THERAPEUTICS

Atypical antipsychotic drugs

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The "typical" (first generation) antipsychotic drugs (such as haloperidol, chlorpromazine, and trifluoperazine) have been used to treat schizophrenia since the 1950s. The "atypical" (second generation) antipsychotics (table 1) were introduced into routine practice from the 1990s. Both classes are used in the acute phase of schizophrenia and related psychoses and for long term maintenance and prevention of relapse. Typical antipsychotic drugs have a range of adverse effects, notably extrapyramidal features such as dystonia, parkinsonism, akathisia, and tardive dyskinesia. Although atypical antipsychotics are less likely to cause extrapyramidal symptoms, they may also have important adverse effects, including metabolic effects.[3] Some atypical antipsychotics are also licensed to treat mood disorders, and table 1 summarises licensed indications in the United Kingdom. However, this article considers their use for the treatment of non-affective psychosis only.

Antipsychotics are a pharmacologically heterogeneous group of compounds, but all act as D_2 dopamine receptor antagonists, an action linked to their antipsychotic effect.[4] While the term atypical originally referred to antipsychotic drugs that did not cause catalepsy in animal models, recent academic and marketing literature uses this term to refer to both clinical properties (reduced incidence of extrapyramidal effects) and chemical properties (receptor profile).[5 6] 5-HT_{2A} antagonism and/or 5-HT_{1A} agonism may be important in the therapeutic effects of atypical antipsychotics,[3] and adverse effects seem to be dose related and often linked to their action at histaminergic, cholinergic, alpha-adrenergic, and other receptor sites.

CASE SCENARIO

A 19 year old student has a six month history of social withdrawal, and bizarre behaviour. He becomes suspicious of his fellow students and believes that his teachers are monitoring his activity on Facebook. He is heard laughing and shouting when he is alone. Paranoid psychosis is diagnosed, and an atypical antipsychotic drug is prescribed alongside other psychosocial interventions (a combination recommended by current guidelines from the National Institute for Health and Clinical Excellence (NICE)[1]

How well do atypical antipsychotic drugs work?

Evidence on the efficacy of typical versus atypical antipsychotics is contentious and often difficult to interpret owing to methodological heterogeneity. A recent meta-analysis of 150 double blind, mainly short term randomised controlled trials involving 21 533 participants with schizophrenia and related disorders concluded that four of the atypical antipsychotic drugs (amisulpride, clozapine, olanzapine, and risperidone) were more effective than some first generation drugs (haloperidol in 95 of the studies) in improving mean overall symptom scores.[7] Effect sizes, however, were modest, with numbers needed to treat ranging from 6 (amisulpride) to 15 (risperidone).[7] Aripiprazole,

Table 1 | Current licensed (UK) atypical antipsychotics, with their licensed indications and available formulations[2]

Drug	Licensed indications	Available formulations
Amisulpride	Schizophrenia	Tablets, oral solution
Aripiprazole	Schizophrenia; agitation and disturbed behaviour in schizophrenia; mania	Tablets, orodispersible tablets, oral solution, intramuscular injection (short acting)
Clozapine	Schizophrenia (including psychosis in Parkinson's disease) in patients unresponsive to or intolerant of conventional antipsychotic drugs	Tablets, oral solution
Olanzapine	Schizophrenia; mania; preventing recurrence in bipolar disorder; agitation and disturbed behaviour in schizophrenia; mania	Tablets, orodispersible tablets, intramuscular injection (short and long acting)
Paliperidone*	Schizophrenia	Tablets
Quetiapine†	Schizophrenia; mania; depression in bipolar disorder; preventing recurrence in bipolar disorder	Tablets, prolonged release tablets
Risperidone	Acute and chronic psychoses; mania; short term treatment of persistent aggression in patients with moderate to severe Alzheimer's dementia unresponsive to non-drug interventions when there is a risk to others; short term treatment of persistent aggression in conduct disorder	Tablets, oral solution, orodispersible tablets, intramuscular injection (long acting)
Sertindole‡	Schizophrenia	Tablets
Zotepine	Schizophrenia	Tablets

*Paliperidone is a metabolite of risperidone.

†The Scottish Medicines Consortium has advised (in April 2009) that quetiapine is not recommended for use within NHS Scotland for the treatment of major depressive episodes associated with bipolar disorder.

‡Sertindole has been reintroduced after an earlier suspension because of concerns about arrhythmias; its use is restricted to patients who are enrolled in clinical studies and who are intolerant of at least one other antipsychotic.

This is one of a series of occasional articles on therapeutics for common or serious conditions, covering new drugs and old drugs with important new indications or concerns. The series advisers are Robin Ferner, honorary professor of clinical pharmacology, University of Birmingham and Birmingham City Hospital, and Philip Routledge, professor of clinical pharmacology, Cardiff University. To suggest a topic for this series, please email us at practice@bmj.com.

Table 2 | Summary of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE)[9] and the Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia (CUtLASS 1)[8] studies. Adapted from National Institute for Health and Clinical Excellence[1]

	CATIE	CUtLASS 1
No of participants	1493	227
Intervention (No of patients randomised)	Typical agent: perphenazine (261) Atypical agents: olanzapine (336), quetiapine (337), risperidone (341), zipasidone* (185)	Typical agents (118) Atypical agents (109)
Inclusion criteria	Diagnosis of schizophrenia; no history of serious adverse reaction to study medication; not experiencing first episode; not resistant to treatment	Diagnosis of schizophrenia; schizoaffective disorder or delusional disorder requiring change of antipsychotic because of inadequate response or intolerance; at least one month since onset of positive psychotic symptoms
Setting	Inpatients and outpatients (United States)	Inpatients and outpatients (United Kingdom)
Duration	Up to 18 months	Up to 12 months
Main findings	Symptom scores improved in all groups, with significant variation in treatment effects over time. Improvement initially greatest with olanzapine, but advantage diminished with time	Quality of life, symptoms, and cost of care were similar for both groups (those taking atypical antipsychotics (other than clozapine) and those taking typical antipsychotics)
	74% of recipients discontinued study medication before 18 months (64% olanzapine, 75% perphenazine, 82% quetiapine, 74% resperidone, 79% ziprasidone)	No significant difference in proportion of recipients remaining on study treatment between atypical (65%) and typical (54%) agents over 1 year
	The time to discontinuation of treatment for any cause was significantly longer in the olanzapine group than in the quetiapine or risperidone groups, but not significantly longer than in the perphenazine or ziprasidone groups	
	Olanzapine was significantly associated with more discontinuation for weight gain and metabolic effects	
	Perphenazine was significantly associated with more discontinuation for extrapyramidal effects	

* Added after licensing by Food and Drug Administration in 2002.

quetiapine, sertindole, ziprasidone (not licensed in the UK) and zotepine were not significantly different from first generation drugs for overall efficacy in this meta-analysis.

Two pragmatic randomised controlled trials, the CUtLASS 1 and CATIE studies, compared the efficacy and tolerability of second versus first generation antipsychotic drugs in patients with schizophrenia and related disorders.[8 9] Neither study found significant differences in overall efficacy between typical and atypical agents, although in the CATIE study, symptom scores improved more rapidly with olanzapine (table 2).

Some evidence exists that clozapine, the prototype of atypical antipsychotics, is more effective for treatment resistant schizophrenia than are other atypical agents. For example, in a randomised controlled trial (CUtLASS 2) comparing clozapine with risperidone, olanzapine, quetiapine, or amisulpride in those with a poor clinical response to at least two previous drugs, clozapine significantly improved positive and negative symptom scores, although quality of life was not significantly affected.[10] Clozapine should be prescribed only in specialist settings because of its adverse effects, especially its propensity to cause agranulocytosis.

The guidance from the National Institute for Health and Clinical Excellence (NICE) has concluded that, with the exception of clozapine, insufficient evidence exists for it to make "any general recommendation for one antipsychotic to be preferred over another."[1]

How safe are atypical antipsychotic drugs?

Common, dose related adverse effects of atypical antipsychotic drugs include sedation (especially with clozapine, olanzapine, and quetiapine); anticholinergic effects, such as dry mouth, constipation and blurred vision (especially with clozapine and olanzapine); and dizziness and postural hypotension resulting from α adrenoceptor antagonism (especially with sertindole, clozapine, risperidone, and quetiapine).[11]

Atypical agents are generally considered to cause fewer extrapyramidal adverse effects than typical agents, although some (such as akathisia) can occur. In the recent meta-analysis described above, clozapine, olanzapine, and risperidone were significantly less commonly associated with extrapyramidal symptoms than were low potency first generation antipsychotics (600 mg a day chlorpromazine or equivalent).[7]

Some atypical agents cause substantial metabolic adverse effects (table 3). This is of concern because of the well established excess of cardiovascular morbidity and mortality in patients with schizophrenia that predates the widespread introduction of atypical drugs.[12] Individual drugs have differing propensities to cause metabolic adverse effects.[13] The CATIE study, for example, showed that olanzapine was more likely to be associated with weight gain (>7% of pretreatment weight) than perphenazine (number needed to harm 5.6), quetiapine (7.2), risperidone (6.3), and ziprasidone (4.4). Olanzapine was also more commonly associated with treatment discontinuation because of weight gain or metabolic effects than perphenazine (12.4), quetiapine (17.6), risperidone (13.4), and ziprasidone (16.7).[14] Table 3 summarises data on adverse effects in this study.

In our experience clozapine, olanzapine, and quetiapine are particularly associated with substantial weight gain, dyslipidaemia, and hyperglycaemia. Both Eli Lilly (which makes olanzapine) and AstraZeneca (quetiapine) have paid substantial settlements to patients in the United Sates after allegations relating to adverse metabolic effects of these drugs.[15 16]

Hyperprolactinaemia is a well recognised adverse effect of some of the atypical drugs, particularly risperidone and amisulpride[17] and may result in gynaecomastia, galactorrhoea, abnormalities of the menstrual cycle, impotence, and osteoporosis (table 3).

Some first generation antipsychotics (such as thioridazine, droperidol, pimozide) can show clinically significant prolongation of the QT interval in the

Table 3 | Summary of the common adverse effects associated with the frequently prescribed atypical antipsychotic drugs in the United Kingdom, based on the authors' appraisal of the evidence and their clinical experience. (Aripiprazole is a relatively new drug with more limited data on adverse effects)

	Sedation	Anticholinergic effects	Postural hypotension	QTc prolongation	Weight gain	Hyperglycaemia, dyslipidaemia*	Hyperprolactinaemia
Amisulpride	+	++	++	++	+	+	+++
Aripiprazole	+	+	+	Discrepant results	+	+	+
Clozapine	++	+++	+++	+	+++	+++	+
Olanzapine	+++	+++	+	+	+++	+++	++
Quetiapine	++	+	+++	+	++	++	+
Risperidone	+	+	+++	+	++	+	+++
Sertindole	+	+	+++	+++	++	+	+

*Same effect for each drug for both hyperglycaemia and dyslipidaemia.

+ =Some effect.

++ =Intermediate effect.

+++ = Greatest effect.

electrocardiogram, which may lead to the ventricular arrhythmia torsade de pointes. With the exception of sertindole and ziprasidone, atypical agents have been less associated with QT prolongation at therapeutic doses.[18]

Antipsychotic drugs, both typical and atypical, may provoke seizures in susceptible patients. For atypical agents, the risk of this effect seems highest for clozapine and lowest for risperidone.[19]

Because clozapine may provoke agranulocytosis, the white blood cell count must be monitored to allow agranulocytosis to be detected early, before it becomes irreversible, thus greatly reducing mortality. Data from the UK Clozaril Patient Monitoring Service show that the incidence of agranulocytosis per 100 000 person weeks of observation is 32.0 in weeks 0-18 (70% of all cases), 2.3 in weeks 19-52, and 1.8 in weeks 53 and beyond; the cumulative incidence is 0.78%.[6] Sialhorroea, ileus, tachycardia, and myocarditis are also reported after clozapine use.

Box 1 provides practical guidance on prescribing antipsychotic agents in schizophrenia. Box 2 provides some tips for patients.

What are the precautions?

- Monitor weight, glycaemic status, and lipids regularly, especially in patients with cardiovascular disease, and manage raised cardiovascular risk according to national guidance. Clozapine, olanzapine, and quetiapine in particular are associated with weight gain and other metabolic disturbances, which may further increase cardiovascular morbidity.
- In individuals known to have a prolonged QT interval on electrocardiography, prescribe antipsychotic drugs at the lowest effective dose, avoiding the drugs associated with more marked electrocardiographic effects (table 3) and monitoring electrocardiographic effects, especially at the start of treatment or if you increase the dose.
- In people with epilepsy, ensure that appropriate anticonvulsant treatment is in place and encourage adherence. Monitor seizure frequency during treatment.
- In pregnancy and breast feeding, discuss the benefits and possible risks of effective treatment with antipsychotics. Little experience has been reported of use of atypical agents in pregnancy and breast feeding, but mother and child are at risk if psychosis is inadequately treated. The lowest effective dose of antipsychotic should be used. Monitor maternal blood glucose, blood pressure, and weight, as well as fetal growth throughout pregnancy. A small prospective case series has reported that in utero exposure to atypical antipsychotic drugs may increase infant birth weight and the risk of babies being large for gestational age.[20] Further information on specific drugs can be obtained from the UK Teratology Information Service (www.uktis.org/). Antipsychotic drugs may be present in breast milk, but serious adverse effects have not been reported, and the benefits of effective treatment probably outweigh risks.
- In elderly patients with dementia, use antipsychotic drugs only when the indications are compelling as they are associated with a small increased risk of mortality and an increased risk of stroke and transient ischaemic attack.[21]
- Ensure that the white blood cell count is being monitored in people prescribed clozapine.

How cost effective are atypical antipsychotic drugs?

Prescribing of antipsychotic drugs (excluding depot injections) in primary care in England has increased by 24% in the past five years, to 1.6 million items per quarter, while costs have increased by 29% to £62.2m (€73m; $101m) per quarter. This increase is largely accounted for by the increased use of atypical antipsychotics; prescribing has risen by 49%, to 1.2 million items, with an increase in costs of 29%, to £59.2m. Prescribing of typical antipsychotic drugs has decreased by 15%, to 439 000 items, and their cost has risen by 21%, to £2.9m.[22]

A systematic review of the economic literature by NICE identified several studies of differing quality from the UK.[1] Most of these compared cost effectiveness between olanzapine, risperidone, and haloperidol. The study findings were not consistent, leading to a high degree of uncertainty about cost effectiveness, but they seemed to indicate that,

Box 1 | Practical guidance for use of antipsychotics for treatment of schizophrenia, based on NICE guidance and authors' opinion

Start of treatment (first episode)

- Offer oral typical or atypical antipsychotic drugs
- The choice of drug should be made jointly by the healthcare professional and the patient (and carer if the patient agrees) after considering the potential for individual drugs to cause extrapyramidal symptoms, metabolic side effects, or other adverse effects
- Before starting antipsychotic drugs offer the patient electrocardiography if physical examination identifies a specific cardiovascular risk, if the patient has a history of cardiovascular disease or a family history of long QT syndrome, or if QT interval prolongation is cited as a potential adverse effect in the drug's summary of product characteristics
- Begin treatment at the lower end of the licensed dose range and slowly titrate upwards. Consider repeating electrocardiography after dose increases for the patient groups defined in the preceding point
- Throughout treatment, and especially during titration, monitor and record clinical response, adverse effects (especially neurological and metabolic), physical health, and adherence

Treatment of recurrence

- Offer oral medication. Base the choice of drug on the criteria above as well as previous treatment response

Maintenance treatment

- Advise the patient of the high risk of relapse if he or she discontinues use in the next one to two years
- When withdrawing drugs, do so gradually and monitor for signs and symptoms of relapse
- Consider a long acting (depot) formulation if the patient would prefer this treatment, or where non-adherence affects recovery
- Where the response to antipsychotic treatment is inadequate, review the diagnosis and the adherence to and dose of medication; consider other causes of non-response, such as comorbid substance misuse

Management of adverse effects

- If extrapyramidal symptoms develop, consider reducing the dose or switching to another drug. Consider also offering drugs effective in treating extrapyramidal side effects (anticholinergic and antihistaminergic drugs are the most commonly used). Tardive dyskinesias do not respond to drug treatment
- Encourage patients to maintain a healthy diet and exercise regularly to counteract weight gain. Routine drug management of weight gain is not recommended
- Manage hyperlipidaemia and hyperglycaemia as in patients not taking antipsychotic drugs. Base any decision to change antipsychotic drugs on a careful assessment of the potential benefits and on the risks of destabilising the mental state

Box 2 | Tips for patients

- There are many different antipsychotic drugs that are effective, but unfortunately they all have side effects. We can't predict who is going to develop side effects, but we will monitor this carefully. If you do develop any side effects we can change the dose or think about a different drug
- Some people will develop a restless feeling (akathisia), stiffness in the arms or legs, or a tremor (parkinsonism). You should let your doctor know if this happens
- After prolonged treatment with antipsychotic drugs, a few people develop involuntary movements (tardive dyskinesia), which usually affect the muscles of the face, neck, or limbs. This seems to be less common with the newer antipsychotic drugs, but if it happens, let your doctor know
- Weight gain, hyperglycaemia (high blood sugar), diabetes, and raised cholesterol and triglycerides can occur, especially with some of the newer drugs. It is important that your GP or psychiatrist monitors your physical health as well as your mental health while you are receiving treatment
- You can take the medication as a tablet, usually once or twice a day. Some drugs are available as an injection, which is usually given every two to four weeks
- Alcohol and illicit drugs can interfere with the effects of antipsychotic drugs and can make your symptoms worse
- If you have a preference for what treatment you would like to receive if you become unwell again, discuss this with a member of your mental health team and make an advance statement specifying how you would like to be treated in the future. This will help the doctors to decide how best to treat you

overall, olanzapine and risperidone might be more cost effective than haloperidol. Importantly, for a first episode of psychosis, early schizophrenia, or prevention of relapse, NICE was unable to draw any reliable conclusions on the relative cost effectiveness of any antipsychotic medication.

How are atypical antipsychotic drugs taken?

Table 1 outlines the available formulations. For patients who may have difficulties with adherence or swallowing, orodispersible tablets or oral solutions may be preferable to tablets. Occasionally, parenteral medication may be necessary to control the acute behavioural disturbances associated with psychosis. Long acting (depot) preparations can be used for treating patients who require long term antipsychotics and prefer this route of administration, or for patients who have difficulties with adherence.

How do atypical antipsychotics compare with other drugs?

The antipsychotics are the only class of drug for which the evidence base shows consistent efficacy in treating the core symptoms of schizophrenia and schizophrenia-like illnesses. Despite the enthusiasm that accompanied the introduction of the atypical antipsychotics, no consistent compelling evidence exists of superior efficacy or cost effectiveness compared with the typical antipsychotics. The accumulating evidence of substantial metabolic disturbance and increased cardiovascular risk associated with some of the atypical drugs must be carefully balanced against the evidence for reduced extrapyramidal adverse effects.

The promotional activity of the drug industry, historical guidelines, and the education and training of the younger generations of psychiatrists who have greater familiarity with these drugs have resulted in atypical antipsychotics being widely used and enjoying the majority of the market share in many countries.[23] On the basis of the current evidence, however, we would concur with NICE that "choosing the most appropriate drug and formulation for an individual may be more important than the drug group."[1]

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A PATIENT'S JOURNEY

Adult atopic eczema

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This is one of a series of occasional articles by patients about their experiences that offer lessons to doctors. The *BMJ* welcomes contributions to the series. Please contact Peter Lapsley (plapsley@bmj.com) for guidance.

In the 13 years since his eczema returned, John has tried the full panoply of treatments and been admitted to hospital many times; he recognises that his is an exceptional case

Just after I graduated from university, my eczema returned. I had been hospitalised with the skin condition as a child, and it had disappeared suddenly before my teens. When it came back, I immediately recognised the telltale sign of an unbearable itch, which initially limited itself to the crooks of my elbows and the backs of my knees.

My general practitioner's treatment regimen of emollients and an ever increasing strength of topical steroids failed as the eczema spread all over my body. My overwhelming early feelings were of anger, helplessness, and dread. I felt the eczema wasn't being treated aggressively enough but knew there was no magic cure and that I might have to live with it for the rest of my life.

I was diagnosed with severe atopic eczema, and my health quickly worsened through a combination of habitual scratching and a barrage of infections that exacerbated the condition. I thought nothing of ripping at my skin continually until the blood was flowing and I was exhausted and in too much pain to continue. My skin was forever dry, inflamed, and covered in open wounds.

I endured a broad range of symptoms in that first year of my relapse, learning all the spiteful ways that atopic eczema can manifest itself. Weeping eczema ruined bedding, stuck to clothes, and was a cloying, unpleasant reminder. Yellow crusting meant infected eczema, which required antibiotics. Inflamed hair follicles caused white, painful spots all over my legs. Meanwhile, I derived a perverse pleasure from picking and scratching at wounds that hadn't healed.

Admitted to hospital

I finally saw a dermatologist who fast tracked my admission to Chelsea and Westminster Hospital. It was both a relief to be well cared for and a worry that things had got so out of hand. I remember feeling ashamed that I hadn't been able to cope at home. Looking back, I should have been referred to secondary care much sooner—not because I somehow deserved better care but because I obviously needed specialist treatment a GP couldn't deliver. The common misconception is that adults with eczema are able to magically cope better just because they are adults.

Alongside all the physical symptoms were the psychological pressures. I felt frustrated, powerless, and embarrassed about the way I looked, and enormously guilty. Eczema is, to my mind at least, like a form of self harm, and to that end I felt responsible for what was happening to me, and still do. Obviously I can rationalise that having eczema is not my fault, but ultimately the root of the problem is the damage done when I tear at my skin on a daily basis.

It was like having a split personality. When the eczema was subdued I could be outgoing, confident, and sociable; the other side of me felt awkward, was ashamed to be seen in public, and would default to his insular world. Staying in meant not being judged, a safety net of sorts; something that continues even today.

I started the immunomodulator, ciclosporin, after that initial spell in hospital, which stabilised my health and

A DOCTOR'S PERSPECTIVE

The prevalence of atopy in the population may be as high as 20% and rising. Up to half of people with atopy will develop atopic eczema at some stage.

The commonest form is in childhood, but the condition can persist into adult life. A prevalence study in the United Kingdom found 38% of cases were in people aged over 16. In a small group of people with childhood eczema the problem recurs in adulthood. For some people this can become a chronic and difficult management problem. John's story is typical of that told by adults with chronic atopic eczema. As the condition is less common in adults, it may not be recognised at an early stage in the disease process, and the intensive treatment that is often needed to bring the condition under control may not be instituted or organised. Lack of public awareness of skin diseases in general, and particularly of severe eczema, often exacerbates the problem by causing embarrassment and therefore increasing psychological pressures.

John's story is an example of how difficult it can be to treat adult atopic eczema. A regimen using ointments and creams is not easy to follow with a heavy work schedule and is often not compatible with wearing the type of clothing expected in some work environments. Many adults with eczema experience difficulties in personal relationships and employment, adding to their stresses.

Adult atopic eczema can respond poorly to treatment. John has worked through a variety of standard recognised treatments without huge benefit, including oral and topical steroids, emollients, ultraviolet light, and ciclosporin and other immunomodulators, and he is currently reasonably controlled by taking methotrexate. Given the treatments he has had, the range of further options is limited, and both he and I are keenly watching the literature for developments in the treatment of this condition.

The treatment of other chronic skin conditions has advanced recently, particularly the introduction of biological agents to treat psoriasis, and it is to be hoped—on behalf of all of those with atopic eczema but particularly those adults with chronic problems—that similar exciting developments are on the horizon for their condition.

Andrew Wright

WHAT HAS WORKED WELL AND WHAT HAS NOT

What has worked well for me

- Being given the time to talk through issues properly with nurses, GPs, and dermatologists. Dealing with eczema is complicated and being spared the time to answer questions really does matter—that dermatology appointment may have been months coming and something to look forward to. Failing that, access by email is a helpful stopgap between appointments
- Identifying the start of a flare and acting quickly—an ice pack and distraction (usually television or a computer game) can sometimes stop a flare before I've had time to do any serious damage
- Reminding myself that it's not my fault. Owing to the nature of eczema, a lot of guilt is wrapped up with it
- Identifying lifestyle changes and triggers that can make a difference. I no longer drink alcohol because it quickly makes me hot, red, and itchy. My skin reacts dreadfully in the sun so I am careful to keep covered up and choose a sensitive cream with the highest protection factor. Rain often irritates my skin, and the herpes simplex virus via a cold sore is dangerous for my eczema and needs treating quickly
- Eczema support groups were not something I readily considered; I felt like I wanted to tackle eczema myself and would never open up to strangers. However, I learnt tips that hadn't occurred to me before, and I was able to pass on knowledge that I've acquired over the years
- The National Eczema Society is a charity offering a huge amount of information about every type of eczema. The ability to tap into accurate medical and lifestyle information has been really useful over the years

What has not worked well

- Dermatologists who pushed me towards their favourite treatment—I was once pressured into ultraviolet light treatment despite protesting that I was very sensitive to the sun. The result set me back several months, and I needed time off work
- When my skin deteriorates beyond a certain point, I might need help all of a sudden. Often getting appointments or access to the right help urgently, given the demands on dermatology departments, is not quick enough

gave me a glimpse of how I could manage my eczema, without it controlling me. Over the next 18 months, my dose of ciclosporin was first increased to the maximum safe level for my body weight to keep the eczema at bay—but when blood tests flagged up potential problems, it had to be gradually lowered, then stopped after it became ineffective.

Since the age of 21, I have been taking ciclosporin, azathioprine, or a combination of oral tacrolimus and mycophenolate at one time or another. All share one characteristic: my body adapts to them and the eczema becomes uncontrollable. In those 12 years, I have been admitted to hospital many times and the number of consultants I've seen stretches into double figures. I'm an extreme case—a fact I often need to remind myself of after a torrid scratch and the usual soul searching.

Along with my systemic medication, the side effects of which included severe nausea, shakes, extreme tiredness, and being prone to dizzy spells, I have been prescribed short courses of oral prednisolone. This has always been successful as a short term fix—but the impact of rebound eczema often makes me regret taking it. A week of respite will always precede a horrendous flare, but to see my skin clear, even for a short time, can be a real boost.

Coping

Coping with eczema, as I've learnt over the years, extends far beyond taking steroids, immunosuppressants, antibiotics, and antihistamines. Eczema interferes with every aspect of life. Tackling people's perceptions and lack of knowledge in the wider world about eczema was a serious shock. I was once warned not to take any more time off work or I would be fired, a week after coming out of hospital. There is no quick fix for eczema, and for some people, whose only reference point may be mild eczema, the severity of my condition is hard to understand.

The unpredictable nature of the condition has made forging a successful career really difficult at times. Taking time off work can be awkward enough, but having no control over the situation and finding a suitably understanding employer has been hit and miss. Additional stresses include an impossible desire to keep my condition secret from a new employer so as not to stand out as troublesome; explaining eczema to new colleagues all over again; applying creams effectively at work; and balancing the drowsy effects of hydroxyzine with being able to do a full day's work.

Needless to say, through all of this a support network is invaluable, and trusting someone with all your worst problems concerning eczema is a vital crutch on which to lean. I often have the same conversation with my father about my skin: he says that he knows how attritional and difficult it can be for me and he wishes he could do something—this in itself is therapeutic.

I am lucky enough to have a wife who accepts me, incessant scratching and all. She is not judgmental, nor does she get angry at me for repeatedly doing such terrible damage to my skin. To be built back up again when at the absolute lowest point is something I've had to rely on a number of times, and it's both a stark warning about how debilitating eczema can get and humbling to have someone there to help and understand. What shouldn't be underplayed is the impact on those who live with someone with eczema. Everything from

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- Alcoholism (*BMJ* 2011;342:d956)
- Rheumatoid arthritis (*BMJ* 2010;341:c7095)
- Heart transplant (*BMJ* 2010;341:c4918)
- Duchenne muscular dystrophy (*BMJ* 2010;341:c4364)
- Vitiligo (*BMJ* 2010;341:c3780)

the lack of sleep to the emotional stress of seeing someone continually hurt themselves has not been lost on me.

Where am I now?

I was in hospital in 2010 with the worst eczema of my life. I've switched to taking methotrexate, which has had some early success with my skin, but the future is a worry. Without that core stability of a successful treatment, I flare constantly and am easily infected. I think I have a reasonable outlook: I have squared that I might live with this forever but want a semblance of control to enable me to lead a normal life.

I am 34 and already scarred from years of scratching. I've taken more oral steroids, antibiotics, and immunomodulators in the past year than ever before and am realistic enough to know there might be consequences when I'm older—but what are my options? I've always taken the approach that if my eczema gets out of hand then we'll try something else. By now, though, I'm not sure there really is anything else, which remains something of a worry. But new treatments do come along, and I'll be the first in line when they do.

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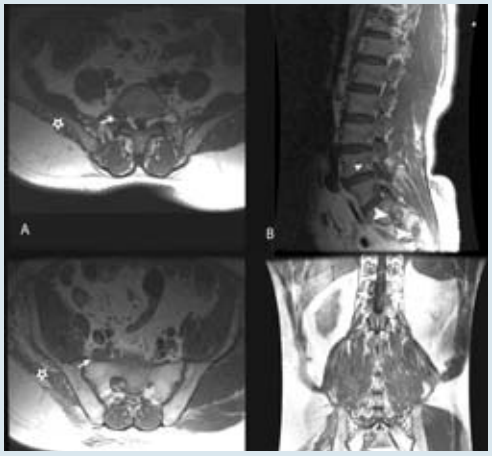
ANSWERS TO ENDGAMES, p 663. For long answers go to the Education channel on bmj.com

PICTURE QUIZ

A painful right leg



(A) Axial T1 weighted magnetic resonance imaging scan showing a thickened right S1 nerve exiting the L5-S1 foramen (arrow) and abnormal signal in the atrophic and denervated gluteal muscles on the right (star). (B) Sagittal T2 weighted fast spin echo sequence magnetic resonance imaging scan showing the thickened abnormal S1 and S2 exiting nerves (large arrowheads), compared with the normal exiting nerves above (small arrowhead). (C) Axial T1 weighted fast spin echo sequence magnetic resonance imaging scan showing enlarged S1 and S2 nerves (arrows). The larger S1 nerve has abnormal heterogeneous signal change within it. The normal S1 nerve on the left can be seen in the left exit foramen for comparison. Abnormal signal can be seen in the atrophic and denervated gluteal muscles on the right (star). (D) Coronal T1 weighted magnetic resonance imaging scan showing abnormal signal within the thickened S1 nerve on the right (arrowheads); the normal S1 nerve can be seen on the left for comparison. The right gluteal muscles are atrophic and infiltrated by fat (star)

1 The clinical signs suggest involvement of spinal nerves L5-S3.

2 The 3 tesla magnetic resonance imaging scans of the pelvis, lumbosacral spine, and plexus in coronal, sagittal, and axial planes with T1 (with and without gadolinium), T2, and fat saturated images show enlargement and thickening of the right L5, S1, and S2 nerves, with S1 being most abnormal (figure). The differential diagnoses for the signs seen on the scans include peripheral nerve sheath tumour (PNST), lymphoma, metastatic tumour (most commonly colorectal cancer, genitourinary cancer, breast tumours, retroperitoneal or pelvic sarcomas, or lymphoma), and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). No lymphadenopathy was seen.

3 Lumbar puncture followed by biopsy, if necessary, should be considered to obtain a histological diagnosis. Complications of lumbar puncture are headache and, rarely, epidural haematoma or damage to nerve roots, causing sensory loss or weakness. Complications of biopsy include the risks associated with anaesthetic; local bleeding and infection; a significant risk of loss of sensation, motor function, or both; and the possibility of a non-diagnostic biopsy.

4 The patient's symptoms should be treated with an appropriate analgesia regime. Opiates are often required to relieve the pain of malignant infiltration. Local radiotherapy can be used for palliation. Depending on further restaging investigations, systemic treatment may be indicated.

ON EXAMINATION QUIZ

Hypertension

Answer A is correct.

STATISTICAL QUESTION

Sampling methods III

Answer *b* best describes the sampling method used.