Streptococcal perianal infection in children is caused by group A Streptococcus pyogenes and is usually confined to the immediate perianal area, though it can spread to the perineum and occasionally the genitalia.1,2

How common is it?
The incidence of perianal infection caused by group A S pyogenes is not known, but since the first case descriptions in 19663 it has been reported in children from around the world. In a US general paediatric practice, perianal streptococcal disease was detected in one consultation per 300, and perineal disease (that is, perianal plus vulvovaginal disease) in one per 200.1 A 1996 audit of our own practice (an urban British practice with 7000 patients and four full time general practitioners), found that 18 cases had been detected over two years by general practitioners highly aware of the condition—about one consultation per 1000 patients (children and adults combined). On this basis, the average general practitioner in the United Kingdom might expect to see childhood streptococcal perianal disease once or twice a year. It occurs in prepubertal children from infancy, with a peak incidence between the ages of 3 and 5 years.4

Why is it missed?
We conducted a postal survey of all general practitioners in north Oxfordshire in 1996 (table) using the presentation from the case scenario in this article. The findings showed that most respondents were not aware of streptococcal disease as a likely diagnosis despite a classic presentation with pain on defecation, erythema, and multiple fissures. The choice of treatments suggests that likely diagnoses were thought to be threadworm infestation, simple constipation, or fungal infection, with nine of the 54 respondents mentioning the possibility of sexual abuse. There is, however, no clear evidence that perianal redness and fissures should in themselves be taken as indicators of possible sexual abuse.5 The main reason that paediatric streptococcal perianal infection is missed in primary care may be lack of awareness.

Why does this matter?
The natural course of untreated perianal streptococcal infection in children is not known, but it is known that it can cause prolonged discomfort, toilet avoidance, and constipation,1,4,6 and given the findings of our 1996 survey we think it might raise unfounded suspicion of child abuse. From our survey and from several case series reports, it seems likely that inappropriate initial treatment is common. Infection can spread to siblings and other children7 and inadequate treatment may be followed by recurrence. Complications include local...
tissue spread and, less commonly, an illness similar to scarlet fever (guttate psoriasis) and glomerulonephritis.

**How is it diagnosed?**

**Clinical features**

Several case series describe the clinical features of perianal streptococcal infection, although variations in reporting make it difficult to specify the exact prevalence or the predictive value against the optimal bacteriological proof:

- Constipation: about half of cases
- Pain on defecation of recent onset: about half of cases
- Itching: a quarter of cases in one series and 78% and 100% in others
- Blood seen in stools: 20-35%
- Erythema: over 90% in most case series, although this is also common in asymptomatic children (41% in a descriptive study of 267 prepubertal, non-abused children). The erythema is often described as bright or “beefy” (figure). A distinct margin may be commoner in streptococcal infection
- Fissures: about a quarter in one series, absent in the normal child population
- Exudate and/or visible bleeding on examination: sometimes mentioned.

**Investigations**

Definitive diagnosis is by the growth of a pure culture of group A streptococcus from a perianal swab.

**How is it treated?**

External anal examination and gentle perianal swabbing should therefore be performed whenever a child presents with clinical features suggestive of this infection. Such examination does not cause distress in the great majority of non-abused preschool children.

### Responses of 54 (68% response rate)* general practitioners in north Oxfordshire to the case presented in the scenario cited in this article when asked: ‘What would be your management at this first consultation?’

<table>
<thead>
<tr>
<th>Suggested Management</th>
<th>No (%) of general practitioners</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treat with anthelmintics</td>
<td>29 (54)</td>
</tr>
<tr>
<td>Treat with antifungal cream</td>
<td>12 (22)</td>
</tr>
<tr>
<td>Treat with topical anaesthetics</td>
<td>15 (28)</td>
</tr>
<tr>
<td>Treat with topical antiseptics</td>
<td>6 (11)</td>
</tr>
<tr>
<td>Take a perianal swab</td>
<td>17 (31)</td>
</tr>
<tr>
<td>Treat with stool softeners</td>
<td>28 (52)</td>
</tr>
<tr>
<td>Treat with antifungal cream</td>
<td>12 (22)</td>
</tr>
<tr>
<td>Treat with anthelmintics</td>
<td>29 (54)</td>
</tr>
</tbody>
</table>

*“Free text” responses (outside the options suggested in the questionnaire) included looking for possible sexual abuse (9; 17%) and looking for inflammatory bowel disease (4; 7%).

*Questionnaires were sent to 80 general practitioners.

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A PATIENT'S JOURNEY

Polycystic kidney disease

K Schipper, Tineke A Abma, Ronald J Hené, Guy A M Widdershoven

Polycystic kidney disease is inherited, so most patients have seen how it has affected their relatives. Young adult patients have no symptoms and need no drugs, but kidney function will slowly deteriorate.

My family and PKD

My journey on the “PKD path” started when I was a child, but my family’s journey began earlier. My grandmother died of polycystic kidney disease (PKD), and my mother was diagnosed as having it shortly after my birth, after having a cerebrovascular accident, which she surprisingly survived. The doctor told her that she shouldn’t be afraid: “She would be able to raise her own kids.” He was right; she only started dialysis after several years of having nausea and tiredness.

When she started dialysis I was 16 years old. I always knew that my mother had a hereditary kidney disease and that I too might have it. But I hadn’t understood the consequences of the disease and its impact on life. I only knew that my mother needed to take her daily medicines and I always thought: “If this is PKD, then I can handle it. It’s not that bad to have a kidney disease.” I hadn’t known that haemodialysis and transplantation might be needed, and because of this I was deeply shocked when my mother started dialysis. I was worried about her: would she survive? But I was also confused, sad, and angry: “Why didn’t my parents tell me this before?”

Suddenly I was confronted with the impact of having a kidney disease and uncertainties about my own future. Probably my ignorance related to the fact that my parents didn’t like to talk about the disease. Their guiding philosophy was: “Don’t talk and complain about your problems, but get on and live your life. Emotions don’t help you to survive, so stay strong and go on.” Later my mother told me: “I didn’t want to know the truth, it was too intense. By putting it away, the disease wasn’t there and because of that I was able to survive and go on.” My parents always wanted us simply to be like other families. Looking back I now think this was impossible; we were not a normal family.

Having a relative with a chronic disease changes the child-parent relationship and the family.

After three years of dialysis my mother received a cadaver donor kidney. The months before she received the kidney were exciting and emotional. She was very ill, and dialysis was more and more problematic as her blood pressure was so low. Every day we were happy she was still alive.

People might think that her journey along the PKD path ended after the transplant. Unfortunately it did not: her patient journey goes on, on a path with side effects of medicines and sometimes fears for the future: “Will I be able to keep this kidney for a long time?” Her path has become easier now, but it still has difficulties.

Deciding to be tested

Because of the confrontation with the real impact of PKD I wished to know if I had it myself. After many conversations with my parents and professionals, however, I decided to postpone “the examination.” If tests showed I had the disease, I would undoubtedly have problems with my future—with insurance, for example, and with getting a job or a boyfriend. At that age it was difficult to get a reliable result; I was advised to wait until I was at least 18 years old.

The next few years were filled with doubts: did I want to know or not? When I was 20 I decided to have the test, but the day before the appointment I

What can medical professionals do?

- Provide information and support for the patient and the whole family, including partner and children, starting from the onset of the disease
- Information includes medical knowledge about the disease, but also practical knowledge of how to deal with the disease in daily life. Fellow patients are particularly helpful to share creative solutions for daily problems
- Medical specialists can provide an automatic referral to an association for renal patients to meet fellow patients
- Support also entails emotional support for accepting the disease and giving it a place in one’s life. Listening to the patient’s story is important to help them find meaning again, and to revalue their life with the disease
- Information and support also covers sensitive topics such as the desire to have children in relation to hereditary diseases
- Taking the patient seriously (concerns, fears, ideas), creating enough time, and a respectful and open attitude is helpful for patients
- Supporting the wish of a patient to remain active in society and life; letting the patient evaluate the risks
Slow progression, while allowing dose reduction and hence the incidence of side-effects. They influence different mechanisms, combining some of these agents may effectively influence the disease. Studies are underway, but adverse effects of these potent drugs are inevitable. Because of these complications, drugs become necessary to treat hypertension and the progressive failure. At any age by means of DNA analysis, the diagnosis is generally made by ultrasound in the late teens or early adulthood. Subsequently, many anxious years follow, even though young adult patients usually have no symptoms at all and need no drugs. Slowly, renal function deteriorates, drugs become necessary to treat hypertension and the progressive failure, at which point dialysis treatment or transplantation is inevitable. In families with a mutation in the gene coding for the protein polycystin-1, localised on chromosome 16, renal failure occurs at about age 50. In families with a mutation for the gene coding for polycystin-2 on chromosome 4, the disease may have a more lingering course.

Hypertension is common in ADPKD. Indeed, antihypertensive agents are currently the only accepted treatment. Other symptoms such as flank pain or fever are related to bleeding or infections of the renal cysts. The many extrarenal manifestations of the disease include early and severe diverticular disease of the colon, mitral valve prolapse, and intracranial aneurysms. The aneurysms, which occur in a subset of families, may lead to cerebral haemorrhage.

Until the 1960s, patients with ADPKD died at a young age because of uraemia or a ruptured intracranial aneurysm. Since then, renal replacement treatment has improved markedly: haemodialysis is much more bearable than it was 30 years ago and the results of (preferably pre-emptive) kidney transplantation have improved greatly. Furthermore, prophylactic, nearly non-invasive coagulation of the aneurysms has become feasible. As ADPKD is an inherited disease, most patients are conscious of its course and complications in their affected relatives. ADPKD is an autosomal dominant disease, so offspring having a 50% chance of being affected. Though the disease can be confirmed at any age by means of DNA analysis, the diagnosis is generally made by ultrasound in the late teens or early adulthood. Subsequently, many anxious years follow, even though young adult patients usually have no symptoms at all and need no drugs. Slowly, renal function deteriorates, drugs become necessary to treat hypertension and the progressive abnormalities in calcium-phosphate metabolism. A stage of life with haemodialysis or (pre-emptive) renal transplantation looms for ADPKD patients, more so than for other patients with progressive renal failure, who have not witnessed these dramatic events in their affected relatives when they were still children. Consequently most ADPKD patients are worried about their future. Many feel as if they are in a long tunnel, with renal replacement treatment waiting behind a closed door at its end.

What are the perspectives in the 21st century? The role of angiotensin converting enzyme inhibitors is still unclear. The HALT-PKD study is designed to test whether ACE inhibitors are superior to other antihypertensive agents in slowing down deterioration of renal function, but its results are still pending.

Fundamental research indicates that cyst formation is caused by ciliary dysfunction, followed by accelerated proliferation and dedifferentiation of the epithelium. Growth of the cysts is related to deterioration of renal function. This process may be slowed down by drugs inhibiting fluid and ion transport into the cysts (vasopressin receptor antagonists and basolateral K+ channel inhibitors). Another approach is inhibiting cell proliferation, for instance with rapamycin. Finally, gene therapy may correct inborn errors of metabolism. Studies are underway, but adverse effects of these potent drugs are inevitable. Because they influence different mechanisms, combining some of these agents may effectively slow progression, while allowing dose reduction and hence the incidence of side-effects. So, there may be a bright light at the end of the tunnel: ADPKD could one day become a treatable disease.

Ronald J Hené, consultant nephrologist

A DOCTOR’S PERSPECTIVE

Autosomal dominant polycystic kidney disease (ADPKD) is a common cause of renal failure, occurring in one person in every 500. Progressive renal damage leads to renal failure, at which point dialysis treatment or transplantation is inevitable. In families with a mutation in the gene coding for the protein polycystin-1, localised on chromosome 16, renal failure occurs at about age 50. In families with a mutation for the gene coding for polycystin-2 on chromosome 4, the disease may have a more lingering course.

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Ronald J Hené, consultant nephrologist
Helping hands along the way

- Support from friends and family
- Contact with fellow sufferers—both for empathy and for advice.
- My specialist in internal medical and my neurologist took me seriously and are respectful, straight, open, concrete, and understandable, taking time and being stringent or sensitive, depending on what I need at the moment
- The appreciation of my experience of the illness in my temporary job as research partner; I can relate to other patients with the condition, and thanks to the disease I’m now a PhD student

I sometimes feel sad and angry when people ask: “When are you going to have children?” The medical risks aren’t that great, and there are some new options like genetic selection, but for me this isn’t an option so the risk of heredity remains. We decided to give up our wish for children. People have tried to convince me of their own opinion, rather than respecting our choice. Also, people say: “Why are you upset, in the future there surely will be new technologies which will cure you” or “Everybody has problems, perhaps you will be fine.” They are trying to help, but it has the opposite effect, making me feel misunderstood and miserable. Accepting my feelings and just being there helps far more than offering “good advice.” On my sad days, I find it difficult to understand why my boyfriend would want to stay with me—he would be better off when finding a new, healthy girlfriend. He helps me most by giving me a big hug and not saying anything at all at these moments.

No longer an enemy

Gradually I have learnt that “putting the illness away and getting on with life” doesn’t help. In my research job I can talk to many fellow kidney patients and have developed a much more realistic picture of living with a kidney disease. Talking to fellow patients and relating their stories to mine has changed my perspective; I have become more aware of the negative and positive aspects of the disease. I’ve stopped trying to change irreversible things, and this makes me happier.

I used to tell people “I seem to have a kidney disease” or “They have told me I have a kidney disease.” The disease wasn’t part of me; I tried to keep it at a distance. It was an enemy, something negative, not a part of me that I had to accept and cope with. With the passing of time, the disease has become a part of me. Through my research, my self-esteem has grown and I use the knowledge gained through my experience within academia to help fellow patients.

Contributors: KS is a PhD student at VU Medical Center studying patient perspectives in clinical studies. TAA, KS’s supervisor, assisted her in developing her own voice, in eliciting experiences, and in the process of writing. RJH is Karen’s medical doctor. GAMW peer reviewed the article internally and made significant contributions to it.

Competing interests: None declared.

Provenance and peer review: Not commissioned; not externally peer reviewed.

10 MINUTE CONSULTATION

Genital warts

Elizabeth K Delaney,1 Steve Baguley2

A 19 year old heterosexual man attends the surgery complaining of “some spots down below.” They are not painful and he says he has no urethral discharge or scrotal pain. He has had a regular female partner for the past two years. On examination he has several warts on the shaft of his penis and no other abnormal findings.

What issues you should cover

History—Should be relevant for each individual patient. Does he have other symptoms? Ask about sexual activity in the past three months: timing and duration of relationships, sex and nationality of partners, condom use. Ask about any previous activity that would put him at risk of HIV—the main activities are sex with men and sex with someone from a country where HIV is relatively common. Is immunosuppression a factor (associated with poorer treatment responses, more relapses, and dysplasia)?

Implications—Anogenital warts, one of the commonest sexually transmitted infections in the UK, are disfiguring and can be psychologically distressing, so treat the patient sensitively. Over 90% of anogenital warts are caused by the human papillomavirus type 6 or 11 (rather than types 16 or 18, which are associated with cervical intraepithelial neoplasia), and for most people the infection is transient. Partner notification is not necessary, 20-30% of patients will have another sexually transmitted infection so appropriate screening should be discussed and offered.

Advice for the patient—Explain to the patient that genital warts are sexually transmitted and caused by a wart virus, and that they are common and relatively harmless. Although evidence is conflicting regarding the protective use of condoms and the acquisition of HPV infection and genital warts, condom use may be beneficial with his current partner at reducing...
re-exposure to the virus. He should also be advised to either use condoms or preferably avoid sexual contact with any new partners until the warts have gone. Explain that warts have a long latent period and that the recurrence of warts in one partner does not mean a recent infidelity.

What you should do

*Diagnosis*—Warts are generally diagnosed from physical appearance. Examine his genitalia in good light (in women, use a speculum to examine vagina and cervix).

*Differential diagnosis* includes molluscum contagiosum, epidermoid cysts, hair follicles, sebaceous glands, pearly penile papules, and, rarely, condylomata lata of secondary syphilis and (pre)malignant tumours. In women, remnants of the hymen and vulval papillomatosis (a variant of the normal vulva anatomy) can sometimes be mistaken for warts. If diagnosis is unclear, refer the patient to the genitourinary medicine department.

*Management*—The patient can be advised to attend the genitourinary medicine clinic for treatment and a sexually transmitted infection screen. Alternatively, he can be offered treatment and further testing by his general practitioner.

*Treating warts*—Correct treatment will speed clearance of the warts. Most treatments can be applied by the patient, thus avoiding repeated visits to the surgery. Ensure the patient fully understands the treatment, finding warts, and applying the cream or liquid. If there is any doubt, the general practitioner or practice nurse can supervise treatment. About 75% of people are clear of warts a month after starting treatment.

- A few warts only—first line treatment is freezing with liquid nitrogen; second line treatment depends on the site (see below).
- Many soft warts—for example, at vaginal introitus, underneath foreskin. First line treatment is podophyllotoxin 0.15% cream. Apply twice daily for three days, then have a four day break before resuming if warts persist. Use for a maximum of five weeks before review. Second line treatment is podophyllotoxin 0.5% liquid with same dosing as cream above, or imiquimod cream, applying half or whole sachet on alternate night, washed off after 6-10 hours. Use for maximum of 16 weeks with a review every four to six weeks.
- Many keratinised warts and site is accessible to patient—for example, the penile shaft. First line treatment is podophyllotoxin 0.5% liquid. Second line treatment is imiquimod cream.
- Perianal warts—first line treatment is imiquimod or liquid nitrogen. Refer to general surgeons if warts persist.
- Cervical warts—refer to your local colposcopy department.
- Urethral meatus—difficult to treat; refer to either genitourinary medicine or urology.

Warn patients that all treatments can cause discomfort and local skin reactions. If these are severe, they should stop treatment and seek advice. Advise patients to stop treatment once the warts disappear. If they are using podophyllotoxin, normal surrounding skin can be protected by applying some petroleum jelly.

Lesions larger than 4 cm must be treated under direct medical supervision. Giving no treatment is also an option, as warts can regress spontaneously.

If the patient is female, reassure her that cervical screening intervals can stay the same. Avoid imiquimod and podophyllotoxin in pregnancy, or if there is any risk of pregnancy.

*Investigations for other sexually transmitted infections*—Send off a urethral swab or a urine sample, ensuring the patient has not urinated in the past one to two hours, for chlamydia and gonorrhoea. Offer tests for HIV, syphilis, hepatitis B and C, as indicated by his sexual history. All positive results can be referred to genitourinary medicine or the chlamydia screening office for follow-up. See the RCGP/BASHH primary care guideline [http://www.bashh.org/documents/702/702.pdf] for additional advice.

*Follow-up*—About 20% of patients have a recurrence in the following three months. If the warts are visible and you are confident that the patient can identify them correctly, then follow-up is usually unnecessary. Review if the warts persist or if the patient has side effects from treatment.

FURTHER READING


RCGP Sex, Drugs and HIV Task Group and BASHH. Sexually Transmitted Infections in Primary Care (March 2006) http://www.bashh.org/documents/702/702.pdf

Patient UK. Anogenital warts (www.patient.co.uk/showdoc/23069188)—comprehensive patient information leaflet

Contributors: EKD came up with original idea for writing the article. Both EKD and SB co-wrote the paper. EKD responded to and amended changes by the original two reviewers, all of which were checked by SB.

Competing interests: None declared.

Provenance and peer review: Commissioned; externally peer reviewed.
Consider optic disc drusen in optic disc swelling to ensure appropriate investigations and management

We report a patient with optic disc drusen, a common anomaly that may mimic papilloedema (swelling of the optic discs as a result of raised intracranial pressure). We suggest that optic disc drusen (globular collections of calcific material in the optic nerve head) should be considered routinely in the differential diagnosis of bilateral optic disc swelling. Although optic disc drusen may coexist with papilloedema, awareness of the former will help to direct appropriate investigations and management.

Case report
A 6 year old girl was referred urgently to our ophthalmology department with a one month history of headache and the finding of swollen optic discs in both eyes. The referring optometrist was concerned that the patient might have papilloedema.

The patient reported that her headache was intermittent, frontal, and associated with nausea. She denied vomiting or visual problems, including transient visual obscurations (sudden blanking of vision lasting seconds) and double vision. Apart from wearing glasses with a small hyperopic prescription, she had no previous ophthalmic or medical history of note. She was not taking any medication.

On examination, her pupils were dilated after pharmacological dilatation by the referring optometrist. Consistent with the expected effect of pupillary dilatation, the visual acuity with glasses was 6/9 in each eye. She had no visual field defect to confrontation, and colour vision was normal. Ocular movements were full, and the rest of the cranial nerve examination was unremarkable. Funduscopy showed swollen optic discs in both eyes, with anomalous branching of the retinal vasculature (fig 1). We started investigations to determine whether optic disc drusen were present.

Fundus photography using special camera filters showed patchy autofluorescence of the optic discs (fig 2). This phenomenon represents the emission of light of wavelength 530 nm from optic disc drusen when exposed to light of wavelength 490 nm.

The patient had ophthalmic ultrasonography two days later. This showed gross optic disc drusen in both eyes (fig 3).

A few days later, visual acuity tested without pharmacologically dilated pupils was 6/6 in each eye. There was no relative afferent pupillary defect. Optical coherence tomography, a non-invasive imaging technique, was used to generate a three dimensional, cross sectional map of each elevated optic disc (fig 4). This showed no obvious swelling of the peripapillary retina.

The appearances of the optic discs and the investigations established the diagnosis of optic disc drusen. Owing to the patient’s history of headaches, magnetic resonance imaging of her head was arranged; this was normal. The headaches resolved spontaneously within a few weeks, and the patient has remained asymptomatic over subsequent months.

Discussion
It is important to consider the diagnosis of optic disc drusen in any patient presenting with swollen optic discs. Provided that there are no features suggesting...
Coexisting papilloedema, the timely diagnosis of optic disc drusen eliminates unnecessary tests for raised intracranial pressure. Investigations for raised intracranial pressure include computed tomography of the head, with its potential morbidity from radiation exposure, or magnetic resonance imaging. If neuroimaging shows no abnormality, lumbar puncture is performed. This is invasive and subject to complications. Importantly, early diagnosis of isolated optic disc drusen spares the patient unnecessary anxiety about intracranial disease.

Optic disc drusen may coexist with papilloedema. Other conditions may contribute to actual or apparent swelling of the optic discs, including bilateral compressive thyroid ophthalmopathy, bilateral anterior ischaemic optic neuropathy, optic neuritis, hyperopia, glial anomalies, and Bergmeister’s papilla. Consequently, swollen optic discs accompanied by features of papilloedema or another optic neuropathy require investigations for these possibilities, even if optic disc drusen are present.

Nevertheless, it is important to identify optic disc drusen at an early stage and to investigate further only if comorbidities are suspected. Input from a multidisciplinary team, including ophthalmologists and neurologists, may help. The aim is to minimise iatrogenic morbidity while ensuring that sinister conditions such as papilloedema are not overlooked. In the present case, neuroimaging excluded an intracranial space-occupying lesion, and further investigations were not required because the patient’s headaches resolved spontaneously and with no evidence of optic neuropathy. For patients in whom coexisting disease is diagnosed, the knowledge that optic disc drusen will cause the discs to appear persistently swollen is valuable during subsequent management.

Recent reports have highlighted how optic disc drusen may masquerade as papilloedema in adults and children. In children, optic disc drusen may be buried beneath the surface of the optic disc and not visible ophthalmoscopically, unlike the exposed disc drusen found in adults. However, the optic discs may still appear swollen, so children are particularly vulnerable to misdiagnosis.

Optic disc drusen occur in 0.3% to 2% of the population, are bilateral in two thirds of cases, and have no bias according to sex or association with refractive error. Whether optic disc drusen are inherited is disputed. They are, however, associated with certain ophthalmic conditions, such as retinitis pigmentosa and angioid streaks, and can cause sight threatening complications such as visual field loss. The drusen may develop when crowding of optic axons at congenitally small optic discs causes interruption of axoplasmic transport. A recent study has questioned this hypothesis.

Optic disc drusen evolve from early childhood. They are initially buried beneath the surface of the optic disc and produce disc elevation. From about age 12, the drusen become exposed at the surface of the disc. As optic disc drusen might be inherited, it may be useful to examine both parents for exposed drusen when buried drusen are suspected in a child.

Unlike isolated optic disc drusen, papilloedema may be associated with symptoms and signs of raised intracranial pressure: progressively worsening headache that is characteristically worse in the morning; nausea...
and vomiting; deterioration of consciousness; transient visual obscurations; and double vision.1,2 The blind spot may be enlarged, but central visual acuity is often reduced late in papilloedema. Exposed drusen appear ophthalmoscopically as round, reflective excrescences at the disc surface. Although it is quite difficult to distinguish between true papilloedema and the pseudopapilloedema associated with buried drusen, their detailed appearances differ.18 Papilloedema is associated with hyeremia of the disc; swelling of the peripapillary retina that obscures the peripapillary retinal vasculature; and sometimes cotton wool spots, exudates, and venous congestion. These signs are absent with buried drusen, although anomalous retinal venous pulsations are often found, including an increased number of vessels, abnormal branching, and increased tortuosity. Peripapillary haemorrhages may occur with both conditions. The presence of spontaneous retinal venous pulsations makes the diagnosis of papilloedema less likely, but does not exclude it.19 Spontaneous retinal venous pulsations are present in most, but not all, normal subjects.

Several tests help in diagnosing optic disc drusen. Both buried and exposed drusen may show the phenomenon of autofluorescence, which can be recorded using a special fundus camera.20 They are echobright on ophthalmic ultrasonography because of their calcium content.1 For the same reason, the drusen can be shown by computed tomography, though this technique is less sensitive than ultrasonography and involves radiation.21 Other investigations include optical coherence tomography,22 which is the optical analogue of ultrasonography, and scanning laser ophthalmoscopy.23 Fundus fluorescein angiography, in which intravenously injected fluorescein is tracked in its passage through retinal blood vessels, is a means of differentiating papilloedema from pseudopapilloedema.24 This test carries a small risk of anaphylaxis, however, and is not usually needed.1

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**DRUG POINT**

**Strontium ranelate may cause alopecia**

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From May 2005 to January 2008, the Spanish pharmacovigilance system received 56 reports in which strontium ranelate, a drug intended for the treatment of osteoporosis, was associated with different adverse reactions; five of them (8.9%) were reports of alopecia (table; figure). From the start of pharmacovigilance activities in Spain in 1982 up to January 2008, 102,540 reports were collected, of which 393 (0.4%) were cases of alopecia; the corresponding reports for postmenopausal women were 39,640, of which 205 (0.5%) cases were of alopecia.

Inorganic strontium has traditionally been a component of depilatory creams.1 Despite limitations as a result of under-reporting, there is a significant statistical association between intake of the drug and onset of alopecia that is greater than that for drugs well known to induce alopecia. As these are the first reported cases of alopecia presumed to have been induced by strontium ranelate, a “notoriety bias” is unlikely to account for this finding; neither are there reasons to think that this drug was prescribed to women prone to develop alopecia. Thus, the temporal sequence, the improvement of most cases after drug withdrawal, and the exclusion of other causes allow us to reasonably suspect a causal relation. In the United Kingdom seven other cases of alopecia related to strontium ranelate have been recorded (www.mhra.gov.uk).

Bisphosphonates are commonly used for treating osteoporosis. Fears of serious adverse effects, such as necrosis of the jaw2 and severe pain,3 might account for women being switched to strontium ranelate, which could put them at risk of developing alopecia. Although alopecia is not life threatening or disabling, it can have serious adverse effects on self esteem, psychological wellbeing, and body image in women.4 Alopecia induced by strontium ranelate should be further investigated. Meanwhile, physicians should not underestimate the importance of alopecia as a cosmetic problem or as a sign of a potentially serious hypersensitivity syndrome in susceptible women.

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Alopecia in case 3 (see table). This was accompanied by some features compatible with those of Stevens-Johnson syndrome; the European Medicines Agency recently issued a warning of severe hypersensitivity syndromes, sometimes fatal, in patients treated with strontium ranelate. Alopecia may be one symptom of a more complex and severe hypersensitivity syndrome.

### Cases of alopecia associated with use of strontium ranelate reported to the Spanish pharmacovigilance system, 2005-8

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Other adverse reactions</th>
<th>Induction period (days)*</th>
<th>Other drugs</th>
<th>Investigations</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>51</td>
<td>No</td>
<td>20</td>
<td>No</td>
<td>Normal</td>
<td>Slow recovery</td>
</tr>
<tr>
<td>2</td>
<td>74</td>
<td>No</td>
<td>1</td>
<td>No</td>
<td>No data</td>
<td>Recovery</td>
</tr>
<tr>
<td>3</td>
<td>57</td>
<td>Eczema; skin exfoliation; conjunctivitis; diarrhoea; dyspepsia</td>
<td>45</td>
<td>No</td>
<td>Normal</td>
<td>No recovery†</td>
</tr>
<tr>
<td>4‡</td>
<td>54</td>
<td>No</td>
<td>40</td>
<td>Levothyroxin; lisinopril; simvastatin</td>
<td>Normal</td>
<td>Recovery</td>
</tr>
<tr>
<td>5¶</td>
<td>54</td>
<td>No</td>
<td>30</td>
<td>Citalopram; lorazepam; flunitrazepam; dipyrone; calcium plus colecalciferol</td>
<td>No data</td>
<td>Recovery</td>
</tr>
</tbody>
</table>

All cases in women; all doses of strontium ranelate were the usual 2 g a day. Reporting odds ratios and 95% CIs for strontium ranelate compared with estimates for other drugs known to induce alopecia in postmenopausal women were 14.2 (5.4 to 37.3) for strontium ranelate; 91.8 (21.8 to 387.0) for acitretin; 4.7 (1.7 to 12.7) for methotrexate; 3.0 (0.4 to 21.8) for doxorubicin and 2.4 (0.3 to 17.2) for valproic acid.

*Corresponding start and stop dates: case 1, 5 April 2006 and 10 November 2006; case 2, 30 May 2006 and stop date unknown; case 3, 1 July 2006 and 18 September 2006; case 4, 10 April 2007 and 6 June 2007; case 5, October 2007 and stop date unknown.

†Not recovered at three months after withdrawal of drug.

‡Patient was being treated with other drugs from 2005 onwards because of hypothyroidism, hypertension, and hypercholesterolaemia.

¶Patient was being treated with other drugs for depression, insomnia, and pain; no information on start or stop dates for these drugs.