education

ART OF MEDICINE

An outbreak of humidifier fever on a warship

During the summer of 1981 a sailor from the warship *HMS Sheffield* mentioned a curious illness affecting his messmates. They would embark after weekend leave and, by late afternoon on Monday, they would have chills, aches, sweats, dry coughs, and sore throats. These symptoms would largely subside through the week and, by the weekend, had disappeared, only to recur the following Monday. Each week the same pattern was repeated. The ship was coming to the end of a prolonged maintenance period, and the ventilation system had recently been restarted after a lengthy shutdown.

Inspection of the ship's sickness log revealed a high number of sick bay attendances on Tuesday and Wednesday mornings from members of one messdeck. All 20 of them gave a similar story of typical symptoms with a periodicity characteristic of humidifier fever. The messdeck itself was dank and chilly. Inside the air treatment units there was a fluffy, white mould, subsequently identified as an actinomycete species—to which all 20 of the men had precipitating antibodies.

The remedy was simple. The air treatment units throughout the ship were dismantled and cleaned. It was the damp, stagnant atmospheric conditions which allowed fungal colonisation during ventilation system shutdown. An aerosol of fungal spores was then blown into the messdeck when the ventilation was restarted.

Ironically the messdeck was blown apart a few months later when, on 4 May 1982, an Argentine Exocet missile slammed into *HMS Sheffield* and destroyed her. She is now a designated war grave for the 20 men lost with her.

Mark Edmondstone, retired consultant physician, Winchester, UK

We welcome contributions to this column via our online editorial office: https://mc.manuscriptcentral.com/bmj.

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PRACTICE UPDATES

NHS reality check

In a report from the Royal College of Physicians, *NHS reality check: Delivering care under pressure*, a survey of 2100 RCP members has shown that:

- 74% of physicians are worried about the ability of their service to deliver safe patient care in the next 12 months
- Over half of physicians believe patient safety has deteriorated, 84% have experienced staffing shortages in their team, and 82% believe the workforce is demoralised
- Only one in five of the doctors surveyed knew who their "freedom to speak up guardian" was at their NHS trust, and less than a third believed that guardians have helped improve the culture of transparency and raising concerns in their organisation.

http://bit.ly/2nsrEKo

Health of employees

NICE has published a quality standard on mental and physical health and wellbeing of employees. It states that:

- Organisations should have a named senior manager who makes employee health and wellbeing a core priority
- Managers should be trained to recognise stress and should support employees' health and wellbeing
- Employees should have the opportunity to contribute to decision making through staff engagement forums.

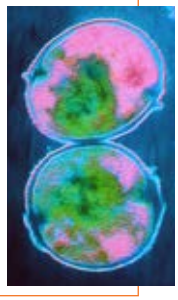
http://bit.ly/2nJwrTA

FAST FACT—INTRAVENOUS ANTIBIOTICS FOR COMMUNITY ACQUIRED PNEUMONIA

Patients with community acquired pneumonia should receive intravenous antibiotics if they have the following:

- High severity pneumonia (CURB-65 score ≥3)
- Functional or anatomical reasons for malabsorption
- Impaired consciousness
- Impaired swallowing reflex.

For more information visit BMJ Learning (http://bit.ly/2mTGSGF).



CNRI/SPL

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STATE OF THE ART REVIEW

Managing restless legs syndrome

Diego Garcia-Borreguero, Irene Cano-Pumarega

CPD READING
0.5 HOURS

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This is an edited version; the full version is on bmj.com

Restless legs syndrome (RLS), also known as Willis-Ekbom disease (WED) is a common neurological disorder, which affects sleep and health.[1-3] Reductions in health related quality of life scores are similar to or worse than those in patients with osteoarthritis, congestive heart failure, depression, or stroke.[2-13]

Until recently, dopaminergic agents were the first line treatment for this disease, but we now know that these drugs can lead to augmentation of symptoms for many patients. This review assesses the latest evidence on the diagnosis, pathophysiology, and treatment.


PHANIE / ALAMY

WHAT YOU NEED TO KNOW

- If symptoms are mild, encourage patients to adopt good sleep habits, reduce smoking and caffeine intake and increase daytime exercise
- Consider treatment when symptoms impair patients' quality of life
- Dopamine agonists have been shown to be effective in treating sensory symptoms, however symptoms may worsen (augmentation) during longer term treatment
- Recent guidelines recommend,whenever possible, to start treatment with α2δ ligands
- The goal of treatment is not to eradicate symptoms completely but to reduce them

How common is RLS?

RLS affects 5-10% of European and North American adults, with 2-3% experiencing moderate to severe symptoms.[4 15] Women are affected about twice as often as men. The mean age of onset is during the third or fourth decade, but paediatric cases are not rare with overall paediatric prevalences of 2-4%.[16 17]

The later in life RLS starts, the more rapid the onset and the greater the likelihood that it is associated with another medical condition such as neuropathy, iron deficiency, or renal disease.

How does it present?

The diagnosis of RLS is made on the basis of the presence of clinical symptoms.[14 32] RLS is mainly characterised by neurosensory symptoms, which are strong feelings of restlessness and distressing paraesthesia-like sensations in the lower legs.[33 34] RLS typically manifests when the patient is at rest, and a state of relaxation or comfort is associated with a greater likelihood of symptoms occurring. Conversely, symptoms usually improve or resolve when the patient begins physical activity; as symptoms arise, patients will experience an intense urge to move in order to relieve the discomfort felt.[35] In addition, the symptoms follow a circadian pattern and are worse in the evening.[36] The symptoms vary considerably in frequency from less than once a month or year to daily; severity ranges from mildly annoying to disabling, and symptoms may also remit for differing periods of time.[14]

How is it diagnosed?

Current diagnostic criteria

RLS is diagnosed by ascertaining symptom patterns that meet the five essential criteria in box 1.[14] These five essential criteria have to be met for a positive diagnosis.

Supporting features

RLS has both a motor symptom—periodic leg movements (PLMs)—and several common clinical patterns that can support a diagnosis, particularly when diagnostic certainty is lacking.

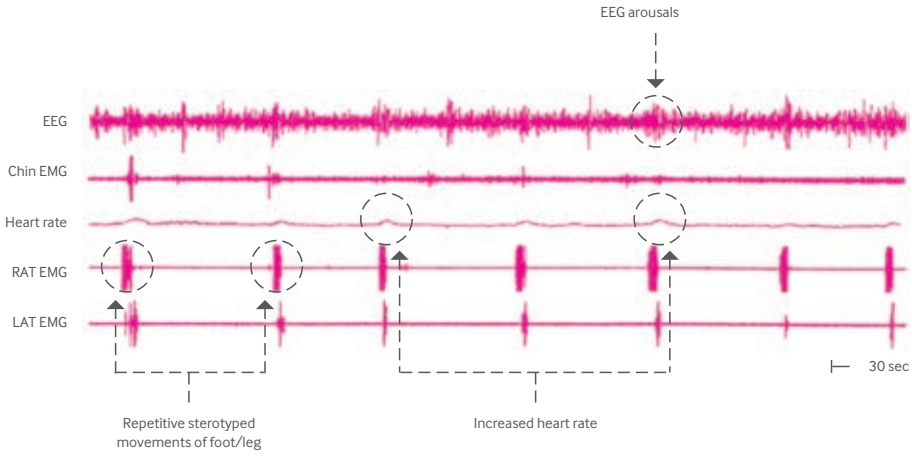

Fig 1 | Periodic leg movements (PLMs) during sleep. The presence of repetitive PLMs causes arousals seen on electroencephalography, which contribute to sleep fragmentation. In addition, repetitive sympathetic arousals are caused, which might lead in the long term to systemic hypertension and increased cardiovascular risk. (RAT EMG, LAT EMG = right, left anterial tibialis electromyogram)

Box 1 | Diagnostic criteria for restless legs syndrome (RLS)[1]

1. An urge to move the legs usually but not always accompanied by or felt to be caused by uncomfortable and unpleasant sensations in the legs
2. The urge to move the legs and any accompanying unpleasant sensations begin or worsen during periods of rest or inactivity such as lying down or sitting
3. The urge to move the legs and any accompanying unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues
4. The urge to move the legs and any accompanying unpleasant sensations during rest or inactivity only occur or are worse in the evening or night than during the day[33]
5. The occurrence of the above features is not solely accounted for by symptoms primary to another medical or behavioural condition (eg, neuropathy, myalgia, venous stasis, leg oedema, arthritis, leg cramps, positional discomfort, or habitual foot tapping)

Periodic leg movements

PLMs are repetitive, stereotyped, flexor withdrawal-like movements of the legs that occur during sleep and are thus called periodic limb movements of sleep (PLMS) (fig 1). PLMs can also occur during wakefulness. PLMS occur in about 80-89% of RLS patients seen in a clinic setting, and PLMs during wakefulness occur at a similar frequency.[44-46]

Dopaminergic treatment response

In general clinical practice, a failure to respond to dopaminergic treatment should raise some concern about the accuracy of diagnosis but does not necessarily exclude a diagnosis of RLS. However, as non-response to dopaminergic drugs is possible but rare, compliance, dose, and concomitant drugs should be checked.

Family history

RLS has been noted to occur commonly in families, indicating important genetic or shared environmental factors for the disease.[45-74] The risk of RLS is nearly six times higher among first degree relatives of RLS patients than in other people.[75]

Lack of profound daytime sleepiness

Patients with moderate to severe RLS have chronic short sleep times but generally do not report a level of daytime sleepiness that would be expected for the degree of sleep loss.[2-80] Profound sleepiness should prompt evaluation for another cause, such as sleep apnoea, narcolepsy, or a drug effect.[84]

Comorbid conditions

A recent review of RLS associated with comorbidities identified an increased prevalence of RLS only in iron deficiency and kidney disease.[85]

Clinical course

A history of remission and relapse in symptoms should be noted as a possible indicator of the subsequent course of the condition. The typical pattern of an insidious onset with gradual progression over a period of years to a clinically significant disease occurs more frequently with early age of onset.[24 25] However, in some cases, relatively rapid symptom development over months to a few years is reported with a variable degree of symptom progression after onset.[87]

What do we know about the cause of RLS?

RLS is a highly familial trait but genetically complex, with estimates of concordance between 54% and 69% reported in twin studies.[76 77]

The most compelling argument in favour of a dopaminergic dysfunction is the striking improvement in symptoms with dopaminergic drugs.[31] However, the mechanism of this improvement has never been fully elucidated.

Iron deficiency has also repeatedly been shown to be associated with RLS.[108] The mechanism by which iron deficiency leads to dopaminergic dysfunction is unclear. Iron has a complex effect on dopaminergic function. It is a cofactor for tyrosine hydroxylase and is integral to D2 receptor function.[102 111]

Other systems, such as the opiate, glutamate, adenosine, and hypocretin systems,[112-114] might also be involved and might thus be future targets of drug action.

How do we diagnose RLS?

Basic laboratory evaluation

Laboratory parameters include complete blood cell count, markers of kidney and liver function, iron metabolism, inflammation, endocrine function (glucose, thyroid hormones), and vitamins (B_{12}, D, and folic acid). Basic biochemistry is also needed, with determination of plasma concentrations of glucose, creatinine, urea, potassium, calcium, and sodium.

For iron metabolism, two variables are of special interest:

- Serum ferritin—Serum ferritin concentrations below 50 ng/mL (<50 µg/L) have been associated with RLS, even in the absence of decreased haemoglobin or serum iron concentrations [122 123]
- A high soluble transferrin receptor (sTR) concentration is considered to be the initial response to declining body iron supply.[125]

Other investigations

In addition to urinalysis, a 12 or 24 hour urine collection for creatinine clearance

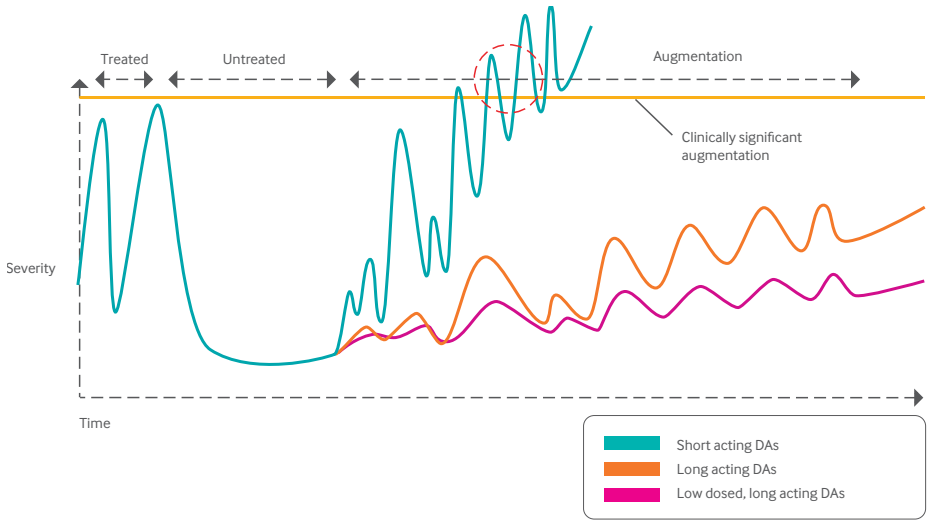

Fig 2 | Therapeutic response during treatment with dopamine agonists (DAs). At the beginning of treatment with dopamine agonist, pre-existing fluctuations in symptom severity cease and initial therapeutic benefit is obtained. However, with longer duration of treatment these fluctuations will eventually re-emerge until the severity matches or even exceeds that before any treatment had been started. This process is called dopaminergic augmentation and can take a variable amount of time to occur. There is general agreement that treatment with long acting dopamine agonists delays the process somewhat. Certainly, the use of low doses delays the process further, prolonging therapeutic response

should be done to determine the glomerular filtration rate in patients at risk of kidney disease. Declining renal function is associated with increasing prevalence of RLS.[126]

Electromyography and nerve conduction studies should be used primarily when peripheral neuropathy is suspected on clinical grounds.[129]

In certain cases, extensive complementary tests (MRI, special cerebrospinal fluid and serum determination, venous ultrasonography of the legs) should be carried out to confirm the existence of other factors and conditions that may contribute to so called "comorbid RLS," such as lumbosacral radiculopathy, Lyme disease, monoclonal gammopathy of undetermined significance, myelopathy, or myelitis.

How do we manage patients with RLS?

Patients who are diagnosed as having RLS will have already tried and tested many non-drug options by the time they seek medical assistance (eg, activities that keep them concentrated, avoidance of caffeine and alcohol, hot baths). Use of drugs that are known to exacerbate RLS symptoms should also be reconsidered—these include antihistamines, dopamine antagonists, anti-nausea drugs, antidepressants, serotonergic reuptake inhibitors, neuroleptics, β blockers, some anticonvulsants, and lithium.[130] Furthermore, measures (including oral iron supplements and, in some cases, intravenous iron administration) should taken to ensure that ferritin concentrations are raised above 50 ng/mL.

Which treatment works best?

Two types of drugs have been extensively investigated for the treatment of RLS: dopamine agonists and α2δ ligands. Both have been shown to be clinically effective in treating sensory symptoms.[149] Dopamine agonists are more effective in treating PLMs, whereas α2δ ligands are effective in consolidating sleep.[149] Several large retrospective cohort studies have examined augmentation rates during long term treatment (5-10 years) with dopaminergic agonists, showing rates of dopaminergic augmentation and no improvement in more than 40% of patients.[147-152]

Because of the link between dopaminergic treatment and a progressive loss of response, the most recent international guidelines recommend that whenever possible the initial treatment of choice should be an α2δ ligand.[153 154]

Furthermore, recent studies have reported on the efficacy of opioids for the treatment of RLS, when resistant to dopamine agonists.[155] Recent guidelines have taken these new data into account and highlight that a low dose of an opioid (prolonged release oxycodone[145] or methadone[147]) may be considered in patients with very severe augmentation.[153 156]

Long term treatment of RLS

During long term treatment of RLS, plasma ferritin concentrations should be kept over 50-75 µg/mL, by using oral iron if necessary. Drugs that are known to exacerbate RLS, such as antidepressants, antihistamines, or dopamine blockers, should obviously be avoided unless strictly necessary. Patients should be encouraged to have good sleep hygiene with regular bedtimes.

If a patient is already being treated with a dopaminergic agent, the lowest possible cumulative daily dose should be used to control the most bothersome RLS symptoms, and the total daily dose should never exceed maximum recommended levels (pramipexole 0.5 mg, ropinirole 4 mg, rotigotine 3 mg)[153]. Physicians should explain to patients that the goal of treatment is not to eradicate symptoms completely but to ensure that they do not interfere with quality of life.[153] If symptoms become bothersome, the dose can be increased cautiously, but this will increase the risk of development of augmentation (fig 2).[153] A non-dopaminergic agent can be added if concerns about the dose of the dopaminergic drug occur.[153]

Intermittent (non-daily) treatment of RLS to prevent augmentation

Starting daily treatment of RLS should be deferred as long as possible until symptoms occur almost daily.

Fluctuating RLS symptoms

In patients with a history of notable fluctuating RLS symptoms, intermittently attempting to reduce the dose or even discontinue the drug may be appropriate to ensure that they are being treated with the lowest effective dose.[153]

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PRACTICE POINTER

Depersonalisation and derealisation

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CPD READING

0.5 HOURS

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Patients who experience depersonalisation and derealisation often have difficulty in describing their symptoms. They experience a sense of unreality and detachment from their sense of themselves (depersonalisation: DP) or their perception of the world (derealisation: DR). In most cases these two symptoms co-occur. This article aims to help clinicians recognise depersonalisation and derealisation (DP DR) symptoms, diagnose the disorder, and discuss current treatment options.

HOW PATIENTS WERE INVOLVED IN THE CREATION OF THIS ARTICLE

The article was co-written by a patient with longstanding DPRD who contributed at every stage in the process. We also had another patient contributor and a patient reviewer.

The patients wished to emphasise the importance of clinicians recognising that DP DR symptoms can occur as a primary diagnosis, distinct from anxiety and depression, as so many people with DP DR symptoms are misdiagnosed resulting in distress and delay in treatment. They also wanted to stress that although there is no definitive treatment, recovery is possible for many people with DPRD.

WHAT YOU NEED TO KNOW

- Depersonalisation and derealisation symptoms include having a sense of unreality and detachment; patients may describe using phrases such as "it is as if…"
- Symptoms are often triggered by adverse life events, severe anxiety, or cannabis use
- Transient symptoms of less than a couple of weeks' duration are common and need no intervention
- Distinguish symptoms of depersonalisation and derealisation that are secondary to another medical or psychiatric diagnosis and treat the underlying problem
- Refer those who appear to have persistent symptoms to a psychiatrist for consideration of primary depersonalisation derealisation disorder

Who experiences depersonalisation and derealisation?

Otherwise healthy people—Transient symptoms of depersonalisation and derealisation are very common in the general population, often during periods of stress or fatigue. One US phone study of more than 1000 people found that nearly a quarter reported a brief episode over the previous one year period.[1]

Those with a range of physical and mental health conditions—Such symptoms are also commonly associated with several medical conditions, such as migraine and temporal lobe epilepsy,[2] and with psychiatric conditions, particularly anxiety disorders, such as panic, depression, or in those with complex post-traumatic stress or personality disorders who report a history of childhood abuse or trauma.[3]

Those with depersonalisation and derealisation disorder as a primary diagnosis—Less well known is that the symptoms of depersonalisation and derealisation can also occur as a chronic primary mental health disorder called depersonalisation derealisation disorder (DPRD). These symptoms can cause distress and affect quality of life and function. Case series from the UK,[4] Germany,[5] and the US[6] find the primary disorder of DPRD affects men and women roughly equally. Several robust epidemiological surveys indicate prevalence rates over the past month of clinically significant DPRD at around 1% of the general population[3] and at 5% within psychiatric outpatient samples.[7] Data suggest that DPRD can be underdiagnosed, or the diagnosis is delayed, with patients typically waiting between seven and 12 years for a diagnosis.[4 5] If left untreated the disorder can have an unremitting course lasting years. Patients report that early diagnosis and information-giving help alleviate the distress typically associated with this condition and promote recovery.

PERSONAL ACCOUNT

My depersonalisation started after severe anxiety with acute physical symptoms. I started being hyper aware of my every movement, word, and breath. When I looked at my hands they felt like they didn't belong to me, my voice was like it was not my own, and I was totally detached looking in a mirror. It was as if I was living in a dream, my head felt very foggy, and I was very numb. I remember at its worse that I would laugh or cry but feel nothing. Already suffering from anxiety, once I fell into the depersonalisation as well I very quickly was on a hamster wheel: I worried about this feeling, which of course fed my anxiety. I couldn't eat or sleep or enjoy anything anymore.

I was put on antidepressants, which helped with the anxiety, and I have been on them ever since (around 20 years). True recovery only started to come to me when, very luckily, I managed to get in touch with a clinical psychologist. I started cognitive behavioural therapy (CBT) specialising in depersonalisation and anxiety, which taught me to not be scared and run away from the feelings. Once I understood what this condition was, and was told it is actually very common and there were lots of people out there like me that had experienced similar symptoms, and most importantly recovered, I started to feel a lot calmer about it, and it felt less like I was being attacked by some strange force.

When I looked at my hands they felt like they didn't belong to me, my voice was like it was not my own, and I was totally detached looking in a mirror

Box 1 | What your patient might say

- I feel as if I'm living in a dream
- I feel like I don't (or the world doesn't) exist anymore
- I feel completely detached from everything or everyone around me
- It's like I'm just watching life from behind glass/projected onto a screen/in a fog
- I'm robotically going through the motions of being alive but feel dead inside

The infographic that accompanies this article summarises the main categories of people who experience depersonalisation and derealisation.

What symptoms do people describe?

Patients might use the language in box 1 when putting their experience into words. Such phrases used by patients might suggest the need for further questioning.

Alongside the core symptoms of unreality and detachment, people with depersonalisation and derealisation can describe emotional numbing of positive *and* negative emotions, and experiences affecting specific parts, or all, of their body. They might report that parts of their body (their reflection, voice, or hands) don't feel like they belong to them and that their actions feel robotic. They might experience blurred vision or perceptual distortions, such as seeing the world in two dimensions. Obsessive existential thoughts about the meaning of life might be present. The person might complain about difficulty concentrating or remembering but these problems are typically not accompanied by clear-cut objective cognitive deficits such as memory or attention impairments on formal testing.[8]

Patients with depersonalisation and derealisation are aware that their experiences are subjective and do not reflect reality, but might present urgently seeking help because of fears that their symptoms indicate incipient psychosis or brain dysfunction. However, the "*as if*…" quality to their descriptions helps to distinguish those with depersonalisation and derealisation from those experiencing psychosis, as the former will not have accompanying hallucinations or delusional beliefs. In US psychiatric classification systems,[9] depersonalisation derealisation disorder is categorised as a dissociative disorder due to the sense of detachment experienced. However it is distinguishable from other dissociative disorders in that discontinuities of memory and identity are rare.

What triggers depersonalisation and derealisation

Current evidence is insufficient to fully characterise or quantify associations with life events or other diagnoses, or to predict who will or won't develop symptoms. However, what data exist suggest that there are some life events and diagnoses that are associated with transient or intermittent symptoms and with the more chronic disorder.

There is a strong association of depersonalisation or derealisation symptoms starting during a period of acute

Primary care guidance

Assessing severity of depersonalisation and derealisation symptoms

Transient symptoms of depersonalisation and derealisation are very common in the general population, often during periods of stress or fatigue, or concurrent with a number of medical conditions. They can also occur as a chronic primary mental health disorder called Depersonalisation/ Derealisation Disorder (DPRD).

What your patient may say

- It's like I'm just watching life from behind glass
- I feel completely detached from everything around me
- I feel as if I'm living in a dream
- I feel like I don't exist anymore

Increasing symptom severity

1 Transient symptoms

Mildly distressing

Seconds to a few days

Typical triggers

Fatigue

Jet lag

Life threatening incidents

After heavy alcohol use

Illicit drug use

Comorbidities and risk factors

None

Intervention

Give the patient a name for their symptom. Explain why it might have been triggered in their case

Review after 2 weeks. If symptoms persist, consider other levels of severity

2 Secondary to other disorder

Moderately distressing

Panic attacks: Minutes

Psychiatric disorders: Weeks to months

Typical triggers

Panic attack

Aura of migraine or seizure

Comorbidities and risk factors

Neurological conditions

Eg, migraine or temporal lobe epilepsy

Psychiatric conditions

Eg, depression or schizophrenia

Anxiety disorders

Particularly those with panic or obsessive compulsive disorder

Intervention

Treat primary condition

Anxiety or depression

Psychopharmacological management

Psychological management

Refer for low intensity psychological therapy

Psychosis

Refer to CMHT*

Review after treatment. If symptoms persist, consider primary DPRD

3 Part of PTSD or personality disorder

Moderately–severely distressing

Functional impairment possible

Months to years

Typical triggers

Period of prolonged stress

Comorbidities and risk factors

History of significant childhood abuse and trauma

Post-traumatic stress disorder

Personality disorders

Particularly borderline personality disorder

Intervention

Treat primary condition

Childhood or adult trauma

Refer for high intensity trauma focused psychological therapy

Personality disorder

Refer to secondary care services

Review after treatment. If symptoms persist, consider primary DPRD

4 Primary DPRD

Moderately–severely distressing

Functional impairment likely

Months to years

Onset often in adolescence

Typical triggers

Acute stress

Use of illicit drugs

Particularly after cannabis use

Comorbidities and risk factors

May be none

A history of anxiety problems

Family history of anxiety disorders

Reported parental emotional abuse, perceived criticism, and/or emotional neglect

Intervention

Elicit concerns, and offer reassurance and hope that they can recover. Signpost patient to self help material, online and phone support, particularly recovery stories

Review after 2 months. If symptoms persist, refer to local secondary care services for psychiatric assessment and intervention

Review after treatment. If symptoms persist, consider referral to tertiary or specialised DPRD centre

*CMHT = Community Mental Health Teams

Box 2 | Assessing DP DR symptoms

The presence and severity of symptoms can be assessed by summing scores on two questions: "Over the past two weeks, how often have you been bothered by the experience of

1. Your surroundings feeling detached or unreal, as if there were a veil between you and the outside world, and

2. Out of the blue, you feel strange, as if you were not real or as if you were cut off from the world."

Scale: 0=not at all; 1=several days; 2=more than half the days; 3=nearly every day.

Clinical cut off score of >=3

stress. This has led to the current understanding that DP DR is part of a normal physiological or psychological coping mechanism ("like a circuit breaker") that is designed to protect us from overwhelming anxiety by creating a sense of detachment and numbing.[10 11] However, in some cases this normally transient coping mechanism can become maintained, leading to the chronic disorder of DPRD.[11]

How to assess and manage someone with symptoms

The suggested key principles for when someone presents with symptoms of depersonalisation or derealisation are laid out in the infographic (based on tables in appendix files). This guide is compiled based on research evidence and clinical experience from authors based at the specialist London based NHS Depersonalisation Disorder Clinic.

Try to distinguish between transient or intermittent symptoms; those that might be suggestive of a concurrent physical or mental health problem where the DP DR is secondary; or symptoms that are suggestive of the chronic disorder of DPRD. Remember DPRD can be a primary disorder or it can be a comorbid problem in the context of substantial history of trauma or a primary mental health disorder. If the latter, then address this history. If there is no significant history of trauma then treat as a primary disorder by following the guidance in this article.

The hardest differential diagnosis is when both an anxiety disorder and depersonalisation derealisation disorder are present and distressing. In these cases it is worthwhile monitoring both conditions on a monthly basis, and if the DP DR does not resolve within a few months, to assume that this is primary DPRD, and to follow the recommendations for this.

Assessing DP DR symptoms—See box 2

You can also ask your patient to complete the 29 item Cambridge Depersonalisation Scale[12] (available for free through internet search). Scores of >=70 are associated with clinical severity. Those diagnosed with primary DPRD are likely to need specifically targeted intervention for DPRD.

Management of DP DR symptoms—In all cases, when there are DP DR symptoms present, normalise these symptoms by explaining the common association with acute stress and fatigue, as well as giving hope that these symptoms are likely to resolve in time. Signpost patients to sources of support.

Treatment for primary depersonalisation derealisation disorder—The evidence base for empirically validated treatments for DPRD is extremely limited. Small open studies suggest some interventions may be promising, but need to be treated with caution. Psychotherapeutic approaches such as cognitive behavioural therapy, specifically adapted for DPRD, have shown good results but are only available in specialist settings.[13] Mindfulness approaches could be beneficial.[14] A study of lamotrigine as an adjunct therapy reported dose related benefits,[15] as did studies using opiate antagonists.[16 17] Repetitive transcranial magnetic stimulation has also been tried and the results show promise.[18 19]

The older literature confirms the large number of treatments tried but ineffective, including anticonvulsants, stimulants, and even electroconvulsive therapy.[20] A recent systematic review[21] found only three double blind randomised control trials (RCTs), with inconsistent results. One RCT involved lamotrigine, which blocks ketamine induced depersonalisation.[22] The second trial had no effect, albeit approaching statistical significance.[23] An RCT of fluoxetine found it no more efficacious than placebo,[24] although with a trend for efficacy in those with a comorbid anxiety disorder. An RCT using biofeedback found no significant therapeutic benefit.[25]

PERSONAL ACCOUNT

I smoked cannabis one evening while at university. I had smoked once before, a year earlier. Shortly after, I began to feel as though my eyes were fixating on parts of the room, and that I was distanced from my environment. This led to me having a panic attack which was only alleviated when I eventually managed to sleep. In the morning I continued to feel distanced, and as though I was a spectator in my own life. I experienced this constantly for many months. Recovery was a gradual process, firstly of being distracted from the feelings of depersonalisation for longer and longer periods while I was engaged in activities, and then later experiencing extended periods where I was actually conscious of feeling present in the moment. Diagnosis was an important part of my recovery, as was continuing with some normal, daily activities, and distracting myself with engaging activities.

In the morning I continued to feel distanced, and as though I was a spectator in my own life

Competing interests: None declared.

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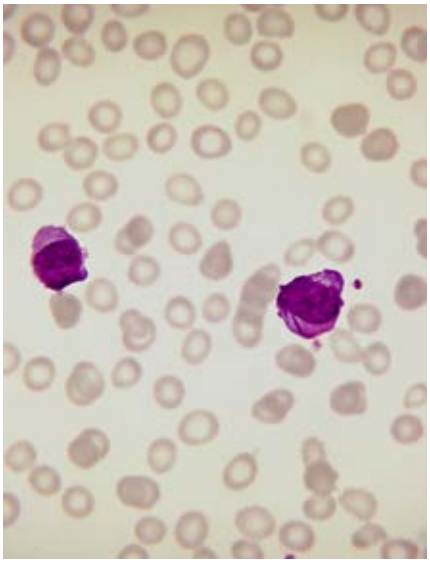
EDUCATION INTO PRACTICE

Did you know that when patients say things like "I don't feel real" they may be suffering from depersonalisation disorder?

Do you know where to refer patients if you suspect they might be suffering from depersonalisation derealisation disorder?

CASE REVIEW

Bruising and abnormal leucocytes on a blood film—a haematological emergency



A 20 year old man was referred to the emergency department by his general practitioner with a one week history of easy bruising, gum bleeding, and lethargy. He had no medical history and took no regular medications. He did not smoke or drink alcohol and had no travel history. On examination, he appeared unwell and had widespread petechiae with evidence of gum bleeding. The rest of the clinical examination, including funduscopy, was normal.

His observations were: heart rate 110 beats per minute, blood pressure 100/80 mm Hg, temperature 38.5°C, respiratory rate 20 breaths/minute, and oxygen saturations 100% on room air.

Blood results showed: haemoglobin 77 g/L (133-167 g/L), white blood cell count 6×10^9 cells/L ($3.5\text{-}11\times10^9$ cells/L), neutrophils 1.1×10^9 cells/L ($2.0\text{-}7.0\times10^9$ cells/L), platelets 45×10^9/L ($150\text{-}410\times10^9$/L), and C reactive protein level 160 nmol/L (0.76 –28.5 nmol/L). A coagulation screen showed INR 1.9 (0.8-1.1), APTT ratio 1.07 (0.85-1.15), fibrinogen 0.8 g/L (2-4 g/L), and D-dimer 3334 ng/ml (<250 ng/ml). Urea, creatinine, and liver function tests including bilirubin were normal.

His blood film at ×40 magnification (figure) showed large promyelocyte blast cells with bilobed nuclei with azurophilic granules and Auer rods within the cytoplasm. His bone marrow aspirate showed a hypercellular marrow packed with large promyelocyte blast cells containing Auer rods.

Flow cytometry from peripheral blood showed a clonal population of cells that were HLADR–, CD34– CD13+, CD33+and CD117+. Cytogenetic testing confirmed the presence of t(15;17) abnormality in these cells.

1 What is the diagnosis?
2 What treatments are available for this condition?
3 What follow-up is necessary for this condition?

Submitted by Selina J Chavda, Sophie Lindsay, Fenella Willis, and Mickey Koh

Patient consent obtained.

Cite this as: *BMJ* 2017;356:j1164

SPOT DIAGNOSIS

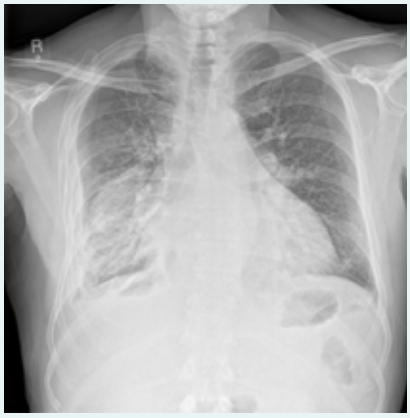
An easily mistaken pulmonary opacity

A 54 year old male smoker of 20 pack years presented with a six week history of fever, anorexia, worsening cough, and dyspnoea. He had previously undergone coronary artery bypass grafting. A chest radiograph showed previous sternotomy, borderline cardiomegaly, pulmonary oedema, right lower zone consolidation, and a right mid zone oval density (figure). What is the diagnosis for this oval density?

Submitted by Timothy Shao Ern Tan and Omar Abdulla

Patient consent obtained.

Cite this as: *BMJ* 2017;356:j1188



If you would like to write a Case Review for Endgames, please see our author guidelines at http://bit.ly/29HCBAL and submit online at http://bit.ly/29yyGSx

answers

CASE REVIEW

Bruising and abnormal leucocytes on a blood film—a haematological emergency

1 The blood film and bone marrow show large promyelocyte blast cells consistent with acute promyelocytic leukaemia. This is confirmed by the flow cytometry results and the presence of characteristic t(15;17) translocation.

2 Patients with a suspected diagnosis of acute promyelocytic leukaemia should be started urgently on all-trans retinoic acid and then given chemotherapy. Coagulopathy should be treated aggressively with blood product support as needed. Arsenic trioxide and all-trans retinoic acid combinations can be used initially in groups at low to intermediate risk.

3 Patients are followed up by haematology teams for three years after treatment and are then discharged back to primary care. Monitoring is performed using molecular PCR techniques on peripheral blood or bone marrow. Patients who relapse should be treated with salvage chemotherapy and might require stem cell transplantation.

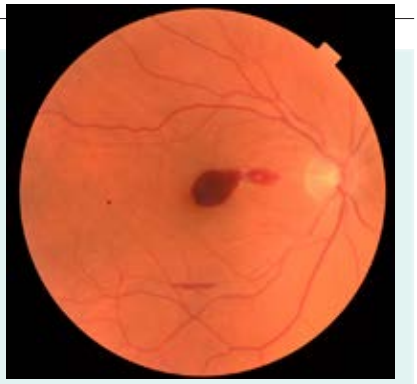
SPOT DIAGNOSIS

An easily mistaken pulmonary opacity

Encysted pleural fluid in the right oblique fissure.

Apart from the right sided encysted pleural fluid, the figure also shows left subpulmonic and right lamellar effusions. Overall, the radiological findings suggest congestive heart failure with coexisting right lobar pneumonia caused by *Mycoplasma pneumoniae* (organism confirmed on laboratory testing).

Branch retinal vein occlusion secondary to sildenafil



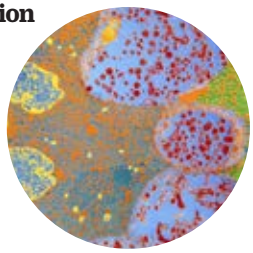
A 73 year old man presented at the eye unit with a cotton wool spot in his right macula (figure). Ten days later he developed a superficial retinal haemorrhage and was diagnosed with a right branch retinal vein occlusion. His Snellen visual acuity was 6/15. He had no history of diabetes mellitus or hypertension, and coagulation screening was normal. No specific cause was found, but further questioning revealed regular use of sildenafil for erectile dysfunction. A known side effect of sildenafil is retinal vascular occlusion. This case highlights the importance of taking a thorough medical and drug history when faced with a vascular ocular lesion without an obvious cause.

Hussein Almuhtaseb, Osama Kanavati, Andrew Lotery (a.j.lotery@soton.ac.uk), Southampton Eye Unit, University Hospital Southampton NHS Foundation Trust, Southampton, UK

Patient consent obtained.

Cite this as: *BMJ* 2017;356:j753

Vertical transmission of chlamydia



Routine testing for *Chlamydia trachomatis* in pregnant women in Finland, using urine nucleic acid amplification tests, shows a carriage rate of 2.7%. Textbooks and guidelines claim that half of the babies born to infected women will acquire the infection, and of these, 25% to 50% will be symptomatic. But a study (*Sex Transm Infect* doi:10.1136/sextrans-2016-052884) shows that the true rate of chlamydial disease in babies is much lower. Using other whole population registries from Finland, possible vertically transmitted chlamydia in infants was estimated at 2.2% per 1000 live births.

Good acute care pays in stroke

The quality of acute care for Australians who suffer stroke was assessed over the years 2010 to 2014 using the Australian Stroke Clinical Registry (*Stroke* doi:10.1161/STROKEAHA.116.015714). The three key components were: admission to an acute stroke unit, effective antihypertensive medication at discharge, and provision of a discharge care plan. Patients who received these aspects of care showed better survival to 180 days and better health related quality of life.

Bariatric surgery reduces heart failure

Two Swedish registers allow large scale indirect comparisons between the effects of intensive lifestyle modification and bariatric surgery. The 25 804 gastric bypass surgery patients had on average lost 18.8 kg more weight after one year, and 22.6 kg more after two years, than the 13 701 lifestyle modification patients (*Circulation* doi:10.1161/CIRCULATIONAHA.116.025629). During a median of 4.1 years, the incidence of heart failure in the surgery patients was half that of the lifestyle group, translating into a five year risk of 0.2% versus 0.4%.

BCG: not magic for preventing other things

Bacillus Calmette-Guérin is an example of a live vaccine that, according to observational evidence from low income settings, might protect children from more than just its target disease, tuberculosis. The Danish Calmette Trial randomised 4262 children to receive BCG or no intervention at seven days of age, to test this hypothesis in a high income setting (*Arch Dis Child* doi: 10.1136/archdischild-2016-310760). Over a period of 15 months, there was no difference in rates of hospitalisation between the groups.

Overdiagnosis victims speak

Many people who have had dubious diagnoses and then unnecessary treatment show high levels of gratitude. Conversely, those who decide against intervention often suffer for it, according to a qualitative study of 22 people who were among the first to question the practice of immediate intervention for their small, incidentally identified thyroid cancers (*JAMA Otolaryngol Head Neck Surg* doi:10.1001/jamaoto.2016.4749). Participants reported receiving non-reassuring, unsupportive responses to their decision not to intervene. They experienced anxiety about disease progression, felt isolated, and most kept their diagnosis a secret because of their experiences.

Distress, observed or felt

Coping with pregnancy termination for fetal abnormality can have profound effects on mothers and those looking after them. A study within three English hospitals interviewed both the staff and the mothers (*BMC Pregnancy Childbirth* doi:10.1186/s12884-017-1238-3) and found good agreement in identifying key coping mechanisms. These included support from others, acceptance, problem solving, avoidance, another pregnancy, and meaning attribution. Health professionals showed high levels of insight and empathy in the short term, but there were no systems in place for longer term support.

Vesalius for your next birthday

De humani corporis fabrica by Andreas Vesalius is no doubt "the most iconic medical book of all time," to use current jargon. Sir William Osler was just one medical luminary who spent years striving to obtain a copy, which he later gave to the Bodleian Library in Oxford. In fact, the magnificent folio editions of 1543 and 1555 are not as rare as once thought, according to a survey (*Soc Hist Med* doi:10.1093/shm/hkw108). There are 146 publicly held copies in the USA, followed by 97 in the UK, which beats Italy with its 63. The last 1543 edition to come on sale in the UK fetched a mere £60 000, far less than the big car with a personal number plate coveted by so many wealthy doctors.

Cite this as: *BMJ* 2017;356:j1344