TEACHING CASE REPORT

Transient monocular visual loss and retinal migraine

The Case: A 40-year-old man was referred because of multiple events of transient monocular visual loss since adolescence. He described the events as small, translucent, grey-coloured spots similar to those seen after looking at a bright light. These visual defects affected both of his eyes equally in frequency but never simultaneously (i.e., each episode was monocular). Episodes lasted about 5–10 minutes, occurred 2–3 times a day on average and were often associated with migrainous headaches, which began within 30 minutes after the onset of the visual symptoms. The headaches were described as unilateral, pounding, lasting up to 4 hours, and sometimes associated with nausea, vomiting, photophobia and phonophobia. On 1 or 2 occasions the headaches also coincided with unilateral jaw and arm numbness, and scintillating scotoma. Although the headaches responded well to ibuprofen, the visual symptoms did not.

On examination, the patient's visual acuity was 20/20 (6/6) in both eyes, and the intraocular eye pressure was 14 mm Hg bilaterally (normal pressure 10–20 mm Hg). Gross examination of the visual fields by confrontation yielded normal findings, as did the rest of the ophthalmologic and the neurologic examinations. Comprehensive blood work revealed only mild hyperlipidemia. Electrocardiography demonstrated sinus rhythm, and neither carotid duplex Doppler ultrasonography nor transthoracic echocardiography revealed any abnormalities. Retinal migraine was diagnosed, and daily therapy with ASA and verapamil was started. The frequency of events of transient visual loss decreased from 2–3 attacks per day to 2–3 attacks per week.

Retinal migraines are transient monocular visual disturbances (scintillations, scotomas or blindness) that can occur simultaneously with migraine headaches or in a patient with a prior history of migraines. They occur because of hypoperfusion of either the eye or the optic nerve. This is in contrast to typical migraine with aura (previously known as classic migraine), which involves the cerebral cortex and is therefore associated with binocular visual phenomena. The International Headache Society's definition of retinal migraine is given in Box 1.[1] The society's definition is limited because it does not account for patients who have visual symptoms without headaches or who have permanent visual scotomas; although rare, both of these presentations have been well documented in the literature.

Retinal migraine affects about 1 of every 200 patients who have migraines. At the time of diagnosis, most patients are less than 40 years old. Nearly 30% have a past history of nonretinal migraine with or without aura, and 25% have a relative with retinal migraines.

Clinically, retinal migraine has a highly variable presentation. Some patients describe primarily negative symptoms (visual loss) consisting of black, grey, white or shaded areas of varying size that may appear instantaneously or gradually progress inward from the peripheral visual field. Others describe positive symptoms such as flashing lights or scintillating scotomas. Symptoms are always monocular. Most events are transient, lasting from 5–20 minutes, and may occur several times a day. When headaches occur in association with the visual changes, they may occur either during or after the visual disturbances.

Specific precipitants for attacks are often unclear. Although the natural history of retinal migraine has not been well studied, the prognosis appears to be similar to that of typical migraine with aura. Symptoms may go into permanent remission after several months or years, they may go into remission but recur at a future date, or they may persist lifelong.

The diagnosis of retinal migraine is by exclusion. The differential diagnosis of transient monocular visual loss is

Box 1: Diagnostic criteria for retinal migraine and migraine without aura[1]

Retinal migraine

A. At least 2 attacks fulfilling criteria B and C
B. Fully reversible monocular positive and/or negative visual phenomena (e.g., scintillations, scotomata or blindness) confirmed by examination during an attack or (after proper instruction) by the patient's drawing of a monocular field defect during an attack
C. Headache fulfilling criteria B–D for migraine without aura that begins during the visual symptoms or follows them within 60 minutes
D. Normal ophthalmologic examination between attacks
E. Not attributed to another disorder

Migraine without aura

A. At least 5 attacks fulfilling criteria B–D
B. Headache attacks last 4–72 hours (untreated or unsuccessfully treated)
C. Headache has at least 2 of the following:
   - Unilateral location
   - Pulsating quality
   - Moderate or severe pain intensity
   - Aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)
D. During headache, at least 1 of the following occurs:
   - Nausea and/or vomiting
   - Photophobia and phonophobia
E. Not attributed to another disorder

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Box 2: Differential diagnosis of transient monocular visual loss

- *Embolism* (carotid, cardiac or aortic source): Usually is nonrecurring event
- *Increased intracranial pressure:* Usually causes bilateral symptoms and papilledema
- *Orbital apex mass:* Usually is accompanied by other signs (e.g., proptosis, abnormal eye movements)
- *Optic neuritis* (e.g., multiple sclerosis): Usually evolves gradually over hours to days and resolves over days to weeks
- *Giant cell arteritis, other vasculitides:* Usually occurs in elderly patients with temple tenderness, jaw claudication and polymyalgia rheumatic symptoms
- *Migraine:* Visual symptoms are bilateral (homonymous hemianopsia) because of occipital cortex involvement
- *Anterior ischemic optic neuropathy:* Usually affects older patients with multiple atherosclerotic risk factors (e.g., hypertension, diabetes mellitus)
- *Retinal migraine:* Diagnosis of exclusion
- *Increased viscosity* (e.g., polycythemia vera, leukemia, lymphoma, dysproteinemia): Is investigated with routine blood work
- *Optic disk coloboma:* Is visible on ophthalmoscopy
- *Optic disk drusen:* Is visible on ophthalmoscopy

given in Box 2. A careful history and physical examination are required, often in conjunction with appropriate investigations, including a complete blood count, erythrocyte sedimentation rate, prothrombin and partial thromboplastin times, electrocardiography, carotid duplex Doppler ultrasonography, transthoracic echocardiography and, if an arrhythmia is suspected, a Holter monitor. A work-up for hypercoagulable states is often indicated if the personal or family history is suggestive. Signs that should raise clinical suspicion of retinal migraine are listed in Box 3.

Management is often done in collaboration with a neurologist or an ophthalmologist. Formal baseline visual field testing is advisable; abnormalities may indicate a need for additional investigation or closer follow-up. If the episodes of transient visual loss have been infrequent, management is often conservative, with reassurance and simple follow-up. Although no guidelines are available, we recommend prophylactic therapy if the episodes are disabling or occur more than twice per week. Low-dose daily ASA therapy is well tolerated and has been reported anecdotally to be effective. Although randomized trials of therapies are lacking, anecdotal reports have suggested that calcium-channel blockers such as verapamil and nifedipine,[2] β-blockers[3] and inhaled amyl nitrate therapy[4] may be effective for prophylaxis.

Box 3: Signs suggestive of retinal migraine

- Age < 40 yr
- Prior history of migraine
- Personal or family history of full recovery after prolonged visual loss
- Recurrent transient episodes in a single day
- Negative diagnostic work-up for other causes of transient monocular visual loss (see Box 2)

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REFERENCES

1. Headache Classification Subcommittee of the International Headache Society. The international classification of headache disorders: 2nd edition. *Cephalalgia* 2004;24(Suppl 1):9-160.
2. Winterkom JMS, Kupersmith MJ, Wirtschafter JD, et al. Brief report: treatment of vasospastic amaurosis fugax with calcium channel blockers. *N Engl J Med* 1993;329:396-9.
3. Kline LB, Kelley CL. Ocular migraine in a patient with cluster headache. *Headache* 1980;20:253.
4. Walter JR, Birchfield WJ. Ocular migraine in a young man resulting in unilateral blindness and retinal oedema. *J Pediatric Ophthalmol* 1971;8:173-6.

PUBLIC HEALTH

'Tis the season: meningococcal disease

Background and epidemiology: Invasive meningococcal disease (IMD) is endemic in Canada, with 2 cases per 100 000 population per year. IMD is more common among young children (≥ 1 year old); incidence declines with age, except for a peak among adolescents (15–19 years). The majority of cases occur during the winter months.[1]

IMD is caused by *Neisseria meningitidis*, a gram-negative coccus. There are 5 main serogroups: A, B, C, W135 and Y. Serogroups B and C are responsible for most endemic disease in Canada: group C accounts for almost half of meningococcal disease during years having outbreaks, and about 30% at other times.[2] Serogroups A, W135 and Y cause disease primarily among international travellers. About 10% of cases of meningococcal disease are fatal,[2] with a higher rate for meningococcal C infections.[1]

Clinical management: IMD usually presents as meningitis or septicemia, and on occasion as orbital cellulitis and septic arthritis. It can progress rapidly to shock and death. Symptoms of meningitis include high fever, headache, stiff neck, vomiting and drowsiness. People may also display photophobia, confusion and nonblanching purpura. Long-term effects such as deafness, seizures and requirements for amputation occur in about 10% of infected patients.[2]

Patients with probable or confirmed meningococcal meningitis need treatment with empiric antibiotics immediately; third-generation cephalosporins are a common choice as the first-line agent. As treatment begins, patients should be kept in respiratory isolation for 24 hours. If the antibiotic used is inadequate to correct nasopharyngeal colonization with *N. meningitidis*, then that should also be treated.[1]

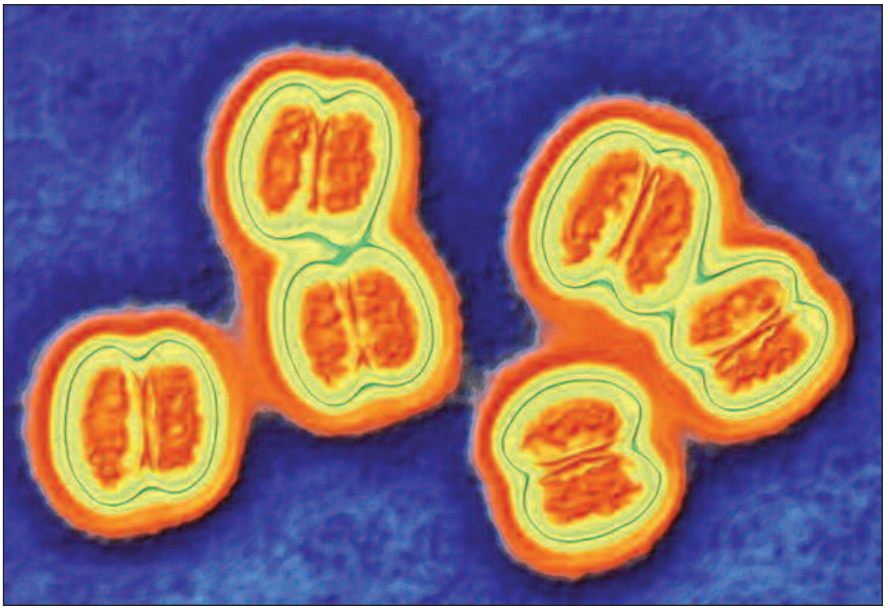
Probable or confirmed cases must be reported to public health authorities. Box 1 outlines updated case definitions of IMD, effective from Jan. 1, 2006.

Diagnosis: A culture of *N. meningitidis* from blood, cerebrospinal fluid (CSF) or sterile site fluid (e.g., joint fluid) is diagnostic for IMD. Samples are best taken before antibiotic therapy, but treatment should not be delayed for testing or to wait for results. Polymerase chain reaction (PCR) testing of blood or CSF samples, which allows rapid diagnosis and serotyping, is also possible. PCR has greater sensitivity than culture, particularly if antibiotics have already been started.[1] Latex agglutination antigen testing is also used. Meningococcal isolates should be sent to the provincial or territorial laboratory for serogrouping and antibiotic susceptibility testing.

Contact management: About 10% of people carry *N. meningitidis* in their nasopharynx at any given time. Because others are at risk of colonization with the bacteria that caused the IMD being treated, everyone in close contact during the incubation period (7 days before symptom onset to 24 hours after the start of effective treatment), regardless of immunization status, should be offered clearance antibiotics to reduce nasopharyngeal carriage and prevent further spread in the community (Box 2). Table 1 lists appropriate agents for chemoprophylaxis.

Clearance antibiotics should be given within 24 hours of diagnosis, although they may be given up to 10 days after the last contact with the index case. Clearance antibiotics should likewise not be delayed for laboratory results.

People who have had close contact are also at increased risk of IMD, since clearance antibiotics do not prevent disease in a person in whom IMD is al-



PLoS

Neisseria meningitidis, cause of invasive meningococcal disease.

Box 1: Case definitions* of invasive meningococcal disease

Confirmed case — Invasive disease with laboratory confirmation of infection, by either of these means:

- Isolation of *Neisseria meningitidis* from a normally sterile sample site (e.g., blood, CSF or joint, pleural or pericardial fluid)
- Demonstration of *N. meningitidis* DNA by appropriately validated NAT from a normally sterile site

Probable case — Invasive disease with purpura fulminans or petechiae and no other apparent cause, in the absence of either factor bulleted above, with or without a finding in CSF of *N. meningitidis* antigen

Note: CSF = cerebrospinal fluid, NAT = nucleic-acid amplification technology.
*Adapted from *Can Commun Dis Rep* 2005; 31S1:1-20,[1] available at www.phac-aspc.gc.ca/publicat /ccdr-rmtc/05vol31/31s1/index.html (accessed 2005 Oct 6).

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Box 2: People considered* to have close contact† with someone infected with invasive meningococcal disease

- Members of the same household
- Anyone sharing a sleeping area
- Anyone with direct nose or mouth contamination with oral or nasal secretions of an infected person (e.g., kissing on the mouth or sharing cigarettes or drinking bottles)
- Health care workers with intensive unprotected contact (e.g., intubation or resuscitation) with an infected patient
- Other children and staff in child care and nursery school facilities
- Airline passengers who sat immediately beside an infected person (but not across the aisle) on trips taking 8 hours or longer

*Adapted from *Can Commun Dis Rep* 2005;31 S1:1-20,[1] available at www.phac-aspc.gc.ca /publicat/ccdr-rmtc/05vol31/31s1/index .html (accessed 2005 Oct 6).
†During the incubation period or early symptomatic phase of the infection.

Table 1: Chemoprophylaxis for close contacts of people with IMD*

Drug and dosage	Comment
Ciprofloxacin, 1 dose PO • Adults (≥ 18 yr): 500 mg	Contraindicated during pregnancy and lactation Approved for adults only; not recommended for prepubertal children
Rifampicin, 4 doses PO q 12 h • Adults: 600 mg • Children (≥ 1 mo): 10 mg/kg (to a maximum of 600 mg) • Infants (< 1 mo): 5 mg/kg	Contraindicated in pregnancy Urine and tears may be stained red, which may also stain contact lenses Can reduce effectiveness of oral contraceptives
Cetriaxone, 1 dose IM • Adults: 250 mg • Children: 125 mg	The recommended drug for pregnant women Alternative for people who cannot tolerate oral medication Dilute in 1% lidocaine to reduce pain of injection

Note: IMD = invasive meningococcal disease, PO = by mouth, q = every, IM = intramuscular.
*Adapted from *Can Commun Dis Rep* 2005;31S1:1-20,[1] available at www.phac-aspc.gc.ca/publicat/ccdr -rmtc/05vol31/31s1/index.html (accessed 2005 Oct 6).

ready developing. Such people should be advised to seek medical attention immediately if they develop a fever or an IMD-type illness. For those who are susceptible, vaccination is also recommended and may further reduce the risk of secondary cases.[1]

Vaccination: Vaccines against meningococcal disease either are directed against several serogroups (e.g., Men-ACYW-P for serogroups A, C, Y and W135) or are conjugate meningococcal vaccines with activity only against meningococcal C.

Meningococcal C conjugate vaccine is recommended for all children. They should receive three doses, at ages 2, 3 and 4 months. Older children (5 months to 18 years) were vaccinated as part of a catch-up vaccination program with these recommendations, introduced in 1999. Vaccine effectiveness has been estimated at 87%–98%, with no significant differences across age groups.[3] Because data for meningococcal C vaccination have been available for less than 5 years, the need for revaccination is currently unclear.

Polysaccharide vaccines against multiple serogroups have a shorter duration of protection and are not immunogenic for children younger than 2 years.[1] They are recommended for outbreak control, travellers to places where IMD is endemic or epidemic, and suspectible close contacts of patients with known relevant serogroup disease. They are not recommended for routine vaccination.

No vaccine is currently available in Canada for serogroup B disease.

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REFERENCES

1. Public Health Agency of Canada. Guidelines for the prevention and control of meningococcal disease. *Can Commun Dis Rep* 2005;31S1:1-20. Available: www.phac-aspc.gc.ca/publicat/ccdr-rmtc /05vol31/31s1/index.html (accessed 2005 Oct 6).
2. Meningococcal vaccine. Ottawa: Health Canada. Available: www.hc-sc.gc.ca/iyh-vsv/med/mening _e.html (accessed 2005 Oct 6).
3. National Advisory Committee on Immunization. Update on meningococcal C conjugate vaccines. *Can Commun Dis Rep* 2005;31(ACS3):1-4. Available: www.phac-aspc.gc.ca/publicat/ccdr-rmtc /05pdf/acs-dcc3103.pdf (accessed 2005 Oct 6).

Clinical Vistas

A case of painful elbow: What's your diagnosis?

DOI:10.1503/cmaj.051162

The Case: A 29-year-old male who had previously been healthy discovered, upon awakening, swelling and pain over the left olecranon. Despite numerous complaints to his wife, this condition was ignored for several hours. The pain increased steadily over this period, during which the left elbow developed a large golf-ball appearance, resulting in a large amount of self-pity.

The patient immediately sought the help of 2 family physicians. He was observed to favour the left arm rather dramatically and repeatedly entreat sympathetic responses from bystanders.

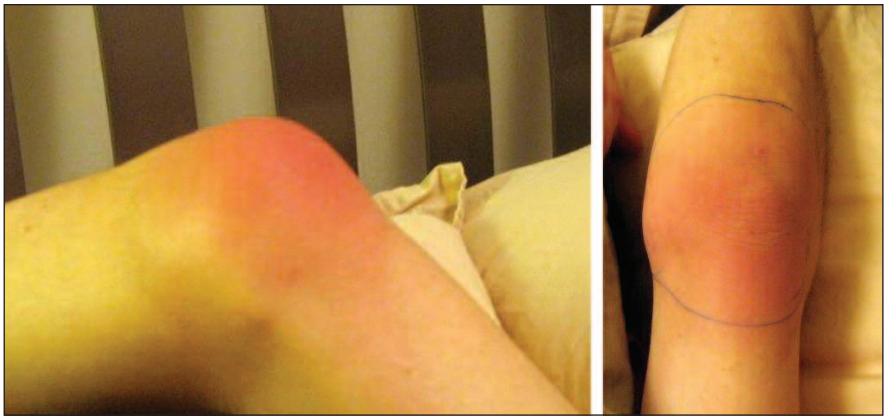

Fig. 1: Patient's right elbow.

The left elbow was erythematous and swollen, tender and warm to the touch. The area of erythema had spread to much of the soft tissue surrounding the olecranon (Fig. 1).

What is your diagnosis? What do you think caused the problem?

Answer on page 1446

"Playboy Rabbit" sign: What's your diagnosis?

DOI:10.1503/cmaj.050428

The Case: A 35-year-old, otherwise healthy woman arrived with complaints of shortness of breath and abdominal pain. Results of a physical examination, electro- and echocardiography, and chest radiography were all normal. An ultrasound scan of the liver was done (Fig. 1). What is your diagnosis?

Answer on page 1446

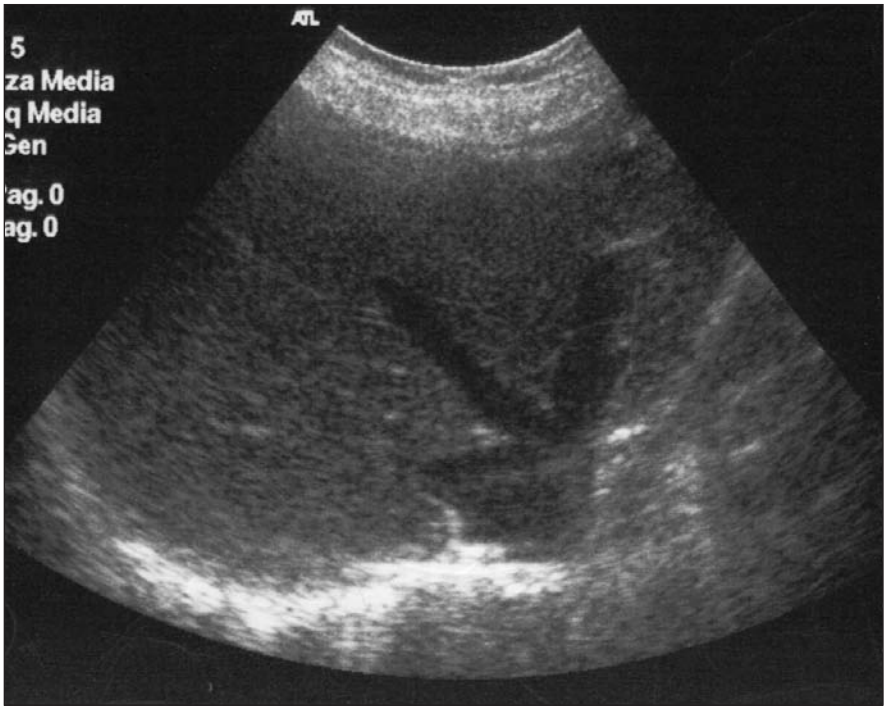

Fig. 1: Ultrasound image of the patient's liver.

Answer to Clinical Vistas:

A case of painful elbow

The Diagnosis: After considering the patient's primary occupation (Fig. 2), both examining clinicians (on separate occasions) diagnosed olecranon bursitis and prescribed cephalexin 500 mg QID and celecoxib 200 mg OD. Despite the certainty of these 2 physicians of their diagnosis, the patient sought the opinions of a rheumatologist, a rheumatology fellow, a nephrology fellow, a cardiology fellow, 3 endocrinologists, 3 internal medicine residents, a clinical clerk, a ward aide, and anyone else he ran into that day. After at least 14 concurring opinions, the patient accepted the diagnosis.

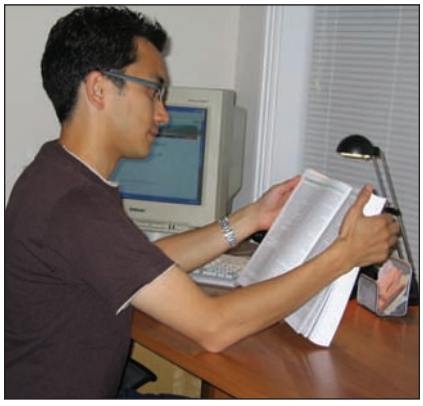

Fig. 2: The patient (D.H.S.) studying for his Royal College exams.

Over the next 48 hours, the patient's symptoms increased, and he began to show signs of a delusional state, babbling on about necrotizing fascitis devouring his left arm. He entered a panicky state, describing visions of trying to hold Harrison's or demonstrating physical examination techniques with one arm.

After 48 hours, the swelling began to stabilize and regress; and as the physical symptoms resolved, the patient's delusional state returned to normal. After receiving careful instruction not to lean on his elbows, the patient recovered sufficiently to continue his studying, although whining behaviour persisted for some weeks.

This case represents an underreported hazard of residency training. Much publicity has surrounded the effect of long hours on residents' health,[1–3] but the hazards of academic and licensing examinations have received little media attention. Although associated with increased stress, insomnia, weight gain and loss of social skills, studying for exams (sometimes called "cramming") has never before been reported as a cause of infectious complications. We, the authors, believe more attention should be given to this important area, as it may prevent future incidents and unnecessary clinical and spousal stress. Future Royal College prep sessions should include warnings about the dangers of Royal College bursitis, and the prophylactic possibilities of elbow pads.

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REFERENCES

1. Barger LK, Cade BE, Najib MS, et al. Extended work shifts and the risk of motor vehicle crashes among interns. *N Engl J Med* 2005;352:125-34.
2. Daugherty SR, Baldwin DC, Rowley BD. Learning, satisfaction, and mistreatment during medical internship. *JAMA* 1998;279:1194-9.
3. Thomas NK. Resident burnout. *JAMA* 2004;292: 2880-9.

Answer to Clinical Vistas:

"Playboy Rabbit" sign

The Diagnosis: The ultrasound scan showed a rabbit-shaped image caused by the confluence of the middle and right hepatic veins. The strongly suggestive image, also known as Mumoli's sign (named after the senior author), shows the hepatic veins joining together into the inferior vena cava. It is highly reproducible with a transverse subcostal view in deep inspiration during ultrasound scanning of the normal liver.

We were unable to find any previous report describing a rabbit-like sign.

The patient was given assurance that she had no physical abnormality and was discharged with a diagnosis of anxiety. Indeed, the woman returned immediately to her work as a waitress in a nightclub.

In the preface to the first edition of his *Principles of Internal Medicine*, Tinsley R. Harrison stated that physicians need "technical skill, scientific knowledge, and human understanding ... courage, humility, and wisdom."[1] Although these words have proven true many times, we believe that a little bit of curiosity and humour can help physicians to face their heavy duty to serve the suffering human being.

And sometimes, upon receiving the results of an imaging scan, one simply has to do a double-take.

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Competing interests: None declared.

HEALTH AND DRUG ALERTS

Suicidal ideation among children taking atomoxetine (Strattera)

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Reason for posting: As a nonstimulant, atomoxetine is a popular new treatment for attention-deficit hyperactivity disorder (ADHD). However, the US Food and Drug Administration and Health Canada recently warned of increased rates of suicidal ideation among children taking the drug in placebo-controlled trials. This comes in addition to postmarketing reports of suicidal ideation in and suicide attempts and completed attempts by some children and adults given the drug.[1]

Box 1: Adverse effects of atomoxetine

Serious effects

- Hepatotoxicity
- Sedation, impaired motor skills
- Suicidal thoughts or actions
- Weight loss or slowed growth

Effects common among children

- Decreased appetite
- Dizziness
- Fatigue
- Gastrointestinal upset
- Mood swings
- Nausea, vomiting

Effects common among adults

- Appetite decline
- Constipation
- Appetite decline
- Dry mouth
- Dysmenorrhea
- Erectile or ejaculatory dysfunction
- Nausea
- Sleep problems
- Urinary hesitancy

Adapted from the US Food and Drug Administration patient information handout available at www.fda.gov/cder/drug/infopage/atomoxetine/default.htm (accessed 9 Nov 2005).

The drug: ADHD is hypothesized to involve altered central dopaminergic and noradrenergic tone, and atomoxetine acts as a selective norepinephrine reuptake inhibitor. It is metabolized in the liver by the CYP2D6 enzyme, glucouronidated and then excreted renally. Depending on whether the patient carries a polymorphism of CYP2D6 that makes him or her a "poor metabolizer" (about 5%–10% of patients), the drug's half-life ranges between 5 and 22 hours.[2] It is more effective than placebo but may be less effective and slower-acting than stimulants such as methylphenidate.[3] Serious and common adverse effects of atomoxetine are listed in Box 1.

The unpublished meta-analysis that prompted the warnings reviewed 12 studies, 11 of ADHD and 1 of enuresis. The studies were of 6–18 weeks' duration, but other key clinical details (e.g., baseline characteristics of the participants, screening tools used, comorbidities, concomitant medications, doses) are not available. Suicidal ideation is reported to have occurred in 5 (0.37%) of 1357 children given atomoxetine but none of 851 children given placebo.[1] All reports of suicidal ideation were in children aged 7–12 years; one attempted suicide. Older adolescents made up a quarter of the children studied, but none reported suicidal ideation. A separate analysis of clinical trials involving adults apparently showed no difference in rates of suicidal ideation.[1]

What to do: Suicidality is a rare but serious adverse effect of this drug. Although atomoxetine is not indicated for use as an antidepressant, it acts using a similar mechanism (inhibition of synaptic neurotransmitter reuptake). Around 1 in 50 children prescribed antidepressants have increased thoughts of suicide (www.fda.gov/cder/drug/infopage/effexor/default.htm). Parents should be warned to watch for this newly recognized serious adverse effect, and anyone prescribed the drug should be screened at baseline and regularly thereafter for symptoms of depression, irritability, anxiety, suicidality, agitation or behavioural disturbances.

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REFERENCES

1. Warning for atomoxetine regarding the potential for behavioural and emotional changes, including risk of self harm. [Dear Healthcare Professional Letter]. Available: www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/strattera_hpc-cps_e.html (accessed 9 Nov 2005).
2. Atomoxetine (Strattera) for ADHD. *The Medical Letter* 2003;45(1149):11-2.
3. Atomoxetine (Strattera) Revisited. *The Medical Letter* 2004;46(1189):65.

Early release
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