Management of adult testicular germ cell tumours: summary of updated SIGN guideline

G C W Howard,¹ M Nairn,² on behalf of the Guideline Development Group

Testicular germ cell tumours are rare. In 2008, 203 new cases were diagnosed in Scotland,¹ with a crude incidence of 8.1 cases per 100 000 of the male population.² It is the 15th most common cancer among all men in Scotland³ and the most common cancer in younger adult men.¹ It is one of the few curable solid cancers, even when it has metastasised, and has a crude overall five year survival rate in Scotland of 95.8%.³ Although the cure rate is high, the toxicity of treatment is substantial, resulting in treatment related deaths and long term adverse effects. Potential effects on employment and fertility are of particular importance in this age group.

This article summarises the most recent recommendations from the Scottish Intercollegiate Guidelines Network (SIGN) on the management of adult testicular germ cell tumours,³ updating 1998 SIGN guidelines on this condition.

Recommendations
SIGN recommendations are based on systematic reviews of best available evidence. The strength of the evidence is graded as A, B, C, or D (figure), but the grading does not reflect the clinical importance of the recommendations. Recommended best practice (“good practice points”), based on the clinical experience of the Guideline Development Group, is also indicated (as GPP).

Initial assessment and referral in primary care
• Presenting symptoms and history of patients with testicular cancer include³:
  - A painless, solid, unilateral mass in the scrotum (most cases)
  - Enlarged testicle
  - Scrotal pain (20% of cases)
  - Backache (11%)
  - Gynaecomastia (7%)
  - Dragging sensation in the scrotum
  - Incidental recent trauma (it is not thought that the trauma causes the cancer, but rather that it brings an existing tumour to the attention of the patient and physician).
• Examine patients presenting with a scrotal swelling carefully, and try to distinguish between lumps arising from the body of the testes and other intrascrotal swellings (GPP). To make the distinction, conduct ultrasonography if available (GPP).
• For patients suspected of having a testicular malignancy (that is, have a lump in the testis, doubtful epididymo-orchitis, or orchitis not resolving within two to three weeks), refer urgently for urological assessment within two weeks (D). An increasing tumour bulk is associated with more advanced disease, requiring more toxic treatment, with poorer outcomes.⁶
• Abnormal masses in the epididymis are unlikely to be testicular tumours and do not require urgent referral.

Initial specialist management
• Preoperative investigations should include assay of tumour markers (α-fetoprotein, human choriongonadotrophin, and lactate dehydrogenase, bilateral testicular ultrasonography, and chest radiography (D).
• After a germ cell tumour has been confirmed, refer all patients to a specialist centre for the management of testicular tumours (D).
• For patients with metastases in whom the diagnosis is not in doubt (when there are high levels of tumour markers and a testicular mass on physical examination or ultrasound scan), immediate chemotherapy may be indicated. In such cases, perform a delayed orchidectomy either at the time of excision of residual masses or, for those patients who are not having additional surgery, after chemotherapy (GPP).
• When possible, perform an inguinal orchidectomy (D).
• Offer a testicular prosthesis to all patients (D).
• When appropriate, offer sperm storage to men who may require chemotherapy or radiotherapy (D).
• Involve clinical specialist nurses as early as possible in the management (GPP).
• Check serum markers before orchidectomy, 24 hours after, then weekly thereafter until concentrations are normal (GPP). Follow-up monitoring of serum α-fetoprotein and human choriongonadotrophin concentrations is essential for non-seminomatous germ cell tumours (C), but lactate dehydrogenase concentrations have not been shown to be helpful in this context.
• Owing to the rarity of testicular malignancy and its complex and potentially toxic treatments, ensure that the patient’s general practitioner and other community services are well informed and involved throughout treatment and follow-up (GPP).
The grade of recommendation relates to the strength of the supporting evidence on which the evidence is based. It does not reflect the clinical importance of the recommendation.

**A**
- At least one high quality meta-analysis, systematic review of randomised controlled trials, or randomised controlled trial with a very low risk of bias and directly applicable to the target population; or
- A body of evidence consisting principally of well conducted meta-analyses, systematic reviews of randomised controlled trials, or randomised controlled trials with a low risk of bias directly applicable to the target population, and demonstrating overall consistency of results.

**B**
- A body of evidence including studies rated as high quality systematic reviews of case-control or cohort studies, and high quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal and which are directly applicable to the target population, and with overall consistency of results; or
- Extrapolated evidence from studies described in **A**

**C**
- A body of evidence including well conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal and which are directly applicable to the target population and with overall consistency of results; or
- Extrapolated evidence from studies described in **B**

**D**
- Non-analytic studies, such as case reports, case series, expert opinion; or
- Extrapolated evidence from studies described in **C**

**Good Practice Points (GPP)**
Recommended best practice based on the clinical experience of the guideline development group.

**Explanation of SIGN grades of recommendations**

**Management of the contralateral testis**
- For patients who are aged ≤30 years at diagnosis and who have a small (<12 ml) contralateral testis, consider biopsy of the contralateral testis to diagnose carcinoma in situ (C). About 5% of all men with testicular cancer have contralateral carcinoma in situ, but the prevalence is much higher (34%) in those in this age group who have a small contralateral testis.8
- When possible, perform contralateral testicular biopsy after all sperm samples have been obtained for storage and before chemotherapy or any secondary treatment (GPP).
- If carcinoma in situ is diagnosed, discuss with the patient the options of surveillance, prophylactic orchidectomy, and testicular radiotherapy (D).

**Clinical staging**
- Use serum marker concentrations along with imaging techniques to determine the prognostic group (D).
- Contrast enhanced computed tomography of the thorax, abdomen, and pelvis is essential for staging (D).
- Complete and review all staging at a uro-oncology multidisciplinary team meeting no later than three weeks after surgery, but be aware that immediate postoperative scans may be misleading (GPP).

Detailed recommendations on the management of stage I disease, metastatic disease, residual masses after chemotherapy, and treatment of relapsed disease are included in the full SIGN guideline.4 Table 1 summarises different stages and their treatment.

**Management of metastatic disease**
The International Germ Cell Consensus Classification defines three prognostic groups (good, intermediate, and poor) on the basis of tumour markers and the presence of metastases (table 2).10

**Management of residual masses after chemotherapy**
- Patients with seminoma who have residual masses after chemotherapy can generally be managed by a policy of observation rather than radiotherapy. Surgery is not routinely indicated (D).
- Patients with non-seminomatous germ cell tumours who have residual masses after chemotherapy and whose markers have normalised should be treated with complete surgical excision (D).

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**Table 1: Treatment summary; primary orchidectomy is the initial surgical treatment of choice for most testicular tumours**

<table>
<thead>
<tr>
<th>Stage and definition of disease</th>
<th>Seminoma and non-seminomatous germ cell tumours (NSGCT)</th>
<th>Treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage I:</strong> defined as no known residual disease after orchidectomy, with no evidence of metastatic disease on clinical examination and with normal computed tomogram of chest, abdomen, and pelvis, and normal postoperative tumour markers*</td>
<td>Seminoma</td>
<td>Discuss with patients the advantages and disadvantages of options for treatment after orchidectomy, including surveillance, single dose adjuvant carboplatin, and adjuvant radiotherapy</td>
</tr>
<tr>
<td><strong>NSGCT or mixed tumour (seminoma plus NSGCT) with no high risk features</strong>&lt;sup&gt;†&lt;/sup&gt;</td>
<td>Surveillance after inguinal orchidectomy</td>
<td></td>
</tr>
<tr>
<td><strong>NSGCT or mixed tumour (seminoma plus NSGCT) with high risk features (blood vessel and/or lymphatic invasion)</strong>&lt;sup&gt;‡&lt;/sup&gt;</td>
<td>Consider two courses of adjuvant chemotherapy (bleomycin, etoposide, and cisplatin)</td>
<td></td>
</tr>
<tr>
<td><strong>Stage II (A-D): defined as metastatic infradiaphragmatic lymph node involvement. Stages A-D are defined with increasing maximum diameter of nodes†</strong></td>
<td>IIA seminoma</td>
<td>Chemotherapy and radiotherapy should be considered and discussed with the patient</td>
</tr>
<tr>
<td><strong>IIB seminoma</strong></td>
<td>Sequential chemotherapy and radiotherapy can be considered as an alternative to radiotherapy or chemotherapy alone</td>
<td></td>
</tr>
<tr>
<td><strong>IIC and IID seminoma</strong></td>
<td>Chemotherapy</td>
<td></td>
</tr>
<tr>
<td><strong>NSGCT (with good prognosis)</strong></td>
<td>Three cycles of adjuvant chemotherapy (bleomycin, etoposide, and cisplatin)</td>
<td></td>
</tr>
<tr>
<td><strong>NSGCT (with intermediate and poor prognosis)</strong></td>
<td>Four cycles of chemotherapy (bleomycin, etoposide, and cisplatin) is standard. Consider entry into appropriate trials</td>
<td></td>
</tr>
<tr>
<td><strong>Stage III:</strong> defined as metastatic supradiaphragmatic and infradiaphragmatic node involvement. Stages A-D are defined with increasing maximum diameter of nodes†</td>
<td>Seminoma</td>
<td>As for stage II</td>
</tr>
<tr>
<td><strong>NSGCT (with good prognosis)</strong></td>
<td>Three cycles of adjuvant chemotherapy (bleomycin, etoposide, and cisplatin)</td>
<td></td>
</tr>
<tr>
<td><strong>NSGCT (with intermediate and poor prognosis)</strong></td>
<td>Four cycles of chemotherapy (bleomycin, etoposide, and cisplatin) is standard. Consider entry into appropriate trials</td>
<td></td>
</tr>
<tr>
<td><strong>Stage IV:</strong> defined as involvement of extralymphatic metastases</td>
<td>Seminoma and NSGCT</td>
<td>As for stage III</td>
</tr>
</tbody>
</table>

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* Ninety per cent of seminomas and 57% of non-seminomatous germ cell tumours present as stage I disease.4
† About 15% of patients fall into the stage II category.
### Follow-up after treatment

The aim is to detect relapse early, monitor and treat toxicity that is related to treatment, detect metastatic carcinomas, and offer support and counselling, particularly on issues such as employment and fertility. Follow-up protocols, including the frequency of clinic visits, blood tests, and radiology investigations, will vary according to tumour stage and are outlined in the full guidance.

### Overcoming barriers

Rising incidence rates, improved treatment, and increased life expectancy result in a larger number of people living for many years after a diagnosis of testicular cancer, sometimes with serious sequelae. To most effectively prevent the onset of secondary disease and manage complications, patients should be advised of their increased risks and general practitioners should reinforce advice on healthy living at every opportunity.

SIGN thanks Alan James, consultant clinical oncologist, and Peter Correra, specialist registrar in clinical oncology, both of Beatson West of Scotland Cancer Centre, Glasgow, for their contribution to appendix 2 of the latest guideline; and the Guideline Development Group responsible for the development of SIGN 28 (Management of Adult Testicular Germ Cell Tumours), on which this new guideline is based.

### Contributors

Both authors contributed to reviewing the evidence and writing and correcting the article. MH is the guarantor.

### Funding

No funding was received for writing this summary.

### Competing interests

Both authors have completed the Unified Competing Interest form at www.icmje.org/coiDisclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation that might have an interest in the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

### Provenance and peer review

Commissioned, not externally peer reviewed.

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### Table 2: Prognosis for seminomas and non-seminomatous germ cell tumours, according to International Study of Germ Cell Cancer Collaborative Group

<table>
<thead>
<tr>
<th>Prognosis Type</th>
<th>Diagnoses and Tumour Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Good prognosis</strong></td>
<td>Any primary site; no non-pulmonary visceral metastases; normal or elevated lactate dehydrogenase (&lt;15 x upper limit of normal).</td>
</tr>
<tr>
<td><strong>Intermediate prognosis</strong></td>
<td>Any primary site; no non-pulmonary visceral metastases; any human choriongonadotrophin; any lactate dehydrogenase (≥50,000 IU/L or lactate dehydrogenase ≥1.5 x upper limit of normal).</td>
</tr>
<tr>
<td><strong>Poor prognosis</strong></td>
<td>No patients classified as poor prognosis.</td>
</tr>
</tbody>
</table>

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### Treatment of relapsed disease

After complete remission with chemotherapy for metastatic testicular cancer, relapse is highly unlikely in patients whose disease is associated with a good prognosis (<10%) but is more likely in patients with more advanced disease. Salvage treatment may be curative, and choice of treatment depends on several factors, including initial sensitivity to chemotherapy, tumour marker concentrations, and time to relapse. Treatments include further chemotherapy (which may be high dose with stem cell rescue) and surgery.

### Late toxicity

- **Potential short, medium, and long term effects of treatment include neurotoxicity, nephrotoxicity, pulmonary toxicity, and androgen deficiency;** the most serious late effects are the risk of second cancers and cardiovascular events.
- **Oncologists should advise survivors of testicular cancer and their general practitioners of the increased risk of cardiovascular disease and of non-germ cell second malignancies (GPP).** The latter risk is greatest for those treated before age 30 years and continues for more than 15 years after treatment.
- **Advise survivors of testicular cancer not to smoke (C).** No evidence was identified to support routine cardiovascular screening in people with testicular cancer.
- **Advise patients to remain vigilant for any unusual or “alert” symptoms,** particularly relating to the gastrointestinal, respiratory, or urinary tracts, and to report these promptly to their general practitioners (GPP).
- **Advise of the increased risk of haematological malignancies (especially after chemotherapy) and of solid malignancies in or near the fields of radiotherapy.** Advise patients to report any alert symptoms to their general practitioners, who should have a low threshold for further investigation and appropriate referral to secondary care. Consider annual urine analysis for haematuria (GPP).

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### References

1. Information and Statistics Division Scotland. Male genital organ cancers. www.isdscotland.org/isd/1488.html#Summary statistics for male genital organ cancers
UNCERTAINTIES PAGE

Does first trimester progesterone prophylaxis increase the live birth rate in women with unexplained recurrent miscarriages?

Arri Coomarasamy,¹ Ewa G Truchanowicz,⁵ Raj Rai²

Miscarriage is the commonest complication of pregnancy, occurring in one in six clinically recognised pregnancies.¹ Recurrent miscarriage is the loss of three or more consecutive pregnancies. Women with recurrent miscarriage (in contrast to women with sporadic miscarriage) tend to lose genetically normal pregnancies.² After comprehensive investigation, a cause for recurrent miscarriage is identified in less than half of couples.³ Most couples are therefore labelled as having unexplained recurrent miscarriage.

Progesterone, secreted by the corpus luteum and the placenta, has a central role in maintaining a pregnancy.⁴ It is theoretically plausible that progesterone supplementation may reduce the risk of miscarriage in women with a history of recurrent miscarriages, and the first trial using progesterone for such women was published in the BMJ in 1953.² This was followed over the decades by several small trials. However, uncertainty remains about the evidence: a survey we conducted in the United Kingdom in 2008 found that of the 102 obstetricians and gynaecologists who responded, 2% used progesterone routinely and 3% used it selectively; 90% called for a definitive placebo controlled randomised trial (unpublished data, AC and RR).

What is the evidence of the uncertainty?

We searched Medline, Embase, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, DARE (Database of Abstracts of Reviews of Effects), ISI proceedings, the International Standard Randomised Controlled Trial Number (ISRCTN) register, and the mRCT database for published and ongoing randomised trials. The search terms were “progesterone”, “progestagen”, “progestogen”, “progestin”, and “progestational [hormone or agent]”, which were combined with search terms for miscarriage.

Four randomised trials were identified.²⁻⁵ The quality of the four trials was poor (modified Jadad quality scores ranged from 0/5 to 2/5 (table). Participant numbers were small even when the trials were combined in meta-analysis, with only 132 women treated with progesterone. Although all four trials showed a trend towards benefit, with a 42–69% reduction in rate of miscarriage, the confidence intervals were wide and differences were not statistically significant.

This randomised, double blind, placebo controlled multicentre trial is studying the effect of progesterone treatment given in the first trimester of pregnancy in women with a history of unexplained recurrent miscarriages.

Population—Women with a history of unexplained recurrent miscarriages (three or more), who conceive naturally

Intervention—400 mg of vaginal progesterone pessaries twice daily, started as soon after a positive urinary pregnancy test as possible (but no later than six weeks of gestation) and continued to 12 weeks of gestation

Comparison—Placebo of identical appearance

Primary outcome—Live birth beyond 24 completed weeks

Sample size—The total number of participants required will be 790 (395 in each trial arm) to detect a minimally important difference of 10% in live birth beyond 24 weeks (from 60% to 70%) for an alpha error rate of 5% and beta error rate of 20%, after adjustment for a loss to follow-up rate of 5%

The full protocol is available at www.hta.ac.uk/project/1764.asp

This is one of a series of occasional articles that highlight areas of practice where management lacks convincing supporting evidence. The series advisers are Robin Minhas, clinical director, BMJ Evidence Centre, and David Tovey, editor in chief, the Cochrane Library. This paper is based on a research priority identified and commissioned by the National Institute for Health Research’s Health Technology Assessment programme on an important clinical uncertainty. To suggest a topic for this series, please email us at uncertainties@bmj.com.

| Characteristics of the randomised trials of progesterone in recurrent miscarriage |
|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| Goldzieher 1964¹ (n=18) | Le Vine 1964¹ (n=30) | Swyer 1953² (n=67) | El-Zibdeh 2005⁵ (n=130) |
| **Clinical characteristics** | **Clinical characteristics** | **Clinical characteristics** | **Clinical characteristics** |
| Population | Analysis restricted to those with a history of ≥3 miscarriages | History of three consecutive miscarriages | Analysis restricted to those with a history of ≥3 miscarriages |
| Intervention | Medroxyprogesterone 10 mg/day (oral) | Hydroxyprogesterone caproate 500 mg/week (intramuscular) | Progestrone pellets 6 x 25 mg inserted into gluteral muscle |
| Duration of treatment | Unclear | Until miscarriage or 36 weeks | Unclear |
| Quality features | | | From diagnosis of pregnancy to 12 weeks |
| Randomisation method | “Sequentially numbered bottles” | Alternation | Alternation | “Randomised” (method not given) |
| Allocation concealment | Unclear | Unclear | Inadequate | Unclear |
| Blinding | Double | Double | No | No |
| Intention to treat analysis | Unreported | No | Unreported | Yes |
| Follow-up rates (%) | 100 | 54 (26/56 participants excluded) | 100 | 100 |
| Jadad score | 2/5 | 0/5 | 1/5 | 0/5 |

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doi: 10.1136/bmj.d1914
Significant for all but one of the four trials. Meta-analysis showed a statistically significant reduction in miscarriages (figure). We found no evidence of statistical heterogeneity in the results (heterogeneity, $P=0.94$). Data were not available for other clinically relevant outcomes such as live birth. Our review findings are consistent with the findings of a Cochrane review on this subject, published earlier and including three of the above four studies.

Although the pooled analysis shows a statistically significant reduction in miscarriage rate, it is not surprising, given the poor quality of the trials (for example, none of them had evidence of allocation concealment), that most clinicians have called for a definitive placebo controlled randomised trial targeting live birth as the primary outcome.

**Is ongoing research likely to provide relevant evidence?**

We identified ongoing studies from the ISRCTN register and the mRCT database. The results of a randomised study of oral dydrogesterone 20 mg a day versus placebo in women with recurrent miscarriages are awaited (clinical trial number: NCT00193674). Although the study is small ($n=77$) and the primary outcome is the cytokine ratio of interferon to interleukin 10, useful information on pregnancy outcome may emerge from this study.

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**10-MINUTE CONSULTATION**

**Epididymo-orchitis**

A 22 year old student presents with a three day history of painful swollen left scrotum. He has also noticed a burning sensation when he passes urine.

**What you should cover**

There are three main diagnoses to consider in this patient. Epididymo-orchitis is the commonest cause of acute scrotal pain and refers to inflammation of the epididymis and testis. However, the most important differential diagnosis that should be excluded is testicular torsion; this is a surgical emergency where prompt intervention is required. Trauma is an important diagnosis to think about in all patients and is usually suggested by the history.

Two much rarer causes of acute scrotal pain and/or swelling include a rapidly growing testicular tumour, which in most cases will present as a painless testicular lump. Idiopathic scrotal oedema usually presents in childhood with bilateral oedema and bruising over the scrotal skin. The testes should not be tender on examination.

**Taking history**

- Onset: insidious presentation suggests infection. Sudden onset of symptoms should raise suspicions of torsion
- Pain: usual presentation of epididymo-orchitis is with unilateral-scrotal pain that may radiate to the groin
- Swelling
- Any recent trauma
- Urinary symptoms: may be present if there is urinary tract infection
• Sexual history: ask about recent changes in sexual partners and any associated symptoms such as urethral discharge
• Recent viral illness: may point towards rarer causes such as mumps orchitis. Testicular swelling in mumps normally occurs 7-10 days after the characteristic fever and parotid swelling.

Taking the patient’s history is important to aid diagnosis and to help you decide the most likely pathogenesis. As there is a high incidence of sexually acquired infections in men under 35 these should be excluded in all cases. This 22 year old man is currently sexually active and is therefore at risk of a sexually transmitted pathogen, such as Chlamydia trachomatis or Neisseria gonorrhoea.

In patients with associated urinary symptoms and recent instrumentation (such as bladder catheterisation or cystoscopy) gram negative organisms such as Escherichia coli are the most likely cause. Mumps is a notifiable disease and is possible in those who have not been immunised. Rarer causes such as extra-pulmonary tuberculosis should be considered in those who are immunosuppressed.

What you should do
Perform a urine dipstick that includes a leucocyte esterase and nitrite test. Positive leucocytes, nitrites, and blood would point towards an underlying infection, but this finding is not diagnostic.

Urine should be sent for further microbiological analysis. First pass urine (the first part of the urine the patient passes) is recommended when testing (nucleic acid amplification) for Chlamydia trachomatis and Neisseria gonorrhoea. Patients should be instructed to collect the first part of the urine they pass when giving a specimen. This urine specimen should also be sent for microscopy and culture.

As a rule, examine the scrotum with the patient in the standing position, and look for:
• Enlarged, erythematous scrotum
• Tenderness to palpation of the testis, epididymis, or the cord on the affected side
• In early presentations of epididymo-orchitis the epididymis may be tender and thickened
• In later stages of epididymo-orchitis the entire hemi-scrotum may be oedematous.

Clinical care pathway for management of epididymo-orchitis. Adapted from 2010 national guidelines (http://www.bashh.org/guidelines)
It may be difficult to differentiate between epididymo-orchitis and testicular torsion on clinical examination. In torsion, the testis will be very tender whereas, typically in epididymo-orchitis, elevating and supporting the scrotum with the patient standing may reduce their pain.

However, if there is any doubt in diagnosis, the patient should be referred immediately for surgical exploration.

Treatment

- If testicular torsion is suspected, refer the patient urgently for surgical exploration.
- If the diagnosis is epididymo-orchitis, advise about appropriate rest and analgesia.
- Give empirical antibiotics in all patients with epididymo-orchitis. The preferred antibiotic regimen depends on history and whether a sexually acquired micro-organism is likely (figure).

Once treatment has been started, advise all patients to attend the genitourinary medicine department for further investigations and anonymous partner tracing.

Ask patients to return if there is no improvement within 72 hours. The scrotal swelling could take up to six weeks to resolve completely, but after 3-5 days of antibiotics the pain should be substantially better and the scrotum should be less erythematous. If no improvement occurs, exclude a scrotal abscess through referral to an on call urologist for assessment with clinical and radiological examination.

UK National Guidelines recommend further investigation of the urinary tract in patients with confirmed gram-negative enteric organisms (box). Further investigation is strongly advised in patients older than 50 years. In patients with recurrent infections and prostatic symptoms the clinical suspicion of an underlying obstruction should be higher. Adopt a lower threshold for urology referral for these patients.

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Competing interests: All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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

**CORRECTIONS AND CLARIFICATIONS**

Iatrogenic radiation, and unethical health reforms

In the opening paragraph of her Editor’s Choice, Fiona Godlee mistakenly underestimated the radiation dose from computed tomography of the abdomen (BMJ 2011;342:d1551, print publication 12 March). The third sentence should have read (to reflect correctly the article she was citing): “A CT scan of the abdomen delivers 400 times [not eight times] the dose of a chest radiograph.”

Prevention of Leishmania donovani infection

The photograph accompanying this editorial by Philippe Desjeux (BMJ 2010;341:c6751, print publication 8 January 2011, pp 60-1) was misleading. It showed cutaneous leishmaniasis, rather than visceral leishmaniasis—the focus of the article.

How small changes led to big profits for insulin manufacturers


The life imprisonment of Dr Binayak Sen

In this editorial by P Zachariah and colleagues (BMJ 2011;342:d262, print publication 22 January, pp 182-3) Noam Chomsky was wrongly credited with a Nobel prize—only Amartya Sen is a Nobel laureate.

Wakefield’s article linking MMR vaccine and autism was fraudulent

The fraud behind the MMR scare

Institutional and editorial misconduct in the MMR scare

The BMJ should have declared competing interests in relation to these three articles (the first was an editorial by Fiona Godlee and colleagues (BMJ 2011;342:c7452, 8 January, pp 64-6) and the second and third were Editor’s Choice articles by Fiona Godlee (BMJ 2011;342:d22 and BMJ 2011;342:d378, both also published in the 8 January issue)). The BMJ Group receives advertising and sponsorship revenue from vaccine manufacturers, and specifically from Merck and GSK, which both manufacture MMR vaccines. For further information see the rapid response from Godlee (www.bmj.com/content/342/bmj.d1335.full/reply#bmj_el_251470).

Effect on gastric function and symptoms of drinking wine, black tea, or schnapps with a Swiss cheese fondue: randomised controlled crossover trial

In this Christmas article by Henriette Heinrich and colleagues, the corresponding author’s affiliations need clarification (BMJ 2010;341:1284, print publication 18-25 December, pp 1284-5). Along with the two addresses in Zurich, Mark Fox is also affiliated with the Queen’s Medical Centre, Nottingham, the address given for correspondence.

FURTHER READING

For patients

- Patient UK (http://www.patient.co.uk/health/Epididymo-orchitis.htm)
- BBC Health (http://www.bbc.co.uk/health/ask_the_doctor/epididymo.shtml)
- NHS Choices (http://www.nhs.uk/Livewell/Sexualhealthtopics/Pages/Sexual-health-hub.aspx)

For healthcare professionals


For healthcare professionals