination to put my body back together, and if it wasn't for the huge improvements in functioning and movement, and the payback of improved performance in class, I would have given up long ago.

After treating me for about six months my physiotherapist did some hands-on work on me and realised that my tissue response was somewhat unusual. For example, she might treat one area (the right hip, say), move to another area, then return to the starting point and find my tissues had gone back to where they were—therefore progress was seemingly nil. At the same time I was having considerable trouble with fatigue,

A DOCTOR'S PERSPECTIVE

Joint hypermobility implies that the patient has joints with a wider range of movement than would normally be expected. Conventionally, this is identified by the nine point Beighton scoring system, devised in 1973 for epidemiological work in an African population (http://ard.bmj.com/content/32/5/413.full.pdf+html). This in itself does not give information about the factors that are contributing to the increased range of movement of joints. The structure of collagen and the shape of the bony articulating surfaces both contribute, as may neuromuscular tone and possibly proprioception. Collagen is ubiquitous and when lax in the joint capsule it may also be lax at other sites in the body. If this occurs, and particularly if the joints are painful, it is normally described as a joint hypermobility syndrome. Separate criteria (the Brighton criteria, published in 2000; www.ncbi.nlm.nih.gov/pubmed/10914867) allow hypermobility to be diagnosed on the basis of fewer affected joints, especially if there are supporting features.

The multifaceted nature of the condition often leads to confusion in making a diagnosis, and I can sympathise with Isobel's difficulty in finding a general practitioner, even a rheumatologist, with the skill and experience to make the diagnosis and then to analyse why the condition was present, which informs management. Management is likely to involve close collaboration between physician, physiotherapist, occupational therapist, and podiatrist. The websites of self help groups contain valuable educational material.

Isobel would clearly have benefited from earlier diagnosis and advice on treatment from a doctor or physiotherapist who was prepared to consider the body as a whole rather than just the joints. Interactions between hypermobility and the hormonal environment can be complex, as are some of the developmental orthopaedic abnormalities that are often associated with this condition.

Irritable bowel syndrome is common, partly because of stasis and partly because of the mild autonomic neuropathy that is often present in these patients. Laxity at the bladder neck can lead to stress incontinence. Easy bruising, severe Raynauld's phenomenon, hypotension, and asthma all occur. Some patients seem to fracture easily. In women, hormonal levels often correlate with symptoms. Anxiety state is a recognised association, and some developmental psychological conditions may be related to the syndrome.

In more severe inherited conditions associated with hypermobility, such as Marfan syndrome, prophylaxis with losartan and even cytokine modulation to alter the rate of collagen formation may become possible. Specialised clinics devoted to these complex patients are few and far between and completely absent in some areas.

Isobel's story draws attention to one of the benefits often conferred by hypermobile joints, which is prowess in dance as well as in some sports. Although joint laxity is generally advantageous in dancers, certain variants may be less suited to particular styles of dance. This is a complex area of performing arts medicine, and it demands not only a high degree of applied musculoskeletal expertise and knowledge of anatomy on the part of the practitioner but also an empathy with the artistic temperament.

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SUPPORT FOR PEOPLE WITH HYPERMOBILITY SYNDROME

Hypermobility Syndrome Association—HMSA is a charity run by and for people with a diagnosis of hypermobility syndrome. The website (www.hypermobility.org) includes a discussion forum (www.hypermobility.org/forum/index.php) and patient support boards. The telephone line (tel 0845 345 4465) has a 24 hour answering service, and the association aims to reply to all messages within one working day.

Laban Health—Based in South East London, Laban Health (www.laban.org/health.phtml) has treatment rooms for physical therapy, a dance science laboratory and one of the largest pilates studios in the UK. Its multidisciplinary team of therapists specialise in dance and sports related conditions. They encourage a preventive approach to injury management and the development of cutting edge treatment strategies. Laban Health's services are open to everyone.

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not for the first time in my life. I was regularly feeling "run over" and disproportionately exhausted. It was at this point that my physiotherapist thought that I might not just be hypermobile, but have joint hypermobility syndrome. My history of chronic pain and frequent soft tissue trauma made this diagnosis more likely. Also, I had been a very late walker, had not crawled, and had night cramps and growing pains, including problems with motor control (my coordination was and still is very poor); these are all indicative of the syndrome.

Joint hypermobility syndrome is formally diagnosed, often by using the Beighton score and the Brighton criteria. The Brighton criteria differentiate the hypermobile patient from the one who has the syndrome, because of positive responses to joint pain and signs indicative of faulty collagen—for example, skin extensibility, prolapses, and varicose veins. My overriding message to the medical profession would be to "think outside the box" in the case of a patient who regularly presents with joint pain and injuries. I believe that some of my injuries and traumas could have been prevented if I had been diagnosed when much younger and been given the appropriate remedial strengthening and stability work from the outset.

Joint hypermobility syndrome is an invisible condition, but it is hard work controlling limbs that have such an extra range of movement. Indeed, I am lucky that I have not subluxated or dislocated any joints, as this is a regular problem for many patients with joint hypermobility syndrome. Pain and fatigue are a large part of this condition, but the range of symptoms is wider. For example, irritable bowel syndrome and asthma are related to the syndrome because it is a connective tissue disorder and the problems stem from having abnormally stretchy collagen fibres, as I understand it. Given that the guts and lungs are stretchy tissues in themselves, one can perhaps begin to understand the repercussions of faulty connective tissues.

On the whole, people are not sympathetic to the condition, and I have lost relationships because of being in pain so often. Even friendships have suffered because I have often been so exhausted at the end of a working day that I had no reserves for going out and socialising. I suppose that because I look healthy and well and I dance, people dismiss my symptoms. Sometimes it gets hard to deflect people's lack of sympathy and negative comments. Talking to other patients—for example, via the Hypermobility Syndrome Association forum (see box)—can be supportive and helpful.

I am one of the lucky ones. I have a wonderful physiotherapist who is incredibly supportive and who has really helped me. My body has changed beyond all recognition over the past two years. With the help of regular pilates sessions and ongoing physiotherapy, I am still managing to do ballet classes. I will probably have to do remedial exercises for the rest of my life, but at last I am starting to have some sense of control over my body, compared with the chaos of the past. I have a mission to ensure that others with the condition are helped. Since completing my MSc in Dance Science, I have been researching the condition and am now writing a patient led book on joint hypermobility syndrome, to be published in mid-2011.

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GUIDELINES

Management of generalised anxiety disorder in adults: summary of NICE guidance

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This is one of a series of *BMJ* summaries of new guidelines based on the best available evidence; they highlight important recommendations for clinical practice, especially where uncertainty or controversy exists. The supporting evidence statements and further information about the guidance are in the full version on bmj.com.

Generalised anxiety disorder affects about 4.4% of the adult population in England.[1] It is characterised by worry and apprehension. Worries are typically widespread, involving everyday issues and a shifting focus of concern; a person with this disorder finds it difficult to control their worries.[2 3] Like other anxiety disorders, it is often chronic if untreated,[2] and it is associated with substantial disability equivalent to other chronic physical health problems such as arthritis and diabetes.[4] People with generalised anxiety disorder have high levels of service use (visits to general practitioners and hospital), a consequence of somatic symptoms and worries commonly associated with the disorder and because it commonly coexists with chronic physical health problems.[5-7]

This article summarises the most recent recommendations from the partially updated guideline from the National Institute for Health and Clinical Excellence (NICE) on generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults.[8] Only recommendations for the management of generalised anxiety disorder have been updated, and these are described here.

Recommendations

NICE recommendations are based on systematic reviews of best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Development Group's experience and opinion of what constitutes good

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practice. Evidence levels for the recommendations are in the full version of this article on bmj.com.

A "stepped care" model is used to organise and integrate the provision of care by general practices and community services and to help in choosing the most effective interventions. With this approach, patients are first offered the least intrusive intervention that might be effective, with a "step up" to more intensive interventions if they do not improve.

Identification, assessment, and initial treatment

- Consider a diagnosis of generalised anxiety disorder in people presenting with anxiety or substantial worry and in people who attend primary care frequently who have a chronic physical health problem or do not have a physical health problem but are seeking reassurance about somatic symptoms or are repeatedly worrying about a wide range of different issues. (New recommendation.)
- Conduct a comprehensive assessment that considers the degree of distress and functional impairment; the effect of any comorbid mental health disorder, substance misuse, or medical condition; and past response to treatment. (New recommendation.)
- For all known and suspected presentations of this disorder, provide education about it and the treatment options. Monitor the person's symptoms and functioning. Education and active monitoring may improve less severe presentations and avoid the need for further interventions. (New recommendation.)
- For people with a comorbid depressive or other anxiety disorder, treat the primary disorder first (that is, the one that is more severe and treatment of which is more likely to improve overall functioning). (New recommendation.)
- For those with harmful and dependent substance misuse, treat the substance misuse first as this may lead to substantial improvement in the symptoms of generalised anxiety disorder. (New recommendation.)
- Discuss the use of over the counter preparations. Explain the potential for interactions with other medications (for example, St John's wort with oral contraception) and that insufficient evidence exists to support their safe use. (New recommendation.)

Further treatment of diagnosed generalised anxiety disorder

If symptoms have not improved after education and active monitoring

- Offer one or more of the following first line, low intensity interventions, guided by the person's preference (new recommendation):
  - -Individual non-facilitated self help (usually involving minimal contact with a healthcare professional)
  - -Individual guided self help (supported by a trained practitioner, who facilitates the programme and reviews progress and outcome)
  - -Participation in psychoeducational groups (conducted by trained practitioners and based on the principles of cognitive behavioural therapy; groups should have a ratio of one therapist to about 12 participants).
- Individual non-facilitated and guided self help should include printed or electronic materials of a readability level suitable for the individual based on the treatment principles of cognitive behavioural therapy. (New recommendation.)

If functional impairment is marked or symptoms have not improved after low intensity interventions

- Offer a choice of the following:
  - -An individual, high intensity psychological intervention (cognitive behavioural therapy or applied relaxation, in which people learn to apply relaxation skills in anxiety provoking situations) (new recommendation) or
  - -Drug treatment.
- Select the treatment according to patient preference as no evidence exists that either treatment is better. (New recommendation.)
- Base cognitive behavioural therapy or applied relaxation on treatment manuals used in the clinical trials. They should be delivered by trained and competent practitioners. (New recommendation.)
- If a person chooses drug treatment, offer a selective serotonin reuptake inhibitor. Consider offering sertraline first because it is the most cost effective drug. If sertraline is ineffective, offer an alternative selective serotonin reuptake inhibitor or a serotonin noradrenaline reuptake inhibitor. (New recommendation.)
- If the person cannot tolerate selective serotonin reuptake inhibitors or serotonin noradrenaline reuptake inhibitors, consider offering pregabalin. (New recommendation.)
- Do not offer a benzodiazepine to treat generalised anxiety disorder in primary or secondary care except as a short term measure during crises. (New recommendation.)
- Do not offer an antipsychotic to treat this disorder in primary care as the evidence for clinical efficacy is poor, while the risk of serious side effects are well known. (New recommendation.)
- Before prescribing any medication, discuss the treatment options and any concerns the person has about taking medication. (New recommendation.)
- Review the effectiveness and side effects of the drug every two to four weeks during the first three months of treatment and every three months thereafter. (New recommendation.)
- If the drug is effective advise continuation for at least a year as the likelihood of relapse is high. (New recommendation.)

If response to psychological or drug interventions is inadequate

- If the condition has not responded to a full course of a high intensity psychological treatment, offer a drug treatment. (New recommendation.)
- If the condition has not responded to a drug treatment, offer either a high intensity psychological intervention or an alternative drug treatment. (New recommendation.)

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- If the condition has partially responded to drug treatment, consider offering a psychological intervention in addition to drug treatment. (New recommendation.)

If the disorder is complex and refractory to treatment, if functional impairment is very marked, or if patient has a high risk of self harm

- For those who have not been offered, or have refused, the recommended interventions, inform them about the potential benefits of these interventions and offer them any they have not tried. (New recommendation.)
- Consider offering combinations of psychological and drug treatments, combinations of antidepressants, or augmentation of antidepressants with other drugs, but be aware that evidence for the effectiveness of combination treatments is lacking. Combination treatments should be undertaken only by practitioners with expertise in the psychological and drug treatment of complex anxiety disorders that are refractory to treatment. (New recommendation.)

Overcoming barriers

Generalised anxiety disorder is under-recognised.[9 10] People may present with the physical or somatic symptoms of the disorder[11 12] or with worries about their health, but these worries may be just one of the many worries that are part of the condition.[13] Therefore it is only after a succession of consultations that it becomes apparent that the person has multiple worries and that reassurance has only a temporary impact. The guideline encourages clinicians to consider the possibility of generalised anxiety disorder in people with or without a chronic physical health problem who present frequently with health concerns and to ask about other worries that would confirm this diagnosis.

Limited availability of cognitive behavioural therapy has been a barrier to effective treatment,[14] and many people do not wish to use medication. Use of low intensity psychological interventions based on cognitive behavioural therapy, as part of a stepped care framework, may increase access to effective psychological interventions.

NICE does not often recommend the use of drugs for conditions for which their use is not licensed (except in the case of children, for whom many drugs are not licensed specifically). In this guideline, sertraline emerged as clearly the most cost effective drug for generalised anxiety disorder compared with other drugs licensed for use in this disorder. Sertraline use in this context is acceptable, but patients should be advised about the evidence for its use and warned that no marketing authorisation (licence) has been issued for the drug's use in generalised anxiety disorder.

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STATISTICAL QUESTION

Meta-analyses III

Answers *a* and *c* are true, whereas *b* and *d* are false.

ON EXAMINATION QUIZ

Gynaecomastia

Answers A and E are true, whereas B, C, and D are false.

PICTURE QUIZ

An odd eruption

1 **The most likely diagnosis is cutaneous sarcoidosis.**
2 **Full blood count, erythrocyte sedimentation rate, and liver function tests; bone profile blood test; and serum angiotensin converting enzyme test should be performed, and a skin biopsy sample should be sent for histology and culture. Chest radiograph, Mantoux test, high resolution computed tomography, and transfer factor test are also recommended.**
3 **Cutaneous sarcoidosis should be managed using a potent topical steroid, intralesional steroids, topical tacrolimus, antimalarials, and immunosuppressants, including methotrexate or azathioprine.**